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TERPENOIDS—XIV[1]

FORMAL CHEMICAL CONVERSION OF ENMEIN INTO *ent*-KAURENE, ATISINE, GARRYINE AND VEATCHINE

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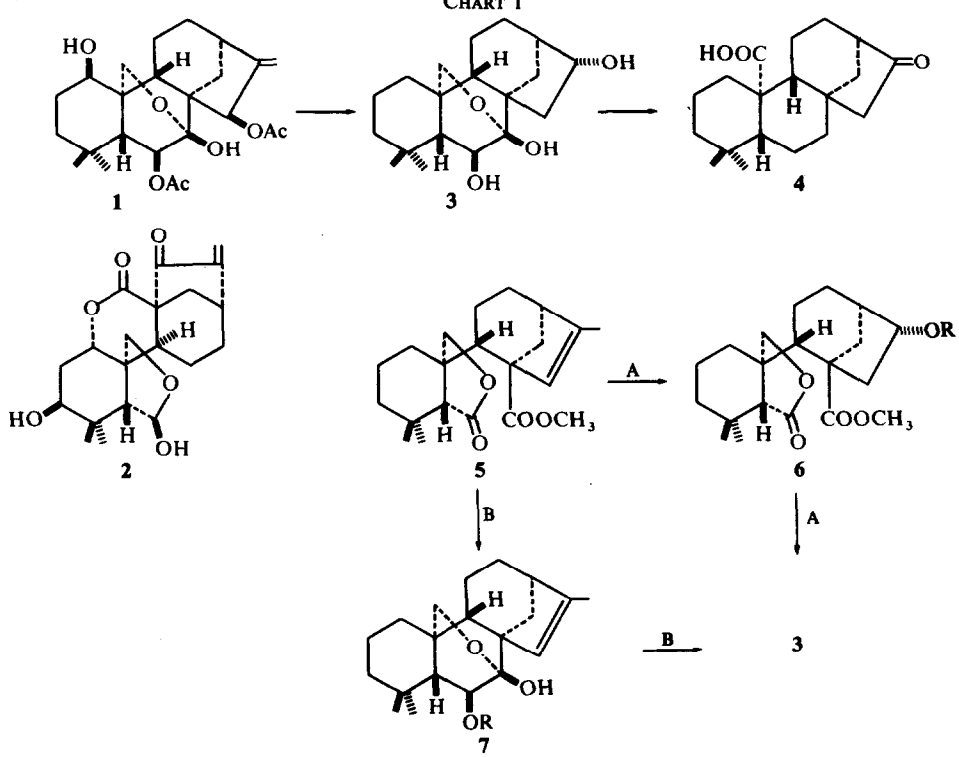
Abstract—Lactone ester **5** derived from enmein **(2)** was subjected to acyloin condensation to give **18** as a main product. Compound **18** was converted into **27**, which on ozonolysis gave ketone **31**. The latter was treated with Ca in liquid NH_3 to afford **3**. The work constitutes a formal chemical conversion of enmein into *ent*-kaurene, atisine, garryine and veatchine.

RECENTLY, the chemical conversion of trichokaurin **(1)**[2] into keto-carboxylic acid **4**[3] *via* hemiketal diol **3** was accomplished,[2] which corresponded to a success of a formal chemical conversion of trichokaurin into *ent*-kaurene,†[3, 4] atisine,[5] garryine[6a, b] and veatchine.[6a, 7]

CHART 1



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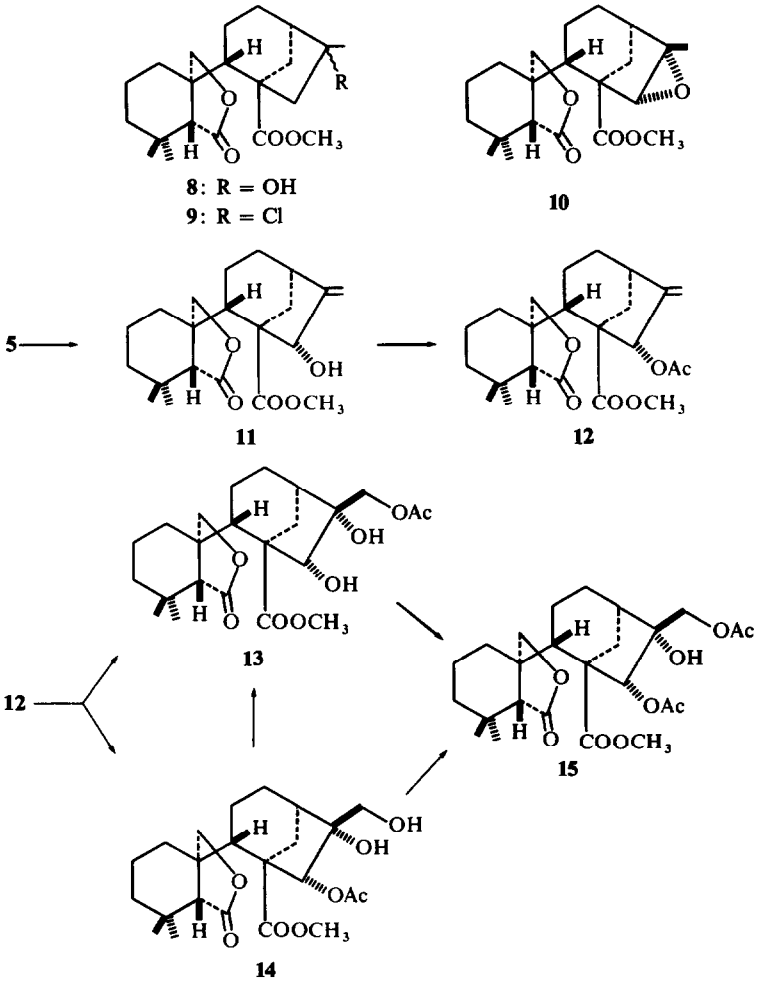
† (-) -Kaurene is named like this in accordance with a proposal for nomenclature of cyclic diterpenes subscribed to by many workers in this area. (J. W. Rowe in preparation.)

This paper deals with the details of chemical conversion of enmein (**2**) into compound **3**.

Enmein,[8] major bitter diterpenoid from the leaves of *Isodon trichocarpus* Kudo and *I. japonicus* Hara, was converted into unsaturated lactone ester **5**[9a, b] Subsequent routes to **3** were investigated in two ways: the one is the route A *via* **6** to **3**, and the other is the route B *via* **7** to **3**.

Route A. An attempted rearrangement of *endo-* into *exo*-double bond by treatment of **5** with I_2 in dry benzene[10] or with dil HCl in acetone[11] was unsuccessful. Treatment of **5** with 6N HCl in acetone at reflux gave t-alcohol **8**, while **5** was treated with 35% HCl in acetone to give hydrochloride **9**. The epoxide **10**[9b] on treatment with Zn in EtOH or with $ZnBr_2$ in EtOH[12] gave only the recovered material. Treatment of **10** with $ZnBr_2$ in benzene at reflux gave a mixture of at least seven unidentified products. Neither the heating of **10** in EtOH–AcOH (9 : 1 in volume) under reflux[10] nor treatment

CHART 2

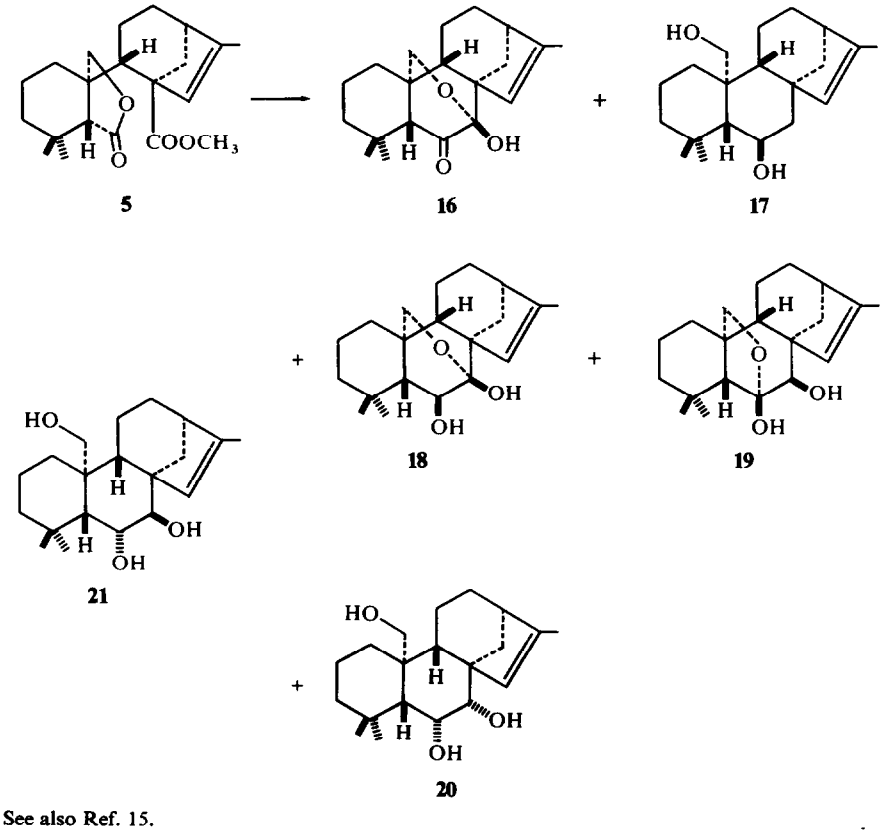


of **10** with $MgBr_2$ in Et_2O–benzene[10, 13] at room temperature gave the desired product **11**.

