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Terpenoids. XXXIII.[1] Chemical Conversion of Enmein into Enmelol

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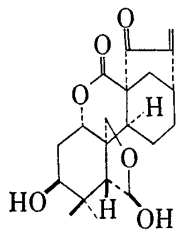
After several preliminary experiments, enmein (**1**) was converted into enmelol (**2**). The route consists of the following steps: (i) Enmein (**1**) was converted into lactone ester **40** *via* **3**, **8**, **9**, and **10**. (ii) An acyloin product **42** derived from **40** was transformed into 15-kaurene derivative **61**, *via* epoxide **56**, 1β-ol **57**, acetate **58**, and 15-ol **59**. (iii) By photosensitized oxygenation of **61**, allyl alcohol **62** and $\alpha\beta$-unsaturated ketone **63** were yielded. (iv) Enmelol (**2**) and 15-epienmelol (**69**) were derived from **63** and **62**, respectively.

The total synthesis of enmein (**1**), a major bitter principle of leaves of *Isodon japonicus* Hara and *I. trichocarpus* Kudo, was recently accomplished in our laboratory.[3] The chemical conversions of enmein (**1**) into *ent*-kaurane,[4,5] enmein-3-acetate,[6] isodocarpin,[7,8] isodotricin,[9] *ent*-abietane,[10] *ent*-16-kaurene,[11,12] *ent*-15-kaurene,[11] and gibberellin A_{15}[13] as well as the formal chemical conversions[12] of enmein into atisine, garryine, and veatchine have also been achieved. Chemical transformation of enmein into any natural kaurene-type diterpenoid having an



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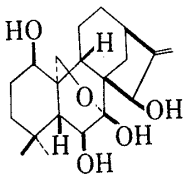

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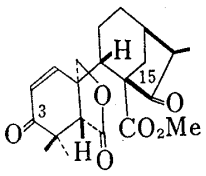

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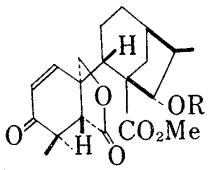
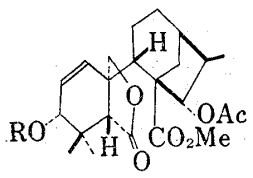


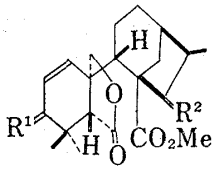
4 : R=H
5 : R=Ac
15 : R=

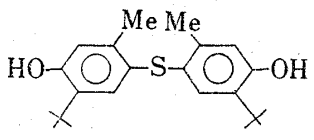
1) Part XXXII: E. Fujita, I. Uchida, and T. Fujita, *J. C. S. Perkin I*, **1974**, 1547.
2) Location: *Uji, Kyoto-Fu, 611, Japan*; *a*) Present address: *Research Laboratory, Daiichi Pharmaceutical Co., Ltd., Edogawa-ku, Tokyo, 132, Japan.*
3) E. Fujita, M. Shibuya, S. Nakamura, Y. Okada, and T. Fujita, *J. C. S. Perkin I*, **1974**, 165.
4) K. Shudo, M. Natsume, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **13**, 1019 (1965).
5) E. Fujita, T. Fujita, K. Fuji, and N. Ito, *Chem. Pharm. Bull.* (Tokyo), **13**, 1023 (1965); *Tetrahedron* **22**, 3423 (1966).
6) E. Fujita, T. Fujita, and M. Shibuya, *Chem. Comm.*, **1966**, 297; *Yakugaku Zasshi*, **87**, 1076 (1967).
7) E. Fujita, T. Fujita, and H. Katayama, *J. Chem. Soc.* (*C*), **1970**, 1681.
8) E. Fujita, T. Fujita, and M. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1573 (1968).
9) E. Fujita, T. Fujita, Y. Okada, S. Nakamura, and M. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **20**, 2377 (1972).
10) *a*) E. Fujita, T. Fujita, and H. Katayama, *Chem. Comm.*, **1967**, 968; *b*) E. Fujita, T. Fujita, H. Katayama, and Y. Nagao, *Tetrahedron*, **25**, 1335 (1969).
11) E. Fujita, T. Fujita, and Y. Nagao, *Tetrahedron*, **28**, 555 (1972).
12) E. Fujita, T. Fujita, and H. Katayama, *Tetrahedron*, **26**, 1009 (1970).
13) M. Somei and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 2135 (1970); *Yakugaku Zasshi*, **92**, 397 (1972).

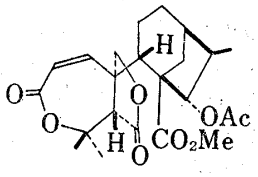
oxygen-function at C-1, however, has not yet been published. Now, we tried the chemical conversion of enmein (**1**) into enmelol (**2**),[14] and accomplished it.

The known compound **3**[5] derived from enmein (**1**) *via* three steps, on ketalization at 3-ketone, sodium borohydride reduction of 15-ketone, and subsequent acid hydrolysis, gave 15α-ol **4**, whose acetate **5** on sodium borohydride reduction afforded 3α-ol **6**.









6 : R=H
7 : R=Ac

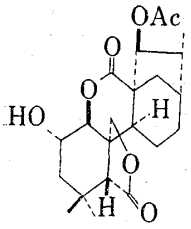
8 : R^1=$-S(CH_2)_2S-$, R^2=O
9 : R^1=H_2, R^2=O
10 : R^1=H_2, R^2=α-OH, β-H
11 : R^1=H_2, R^2=α-OAc, β-H

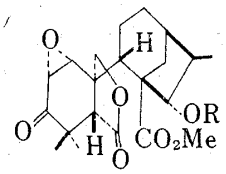
12

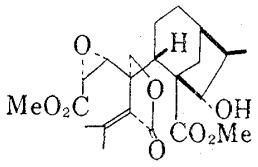
13

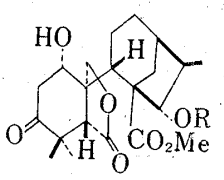
On the other hand, compound **3** was converted into 3-deoxy-15-acetate **11** *via* thioketal **8**, 3-deoxo-15-one **9**, and 15α-ol **10**.

Compound **6** on heating with perbenzoic acid at reflux in benzene for 7 hours under the presence of 4,4′-thiobis-(6-*tert*-butyl-*m*-cresol) (**12**), a radical inhibitor, regenerated ketone **5**, while in 1,2-dichloroethane it gave lactone **13**, a Baeyer-Villiger oxidation product from **5**. Acetate **7** on heating[15] with *m*-chloroperbenzoic acid at 80—84° in 1,2-dichloroethane for 12 hours under the presence of a radical inhibitor resulted in a complete recovery of the starting material. The same reaction with compound **11** gave an unseparable mixture of the starting material and an epoxide, and a small amount of compound **14**, which corresponded to a secondary product formed from the initial α-epoxide product by 1β-attack of carboxylate. Thus, attempts for introduction of the oxygen-function to C-1 by peracids were unsuccessful.









14

16 : R=
20 : R=H
21 : R=Ac

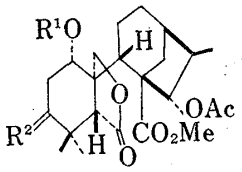
17

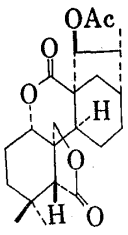
18 : R=
19 : R=H

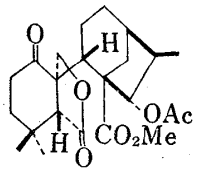
Subsequently, investigation was directed for the method of the direct 1,2-epoxide formation from compound **4**. Protection of the 15-hydroxy group by tetrahydropyranylation and epoxidation of the resulting tetrahydropyranyl ether **15** with hydrogen peroxide in the presence of alkali[16] resulted in the formation of an epoxide in 25—30% yield, but this epoxide was shown to be α-epoxide **16** as will be described. The acidic product was methylated by diazomethane to yield ester **17**, which was formed by successive epoxidation, Baeyer-Villiger reaction, alkaline hydrolysis followed by dehydration, and esterification. The epoxide **16** on heating with zinc dust under addition of a catalytic amount of zinc dichloride in absolute

14) S. Mori, T. Koizumi, K. Shudo, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 884 (1970).
15) Y. Kishi, M. Aratani, H. Tanino, T. Fukuyama, and T. Goto, *J. Chem. Soc.* (*D*), **1972**, 62.
16) C.A. Bunton and G.J. Minkoff, *J. Chem. Soc.*, **1949**, 665.

ethanol at reflux gave 62% yield of alcohol **18**. Attempted thioketalization of 3-ketone with ethanedithiol in the presence of boron trifluoride at −2 to −6°, however, resulted in hydrolysis of the tetrahydropyranyl ether to yield diol **19**. Then, acetate group was tried as the protecting group of the 15-ol instead of tetrahydropyranyl ether. The compound **16** was hydrolyzed with hydrochloric acid in methanol to give alcohol **20**, whose acetate **21** was refluxed with zinc dust under the addition of a catalytic amount of zinc dichloride in absolute ethanol to yield the desired 1-ol **22** in 40% yield accompanied by 30—40% yield of $\alpha\beta$-unsaturated ketone **5**, the dehydration product. Thioketalization of **22** gave **23**, which was subjected to reduction with Raney nickel to afford 3-deoxo compound **24** quantitatively. The mother liquor from recrystallization of **23** was desulfurized by the same way as above and purified by chromatography on silica gel column to give compound **25**.





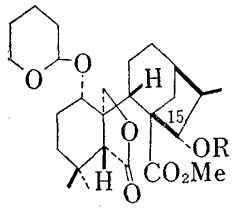


22 : R^1=H, R^2=O
23 : R^1=H, R^2=$-S(CH_2)_2S-$
24 : R^1=H, R^2=H_2
26 : R^1=Ac, R^2=H_2

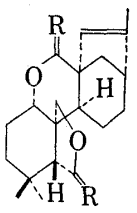
25 **27**

The stereochemistry of the 1-ol of compound **24** was assigned an equatorial conformation *i.e.* α-configuration, on the basis of the nuclear magnetic resonance (NMR) data (δ 5.10, q, J=10 and 5 Hz) of 1-H in its acetate **26**. Hence, the original compound **16** must have an α-epoxide at 1 and 2 positions. The stereomodel of compound **15** shows that the β-side is sterically more hindered. Jones oxidation[17] of **24** gave ketone **27**, but its Meerwein-Ponndorf reduction for getting the 1β-ol resulted in the recovery of the starting material. Then, the 1α-ol **24** was subjected to tetrahydropyranylation to give **28**, which was hydrolyzed with alkali to yield 15-ol **29**. Its mesylate **30** was heated carefully at 110—115° to yield the desired 15-ene derivative **32** quantitatively, but it was transformed into dilactone **31** quantitatively under more drastic conditions, *i.e.* under heating at 150° in dimethylsulfoxide or at 125° in pyridine. The structure of **32** is supported by its NMR data, but this compound remains as an oil and is easily transformed into **31** even when the oil is allowed to stand. Thus, compound **32** was subjected to the acyloin condensation, in order to synthesize the desired product **33**. Surprisingly, the major product was found to be dihemiacetal **34**. This compound on acetylation gave diacetate **35**, and on Jones oxidation gave dilactone **31**. Hence, the starting material was checked again by NMR, and the apparent starting material **32** used for the acyloin condensation was found to be, in fact, not **32** but already transformed dilactone **31**, which was crystallized from ether and dichloromethane and confirmed by direct comparison with the authentic sample. Thus, compound **32** having a double bond between 15 and 16 was lactonized much more easily than compound **24**, the reason for which might be reasonably considered as follows: the compound **32** which was purified by chromatography on silica gel column must be catalyzed by a slightly contaminated acid to be easily transforemd into **31** *via* **36**, while in the case of **24** there might be a large interaction between the 15-acetoxy group and the 7-methoxy group in the intermediate transition state **37**.

