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Terpenoids. XXXVII.[1] Hypoiodite Reactions with 6-Hydroxy-17-norkaurane- and 7-Norgibberellane-derivatives

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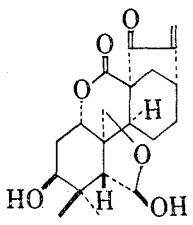
On the hypoiodite reaction, 17-norkauran-6α-ols **3**, **5**, **13**, **17**, and **22** gave **4**, **6**, **14**, **18**, and **28**, respectively. The same reactions on 7-norgibberellane derivatives, **30** and **32** afforded **31** and **33**, respectively. Finally 17-norkauran-6β-ols **36**, **38**, and **41** on the same reaction yielded **37**, a mixture of **39** and **40**, and **42**, respectively. Thus, the O-functionalization of the inactive C-19 methyl group of 17-norkauran-6-ols was achieved by means of the hypoiodite reaction with 6β-ols.

Recently, we published[3] chemical conversions of enmein (**1**) into methyl esters of gibberellin A_{15} and gibberellin A_{37} and also more direct syntheses of these esters from the important intermediate **2** in the total synthesis[4] of enmein. In these works, the selective oxidation of the inactive methyl group at C-19 in kaurene derivatives was necessary. In this paper, the details of the investigations for this requirement are described.

Up to date, several selective oxidation methods for an inactive methyl group have been developed.[5,6] We picked up the hypoiodite reaction[6] because of its simple and easy procedure. First, the reaction was tried on 17-norkaurane derivative (**3**), but oxidation occurred selectively at C-20 to give hemiacetal acetate (**4**) as a sole product in quantitative yield. Treatment of this compound with alkali gave compound (**5**), which on the hypoiodite reaction afforded 6-formate (**6**), that is, the product formed from bond cleavage between C-10 and C-20 accompanied by the formation of a double bond between C-1 and C-10. This reaction seems available for syntheses of C_{19} gibberellins. The similar C-C bond cleavage has been observed by the formation of compound (**8**) in the hypoiodite reaction of isodocarpin dihydro-derivative (**7**).[7]



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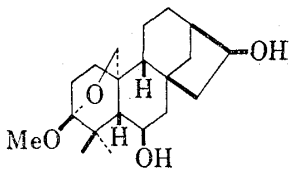

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1) Part XXXVI: E. Fujita, Y. Nagao, K. Kaneko, S. Nakazawa, and H. Kuroda, *Chem. Pharm. Bull.* (Tokyo), **24**, 2118 (1976).
2) Location: *Uji, Kyoto, 611, Japan.*
3) M. Node, H. Hori, and E. Fujita, *J. C. S. Chem. Commun.*, **1975**, 898.
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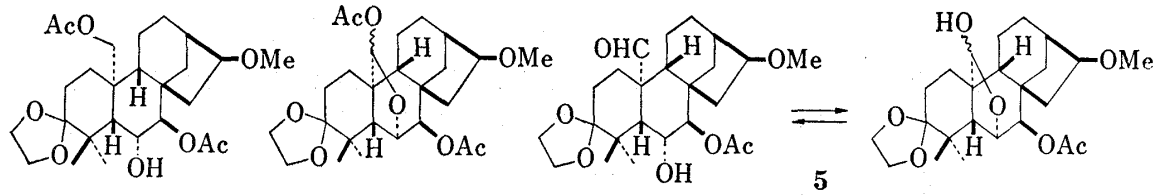
6) K. Heusler and J. Kalvoda, *Angew. Chem.*, **76**, 518 (1964); J. Kalvoda and K. Heusler, *Synthesis*, **1971**, 501.
7) E. Fujita, I. Uchida, and T. Fujita, *Chem. Pharm. Bull.* (Tokyo), **32**, 1656 (1974).



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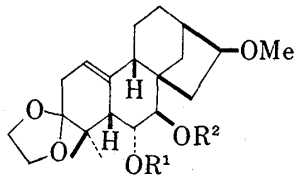
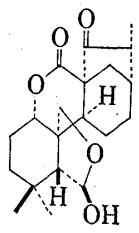
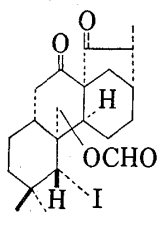
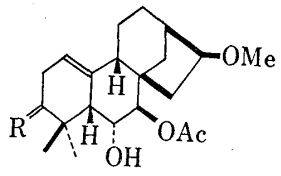






6 : R^1=CHO, R^2=Ac
9 : R^1=R^2=H
10 : R^1=H, R^2=Ac

7 8



11 : R=H, OAc
12 : R=O

Compound (**6**) was treated with lithium aluminum hydride to give diol (**9**), whose 7-acetate (**10**) on the hypoiodite reaction resulted in only the recovery of the material. The same reactions with compounds (**11** and **12**) derived from **10** were also unsuccessful; the former remained unchanged, while the latter gave unseparable mixture of many products.

As shown in the foregoing results, the hypoiodite reaction with 6α-hydroxykaurane derivatives having the chair form of the ring A did not give any C-19 oxygenated products. Previously, Somei and Okamoto[5k] also published an unsuccessful result of the Barton's reaction[5g] with the C-6 axial hydroxy group of a kaurene derivative in the hope of oxygenation at C-19.

The reason why the C-19 methyl group was inactive on the hypoiodite reactions with the foregoing 6α-hydroxykaurane derivatives is probably due to mobility of the C-19 methyl group accompanied by a change from typical chair to twisted chair conformation preferable for release of 1,3-diaxial interactions of the bond between C-4 and C-19 with that between C-10 and C-20 and with that between C-6 and oxygen atom. On the other hand, the C-20 methyl group is located in an angular position fixed in a conformationally rigid form, hence the hypoiodite reaction with compound (**3**) yields only the product (**4**) oxidized selectively at C-20.

