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TERPENOIDS—XIX[1]

CHEMICAL CONVERSION OF ENMEIN INTO *ENT*-15-KAURENE AND *ENT*-16-KAURENE

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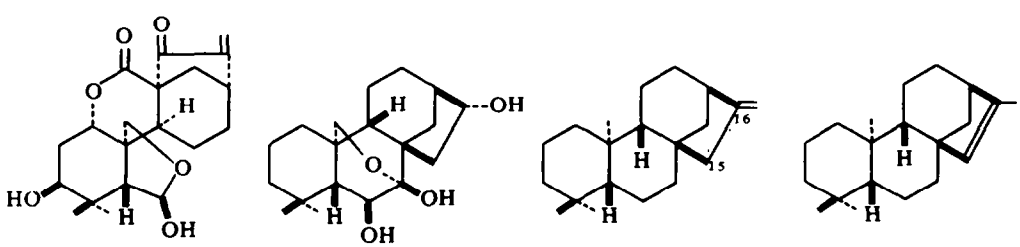
Abstract—Acyloin **6** and its acetate **7** were treated with zinc powder in acetic acid containing a trace of hydrochloric acid to yield unexpected *ent*-beyerane derivatives, **11** and **12**. Diol **15** was oxidized to keto-aldehyde **16**, which was subjected to Huang-Minlon modification of Wolff-Kishner reduction to give *ent*-15-kaurene(**4**), *ent*-16-kaurene(**3**), and *ent*-kaurane(**17**).

PREVIOUSLY, we[2] converted enmein(**1**), a major diterpenoid in the leaves of *Isodon trichocarpus* Kudo, into *ent*-kaurane (**17**) and provided chemical evidence for the absolute configuration of the former. Recently, we carried out a chemical conversion of enmein into a hemiketal diol (**2**)[3] which had been transformed into *ent*-16-kaurene (**3**). Thus, a formal chemical conversion of enmein into **3** has been achieved,[3] but by a rather roundabout route. Now, we attempted to convert enmein into **3** and its isomer, *ent*-15-kaurene (**4**), *via* a more convenient and shorter route. *ent*-16-Kaurene (**3**) is a metabolite from *Gibberella fujikuroi*[4] and also a major diterpene in the leaves of *Cryptomeria japonica* D. Don.[5] Moreover, it has been proved by Cross *et al.*[6] to be a precursor of gibberellin-A_3, and it must be a precursor of enmein. Thus, the present attempt seems interesting and significant.



1 **2** **3** **4**

CHART 1

First we tried the hydrogenolysis of 7-hemiketal derivative **6**,[3] a main product of the acyloin condensation with the lactone ester **5**[7] derived from enmein, in order to get a hemiketal **8**. Reaction of **6** with Zn powder in AcOH containing a trace of HCl, however, did not give the desired product **8**, but gave two products in rather low

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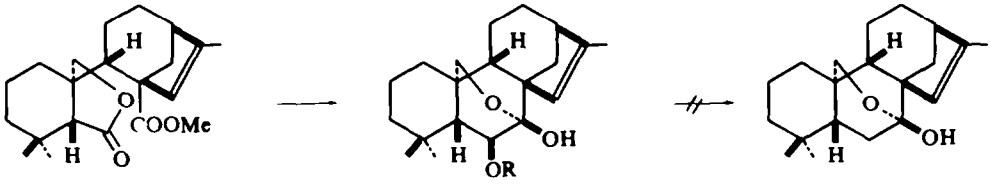
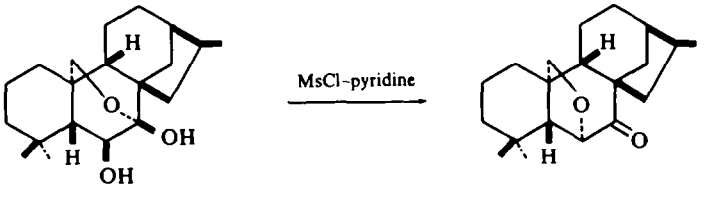
yield.* One of them had m.p. 145–149° and its IR absorption at 1717 cm^{-1} suggested the presence of a six-membered ring ketone. In its NMR spectrum, three singlets were observed at δ 0·93, 1·00, and 1·18, which indicated the presence of three Me groups on tertiary carbon atoms. From the high resolution mass spectrum† of this compound, the molecular formula, $C_{20}H_{29}O_2Cl$, was determined. A broad multiplet NMR signal of a proton attached to the carbon carrying the chlorine was recognized



5 **6** R = H, **7** R = Ac **8**

CHART 2

near δ 3·88. Considerations of these data and mechanism led to the assumption of an *ent*-beyerane type structure **11**. A broad singlet at δ 4·20 was assigned to C-6—H, while an AB type signal at δ 3·93 and 3·85 (J = 9 Hz) to C-20 H_2. The foregoing IR and mass spectral data also reasonably account for this structure. Such a 1,2 shift of the C—O bond accompanied by elimination as this has been recognized in the kaurene series,[8] as shown in Chart 3 (**9** → **10**).