Compound **5**, dissolved in pyridine, was subjected to photosensitized oxygenation[10, 14] by passing O_2 gas through the solution in the presence of hematoporphyrin as photosensitizer under irradiation by fluorescent lamps to yield the desired allyl alcohol **11** accompanied by epoxide **10**. The assignment of the structure was based on the IR and NMR soectra. The acetate **12** was oxidized with OsO_4 to afford two glycols **13** and **14**, both of which on acetylation gave diacetate **15**. Glycol **14** was easily converted into **13** by treatment with HCl. These facts and NMR data supported the structures of the glycols. The yields of **11** and **14**, however, were low, so the route A was abandoned.

Route B. The acyloin condensation with **5** by Na in liquid NH_3 was investigated.* Into a solution of a large excess Na in liquid NH_3, an ethereal solution of **5** was added at $-60°$ within 30 min, and the mixture was stirred for 2 hr. The reaction resulted in the formation of **16**, **17** and **18**. The IR spectrum (ν_{max} 3470 and 1715 cm^{-1}) of **16** suggested the presence of OH and cyclohexanone, and its NMR spectrum showed a singlet signal of C-5 proton at δ 2·16, a singlet signal of C-20 protons at δ 4·07 and a

CHART 3

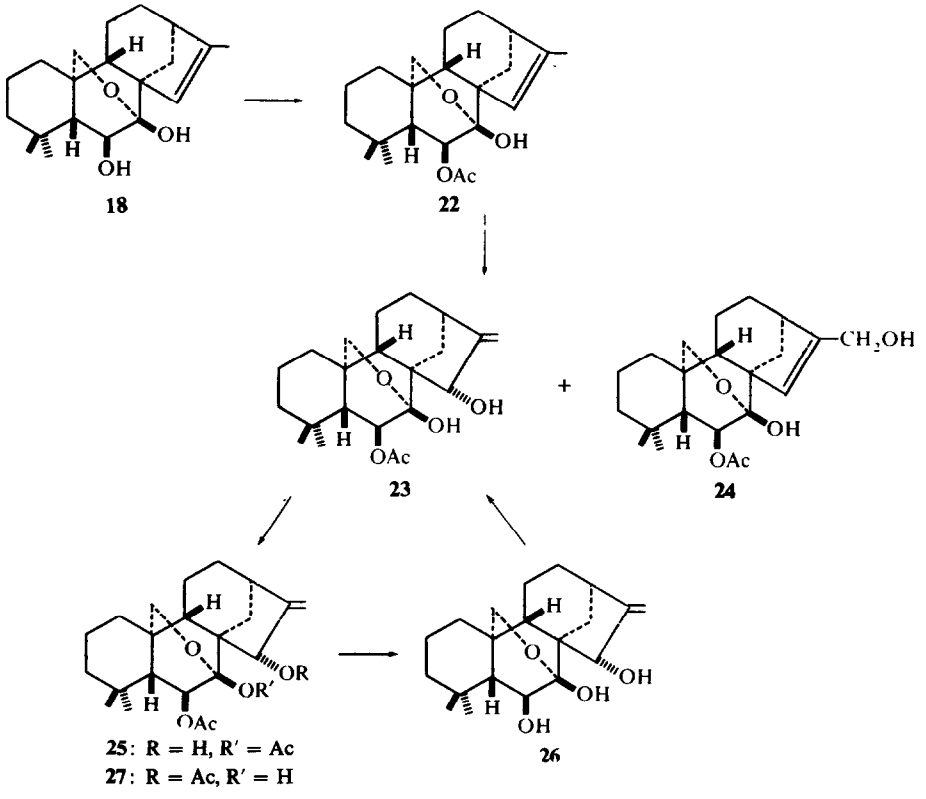


* See also Ref. 15.

singlet signal of C-7 OH proton at δ 4·22 ppm. The IR spectrum (ν_{max} 3350, 1048 and 1031 cm^{-1}) of **17**, and a multiplet signal at δ 3·93 (C-6—H) and a C-20 protons singlet signal at δ 4·02 ppm in its NMR spectrum suggested the diol structure. Catalytic hydrogenation of **17** gave the known dihydro-derivative.[8] Compound **18** was shown to have two OH groups by IR ($\nu_{max}^{CHCl_3}$ 3590 and 3430 cm^{-1}) and NMR signals at δ 2·40 and 2·98 ppm assignable to OH protons, and a doublet at δ 3·80 ppm assignable to C-6 proton. Catalytic hydrogenation of **18** gave the known dihydro-derivative.[8] Oxidation of **18** afforded ketone **16**.[15] In the second case, an ethereal solution of **5** was added into 1·3 equivalents of Na in liquid NH_3 at $-75°$ within 1·5 hr and the mixture was stirred for 2 hr. The reaction afforded **19** and **18**. The molecular formula of **19** was the same as that of **18**, and on treatment with methanolic 0·01N NaOH **19** was converted into **18**. The NMR spectrum gave a singlet signal due to C-7 proton at δ 3·34, besides two OH protons signals at δ 3·25 and 2·29 supporting the structure **19**. The configuration of OH at C-7 of **19** was confirmed by its conversion into triol **21**[15] with $NaBH_4$. Through several times of reactions under the same conditions, the best yield of the desired compound **18** was 49·8%. In addition to the above products, triol **20** was also formed as a minor product.

Recently, a high yield of acyloin was reported, when the reaction was carried out in the presence of trimethylsilyl chloride in nonpolar solvent.[16] This procedure was tried for the acyloin condensation of **5**. The VPC of the products showed at least 7 peaks. The NMR and IR spectra of the mixture did not show the presence of OH,

CHART 4



but the IR (in $CHCl_3$) absorption bands at 1248 (Si-C bending vibration) and 842 cm^{-1} (Si-C stretching)[17] suggested the presence of trimethylsilyl ether. The mixture was treated with dil HCl to give free alcohols, which were column-chromatographed to give only a low yield of 7-hemiketal-6-ol **18**.

The key intermediate **18** was first acetylated to give 6-acetate **22**, which was oxygenated with an O_2 stream under irradiation by fluorescent lamps in the presence of hematoporphyrin to afford the expected allyl alcohol **23** in 71·5% yield accompanied by a small quantity of an isomer **24**.