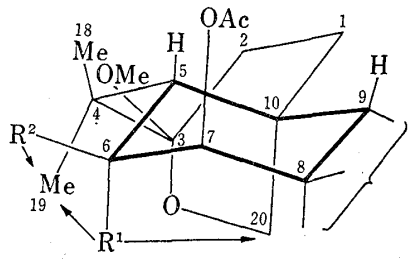
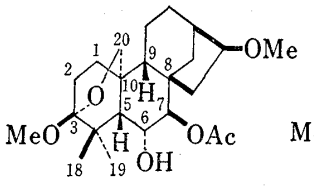


Fig. 1



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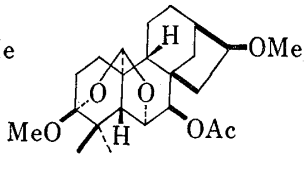

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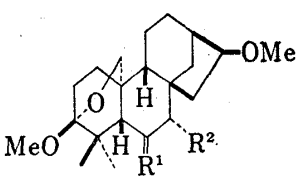
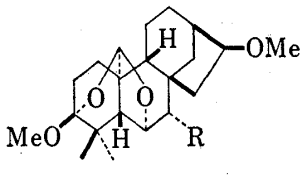
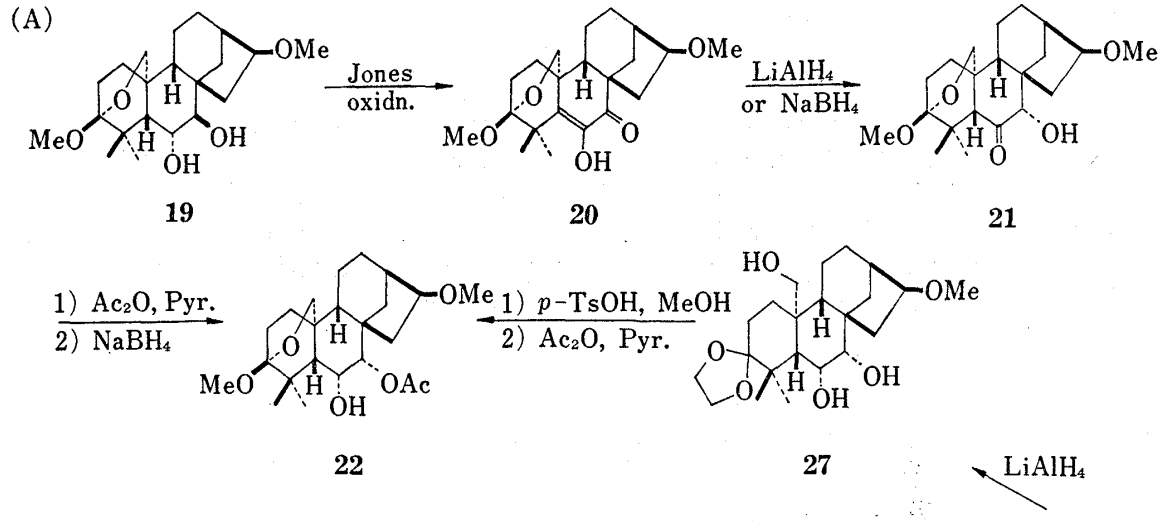
Then, the conformation of the ring A was made rigid. Thus, compound (**13**)[3] with the rigid boat form of ring A fixed by the condensation with an acetal ring has both C-19 and C-20 located in positions where are subject to the attack from the C-6α-hydroxy group, as recognized by the Dreiding model. (See Fig. 1; R^1=OH, R^2=H). The hypoiodite reaction for this compound also gave a sole product (**14**) quantitatively.



15 : $R^1=\alpha$-H, β-OH; R^2=H
16 : R^1=O; R^2=H
17 : $R^1=\alpha$-OH, β-H; R^2=H



18 : R=H
28 : R=OAc



19 **20** **21** **22** **27** **23** **24** **25** **26**

Pyr.=pyridine

Chart 1

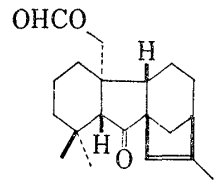
Subsequently, compound (**17**) having no substituent at C-7 was prepared by Jones oxidation of 6β-ol (**15**)[3] followed by sodium borohydride reduction of the resulting ketone (**16**), and it was subjected to the hypoiodite reaction to yield product (**18**) in high yield. Furthermore, the C-7 epimer of compound (**13**), that is, compound (**22**) was synthesized either from 6α,7β-diol (**19**)[3] *via* route A or from 6α,7β,20-triol (**23**)[3] *via* route B in Chart 1, and it was subjected to the same reaction. Also in this case, the product obtained was compound (**28**) formed by the selective attack to C-20. Thus, in this reaction, no effect was observed concerning the C-7 stereochemistry.

The foregoing results suggest that a big difference between the reactivities of the C-19 and C-20 atoms to the C-6α hydroxy group is probably due not to each distance, but to the difference of the reactivity between the primary carbon atom and the secondary carbon atom.

In relation to these kaurene derivatives, the additional findings for the hypoiodite reaction on the 7-norgibberellane derivatives are described. The reaction with 7-nor-6-on-20-ol (**30**) derived from compound (**29**)[8] gave a high yield of 3,20-ether (**31**). This procedure is probably

8) E. Fujita, T. Fujita, H. Katayama, M. Shibuya, and Y. Nagao, Symposiun Papers of 12th Symposium on the Chemistry of Natural Products (Sendai), 1968, 298.

available to functionalization at C-3 position.[9] The second hypoiodite reaction with the α-ol (**32**), that is, the reduction product of ketone (**31**), took place between C-6 and C-20 and gave compound (**33**), whose oxidation by the Jones reagent afforded ketolactone (**34**).