9 **10**

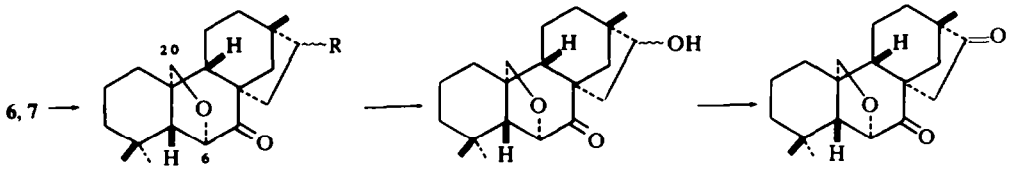
CHART 3

Another product, m.p. 189–193°, was deduced to have an AcO group from its IR($CHCl_3$) (1715 and 1250 cm^{-1}) and NMR (δ 2·02, s, —O—COC<u>H</u>$_3$, and 4·78, m, —C<u>H</u>—OAc) spectra. Its NMR spectrum exhibited three protons singlets at 0·93, 0·97, and 1·00, and an AB type signal at δ 3·92 and 3·80 (J = 8·5 Hz), suggesting the same skeleton as **11**. Its high resolution mass spectral pattern was similar to that of **11** especially in the field below M^+–AcOH. On the basis of these data, formula **12** was proposed for this product. In order to confirm this structure, **12** was hydrolysed with Na_2CO_3 to afford an alcohol **13**, m.p. 154–155°, which on oxidation with CrO_3 gave a diketone **14**, m.p. 172–174°. The structure of **14** was supported by IR($CHCl_3$)

* The same reaction with acetate **7** resulted in yielding the same products as in the reaction with **6**

† See Table 1 and Fig 1

(1739 and 1720 cm^{-1}) and mass spectral data. A strong negative Cotton effect in its ORD spectrum at about 300 nm also supported the stereochemistry of the rings C and D shown in **14**.[9]*



11 R = Cl
12 R = OAc

13 **14**

CHART 4

The high-resolution mass spectral data of **11** and **12** are given in Table 1, and their fragmentation pattern is shown in Fig 1.

TABLE 1. HIGH-RESOLUTION MASS SPECTRA OF **11** AND **12**

		Ions	Compositions	*m/e* Calcd.	*m/e* Obsd.
Compd. **11**	A	M^+	$C_{20}H_{29}O_2{}^{35}Cl$	336·186	336·184
	B	M^+–HCl	$C_{20}H_{28}O_2$	300·209	300·207
	C	B–CH_3	$C_{19}H_{25}O_2$	285·185	285·185
	D	B–CO	$C_{19}H_{28}O$	272·214	272·217
	E		$C_{10}H_{16}O$	152·120	152·117
	F		$C_{10}H_{15}O$	151·112	151·114
	G		$C_{10}H_{14}O$	150·104	150·105
Compd. **12**	A′	M^+	$C_{22}H_{32}O_4$	360·230	360·227
	H	M^+–CH_3	$C_{21}H_{29}O_4$	345·207	345·209
	B′	M^+–CH_3COOH	$C_{20}H_{28}O_2$	300·209	300·208
	C′	B′–CH_3	$C_{19}H_{25}O_2$	285·185	285·188
	D′	B′–CO	$C_{19}H_{28}O$	272·214	272·214
	E′		$C_{10}H_{16}O$	152·120	152·117
	F′		$C_{10}H_{15}O$	151·112	151·112
	G′		$C_{10}H_{14}O$	150·104	150·104

Now, we attempted another route from enmein to *ent*-kaurene involving diol **15** as key compound. Investigation of the reaction conditions led to success in getting the desired compound efficiently, that is, an acyloin condensation with **5** using about 8·3 times the calculated amount of Na gave diol **15** as main product.† Epoxide **20**, m.p. 199–201°, prepared from a reaction of **15** with perbenzoic acid, exhibited a three proton singlet at δ 1·23, a six proton singlet at δ 1·47, and a one proton singlet

* An ORD spectrum of compound **12** showed a positive Cotton effect at almost the same wave length, but it was overcome by an opposite Cotton effect due to C-16 ketone in compound **14**.

† For the investigation of the reaction conditions carried out so far, see references 1[b] and 3.

