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Terpenoids. XLIII.[1] Total Synthesis of *rac*-Kaur-16-ene-11α,15α-diol

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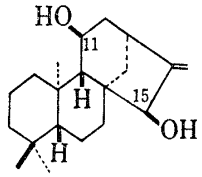
Total synthesis of *rac*-kaur-16-ene-11α,15α-diol (**1**) *via* a sequence of reactions including the Birch reduction of alcohol **4** and the Claisen rearrangement of vinyl ether **34** as the key steps is described.

Keywords——kaurane-type diterpenes; *rac*-kaur-16-ene-11α,15α-diol; total synthesis; Birch reduction; neighboring group participation; Claisen rearrangement; calliterpenone

Connolly, *et al.*[3] isolated *ent*-kaur-16-ene-11α,15α-diol (**1**) and determined its structure on the basis of chemical and spectroscopic evidence. Recently, Kitahara (the late), *et al.*[4] converted *ent*-16-kaurene into this compound. Now, we have completed the total synthesis of racemate of this natural product, which we wish to report here.

In the total syntheses of tetracyclic diterpenes, *i.e.*, 13β-kaurene[5] and *ent*-16-kauren-19-oic acid,[6] and diterpene alkaloids, *i.e.*, veatchine[7] and garryine,[7] the compounds, **2a** and **2b**, were used as the intermediate in the syntheses. The Birch reduction of the ring C, however, does not easily take place, hence the catalytic hydrogenation is necessary. In this case, only the saturated alcohols are obtained, which limits the range for the application of this method. Recently, the diol **3** was subjected to the Birch reduction to give saturated ketones in good yield.[8] The intramolecular participation of the two hydroxyl groups made the reaction easy. The similar participations have also been published.[9]



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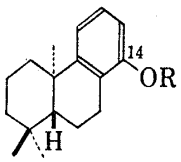
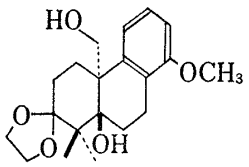


2a: R=H
2b≡**21**: R=CH_3



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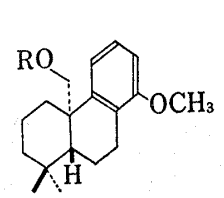
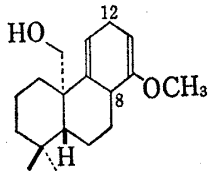
If compound **4**[10] is subjected to the Birch reduction, then the 8,12-dihydro compound **5** rather than the 9,13-dihydro derivative **6** will be easily formed. Its hydrolysis will readily

1) Part XLII: E. Fujita and M. Ochiai, *Chem. Pharm. Bull.* (Tokyo), **25**, 3013 (1977).
2) Location: *Uji, Kyoto-Fu, 611, Japan.*
3) J.D. Connolly and I.M.S. Thornton, *J.C.S. Perkin I*, **1973**, 736.
4) N. Fukazawa, M. Funamizu, Y. Kitahara, and T. Kato, *Chemistry Letters*, **1976**, 1253.
5) R.B. Turner, K.H. Gänshirt, P.E. Shaw, and J.D. Tauber, *J. Am. Chem. Soc.*, **88**, 1776 (1966).
6) K. Mori and M. Matsui, *Tetrahedron*, **24**, 3095 (1968).
7) R.W. Guthrie, W.A. Henry, H. Immer, C.M. Wong, Z. Valenta, and K. Wiesner. *Coll. Czech. Chem. Comm.*, **31**, 602 (1966).
8) E. Fujita, M. Shibuya, S. Nakamura, Y. Okada, and T. Fujita, *J.C.S. Perkin I*, **1974**, 165.
9) *a*) W.S. Johnson, R. Pappo, and W.F. Johns, *J. Am. Chem. Soc.*, **78**, 6339 (1956); *b*) T.B. Windholz, R.D. Brown, and A.A. Patchett, *Steroid*, **6**, 409 (1965); *c*) A.J. Birch and E.G. Hutchinson, *J.C.S. Perkin I*, **1972**, 1546.
10) The following compounds are all racemates, but they are conveniently represented as one of the enantiomers. The stereochemistry is discussed on the basis of the formulas depicted.

give $\beta\gamma$-unsaturated ketone **7**. Since the 9,11-double bond in the compound can be regarded as being equivalent to the 11-hydroxyl group synthetically, the compound **7** will be an important intermediate for the synthesis of the desired compound (**1**). The planning of the synthetic route was made on the basis of the foregoing consideration, and the initial purpose was directed toward the synthesis of compound **4**.



4 ≡ **20** : R=H
19 : R=Ac



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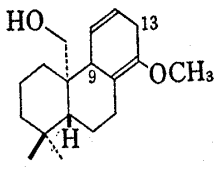

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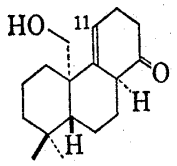
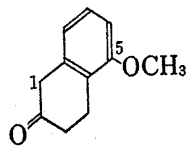


7 ≡ **22**



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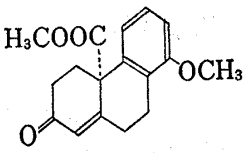

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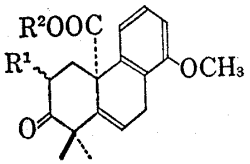
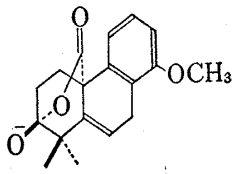


10 : $R^1=R^2=H$
11 : $R^1=R^2=CH_3$
12 : $R^1=H$, $R^2=CH_3$



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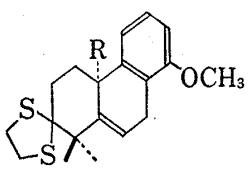
5-Methoxy-2-tetralone (**8**),[11] on methoxycarbonylation with dimethyl carbonate, alkylation with 1-N-piperidinobutan-3-one methiodide,[12] and subsequent heating with sodium methoxide in methanol, gave an $\alpha\beta$-unsaturated ketone in 57% yield. Since methoxycarbonylation[8] has been known to occur at C-1 position of **8**, the formula **9** is assignable to this unsaturated ketone. Dimethylation on the C-4 atom proceeded by the reaction with methyl iodide and potassium *t*-butoxide in the presence of a little water to give a carboxylic acid **10** in good yield. Without water, the major product was 2,4,4-trimethyl compound **11**. The reason why the methylation on the C-2 atom did not proceed in the presence of water was initially assumed to be attributed to the formation of pseudoacid type anion **13** which prevents enolization. But, enolization at C-2 proved to be possible by the deuterium exchange experiment described in the experimental section. Perhaps the steric hindrance in the α-side due to the solvated bulky carboxylate anion and that in the β-side by the ring-C would be the main reason.

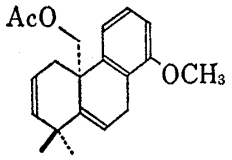
The methyl ester **12**[8] derived from carboxylic acid **10** was converted into acetate **16** *via* dithioacetalization (to **14**) and lithium aluminum hydride reduction (to **15**) in 76% overall yield. The compound **16** on desulfurization with Raney nickel gave a mixture of diene **17** and monoolefin **18**, which on catalytic hydrogenation on palladium-charcoal in acetic acid (to **19**) and treatment with lithium aluminum hydride afforded alcohol **20** in 76% overall yield (from **16**). The alcohol **20** on Jones oxidation followed by Wolff-Kishner reduction yielded the known compound **21**,[5] which established the *trans* juncture between the rings A and B in compound **20**.

The second problem is the Birch reduction of compound **20**. The use of the tertiary alcohol as the proton source seemed more effective for utilization of the intramolecular participation of the hydroxyl group, because the rate of protonation to the radical anion has

11) J.W. Cornforth and R. Robinson, *J. Chem. Soc.*, **1949**, 1855.
12) A.L. Wilds and R.G. Werth, *J. Org. Chem.*, **17**, 1149 (1952).