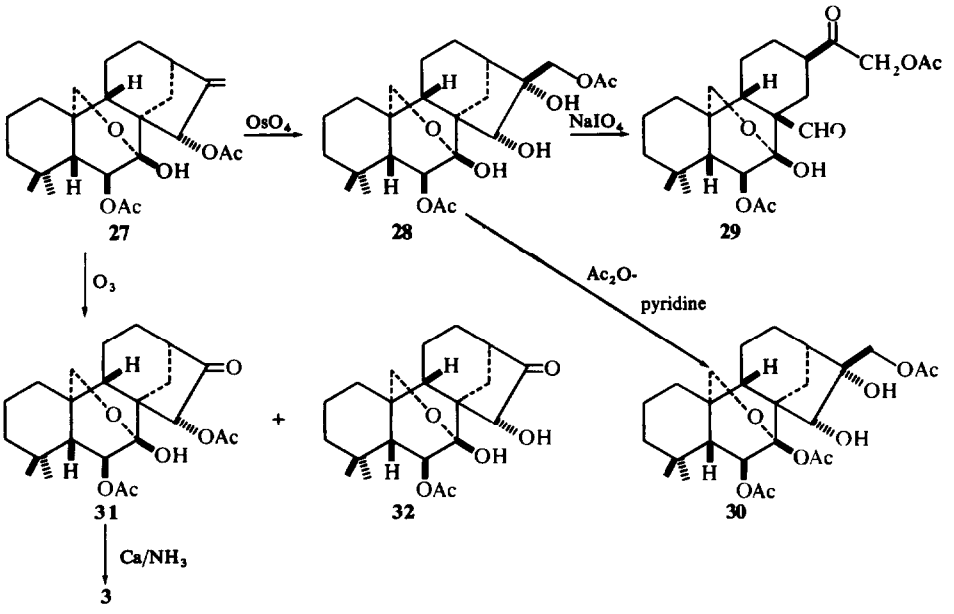
The IR ($\tau_{max}^{CHCl_3}$ 1662, 977, 922 and 908 cm^{-1}) and NMR (δ 5·13 and 5·24 ppm) spectra of **23** suggested the presence of exocyclic methylene group in the molecule, and a singlet signal at δ 4·26 in its NMR spectrum was assignable to C-15 βH. A comparison of the NMR spectrum of **24** with that of **23** and the identity of the molecular formulas of two compounds gave a reasonable assignment of the structure to the minor isomer. The usual acetylation of **23** by Ac_2O–pyridine at room temp resulted in the recovery of the material, because of a hydrogen bonding between C-7- and C-15-α-OH groups [$\nu_{max}^{CHCl_3}$ 3450 cm^{-1}; δ^{CDCl_3} 3·33 and 4·37 ppm (each 1H, m, O<u>H</u>)]. The same reaction at 105 ~ 110° gave amorphous triacetate and a mixture of diacetates **25** and **27**. When the mixture of diacetates was warmed with aqueous AcOH, only acetate at C-7 in **25** was hydrolyzed and diacetate **27** was isolated as crystals. The mixture of **25** and **27** on treatment with LAH in Et_2O gave alcohol **26**, in which a strong intramolecular H-bonding was recognized, thus, it had an unchangeable OH signal on treatment with D_2O in its NMR spectrum. On acetylation at room temp, **26** gave monoacetate **23**. The best way for getting **27** among the investigated procedures was treatment of **23** with Ac_2O–NaOAc in $CHCl_3$ at reflux for 22 hr. The structure **27** was supported by the NMR and IR data.

The Lemieux-Johnson's oxidation[2, 18] was tried on **27** in THF, but only a very low yield of α-ketol **32** was obtained. Now, diacetate **27** on OsO_4 oxidation in ether-pyridine[19] gave an amorphous glycol in 64% yield. The foregoing result of the reaction with compound **12** and the NMR data of the glycol [δ 2·10, 2·11 (C<u>H</u>$_3$CO), 3·60 (1H, d, J = 1·5 Hz, C-15—H), 3·80, 3·98 (each 1H, AB-type, J = 10·5 Hz, C-20<u>H</u>$_2$), and 4·18 (2H, s, C-17<u>H</u>$_2$)] led to an assumption that the glycol is not the normal C-16, C-17 glycol, but the acetyl-migrant[20] C-15, C-16 glycol **28**. The assumption was proved to be correct by $NaIO_4$ cleavage of the glycol: the product was an aldehyde **29** which had an acetoxyacetyl-group as shown by IR (ν_{max}^{KBr} 1724 cm^{-1}) and NMR data [δ 2·00, 2·12 (C<u>H</u>$_3$CO), 4·67 (2H, s, C-17<u>H</u>$_2$)]. The compounds **28** and **29** were also obtained by Lemieux-Johnson's oxidation of **27** in dioxan.[21] The glycol **28** on acetylation with Ac_2O–pyridine at room temp gave a triacetate, whose structure was, unexpectedly, shown to be **30** on the basis of IR ($\tau_{max}^{CHCl_3}$ 1770 cm^{-1}) and NMR data [δ 3·67 (1H, d, J = 1·5 Hz, C-15—<u>H</u>) and 6·03 ppm (1H, d, C-6—<u>H</u>)]. The migration of acetyl group during the reactions of **12** and **27** with OsO_4 seemed very characteristic for these C/D ring compounds.

In order to prevent the acetyl-migration, mesylation at C-15 OH-group of **23** was tried, but the expected mesylate could not be obtained.[22]

Finally, ozonolysis[23] was successfully carried out to yield the desired compound **31** as a major product (55% yield) and **32** as a minor product. The latter on acetylation with Ac_2O–NaOAc in chloroform gave the former, while the former, dissolved in chloroform, was allowed to stand on addition of the catalytic quantity of conc HCl

CHART 5



for 2 days to give the latter. These facts and IR and NMR spectra reasonably led to the assignment of the structures **31** and **32**. α-Acetoxyketone **31** was subjected to hydrogenolysis with Ca in liquid NH_3[2, 24] to afford alcohol **3**, which constitutes the formal chemical conversion of enmein into *ent*-kaurene, atisine, garryine and veatchine.

EXPERIMENTAL

All m.ps were determined by a micro m.p. apparatus (Yanagimoto) and were uncorrected. Unless otherwise stated, IR spectra were run in KBr discs on a Hitachi model EPI-S2 spectrophotometer and NMR spectra in $CDCl_3$ with TMS as an internal standard on a Varian A-60 spectrometer. Mass spectra were taken on a Hitachi RMU 6D mass spectrometer using a direct inlet system. GLC was carried out with a Shimadzu GC-1C equipped with hydrogen ionization detector. Extracts were dried over Na_2SO_4. Mallinckrodt silicic acid or Kieselgel 0·05 ~ 0·20 mm (Merck) was used for column chromatography. TLC plates were coated with Silicagel G nach Stahl (Merck) or Nakarai Silica Layer G.

Attempted rearrangement of endo- *into* exo-*double bond of unsaturated lactone ester* **5**

(a) Material **5** (54 mg) was dissolved in dry benzene (5 ml) and I_2 (0·5 mg) was added. The mixture was heated under reflux for 2 hr. A usual work up, after washing with $Na_2S_2O_3$ aq, gave the recovered material (54 mg), which was identified by TLC (10% $AgNO_3$ impregnated SiO_2[25], $CHCl_3$: acetone = 95:5), GLC (QF −1:1·5%, 0·75 m × 0·4 mm, N_2 carrier) and IR ($CHCl_3$).

(b) A soln of material **5** (50 mg) in glacial AcOH (5 ml) was heated under reflux for 2 hr to give the recovered material.

(c) To a soln of **5** (48 mg) in acetone (4 ml), 3·5% HCl (1 ml) was added and the mixture was heated under reflux for 2 hr. After pouring into NaCl aq, extraction with Et_2O and a usual work up recovered the material (46 mg).

(d) After a mixture of **5** (90 mg) and 6N HCl (3 ml) in acetone (3 ml) was heated under reflux, the reaction mixture was poured into H_2O and extracted with Et_2O. A usual treatment of the extract gave a neutral fraction (77 mg), which was chromatographed on SiO_2 (2 g) column by elution with $CHCl_3$ to give the recovered material (48 mg) and *a hydroxy lactone ester* **8** (28 mg). An eluate with $CHCl_3$ – acetone (9:1) gave an additional quantity (10 mg) of the latter. Recrystallization from MeOH–H_2O afforded colourless

crystals, m.p. 164 ~ 165° (changed to needles at near 100°); IR ν_{max}: 3600 ~ 3300; 1762; 1727 cm^{-1}. (Found: C, 68·08; H, 9·17. $C_{21}H_{32}O_5 \cdot 1/2\ Me_3OH$ requires: C, 67·86; H, 9·01%).

(e) To a soln of **5** (53 mg) in acetone (2·5 ml), 35% HCl (1 ml) was added, and the mixture was heated under reflux for 30 min. The reaction mixture was poured into NaCl aq and extracted with Et_2O. The extract was treated as usual to give a crude product (60 mg), which was chromatographed on SiO_2 (1·2 g) column by elution with $CHCl_3$ to give *hydrochloride* **9** (28 mg). Purification by recrystallization from Et_2O yielded pure compound **9**, m.p. 143 ~ 146°. Beilstein reaction: positive (green); IR ν_{max}: 1750; 1727 cm^{-1}, NMR δ_{ppm}: 0·98 (3H, s); 1·18 (3H, s); 1·73 (3H, s, >C(Cl)—C<u>H</u>$_3$); 3·72 (3H, s, COOC<u>H</u>$_3$); 3·96 (2H, s, C-20 <u>H</u>$_2$). (Found: C, 65·95; H, 8·25. $C_{21}H_{32}O_4$ requires: C, 65·09; H, 8·41%).

Attempted conversion of epoxide **10** *into* **11**

(a) Epoxide **10** (15 mg) and $ZnBr_2$ (529 mg) were added into a mixture of dry benzene (4 ml) and abs EtOH (1 ml), and the mixture was heated under reflux for 9·5 hr. A usual treatment gave a crude substance (15 mg) which exhibited at least 7 spots on TLC ($CHCl_3$: acetone = 97:3) including the spot of the starting material.