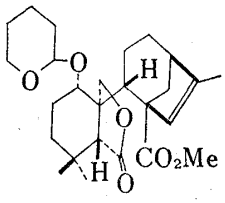
17) K. Bowden, I.M. Heilbron, E.R.H. Jones, and B.C.I. Weedon, *J. Chem. Soc.*, **1946**, 39.



28 : R=Ac
29 : R=H
30 : R=Ms



31 : R=O
34 : R=α-H, β-OH
35 : R=α-H, β-OAc



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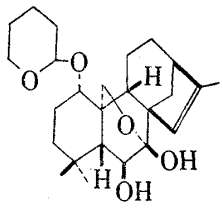

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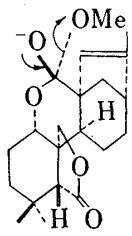

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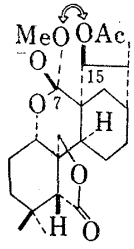
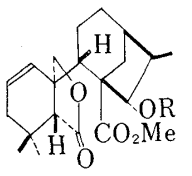
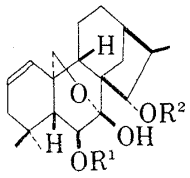


37

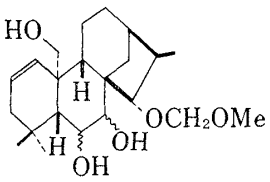
Consequently, an attempted chemical conversion of **32** into acyloin **33** was given up. Subsequently, an acyloin condensation with the compound **38**, the tetrahydropyranyl ether of **10**, was tried, but the desired acyloin product was hardly isolated. The protecting group was then changed to the methoxymethyl group. Compound **10** on treatment with chloromethyl methyl ether[18] in dimethylformamide under the presence of sodium hydride gave the methoxymethyl ether **40** in 70% yield accompanied by 20% yield of formate **41**.



38 : R=
40 : R=CH_2OMe
41 : R=CHO



39 : R^1=H, R^2=
42 : R^1=H, R^2=CH_2OMe
46 : R^1=Ac, R^2=CH_2OMe
47 : R^1=Ac, R^2=H



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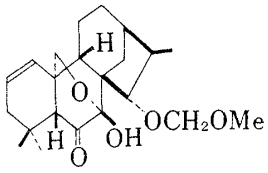

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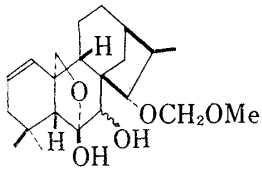

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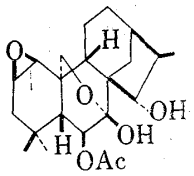
Acyloin condensation with lactone ester **40** gave 7-hemiketal-6-ol **42** as the major product in 26—50% yield accompanied by the by-products, **43**, **44**, **45**, and another compound whose

18) L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons Inc., London, Vol. 1, 1967 p. 132.

structure was not clarified. On sodium borohydride reduction in ethanol, compound **44** was converted into **42** quantitatively. The major product **42** on acetylation gave acetate **46** whose NMR spectrum showed a doublet signal (J=8 Hz) at δ 5.40 assignable to 6-H. This suggested 6-acetoxy group to have β-configuration. Methoxymethyl ether **46** on hydrolysis with hydrochloric acid in methanol gave 15-ol **47**, whose epoxidation with *m*-chloroperbenzoic acid took place from the less hindered side. In the NMR spectrum of this epoxide product, an AB part signal of the ABX_2 type resonance was observed at δ 2.68 and 3.23 (each 1H), and a doublet (J=6.5 Hz) due to 6-H at δ 5.55. All of the NMR data supported the β-epoxide structure **48**. The compound **48** on treatment with mesyl chloride in pyridine gave two products, **49** and **50**. The former remains as an oil, but the latter was obtained as crystals. In the NMR spectrum of **49**, an allyl methyl doublet signal (J=1.5 Hz) at δ 1.70, the AB part of an ABX_2 type at δ 2.63 and 3.20 due to 1-H and 2-H, a doublet (J=6 Hz) at δ 5.05 assignable to 6-H, and the 15-vinyl proton quartet (J=1.5 Hz) at δ 5.73 were observed, which supported its structure. Compound **50** showed a positive Beilstein reaction, and its mass spectrum exhibited the molecular ions *m/e* 410 and 412 in a ratio of 3: 1, which indicated the presence of chlorine in the molecule. This means the formation of a chlorohydrin by a reaction of the epoxide with hydrochloric acid. In the compound **48**, the stereochemistry of the epoxide should be β, because of the attack of the peracid from the less hindered side. Subsequent cleavage of the epoxide by acid should take place to form a 1,2-diaxial substituted product.[19] Accordingly, the chlorohydrin product must have 1β-hydroxy-2α-chloro structure **50**. The NMR spectrum, in which the allyl 17-methyl doublet (J=1.5 Hz) at δ 1.76, the 1-H doublet (J=2 Hz) at δ 3.97, the 2-H multiplet at δ 4.63, the 6-H doublet (J=4 Hz) at δ 5.83, and the vinyl 15-H quartet (J=1.5 Hz) at δ 6.28 were observed, supported this structure.



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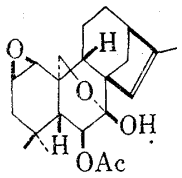

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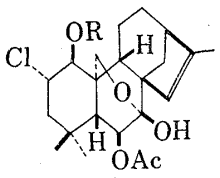
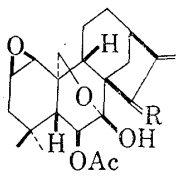
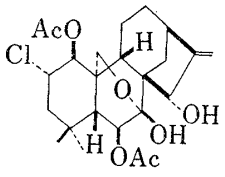


50 : R=H
53 : R=Ac

Photosensitized oxygenation[20] with compound **49** gave the desired allyl alcohol **51** in 64% yield. However, oxidation of alcohol to ketone **52** was not successful, although Collins reagent[21] and chromic acid-pyridine complex were tried. Moreover, diacetate **53** was subjected to the photosensitized oxygenation to give allyl alcohol **54**, whose oxidation with several reagents for oxidation of allyl alcohol was not successful. Jones oxidation gave only a low yield



51 : R=α-OH, β-H
52 : R=O



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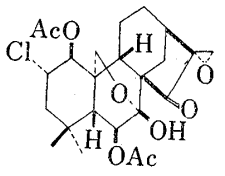
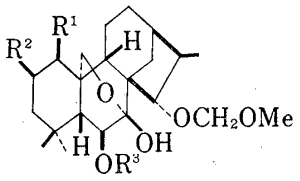


55

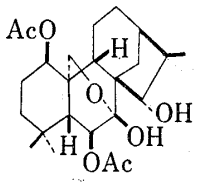
19) A. Fürst and P.A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).
20) A. Nichon and J.F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961); E. Fujita, T. Fujita, and H. Katayama, *Tetrahedron*, **26**, 1009 (1970).
21) J.C. Collins, W.W. Hess, and F.J. Frank, *Tetrahedron Letters*, **1968**, 3363.

of epoxide ketone **55**. The large resistance to oxidation observed may be due to a strong hydrogen-bonding between 7-hydroxy and 15α-hydroxy groups.

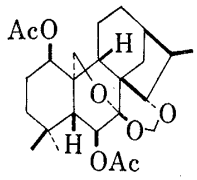
Subsequently, compound **42** was converted to the epoxide **56** by *m*-chloroperbenzoic acid. The lithium aluminum hydride reduction of epoxide **56** gave a quantitative yield of 1β-ol **57**, whose acetylation afforded 1,6-diacetate **58**. The NMR spectrum supported this structure: a singlet due to six protons of two acetoxy groups at δ 2.09, a singlet due to methyl protons of methoxymethyl ether at δ 3.35, the 1-H triplet (J=2 Hz) at δ 4.57, and the 6-H doublet (J=6 Hz) at δ 5.33 were observed. Hydrolysis of methoxymethyl ether in **58** with methanolic hydrochloric acid yielded the desired alcohol **59** accompanied by a small amount of methylenedioxy compound **60**, whose structure was assigned on the basis of spectroscopic data. Alcohol **59** on treatment with mesyl chloride in pyridine at room temperature gave 15-ene product **61**, whose NMR spectrum showed an allyl methyl doublet (J=1 Hz) at δ 1.71, two singlets due to two acetate groups at δ 2.08 and 2.15, the 1-H triplet (J=2.5 Hz) at δ 4.60, the 6-H doublet (J=4 Hz) at δ 5.15, the 15-vinyl H quartet (J=1 Hz) at δ 5.73, and an AB type due to 20-methylene protons at δ 3.85 and 4.03 (J=10 Hz).



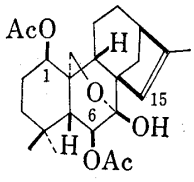
56 : R^1, R^2=−O−, R^3=H
57 : R^1=OH, R^2=R^3=H
58 : R^1=OAc, R^2=H, R^3=Ac



59

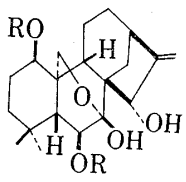


60

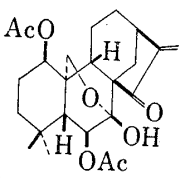


61

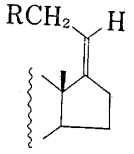
The photosensitized oxygenation with diacetate **61** gave allyl alcohol **62** and $\alpha\beta$-unsaturated ketone **63** in 50 and 10% yield, respectively. The product **63** has IR absorptions at 1710 and 1645 cm^{-1} and a ultraviolet (UV) absorption at 234 nm. Its NMR spectrum showed two singlets due to two acetate groups at δ 2.07 and 2.33, a singlet due to 20-methylene protons at δ 4.00, the 1-H triplet (J=2 Hz) at δ 4.63, the 6-H doublet (J=5 Hz) at δ 5.05, and two singlets due to the 17-exocyclic methylene protons at δ 5.28 and 5.86. The direct formation of an $\alpha\beta$-unsaturated ketone in the photosensitized oxygenation was pointed out by Nichon, *et al.*,[20] but not isolated. W.P. Schneider, *et al.*[22] have reported the preparation of an $\alpha\beta$-unsaturated ketone **66** by dehydration with acetic anhydride of hydroperoxide **65** which was formed in the photosensitized oxygenation of a steroid derivative **64**.