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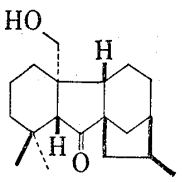

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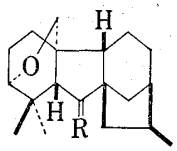
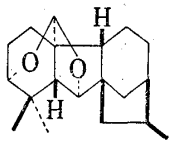


31 : R=O
32 : R=α-OH, β-H



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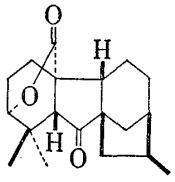
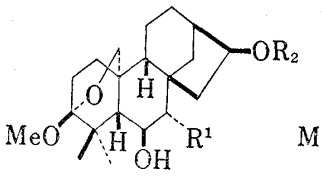
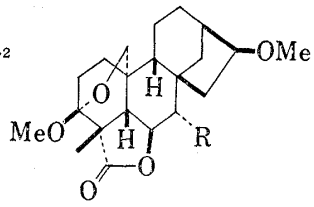


34

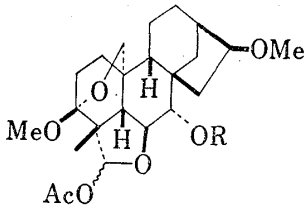
Thus, we gave up the oxidation of C-19 from 6α-hydroxy group and tried the application of 6β-hydroxy group. As observed from the Dreiding model (Fig. 1; R^1=H, R^2=OH), the 6β-hydroxy group is located in a position where it can attack only the C-19 methyl group in the compound possessing the rigid boat form of ring A. Since the hypoiodite reaction with diol (**35**)[4] gave the ring D-cleaved products,[10] the same reaction was carried out on methyl ether (**36**).[3] As the result, the desired product oxygenated at C-19, that is, lactone (**37**) was obtained in 75% yield.



35 : R^1=R^2=H (=**2**)
36 : R^1=H, R^2=Me
38 : R^1=OAc, R^2=Me
41 : R^1=OMs, R^2=Me
43 : R^1=OH, R^2=Me



37 : R=H
39 : R=OAc



40 : R=Ac
42 : R=Ms

Furthermore, the reaction with 7α-acetate (**38**) gave lactone (**39**) and hemiacetal acetate (**40**) in a ratio of *ca.* 2.4: 1. The reaction with 7α-mesylate (**41**) afforded hemiacetal acetate **42** as the major product. The observed results of the hypoiodite reactions on **36**, **38**, and **41** indicate the substituent effect at C-7. The materials (**38** and **41**) were prepared by acetylation and by mesylation of diol (**43**),[3] respectively.

In conclusion, we succeeded in the O-functionalization of C-19 methyl group by means of the hypoiodite reaction with kaurane-6β-ol derivatives which had a rigid boat form of ring A.

Experimental

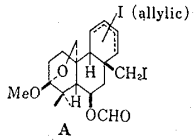
Melting points were taken on a micro hot-stage and uncorrected. Unless otherwise stated, infrared (IR) spectra were recorded in KBr discs on a Hitachi model EPI-S2 spectrometer and nuclear magnetic resonance (NMR) with Varian T-60 and A-60 spectrometer in deuteriochloroform; signals are reported in ppm from trimethyl silane (TMS) as internal standard. The mass spectra were determined on a JMS-OISG double-focusing mass spectrometer. Extracts were dried over Na_2SO_4. Mallinckrodt silicic acid or Kieselgel 0.06—0.2 mm (Merk) was used for column chromatography, and Kieselgel G nach Stahl (Merk) for thin-layer chromatography (TLC).

9) *cf.* T. Nakata and A. Tahara, *Chem. Pharm. Bull.* (Tokyo), **23**, 2323 (1975).
10) See experimental.

Table I. Experimental Data of the Hypoiodite Reactions

Material (mg)	Reaction Time (min)	Product (ratio)	Yield (%)
3(135)	40	**4**[a]	95.5
5(132)	30	**6**[b]	81
13(60)	120	**14**	98
17(15)	40	**18**	87
22(16)	30	**28**	93.7
30(250)	90	**31**	74
32(25)	90	**33**	80
35(53)	40	a mixture[c]	30
36(500)	180	**37**	75[d]
38(305)	240	**39**+**40**(2.4:1)	73.5[d]
41(7)	90	**42**[a]	32

a) a mixture of epimeric hemiacetal acetates
b) a mixture of **6** (major component) and its $\Delta^{5,10}$- and $\Delta^{9,10}$-isomers (minor components)
c) The major two isomeric products were separated, and they were assigned structure A on the basis of spectral data.
d) In the large scale of experiments, vigorous stirring was required for increasing the yield.



A

Hypoiodite Reaction——General Procedure: A suspension of lead tetraacetate (6 mol equiv.) and carcium carbonate (10 mol equiv.) in dry cyclohexane was warmed for 10 min, to which the starting material (alcohol) (1 mol equiv.) and iodine (2 mol equiv.) were added. The mixture was refluxed under irradiation by 500W tungsten lamp until the color of the solution and the starting material on TLC disappeared. After filtration the filtrate and the washing (ether) of the residue were combined and washed with aqueous sodium thiosulfate and water. Evaporation of the solvent *in vacuo* after drying left a residue, which was chromatographed (SiO_2) to separate products.

The detailed data are shown in Table I.

Physical Data of Hypoiodite Reaction Products——(i) Compound (4)[11]: Crystals (from MeOH). *Anal.* Calcd. for $C_{26}H_{38}O_8$: M, 478.256. Found: M+, 478.256. IR ν_{max} ($CHCl_3$) cm^{-1}: 1735, 1370, 1235, and 1010. NMR δ: 0.85, 1.13, 1.15† (total 6H, s), 2.07, 2.12, 2.20† (total 6H, s, 2×OAc), 3.32, 3.35† (total 3H, s, OCH_3), *ca.* 3.7 (1H, m, 16-H), 3.99 (4H, s, OCH_2CH_2O), 4.13,† 4.44, 4.74, 4.83† (total 2H, AB type, J=5.5 Hz, 6-H and 7-H), 6.40 (1H, s, 20-H). † Marks indicate signals of one of epimers.

(ii) Compound (6)[12]: Needles (from MeOH). *Anal.* Calcd. for $C_{24}H_{34}O_7$: M 434.230. Found: M+, 434.226. IR ν_{max} ($CHCl_3$) cm^{-1}: 1760 (shoulder), 1735, 1370, 1235, 1100, and 1030. NMR δ: 0.92, 1.05 (each 3H, s), 2.10 (3H, s), *ca.* 3.8 (1H, m, 16-H), 3.33 (3H, s), 3.92 (4H, A_2B_2 type, OCH_2CH_2O), 4.64 (1H, d, J=4 Hz, 7-H), 5.25 (1H, m, 6-H), 5.55 br (1H, s, 1-H), and 7.97 (1H, s, CHO).