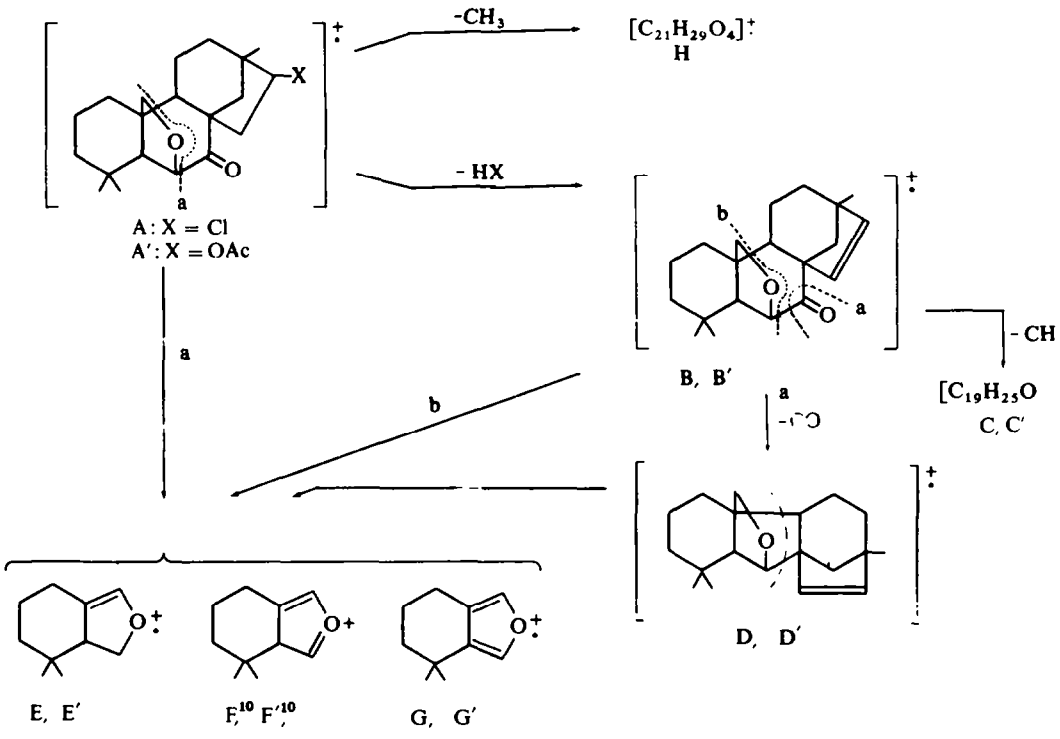


FIG 1. Fragmentation patterns of **11** and **12***

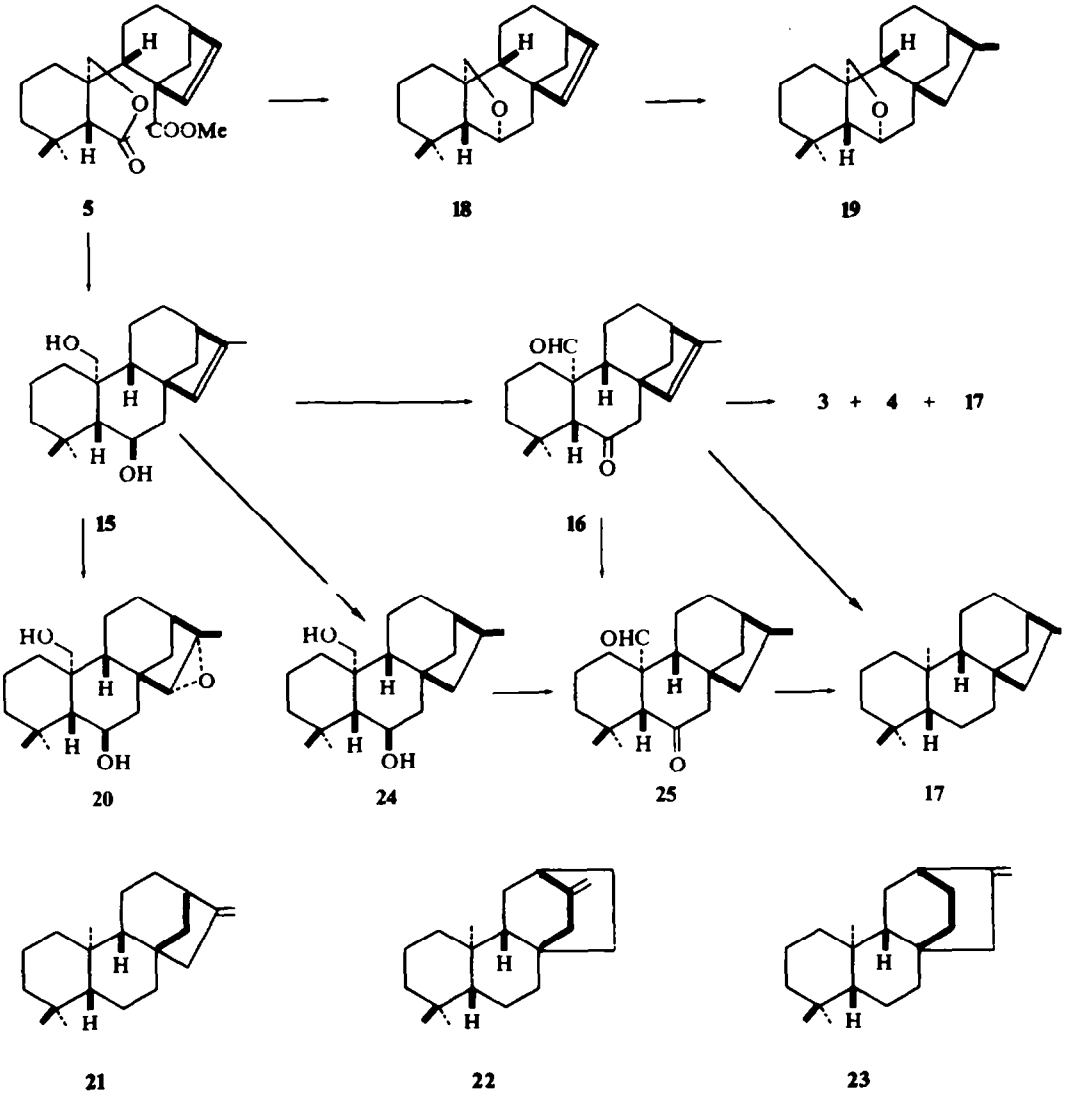
at δ 3·07 (assignable to C-15—H) supporting the presence of a double bond between C-15 and C-16 in the original diol. Catalytic hydrogenation of **15** yielded the known saturated diol **24**.[2] Thus, structure **15** was established.