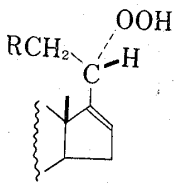
62 : R=Ac
69 : R=H



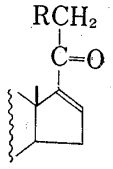
63



64



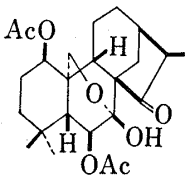
65



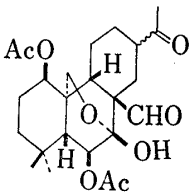
66

22) D.N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Publishing Co., London, 1968 p. 435. (W.P. Schneider, D.E. Ayer, and J.E. Huber, *Abstr. 2nd Intern. Congr. Hormonal Steroids*, Milan, 24 (1966)).

Finally, the compound **63** was reduced with sodium borohydride in methanol at 0°[23] and subsequently treated with lithium aluminum hydride to yield *ent*-7β,20-epoxy-16-kaurene-1α,6α,7α,15α-tetraol (**2**), which was proved to be identical with enmelol. Thus, the chemical conversion of enmein (**1**) into enmelol (**2**) was accomplished. Since enmein (**1**) has been synthesized,[3] the present conversion constitutes a formal total synthesis of enmelol (**2**).



67



68

Attempted oxidation of **62** to **63** was unsuccessful, just like the preliminary investigations described above. Jones oxidation was tried with compound **59**, but ketone **67** was not obtained, but compound **68**, a ring-D cleaved product, was yielded as a major product.

The 15α-ol **62** on treatment with lithium aluminum hydride gave 15-epienmelol (**69**). Although this compound has not been found in nature, this conversion means a formal total synthesis of this epimer of enmelol.

Experimental[24]

Conversion of the Known 15-Ketone 3 into 15α-ol 4——Compound 3[5] (20 g) derived from enmein, ethylene glycol (20 ml) and *p*-toluenesulfonic acid (1 g) were added in benzene (1 liter), and the mixture was refluxed under removing H_2O by distillation for 24 hr. Usual work-up gave the crude 3-ethylenketal (22 g), whose solution in MeOH (500 ml) was reduced with $NaBH_4$ (6.5 g) under stirring for 2 days. Subsequently, 3.6% HCl (200 ml) was added and stirred overnight. After neutralization with aq. Na_2CO_3 and evaporation of MeOH *in vacuo*, usual work up on the CH_2Cl_2 extract gave an oily product (20 g), which was purified by chromatography to yield a crystalline product (17 g). Its recrystallization from ether afforded 15α-ol **4** as prisms, mp 154—155°. *Anal.* Calcd. for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.76; H, 7.61. UV λ_{max}^{MeOH} nm (ε): 227 (9400). IR ν_{max} cm^{-1}: 3500 and 1776. NMR δ: 1.12 (3H, d, J=8 Hz), 1.20, 1.40 (each 3H, s), 3.08 (1H, s), 3.58 (1H, d, J=4.5 Hz) 3.70 (3H, s), 4.03, 4.25 (each 1H, AB type, J=10 Hz, 20 H_2), 5.98, and 6.60 (each 1H, AB type, J=11 Hz, 1-H, 2-H).

Acetylation of 4 to 5——Alcohol **4** (300 mg) was dissolved in pyridine (5 ml), to which Ac_2O (5 ml) was added. The mixture was allowed to stand overnight, and was treated as usual to give the crude product, which was chromatographed to isolate acetate **5** (296 mg) as crystals, mp 193—194° (from ether). *Anal.* Calcd. for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 66.00; H, 7.23. UV λ_{max}^{MeOH} nm (ε): 226 (7900). IR ν_{max} cm^{-1}: 1772, 1740, and 1690. NMR δ: 1.12 (3H, d, J=8 Hz, 16-Me), 1.20, 1.40, 2.00, 3.70 (each 3H, s), 4.07, 4.37 (each 1H, AB type, J=11 Hz, 20 H_2) 4.98 (1H, d, J=5 Hz, 15-H), 6.03 and 6.70 (each 1H, AB type, 1-H, 2-H).

Sodium Borohydride Reduction of Ketone 5 to Alcohol 6——To a solution of **5** (200 mg) in a mixture of MeOH (6 ml) and CH_2Cl_2 (1 ml) was added $NaBH_4$ (100 mg) and the mixture was stirred for 5 hr. After neutralization with dil. HCl, evaporation of the solvent *in vacuo*, and extraction with CH_2Cl_2, usual work-up on the extract gave an oil, which was chromatographed to give a crude crystalline product (182 mg). Recrystallization from ether yielded alcohol **6**, mp 168—170°, as prisms. Mass Spectrum *m/e*: 420.216 (M^+) (Calcd. for $C_{23}H_{32}O_7$, 420.214). IR ν_{max} cm^{-1}: 3475 and 1748. NMR δ: 0.89 (3H, s), 1.10 (3H, d, J=7 Hz, 16-Me), 1.34, 1.98, 3.65 (each 3H, s), 3.88, 4.16 (each 1H, AB type, J=10.5 Hz, 20 H_2), 4.16 br (1H, s, 3-H), 4.93 (1H, d, J=4 Hz, 15-H), 5.50, and 5.70 (each 1H, ABX type, J_{AB}=10, J_{AX}=2 Hz, 1-H, 2-H).

Acetylation of Alcohol 6——A solution of **6** (120 mg) in a mixture of pyridine (1.5 ml) and Ac_2O (1.5 ml) was allowed to stand overnight. Evaporation *in vacuo* left an oily residue, which was chromatographed to give crude crystals (114 mg). Recrystallization from Et_2O yielded acetate **7**, mp 159—161°, as fine crystals. Mass Spectrum *m/e*: 462.227 (M^+) (Calcd. for $C_{25}H_{34}O_8$, 462.225). IR ν_{max} cm^{-1}: 1780 and 1760. NMR δ: 0.98 (3H, s), 1.09 (3H, d, J=7.5 Hz, 16-Me), 1.26, 1.98, 2.13 (each 3H, s), 2.83 (1H, s, 5-H), 3.65 (3H, s), 3.87, 4.18 (each 1H, AB type, J=10 Hz, 20 H_2), 4.95 (1H, d, J=4 Hz, 15-H), 5.29 (1H, s, 3-H), and 5.59 (2H, s, 1-H, 2-H).

Oxidation of 6 with *m*-Chloroperbenzoic Acid in Benzene——To a solution of **6** (100 mg) in benzene (12 ml) were added *m*-chloroperbenzoic acid (500 mg) and 4,4′-thiobis(6-*tert*-butyl-*m*-cresol) (15 mg), and the mixture was refluxed for 7 hr. Usual work-up of the mixture gave a crystalline product (51 mg), mp 193—194° (from ether), which was proved to be identical with ketone **5**. (m.mp, IR, NMR, and TLC)

23) M.F. Barnes and J. MacMillan, *J. Chem. Soc.*, **1967**, 361.
24) General details are given in Part XXX: E. Fujita, I. Uchida, and T. ujjta, *Chem. Pharm. Bull.* (Tokyo), **22**, 1656 (1947).

Oxidation of 6 with *m*-Chloroperbenzoic Acid in 1,2-Dichloroethane——To a solution of **6** (100 mg) in 1,2-dichloroethane (7 ml) were added *m*-chloroperbenzoic acid (500 mg) and 4,4′-thiobis(6-*tert*-butyl-*m*-cresol) (15 ml), and the mixture was refluxed for 7 hr. Usual work-up gave an oily product (109 mg), which was crystallized by column chromatography and treatment with ether to give lactone **13** (49 mg), mp 220—224° (from ether), as prisms. *Anal.* Calcd. for $C_{23}H_{30}O_8$: C, 63.58, H, 6.96. Found: C, 63.30; H, 7.06. Mass Spectrum *m/e*: 434 (M^+) (Calcd. for $C_{23}H_{30}O_8$, 434). IR ν_{max} cm^{-1}: 1770, 1745, and 1680. NMR δ: 1.10 (3H, d, J=7 Hz, 16-Me), 1.50, 1.57, 2.00 (each 3H, s), 2.80 (1H, s), 3.70 (3H, s), 3.95, 4.33 (each 1H, AB type, J=11 Hz, 20 H_2), 4.90 (1H, d, J=4 Hz, 15-H), 5.01 and 6.37 (each 1H, AB type, J=8 Hz, 1-H, 2-H).

Chemical Conversion of 3 into 3-Deoxo-derivative 9——Ketone **3** on thioketalization as usual gave 3-thioketal **8**. To a solution of **8** (5 g) in acetone (100 ml) was added Raney Ni W-2 (13.8 g) and refluxed for 2.5 hr. After filtration from Raney Ni, evaporation of acetone left a crude crystalline residue (3.2 g), which was chromatographed and recrystallized from ether–CH_2Cl_2 to yield **9**, mp 184—187°, as needles. *Anal.* Calcd. for $C_{31}H_{28}O_5$: C, 69.97; H, 7.83. Found: C, 70.05; H, 7.76. IR ν_{max} cm^{-1}: 1768, 1755, and 1720. NMR δ: 0.95 (3H, s), 1.10 (3H, d, J=7 Hz), 1.29 (3H, s), 2.76 (1H, s), 3.72 (3H, s), 3.90, 4.05 (each 1H, AB type, J=10 Hz, 20 H_2), 5.70 (2H, AB part of ABX_2 type, 1-H, 2-H).

Reduction of 15-Ketone 9 to Alcohol 10——To a solution of **9** (4.01 g) in MeOH (30 ml) was added $NaBH_4$ (0.8 g) and stirred overnight. After addition of H_2O (5 ml), the mixture was stirred further overnight. Neutralization with AcOH, evaporation of MeOH *in vacuo*, extraction with CH_2Cl_2, and subsequent usual treatment of the extract gave a crude crystalline product (3.8 g), which was purified by recrystallization to yield pure alcohol **10**, mp 159—160° (from ether–CH_2Cl_2), as needles. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.51; H, 8.30. IR ν_{max} cm^{-1}: 3500, 1765, and 1735. NMR δ: 0.92 (3H, s), 1.10 (3H, d, J=7 Hz), 1.30 (3H, s), 2.80 (1H, s), 3.70 (3H, s), 3.90, 4.17 (each 1H, AB type, J=10 Hz, 20 H_2), and 5.70 (2H, AB part of ABX_2 type, 1-H, 2-H).

Acetylation of Alcohol 10——Alcohol **10** (100 mg) was treated as usual with pyridine (1 ml) and Ac_2O (1 ml) to give a crystalline product (102 mg), which was purified by recrystallization to yield acetate **11**, mp 160—162° (from ether–petroleum ether), as prisms. *Anal.* Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.13; H, 7.94. IR ν_{max} cm^{-1}: 1768, 1750, and 1730. NMR δ: 0.92 (3H, s), 1.08 (3H, d, J=7 Hz), 1.30, 1.97, 3.62 (each 3H, s), 3.87, 4.18 (each 1H, AB type, J=10 Hz, 20 H_2), 4.95 (1H, d, J=5 Hz, 15-H), and 5.70 (2H, AB part of ABX_2 type, 1-H, 2-H).