14 : R=$COOCH_3$
15 : R=CH_2OH
16 : R=CH_2OAc



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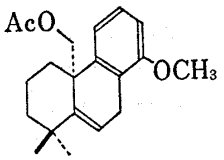

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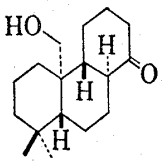

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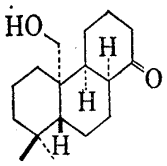

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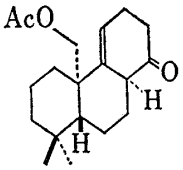

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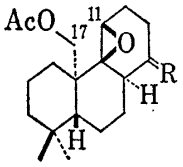
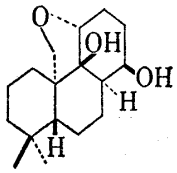


26 : R=O
27 : R=α-H, β-OH



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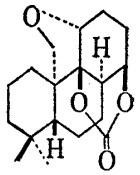
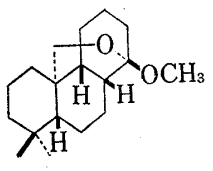


29

been known to be slower in tertiary alcohol than in primary alcohol.[13] Thus, the compound **20** was subjected to the Birch reduction, in which *t*-butanol was used as the proton source, to give the desired unsaturated ketone **22** (62%) as the major product and saturated ketones, **23** (10%) and **24** (6%), as the minor products.

The structure and stereochemistry of the major product were determined by the vinyl proton signal at δ 5.67 in the nuclear magnetic resonance (NMR) spectrum and the following reactions: the compound **22** was converted into dihydroxyether **28** *via* acetate **25**, epoxyacetate **26**, epoxyalcohol **27**, and subsequent treatment of the latter with methanolic potassium hydroxide. The intramolecular hydrogen-bondings were recognized from the infrared (IR) and NMR spectra between epoxy and hydroxyl groups in compound **27** and between two hydroxyl groups in compound **28**. The easy conversion of **27** into **28** suggested the β-configuration of the epoxy group of compounds, **26** and **27**. Thus, the 17-hydroxylate anion formed by hydrolysis of **27** attacked the 11-carbon atom from the α-side through an intramolecular S_N2-type reaction to open the epoxide ring. Furthermore, the compound **28** on treatment with phosgene gave cyclic carbonate **29**, which indicated the 1,3-diaxial stereochemistry of two hydroxyl groups and the *trans*-diaxial stereochemistry between the 9-hydroxyl group and the 8-hydrogen in compound **28**. Since epimerization at the C-8 atom can not take place during a series of reactions from **22**, the stereochemistry of the C-8 atom is established.



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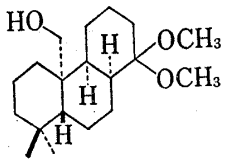

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One of the minor products on treatment with BF_3-etherate in methanol gave methylacetal **30**. Only in the case of the β-configuration of both hydrogens on the C-8 and C-9 atom, such an intramolecular acetal formation is possible. The acetal **30** on hydrolysis regenerated the original saturated ketone, which even on refluxing in methanol with sodium methoxide caused no epimerization and was recovered. Thus, the thermodynamically stable *trans*, *anti*, and *trans* formula (**23**) is assigned to this minor product.[5,14] Thus, epimerization at C-8 was observed to occur in the reaction of **23** to **30**.

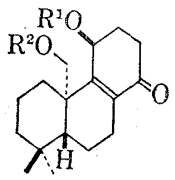
13) A.P. Krapcho and A.A. Bothner-By, *J. Am. Chem. Soc.*, **81**, 3658 (1959).
14) W.S. Johnson, *Experientia*, **1**, 315 (1951).

Another minor product on heating in methanol with sodium methoxide did not cause any epimerization but was recovered. On refluxing in methanol in the presence of *p*-toluenesulfonic acid, it gave dimethylacetal **31**. On the basis of these facts, the *trans*, *syn*, and *cis* formula (**24**) was assigned to this compound.[5,14]

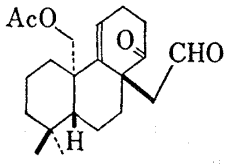
A Formal Total Synthesis

Kitahara (the late) and coworkers[4] converted *ent*-16-kaurene into the natural diterpene **1** *via* diol **45**. Hence the synthesis of **45** would constitute its formal total synthesis.

The foregoing epoxide **26** on treatment with sodium acetate in dimethylformamide (DMF) gave an unsaturated ketol **32** (72%) and diol **33** (12%). This reaction has been known to be "concerted".[15] The stereochemistry of the C-8 and C-9 positions has a suitable *trans* relation. The 11-hydroxyl group of **32** holds the stereochemistry of the epoxide in **26** *i.e.* the *β*-configuration which is suitable for the ring D construction. Transetherification with ethyl vinyl ether in the presence of mercuric acetate converted the compound **32** into vinyl ether **34**, which was subjected to the Claisen rearrangement by heating at 200° to give keto aldehyde **35** stereoselectively. Since the compound **35** was unstable, it was, without purification, heated with sodium acetate in DMF at 100° for 2 hr to afford two aldol condensation products, the minor one (25% from **34**) of which on heating with sodium acetate in hexamethylphosphoramide was transformed into the major product (38% from **34**). Thus, the major product was assignable to the more stable epimer's formula (**37**), while the minor one to the formula **36**.



32: $R^1=H$; $R^2=Ac$
33: $R^1=R^2=H$
34: $R^1=CH=CH_2$; $R^2=Ac$



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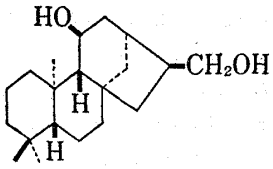

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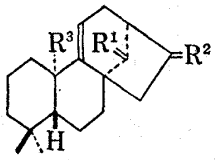


36: $R^1=O$; $R^2=\alpha$-H, β-OH; $R^3=CH_2OAc$
37: $R^1=O$; $R^2=\alpha$-OH, β-H; $R^3=CH_2OAc$
38: $R^1=O$; $R^2=\alpha$-OTHP, β-H; $R^3=CH_2OAc$
39: $R^1=O$; $R^2=\alpha$-OTHP, β-H; $R^3=CH_2OH$
40: $R^1=O$; $R^2=\alpha$-OTHP, β-H; $R^3=CHO$
41: $R^1=H_2$; $R^2=\alpha$-OTHP, β-H; $R^3=CH_3$
42: $R^1=H_2$; $R^2=\alpha$-OH, β-H; $R^3=CH_3$
43: $R^1=H_2$; $R^2=O$; $R^3=CH_3$
44: $R^1=H_2$; $R^2=CH_2$; $R^3=CH_3$

Compound **37** on tetrahydropyranylation and alkaline hydrolysis gave alcohol **39** *via* **38**. Collins oxidation of **39** to aldehyde **40** and subsequent Huang-Minlon reduction[16] of the latter under the conditions used by Barton, *et al.*[17] afforded *rac*-unsaturated alcohol tetrahydropyranylether **41** in 38% overall yield from **37**. Tetrahydropyranylether on hydrolysis gave alcohol **42**, whose Jones oxidation afforded ketone **43**. The Witting reaction with the latter gave diene **44** in 65% overall yield from **41**. The final hydroboration converted this diene (**44**) into *rac*-kaurane-11α,17-diol (**45**) although in a low yield. This compound was shown to be identical with the authentic sample prepared from its 11-benzoate[4] provided by Kitahara by treatment with lithium aluminum hydride. Thus a formal total synthesis of **1** was accomplished.