The use of a greater excess of Na in the acyloin condensation resulted in the formation of an ether **18**, which might be derived from **15**. The structure was deduced from NMR and mass spectra, and was established by hydrogenation to the known compound **19**.[2]

The key compound **15** on Jones oxidation gave the desired keto-aldehyde **16** in good yield. The spectral data supported the structure. The Nagata's modification[11] of the Wolff–Kishner reduction on **16** under the presence of hydrazine hydrochloride did not give the desired *ent*-15-kaurene (**4**), but afforded only *ent*-kaurane **17**[2] in 29% yield.† A reaction of **16** with Na and 98·5% hydrazine in MeOH for 14 hr in a sealed tube according to Wenkert's procedure[12] gave a mixture of **4**, **3**, and **17** (3:1:1), but its yield was very poor. Reaction under stronger conditions, the so-called Barton-like Huang–Minlon's modification,[13] heating of **16** with Na and anhyd hydrazine at 180–190° in triethyleneglycol for 24 hr gave a fairly good yield of crude crystals, which were analysed by gas chromatography to be a mixture of **4**, **3**, and **17** in a ratio of 5:2:3. Chromatography on silica gel containing 2·5% $AgNO_3$ succeeded in separation into **17**, **3**, and **4**. Each was identified by comparing

* Symbols A ~ H and A' ~ G' correspond to those in Table 1.

† The mechanism of hydrogenation during this reaction will be discussed elsewhere



5 18 19

15 16

20 24 25 17

21 22 23

CHART 5

the IR spectrum, TLC, and GC with those of the authentic samples, 17,[2] 3,[4] and 15-kaurene,[13] and by m.m.p. determination for the first two. The yields of **17**, **3**, and **4** from **16** were 10, 5, and 18%, respectively. Thus, the attempted chemical conversion of enmein into *ent*-15-kaurene and *ent*-16-kaurene was accomplished. As the chemical conversion of *ent*-16-kaurene into *ent*-phyllocladene (**21**), atisirene (**22**), and neo-atisirene (**23**) has been reported by McCrindle *et al.*,[14] so the present work means a formal chemical conversion of enmein into these three diterpenes.

Previously, we tried unsuccessfully a chemical transformation of ketoaldehyde **25** into *ent*-kaurane (**17**) by Wolff–Kishner reduction.[2] Now, the same compound (**25**),

m.p. 143–144°,* prepared from diol **24** by Jones oxidation, was subjected to the Huang–Minlon modification of Wolff–Kishner reduction to give 55% of **17**. The steric effect of the Wolff–Kishner type reaction at C-6 carbonyl group in **16** and **25** seems less than expected.

The migration of the double bond observed in the Wolff–Kishner reaction of **16** might be due to an abstraction[15] of the proton at the allylic position by base in the medium under the reaction conditions. In this connection, **3** was heated with Na in diethyleneglycol and EtOH at 180–190° for 22 hr to give a mixture of **3** and **4** in a ratio of 1:1·4, which was separated by column chromatography on silica gel containing 2·5% of $AgNO_3$ into each component. It has been reported that treatment of **3** with I_2[13] or acids[16, 17] afforded a mixture of several diterpenes possessing the rearranged nucleus. In the basic treatment, however, no rearrangement was observed.

EXPERIMENTAL

All m.ps were determined by a micro m.p. apparatus (Yanagimoto) and are uncorrected. Unless otherwise stated, IR spectra were recorded for $CHCl_3$ soln on a Hitachi model EPI-S2 spectrophotometer, NMR spectra in $CDCl_3$ with TMS as an internal standard on a Varian A-60 spectrometer, and mass spectra on a JEOL model JMS-OISG mass spectrometer. The ORD spectra were taken on a JASCO model ORD/UV-5. Hitachi model F-6 equipped with Golay-type capillary column (45 m) coated with SE-30 and hydrogen flame ionization detector were used for gaschromatography. Extracts were dried over anhyd Na_2SO_4. Merck Kieselgel (0·05–0·2 mm) and Mallinckrodt silicic acid were used for column chromatography. The TLC plates were coated with Merck Kieselgel G.