Oxidation of 11 with *m*-Chloroperbenzoic Acid in 1,2-Dichloroethane——To a solution of **11** (324 mg) in 1,2-dichloroethane (10 ml) were added *m*-chloroperbenzoic acid (200 mg) and 4,4′-thiobis(6-*tert*-butyl-*m*-cresol) (15 mg) and heated at 80° for 12 hr. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. Usual work up of the extract gave a mixture of oily products (319 mg), which was chromatographed to separate two fractions. The less polar fraction was found to be a mixture of epoxide and starting material by NMR investigation. The more polar fraction was obtained as a crystalline form and purified by recrystallization to yield compound **14** (74 mg), mp 204—205° (from ether), as needles. *Anal.* Calcd. for $C_{22}H_{30}O_7$: C, 65.01; H, 7.44. Found: C, 64.74; H, 7.51. Mass Spectrum *m/e*: 406 (M^+) (Calcd. for $C_{22}H_{30}O_7$: 406). IR ν_{max} cm^{-1}: 3500, 1760, and 1730. NMR δ: 1.13 (3H, d, J=7 Hz), 1.23 (6H, s), 2.10 (3H, s), 3.93 br (1H, s, OH), 3.95, 4.98 (each 1H, AB type, J=9 Hz, 20 H_2), 4.20 (1H, m, 2-H), 4.40 (1H, d, J=5 Hz, 15-H), and 4.43 (1H, d, J=2.5 Hz, 1-H).

Tetrahydropyranylation of Alcohol 4——To a solution of alcohol **4** (15 g) in $CHCl_3$ (dried over P_2O_5) (300 ml) was dropwise added dihydropyran (4.7 g). The reaction was accomplished, when the addition of the reagent was finished. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. The extract was treated as usual to give a crude crystalline product (19 g), which was recrystallized from ether–petroleum ether to yield tetrahydropyranyl ether **15**, mp 142—148°, as prisms. *Anal.* Calcd. for $C_{26}H_{36}O_7$: C, 67.80; H, 7.88. Found: C, 67.54; H, 8.11. UV λ_{max}^{MeOH} nm (ε): 227.5 (5230). IR ν_{max} cm^{-1}: 1775, 1735, and 1685. NMR δ: 1.08 (3H, d, J=7 Hz), 1.20, 1.40 (each 3H, s), 3.68 (2/3×3H, s),[25] 3.72 (1/3×3H, s), 4.35 (each 1H, AB type, J=11 Hz), 4.53 br (2/3×1H, s, –OĊHO–), 4.90 br (1/3×1H, –OĊHO–), 6.03, and 6.70 (each 1H, AB type, J=10 Hz, 1-H, 2-H).

Epoxidation of 15 with H_2O_2 and Alkali——After addition of 30% H_2O_2 (100 ml) to a solution of **15** (8 g) in MeOH (150 ml), 10% aq. NaOH (3.8 ml) was added under stirring. The mixture was stirred for 34 hr. Neutralization with aq. AcOH and evaporation of MeOH *in vacuo* left a crude mixture, which was extracted with ether. The ether layer was washed with aq. NaOH to remove acidic substance and then with H_2O. Evaporation of ether after drying gave an oily product (8.1 g), which was purified by chromatography to give epoxide **16** (4.2 g) as an oil. NMR δ: 1.10 (3H, d, J=7 Hz), 1.35, 1.40 (each 3H, s), 3.45, 3.80 (each 1H, AB type, J=5 Hz, 1-H, 2-H), 3.70 (2/3×3H, s), 3.73 (1/3×3H, s), 4.30, 4.53 (each 1H, AB type, J=10 Hz, 20 H_2), 4.53 br (2/3×1H, s, –OĊHO–), and 4.85 br (1/3×1H, s, –OĊHO–). The alkaline layer was acidified by HCl and extracted with AcOEt. The extract was treated as usual to give an oil, which was methylated by CH_2N_2 in MeOH and ether. Evaporation of the solvents and recrystallization of the crystalline residue

25) Tetrahydropyranyl ethers are always a mixture of the stereoisomers at 2′-position of the substituted group.

gave diester **17**, mp 232—235° (from ether), as prisms. *Anal.* Calcd. for $C_{22}H_{30}O_8$: C, 62.54; H, 7.16. Found: C, 62.26; H, 7.36. Mass Spectrum *m/e*: 422 (M^+) (Calcd. for $C_{22}H_{30}O_8$: 422). UV λ_{max}^{MeOH} nm (ε): 238 (7800). IR ν_{max} cm^{-1}: 3525, 1740, 1705, and 1604. NMR δ: 1.15 (3H, d, J=7 Hz), 1.97, 2.20 (each 3H, s), 3.37, 3.53 (each 1H, AB type, J=5 Hz, 1-H, 2-H), 3.60, 3.67 (each 3H, s), and 4.67 (2H, s, 20 H_2).

Zinc Dust Reduction of $\alpha\beta$-Epoxy-ketone 16——To a solution of epoxide **16** (820 mg) in absolute EtOH (27 ml) were added Zn dust (14.5 g) and $ZnCl_2$ (20 mg) and refluxed for 3.5 hr. The EtOH layer collected by repeated decantations under additions of EtOH was evaporated *in vacuo* to leave a residue, which was dissolved in CH_2Cl_2 and filtered through a Na_2SO_4 column to remove Zn dust completely. Chromatography gave an oily substance (513 mg), which was crystallized and recrystallized from ether–petroleum ether to yield a hydroxy ketone **18**, mp 194—199°, as prisms. *Anal.* Calcd. for $C_{26}H_{38}O_8$: C, 65.25: H, 8.00. Found: C, 65.51; H, 7.74. IR ν_{max} cm^{-1}: 3515, 3450, 1753, and 1720. NMR δ: 1.10 (3H, d, J=6 Hz), 1.21, 1.25 (each 3H, s), 3.53 br. (1H, s, 15-H), 3.73 (2/3×3H, s), 3.75 (1/3×3H, s), 4.13, 4.53 (each 1H, AB type, J= 11 Hz, 20 H_2), 4.52 br. (2/3×1H, s, –OĊHO–), and 4.88 br. (1/3×1H, s, –OĊHO–).

Attempted Thioketalization of Ketone 18——To a solution of ketone **18** (270 mg) in $CHCl_3$ (3 ml) was added ethanedithiol (5 drops) and stirred at −2∼−6°. To this mixture was added BF_3–etherate (2 drops) and stirred for 40 min. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. The extract was treated as usual to give a crude crystalline substance (186 mg), which was recrystallized from MeOH–ether to yield diol **19**, mp 220—224°, as prisms. *Anal.* Calcd. for $C_{21}H_{30}O_7$: C, 63.94; H, 7.66. Found: C, 63.97; H, 7.78. Mass Spectrum *m/e*: 394 (M^+) (Calcd. for $C_{21}H_{30}O_7$, 394). IR ν_{max} cm^{-1}: 3500, 1760, 1740, and 1708. NMR δ (D_5–pyridine): 1.12 (3H, d, J=7 Hz,) 1.55 (6H, s), 3.80 (3H, s), 3.94 (1H, d, J=4.5 Hz, 15-H), 4.38 (1H, t, J=4.5 Hz, 1-H), 4.84, and 5.10 (each 1H, AB type, J=11 Hz, 20 H_2).

Chemical Conversion of Tetrahydropyranyl Ether 16 into Acetate 21——To a solution of **16** (14.5 g) in MeOH (400 ml) were added conc. HCl (1 ml) and H_2O (180 ml) and the mixture was stirred overnight. Neutralization with aq. Na_2CO_3 and evaporation of MeOH *in vacuo* left a residue, which was extracted with CH_2Cl_2. Usual work up of the extract gave an oil (14.2 g). Purification by chromatography gave alcohol **20** as an oil (10.4 g). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1770, and 1715. NMR δ: 1.11 (3H, d, J=7 Hz), 1.35, 1.38 (each 3H, s), 3.41, 3.72 (each 1H, AB type, J=4 Hz, 1-H, 2-H), 3.65 (1H, d, J=4 Hz, 15-H), 3.73 (3H, s), 4.23, and 4.57 (each 1H, AB type, J=10 Hz, 20 H_2). Alcohol **20** (10.4 g) was dissolved in pyridine (50 ml), to which Ac_2O (50 ml) was added. The mixture was allowed to stand overnight. Evaporation *in vacuo* left a residue, which was chromatographed to give a crude crystalline substance (10.1 g). Treatment with ether–petroleum ether crystallized it, which was recrystallized to yield acetate **21**, mp 141—142° (from ether–petroleum ether), as prisms. *Anal.* Calcd. for $C_{23}H_{30}O_8$: C, 63.58; H, 6.96. Found: C, 63.78; H, 7.19. Mass Spectrum *m/e*: 434 (M^+) (Calcd. for $C_{23}H_{30}O_8$: 434). IR ν_{max} cm^{-1}: 1775, 1740, and 1730. NMR δ: 1.10 (3H, d, J=7 Hz), 1.35, 1.38, 1.98 (each 3H, s), 3.43, 3.75 (each 1H, AB type, J=4 Hz, 1-H, 2-H), 3.70 (3H, s), 4.25, 4.53 (each 1H, AB type, J=10 Hz, 20 H_2), and 4.95 (1H, d, J=4 Hz, 15-H).

Zinc Dust Reduction of $\alpha\beta$-Epoxy-ketone 21——To a solution of ketone **21** (4.4 g) in absolute EtOH (300 ml) were added Zn dust (80 g) and $ZnCl_2$ (400 mg) and refluxed for 6 hr. After cooling, the same treatment as in **16** gave an oil (4.1 g), which was chromatographed to separate two crystalline products. The less polar product (1.45 g) was proved to be identical with $\alpha\beta$-unsaturated ketone **5**. (m.m.p, IR, NMR, and TLC) The more polar product (1.9 g), mp 205—206° (from ether–petroleum ether), obtained as fine crystals, was proved to be the desired compound **22**. *Anal.* Calcd. for $C_{23}H_{32}O_8$: C, 63.28; H, 7.39. Found: C, 63.00; H, 7.60. Mass Spectrum *m/e*: 436 (M^+) (Calcd. for $C_{23}H_{32}O_8$: 436). IR ν_{max} cm^{-1}: 3450, 1760, 1740, and 1715. NMR δ: 1.10 (3H, d, J=7 Hz), 1.23, 1.30, 2.00 (each 3H, s), 3.12 (1H, d, J=5 Hz, OH, disappeared with D_2O), 3.77 (3H, s), 4.15 br. (1H, m, 1-H), 4.18, 4.52 (each 1H, AB type, J=12 Hz, 20 H_2), and 5.03 (1H, d, J=5 Hz, 15-H).

Thioketalization of Ketone 22——To a solution of **22** (2.15 g) in $CHCl_3$ (20 ml) was added ethanedithiol (2 ml). To the mixture was added BF_3-etherate (1.5 ml) at 0° under stirring and further stirred for 30 min. The mixture was poured into aq. Na_2CO_3 and extracted by CH_2Cl_2. The usual treatment of the extract gave a crude crystalline product which was washed with ether. Recrystallization of this substance (2.19 g) from MeOH yielded ethylenethioketal **23**, mp 278—285° (decomp.), as needles. *Anal.* Calcd. for $C_{25}H_{36}O_7S_2$: C, 58.54; H, 7.08; S, 12.48. Found: C, 58.31; H, 7.07; S, 12.41. Mass Spectrum *m/e*: 512 (M^+) (Calcd. for $C_{25}H_{36}O_7S_2$: 512). IR ν_{max} cm^{-1}: 3400, 1765 (shoulder), and 1735. NMR δ: 1.13 (3H, d, J=7 Hz), 1.20, 1.46, 2.00 (each 3H, s), 3.30 br (4H, s, $-SCH_2CH_2S-$), 3.70 (3H, s), 4.07, 4.23 (each 1H, AB type, J=12 Hz, 20 H_2), and 4.98 (1H, d, J=5 Hz, 15-H).