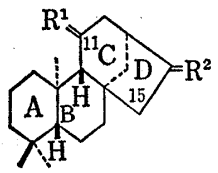
15) D.H.R. Barton and Y. Houminer, *J.C.S. Perkin I*, **1972**, 919.
16) Huang-Minlon, *J. Am. Chem. Soc.*, **71**, 3301 (1949).
17) D.H.R. Barton, D.A.J. Ives, and B.R. Thomas, *J. Chem. Soc.*, **1955**, 2057.

Total Synthesis of *rac*-Kaur-16-ene-11α,15α-diol (1)

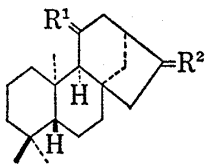
Alcohol **42** on hydroboration[18] gave two diols, **46** and **47**, in a ratio of about 3:4. Their Jones oxidation gave diketones, **48** and **49**, respectively. The latter (**49**) on refluxing in methanolic potassium hydroxide for half an hour gave the former, that is, the thermodynamically more stable epimer (**48**). Hence, diol **46** must have the 11β-OH group as well as the *cis*-ring juncture between rings B and C.

Diketone **48** was shown to be not identical with the dioxo-product obtained from calliterpenone[19] by Jones oxidation. Hence the formula postulated for calliterpenone by Chatterjee, *et al.*[19a] in 1972 was indicated to be incorrect.[20]

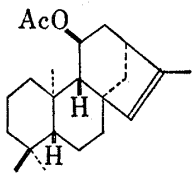
In the following synthesis, it was necessary to distinguish two hydroxyl groups in the compound **46**. Its diacetate **50** on partial hydrolysis by 1.5 equivalents of potassium carbonate gave 16-ol **51**, whose Jones oxidation into ketone (**52**) followed by Wittig reaction gave exocyclic methylene compound **53** in 48% overall yield from **46**.



46: R^1=α-H, β-OH; R^2=α-OH, β-H
48: $R^1=R^2$=O
50: R^1=α-H, β-OAc; R^2=α-OAc, β-H
51: R^1=α-H, β-OAc; R^2=α-OH, β-H
52: R^1=α-H, β-OAc; R^2=O
53: R^1=α-H, β-OAc; $R^2=CH_2$



47: $R^1=R^2$=α-OH, β-H
49: $R^1=R^2$=O



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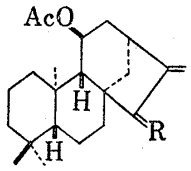

55: R=α-OOH, β-H
56: R=O

On heating with iodine in benzene, the compound **53** was converted into endocyclic ene compound **54** in 86% yield. Compared to the similar reaction with *ent*-16-kaurene,[21] this isomerization proceeded more easily, which was probably due to an unfavored nonbonded interaction between the 11β-acetoxyl group and 15β-hydrogen in compound **53**. The photosensitized oxygenation with compound **54** using hematoporphyrin in pyridine was carried out, and the reaction mixture was allowed to stand for 5 days after addition of acetic anhydride[22] to afford the αβ-unsaturated ketone **56** in 88% yield *via* dehydration of the initially formed hydroperoxide (**55**). The ketoacetate **56** on treatment with lithium aluminum hydride yielded the desired compound, *rac*-kaur-16-ene-11α,15α-diol (**1**), as the crystals of mp 159—160°. The identity with the authentic sample was proved by the coincidence of their IR (in chloroform) and mass spectra and also their same behavior on thin-layer chromatography (TLC).

Experimental

Melting points were taken on a micro hot-stage and are uncorrected. IR spectra were taken with a Hitachi model EPI-S2 spectrometer and NMR spectra with a Varian T-60 spectrometer using tetramethyl-

18) F. Piozzi, S. Passannanti, M.L. Marino, and V. Spiro, *Can. J. Chem.*, **50**, 109 (1972).
19) *a*) A. Chatterjee, S.K. Desmukh, and S. Chandrasekharan, *Tetrahedron*, **28**, 4319 (1972); *b*) S.A. Ahmad and A. Zaman, *Tetrahedron Lett.*, **1973**, 2179; *c*) E. Fujita, M. Ochiai, I. Uchida, A. Chatterjee, and S.K. Desmukh, *Phytochemistry*, **14**, 2249 (1975).
20) For the correct structure, see references 18*b* and 18*c*.
21) *a*) M.F. Barnes and J. MacMillan, *J. Chem. Soc.* (*C*), **1967**, 361; *b*) A. Yoshikoshi, M. Kitadani, and Y. Kitahara, *Tetrahedron*, **23**, 1175 (1967).
22) D.N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanism," Elsevier Publishing Co., London, 1968, p. 435.

silane as internal standard. Mass spectra were determined on a JEOL model JMS-OISG double-focusing mass spectrometer. Unless otherwise stated, Mallinckrodt silicic acid and Kieselgel 0.05—0.2 mm(Merck) were used for column chromatography. TLC plates were coated with silica gel G nach Stahl (Merck). Extracts were dried over anhydrous Na_2SO_4.

$\alpha\beta$-Unsaturated Ketone 9——To a mixture of ether (1.1 ml) and sodium hydride (50% in oil; 330 mg) was added a solution of dimethyl carbonate (660 mg) in benzene (2.2 ml). Then a solution of 5-methoxy-2-tetralone (1 g) in benzene (5.5 ml) was added dropwise. After refluxing for 3 hr, the mixture containing the insoluble sodium salt was cooled in an ice-bath, and methanol (1 ml) was added. 1-N-piperidinobutan-3-one methiodide (3.5 g) in methanol (10 ml) was then added dropwise. The solution was stirred for 4 hr, and refluxed for further 2 hr. After cooling, ice-water and 5% hydrochloric acid were added to weak acidity, and the mixture was extracted with ethyl acetate. Usual work-up gave a crude substance (1.9 g), which was dissolved in methanol (35 ml). The solution was refluxed with sodium methoxide (445 mg) for 40 min. After cooling and addition of acetic acid, the mixture was extracted with ethyl acetate. Usual work-up gave a crude crystalline product, which was recrystallized from methanol to give the α,β-unsaturated ketone **9** (897 mg, 57% yield), mp 153—155°. IR ν_{max}^{KBr} cm^{-1}: 1720, 1665, 1625, 784, and 735. NMR ($CDCl_3$) δ: 3.70, 3.87 (each 3H, s), and 6.07 (1H, s, 1-H). MS *m/e*: 286 (M^+). *Anal.* Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.19; H, 6.53.

4,4-Dimethylation of Unsaturated Ketone (9)——a) Absence of Water: To a solution of potassium (468 mg, 12 mmol) in dry *t*-butyl alcohol (14 ml) was added a solution of unsaturated ketone **9** (572 mg, 2 mmol) in dry *t*-butyl alcohol (2 ml) under nitrogen at room temperature. After stirring for 1.5 hr at room temperature, methyl iodide (1.48 ml, 24 mmol) was added all at once, and stirring was continued for 2 hr. After neutralization by acetic acid, the mixture was extracted with ethyl acetate to give an oily product. Chromatography separated three products besides the material (**9**) (25 mg). The product of largest *Rf* value, methyl *rac*-14-methoxy-2,4,4-trimethylpodocarpa-5,8,11,13-tetraen-3-on-17-oate (**11**), was obtained as prisms (223 mg, 34% yield), mp 153—154° (from chloroform–methanol). IR ν_{max}^{KBr} cm^{-1}: 1723, 1708, 1671, and 786. NMR ($CDCl_3$) δ: 1.08 (3H, d, J=6 Hz, 2-CH_3), 1.25, 1.33 (each 3H, s), 3.57, 3.80 (each 3H, s, -OCH_3), and 6.08 (1H, t, J=4 Hz, 6-H). *Anal.* Calcd. for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37; M, 328.167. Found: C, 73.28; H, 7.43; M^+, 328.167. The product of middle *Rf* value, methyl *rac*-14-methoxy-4,4-dimethylpodocarpa-5,8,11,13-tetraen-3-on-17-oate (**12**), was obtained as plates (143 mg, 23% yield), mp 103—104° (from methanol), identical with the authentic sample of **12**. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715, 1667, and 1260. MS *m/e*: 314 (M^+). *Anal.* Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.97; H, 7.21. The product of smallest *Rf* value, *rac*-14-methoxy-4,4-dimethylpodocarpa-5,8,11,13-tetraen-3-on-17-oic acid (**10**), was obtained as plates (30 mg, 5% yield), mp 228—229° (dec.) (from methanol). IR ν_{max}^{KBr} cm^{-1}: 3210, 3000—2500, 1720, and 1688. NMR (C_5D_5N) δ: 1.45, 1.63 (each 3H, s), 3.70 (3H, s, -OCH_3), 6.18 (1H, t, J=4 Hz, 6-H), 9.02 (1H, -COOH, disappeared with D_2O). *Anal.* Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71; M, 300.136. Found: C, 72.27; H, 6.80; M^+, 300.140.