ent-6,20-*Epoxy*-16-*chlorobeyeran*-7-*one*(**11**) *and* ent-6,20-*epoxy*-16-*acetoxybeyeran*-7-*one*(**12**). (a) To a suspension of 7-hemiketal **6** (132 mg) in AcOH (10 ml)–HCl (0·5 ml), dried Zn powder (500 mg) was added. The mixture was heated at 130–140° (oil bath) for 23 hr, and filtered. Evaporation of the filtrate *in vacuo* gave a gummy residue (104 mg), which was chromatographed on SiO_2 (5 g) column. The first fraction eluted with $CHCl_3$ (30 ml) was evaporated and the eluate was crystallized and recrystallized from EtOH to give ent-6,20-*epoxy*-16-*chlorobeyeran*-7-*one*(**11**) (19 mg) as colourless fine crystals, m.p. 145–149°: ν_{max}: 1717 cm^{-1}: NMR δ_{ppm}: 0·93 (3H, s): 1·00 (3H, s): 1·18 (3H, s): 3·93, 3·85 (each 1H, AB type, J = 9 Hz, C-20 $\underline{H}_2$): 3·88 (1H, m, C-16'–$\underline{H}$): 4·20 (1H, br s, C-6–$\underline{H}$): mass spectrum M^+ *m/e* 336·184 ($C_{20}H_{29}O_2Cl$ requires: 336·186): Beilstein's test: positive: ORD (*c* 0·040, dioxane): $[\Phi]_{360}$ −3696, $[\Phi]_{334}$ −4704. $[\Phi]^{max}_{322}$ −1680, $[\Phi]_{312}$ −4704, $[\Phi]_{310}$ −3696, $[\Phi]_{306}$ −6384, $[\Phi]_{296}$ −11760, $[\Phi]_{276}$ −14784, $[\Phi]_{250}$ −18,480.

The following fraction eluted with $CHCl_3$ (20 ml) was treated as usual to give ent-6,20-*epoxy*-16-*acetoxybeyeran*-7-*one*(**12**) (20 mg) as colourless fine crystals (from EtOH), m.p. 189–193°: ν_{max}: 1715: 1250 cm^{-1}: NMR δ_{ppm}: 0·93 (3H, s): 0·97 (3H, s); 1·00 (3H, s): 2·02 (3H, s): 3·80, 3·92 (each 1H, AB type, J = 8·5 Hz, C-20 $\underline{H}_2$): 4·20 (1H, br s, C-6–$\underline{H}$): 4·78 (1H, br m, C-16–$\underline{H}$): mass spectrum M^+ *m/e* 360·227 ($C_{22}H_{32}O_4$ requires: 360·230): ORD (*c* 0·049, dioxane): $[\Phi]_{360}$ −1176, $[\Phi]_{334}$ −2057, $[\Phi]^{max}_{322}$ −294, $[\Phi]_{308}$ −2057, $[\Phi]_{294}$ −4702, $[\Phi]_{274}$ −5878, $[\Phi]_{236}$ −8229, $[\Phi]_{212}$ −25861.

(b) To a suspension of compound **7** (86 mg) in AcOH (7 ml)–HCl (0·5 ml), dried Zn powder (350 mg) was added. The mixture was heated at 130–140° (oil bath) for 20 hr. A usual work up of the mixture and chromatography of the crude product (48 mg) on SiO_2 (4 g) column with elution by $CHCl_3$ gave **11** (7 mg) and **12** (15 mg) as crystals (from EtOH).

ent-6,20-*Epoxybeyeran*-7-*on*-16-*ol* (**13**). A suspension of acetate **12** (15 mg) in a mixture of MeOH (1·5 ml) and conc Na_2CO_3aq (0·5 ml) was stirred overnight, but no reaction occurred. Then, the mixture was heated at 110° (oil bath) for 6 hr. Work up and purification of the crystalline crude product (10 mg) by chromatography on SiO_2 column by elution with $CHCl_3$ and $CHCl_3$–Me_2CO (9:1) afforded ent-6,20-*epoxybeyeran*-7-*on*-16-*ol* (**13**) (6 mg) as colourless needles (from MeOH), m.p. 154–155°: ν_{max}: 3427: 1715 cm^{-1}: NMR $\delta^{CDCl_3-D_2O}_{ppm}$: 0·92 (3H, s): 1·00 (6H, s): 3·63 (1H, m, C-16–$\underline{H}$): 3·74, 3·84 (each 1H, AB type, J = 9 Hz, C-20 $\underline{H}_2$): 4·12 (1H, s, C-6–$\underline{H}$): mass spectrum M^+ *m/e* 318 ($C_{20}H_{30}O_3$ requires: 318).