Reduction of the Ethylenethioketal 23 with Raney Ni——To a solution of **23** (2.486 g) in EtOH (210 ml) was added Raney-Ni W-2 (6 g), and the mixture was refluxed for 11 hr. Filtration from the catalyst and evaporation of EtOH gave a crude crystalline compound (1.87 g), which on recrystallization yielded 3-deoxo product **24**, mp 205—207° (from ether), as needles. *Anal.* Calcd. for $C_{23}H_{34}O_7 \cdot 1/3H_2O$: C, 64.46; H, 8.07. Found: C, 64.67; H, 7.96. Mass Spectrum *m/e*: 422 (M^+) (Calcd. for $C_{23}H_{34}O_7$: 422). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3450, 1765, and 1735. NMR δ: 1.00 (3H, s), 1.10 (3H, d, J=7 Hz), 1.20, 2.00, 3.73 (each 3H, s), 3.90 br (1H, q-like), 4.07, 4.20 (each 1H, AB type, J=11 Hz, 20 H_2), and 4.97 (1H, d, J=5 Hz, 15-H).

Isolation of Lactone 25 from Reduction of the Mother liquor of 23——A combined mixture of the ether washing of the crude thioketal **23** and the mother liquor of recrystallization of the thioketal **23** was eva-

porated *in vacuo* to leave a residue, which was dissolved in EtOH and reduced with Raney-Ni. Usual work up of the reaction mixture and purification of the crude product by chromatography gave crystals, which were recrystallized to yield lactone **25**, mp 255—257° (from ether–CH_2Cl_2), as triangular crystals. *Anal.* Calcd. for $C_{22}H_{30}O_6$: C, 67.67; H, 7.74. Found: C, 67.51; H, 8.02. Mass Spectrum *m/e*: 390 (M^+) (Calcd. for $C_{22}H_{30}O_6$: 390). IR ν_{max} cm^{-1}: 1755 and 1735. NMR δ: 1.07 (3H, s), 1.10 (3H, d, J=7 Hz), 1.20, 2.10 (each 3H, s), 4.27, 4.67 (each 1H, AB type, J=10 Hz, 20 H_2), 4.30 (1H, q, J=9 and 6 Hz, 1-H), and 4.40 (1H, d, J=5 Hz, 15-H).

Acetylation of Alcohol 24——Usual work up of a mixture of **24** (115 mg), pyridine (0.5 ml), and Ac_2O (0.5 ml) gave an oil, which was crystallized (89 mg) by chromatography. Recrystallization from ether–petroleum ether yielded acetate **26**, mp 152—154°, as prisms. *Anal.* Calcd. for $C_{25}H_{36}O_8$: C, 64.63; H, 7.81. Found: C, 64.71: H, 7.66. Mass Spectrum *m/e*: 464 (M^+) (Calcd. for $C_{25}H_{36}O_8$: 464). IR ν_{max} cm^{-1}: 1770 and 1745. NMR δ: 1.01 (3H, s), 1.17 (3H, d, J=8 Hz), 1.21 (3H, s), 1.97, 2.10, 3.70 (each 3H, s), 4.20 (2H, s, 20 H_2), 4.95 (1H, d, J=5 Hz, 15-H), and 5.10 (1H, q, J=10 and 5 Hz, 1-H).

Jones Oxidation of Alcohol 24——To an ice-cooled and stirred solution of **24** in acetone (10 ml) was added Jones reagent. Usual work up gave an oil, which was crystallized by chromatography. The crystalline product (105 mg) on recrystallization yielded ketone **27**, mp 137—138° (from ether–petroleum ether), as needles. *Anal.* Calcd. for $C_{23}H_{32}O_7$: C, 65.69; H, 7.67. Found: C, 65.63; H, 7.53. Mass Spectrum *m/e*: 420 (M^+) (Calcd. for $C_{23}H_{32}O_7$: 420). IR ν_{max} cm^{-1}: 1770, 1748, and 1695. NMR δ: 0.90 (3H, s), 1.10 (3H, d, J=7 Hz), 1.36, 1.98, 3.63 (each 3H, s), 4.02, 4.42 (each 1H, AB type, J=11 Hz, 20 H_2), and 4.95 (1H, d, J=4.5 Hz, 15-H).

Tetrahydropyranylation of Alcohol 24——To a solution of **24** (1.28 g) in $CHCl_3$ (20 ml; dried over P_2O_5) was added dihydropyran (310 mg) under stirring and the mixture was stirred for 3 hr. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. Usual treatment of the extract gave an oil (1.7 g), which was purified by chromatography to give an amorphous product **28** (1.3 g). Mass Spectrum *m/e*: 506.290 (Calcd. for $C_{28}H_{42}O_8$: 506.287). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 and 1735. NMR δ: 1.00 (3H, s), 1.12 (3H, d, J=7 Hz), 1.18, 1.98, 3.70 (each 3H, s), 4.25 (2H, s, 20 H_2), 4.73 br (1H, s, –OCHO–), and 4.93 (1H, d, J=5 Hz, 15-H).

Alkaline Hydrolysis of Acetate 28——A mixture of **28** (1.1 g), MeOH (20 ml), and 5% Na_2CO_3 (10 ml) was stirred for 2 days. Neutralization with dil. AcOH, evaporation *in vacuo*, extraction with CH_2Cl_2, and usual treatment of the extract gave an oil (1.0 g), which was purified by chromatography to yield alcohol **29** as an oil (751 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3450, 1768, and 1740. NMR δ: 1.00 (3H, s), 1.10 (3H, d, J= 7 Hz), 1.19 (3H, s), 3.73 (2/3×3H, s), 3.74 (1/3×3H, s), 4.13 (2/3×2H, s, 20 H_2), 4.23 (1/3×2H, s, 20 H_2), and 4.70 br (1H, s, –OCHO–).

Mesylation of Alcohol 29——To a solution of **29** (751 mg) in pyridine (4 ml) was added mesyl chloride (700 mg) and the mixture was stirred overnight. Evaporation *in vacuo* left a residue, which, after addition of some H_2O, was extracted with CH_2Cl_2. Usual treatment of the extract gave an oil, which was chromatographed to give mesylate **30** as an oil (752 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1763 and 1730. NMR δ: 1.00 (3H, s), 1.20 (3H, s), 1.22 (3H, d, J=7 Hz), 3.00 (3H, s, CH_3SO_2–), 3.77 (3H, s), 4.15 (2/5×2H, s, 20 H_2), 4.21 (3/5×2H, s, 20 H_2), 4.59 br (1H, s, –OCHO–), and 4.70 (1H, d, J=5 Hz, 15-H).

Elimination Reaction of Mesylate 30——A solution of mesylate **30** (100 mg) in pyridine (3 ml) was heated at 110—115° for 3 hr in a sealed tube. Evaporation of pyridine *in vacuo* left a residue, which was extracted with CH_2Cl_2. The extract was treated as usual to give an oil (100 mg), which was purified through chromatography to give 15-ene derivative **32** as an oil (82 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1763 and 1725. NMR δ: 1.00 (3H, s), 1.23 (3H, s), 1.75 (3H, d, J=1.5 Hz), 3.70 (3H, s), 4.13 (2H, s, 20 H_2), 4.70 br (1H, s, –OCHO–), and 5.60 (1H, q, J=1.5 Hz, 15-H).

Formation of Lactone 31 from Mesylate 30——A solution of mesylate **30** (285 mg) in pyridine (5 ml) was heated at 125° for 5 hr in a sealed tube. Evaporation of pyridine *in vacuo*, extraction of the residue with CH_2Cl_2, and usual treatment of the extract gave an oil (206 mg), which was chromatographed to give a crystalline compound (169 mg). Purification by recrystallization yielded lactone **31**, mp 252—256° (from ether–CH_2Cl_2), as needles. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.85; H, 7.86. Mass Spectrum *m/e*: 330 (M^+) (Calcd. for $C_{20}H_{26}O_4$: 330). IR ν_{max} cm^{-1}: 1775 and 1733. NMR δ: 1.05, 1.20 (each 3H, s), 1.77 (3H, d, J=1.5 Hz), 3.73, 4.35 (each 1H, AB type, J=10 Hz, 20 H_2), 4.50 (1H, q, J=10 and 7 Hz, 1-H), 5.70 (1H, q, J=1.5 Hz). This compound was confirmed to be identical with the authentic sample[26] of compound **31** (mp, IR, and NMR).

Reaction of Dilactone 31 with Na in Liquid NH_3——A solution of dilactone **31** (232 mg) in a mixture of ether (10 ml) and THF (10 ml) was added dropwise into a solution of Na (80 mg) in anhydrous liquid NH_3 (50 ml) under stirring over a period of 20 min. After stirring for 2 hr, the excess of Na was treated with a mixture of ether and MeOH, and NH_3 was evaporated. Extraction with ether and usual treatment of the extract gave an oil, which was chromatographed to give an oily product **34** (94 mg). Mass Spectrum *m/e*: 334 (M^+) (Calcd. for $C_{20}H_{30}O_4$, 334). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 and 3557. NMR δ: 0.90, 0.99 (each 3H, s), 1.72 (3H, d, J=1.5 Hz). 3.81, 4.08 (each 1H, AB type, J=8 Hz, 20 H_2), 5.20, 5.22 (each 1H, s), and 5.30 (1H, q, J=1.5 Hz, 15-H).

26) E. Fujita and S. Nagakura, unpublished.

Acetylation of Dihemiacetal 34——To a solution of **34** (51 mg) in pyridine (1 ml) was added Ac_2O (0.5 ml) and the mixture was allowed to stand for 7 hr at room temperature. Evaporation *in vacuo* left an oily residue, which was chromatographed to separate monoacetate (7 mg) and diacetate (29 mg). Monoacetate was an oil. Mass Spectrum *m/e*: 376 (M^+) (Calcd. for $C_{22}H_{32}O_5$: 376). NMR δ: 0.95, 1.03 (each 3H, s), 1.70 (3H, d, J=1.5 Hz), 2.03 (3H, s), 3.82, 4.15 (each 1H, J=10 Hz, 20 H_2), 5.20 (1H, q, J=1.5 Hz), 5.35, and 6.05 (each 1H, s).

Diacetate **35** was obtained as prisms, mp 149—151° (from ether). *Anal.* Calcd. for $C_{24}H_{34}O_6$: C, 68.87; H, 8.19. Found: C, 68.99; H, 8.46. Mass Spectrum *m/e*: 418 (M^+) (Calcd. for $C_{24}H_{34}O_6$: 418). IR ν_{max} cm^{-1}: 1743 and 1720. NMR δ: 0.95, 1.03 (each 3H, s), 1.72 (3H, d, J=1.5 Hz), 2.03, 2.08 (each 3H, s), 3.90, 4.25 (each 1H, AB type, J=9 Hz), 5.30 br (1H, s, 15-H), 6.07, and 6.17 (each 1H, s, 6-H, 7-H).

