Terpenoids. Part 8.[1] Partial Syntheses of *ent*-11β-, 12α-, and 12β-Hydroxykaur-16-en-19-oic Acids from Grandiflorenic Acid

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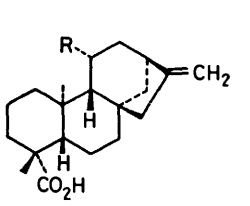
The partial syntheses of the title compounds are described from grandiflorenic acid [*ent*-kaura-9(11),16-dien-19-oic acid]. Some unsuccessful routes are also discussed.

In recent years several 11- and 12-hydroxygibberellins have been isolated from higher plants.[2] The partial synthesis of these gibberellins from accessible fungal gibberellins presents difficulties. However, the mutant B1-41a of the fungus, *Gibberella fujikuroi*, has been shown [3-6] to convert analogues of the natural gibberellin precursor, *ent*-kaurenoic acid (1), into analogues of the normal fungal gibberellins. This paper describes the partial synthesis of *ent*-11β-, 12β-, and 12α-hydroxykaurenoic acids (2), (3), and (4) from grandiflorenic acid [*ent*-kaura-9(11),16-dien-19-oic acid] (5). The microbiological metabolism of these acids will be described in a subsequent publication.

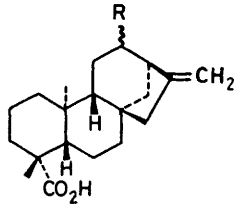
The starting compound, grandiflorenic acid (5), has been isolated from several sources,[7] the most common being *Espeletia* species. It has been isolated by two groups [8-10] from the resin gall from *E. schultzii*, and this was our source. In our hands, methanol extraction was found to be more effective than the light petroleum or diethyl ether used by the previous workers.[8-10] Column chromatography of the acids from the methanolic extract gave a mixture of grandiflorenic acid (5) and *ent*-kaurenoic acid (1) in the ratio 2 : 1 (by g.l.c.). The only effective method of separating these two acids was by fractional crystallisation from methanol; even so, the two acids co-crystallised when the ratio dropped to *ca.* 1 : 1.

The route from grandiflorenic acid (5) to *ent*-11β-hydroxykaurenoic acid (2), shown in Scheme 1, is based upon hydroboronation of the 9(11)-double bond which, with the 16,17-dihydro-derivative, gives [10] the 11α,19-diol (7) as the major product. The first approach, namely, hydroboronation of methyl grandiflorenate (6) to the 11α,17-diol (8), thence selective bromination to the 17-bromo-compound (9) followed by dehydrobromination, was unsuccessful. Treatment of methyl grandiflorenate (6) with diborane, generated *in situ*, gave, not the expected 11α,17-diol (8), but the 11β,17-diol (10), the stereochemistry at C-11 being assigned from the ^{1}H-n.m.r. spectrum. This stereochemistry was supported by the fact that attempted bromination at C-17 with carbon tetrabromide and triphenylphosphine gave the 11,17-ether (11) [11] and not the required 17-bromo-compound (9). Formation of the 11β,17-diol (10) probably occurs *via* the cyclic dialkylborane (12).

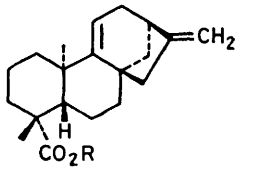
In the successful route (Scheme 1) to *ent*-11β-hydroxykaurenoic acid (2), the exocyclic double bond in grandiflorenic acid (5) was oxidised by osmium tetraoxide–sodium metaperiodate. Sodium borohydride reduction of the resultant norketone (14) gave the alcohol (15). Hydroboronation of the potassium salt of this alcohol (15) was unsuccessful but, after methylation, the diol (16) was slowly formed on reaction with diborane, generated *in situ*. This diol (16), the stereochemistry of



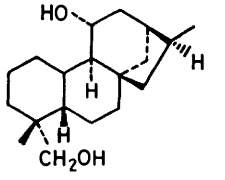
(1) R = H
(2) R = OH



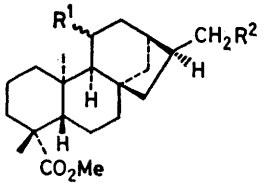
(3) R = α–OH
(4) R = β–OH



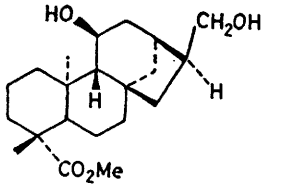
(5) R = H
(6) R = Me



(7) (7)