b) Presence of Water: To a solution of potassium (234 mg, 6 mmol) in *t*-butyl alcohol (7 ml) and water (0.05 ml) was added a solution of unsaturated ketone **9** (286 mg, 1 mmol) in *t*-butyl alcohol (1 ml) in a nitrogen atomosphere at room temperature. After stirring for 10 min at room temperature, methyl iodide (0.74 ml, 12 mmol) was added at once, and the mixture was stirred for 2 hr. The same treatment as in a) gave a crude product, which was crystallized from methanol to give the carboxylic acid **10** (238 mg, 79% yield).

Deuterization of Carboxylic Acid (10)——To a solution of K (117 mg) in a mixture of *t*-BuOD (3.5 ml) and D_2O (0.025 ml) in a nitrogen atomosphere at room temperature was added the unsaturated ketone (**10**) (143 mg), and the mixture was stirred for 2 hr. When the D_2O (2 ml) was added and the mixture was acidified with 5% HCl, a white crystalline precipitate separated. The precipitate was collected by filtration, washed with water, and recrystallized from methanol to give plates (110 mg), mp 224—225°. IR ν_{max}^{KBr} cm^{-1}: 3250, 3100—2700, 2420, 2280, 1720, and 1690. NMR (C_5D_5N) δ: 1.43, 1.55 (each 3H, s), 2.10, and 3.17 (each 1H, AB type, J=13 Hz, 1-H_2). The signals of δ 2.4—3.0 observed in the NMR spectrum of **10** disappeared in that of the deuterized compound, and the signals of protons on the C-1 atom appeared as an AB type. Therefore it is obvious that two protons on the C-2 atom were exchanged by deuterium.

Methylation of Carboxylic Acid 10 with Diazomethane——To a solution of **10** (1 g) in a small amount of benzene was added a solution of excess diazomethane in ether. Evaporation left the foregoing ester **12** (994 mg, 95% yield) as plates (from methanol).

Thioacetalization of Compound 12——To an ice-cooled solution of **12** (1 g) in chloroform (30 ml) dried over phosphorus pentoxide was added ethanedithiol (3 ml) and then boron trifluoride etherate (2 ml). After stirring for 10 min, the mixture was poured into aq. sodium carbonate and extracted with methylene chloride. The usual treatment of the extract gave a crystalline residue. Recrystallization of this substance (1.217 g) from chloroform–methanol yielded ethylenethioacetal **14** as plates, mp 161—162°. IR ν_{max}^{KBr} cm^{-1}: 1723 and 1664. NMR ($CDCl_3$) δ: 1.20, 1.50, 3.52, 3.83 (each 3H, s), and 6.12 (1H, t, J=4 Hz, 6-H). MS *m/e*: 390 (M^+). *Anal.* Calcd. for $C_{21}H_{26}O_3S_2$: C, 64.60; H, 6.71. Found: C, 64.18; H, 6.88.

Lithium Aluminum Hydride Reduction of Ester 14——To a solution of **14** (200 mg) in ether (8 ml) was added lithium aluminum hydride (100 mg) and the mixture was refluxed for 1 hr. After cooling, the mixture

was added to a large quantity of cold ethyl acetate. After usual work-up, evaporation left a crystalline residue, which gave the alcohol **15** (157 mg, 85% yield) as plates, mp 163—165° (from chloroform–methanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1582, and 1468. NMR ($CDCl_3$) δ: 1.45, 1.57 (each 3H, s), 3.83 (3H, s, $-OCH_3$), 6.28 (1H, dd, $J=3$ and 6 Hz, 6-H). MS *m/e*: 362 (M^+). *Anal.* Calcd. for $C_{20}H_{26}O_2S_2$: C, 66.28; H, 7.23. Found: C, 65.97; H, 7.44.

Acetylation of the Alcohol 15——Acetylation of **15** (100 mg) with acetic anhydride (1 ml) in pyridine (2 ml) was carried out as usual to give the acetate **16** (103 mg, 92% yield) as plates, mp 130—130.5° (from chloroform–methanol). IR ν_{max}^{KBr} cm^{-1}: 1725, 1583, and 1468. NMR ($CDCl_3$) δ: 1.40, 1.55 (each 3H, s), 1.85 (3H, s, –OAc), 3.82 (3H, s, $-OCH_3$), 4.15, 4.32 (each 1H, AB type, $J=11$ Hz, 17-H_2), and 6.42 (1H, dd, $J=3$, and 6 Hz, 6-H). MS *m/e*: 404 (M^+). *Anal.* Calcd. for $C_{22}H_{28}O_3S_2$: C, 65.33; H, 6.98. Found: C, 65.31; H, 7.14.

Desulfurization of the Dithioacetal 16 with Raney Ni——To a solution of **16** (1.74 g) in ethanol (85 ml) was added excess Raney Ni (W-2), and the mixture was refluxed for 3 hr. Filtration from the catalyst and evaporation of ethanol gave a crude oil, which was chromatographed to give a mixture of two components, **17** and **18** (1.4 g). MS *m/e*: 314 [M^+ for monoolefin (**17**)] and 312 [M^+ for diene (**16**)].

Catalytic Hydrogenation of the Mixture of 17 and 18——The mixture of **17** and **18** (100 mg), dissolved in acetic acid (10 ml), was hydrogenated over 5% palladium-charcoal (60 mg) at 80° for 6 hr to give a crude product, which was chromatographed to yield the acetate **19** (78 mg) as prisms, mp 62—63° (from methanol). IR ν_{max}^{KBr} cm^{-1}: 1740, 775, and 718. NMR ($CDCl_3$) δ: 0.97 (6H, s), 1.90 (3H, s, –OAc), 3.80 (3H, s, $-OCH_3$), 4.20, and 4.50 (each 1H, AB type, $J=11$ Hz, 17-H_2). *Anal.* Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92; M, 316.204. Found: C, 75.70; H, 9.06; M^+, 316.199.

Lithium Aluminum Hydride Reduction of the Acetate 19——To a solution of **19** (100 mg) in ether (2 ml) was added lithium aluminum hydride (50 mg) and the mixture was refluxed for 1 hr. Usual treatment of the mixture gave a crystalline residue, which gave the alcohol **20** (86 mg, 99% yield) as prisms, mp 105—106° (from methanol). IR ν_{max}^{KBr} cm^{-1}: 3400, 774, and 715. NMR ($CDCl_3$) δ: 0.93 (6H, s), 3.82 (3H, s, $-OCH_3$), 3.68, and 3.92 (each 1H, AB type, $J=11$ Hz, 17-H_2). MS *m/e*: 274 (M^+). *Anal.* Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.94; H, 9.48.