Jones Oxidation of Dihemiacetal 34——To a solution of **34** (47 mg) in acetone (5 ml) was added Jones reagent (2 drops) at 0° under stirring and the mixture was stirred for 30 min. Addition of MeOH, neutralization with aq. Na_2CO_3, evaporation *in vacuo*, extraction with CH_2Cl_2, and usual treatment of the extract gave crude crystals (29 mg), which were recrystallized from ether–CH_2Cl_2 to give pure compound **31** (Identified with the authentic sample by m.mp NMR, and TLC).

Methoxymethylation of Alcohol 10——A solution of alcohol **10** (724 mg) in anhydrous DMF (4 ml) was added to NaH (140 mg) at 0° in dry nitrogen. Subsequently, a solution of chloromethyl methyl ether (1 ml) in DMF (6 ml) was added dropwise at 0° to this mixture, then the mixture was stirred for 30 min, and was poured into aq. Na_2CO_3. It was extracted with Et_2O, and the organic layer was washed with aq. Na_2CO_3 and H_2O to remove acid and DMF. After drying over Na_2SO_4, ether was evaporated off to leave an oil (740 mg), which was chromatographed to separate a formylate **41** (142 mg) and the desired methoxymethyl ether **40** (520 mg). The former was obtained as needles, mp 137—138° (from ether–CH_2Cl_2). *Anal.* Calcd. for $C_{22}H_{30}O_6$: C, 67.67; H, 7.74. Found: C, 67.45; H, 7.50. Mass Spectrum *m/e*: 390 (M^+) (Calcd. for $C_{22}H_{30}O_6$: 390). IR ν_{max} cm^{-1}: 1760 and 1730. NMR δ: 0.93 (3H, s), 1.11 (3H, d, J=7 Hz), 1.30, 3.63 (each 3H, s), 3.90, 4.20 (each 1H, AB type, J=10 Hz, 20 H_2), 5.10 (1H, d, J=4.5 Hz, 15-H), 4.99, 5.85 (each 1H, AB part of ABX_2 type, J_{AB}=10, J_{AX}=5 and 2 Hz, J_{BX}=2Hz, 1-H, 2-H), and 7.97 (1H, s, CHO).

The latter **40** was obtained as needles, mp 100—103° (from ether–petroleum ether). *Anal.* Calcd. for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43. Found: C, 68.04; H, 8.63. Mass Spectrum *m/e*: 406 (M^+) (Calcd. for $C_{23}H_{34}O_6$: 406). IR ν_{max} cm^{-1}: 1760 and 1735. NMR δ: 0.93 (3H, s), 1.10 (3H, d, J=7 Hz), 1.28, 3.30 (each 3H, s), 3.50 (1H, d, J=4 Hz), 3.67 (3H, s), 3.83, 4.23 (each 1H, AB type, J=10 Hz, 20 H_2), 4.53 (2H, s, $-OCH_2O-$), and 5.67 (2H, AB part of ABX_2 type, 1-H, 2-H).

Tetrahydropyranylation of Alcohol 10——To a solution of alcohol **10** (120 mg) in $CHCl_3$ (2 ml) dried over P_2O_5 was added dihydropyran (4 drops) and stirred for 20 min. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. An oily substance obtained by usual treatment of the extract was chromatographed to give crystals (130 mg), which on recrystallization gave tetrahydropyranyl ether **38**, mp 111—115° (from ether–petroleum ether), as needles. *Anal.* Calcd. for $C_{26}H_{38}O_6 \cdot 1/3H_2O$: C, 68.99; H, 8.46. Found: C, 69.13; H, 8.68. IR ν_{max} cm^{-1}: 1765 and 1730. NMR δ: 0.93 (3H, s), 1.10 (3H, d, J=7 Hz), 1.30 (3H, s), 3.63 (1/2×3H, s), 3.67 (1/2×3H, s), 3.80, 4.18 (each 1H, AB type, J=10 Hz, 20 H_2), and 5.70 (2H, AB part of ABX_2 type, 1-H, 2-H).

Acyloin Condensation with 40——A solution of **40** (1.624 g) in dry ether (40 ml) was added dropwise into a solution of Na (460 mg) in a dry mixture of liquid NH_3 (250 ml) and ether (20 ml) at −70° under vigorous stirring over a period of 1.5 hr. After stirring for further 4 hr, NH_3 was allowed to be evaporated off. Extraction with CH_2Cl_2 and usual treatment of the extract gave an oil (1.6 g), which was chromatographed to separate **44** (327 mg), unknown compound (186 mg), **45** (7 mg), **42** (414 mg), and **43** (89 mg), successively. Compound **44** was an oil. Mass Spectrum *m/e*: 376 (M^+) (Calcd. for $C_{22}H_{32}O_5$: 376). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 and 1738. NMR δ: 1.10 (3H, s), 1.13 (3H, d, J=7 Hz), 1.45 (3H, s), 3.20 br (1H, s, 15-H), 3.30 (3H, s), 3.95 (2H, s, 20 H_2), 4.45, 4.70 (each 1H, AB type, J=8 Hz, $-OCH_2O-$), 4.45 (1H, s, OH, disappeared with D_2O), 5.46, and 5.80 (each 1H, AB part of ABX_2 type, J_{AB}=11.5 Hz, 1-H, 2-H). Compound **45** was obtained as needles, mp 147—148° (from ether–CH_2Cl_2). Mass Spectrum *m/e*: 378.243 (M^+) (Calcd. for $C_{22}H_{34}O_5$: 378.240). IR ν_{max} cm^{-1}: 3380. NMR δ: 1.20 (3H, d, J=7 Hz), 1.27 (6H, s), 3.42 (3H, s), 3.53 br (1H, s, 15-H), 3.69 (1H, s, 7-H), 3.85, 3.92 (each 1H, AB type, J=9 Hz, 20 H_2), 4.40 (1H, s, OH, disappeared with D_2O), 4.67, 4.82 (each 1H, AB type, J=7 Hz, $-OCH_2O-$), and 5.73 br (2H, s, 1-H, 2-H). Compound **42** was obtained as needles, mp 193—195° (from ether–CH_2Cl_2). *Anal.* Calcd. for $C_{22}H_{34}O_5 \cdot 1/3H_2O$: C, 68.72; H, 8.91. Found: C, 68.98; H, 9.08. Mass Spectrum *m/e*: 378 (M^+) (Calcd. for $C_{22}H_{34}O_5$: 378). NMR δ: 1.03, 1.08 (each 3H, s), 1.08 (3H, d, J=7 Hz), 3.40 (3H, s), 3.41 br (1H, s, 15-H), 3.80 (1H, d, J=6 Hz, 6-H), 3.87 (2H, s, 20 H_2), 4.66, 4.75 (each 1H, AB type, J=6 Hz, $-OCH_2O-$), 5.12 (1H, s, OH, disappeared with D_2O), 5.30 and 5.77 (each 1H, AB part of ABX_2 type, J_{AB}=11 Hz, J_{AX}=2 and 5 Hz, J_{BX}=2 Hz). Compound **43** was obtained as prisms, mp 219—235° (from ether–CH_2Cl_2). *Anal.* Calcd. for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.26; H, 9.60. Mass Spectrum *m/e*: 362 (M^+-18) (Calcd. for $C_{22}H_{34}O_4$: 362). IR ν_{max} cm^{-1}: 3540 and 3150. NMR δ: 1.12 (3H, s), 1.17 (3H, d, J=6 Hz). 1.21, 3.40 (each 3H, s), 3.50 (1H, d, J=4 Hz, 15-H), 3.53, 3.80 (each 1H, AB type, J=12 Hz, 20 H_2), 3.78 (1H, d, J=3 Hz, 7-H), 4.17 (1H, t, J=3 Hz, 6-H), 4.68, 4.81 (each 1H, AB type, J=6 Hz, $-OCH_2O-$), and 5.40 br (2H, s, AB part of ABX_2 type, 1-H, 2-H).

Sodium Borohydride Reduction of 6-Oxo-7-hemiketal Derivative 44——To a solution of **44** (200 mg) in EtOH (10 ml) was added $NaBH_4$ at 0° and stirred for 1 hr. Neutralization with dil. AcOH and evaporation of EtOH *in vacuo* gave a residue, which was extracted with CH_2Cl_2. Usual treatment of the extract gave crude crystals (186 mg), which were purified by chromatography and recrystallization from ether–CH_2Cl_2 to give a pure crystalline compound. It was proved to be identical with **42** (m.mp, IR, NMR, and TLC).

Acetylation of 7-Hemiketal-6-ol 42——To a solution of **42** (100 mg) in pyridine (1 ml) was added Ac_2O (1 ml) and the mixture was heated at 60—65° for 4 days. Evaporation *in vacuo* left an oily residue, which was chromatographed to give crystals (98 mg). Recrystallization from ether–CH_2Cl_2 yielded acetate **46**, mp 155—156°, as needles. *Anal.* Calcd. for $C_{24}H_{36}O_6$: C, 68.54; H, 8.63. Found: C, 68.25; H, 8.57. Mass Spectrum *m/e*: 420 (M^+) (Calcd. for $C_{24}H_{36}O_6$: 420). IR ν_{max} cm^{-1}: 3400 and 1745. NMR δ: 0.96, 1.07 (each 3H, s), 1.13 (3H, d, J=6 Hz), 2.09, 3.40 (each 3H, s), 3.40 (1H, 15-H), 3.91 (2H, s, 20 H_2), 4.69, 4.81 (each 1H, AB type, J=6 Hz, $-OCH_2O-$), 5.33, 5.78 (each 1H, AB part of ABX_2 type, J_{AB}=11 Hz, J_{AX}=5 and 2 Hz, J_{BX}=2 Hz), and 5.40 (1H, d, J=8 Hz, 6-H).

Acidic Hydrolysis of 15-Methoxymethyl Ether 46——To a solution of **46** (657 mg) in MeOH (32 ml) were added 3.6% HCl (1.5 ml) and H_2O (10 ml) and the mixture was heated at 65° for 3 days. The mixture was neutralized by aq. Na_2CO_3 and evaporated *in vacuo* to leave a residue, which was extracted with CH_2Cl_2. The extract was treated as usual to give crystals, which were recrystallized from ether–CH_2Cl_2 to yield alcohol **47** (483 mg), mp 225—230°, as needles. *Anal.* Calcd. for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57. Found: C, 69.92; H, 8.64. Mass Spectrum *m/e*: 376 (M^+) (Calcd. for $C_{22}H_{32}O_5$: 376). IR ν_{max} cm^{-1}: 3450, 3220, and 1745. NMR δ: (d_5-pyridine): 0.97, 1.03 (each 3H, s), 1.10 (3H, d, J=7 Hz), 2.20 (3H, s), 4.00 (2H, s, 20 H_2), 4.00 (1H, 15-H), 4.80 (1H, s, OH, disappeared with D_2O), 5.37, 5.75 (each 1H, AB part of ABX_2 type, J_{AB}=11 Hz, 1-H, 2-H), and 5.68 (1H, d, J=7.5 Hz, 6-H).