(iii) Compound (14): Needles, mp 194—195°. *Anal.* Calcd. for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43, M 406.235. Found: C, 67.66; H, 8.35, M+ 406.233. IR ν_{max} cm^{-1}: 1727, 1367, 1240, 1158, 1110, and 1025. NMR δ: 0.97, 1.03 (each 3H, s), 2.03 (3H, s), 3.33 (6H, s), 3.74 (1H, quintet, J=5 Hz, 16-H), 4.28, 4.82 (each 1H, AB type, J=5 Hz, 6-H and 7-H), and 5.32 (1H, s, 20-H).

(iv) Compound (18): Prisms, mp 164—166°. *Anal.* Calcd. for $C_{21}H_{32}O_4$: M 348.230. Found: M+ 348.235. IR ν_{max} ($CHCl_3$) cm^{-1}: 980 and 910. NMR δ: 1.00 (6H, s), 3.25, 3.29 (each 3H, s), 3.67 (1H, quintet, J=5 Hz, 16-H), 4.27 br (1H, d, J=4 Hz, 6-H), and 5.28 (1H, s, 20-H).

(v) Compound (28): Needles, mp 215—217°. *Anal.* Calcd. for $C_{23}H_{34}O_6$: M 406.235. Found: M+ 406.233. IR ν_{max} ($CHCl_3$) cm^{-1}: 1730, 1245, and 960. NMR δ: 1.00, 1.02 (each 3H, s), 2.12 (3H, s), 3.30, 3.33 (each 3H, s), 3.73 (1H, quintet, J=5 Hz, 16-H), 4.14 (1H, s, 6-H), 4.73 (1H, s, 7-H), and 5.33 (1H, s, 20-H).

(vi) Compound (31): Prisms (from MeOH), mp 105—107°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: M 288.209. Found: M+ 288.208. IR ν_{max} cm^{-1}: 1725 and 1040. NMR δ: 0.94 (3H, d, J=7 Hz), 0.78, 1.21 (each 3H, s), 3.37, 3.73 (each 1H, AB type, J=9.5 Hz, 20-H_2. Higher field signal becomes broad signal because of a long range coupling with 1β-H), and 4.38 br (1H, t, J=*ca.* 5.5 Hz, 3-H).

(vii) Compound (33): Needles (from MeOH), mp 126—129°. *Anal.* Calcd. for $C_{19}H_{28}O_2$: M 288.209. Found: M+ 288.208. IR ν_{max} cm^{-1}: 930. NMR δ: 0.90, 0.98 (each 3H, s), 1.04 (3H, d, J=6 Hz), 3.94 (1H, d, J=3 Hz, 6-H), 4.10 (1H, dd, J=5 and 3 Hz, 3-H), and 5.22 (1H, s, 20-H).

11) See Table I footnote *a*).
12) See Table I footnote *b*).

(viii) Compound (A)[13]: 1) Substance having smaller *Rf* value on TLC: Crystalline, *Anal.* Calcd. for $C_{20}H_{28}O_4I_2$: M 586.008. Found: M^+ 586.005. IR ν_{max} ($CHCl_3$) cm^{-1}: 1723 and 1180. NMR δ: 1.00, 1.12 (each 3H, s), 3.27 (3H, s), 3.58 (2H, s, 15-H_2), 3.75, 4.05 (each 1H, AB type, J=9.5 Hz, 20-H_2), *ca.* 4.40 (1H, m, CH-I), 5.0—5.6 (2H, m, CH=CH), and 8.07 (1H, s, OCHO). 2) Substance having larger *Rf* value on TLC: NMR δ: 1.05, 1.13 (each 3H, s), 3.29 (3H, s), 3.6—4.5 (*ca.* 3H, CH-I and 20-H_2), 5.0—5.5 (2H, m, CH=CH), 8.08 (1H, s, OCHO).

(ix) Compound (**37**): Needles (from MeOH), mp 220—221°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34. Found: C, 69.49; H, 8.49. IR ν_{max} cm^{-1}: 1765, 1105, and 1040. ν_{max} ($CHCl_3$) cm^{-1}: 1772 and 1040. NMR δ: 1.30 (3H, s), 3.33, 3.38 (each 3H, s), 3.91 4.58 [each 1H, AB type, J=10 Hz, 20-H_2. Lower field signal showed a long range coupling (J=3 Hz)], *ca.* 3.80 (1H, m, 16-H), and 4.37 (1H, sextet, J=5, 10, and 10 Hz, 6-H).

(x) Compound (**39** and **40**): **39**, Needles (from MeOH), mp 219—221°. *Anal.* Calcd. for $C_{23}H_{32}O_7$: M 420.215. Found: M^+ 420.218. IR ν_{max} cm^{-1}: 1780, 1735, and 1028. NMR δ: 1.33 (3H, s), 2.13 (3H, s) 3.33, 3.38 (each 3H, s), *ca.* 3.80 (1H, m, 16-H), 3.90, 4.58 [each 1H, AB type, J=10 Hz, 20-H_2. Lower field signal showed a long range coupling (J=3 Hz).], 4.33 (1H, t, J=10.5 Hz, 6-H), and 5.18 (1H, d, J=10.5 Hz, 7-H). **40** (contaminated with some **39**): 1.03 (3H, s), 2.13 (6H, s), 3.24, 3.33 (each 3H, s), 3.6—4.0 (3H, 6-H, 20-H, and 16-H), *ca.* 4.5 (1H, 20-H), 5.10 (1H, d, J=10.5 Hz, 7-H), and 6.25 (1H, s, 19-H).

(xi) Compound (**42**)[11]: Oily, NMR δ: 1.28 (1.05)† (s, 18-H_3), 2.13 (2.06)† (s, OAc), 3.19 (s, OMs), 3.26, 3.33 (s, 2×OMe), 3.6—5.4 (6-H, 7-H, 16-H, and 20-H_2), and 6.22 (s, 19-H). †The signals of the minor product are indicated in the parentheses.