Jones Oxidation of the Alcohol 20——To an ice-cooled solution of **20** (209 mg) in acetone (40 ml) was added excess Jones reagent. Usual work up gave an oily residue, which was purified by chromatography to yield an aldehyde, *rac*-14-methoxy-podocarpa-8,11,13-trien-17-al (178 mg) as needles, mp 132—134° (from chloroform–methanol). IR ν_{max}^{KBr} cm^{-1}: 2750, 1700, 785, and 723. NMR ($CDCl_3$) δ: 0.83, 1.00 (each 3H, s), 3.80 (3H, s, $-OCH_3$), and 9.97 (1H, d, $J=1$ Hz, 17-H). MS *m/e*: 272 (M^+). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.27; H, 8.98.

Wolff-Kishner Reduction of the Aldehyde using Nagata's Modification[23]——A mixture of the foregoing aldehyde (60 mg), 98% hydrazine hydrate (3 ml), hydrazine dihydrochloride (760 mg) and triethylene glycol (4 ml) was heated at 140° for 10 hr. After adding potassium hydroxide pellets (4 g), the temperature was gradually raised to 210° by distilling the low boiling material out and the solution was heated at this temperature for 2.5 hr. After cooling, water was added, and the mixture was extracted with ether. After washing with water and drying, evaporation of ether left a residue, which was chromatographed to yield compound **21** (25 mg) as plates, mp 118—119° (from ethanol) (lit.,[3] 114—115°). NMR ($CDCl_3$) δ: 0.95 (6H, s), 1.20 (3H, s), and 3.80 (3H, s, $-OCH_3$). *Anal.* Calcd. for $C_{18}H_{26}O$: 258.198 (M). Found: 258.197 (M^+).

Birch Reduction followed by Acid Hydrolysis of Compound 20——To the liquid ammonia (1.5 l) was added lithium (11.3 g). After stirring for 10 min, a solution of **20** (8.4 g) in dry tetrahydrofuran (40 ml) and successively dry *t*-butanol (200 ml) were added at *ca.* −70°. After stirring for 6 hr, the excess metal was destroyed with ammonium chloride, and ammonia was evaporated off to leave a residue, which was extracted with ether. Usual treatment of the ether layer gave a crude mixture. To the acetone solution (420 ml) of this substance was added a solution of oxalic acid dihydrate (7 g) in water (60 ml), and the mixture was stirred for 12 hr. After neutralization with sodium carbonate, acetone was evaporated off *in vacuo* to leave a residue, which was extracted with ethyl acetate and treated as usual to yield a crystalline mass. Recrystallization from *n*-hexane yielded a β,γ-unsaturated ketone **22** (4 g) as prisms, mp 128—130°. IR ν_{max}^{KBr} cm^{-1}: 3500, 1695, 1650, and 735. NMR ($CDCl_3$) δ: 0.82, 0.88 (each 3H, s), 3.78 (2H, s, 17-H_2), and 5.67 (1H, m, 11-H). MS *m/e*: 262 (M^+) and 231 (M^+-CH_2OH). *Anal.* Calcd. for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.75; H, 10.20. Chromatography of the mother liquor separated two products besides **22** (1 g, total 62% yield). The product of larger *Rf* value, the ketone **23**, was obtained as prisms (791 mg, 10% yield), mp 111—112° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 3450 and 1687. NMR ($CDCl_3$) δ: 0.88 (6H, s) and 3.97 (2H, s, 17-H_2). MS *m/e*: 264 (M^+). *Anal.* Calcd. for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.14; H, 10.51. The product of smaller *Rf* value, the ketone **24**, was obtained as needles (450 mg, 6% yield), mp 132—132.5° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 3450 and 1690. NMR ($CDCl_3$) δ: 0.78, 0.88 (each 3H, s), 3.78, and 3.92 (each 1H, AB type, $J=11$ Hz, 17-H_2). MS *m/e*: 264 (M^+). *Anal.* Calcd. for $C_{17}H_{28}O_2$: C,

23) W. Nagata and H. Itazaki, *Chem. Ind*, (London), **1964**, 1194.

77.22; H, 10.67. Found: C, 76.97; H, 10.83.

Acetylation of the Unsaturated Ketone (22)——Acetylation of **22** (100 mg) was carried out as usual to give the acetate **25** (95 mg, 82% yield) as plates, mp 94—95° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 1735, 1715, and 1235. NMR ($CDCl_3$) δ: 0.88 (6H, s), 1.98 (3H, s, -OAC), 4.38 (2H, s, 17-H_2), and 5.57 (1H, m, 11-H). MS *m/e*: 304 (M^+). *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.08; H, 9.13.

Epoxidation of the Acetate 25——Into a solution of acetate **25** (100 mg) in chloroform (1 ml) was added *m*-chloroperbenzoic acid (42 mg). The mixture was stirred for 1 hr, and then water was added. Extraction with methylene chloride, washing with sodium carbonate and water, and then evaporation of the solvent left an oil, which was purified by chromatography to give the epoxide **26** (65 mg, 62% yield) as needles, mp 108—109° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 1730, 1700, and 1250. NMR ($CDCl_3$) δ: 0.82, 0.92 (each 3H, s), 2.08 (3H, s, -OAc), 3.43 br (1H, s, 11-H), 4.33, and 4.55 (each 1H, AB type, J=12 Hz, 17-H_2). MS *m/e*: 320 (M^+). *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.15; H, 8.81.

Conversion of 26 into the Cyclic Carbonate 29——To an ice-cooled solution of **26** (20 mg) in methanol (2 ml) was added sodium borohydride (15 mg) and the mixture was stirred for 20 min. The excess sodium borohydride was destroyed with acetone and the solvent was evaporated off *in vacuo* to leave a residue, which was extracted with methylene chloride. Usual treatment of the extract gave the alcohol **27** (15 mg, 75% yield). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 and 1730. NMR ($CDCl_3$) δ: 0.82, 0.93 (each 3H, s), 2.07 (3H, s, -OAc), 3.33 (1H, d, J=4 Hz), 3.65 br (1H, s), and 4.43 (2H, s, 17-H_2). To a solution of potassium hydroxide (100 mg) in ethanol (2 ml) was added the acetate **27** (14 mg), and the mixture was refluxed for 1 hr. After neutralization with 10% hydrochloric acid, ethanol was evaporated off *in vacuo* to leave a residue, which was extracted with ethyl acetate and treated as usual to yield the dihydroxyether **28** (8 mg, 61%). NMR (C_6D_6) δ: 0.55, 0.80 (each 3H, s), 3.57 (1H, m), 3.85 (2H, s, 17-H_2), and 4.08 (1H, m). MS *m/e*: 280 (M^+) and 262 (M^+-H_2O). *Anal.* Calcd. for $C_{17}H_{28}O_3$: 280.204 (M). Found: 280.201 (M^+). The diol **28** (8 mg) was dissolved in chloroform (1 ml) and pyridine (1 ml), to which phosgene in toluene (1 ml) was added. The mixture was stirred for 1 hr with ice-cooling, then was left overnight. It was added to ice-water and extracted with chloroform. The usual work-up gave a crystalline mass, which was chromatographed to yield the cyclic carbonate **29** (5 mg) as plates, mp 185—185.5° (from petroleum ether). IR ν_{max}^{KBr} cm^{-1}: 1740. NMR ($CDCl_3$) δ: 0.67, 0.90 (each 3H, s), 3.93 (2H, s, 17-H_2), 4.20 (1H, m), and 4.48 br (1H, s). MS *m/e*: 306 (M^+), 291 (M^+-CH_3), and 262 (M^+-CO_2). *Anal.* Calcd. for $C_{18}H_{26}O_4$: 306.183 (M). Found: 306.184 (M^+).