Epoxidation of 1-Ene Compound 47——To a solution of **47** (483 mg) in dry CH_2Cl_2 (15 ml) was added *m*-chloroperbenzoic acid (274 mg) and allowed to stand in a dark room for 3 days. The mixture was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. Usual treatment of the extract gave crystals (505 mg), which were purified by chromatography to yield epoxide **48**, mp 222—224° (from ether–CH_2Cl_2), as needles. *Anal.* Calcd. for $C_{22}H_{32}O_6 \cdot 1/3H_2O$: C, 66.31; H, 8.16. Found: C, 66.58; H, 8.20. Mass Spectrum *m/e*: 392 (M^+) (Calcd. for $C_{22}H_{32}O_6$: 392). IR ν_{max} cm^{-1}: 3500, 3250, and 1750. NMR δ (d_5-pyridine): 0.83, 0.97 (each 3H, s), 1.08 (3H, d, J=7 Hz), 2.20 (3H, s), 2.68 (1H, d, J=4 Hz, 1-H), 3.23 (1H, m, 2-H), 3.95 br (1H, s, 15-H), 4.18 (2H, s, 20 H_2), and 5.55 (1H, d, J=6.5 Hz, 6-H).

Reaction of Alcohol 48 with Mesyl Chloride——To a solution of **48** (1.5 g) in pyridine (12 ml) was added MsCl (840 mg) and the mixture was stirred for 2 days. Evaporation *in vacuo* left a residue, which was extracted with AcOEt. The extract was treated as usual to give an oil, which was chromatographed to separate **49** (379 mg) and **50** (200 mg). The compound **49** was an oil. Mass Spectrum *m/e*: 374 (M^+) (Calcd. for $C_{22}H_{30}O_5$: 374). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 and 1725. NMR δ: 0.79, 1.08 (each 3H, s), 1.70 (3H, d, J=1.5 Hz), 2.10 (3H, s), 2.63 (1H, d, J=4 Hz, 1-H), 3.20 (1H, m, 2-H), 4.03, 4.17 (each 1H, AB type, J=10 Hz, 20 H_2), 5.05 (1H, d, J=6 Hz, 6-H), and 5.73 (1H, q, J=1.5 Hz, 15-H). The chlorohydrin compound **50** was obtained as prisms, mp 153—155° (from MeOH–CH_2Cl_2). Beilstein test: positive. Mass Spectrum *m/e*: 410.185 (M^+) (Calcd. for $C_{22}H_{31}O_5Cl$: 410.186). IR ν_{max} cm^{-1}: 3450 and 1725. NMR δ: (d_5-pyridine): 1.00, 1.51 (each 3H, s), 1.76 (3H, d, J=1.5 Hz), 2.12 (3H, s), 3.97 (1H, d, J=2 Hz, 1-H), 4.32, 5.02 (each 1H, AB type, J= 10 Hz, 20 H), 4.63 (1H, m, 2-H), 5.83 (1H, d, J=4 Hz, 6-H), and 6.28 (1H, q, J=1.5 Hz, 15-H).

Photosensitized Oxygenation with 15-Ene Compound 49——To a solution of **49** (379 mg) in pyridine (15 ml) was added haematoporphyrin (35 mg), and oxygen was passed through the solution under irradiation with fluorescent tubes (20W×4) for 98 hr. The mixture was evaporated *in vacuo* below 45° to leave a residue, which was dissolved in EtOH (25 ml), to which a solution of KI (700 mg) in H_2O (7 ml) was added, and the mixture was allowed to stand for 1 hr. After decomposition of iodine liberated with aq. $Na_2S_2O_3$ followed by concentration *in vacuo* and addition of H_2O, the mixture was extracted with ether. The extract was treated as usual to give an oil (402 mg), which was chromatographed to give crystals (244 mg). Purification by recrystallization yielded the desired allyl alcohol **51**, mp 207—210° (from ether–CH_2Cl_2), as prisms. *Anal.* Calcd. for $C_{22}H_{32}O_6$: C, 67.67; H, 7.74. Found: C, 67.77; H, 7.53. Mass Spectrum *m/e*: 392 (M^+) (Calcd. for $C_{22}H_{32}O_6$: 392). IR ν_{max} cm^{-1}: 3450, 3280, and 1750. NMR δ: (d_5-pyridine) 0.84, 0.98, 2.19 (each 3H, s), 2.66 (1H, J=4 Hz, 1-H), 3.23 (1H, m, 2-H), 4.20 (2H, s, 20 H_2), 4.61 (1H, d, s, 15-H), 5.20, 5.40 (each 1H, s, 17 H_2), and 5.60 (1H, d, J=7 Hz, 6-H).

Acetylation of Chlorohydrin 50——A solution of **50** (200 mg) in pyridine (4 ml) and Ac_2O (4 ml) was allowed to stand overnight. Usual work up and chromatography of the crude product gave acetate **53** (198 mg) as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520 and 1732. NMR δ: 0.92, 1.42 (each 3H, s), 1.72 (3H, d, J=1.5 Hz), 2.10, 2.17 (each 3H, s), 4.10, 4.76 (each 1H, AB type, J=11 Hz, 20 H_2), 4.13 (1H, m, 2-H), 4.70 (1H, d, J=2.5 Hz, 1-H), 5.23 (1H, d, J=4.5 Hz, 6-H), and 5.72 (1H, q, J=1.5 Hz, 15-H).

Photosensitized Oxygenation of 15-Ene Compound 53——Compound **53** (198 mg) in pyridine (10 ml) under the presence of haematoporphyrin (24 mg) was subjected to the photosensitized oxygenation under the same conditions as in **49**. The reaction mixture was evaporated *in vacuo* to remove pyridine. To the residue were added EtOH (10 ml), a solution of KI (400 mg) in H_2O (2 ml), and finally AcOH (one drop).

The mixture was allowed to stand overnight, and after decomposition of I_2 with aq. $Na_2S_2O_3$, was evaporated *in vacuo*. The residue, after addition of H_2O, was extracted with ether, and usual treatment of the extract gave an oil, which was chromatographed to give crystals (100 mg). Purification by recrystallization yielded 15α-ol **54**, mp 223—225° (from ether–CH_2Cl_2), as fine crystals. Mass Spectrum *m/e*: 468.190 (M^+) (Calcd. for $C_{24}H_{33}O_7Cl$: 469.191). IR ν_{max} cm^{-1}: 3450 and 1745. NMR δ: 0.95, 1.45, 2.09, 2.20 (each 3H, s), 4.01, 4.77 (each 1H, AB type, J=11 Hz, 20 H_2), 4.18 (1H, m, 2-H), 4.30 (1H, s, 15-H), 4.70 (1H, d, J=3 Hz, 1-H), 5.17, 5.30 (each 1H, s, 17 H_2), and 5.32 (1H, d, J=6 Hz, 6-H).

Jones Oxidation of 54——To a solution of **54** in acetone (2 ml) was added dropwise Jones reagent at room temperature. The reaction was stopped at the point in which the spot of the starting material disappeared on TLC. After addition of MeOH, the mixture was neutralized with aq. Na_2CO_3, and the solvents were evaporated off *in vacuo* to leave a residue, which was extracted with CH_2Cl_2. Usual treatment of the extract gave an oil, which was chromatographed to give crystals (18 mg). Recrystallization gave the pure compound **55**, mp 238—242° (from ether–CH_2Cl_2), as prisms. Beilstein test was positive. *Anal.* Calcd. for $C_{24}H_{31}O_8Cl$: C, 59.68; H, 6.47. Found: C, 59.52; H, 6.54. IR ν_{max} cm^{-1}: 3425, 1750, and 1710. NMR δ: 0.95, 1.43, 2.10, 2.27 (each 3H, s), 2.93, 3.19 (each 1H, AB type, J=6 Hz, 17 H_2), 4.10, 4.85 (each 1H, AB type, J=11 Hz, 20 H_2), 4.20 (1H, m, 2-H), 4.79 (1H, d, J=3 Hz, 1-H), 5.15 (1H, d, J=5 Hz, 6-H), and 5.16 (1H, s, OH, disappeared with D_2O).

Epoxidation of 1-Ene Compound 42——To a solution of **42** (600 mg) in CH_2Cl_2 (20 ml) was added *m*-chloroperbenzoic acid (320 mg) and the mixture was allowed to stand in a dark room for 2 days. It was poured into aq. Na_2CO_3 and extracted with CH_2Cl_2. Usual treatment of the extract gave crystals (623 mg), which were chromatographed and recrystallized to give epoxide **56**, mp 207—212° (from ether–CH_2Cl_2), as needles. *Anal.* Calcd. for $C_{22}H_{34}O_6$: C, 66.98; H, 8.69. Found: C, 67.12; H, 8.93. Mass Spectrum *m/e*: 394 (M^+) (Calcd. for $C_{22}H_{34}O_6$: 394). IR ν_{max} cm^{-1}: 3425. NMR δ: 0.98, 1.02 (each 3H, s), 1.14 (3H, d, J=7 Hz), 2.60 (1H, d, J=4 Hz, 1-H), 3.23 (1H, m, 2-H), 3.40 (3H, s), 3.41 br (1H, s, 15-H), 3.68 (1H, d, J=7 Hz, 6-H), 4.02 (2H, s, 20 H_2), 4.67 (2H, s, $-OCH_2O-$), and 5.30 (1H, s, OH, disappeared with D_2O).

Lithium Aluminum Hydride Reduction of Epoxide 56——To a solution of epoxide **56** (102 mg) in dry ether (25 ml) was added a suspension of $LiAlH_4$ (100 mg) in ether (2 ml) at 0°, and then the mixture was refluxed for 3 hr. Decomposition of the excess of $LiAlH_4$ and neutralization were carried out by dil. HCl at 0°, and the mixture was extracted with AcOEt. The extract was treated as usual to give a crystalline product (100 mg), which was recrystallized from MeOH to yield 1β-ol **57**, mp 192—194°, as fine crystals. *Anal.* Calcd. for $C_{22}H_{36}O_6$: C, 66.64; H, 9.15. Found: C, 66.79; H, 9.24. Mass Spectrum *m/e*: 396 (M^+) (Calcd. for $C_{22}H_{36}O_6$: 396). IR ν_{max} cm^{-1}: 3450. NMR δ: (d_5-pyridine): 1.09 (3H, d, J=6.5 Hz), 1.20, 1.30, 3.31 (each 3H, s), 3.68 (1H, t, J=2 Hz, 1-H), 3.83 br (1H, s, 15-H), 4.08 (2H, s, 20 H_2), 4.20 (1H, d, J=6 Hz, 6-H), 4.80, and 5.11 (each 1H, AB type, J=7 Hz, $-OCH_2O-$).