Syntheses of the Starting Materials——(i) Alcohol (**3**) and Acetate (**24**): A solution of triol **23**[3] (450 mg) in Ac_2O–pyridine (1: 1) (4 ml) was stirred at 80° for 1.5 hr. After addition of MeOH to decompose excess of the reagent, the solvent was evaporated off *in vacuo* to leave a residue, which was chromatographed (SiO_2, CH_2Cl_2) to separate triacetate (**24**) (317 mg) and diacetate (**3**) (192 mg). Recrystallization of **24** from MeOH gave colorless prisms, mp 204°. *Anal.* Calcd. for $C_{28}H_{42}O_9$: C, 64.35; H, 8.10, M 522.282. Found: C, 64.55; H, 8.24, M^+ 522.281. IR ν_{max} cm^{-1}: 1740, 1730, 1240—1220, and 1020. NMR δ: 0.93, 1.07 (each 3H, s), 2.10 (9H, s, 3 OAc), 3.30 (3H, s, OCH_3), 3.73 (1H, quintet, J=5 Hz, 16-H), 3.93 (4H, s, OCH_2CH_2O), 4.67 (1H, d, J=4 Hz, 7-H), 4.87 (2H, s, 20-H_2), and 5.20 (1H, dd, J=2 and 4 Hz, 6-H). Recrystallization of **3** from MeOH gave colorless prisms, mp 192—194°. *Anal.* Calcd. for $C_{26}H_{40}O_8 \cdot 1/2MeOH$: C, 64.12; H, 8.52. Found: C, 64.30; H, 8.48. Mass Spectrum *m/e*: 480.269 (M^+) (Calcd. for $C_{26}H_{40}O_8$: 480.272). IR ν_{max} cm^{-1}: 3500, 1730, 1710, and 1240. NMR δ: 0.83, 1.30 (each 3H, s), 2.05 (6H, s, 2×OAc), 3.32 (3H, s, OCH_3), 3.77 (1H, quintet, J=5 Hz, 16-H), 3.93 (4H, s, OCH_2CH_2O), 4.10 (1H, m, 6-H), 4.54 (1H, d, J=3.5 Hz, 7-H), 4.87 (2H, s, 20-H_2), and 2.20—2.40 (1H, OH).

(ii) Alcohol (**5**): To a solution of **4** (103 mg) in MeOH–H_2O (3: 1) (4 ml) was added Na_2CO_3 (25 mg), and the mixture was stirred at room temperature for 2 hr. After neutralization with dil.HCl, the extract with AcOEt was treated as usual to give a crude product (91 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate a crystalline substance (81 mg; 86.1%) as an equilibrium mixture (**5**). *Anal.* Calcd. for $C_{24}H_{36}O_7$: M 436.246. Found: M^+ 436.249. IR ν_{max} cm^{-1}: 3420, 1730, 1700, 1362, 1235, and 1105. NMR δ: 0.82,* 0.89, 1.10, 1.17* (total 6H, s), 2.03*, 2.08 (total 3H, s), 3.28 (3H, s), *ca.* 3.7 (1H, m, 16-H), 3.92 (4H, s, OCH_2CH_2O), *ca.* 4.3, 4.7 (each 1H, m, 6-H and 7-H), 5.57*, and 10.7 (total 1H, s, 20-H). *Marks indicate signals of hemiacetal.

(iii) Alcohols (**10**, **11**, and **12**): To a solution of crude formates (**6**) (100 mg) in dry ether (30 ml) was slowly added $LiAlH_4$ (140 mg) under ice-cooling and stirring. After 1 hr, the extract with AcOEt was treated as usual to give 75 mg of a mixture, which was chromatographed (SiO_2, CH_2Cl_2: acetone=9: 1) to separate diol **9** (45 mg; 54.2%) and its double bond isomers. Recrystallization from acetone–hexane gave pure substance (**9**) as needles, mp 186—190°. Mass Spectrum *m/e*: 364 (M^+) (Calcd. for $C_{21}H_{32}O_5$: 364). NMR δ: 1.03, 1.10 (each 3H, s), 1.8 br (1H, s, OH), 2.37 br (2H, s, 2-H_2), 3.19 (3H, s), 3.52 (1H, d, J=4 Hz, 7-H), 3.6—4.1 (2H, 6-H and 16-H), 4.05 (4H, s, $-OCH_2CH_2O-$), 5.13 (1H, s, OH), and 5.50 br (1H, s, 1-H). A solution of diol **9** (32 mg) in Ac_2O–pyridine (1: 1) (3 ml) was allowed to stand at room temperature for 13 hr. After addition of MeOH, the solvent was evaporated off *in vacuo* to leave a residue, which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate acetate (**10**) (32 mg). Amorphous, Mass Spectrum *m/e*: 406 (M^+) (Calcd. for $C_{23}H_{34}O_6$: 406). NMR δ: 1.00, 1.10 (each 3H, s), 2.06 (3H, s, OAc), 3.33 (3H, s), 3.6—4.0 (2H, 6-H and 16-H), 4.02 (4H, s, OCH_2CH_2O), 4.77 (1H, d, J=4 Hz, 7-H), 5.12 (1H, s, OH), and 5.32 br (1H, s, 1-H). To a solution of acetate **10** (15 mg) in acetone–water (2: 1) (1.5 ml) were added two drops of 10% aq. HCl and the mixture was stirred at room temperature for 29 hr. The extract with CH_2Cl_2 was treated as usual to give a crude product (14 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate ketone (**12**) (12.5 mg) as a gum. NMR δ: 1.07, 1.26 (each 3H, s), 2.08 (3H, s), 3.00 br (2H, s, 2-H_2), 3.33 (3H, s), 3.72 (1H, quintet, J=5 Hz, 16-H), 3.96 (1H, m, 6-H), 4.60 (1H, d, J=4 Hz, 7-H), 5.66 br (1H, s, 1-H), and 1.90 (1H, OH). To a solution of ketone **12** (36 mg) in MeOH (10 ml) was added slowly $NaBH_4$ (48 mg) under ice-cooling, and the mixture was stirred at room temperature for 20 min. After neutralization with 5% aq.