Acetalization of the Ketone 23——To a solution of **23** (259 mg) in dry methanol (20 ml) was added boron trifluoride etherate (15 ml). After stirring for 20 hr, the mixture was poured into aqueous sodium carbonate and extracted with methylene chloride. The usual treatment of the extract left a residue, which was chromatographed to yield mono-methyl acetal **30** (123 mg, 45% yield) as prisms, mp 80—81° (from acetonitrile). IR ν_{max}^{KBr} cm^{-1}: 1064. NMR ($CDCl_3$) δ: 0.88, 0.97 (each 3H, s), 3.33 (3H, s, -OCH_3), 3.91, and 4.35 [each 1H, AB type, J=12 Hz, 17-H_2; upper field signal showed a long-range coupling (J=2 Hz)]. *Anal.* Calcd. for $C_{18}H_{30}O_2$: C, 77.65; H, 10.80; M, 278.227. Found: C, 77.36; H, 10.60; M^+, 278.225.

Hydrolysis of the Acetal 30——To a solution of **30** (20 mg) in acetone (2 ml) was added 35% hydrochloric acid (0.03 ml) and water (0.1 ml), and the mixture was stirred overnight. Neutralization, extraction with ethyl acetate, usual treatment of the extract, and purification of the crude product by chromatography yielded ketone **23** (15 mg, 79% yield), identical (IR and NMR) with the authentic sample.

Acetalization of the Ketone 24——To a solution of **24** (70 mg) in methanol (2 ml) was added toluene-*p*-sulfonic acid (4 mg), and the mixture was heated at reflux for 3 hr. After cooling, it was made weakly alkaline by aqueous sodium carbonate and extracted with ethyl acetate. After washing with water and drying, evaporation of the solvent left a residue, which was chromatographed to yield dimethyl acetal **31** (70 mg) as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400. NMR ($CDCl_3$) δ: 0.75, 0.83 (each 3H, s), 3.12 (6H, s, 2-OCH_3), and 3.87 (2H, s, 17-H_2).

Treatment of the Ketone 23 with Sodium Methoxide——To a solution of **23** (50 mg) in methanol (4 ml) was added sodium methoxide (10 mg) and the mixture was refluxed for 6 hr. Concentration *in vacuo*, extraction of the residue with methylene chloride, and usual treatment of the extract gave the starting material (**23**) (43 mg).

Treatment of the Ketone 24 with Sodium Methoxide——After refluxing a mixture of sodium methoxide (10 mg) and **24** (40 mg) dissolved in methanol (4 ml) for 10 hr, the same treatment as above recovered the material (**24**) (30 mg).

Ring Cleavage of the Epoxide 26——To a solution of epoxide **26** (50 mg) in dimethylformamide (2 ml) was added anhydrous sodium acetate (25 mg). The mixture was heated at 100° (oil bath temperature) for 25 min with stirring. After cooling, the mixture was poured into ice-water, and extracted with ether. Usual treatment of the organic layer gave a crystalline mass, which was chromatographed to separate two products. The product of larger *Rf* value, acetate **32**, was obtained as plates (36 mg, 72% yield), mp 111—112° (from *n*-hexane–methylene chloride). IR ν_{max}^{KBr} cm^{-1}: 3450, 1725, 1665, and 1625. NMR ($CDCl_3$) δ: 0.90, 0.93 (each 3H, s), 2.03 (3H, s, -OAc), 4.13, 4.60 (each 1H, AB type, J=12 Hz, 17-H_2), and 4.67 (1H, m, 11-H). MS *m/e*: 320 (M^+). *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.52; H, 9.05. The product of smaller *Rf* value, diol **33**, was obtained as needles (5 mg, 12% yield), mp 202—203° (from ethyl acetate). IR ν_{max}^{KBr} cm^{-1}: 3400, 1665, and 1650. NMR ($CDCl_3$) δ: 0.87, 0.92 (each 3H, s), 3.84, 4.03 (each 1H, AB type,

J=11 Hz, 17-H_2), and 4.75 (1H, m, 11-H). MS m/e: 278 (M^+). *Anal.* Calcd. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.21; H, 9.58.

The Vinyl Ether 34——To a solution of allylic alcohol (**32**) (100 mg) in ethyl vinyl ether (10 ml) was added mercuric acetate (100 mg), and the mixture was stirred for 4 days. After addition of an equal volume of ethyl vinyl ether, the mixture was washed with 10% potassium carbonate, and dried over anhydrous potassium carbonate. After removal of the solvent, the residue was chromatographed on alumina [W 200 basic (Woelm), grade II]. Elution with methylene chloride gave crystalline vinyl ether **34** (97 mg, 90% yield) as plates, mp 103—106° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 1745, 1665, 1630, 1240, and 830. NMR ($CDCl_3$) δ: 0.90, 0.93 (each 3H, s), 2.03 (3H, s, -OAc), 4.13, 4.61 (each 1H, AB type, J=11 Hz, 17-H_2), and 6.32 (1H, q, J=6 and 14 Hz). MS m/e: 303 ($M^+-C_2H_3O$). *Anal.* Calcd. for $C_{21}H_{30}O_4 \cdot 1/2H_2O$: C, 70.93; H, 8.82. Found: C, 71.34; H, 8.75.

Claisen Rearrangement with Compound 34 followed by Aldol Cyclization——Vinyl ether **34** (80 mg), dissolved in decalin (4 ml), was heated in an oil bath at 200° under nitrogen, and this temperature was maintained for 3 hr. Decalin was evaporated under reduced pressure to leave aldehyde **35** (79 mg) as an oil, which was a labile substance. NMR ($CDCl_3$) δ: 0.88 (6H, s), 1.91 (3H, s, -OAc), 2.67 (2H, d, J=3 Hz, 15-H_2), 4.15 (2H, s, 20-H_2), 5.78 (1H, t, J=3 Hz, 11-H), and 9.60 (1H, t, J=3 Hz, 16-H). Without purification, **35** was dissolved in dimethylformamide (4 ml), to which anhydrous sodium acetate (80 mg) was added. The mixture was heated at 100° with stirring for 2 hr. After adding ice–water, the mixture was extracted with ether. Washing with water, drying, and evaporation left an oil, which was chromatographed to separate two products. The product of larger *Rf* value was **36** (20 mg, 25% yield), mp 113—114° (from ether). IR ν_{max}^{KBr} cm^{-1}: 3450, 1745, 1645, and 1240. NMR ($CDCl_3$) δ: 0.90 (6H, s), 1.93 (3H, s, -OAc), 4.00, 4.20 (each 1H, AB type, J=11 Hz, 20-H_2), and 5.40 (1H, t, J=3 Hz, 11-H). MS m/e: 346 (M^+), and 286 (M^+-AcOH). *Anal.* Calcd. for $C_{21}H_{30}O_4$: 346.214 (M). Found: 346.209 (M^+). The product of smaller *Rf* value, alcohol **37**, was obtained as prisms (30 mg, 38% yield), mp 131—133° (from ether). IR ν_{max}^{KBr} cm^{-1}: 3450, 1735, 1640, and 1230. NMR ($CDCl_3$) δ: 0.90 (6H, s), 1.90 (3H, s, -OAc), 3.97, 4.21 (each 1H, AB type, J=11 Hz, 20-H_2), 4.23 (1H, q, J=4, and 8 Hz, 16β-H), and 5.20 (1H, t, J=3 Hz, 11-H). MS m/e: 346 (M^+). *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80: H, 8.73. Found: C, 72.30; H, 8.86.

Epimerization of the Alcohol 36——To a solution of **36** (7 mg) in hexamethylphosphoramide (1.5 ml) was added anhydrous sodium acetate (14 mg), and the mixture was heated at 120° with stirring for 2 hr. The same treatment of the mixture as above yielded **37** (5 mg, 71% yield) together with the starting material (**36**) (1 mg).