(b) A soln of **10** (28 mg) in abs EtO ml) and AcOH (1 ml) was heated under reflux for 18·5 hr. The solvent was evaporated off to give a residue (30 mg), which did not exhibit the spot of the desired product on TLC($CHCl_3$: acetone = 97:3).

(c) Into a soln of epoxide **10** (23 mg) in EtOH–benzene (1:1) (2 ml), anhyd $MgBr_2$ (170 mg) was added and the mixture was allowed to stand for 30 hr at room temp. The TLC of the product gave two spots, none of which corresponded to the spot of the desired alcohol **11**.

Alcohol **11**

(a) Unsaturated lactone ester **5** (246 mg) was dissolved in dry pyridine (8 ml) and hematoporphyrin (4 mg) was added to the soln. Oxygen was passed through the soln under irradiation with fluorescent lamps. Pyridine was sometimes added to keep constant the volume of the soln. After 58·5 hr, the reaction mixture was concentrated and a soln of KI (1·7 g) in aq EtOH containing a small quantity of AcOH was added. After the mixture was allowed to stand overnight, the soln was concentrated, and H_2O was added. Extraction with Et_2O, washing with aq thiosulphate soln, and a usual work-up gave a crude product (200 mg), which was chromatographed on SiO_2 (5 g) column (1·3 × 7·5 cm) by elution with CH_2Cl_2. The first eluate (40 ml) gave the recovered material (160 mg), the next eluate (20 ml) gave epoxide **10** (11 mg), and the third eluate (40 ml) gave a mixture (71 mg) of at least three compounds. The latter was subjected to a preparative TLC[SiO_2, 20 × 20 cm, 0·2 mm, 4 plates, eluted with $CHCl_3$–EtOH (9:1)] to give an additional epoxide **10** (10 mg) and alcohol **11** (23 mg). Confirmation of the epoxide was based on the IR($CHCl_3$) and NMR spectra. The alcohol was confirmed by the following evidence shown in (b).

(b) The material **5** (982 mg) and hematoporphyrin (22 mg) were dissolved in dry pyridine (14 ml). The soln was irradiated by four fluorescent tubes (20 W) for 97 hr in a stream of dry oxygen. The crude product (715 mg) was chromatographed on SiO_2 (16 g) column (1·8 × 20 cm) by elution with same solvent as above to give alcohol **11** (330 mg) [32% yield]. Recrystallization from $CHCl_3$–hexane two times afforded colourless crystals, m.p. 193–195°; IR ν_{max}: 3500; 3060; 1745; 1723; 910 cm^{-1}, $\nu_{max}^{CHCl_3}$: 3580; 3480; 1768; 1750; 1726; 1660; 908 cm^{-1}, NMR δ_{ppm}: 0·99 (3H, s); 1·20 (3H, s); 2·12 (1H, s, C-5—<u>H</u>); 2·89 (1H, m), 3·77 (3H, s, COOC<u>H</u>$_3$); 3·94, 4·10 (each 1H, AB-type, J = 11 Hz, C-20<u>H</u>$_2$); 4·23 (1H, broad s, C-15—<u>H</u>); 5·18, 5·28 (each 1H, broad s, C-17<u>H</u>$_2$). (Found: C, 68·01; H, 8·38. $C_{21}H_{30}O_5 \cdot 1/2\ H_2O$ requires: C, 67·90; H, 8·41%). Further elution gave a material (14 mg) which had lower Rf value than alcohol **11**; IR $\nu_{max}^{CHCl_3}$: 3450; 1765 (infl); 1752; 1725 cm^{-1}, NMR δ_{ppm}: 0·99 (3H, s); 1·21 (3H, s).

(c) The material **5** (290 mg) was dissolved in dry pyridine (12 ml) and eosin Y (15 mg) was added. The soln was irradiated by fluorescent tubes in a stream of O_2. After similar treatment to that described in (a), the crude product (283 mg) showed only a small spot of alcohol **11** on TLC($CHCl_3$: acetone = 95:5) besides a big spot of the starting material **5**.

Acetate **12**. Alcohol **11** (53 mg) was acetylated with Ac_2O (1 ml)–pyridine (1 ml) for 43 hr. Addition of MeOH and evaporation *in vacuo* gave a crude acetate (63 mg), which was chromatographed on SiO_2 (1·5 g) column (1 × 9 cm) by elution with $CHCl_3$ to yield *acetate* **12** (46 mg). Crystallization with petroleum–benzine and recrystallization from acetone–petroleum benzine afforded colourless rods, m.p. 182–184°.

IR ν_{max}: 3030; 1770; 1740; 1730; 1235; 912 cm^{-1}, NMR δ_{ppm}: 0·99 (3H, s); 1·20 (3H, s); 1·98 (3H, s); 2·13 (1H, s, C-5—H); 2·89 (1H, m); 3·69 (3H, s, $COOCH_3$); 3·91, 4·09 (each 1H, AB-type, J = 11 Hz, C-20 H_2). 5·13 (1H, broad s, C-15—H); 5·19, 5·59 (each 1H, broad s, C-17 H_2). (Found: C,67·66; H, 7·96, $C_{23}H_{32}O_6$ requires: C, 68·29; H, 7·97%).

Osmium tetroxide oxidation of acetate **12**

Glycol **13** *and glycol* **14**. Acetate **12** (63 mg) was allowed to react with OsO_4 (82 mg) in Et_2O (5 ml) and pyridine (3 drops) for 40 hr at room temp. The osmate was collected and dissolved in $CHCl_3$. H_2S gas was passed through the soln. The ppt was filtered and evaporation of filtrate gave a crude glycol (65 mg). The filtrate of osmate on similar treatment afforded an additional crop of crude glycol (11 mg), which showed nearly one spot on TLC ($CHCl_3$: acetone = 8:2). The chromatography of glycol (76 mg) on SiO_2 (2·7 g) by elution with $CHCl_3$-acetone (90:10) (30 ml) gave *glycol* **13** (22 mg), which was recrystallized from EtOAc-hexane to yield colourless crystals, m.p. 170–171°; IR ν_{max}: 3470; 1762; 1734 cm^{-1}, NMR δ_{ppm}: 0·96 (3H, s); 1·19 (3H, s); 2·01 (1H, s, C-5—H); 2·10 (3H, s); 3·61 (1H, s, OH); 3·72 (3H, s, $COOCH_3$); 3·80 (1H, s, C-15—H); 3·94 (2H, s, C-20 H_2); 4·32 (2H, AB-type, J = 12 Hz, C-17 H_2), Mass spectrum: M^+ *m/e* 438.

Elution with $CHCl_3$-acetone (80:20) (10 ml) afforded a mixture (5 mg) of **13** and **14**, and further elution (30 ml) gave the *glycol* **14** (27 mg), which was recrystallized from EtOAc-hexane to yield colourless crystals, m.p. 152–154°; IR ν_{max}: 3470; 1758; 1730; 1708 cm^{-1}, NMR δ_{ppm}: 0·96 (3H, s); 1·19 (3H, s); 2·03 (1H, s, C-5—H); 2·07 (3H, s); 2·97 (1H, broad s, OH); 3·63, 3·71 (each 1H, AB-type, J = 11 Hz, C-17 H_2); 3·70 (3H, s, $COOCH_3$); 3·93 (2H, s, C-20 H_2); 4·98 (1H, s, C-15—H).

Migration of acetyl group from glycol **14** *to glycol* **13**

Glycol **14** (5 mg), which contains very small amount of glycol **13** on TLC, was allowed to stand in $CHCl_3$ with a drop of conc HCl for 45 min at room temp. The product was isolated by extraction with CH_2Cl_2 in aq NaCl. It showed a single spot on TLC ($CHCl_3$: acetone = 80:20). After filtration on SiO_2 column, a reaction product was recrystallized from EtOAc-hexane to afford crystals (2 mg), which were identified with glycol **13** by IR (KBr) and TLC ($CHCl_3$: acetone = 80:20) comparisons. A fraction (1 mg) which seems to be triol was also obtained.

Diacetate **15**

(a) Monoacetate **13** on acetylation with Ac_2O-pyridine gave a crude diacetate (5 mg), which was chromatographed on SiO_2 (100 mg) by elution with CH_2Cl_2-acetone (90:10) to afford a pure *diacetate* **15** (3 mg).

(b) Monoacetate **14** on a similar acetylation and purification [chromatography on SiO_2 (150 mg) by elution with CH_2Cl_2-acetone (90:10)] gave diacetate **15** (5 mg); IR $\nu_{max}^{CHCl_3}$: 3550, 1758–1730; 1056; 1036; 1020 cm^{-1}, NMR δ_{ppm}: 0·96 (3H, s); 1·18 (3H, s); 2·02, 2·06 (each 3H, s); 2·03 (1H, s, C-5—H); 3·70 (3H, s, $COOCH_3$); 3·92 (2H, s, C-20 H_2); 4·04, 4·36 (each 1H, AB-type, J = 11·5 Hz, C-17 H_2); 5·21 (1H, d, J = 1·5 Hz, C-15—H).