13) See Table I footnote *c*).

HCl, the extract with CH_2Cl_2 was treated as usual to give a crude product (38 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=9: 1) to separate non-crystalline diol (31 mg). *Anal.* Calcd. for $C_{19}H_{28}O_3$: M 304.204. Found: M^+ 304.200. NMR δ: 0.96, 1.07 (each 3H, s), 2.10 (3H, s), 3.36 (3H, s), 3.48 br (1H, s, 3-H), 3.6—4.0 (1H, m, 16-H), 3.78 (1H, t, J=3.8 Hz, 6-H), 4.70 (1H, d, J=3.8 Hz, 7-H), 5.52 br (1H, s, 1-H), and 5.4—5.8 br (2H, s, 2×OH). A solution of above diol (10 mg) in Ac_2O–pyridine (1: 1) (2 ml) was allowed to stand at room temperature overnight. After addition of MeOH, the solvent was evaporated off *in vacuo* to leave a residue, which was chromatographed (SiO_2, CH_2Cl_2) to separate non-crystalline triacetate (5.5 mg), Mass Spectrum *m/e*: 388 (M^+−60) (Calcd. for $C_{25}H_{36}O_7$: 448). NMR δ: 0.92, 1.00 (each 3H, s), 2.03, 2.06, 2.08 (each 3H, s, 3×OAc), 3.33 (3H, s), 3.80 (1H, quintet, J=5 Hz, 16-H), 4.5—4.8 (1H, m, 6-H), 4.70 (1H, d, J=3.8 Hz, 7-H), 5.13 br (1H, s, 3-H), and 5.60 br (1H, s, 1-H), and amorphous diacetate **11** (3.5 mg), Mass Spectrum *m/e*: 346 (M^+−60) (Calcd. for $C_{23}H_{34}O_6$: 406). IR ν_{max} cm^{-1}: 3500, 1732, and 1240. NMR δ: 1.03 (6H, s), 2.10 (6H, s, 2×OAc), 3.35 (3H, s), 3.6—4.0 (2H, m, 6-H and 16-H), 4.00 (1H, s, OH), 4.80 (1H, d, J=3.8 Hz, 7-H), 4.02 br (1H, s, 3-H), and 5.35 br (1H, s, 1-H).

(iv) Alcohol (**17**): To an ice-cooled and stirred solution of alcohol (**15**)[3] (26 mg) in acetone (1.5 ml) were added two drops of Jones reagent. Usual work-up gave a crystalline product (25 mg). Its recrystallization (from MeOH) yielded pure ketone (**16**) as needles, mp 156—158°. *Anal.* Calcd. for $C_{21}H_{32}O_4$: M 348.230. Found: M^+ 348.234. IR ν_{max} ($CHCl_3$) cm^{-1}: 1710, 1100, and 910. NMR δ: 1.12, 1.30 (each 3H, s), 3.30 (6H, s), 3.80 (1H, quintet, J=5 Hz, 16-H), 3.97, 4.39 (each 1H, AB type, J=9 Hz, 20-H_2. Each signal showed a long range coupling splitted with J=1 and 3 Hz, respectively). To an ice-cooled and stirred solution of ketone (**16**) (23 mg) in MeOH (3 ml) was slowly added $NaBH_4$ (25 mg). After 30 min, a small amount of acetic acid was added, and then the extract with CH_2Cl_2 was treated as usual to give a crude product (22 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate alcohol (**17**) (18 mg). Recrystallization (from MeOH) gave colorless needles, mp 165—167°. *Anal.* Calcd. for $C_{21}H_{34}O_4$: M 350.245. Found: M^+ 350.247. IR ν_{max} cm^{-1}: 3410, 1150, and 1040. NMR δ: 1.03, 1.22 (each 3H, s), 3.28, 3.34 (each 3H, s), *ca.* 3.80 (1H, m, 16-H), 3.86, 4.87 [each 1H, AB type, J=9 Hz, 20-H_2. Each signal showed a long range coupling (J=1 and 3 Hz, respectively).], 4.27 (1H, m, 6-H), and *ca.* 2.03 (1H, OH).