* We reported m.p. 87–116° for this compound,[5] but now, the purified sample was found to have the datum shown

ent-6,20-*Epoxybeyerane*-7,16-*dione* (**14**). To a soln of alcohol **13** (4 mg) in anhyd pyridine (0·5 ml), a soln (0·5 ml) of a small excess amount of CrO_3–pyridine complex in pyridine was added, and the mixture allowed to stand overnight. Work up gave ent-6,20-*epoxybeyerane*-7,16-*dione* (**14**) (2·5 mg) as fine needles (from MeOH), m.p. 172–174°: ν_{max}: 1739: 1720 cm^{-1}: mass spectrum: M^+ *m/e* 316·202 ($C_{20}H_{28}O_3$ requires: 316·204): ORD (*c* 0·090 dioxane): $[\Phi]_{396}$ −1966, $[\Phi]_{350}$ −3511, $[\Phi]_{332}$ −5618, $[\Phi]^{max}_{319}$ −10246, $[\Phi]_{310}$ −4915, $[\Phi]_{300}$ 0, $[\Phi]^{max}_{289}$ +3932, $[\Phi]_{252}$ −8482. a ≒ −142 D.

Acyloin condensation with methyl ent-6,7-*secokaur*-15-*en*-6,20-*olide*-7-*oate* (**5**). (a) In a mixture of anhyd Et_2O (60 ml) and liquid NH_3 (*ca* 300 ml), Na (2 g) was added and dissolved under stirring. Then, a soln of the material **5** (1·25 g) in anhyd Et_2O (60 ml) was dropwise added into the above soln over a period of 1 hr under stirring in an N_2 atmosphere. After further stirring for 2 hr, a mixture of MeOH–Et_2O (1:3) was slowly added until the blue colour of excess of Na disappeared. Evaporation of NH_3, neutralization with cold 10% HCl, extraction with Et_2O, followed by a usual work up of the ethereal extract gave a gummy crude product, purified by chromatography on SiO_2 column (50 g) by elution with CH_2Cl_2 to yield *ent*-15-kaurene-6α, 20-diol (**15**) (568 mg) as colourless crystals (from Et_2O). Identification was accomplished by comparisons with m.p. and IR of the authentic sample.[3]

(b) A soln of the material **5** (1·3 g) in anhyd Et_2O (60 ml) was added into a soln of Na (5 g) in NH_3 (300 ml) and Et_2O (100 ml) under stirring over a period of 1 hr, then the mixture was stirred for further 3 hr. A usual work up and purification of the crude product by chromatography on SiO_2 (50 g) column by elution with CH_2Cl_2 afforded ent-6,20-*epoxy*-15-*kaurene* (**18**) (120 mg) from the first fraction (70 ml) as colourless fine needles (from Me_2CO), m.p. 90–93°: ν_{max}: 1050: 1030 cm^{-1}: NMR δ_{ppm}: 0·91 (3H, s): 0·96 (3H, s): 1·72 (3H, d, *J* = 1·5, C-16 $C\underline{H}_3$): 3·66, 4·09 (each 1H, AB type, *J* = 9 Hz, C-20 $\underline{H}_2$): 4·20 (1H, m. C-6—$\underline{H}$): 5·10 (1H, m, C-15—$\underline{H}$): mass spectrum: M^+ *m/e* 286·230 ($C_{20}H_{30}O$ requires: 286·230). The following fractions (90 ml) afforded the known 6-keto-7-hemiketal(ent-7β,20-epoxy-15-kauren-6-on-7α-ol)[3] (7 mg) as colourless needles (from Me_2CO) and the foregoing diol **15** (160 mg) as crystals (from Et_2O).

Unsaturated ether **18** (10 mg), dissolved in MeOH (1·5 ml), was mixed with PtO_2 (*ca* 6 mg) and AcOH (2 drops), and subjected to hydrogenation to give a saturated ether **19** (3 mg) as colourless needles (from Me_2CO), whose m.p. and IR were identical with those of an authentic sample.[2] Mass spectrum: M^+ *m/e* 288 (Calcd. for $C_{20}H_{32}O$: 288).

ent-15β,16β-*Epoxykaurane*-6α,20-*diol* (**20**). To a soln of diol **15** (133 mg) in $CHCl_3$–benzene (2:1) (3 ml), a $CHCl_3$ soln (1·5 ml) containing perbenzoic acid (96 mg) was added, and the mixture kept under cooling overnight. A usual work up gave a crude product (70 mg), chromatographed on SiO_2 column by elution with CH_2Cl_2 to afford ent-15β,16β-*epoxykaurane*-6α,20-*diol* (**20**) (64 mg) as colourless needles (from MeOH–Et_2O), m p. 199–201°: ν^{KBr}_{max}: 3360: 1265: 912: 840 cm^{-1}: NMR $\delta^{C_5D_5N-D_2O}_{ppm}$: 0·88, 1·80 (each 1H, AB type, *J* = 13 Hz, C-14 $\underline{H}_2$): 1·23 (3H, s): 1·47 (6H, s): 3·07 (1H, s, C-15 $\underline{H}$): 4·18 (2H. br s. C-20 $\underline{H}_2$): 3·96–4·47 (1H, br m, C-6—$\underline{H}$): mass spectrum: M^+ *m/e* 320·235 ($C_{20}H_{32}O_3$ requires: 320·235).