Acyloin condensation with unsaturated lactone ester **5**

(a) A soln of **5** (497 mg, 1·456 mmole) in dry Et_2O (30 ml) was dropwise added under vigorous stirring into a soln of Na (174 mg, 5·2 eq) in a mixture of liquid NH_3 (50 ml) and dry Et_2O (30 ml) at −60° in an atmosphere of N_2. After 10 min, the blue violet colour disappeared, then Na (214 mg) was added, and further addition of the soln of **5** was followed over a period of 30 min. The reaction mixture was left at same temp for 2 hr. Excess Na was decomposed by addition of a mixture of EtOH–ET_2O, and NH_3 was evaporated by a stream of N_2. The residue was acidified with HCl, and extracted with Et_2O 3 times. Removal of acidic fraction (26 mg) by Na_2CO_3aq gave a neutral product (328 mg), which was chromatographed on SiO_2 (15 g) column (1·8 × 14 cm). By elution with $CHCl_3$ (120 ml) and $CHCl_3$-acetone (97:3) (20 ml), 6-*keto*-7-*hemiketal* **16** (86 mg) was obtained. It was recrystallized from EtOH 2 times to give colourless needles **16**, m.p. 141–145°; IR ν_{max}: 3470; 3030; 1715; 1640 cm^{-1}, NMR δ_{ppm}: 1·02 (3H, s); 1·36 (3H, s); 1·68 (3H, d, J = 1·5, C-16—CH_3); 2·16 (1H, s, C-5—H); 4·07 (2H, s, C-20 H_2); 4·22 (1H, s, OH); 5·17 (1H, d, J = 1·5 Hz, C-15—H).

A part of crystals **16**, dissolved in EtOH, was catalytically hydrogenated. The reaction product was recrystallized from EtOH 2 times to give pure colourless dihydro compound, which was identified with authentic sample by IR (KBr) and mixture melting point determination.

Further elution with same solvent (40 ml) yielded *diol* **17** (92 mg), which was recrystallized from Et_2O-hexane 3 times to give colourless crystals, m.p. 155·5–156·5°; IR ν_{max}: 3350; 1048; 1031; 815 cm^{-1}, NMR

δ_{ppm}: 1·06 (3H, s); 1·17 (3H, s); 1·72 (3H, d, J = 1·5, C-16—C$\underline{H}_3$): 3·93 (1H, m, C-6—$\underline{H}$); 4·02 (2H, s, C-20 $\underline{H}_2$); 5·11 (1H, q, J = 1·5 Hz, C-15—$\underline{H}$). (Found: C, 78·66; H, 10·59. $C_{20}H_{32}O_2$ requires: C, 78·89; H, 10·59%).

A part of these crystals was hydrogenated on PtO_2 in EtOH. Dihydro-compound, recrystallized from MeOH. was proved to be identical with the authentic specimen by IR (KBr) and mixture melting point determination.

Further eluate with $CHCl_3$-acetone (97:3) (80 ml) gave 7-*hemiketal-6-ol* **18** (85 mg), which was crystallized with hexane and recrystallized from $CHCl_3$-hexane to afford colourless crystals, m.p. 167·5–168°; IR ν_{max}: 3450; 3310; 1640 (broad); 813 cm^{-1}. Colourless needles obtained by crystallization and recrystallization from $CHCl_3$-hexane showed m.p. 229–234° and IR ν_{max}: 3500; 3360; 1660; 820 cm^{-1}. The IR spectrum in $CHCl_3$ of both crystals were identical; IR $\nu_{max}^{CHCl_3}$: 3590; 3430; 1603, 1060 cm^{-1}; NMR δ_{ppm}: 1·00 (3H, s); 1·06 (3H, s); 1·68 (3H, d, J = 1·5, C-16—C$\underline{H}_3$); 2·40 (1H, broad s, O$\underline{H}$); 2·98 (1H, s, O$\underline{H}$); 3·80 (1H, d, J = 4·5, C-6—$\underline{H}$); 3·90 (2H, s, C-20 $\underline{H}_2$); 5·99 (1H, q, J = 1·5 Hz, C-15—$\underline{H}$). (Found: C, 75·25; H, 9·51. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%).

Dihydro compound of **18**, colourless needles with m.p. 215–217°, was identified with the authentic sample.

Filtrate from recrystallization of diol **17** was chromatographed on SiO_2 (7 g) column (1·3 × 19 cm) using $CHCl_3$ for elution to give unknown crystals, which were estimated to be 7-*keto-6-hemiketal*, accompanied by a small amount of **17**. Recrystallization of the former from Et_2O-hexane yielded colourless needles, m.p. 143–151°; IR ν_{max}: 3500; 3030; 1718; 1642 cm^{-1}.

(b) Unsaturated lactone ester **5** (947 mg, 2·815 mmole) was dissolved in dry Et_2O (70 ml) and the soln was dropwise added to a soln of Na (342 mg, 1·32 eq) in NH_3 (150 ml) and dry Et_2O (70 ml) over a period of 1·5 hr in an atmosphere of N_2 at −75°. The mixture was stirred for an additional 2 hr under the same conditions. Decomposition of excess Na and usual treatment of the reaction mixture gave a neutral fraction (740 mg), which was crystallized from $CHCl_3$-hexane to give 6-*hemiketal-7-ol* **19** (276 mg, 30% yield). Recrystallization from Et_2O and acetone yielded pure colourless needles, m.p. 178·5–180°; IR ν_{max}: 3420; 3260; 3030 cm^{-1}, NMR δ_{ppm}: 1·10 (3H, s); 1·28 (3H, s); 1·72 (3H, s); 2·29 (1H, broad s, O$\underline{H}$); 3·25 (1H, s, O$\underline{H}$); 3·34 (1H, s, C-7—$\underline{H}$); 3·88 (2H, AB-type, J = 9 Hz, C-20 $\underline{H}_2$); 5·59 (1H, m, C-15—$\underline{H}$). (Found: C, 75·34; H, 9·73. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%). Chromatography of the residue of **19** on SiO_2 (10 g) using $CHCl_3$-acetone (95:5) gave a fraction (170 mg) mainly of 6-hemiketal-7-ol **19** and 7-hemiketal-6-ol **18** (178 mg, 20% yield).

(c) A soln of **5** (1·380 g, 3·99 mmole) in dry Et_2O (70 ml) was dropwise added under stirring into a soln of Na (477 mg, 1·3 eq) in NH_3 (200 ml) and dry Et_2O (80 ml) over a period of 1 hr in a N_2 atmosphere (−75°). After stirring for 2 hr, a usual treatment of the reaction mixture gave a crude product (1·11 g), which was chromatographed on SiO_2 (45 g) column (3 × 12·5 cm) using $CHCl_3$-acetone (95:5) for elution to yield diol fraction (202 mg) and 7-hemiketal-6-ol **18** (675 mg, 49·8% yield).

(d) Compound **5** (1·818 g) was dissolved in dry Et_2O (90 ml) and the soln was dropwise added into a soln of Na (628 mg, 1·3 eq) in NH_3 (200 ml) and dry Et_2O (70 ml) over a period of 1 hr at −75°. After a usual treatment of the reaction mixture, the neutral fraction (1·56 g) was refluxed with 0·05 N–NaOH for 2 hr. The product (1·8 g) was chromatographed on SiO_2 (40 g), and eluted with $CHCl_3$-acetone (95:5) and $CHCl_3$-acetone (90:10) to give **18** (500 mg), a mixture (24 mg) of **18** and **20** and triol **20** (18 mg), which was recrystallized from acetone-hexane and was identified with an authentic sample.

(e) Acidic fraction collected from above reactions was methylated with CH_2N_2 to give ester (320 mg) which was chromatographed on SiO_2 (15 g). Elution with $CHCl_3$ (100 ml) afforded the starting material **5** (240 mg), which was purified by recrystallization from MeOH and identified with the authentic sample by IR comparison.