(v) Alcohol (**22**): Method A: To a solution of diol (**19**)[3] (70 mg) in CH_2Cl_2 (5 ml) was added CrO_3–pyridine complex (280 mg) under ice-cooling and stirring. After 1 hr, a black deposit was filtered off and the filtrate on column chromatography (SiO_2, CH_2Cl_2) gave diosphenol (**20**) (23 mg) and 6-oxo-7-β-ol (30 mg). Recrystallization of **20** (from MeOH) yielded crystalline powder, mp 119—122°. *Anal.* Calcd. for $C_{21}H_{30}O_5$: M 362.209. Found: M^+ 362.213. IR ν_{max} cm^{-1}: 3370, 1665, 1637, 1210, 1140, 1100, and 1040. NMR δ: 1.36, 1.39 (each 3H, s), 3.36 (6H, s), 3.8 (1H, m, 16-H), 4.20, 4.50 [each 1H, AB type, J=8 Hz, 20-H_2. Lower field signal showed a long range coupling (J=3 Hz).], and 6.34 (1H, s, 6-OH). UV λ_{max} (95% EtOH) gave a bathochromic shift from 280 to 355 nm by addition of alkali. The foregoing 6-oxo-7-β-ol (18 mg) was transformed to diosphenol (**20**) (7 mg) by autooxidation when treated with Na_2CO_3 (15 mg) in MeOH–water (4: 1) (5 ml) at room temperature. 6-Oxo-7β-ol, IR ν_{max} cm^{-1}: 3400, 1703, 1100, and 1030. NMR δ: 0.97, 1.10 (each 3H, s), 3.26, 3.30 (each 3H, s), 3.70 (1H, quintet, J=5 Hz, 16-H), 4.17, 4.23 [each 1H, AB type, J=9 Hz, 20-H_2. Each signal showed a long range coupling (J=1 and 3 Hz, respectively).], and 3.65 (1H, OH). To a solution of diosphenol (**20**) (40 mg) in MeOH (3 ml) was added $NaBH_4$ (50 mg) under ice-cooling and stirring. After 11 hr, a small amount of 5% HCl was added, and then the extract with CH_2Cl_2 was treated as usual to give a crude product (41 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate acyloin (**21**) as crystals (20 mg) (from MeOH). IR ν_{max} cm^{-1}: 3470, 1700, 1080, and 1030. NMR δ: 1.10, 1.25 (each 3H, s), 3.30, 3.33 (each 3H, s), 3.7 (1H, OH), 3.80 (1H, quintet, J=5 Hz, 16-H), 3.87 (1H, s, 7-H), 3.92, and 4.30 [each 1H, AB type, J=9 Hz, 20-H_2. Each signal showed a long range coupling (J=1 and 3 Hz, respectively).]. Reduction of **20** with $LiAlH_4$ gave **21** in 38% yield. To a solution of **21** (12 mg) in pyridine (0.5 ml) was added Ac_2O (0.5 ml) and the mixture was allowed to stand overnight at room temperature. After addition of MeOH, evaporation *in vacuo* left a crude acetate (13 mg). IR ν_{max} cm^{-1}: 1740, 1725, 1230, 1100, and 1050. NMR δ: 1.06, 1.40 (each 3H, s), 2.18 (3H, s), 3.27, 3.30 (each 3H, s), *ca.* 3.80 (1H, m, 16-H), 3.93, 4.33 [each 1H, AB type, J=9 Hz, 20-H_2. Lower field signal showed a long range coupling (J=3 Hz).], and 4.97 (1H, s, 7-H). To a solution of acetate (6 mg) in MeOH (2 ml) was added $NaBH_4$ (10 mg) under ice-cooling and stirring. After 12 hr, usual work-up gave a crude product (5 mg). Recrystallization (from MeOH) yielded pure 6α-alcohol (**22**) as needles, mp 265—266°. Mass Spectrum *m/e*: 408 (M^+) (Calcd. for $C_{23}H_{36}O_6$: 408). IR ν_{max} cm^{-1}: 3450, 1733, 1250, and 1050. NMR δ: 1.03, 1.21 (each 3H, s), 2.15 (3H, s), 3.30, 3.33 (each 3H, s), *ca.* 3.80 (1H, m, 16-H), 3.86, 4.90 [each 1H, AB type, J=9 Hz, 20-H_2. Lower field signal showed a long range coupling (J=3 Hz).], 4.23 (1H, m, 6-H), and 4.70 (1H, d, J=2.5 Hz, 7-H).

Method B: To a solution of triacetate (**24**) (60 mg) in MeOH (3 ml) was added Na_2CO_3 (20 mg), and then the mixture was stirred at room temperature for one day. After neutralization with dil.HCl, the extract with CH_2Cl_2 was treated as usual to give a crude product (56 mg), which was chromatographed (SiO_2, CH_2Cl_2: acetone=19: 1) to separate amorphous 7β-ol-6α, 20-diacetate (**25**) (48 mg). *Anal.* Calcd. for $C_{26}H_{40}O_8$: M 480.272. Found: M^+ 480.272. NMR δ: 0.97, 1.12 (each 3H, s), 2.08 (6H, s), *ca.* 2.40 (1H, OH), 3.33 (3H, s), *ca.* 3.4 (1H, 7-H), *ca.* 3.8 (1H, m, 16-H), 3.97 (4H, s, OCH_2CH_2O), 4.90 (2H, s, 20-H_2), and 5.25 (1H, m, 6-H). The diacetate (40 mg) was dissolved in dry CH_2Cl_2 (10 ml), to which CrO_3–pyridine complex (280 mg) was added. The mixture was stirred at room temperature for 5 hr. A black deposit was filtered off and the

filtrate gave 40 mg of ketone (**26**) by column chromatography (SiO_2, CH_2Cl_2). Recrystallization (from MeOH) gave pure compound as colorless needles, mp 192—193°. *Anal.* Calcd. for $C_{26}H_{38}O_8$: C, 65.25; H, 8.00. Found: C, 65.15; H, 8.10. IR ν_{max} cm^{-1}: 1735, 1700, 1240, and 1028. NMR δ: 0.92, 1.22 (each 3H, s), 1.96, 2.12 (each 3H, s), *ca.* 3.8 (1H, m, 16-H), 3.96 (4H, s, OCH_2CH_2O), 4.15, 4.81 (each 1H, AB type, $J=13$ Hz, 20-H_2), and 5.41 (1H, d, $J=6.5$ Hz, 6-H). To a solution of keto acetate (**26**) (39 mg) in dry ether (10 ml) was slowly added $LiAlH_4$ (60 mg) at 0°, and then the mixture was stirred for 2 hr. Excess of $LiAlH_4$ was decomposed by addition of AcOEt at 0°, and the mixture was extracted with ether. The extract was treated as usual to give 24 mg of 6α,7α,20-triol(**27**) as prisms (from MeOH), mp 199—200°. *Anal.* Calcd. for $C_{22}H_{36}O_6$: M 396.251. Found: M^+ 396.251. IR ν_{max} cm^{-1}: 3350 and 1090. NMR δ: 0.97, 1.32 (each 3H, s), 3.33 (3H, s), *ca.* 3.2 br (1H, s), 3.97 (4H, s, OCH_2CH_2O), 3.5—4.2 (4H), and 4.55 br (3H, s, 3×OH). A mixture of triol (24 mg) and *p*-toluene sulfonic acid (6 mg) in absolute MeOH (3 ml) was stirred at room temperature for one day. After neutralization with aq. Na_2CO_3 and evaporation of MeOH *in vacuo*, the residue was extracted with $CHCl_3$. Usual treatment of the extract gave the crude crystals (19 mg) of *ent*-3β,20-epoxy-3,16α-dimethoxy-17-norkaurane-6β,7β-diol, which were purified by chromatography. NMR δ: 1.04, 1.23 (each 3H, s), 2.2—2.5 (2H, 2×OH), 3.29, 3.34 (each 3H, s), *ca.* 3.75 (1H, m, 16-H), 3.83, 4.82 [each 1H, AB type, $J=$ 8 Hz, 20-H_2. Lower field signal showed a long range coupling ($J=3$ Hz).], and 4.20 br (1H, s, 6-H). A solution of diol (15 mg) in Ac_2O–pyridine (1: 1) (2 ml) was stirred at room temperature for 1.5 hr. After addition of MeOH under ice-cooling, the solvent was evaporated off *in vacuo* to leave a crystalline residue (16 mg). Recrystallization (from MeOH) gave pure crystals of the foregoing 6-ol-7-acetate (**22**).