Tetrahydropyranylation of the Alcohol 37——To a solution of **37** (60 mg) in chloroform (15 ml) (dried with phosphorus pentoxide) was added dihydropyran (200 mg), and the mixture was stirred for 1 hr. It was made alkaline by aqueous sodium carbonate and extracted with methylene chloride. The organic layer was washed with water, dried, and concentrated *in vacuo* to give an oil, which was chromatographed to yield tetrahydropyranyl ether **38** as needles (70 mg, 94% yield), mp 117—119° (from *n*-hexane–ether). IR ν_{max}^{KBr} cm^{-1}: 1745, 905, and 870. NMR ($CDCl_3$) δ: 0.90 (6H, s), 1.90 (3H, s, -OAc), and 5.23 (1H, t, J=3 Hz, 11-H). MS m/e: 430 (M^+), 370 (M^+-AcOH), 346 ($M^+-C_5H_8O$), and 286 [$M^+-(AcOH+C_5H_8O)$]. *Anal.* Calcd. for $C_{26}H_{38}O_5$: 430.272 (M). Found: 430.268 (M^+).

Hydrolysis of Acetate 38——To a solution of acetate **38** (120 mg) in methanol (1 ml) was added 1% sodium hydroxide in methanol–water (1: 1) (3 ml), and the mixture was stirred for 36 hr. After removal of methanol *in vacuo*, the residue was extracted with ethyl acetate. Washing with water, drying, and evaporation left an oil, which was chromatographed to yield the alcohol **39** (100 mg, 92% yield) as needles, mp 136—137° (from *n*-hexane). IR ν_{max}^{KBr} cm^{-1}: 3530, 1740, 1630, and 870. NMR ($CDCl_3$) δ: 0.88 (1H, s,) and 5.30 (1H, t, J=3 Hz, 11-H). MS m/e: 388 (M^+). *Anal.* Calcd. for $C_{24}H_{36}O_4$: C, 73.36; H, 9.64. Found: C, 73.56; H, 9.53.

Collins Oxidation of the Alcohol 39——To a solution of alcohol **39** (774 mg) in methylene chloride (30 ml) was added a suspension of Collins reagent (3.26 g) in methylene chloride (40 ml), and the mixture was stirred for 10 min. The reaction mixture was decanted, and the precipitate remaining in the flask was rinsed with methylene chloride. The solvent was evaporated off *in vacuo* to leave a residue, which was extracted with ether. Usual treatment of the extract gave an oil, which was chromatographed to yield the aldehyde **40** (514 mg, 67% yield) as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2725, 1745, and 1708. NMR ($CDCl_3$) δ: 0.80, 0.93 (each 3H, s), 5.42 (1H, t, J=3 Hz, 11-H), and 9.57 (1H, s, 20-H). MS m/e: 386 (M^+), 357 (M^+-CHO), 302 ($M^+-C_5H_8O$), and 273 [$M^+-(C_5H_8O+CHO)$]. *Anal.* Calcd. for $C_{24}H_{30}O_4$: 386.246 (M). Found: 386.242 (M^+).

Wolff-Kishner Reduction of the Keto Aldehyde 40——To a solution of keto aldehyde **40** (30 mg) in triethylene glycol (1.5 ml) was added hydrazine (heated at reflux over sodium hydroxide, and distilled) (410 mg), and the mixture was heated at 160° (oil bath temperature) for 6 hr under a nitrogen atmosphere. After the addition of hydrazine (200 mg), the solution of sodium (60 mg) in triethylene glycol (1.5 ml) was added, then the temperature was raised to 210° by distilling the low boiling material out and the solution was heated at this temperature for 1.5 hr. After cooling, water was added. and the mixture was extracted with ether. Usual work-up of the extract gave a crude product, chromatography of which yielded **41** (18 mg, 64.7%) as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 900 and 865. NMR ($CDCl_3$) δ: 0.82, 0.88, 1.02 (each 3H, s), and 5.05 (1H, m, 11-H). MS m/e: 358 (M^+), 343 (M^+-CH_3), and 274 ($M^+-C_5H_8O$).

Acidic Hydrolysis of Tetrahydropyranyl Ether (41)——To a solution of **41** (60 mg) in acetone (10 ml) were added 35% hydrochloric acid (0.05 ml) and water (1 ml), and the mixture was stirred overnight. After neutralization with aqueous sodium carbonate, concentration to *ca.* half volume, extraction with ethyl acetate, washing with water, drying, and evaporation left a crystalline residue. Chromatography of the residue yielded alcohol **42** as needles (40 mg, 87% yield), mp 129—129.5° (from acetonitrile). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 830. NMR ($CDCl_3$) δ: 0.82, 0.90, 1.02 (each 3H, s), and 5.00 (1H, t, J=3 Hz, 11-H). MS *m/e*: 274 (M^+). *Anal.* Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.06; H, 11.21.

Jones Oxidation of the Alcohol 42——To an ice-cooled solution of **42** (50 mg) in acetone (7 ml) was added excess Jones reagent. Usual work-up gave a crystalline mass, which was purified by chromatography to yield the ketone **43** as needles (40 mg, 81% yield), mp 89—89.5° (from methanol–water). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735. NMR ($CDCl_3$) δ: 0.82, 0.92, 1.08 (each 3H, s) and 5.20 (1H, m, 11-H). MS *m/e*: 272 (M^+). *Anal.* Calcd. for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.87; H, 10.13.

Wittig Reaction of the Ketone 43——To a suspension of methyltriphenylphosphonium iodide (325 mg) in ether (5 ml) was added a 1 M *t*-butanolic potassium *t*-butoxide solution (0.65 ml) under nitrogen, and the mixture was stirred for 30 min at room temperature. To this yellow solution was added a solution of **43** (44 mg) in benzene (1 ml), and the reaction mixture was stirred at room temperature for 3 hr. Water was added and the mixture was neutralized with 5% hydrochloric acid. Extraction with *n*-hexane, drying, and evaporation left an oil, which was chromatographed to yield the diene **44** (40 mg, 92% yield) as an oil, NMR ($CDCl_3$) δ: 0.85, 0.92, 1.07 (each 3H, s), 4.88 br, 4.77 br (each 1H, s, 17-H_2), and 5.13 (1H, t, J=3 Hz, 11-H). MS *m/e*: 270 (M^+).

Hydroboration of the Diene 44——To the ice-cooled solution of **44** (7 mg) in tetrahydrofuran (0.5 ml) was added a solution of 0.33 M borane in tetrahydrofuran (0.17 ml) under nitrogen. The mixture was stirred at room temperature for 2 days. After the hydrolysis of the reaction mixture by water (0.5 ml), 3 N sodium hydroxide (0.5 ml) was added, and then the oxidation was carried out by adding 30% hydrogen peroxide (1 ml). After cooling, the mixture was extracted with ethyl acetate. The extract was treated as usual to give a crude product, which was chromatographed to yield the diol **45** (1 mg) as crystalline solid. IR ν_{max}^{KBr} cm^{-1}: 3580 and 3400. Its TLC and NMR spectrum were identical with those of the authentic sample of **45** prepared from the 11-benzoate of diol **45**, as follows. To a solution of 11-benzoate of diol **45** (5 mg) in tetrahydrofuran (1 ml) was added lithium aluminum hydride (5 mg) and the mixture was stirred for 2 hr. Usual treatment of the mixture gave a crystalline residue, which was chromatographed to yield the diol (**45**) (2 mg), mp 140—141° (from *n*-hexane).