Acyloin condensation of **5** *in the presence of trimethylsilylchloride*

(a) Sodium (310 mg) was added to dry toluene (30 ml) and the suspension was refluxed and crushed under vigorous stirring in N_2 atmosphere. After cooling to room temp, a soln of trimethylsilyl-chloride (500 mg) in dry toluene (1 ml) was added, and **5** (490 mg, 1·41 mmole), dissolved in dry toluene (10 ml), was dropwise added into the soln during 10 min. The mixture was refluxed under N_2 for 13·5 hr. The ppt was filtered, and the filtrate was evaporated *in vacuo* to give crude product (267 mg), which showed at least 7 peaks on GLC (SE-30 1·5%, 0·4 mm × 0·75 m, oven temp 180°). Crude product (100 mg) was distilled under reduced press to give distillate 1 (3 mg, 95–100°/0·9 mm Hg), distillate 2 (14 mg, 115°/0·9 mm Hg), distillate 3 (22 mg, 135°/0·9 mm Hg) and the residue (62 mg). Distillates 1 and 2 were shown to be mixtures of several products by NMR in which the signals due to trimethylsilyl ether were recognized between δ 0·0–0·2 ppm. IR $\nu_{max}^{CHCl_3}$ 1720; 1713; 1248; 878; 842 cm^{-1}.

(b) Unsaturated lactone **5** (175 mg, 0·505 mmolc) was treated with Na (46 mg, 1 eq) in toluene (10 ml) in the presence of trimethylsilyl chloride (233 mg) for 7 hr in a same manner as above. The filtrate was evaporated *in vacuo* to give crude product, to which THF (10 ml) and 3·5% HCl (2 ml) was added, and the mixture was refluxed in N_2 atmosphere for 1 hr. Then, it was concentrated and H_2O was added. Extraction with Et_2O 2 times gave a crude product (144 mg), which was chromatographed on SiO_2 (6 g) column (1·8 × 5·5 cm). Elution with CH_2Cl_2 (20 ml) recovered the starting material **5** (8 mg). The eluate with CH_2Cl_2-acetone (99:1) (40 ml) was a mixture (47 mg) and the following eluate with CH_2Cl_2-acetone (95:5) was shown to be **18** (47 mg), which was crystallized from $CHCl_3$-hexane and identified with the authentic specimen. The above mixture on TLC ($CHCl_3$: acetone = 90:10) gave a spot, whose R_f was identical with that of diol. besides unidentified 3 spots.

Distillate **2** (14 mg) contained no **18** on TLC. It was dissolved in a soln of THF (3 ml) and 3·5% HCl (0·5 ml) and refluxed for 1·5 hr to give a single product which was identified with **18** on TLC ($CHCl_3$: acetone = 90:10).

Isomerization of 6*-hemiketal-*7*-ol* **19** *into* 7*-hemiketal-*6*-ol* **18**

6-Hemiketal **19** (20 mg) was dissolved in 0·01N methanolic NaOH and was left at room temp for 1 hr, but no reaction was observed on TLC ($CHCl_3$:acetone = 90:10). Then, the mixture was refluxed for 30 min, and concentrated *in vacuo* after neutralization to give colourless needles (2 mg), m.p. 229–232°, which were shown to be identical with **18**. The filtrate was extracted with Et_2O and the extract was treated as usual to give additional crystals **18** (8 mg).

Acetate **22**: *ent-*7β,20*-epoxy-*6α,7α*-dihydroxykaur-*15*-ene* 6*-monoacetate*

7-Hemiketal **18** (157 mg) was allowed to react with Ac_2O-pyridine (1:1) at room temp overnight. Addition of MeOH and evaporation gave a crude acetate (170 mg), which was chromatographed on SiO_2 (4 g) column (1·3 × 10 cm) using $CHCl_3$ for elution to yield *acetate* **22** (151 mg). It was recrystallized from $CHCl_3$-hexane 2 times to give colourless crystals **22**, m.p. 154·5–155·5°; IR ν_{max}: 3550; 1727; 1240 cm^{-1}, NMR δ_{ppm}: 0·83 (3H, s); 1·11 (3H, s); 1·72 (3H, d, J = 1·5, C-16-C$\underline{H}_3$); 2·12 (3H, s); 3·42 (1H, s, O$\underline{H}$); 3·93 (2H, s, C-20 $\underline{H}_2$): 5·09 (1H, d, J = 5, C-6-$\underline{H}$); 5·73 (1H, q, J = 1·5 Hz, C-15-$\underline{H}$). (Found: C, 73·42; H, 9·09. $C_{22}H_{32}O_4$ requires: C, 73·30; H, 8·95%).

Photo-sensitized oxygenation of **22**.

Acetate **22** (323 mg) and hematoporphyrin (11 mg) were dissolved in dry pyridine (12 ml) and oxygen was passed through the soln under irradiation with fluorescent tubes (20W × 4). After 98 hr, the mixture was concentrated *in vacuo* below 40° and a soln of KI (0·6 g) in EtOH (10 ml) and AcOH (0·3 ml) was added and kept at room temp overnight. After decomposition of iodine liberated with $Na_2S_2O_3$aq followed by concentration *in vacuo* and addition of H_2O, the soln was extracted with Et_2O (50 ml) and treated as usual to afford a crude product (324 mg), which was crystallized from $CHCl_3$-hexane to give crystals **23** (170 mg). The filtrate was evaporated to give a residue (190 mg) which was chromatographed on SiO_2 (4 g) column (1·2 × 12 cm). Elution with CH_2Cl_2-acetone (95:5) (30 ml) gave a mixture (50 mg) (3 spots) and the following fraction (60 ml) afforded *compound* **23** (74 mg; total 244 mg, 71·5%), which was crystallized from $CHCl_3$-hexane to give crystals, m.p. 187–189°; IR ν_{max}: 3450; 3220; 1732; 1662; 1238 cm^{-1}, $\nu_{max}^{CHCl_3}$: 3650; 3450; 1723; 1662; 977; 922; 908 cm^{-1}, NMR δ_{ppm}: 0·88 (3H, s); 1·15 (3H, s); 2·16 (3H, s); 2·65 (1H, m); 3·33 (1H, m, O$\underline{H}$); 3·87, 4·05 (each 1H, AB-type, J = 10, C-20 $\underline{H}_2$); 4·26 (1H, s. C-15—$\underline{H}$); 4·37 (1H, m, O$\underline{H}$); 5·18 (1H, d, J = 5 Hz, C-6—$\underline{H}$); 5·13, 5·24 (each 1H, s, C-17 $\underline{H}_2$). (Found: C, 70·33; H, 8·68. $C_{22}H_{32}O_5$ requires: C, 70·18; H, 8·57%).

Fractions eluted with Et_2O (10 ml) and acetone (10 ml) were collected and recrystallized from MeOH 3 times to give *colourless needles* **24**, m.p. 204–205·5°; IR ν_{max}: 3370; 1725; 1638 cm^{-1}, NMR $\delta_{ppm}^{D_5\text{-pyridine}}$: 0·93 (3H, s); 1·08 (3H, s); 2·00 (3H, s); 4·03 (2H, s, C-20 $\underline{H}_2$); 4·56 (2H, d, J = 1·5, C-17 $\underline{H}_2$); 5·63 (1H, d, J = 5 Hz, C-6—$\underline{H}$); 6·67 (1H, m, C-15—$\underline{H}$), $\delta_{ppm}^{D_5\text{-pyr.}+D_2O}$: 0·92 (3H, s); 1·08 (3H, s); 2·12 (3H, s); 4·03 (2H, s, C-20 $\underline{H}_2$)4·54 (2H, d, J = 1·5, C-17 $\underline{H}_2$); 5·61 (1H, d, J = 5 Hz, C-6—$\underline{H}$); 6·62 (1H, m, C-15—$\underline{H}$). (Found: C, 70·40; H, 8·53. $C_{22}H_{30}O_5$ requires: C, 70·18; H, 8·57%).

Acetylation of **23**

(a) Compound **23** (348 mg) and anhyd NaOAc (410 mg) were dissolved in a soln of Ac_2O (20 ml) and $CHCl_3$ (40 ml) and refluxed for 22 hr. The reaction mixture was poured into cold H_2O, then concentrated. Extraction with $CHCl_3$ gave a crude acetate (345 mg), which was chromatographed on SiO_2 (10 g) column

(1·8 × 2 cm) using $CHCl_3$ for elution to separate a mixture (33 mg) of triacetate and diacetate, from which crystalline *diacetate* **27** (9 mg) was obtained by recrystallization, crystalline *diacetate* **27** (114 mg), and diacetate mixture (24 mg). The following fraction with $CHCl_3$-acetone (95:5) resulted in the recovery of the starting material (136 mg), which was acetylated with a soln of Ac_2O (10 ml) and $CHCl_3$ (10 ml) containing NaOAc (150 mg) for 10 hr to give crystalline **27** (60 mg) (total yield 47%) and amorphous diacetate mixture (31 mg). The best yield of **27** in the same procedures was 48·1%. The **27** was recrystallized from $CHCl_3$-light petroleum to give colourless crystals, m.p. 189–190°; IR ν_{max}: 3550; 1738; 1650; 1246; 902 cm^{-1}, $\nu_{max}^{CHCl_3}$: 3530; 1732 cm^{-1}, NMR δ_{ppm}: 0·83 (3H, s); 1·12 (3H, s); 1·99 (3H, s); 2·01 (3H, s); 3·72 (1H, s, O<u>H</u>); 3·83, 4·09 (each 1H, AB type, J = 9·5, C-20 <u>H_2</u>; the higher-field doublet has a long range coupling with J = 2); 5·19 (1H, d, J = 3, C-15-<u>H</u>); 5·24 (1H, d, J = 5 Hz, C-6—<u>H</u>); 5·49 (2H, broad s, C-17 <u>H_2</u>). (Found: C, 68·67; H, 8·38. $C_{24}H_{38}O_6$ requires: C, 68·87; H, 8·19%). Diacetate mixture (13 mg), dissolved in a soln of AcOH (1 ml) and H_2O (0·5 ml), was warmed on a water bath for 4 hr. After addition of H_2O, the soln was concentrated and extracted with Et_2O to yield crude product, which was chromatographed on SiO_2 to give crystalline diacetate **27** (5 mg).