(vi) Alcohol (**30**): To a solution of the crude formate (**29**)[8] (755 mg) in MeOH (15 ml) was added aq. Na_2CO_3 (1 g/5 ml) and then the mixture was stirred at room temperature for 3 hr. After neutralization with 5% HCl, the extract with AcOEt was treated as usual to give a crude product (*ca.* 1 g). It was dissolved in MeOH (40 ml) and the solution was subjected to hydrogenation over PtO_2 for 5 hr. The catalyst was filtered off, and the filtrate was evaporated *in vacuo*. The residue (651 mg) was eluted with CH_2Cl_2: acetone (9: 1) on silica gel column to give crystals (336 mg), which were recrystallized(from MeOH) to give **30** as needles, mp 186—188°. *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41; M 290.225. Found: C, 78.66; H, 10.59; M^+ 290.227. IR ν_{max} cm^{-1}: 3500, 1725, and 1070. NMR δ: 1.0 (3H, d, $J=6$ Hz, 16-CH_3), 1.19 (6H, s), *ca.* 1.68 (1H, OH), 3.58, and 3.94 [each 1H, AB type, $J=12$ Hz, 20-H_2. Each signal showed a coupling with proton of alcohol ($J=5$ Hz).].

(vii) Alcohol (**32**): To a solution of **31** (77 mg) in dry ether (10 ml) was slowly added $LiAlH_4$ (77 mg) under ice-cooling and stirring. After refluxing for 1 hr and subsequent decomposition of excess $LiAlH_4$ with a small amount of AcOEt, the mixture was extracted with ether. The extract was treated as usual to give 6α-ol **32** (62 mg). Recrystallization (from MeOH) yielded pure substance as needles, mp 169—172°. *Anal.* Calcd. for $C_{19}H_{30}O_2$: M 290.225. Found: M^+ 290.224. IR ν_{max} cm^{-1}: 3350, 1120, and 1010. NMR δ: 0.98, 1.09 (each 3H, s), 1.02 (3H, d, $J=7$ Hz), 1.53 (1H, s, OH), 3.64, 4.12 (each 1H, AB type, $J=9$ Hz, 20-H_2. Lower field signal becomes broad signal because of a long range coupling with 1β-H), 4.26 br (1H, t, $J=$*ca.* 5 Hz, 3-H), and 4.35 (1H, d, $J=6$ Hz, 6-H).

(viii) Alcohol (**38**): A solution of diol **43**[3] (303 mg) in Ac_2O–pyridine (1: 1) (1 ml) allowed to stand overnight at room temperature. After addition of MeOH, the solvent was evaporated off *in vacuo* to leave a crystalline substance (320 mg), which was recrystallized (from MeOH) to give **38** (292 mg) as needles, mp 248—248.5°. *Anal.* Calcd. for $C_{23}H_{36}O_6 \cdot 1/2MeOH$: C, 66.51; H, 9.02. Found: C, 66.80; H, 9.31. Mass Spectrum *m/e*: 420 (M^+) (Calcd. for $C_{23}H_{36}O_6$: 420). IR ν_{max} cm^{-1}: 3540, 1728, 1238, and 1025. NMR δ: 1.15, 1.27 (each 3H, s), *ca.* 1.8 (1H, OH), 2.16 (3H, s), 3.30 (6H, s), 3.73 (1H, m, 16-H), 3.7—4.2 (2H, 6-H and one proton of 20-H_2), 4.33 [1H, one part of AB type, 20-H. This signal showed a long range coupling ($J=2.5$ Hz)], and 4.70 (1H, d, $J=10$ Hz, 7-H).

(ix) Alcohol (**41**): To a solution of diol (**43**) (20 mg) in pyridine (1 ml) were added three drops of mesyl chloride under ice-cooling and stirring. After 2 hr, small amount of MeOH was added and the mixture was extracted with CH_2Cl_2. The extract was washed with 5% HCl and the CH_2Cl_2 layer was treated as usual to give a residue, which was separated by preparative TLC to give mesylate (**41**) (9 mg) besides recovery of the starting material (8 mg). Recrystallization of **41** (from MeOH) yielded pure compound as needles, mp 184—185°. *Anal.* Calcd. for $C_{22}H_{36}O_7S$: M 444.218. Found: M^+ 444.219. IR ν_{max} cm^{-1}: 3540, 1335, 1165, and 920. NMR δ: 1.16, 1.23 (each 3H, s), 2.32 (1H, OH), 3.19 (3H, s, OSO_2CH_3), 3.29, 3.32 (each 3H, s, 2×O-CH_3), 3.60—4.20 (3H, 6-H, 16-H, and one proton of 20-H_2), 4.32 (1H, dd, $J=9$ and 3 Hz, 20-H), and 4.45 (1H, d, $J=10$ Hz, 7-H).

Jones Oxidation of Acetal (33)——To a solution of acetal (**33**) (19 mg) in acetone (1.5 ml) were added three drops of Jones reagent under ice-cooling and stirring. After stirring for 1 hr and subsequent addition of MeOH, the extract with AcOEt was treated as usual to give a crude crystalline product (19 mg), which was recrystallized from MeOH to yield keto-lactone **34** (9 mg) as needles, mp 165—167°. *Anal.* Calcd. for $C_{19}H_{26}O_3$: M 302.188. Found: M^+ 302.190. IR ν_{max} cm^{-1}: 1735 and 1160. NMR δ: 1.08 (3H, d, $J=6$ Hz), 1.24, 1.32 (each 3H, s), 2.14 (1H, s, 5-H), and 4.87 (1H, t, $J=5.5$ Hz, 3-H).

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