Acetylation of Alcohol 57——A solution of **57** (420 mg) in pyridine (10 ml) and Ac_2O (10 ml) was heated at 70° for 3 days. Evaporation *in vacuo* left an oil, which was chromatographed to give crude crystalline diacetate (260 mg). Its recrystallization from ether yielded 1,6-diacetate **58**, mp 164—166°, as prisms. *Anal.* Calcd. for $C_{26}H_{40}O_8$: C, 64.98; H, 8.39. Found: C, 65.22; H, 8.65. IR ν_{max} cm^{-1}: 3410 and 1740. NMR δ: 0.90 (3H, s), 1.11 (3H, d, J=7 Hz), 1.18 (3H, s), 2.09 (6H, s), 3.35 (3H, s), 3.50 br (1H, s, 15-H), 3.91 (2H, s, 20 H_2), 4.57 (1H, t, J=2 Hz, 1-H), 4.73 (2H, s, $-OCH_2O-$), 5.09 (1H, s, OH, disappeared with D_2O), and 5.33 (1H, d, J=6 Hz, 6-H).

Acid Hydrolysis of Methoxymethyl Ether of Compound 58——A mixture of **58** (870 mg), MeOH (30 ml), 3.6% HCl (1.5 ml), and H_2O (15 ml) was heated at 65° for 2 days under stirring. After neutralization with aq. Na_2CO_3, MeOH was evaporated off *in vacuo* and the remaining mixture was extracted with CH_2Cl_2. The extract was treated as usual to give crude crystals, which on recrystallization gave crystals (470 mg). Further recrystallization from ether–CH_2Cl_2 yielded 15-ol **59**, mp 216—218°, as prisms. *Anal.* Calcd. for $C_{24}H_{36}O_7 \cdot 1/3H_2O$: C, 65.13; H, 8.18. Found: C, 65.05; H, 8.28. Mass Spectrum *m/e*: 436 (M^+) (Calcd. for $C_{24}H_{36}O_7$: 436). IR ν_{max} cm^{-1}: 3450, 3200, and 1745. NMR δ: 0.90 (3H, s), 1.10 (3H, d, J=6 Hz), 1.15, 2.10, 2.13 (each 3H, s), 3.53 br (1H, s, 15-H), 3.90 (2H, s, 20 H_2), 4.58 (1H, t, J=2 Hz, 1-H), and 5.17 (1H, d, J=5 Hz, 6-H). The mother liquor of recrystallization of **59** was concentrated, and chromatographed to separate the starting material (18 mg) and another crystalline compound **60** (23 mg). The latter was recrystallized from ether to yield prisms, mp 185—190°. Mass Spectrum *m/e*: 448.248 (M^+) (Calcd. for $C_{25}H_{36}O_7$: 448.246). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. NMR δ: 0.91 (3H, s), 1.10 (3H, d, J=7 Hz), 1.13 (3H, s), 2.07 (6H, s), 3.60 (1H, d, J=4 Hz, 15-H), 3.93 (2H, s, 20 H_2), 4.60 (1H, t, J=2 Hz, 1-H), 4.80, 5.21 (each 1H, AB type, J=5 Hz, $-OCH_2O-$), and 5.18 (1H, d, J=4 Hz, 6-H).

Reaction of Alcohol 59 with MsCl——To a solution of **59** (400 mg) in pyridine (6 ml) was added MsCl (680 mg) and the mixture was stirred for 2 days. Evaporation of pyridine *in vacuo*, extraction of the residue with CH_2Cl_2, and usual treatment of the extract gave an oil, which was chromatographed to isolate an crystalline product (250 mg). It was recrystallized from ether–petroleum ether to yield 15-ene **61**, mp 191—193°, as prisms. Mass Spectrum *m/e*: 418.233 (M^+) (Calcd. for $C_{24}H_{34}O_6$: 418.235). IR ν_{max} cm^{-1}: 3450 and 1735. NMR δ: 0.90, 1.15 (each 3H, s), 1.71 (3H, d, J=1.0 Hz), 2.08, 2.15 (each 3H, s), 3.53 (1H, s, OH, disappeared with D_2O), 3.85, 4.03 (each 1H, AB type, J=10 Hz, 20 H_2), 4.60 (1H, t, J=2.5 Hz, 1-H), 5.15 (1H, d, J=4 Hz, 6-H), and 5.73 (1H, q, J=1.0 Hz, 15-H).

Photosensitized Oxygenation of 15-Ene Compound 61——The reaction conditions were the same as described above on 49 and **53**. In this case, **61** (240 mg), pyridine (10 ml), and haematoporphyrin (25 mg) were used and the reaction was carried out for 168 hr. Evaporation of pyridine *in vacuo* below 40° left a residue, which was dissolved in EtOH (15 ml). To this solution were added a solution of KI (500 mg) in H_2O (8 ml) and AcOH (1 drop), and the mixture was allowed to stand overnight. Decomposition of I_2 with aq. $Na_2S_2O_3$, evaporation of EtOH *in vacuo*, extraction of the residue with CH_2Cl_2, and usual treatment of the extract gave an oil, which was chromatographed to separate the less polar product **63** (24 mg) and the more polar product **62** (120 mg). Allyl alcohol **62** was obtained as prisms, mp 198—202° (from ether–CH_2Cl_2). *Anal.* Calcd. for $C_{24}H_{34}O_7$: C, 66.34; H, 7.89. Found: C, 66.13; H, 8.09. Mass Spectrum *m/e*: 434 (M^+) (Calcd. for $C_{24}H_{34}O_7$: 434). IR ν_{max} cm^{-1}: 3425 and 1740. NMR δ: 0.89, 1.18, 2.07, 2.17 (each 3H, s), 3.97 (2H, s, 20 H_2), 4.30 br (1H, s, 15-H), 4.60 (1H, t, J=2 Hz, 1-H), 4.63 (1H, s, OH, disappeared with D_2O), 5.18, 5.27 (each 1H, s, 17 H_2), and 5.22 (1H, d, J=6 Hz, 6-H). The $\alpha\beta$-unsaturated ketone **63** was obtained as prisms, mp 218—220° (from ether–CH_2Cl_2). Mass Spectrum *m/e*: 432.214 (M^+) (Calcd. for $C_{24}H_{32}O_7$: 432.214). UV λ_{max}^{MeOH} nm (ε): 234 (8530). IR ν_{max} cm^{-1}: 3425, 1730, 1710, and 1645. NMR δ: 0.94, 1.15, 2.07, 2.33 (each 3H, s), 4.00 (2H, s, 20 H_2), 4.63 (1H, t, J=2 Hz, 1-H), 5.05 (1H, d, J=5 Hz, 6-H), 5.28, 5.86 (each 1H, s, 17 H_2), and 5.39 (1H, s, OH, disappeared with D_2O).

Conversion of Compound 63 to Enmelol (2)——To a solution of **63** (23 mg) in absolute MeOH (3 ml) was added NaB^3H_4 (8 mg) at 0° and stirred for 1 hr. Further slow addition of $NaBH_4$ (27 mg) and stirring at 0° were carried out over a period of 9 hr. Neutralization with dil. AcOH, evaporation of MeOH *in vacuo*, extraction of the residue with AcOEt, and usual treatment of the extract gave an oil (15 mg), which was chromatographed to isolate a major crystalline compound (5 mg). This compound was dissolved in dry ether (1 ml), to which $LiAlH_4$ (5 mg) was added, and the mixture was refluxed for 20 min. After cooling and decomposition of the excess of the reagent with wet ether, the mixture was extracted with AcOEt. The extract was treated as usual to give a crude crystalline product, which was recrystallized from MeOH to yield *ent*-7β,20-epoxy-16-kaurene-1α,6α,7α,15α-tetraol (**2**) (2.5 mg), mp 283—285°, $[\alpha]_D^{22}$ −90° (c=0.022, EtOH). Mass Spectrum *m/e*: 350.211 (M^+) (Calcd. for $C_{20}H_{30}O_5$: 350.209). Its IR, mass spectra, and TLC were identical with those of the authentic sample of natural enmelol. Furthermore, its comparison with enmelol which was derived from trichokaurin by treatment with $LiAlH_4$ also showed their identity (mp, $[\alpha]_D$, m.mp, IR, and TLC).

Conversion of Trichokaurin into Enmelol (2)——To a solution of trichokaurin[27] (200 mg) in dry ether (20 ml) was added a suspension of $LiAlH_4$ (200 mg) in dry ether (10 ml) under ice-cooling. The mixture was then refluxed for 3 hr. After decomposition of the excess of $LiAlH_4$ with wet ether and extraction of the mixture with AcOEt, the organic layer, after washing with dil. HCl, was treated as usual to give a crude crystalline product (147 mg). The crystals were washed with ether and recrystallized from MeOH to yield enmelol (**2**), mp 283—285°, $[\alpha]_D^{21}$ −90° (c=0.044, EtOH), as triangular crystals. *Anal.* Calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.31; H, 8.83. IR ν_{max} cm^{-1}: 3520 and 3300. NMR δ (d_5-pyridine): 1.12, 1.14 (each 3H, s), 3.72 br (1H, s, 1-H), 4.14 br (2H, s, 20 H_2), 4.30 (1H, d, J=5 Hz, 6-H), 5.17, 5.47 (each 1H, s, 17 H_2), 5.17 (1H, s, 15-H).

Jones Oxidation of Alcohol 59——To a solution of **59** (90 mg) in acetone (15 ml) was added Jones reagent (7 drops) under stirring at room temperature. After decomposition of the excess of chromic acid with MeOH and neutralization with aq. Na_2CO_3, acetone was evaporated off *in vacuo* and the residue was extracted with CH_2Cl_2. Usual treatment of the extract gave an oil (88 mg), which was chromatographed to separate aldehyde **68** (44 mg) from unseparable mixture (32 mg) containing the desired ketone **67**. Aldehyde **68** was an oil. Mass Spectrum *m/e*: 450 (M^+) (Calcd. for $C_{24}H_{34}O_8$: 450). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 3400, and 1729. NMR δ: 0.83, 1.13 (each 3H, s), 2.03, 2.03, 2.13 (each 3H, s), 3.90 (2H, s, 20 H_2), 4.67 (1H, t, J=2 Hz, 1-H), 5.07 (1H, d, J=5 Hz, 6-H), and 9.50 (1H, s, CHO).

Conversion of Compound 62 into 15-Epienmelol (69)——To a solution of **62** (40 mg) in dry ether (7 ml) was added a suspension of $LiAlH_4$ (60 mg) in dry ether (2 ml) under ice-cooling, and then the mixture was refluxed. After decomposition of the excess of the reagent with dil. HCl and extraction of the mixture with AcOEt, usual treatment of the extract gave a crude crystalline product, which was recrystallized from EtOH–MeOH to yield 15-epienmelol (**69**) (26 mg), mp 203—205°, $[\alpha]_D^{17}$ −98° (c=0.13, MeOH). *Anal.* Calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.77; H, 8.92. Mass Spectrum *m/e*: 350 (M^+) (Calcd. for $C_{20}H_{30}O_5$: 350). IR ν_{max} cm^{-1}: 3425. NMR δ (d_5-pyridine): 1.22, 1.33 (each 3H, s), 3.70 br (1H, s), 4.15 (2H, s, 20 H_2), 4.38 (1H, d, J=5 Hz, 6-H), 5.07 (1H, s, 15-H), 5.18, and 5.32 (each 1H, s, 17 H_2).

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27) E. Fujita, T. Fujita, M. Shibuya, and T. Shingu, *Tetrahedron*, **25**, 2517 (1969): The structure of trichokaurin corresponds to enmelol-6,15-diacetate.