(b) Acetylation of **23** with the following conditions afforded amorphous diacetate mixture. (i) The material was allowed to react with Ac_2O and pyridine at ca 80° for 5 hr. (ii) The material (64 mg) and anhydrous NaOAc (61 mg) were dissolved in a soln of Ac_2O (3 ml) and abs pyridine (5 ml) and heated for 1·1 hr on a boiling water bath. (iii) The material (23 mg) was dissolved in a mixture of Ac_2O (1 ml), pyridine (1 ml), and $CHCl_3$ (1 ml), and the soln was heated under reflux for 4·3 hr. (iv) The material (23 mg) was warmed together with a mixture of Ac_2O (1 ml), pyridine (1 ml), and $CHCl_3$ (2 ml) for 5 hr. (v) The material (40 mg) was warmed togehter with a mixture of Ac_2O (2 ml), NaOAc (45 mg) and $CHCl_3$ (1 ml) for 7·5 hr.

(c) Monoacetate **23** (22 mg) was mixed with Ac_2O (3 ml) and NaOAc (13 mg) and warmed for 8·5 hr to give a crude product, which was chromatographed on SiO_2 (1 g). Diacetate fraction (23 mg) isolated was recrystallized from $CHCl_3$-hexane to give crystals **27** (12 mg).

(d) Monoacetate **23** (190 mg) was allowed to react with Ac_2O (8 ml) in pyridine (7 ml) at 105–110° for 2 hr. The reaction mixture was concentrated to give a crude product which contained about equal amount of two substances on TLC. The product was chromatographed on SiO_2 (4 g) column (1·6 × 5·5 cm) using $CHCl_3$ for elution to give triacetate fraction (145 mg) and diacetate fraction (57 mg), which showed double spots on TLC [Kieselgel GF_{254} (Merck), plate 5 × 20 cm × 0·2 mm, $CHCl_3$-acetone (95:5)]. The column-chromatography of triacetate fraction collected from the above procedures on SiO_2 using $CHCl_3$ for elution 2 times gave a one spot fraction (50 mg), but it was shown to be a mixture of triacetates by NMR; IR $\nu_{max}^{CHCl_3}$: 1750; 1724; 1663 cm^{-1}.

(e) Monoacetate **23** (35 mg) was acetylated with Ac_2O (4 ml)-pyridine (1 ml) at ca. 80° for 1·5 hr. The crude product (41 mg) was subjected to preparative TLC [Kieselgel GF_{254} (Merck), plate 20 × 20 cm × 0·3 mm, $CHCl_3$-acetone (92:8)]. The diacetate bands were collected and eluted with $CHCl_3$-acetone to afford diacetate (30 mg), which was purified on silicic acid column. This diacetate, which showed a single spot with a little larger R_f value than the above **27**, was estimated to be 6,7-diacetate **25**: *ent*-7β,20-*epoxy*-6α,7α,15β-*trihydroxykaur*-16-*ene* 6,7-*diacetate*; IR $\nu_{max}^{CHCl_3}$: 3550; 1763; 1738 cm^{-1}, NMR δ_{ppm}: 0·88 (3H, s); 1·20 (3H, s); 2·00 (3H, s); 2·12 (3H, s); 2·81 (1H, s, O<u>H</u>); 3·88, 4·16 (each 1H, AB type, J = 9, C-20 <u>H_2</u>); 4·32 (1H, s C-15—<u>H</u>); 5·16, 5·24 (each 1H, broad 2, C-17—H_2); 6·13 (1H, d, J = 5 Hz, C-6—<u>H</u>).

Alcohol **26**: *ent*-7β,20-*epoxy*-6α,7α,15β-*trihydroxykaur*-16-*ene*

(a) A soln of triacetate fraction (50 mg) in Et_2O (10 ml) was dropwise added into a soln of LAH (145 mg, 3·9 mmole) in Et_2O (9 ml) over a period of 20 min. The reaction mixture was refluxed for 1 hr and the usual treatment gave a crude product (30 mg), which was crystallized from Et_2O to give colourless crystals, m.p. 172·5–181·5°, which were proved to be identical with **26** derived from procedure (b) by IR (KBr).

(b) Diacetate mixture and triacetate mixture were collected (70 mg) and were reduced with LAH (205 mg) in a similar manner as (a) to afford crystals (24 mg), which were recrystallized from $CHCl_3$-Et_2O 4 times to give *colourless needles* (**26**), m.p. 190–194·5°; IR ν_{max}: 3500; 3310; 3060; 1663 cm^{-1}, NMR δ_{ppm}: 1·05 (3H, s); 1·08 (3H, s); 3·80, 4·00 (each 1H, AB type, J = 9·5, C-20 <u>H_2</u>); 3·80 (1H, d, J = 4·5 Hz, C-6—<u>H</u>); 4·38 (1H, broad s, C-15—<u>H</u>); 5·17 (2H, m, C-17 <u>H_2</u>); 5·45 (1H, broad s, O<u>H</u>). (Found: C, 71·66; H, 9·15. $C_{20}H_{30}O_4$ requires: C, 71·82; H, 9·04%).

Acetylation of alcohol **26**. Alcohol **26** (22 mg) was acetylated with Ac_2O-pyridine (equal volume) at room temp overnight. The acetate (27 mg) was chromatographed on SiO_2 (700 mg) column (0·8 × 3·5 cm). Elution with CH_2Cl_2-acetone (95:5) gave diacetate (5 mg) and monoacetate fraction (20 mg), which was recrystallized from CH_2Cl_2-hexane and identified with **23** by IR (KBr, $CHCl_3$).

Lemieux–Johnson oxidation of diacetate **27**

(a) Diacetate **27** (62 mg) in THF (13 ml) and H_2O (10 ml) was treated with a piece of OsO_4. After 30 min, sodium metaperiodate (1 g) was added and left overnight. The soln was saturated with H_2S, filtered and extracted with Et_2O to yield a crude product, which was chromatographed on SiO_2 (3 g) and eluted with $CHCl_3$ and $CHCl_3$-acetone (90:10) to give colourless crystals (8 mg), m.p. 250–253°. They were identified by IR (KBr) with *ketomonoacetate* **32**, which was obtained by ozonolysis of **27** (*vide infra*).

(b) Diacetate **27** (11 mg) was dissolved in dioxan-H_2O (3:1) (3 ml) and stirred for 30 min with a piece of OsO_4 until darkness of the soln was reached to maximum. Then, sodium metaperiodate (7 mg, 1·3 eq) was slowly added and stirring was kept for 3 hr, when the second portion of periodate (8 mg) was added. After 16 hr at room temp, sodium metabisulphite was added and left for 10 min. Dilution with NaClaq and extraction with Et_2O gave a crude product (11 mg), which was chromatographed on SiO_2 (800 mg). Elution with $CHCl_3$ gave a mixture (3 mg) containing the starting material and further elution gave *aldehyde* **29** (1 mg), which was identified with an authentic sample (*vide infra*) by IR ($CHCl_3$). Following fraction with $CHCl_3$-acetone (50:50) gave *glycol* **28** (4 mg) identified by IR($CHCl_3$).