(8) R^1 = α–OH, R^2=OH
(9) R^1 = α–OH, R^2 = Br



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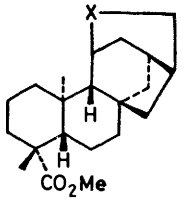
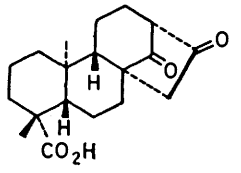
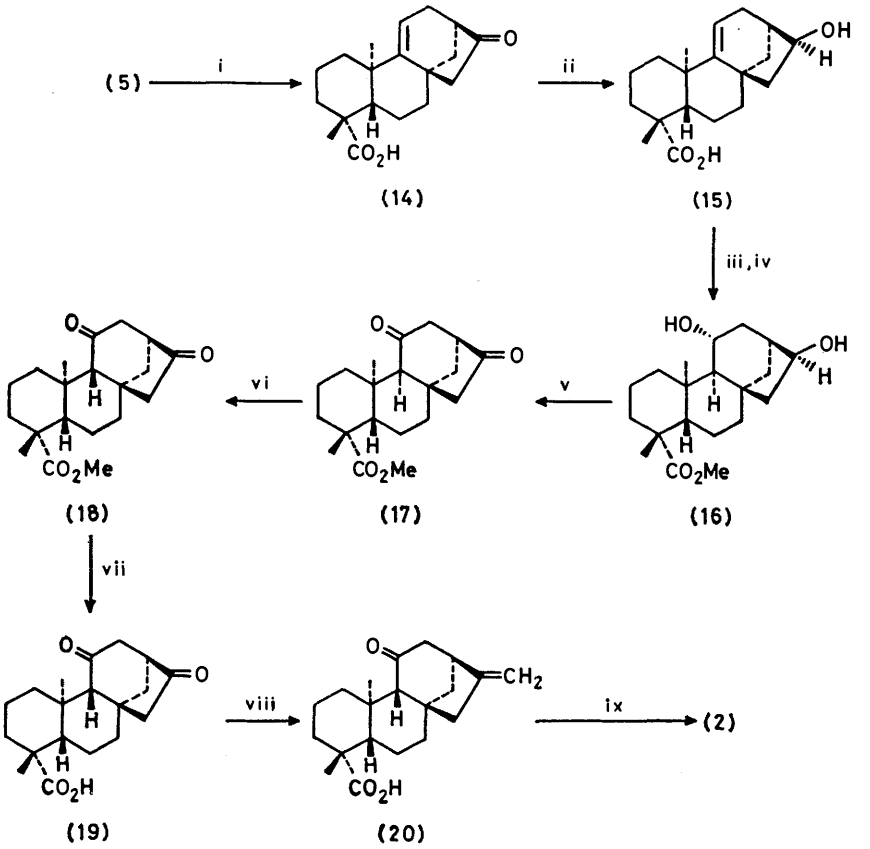


(11) X = O
(12) X = BH



(13)

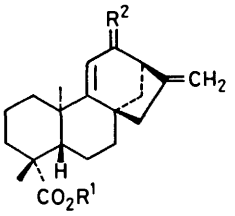
which was assigned from the position of the 10-methyl signal, downfield from the 4-methyl signal in the ^{1}H-n.m.r. spectrum, was oxidised with Jones reagent to the diketone (17). This diketone (17), which slowly epimerised to the *ent*-kaurenoic acid derivative (18), was converted completely into the latter compound (18) by refluxing with methanolic potassium hydroxide [10] for 1 h. The diketone (18) was then demethylated using lithium iodide–collidine [12-14] to give the acid (19). Demethylation was performed at this stage to avoid the hydroxy-kaurenoic acids, shown in Scheme 2 and discussed later, is based upon the discovery that grandiflorenic acid (5) is oxidised by t-butyl chromate to the 12-oxo-derivative (21). The regioselectivity of this oxidation is surprising although the oxidation, allylic to an endocyclic, in preference to an exocyclic, double bond has been previously noted [18] in monoterpene chemistry. t-Butyl chromate oxidation is now believed to be a radical process [18,19] and the observed regio-selectivity probably reflects the greater stability of the endocyclic