Hydroboration of the Alcohol 42——To the ice-cooled solution of **42** (50 mg) in tetrahydrofuran (5 ml) was added a solution of 0.25 M borane in tetrahydrofuran (5 ml) under nitrogen. The mixture was stirred at room temperature for 3 days. The crude product obtained by the same treatment as described above was chromatographed. Elution with 0.5% acetone in methylene chloride gave a crystalline mass (22 mg), the major component of which was shown to be the diol **47**. (*Vide infra*). Elution with 3% acetone in methylene chloride yielded the diol **46** (17 mg) as needles, mp 213—213.5° (from acetone). IR ν_{max}^{KBr} cm^{-1}: 3400. NMR ($CDCl_3$–CD_3OD 1: 1) δ: 0.83, 0.88, 0.93 (each 3H, s), 3.90 (1H, t, J=3.5 Hz, 11α-H), and 4.37 (1H, q, J=3 and 7.5 Hz, 16β-H). MS *m/e*: 274 (M^+–H_2O). *Anal.* Calcd. for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.82; H, 10.82.

A crystalline mass of **47** (22 mg) eluted first was dissolved in acetone (5 ml), and then Jones reagent was added to the ice-cooled solution. After stirring for 15 min, usual work-up gave a crystalline mass. Chromatography gave the diketone **49** (15 mg) as plates, mp 148—152° (from methanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 and 1700. *Anal.* Calcd. for $C_{19}H_{28}O_2$: 288.209 (M). Found: 288.206 (M^+).

Jones Oxidation of the Diol 46——To an ice-cooled solution of **46** (5 mg) in acetone (1 ml) was added Jones reagent. Usual treatment left a crystalline mass, which was purified by chromatography to yield the diketone **48** (4 mg, 81% yield) as plates, mp 146—147° (from methanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1745 and 1695. NMR ($CDCl_3$) δ: 0.87, 0.92, and 1.12 (each 3H, s). MS *m/e*: 288 (M^+). *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 78.87; H, 9.93.

Isomerization of the Diketone 49——A solution of **49** (3 mg) in 10% methanolic potassium hydroxide (1 ml) was heated at reflux for 30 min. After cooling, the mixture was neutralized with 5% hydrochloric acid, and then extracted with ethyl acetate. Usual work-up of the extract gave a crystalline mass, which was chromatographed to yield the diketone **48** (2.5 mg, 83% yield).

Acetylation of the Diol 46——Acetylation of **46** (8 mg) with acetic anhydride (0.5 ml) in pyridine (1 ml) was carried out as usual to give the diacetate **50** (9 mg, 87% yield) as needles, mp 136—137° (from methanol). IR ν_{max}^{KBr} cm^{-1}: 1735 and 1250. NMR ($CDCl_3$) δ: 0.82, 0.87, 0.96 (each 3H, s), 2.02, 2.05 (each 3H, s, –OAc), and 5.13 br (2H, m). MS *m/e*: 316 (M^+—AcOH). *Anal.* Calcd. for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64. Found: C, 73.14; H, 9.65.

Partial Hydrolysis of Diacetate 50——To a solution of diacetate **50** (9 mg) in methanol (0.9 ml) was added a mixture of potassium carbonate (1.7 mg) and water (0.1 ml), and the mixture was stirred for 2 days. After neutralization with acetic acid and concentration of the mixture, it was extracted with ethyl acetate. The crude product obtained by the usual treatment of the extract was chromatographed to yield the alcohol **51** as plates (6 mg, 75% yield), mp 179—183° (from methanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3450, 1725, and 1255.

NMR ($CDCl_3$) δ: 0.82, 0.87, 0.97 (each 3H, s), 0.02 (3H, s, –OAc), 4.28 (1H, q, J=2 and 7 Hz, 16β-H), and 5.07 (1H, t, J=3 Hz, 11α-H). MS *m/e*: 334 (M^+) and 319 (M^+-CH_3). *Anal.* Calcd. for $C_{21}H_{34}O_3$: 334.251 (M). Found: 334.247 (M^+).

Jones Oxidation of the Alcohol 51——The alcohol **51** (10 mg) was oxydized by excess Jones reagent as usual to yield the ketone **52** as prisms (8 mg, 81% yield), mp 159° (from methanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 and 1250. NMR ($CDCl_3$) δ: 0.85, 0.90, 1.07 (each 3H, s), 1.97 (3H, s, –OAc), and 5.20 (1H, t, J=3 Hz, 11α-H). MS *m/e*: 332 (M^+). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.69; H, 9.76.

Wittig Reaction of the Ketone 52——Wittig reaction of **52** (10 mg) was carried out as in the case of **43** to give the olefin **53** as needles (9 mg, 91% yield), mp 120—121° (from ethanol). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1655, 1255, and 875. NMR ($CDCl_3$) δ: 0.81, 0.87, 0.95 (each 3H, s), 1.90 (3H, s, –OAc), 4.65 br, 4.80 br (each 1H, s, 17-H_2), and 5.05 (1H, t, J=3 Hz, 11α-H). *Anal.* Calcd. for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37; M, 330.256. Found: C, 79.92; H, 10.54; M^+, 330.253.

Iodine Catalyzed Isomerization of the Olefin 53——To a solution of **53** (7 mg) in benzene (2 ml) was added iodine (2 mg), and the mixture was heated under reflux for 4 hr. After cooling and adding benzene (10 ml) the mixture was washed with aqueous sodium thiosulfate and water. Drying and evaporation of the solvent left a residue, which was chromatographed on silica gel impregnated with 10% silver nitrate. Elution with *n*-hexane–methylene chloride (8: 2) gave the material (**53**) (1 mg) and elution with *n*-hexane–methylene chloride (1: 1) yielded the olefin **54** as needles, mp 125—126° (from ethanol). IR ν_{max}^{KBr} cm^{-1}: 1730, 1250, and 955. NMR ($CDCl_3$) δ: 0.81, 0.87, 1.01 (each 3H, s), 1.70 (3H, d, J=2 Hz, 17-H_3), 1.97 (3H, s, –OAc), and 5.07 br (1H, s, 15-H). MS *m/e*: 330 (M^+) and 270 (M^+-AcOH). *Anal.* Calcd. for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.71; H, 10.23.

Conversion of Compound 54 into Compound 56——To a solution of **54** (12 mg) in pyridine (3 ml) was added haematoporphyrin (2 mg), and oxygen was passed through the solution under irradiation with fluorescent tubes (20 W×4) for 3 days. Then, acetic anhydride (2 ml) and pyridine (2 ml) was added. The mixture was left for further 3 days. After evaporation of the solvent *in vacuo*, water was added, and the mixture was extracted with ethyl acetate. Washing with water, drying, and evaporation left an oil, which was chromatographed to yield the α,β-unsaturated ketone **56** as prisms (11 mg, 88% yield), mp 142—143° (from methanol). IR ν_{max}^{KBr} cm^{-1}: 1725, 1640, and 1250. NMR ($CDCl_3$) δ: 0.82, 0.88, 1.06 (each 3H, s), 1.83 (3H, s, –OAc), 5.13 (1H, m, 11α–H), 5.22, and 5.88 (each 1H, 17-H_2). MS *m/e*: 344 (M^+), 329 (M^+-CH_3), 284 (M^+-AcOH), and 269 [$M^+-(AcOH+CH_3)$]. *Anal.* Calcd. for $C_{22}H_{32}O_3$: 344.235 (M). Found: 344.235 (M^+).

***rac*-Kaurene-11α,15α-diol (1)**——To an ice-cooled solution of **56** (5 mg) in ether (1 ml) was added lithium aluminum hydride (7 mg), and the mixture was stirred for 1 hr. The mixture was poured into a cold ethyl acetate. Evaporation, after washing with water and drying, left the diol (**1**) as needles (3 mg, 68% yield), mp 159—160° (from *n*-hexane). *Anal.* Calcd. for $C_{20}H_{32}O_2$: 304.240 (M). Found: 304.238 (M^+). Its IR and mass spectra were identical with those of the authentic sample of **1**. The behavior on TLC was also shown to be identical between the synthetic and authentic samples.

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