OsO_4 oxidation of diacetate **27**: *glycol* **28**: *ent*-7β,20-*epoxy*-6α,7α,15β,16β,17-*pentahydroxykaurane* 6,17-*diacetate*

Diacetate **27** (180 mg) was allowed to react with OsO_4 (270 mg) in Et_2O (7 ml) and pyridine (0·8 ml) for 19 hr at room temp, when Et_2O (3 ml) and pyridine (0·3 ml) were added. Chloroform was added into the reaction mixture to dissolve the osmate precipitated, then the osmate was decomposed with H_2S. The ppt was filtered, and evaporation of the filtrate gave a crude product (128 mg). The ppt was washed with MeOH, and evaporation of MeOH yielded further crude product (107 mg). The product (235 mg) was chromatographed on SiO_2 (1 g) using $CHCl_3$-acetone (80:20) for elution to give *glycol* **28** (124 mg, 60% yield); IR $\nu_{max}^{CHCl_3}$: 3380; 1730 cm^{-1}, NMR δ_{ppm}: 0·86 (3H, s); 1·12 (3H, s); 2·10 (3H, s); 2·11 (3H, s); 3·60 (1H, d, J = 1·5, C-15—H); 3·80; 3·98 (each 1H, AB type, J = 10·5, C-20 H_2: the higher field signal has a long range coupling with J = 1); 4·18 (2H, s, C-17 H_2); 5·07 (1H, d, J = 5 Hz, C-6—H).

Cleavage of glycol **28** *with sodium metaperiodate*: *aldehyde* **29**: *ent*-7β,20-*epoxy*-6α,7α,17-*trihydroxy*-15,16-*secokaurane*-15,16-*dione* 6,17-*diacetate*

Glycol **28** (111 mg), dissolved in MeOH (6 ml) containing a few drops of H_2O, was treated with sodium metaperiodate (500 mg) for 47 hr at room temp, during which time a small amount of $NaIO_4$ was added 2 times. The soln was diluted with H_2O and extracted with Et_2O to give crystals (80 mg). During extraction, crystals (28 mg) were separated between two phases. Crystals collected were recrystallized from $CHCl_3$-Et_2O to give pure *carbonyl compound* **29** (81 mg), colourless needles with m.p. 152–153°; IR ν_{max}: 3570; 3260; 2740; 1724; 1620; 1254; 1244 cm^{-1}, $\nu_{max}^{CHCl_3}$: 3550; 3030; 2740; 1728 cm^{-1}, NMR δ_{ppm}: 0·79 (3H, s); 1·09 (3H, s); 1·85 (1H, m, OH, $\frac{1}{2}H_2O$; H_2O of crystallisation); 2·00 (3H, s); 2·12 (3H, s); 3·63 (1H, s, OH); 3·79, 4·02 (each 1H, AB type, J = 10, C-20 H_2); 4·67 (2H, s, C-17 H_2); 5·00 (1H, d, J = 5 Hz, C-6—H); 9·57 (1H, s, CHO); mass spectrum: M^+ m/e 450. (Found: C, 62·47; H, 7·75. $C_{24}H_{34}O_8 \cdot 1/2\ H_2O$ requires: C, 62·72; H, 7·67%).

Triacetate **30**: *ent*-7β,20-*epoxy*-6α,7α,15β,16β,17-*pentahydroxykaurane* 6,7,17-*triacetate*

Glycol **28** (39 mg) was acetylated with Ac_2O (0·5 ml) and pyridine (0·5 ml) at room temp for 2 days. Addition of EtOH and evaporation gave an acetate mixture (2 spots), which was chromatographed on SiO_2 (10 g) column (0·8 × 7 cm) using $CHCl_3$-acetone (90:10) for elution to give *triacetate* **30** (20 mg); IR $\nu_{max}^{CHCl_3}$: 3520; 1770; 1736 cm^{-1}, NMR δ_{ppm}: 0·88 (3H, s); 1·19 (3H, s); 2·03 (6H, s, 2 × Ac); 2·10 (3H, s); 3·67 (2H, s, C-15—H and OH: treatment with D_2O gave 1H, d, J = 1·5, C-15—H); 3·71 (1H, m, OH); 3·82, 4·09 (each 1H, AB type, J = 10, C-20 H_2); 4·20 (2H, s, C-17 H_2); 6·03 (1H, d, J = 4 Hz, C-6—H).

Attempted mesylation of monoacetate **23**. Monoacetate **23** (32 mg), dissolved in dry pyridine (2 ml), was cooled with ice-H_2O, and methanesulphonyl chloride (250 mg) was added. The mixture was stirred for 3 hr at room temp and was poured into NaClaq containing crushed ice. Extraction with $CHCl_3$ resulted in the recovery of the starting material. More vigorous conditions, warming at 80° for 20 min after keeping for 2 days at room temp, gave a crude product containing many compounds on TLC.

Ozonolysis of diacetate **27**: *ketodiacetate* **31** *and ketomonoacetate* **32**

An equivalent amount of ozonized O_2 (0·785 mg O_3/min) was passed through a soln of **27** (140 mg) in dry EtOAc (40 ml) at −75°. The resultant ozonide was catalytically decomposed with neutral pre-reduced

Pd-C in EtOH overnight. Removal of the catalyst gave a crude product (136 mg), which was chromatographed on SiO_2 (4 g) column (1·2 × 10 cm). Elution with CH_2Cl_2-acetone (95:5) (15 ml) yielded a mixture (14 mg), then the following fractions (35 ml) gave *ketodiacetate* **31** (77 mg; 55% yield), which was recrystallized 3 times from $CHCl_3$-hexane to afford colourless triangular crystals, m.p. 201–204°; IR ν_{max}: 3550; 3430; 1752; 1738; cm^{-1}, $\nu_{max}^{CHCl_3}$: 3530; 1752; 1738 cm^{-1}, NMR δ_{ppm}: 0·85 (3H, s); 1·12 (3H, s); 1·68 (1H, O<u>H</u>, 1/2 H_2O: H_2O of crystallization); 2·00 (3H, s); 2·07 (3H, s); 3·83 (1H, s, O<u>H</u>); 3·87, 4·09 (each 1H, AB type, J = 10, C-20 <u>H_2</u>); 4·78 (1H, d, J = 2, C-15—<u>H</u>); 5·10 (1H, d, J = 6 Hz, C-6—<u>H</u>). (Found: C, 65·50; H, 7·47. $C_{23}H_{32}O_7$ requires: C, 65·69; H, 7·67%).

Elution with CH_2Cl_2-acetone (90:10) (10 ml) gave a mixture of **31** and **32**, and the following fraction (30 ml) yielded *monoacetate* **32** (6 mg), which was recrystallized from acetone to give colourless crystals, m.p. 250–253° (dec); IR ν_{max}: 3420; 3250; 1750; 1740; 1231 cm^{-1}, $\nu_{max}^{CHCl_3}$: 3450; 1749; 1728 cm^{-1}, NMR δ_{ppm}: 0·87 (3H, s); 1·14 (3H, s); 2·14 (3H, s); 3·80 (1H, d, J = 2, C-15—<u>H</u>); 3·90, 4·08 (each 1H, AB type, J = 10, C-20 <u>H_2</u>); 4·10 (1H, d, J = 2, C-15—O<u>H</u>); 4·36 (1H, s, C-7—O<u>H</u>); 5·16 (1H, d, J = 5·5 Hz, C-6—<u>H</u>); mass spectrum M^+ m/e 378 ($C_{21}H_{30}O_6$).

Acetylation of ketomonoacetate **32**. Monoacetate **32** (16 mg) and NaOAc (100 mg), dissolved in Ac_2O (1 ml) and $CHCl_3$ (1 ml), were refluxed for 8 hr. The soln was added into NaCl aq and extracted with CH_2Cl_2 to give crude diacetate (12 mg), which was chromatographed on SiO_2 (300 mg). Elution with CH_2Cl_2-acetone (95:5) gave diacetate (5 mg), which was comparatively identified with **31** by IR (KBr) and TLC.

Transformation of **31** *to* **32** *with* HCl. Diacetate **31** (19 mg) in $CHCl_3$ (1 ml) was kept with catalytic amount of conc HCl at room temp for 2 days. The soln was diluted with NaCl aq and extracted with $CHCl_3$ to yield a crude product (10 mg), which was chromatographed on SiO_2 to give ketomonoacetate **32** (6 mg). The IR (KBr) and TLC were completely identical with those of the authentic sample.

Hydrogenolysis of ketodiacetate **31**. Diacetate **31** (42 mg, 0·1 mmole), dissolved in dry dioxan (5 ml), was added under vigorous stirring over a period of 5 min at −65° (bath temp) to a soln of Ca (118 mg, 2·94 mmole) in NH_3 (30 ml).

Then, the reaction mixture was left at room temp for 1 hr under vigorous stirring. Excess Ca was decomposed by addition of NH_4Cl, then NH_3 was removed by a stream of N_2. Addition of H_2O and extraction with Et_2O gave a crystalline product (24 mg), which was recrystallized from EtOH and acetone to give colourless crystals, m.p. 256–260° (12 mg, 37% yield). The crystals were shown to be identical with the authentic specimen **3** (m.p. 255–260°) by mixture melting point determination and comparison of IR (KBr) spectra.

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