ent-*Kaurane*-6α,20-*diol* (**24**). Diol **15** (100 mg) was dissolved in MeOH-n-hexane (1:1) (10 ml), and PtO_2 (10 mg) added. The mixture was stirred for 48 hr under H_2 and treated as usual to yield a crystalline product (95 mg), which was recrystallized from Et_2O to give colourless needles (80 mg). This compound proved to be identical with an authentic sample of *ent*-kaurane-6α,20 diol (**24**)[2] by IR, TLC, and m.p. NMR $\delta^{CD_3COCD_3}_{ppm}$: 1·03 (3H, d, *J* = 7 Hz): 1·07 (3H, s): 1·18 (3H, s): 3·70–4·10 (1H, br m, C-6- $\underline{H}$): 4·02 (2H, s, C-20 $\underline{H}_2$).

ent-15-*Kauren*-6-*on*-20-*al* (**16**). To a soln of diol **15** (93 mg) in Me_2CO (treated with $KMnO_4$ and purified) (20 ml), a small excess of Jones reagent was slowly added under cooling and stirring in N_2 atmosphere. After the mixture was stirred for a further 25 min, the mixture was slowly added onto a cooled conc NaCl aq, and extracted with Et_2O. A usual work up of the extract gave a crystalline crude product (69 mg), whose recrystallization from MeOH yielded ent-15-*kauren*-6-*on*-20-*al* (**16**) (52 mg) as colourless needles, m.p. 113–115°: ν_{max}: 2735: 1710 cm^{-1}: NMR δ_{ppm}: 1·01 (3H, s): 1·07 (3H, s): 1·71 (3H, d, *J* = 1·6, C-16 $C\underline{H}_3$): 2·25, 2·91 (each 1H, AB type, *J* = 12·5 Hz, C-7 $\underline{H}_2$): 2·43 (1H, s, C-5 $\underline{H}$): 5·18 (1H, m, C-15—$\underline{H}$): 10·5 (1H, s, C-20- $\underline{H}$): mass spectrum: M^+ *m/e* 300·212 ($C_{20}H_{28}O_2$ requires: 300·209). (Found: C, 73·28: H, 9·65. $C_{20}H_{28}O_2 \cdot 1{\cdot}5\ H_2O$ requires: C, 73·35: H, 9·54%).

Wolff–Kishner reduction of **16**. (a) Nagata's modification. Hydrazine hydrochloride (380 mg) and keto-aldehyde **16** (30 mg) were added to a mixture of 98·5% hydrazine (3 ml) and triethyleneglycol (4 ml), and the mixture was heated at 140–150° for 14 hr. After cooling, KOH pellets (2 g) were added, and the temperature slowly raised to 150°. The mixture was heated at 150–180° for 2 hr, and at 200–210° for 3 hr. After cooling to room temperature, H_2O (*ca* 10 ml) was added, and the mixture extracted with Et_2O. Work up and purification by chromatography on SiO_2 column by elution with n-hexane gave colourless needles (7 mg),

which were proved to be *ent*-kaurane (**17**) by comparison with an authentic sample[2] (m.p., IR, GC, and mass spectrum).

(b) Wenkert's procedure. In a soln of Na (50 mg) in MeOH (0·3 ml), a soln of keto-aldehyde **16** (22 mg) in MeOH (0·2 ml) and 98·5% hydrazine (0·4 ml) were added, and the mixture heated at 160–170° (oil bath) for 14 hr (sealed tube). The crude product obtained by a usual work up, dissolved in n-hexane, was filtered through a SiO_2 column. The filtrate on evaporation gave a gummy residue (1·5 mg), which crystallized from MeOH as colourless needles. Gas chromatography showed that the product consists of *ent*-kaurane (**17**), *ent*-16-kaurene (**3**), and *ent*-15-kaurene (**4**) in a ratio of 1:1:3.

(c) Huang-Minlon modification under Barton's conditions. To a mixture of anhyd triethyleneglycol (2 ml), Na (90 mg), and anhyd hydrazine (300 mg), keto-aldehyde **16** (169 mg) was added, and the mixture heated at 180–190° for 4 hr. The temperature was raised to 220–230° 8 times at intervals of 15 min to distill off the excess of hydrazine and H_2O. The mixture was further heated at 180–190° for 8 hr. After the accomplishment of the reaction was recognized on TLC (silica gel containing 2·5% of $AgNO_3$: cyclohexane), H_2O (*ca* 20 ml) was added. Extraction with CH_2Cl_2, washing with conc NaCl aq, drying, and distillation of solvent gave a crude product mixture, whose soln in cyclohexane was filtered through a SiO_2 column. The filtrate on concentration afforded colourless needles (14 mg). Gas chromatography showed that the product consisted of *ent*-15-kaurene (**4**), ent-16-kaurene (**3**), and *ent*-kaurane (**17**) in a ratio of 5:2:3.