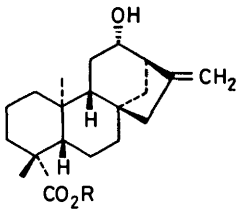
SCHEME 1 Reagents: i, OsO_4–$NaIO_4$; ii, $NaBH_4$ in tetrahydrofuran–EtOH; iii, CH_2N_2; iv, B_2H_6 then H_2O_2–NaOH; v, Jones reagent; vi, KOH–MeOH; vii, LiI, collidine, Ph_3P; viii, $Ph_3P{=}CH_2$; ix, $LiAlH_4$

exo–endo isomerisation, observed [15] with this reagent when the 16,17-double bond is present. Treatment of the trimethylsilyl ester of the diketo-acid (19) with excess of methylenetriphenylphosphorane, followed by hydrolysis of the trimethylsilyl ester, gave *ent*-11-oxokaurenoic acid (20). Regioselectivity at C-16 has also been observed [16] in the Wittig reaction of the diketone (13), and another example is provided later. Reduction of 11-oxokaurenoic acid (20) did not take place with sodium borohydride in ethanol at room temperature and reduction was slow in refluxing 1,2-dimethoxyethane. However with lithium aluminium hydride in ether at room temperature for 26 h, the keto-acid (20) was reduced exclusively to *ent*-11β-hydroxy-kaurenoic acid (2); no trace of the *ent*-11α-epimer [17] was detected by g.l.c.–mass spectrometry.

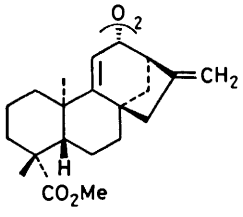
The successful route to *ent*-12α-hydroxy- and *ent*-12β-allylic radical in which there is the possibility of homo-conjugation. Conjugate reduction of the αβ-unsaturated ketone (21) and the corresponding methyl ester (22) with metal hydrides was unsuccessful. The results are shown in the Table. The stereochemical assignments are based upon subsequent results and those of Banerjee *et al.*; [20] the ^{1}H-n.m.r. spectrum of the allylic alcohol (23), the sole product of reduction of the 12-oxo-acid (21) with sodium borohydride in refluxing 1,2-dimethoxy-ethane, is, however, different from that published by Bohlmann and Van.[21] Treatment of the allylic alcohol (24) with thionyl chloride, in an attempt to form the 9-chloro-11-ene, gave two products, assigned the structures (25) and (29) from their mass spectra, and presumably formed *via* the allylic chloride (26) by reaction with water during work-up and by reaction with the allylic alcohol (25).



(21) R^1 = H, R^2 = O
(22) R^1 = Me, R^2 = O
(23) R^1 = H, R^2 = H, β-OH
(24) R^1 = Me, R^2 = H, β-OH
(25) R^1 = Me, R^2 = H, α-OH
(26) R^1 = Me, R^2 = H, β-Cl



(27) R = H
(28) R = Me



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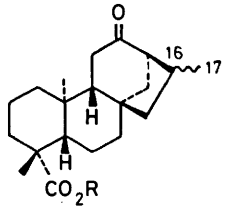
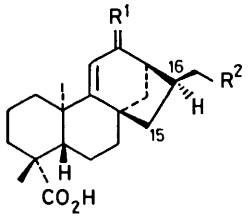
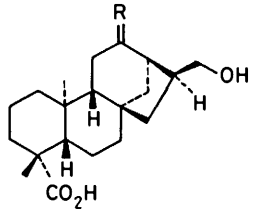


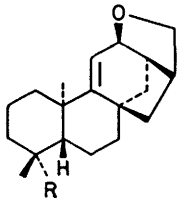
(30) R = H
(31) R = Me
(32) R = H, 16,17-ene



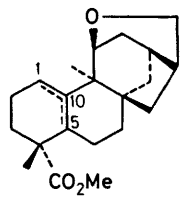
(33) R^1 = H, α-OH, R^2 = H, 15,16-ene
(34) R^1 = O, R^2 = H, 16ξ-H
(35) R^1 = H_2, R^2 = OH
(36) R^1 = H_2, R^2 = OAc
(37) R^1 = O, R^2 = OAc