To a soln of $AgNO_3$ (500 mg) in H_2O (*ca* 60 ml), Malinckrodt silica gel (20 g) was added and mixed sufficiently, then the homogeneous mixture dried at 100° under alternate additions of MeOH and Me_2CO to give a fine powder. This powder containing 2·5% of $AgNO_3$ was suspended in petroleum ether (b.p. 30–70°), and the suspension put in a column 1 cm in diameter. The foregoing crude mixture was chromatographed on this column and the following fractions of 2 ml each were separated: (1) fractions 2–7 (eluted with petroleum ether), (2) fractions 14–26 (eluted with petroleum ether), and (3) fractions 35–44 (eluted with $CHCl_3$). From (1), (2), and (3), *ent*-kaurane (**17**) (15 mg: 10%), *ent*-16-kaurene (**3**) (8 mg: 5%), and *ent*-15-kaurene (**4**) (26 mg: 18%) were isolated, respectively. *ent*-Kaurane (**17**) was identified with an authentic sample[2] (m.p., m.m.p.: 86°; IR; GC; mass spectrum). *ent*-16-Kaurene (**3**) was identified with an authentic sample[4] (m.p., m.m.p.: 49–50°: IR: GC: mass spectrum). ν_{max}^{KBr}: 1650: 870 cm^{-1}: NMR δ_{ppm}: 0·80 (3H, s): 0·84 (3H, s): 1·02 (3H, s): 4·78 (2H, m, C-17 $\underline{H}_2$): ORD: negative plain curve: GC (oven temp: 170°: injection temp: 220°) retention time: 10·2 min: mass spectrum: M^+ *m/e* 272 (Calc. for $C_{20}H_{32}$: 272). *ent*-15-Kaurene (**4**), m.p. 67·5–68·5°, $[\alpha]_D^{28}$ −14° (*c* = 1, $CHCl_3$), was proved to be the enantiomer of an authentic sample of 15-kaurene,[13] m.p. 66–67°, $[\alpha]_D^{25}$ +12° (*c* = 1, $CHCl_3$). ν_{max}^{KBr}: 1640: 820 cm^{-1}: NMR δ_{ppm}: 0·80 (3H, s): 0·83 (3H, s): 1·03 (3H, s): 1·99 (3H, d, *J* = 1·3, C-16—C$\underline{H}_3$): 5·50 (1H, *q*, *J* = 1·3 Hz, C-15—$\underline{H}$): ORD: negative plain curve: GC retention time: 8·8 min: mass spectrum: M^+ *m/e* 272 (Calc. for $C_{20}H_{32}$: 272).

Isomerization of ent-16-*kaurene into* ent-15-*kaurene*. In a soln of Na (90 mg) in anhyd EtOH (0·5 ml) and anhyd diethyleneglycol (2 ml), *ent*-16-kaurene (**3**) (100 mg) was added, and the mixture heated at 180–190° for 22 hr. Extraction with CH_2Cl_2 after addition of H_2O followed by a usual treatment of the extract gave an oily substance. It was dissolved in cyclohexane and filtered through SiO_2. The filtrate was concentrated to afford colourless needles (76 mg). Gas chromatography showed the crystals to be a mixture of *ent*-16-kaurene (**3**) and *ent*-15-kaurene (**4**) in a ratio of 1:1·4, so the mixture was chromatographed on a column of SiO_2 containing 2·5% of $AgNO_3$ by elution with cyclohexane and CH_2Cl_2 to separate *ent*-16-kaurene (**3**) (24 mg: colourless needles recrystallized from Me_2CO) and *ent*-15-kaurene (**4**) (48 mg: colourless needles recrystallized from Me_2CO).

ent-*Kauran-6-on-20-al* (**25**). To a soln of diol **24** (53 mg) in Me_2CO (6 ml), a small excess of Jones reagent was slowly added under cooling. After the mixture was stirred for 25 min with cooling, it was poured into NaCl aq (10 ml), and extracted with Et_2O. Work up gave a crude crystalline product (53 mg), which was purified by chromatography on SiO_2 column with elution by CH_2Cl_2 to yield *ent*-kauran-6-on-20-al (**25**) (33 mg) as colourless needles (from Me_2CO), m.p. 143–144°: ν_{max}: 2730: 1705 cm^{-1}: NMR δ_{ppm}: 1·02 (3H, d, *J* = 6·5): 1·03 (3H, s): 1·10 (3H, s): 2·25, 2·81 (each 1H, AB type, *J* = 12, C-7 $\underline{H}_2$): 2·45 (1H, s, C-5—$\underline{H}$): 10·03 (1H, d, *J* = 1 Hz, C-20—$\underline{H}$): mass spectrum: M^+ *m/e* 302·227 (Calc for $C_{20}H_{30}O_2$: 302·225).

Huang-Minlon reduction of keto-aldehyde **25**. To a soln of Na (50 mg) in anhyd triethyleneglycol (1 ml), anhyd hydrazine (60 ml) and keto-aldehyde **25** (32 mg) were added. The mixture was heated at 180–190° for 16 hr. The temperature was raised up to 220–230° 10 times at intervals of 15 min to distill off the excess of hydrazine and H_2O. Further, heating at 180–190° was continued for 10 hr. Work up yielded colourless

needles (16 mg) (from Me_2CO), which were proved to be identical with an authentic sample of *ent*-kaurane (**17**). (m.p. and IR).

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