(38) R = H, α-OH
(39) R = O

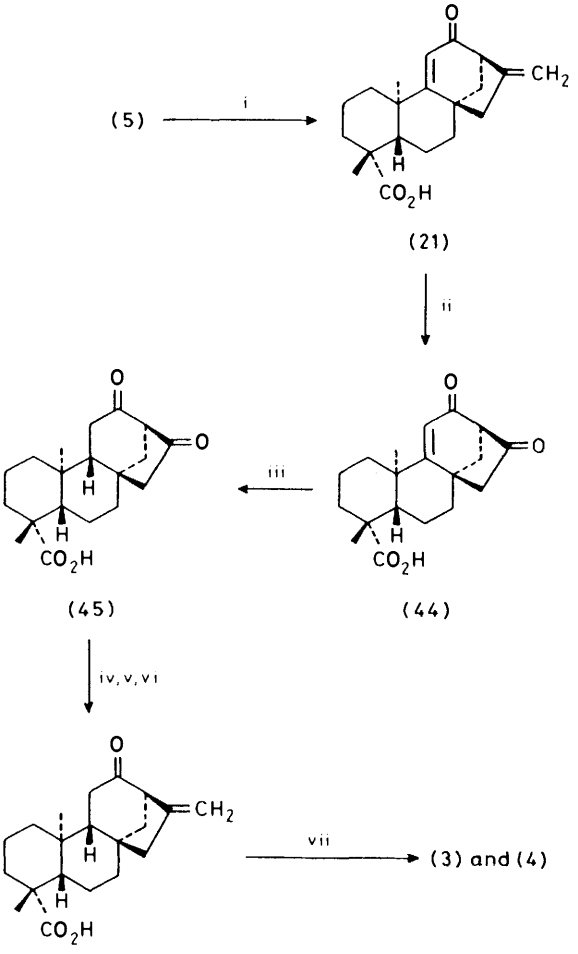


(40) R = CO_2Me
(41) R = Me



(42) 5(10)-ene
(43) 1(10)-ene

Selective reduction of the αβ-unsaturated ketone (21) by dissolving metals, expected [22] to provide the 9β-stereochemistry, was also unsuccessful. With lithium in ethylamine, over-reduction to the tetrahydro-derivative (30) occurred. With sodium in naphthalene starting material (21) and two compounds (32) and (33), tentatively identified by g.l.c.–mass spectrometry, were obtained. With lithium in liquid ammonia the diketone (21) gave the 16,17-dihydro-compound (34) which, when re-subjected to Birch reduction at −33 °C, gave unchanged (34), the compound (30), and its methyl ester (31), formed on work-up. Protection of the double bond by formation of the 17-ol (35) (see later), oxidation of the 17-acetate (36), and Birch reduction of the derived 12-ketone (37) gave an inseparable mixture containing



SCHEME 2 Reagents: i, Bu^tCrO_4; ii, OsO_4–$NaIO_4$; iii, 10% Pd–$CaCO_3$; iv, Me_3SiCl, $(Me_3Si)_2NH$, C_5H_5N; v, $Ph_3P{=}CH_2$; vi, H_3O^+; vii, $NaBH_4$

(g.l.c.–mass spectrometry) the compounds (38) and (39); selective monobromination [23] of compound (39) in this mixture was unsuccessful.

Catalytic reduction of grandiflorenic acid (5), and its derivatives, has been found [9,10,24] to give the 9β-stereochemistry; and, applied to the diketone (21), provides the basis of the successful route (Scheme 2) to the 12-hydroxy-derivatives of *ent*-kaurenoic acid. The diketone (44), prepared by osmium tetraoxide–sodium metaperiodate oxidation of 12-oxograndiflorenic acid (21), gave very low yields of the 16-monoacetal although

similar diketones in the gibberellin series have been selectively acetalised at the 16-position.[25-27] However, direct hydrogenation of the diketone (44) with palladium on calcium carbonate gave *ent*-12,16-dioxo-17-norkaurenoic acid (45), together with 9% (g.l.c.–mass spectrometry) of the presumed 9-epimer. The two isomers could not be separated. Treatment of the trimethylsilyl ester of the mixture (45) with an excess of methylenetriphenylphosphorane gave *ent*-12-oxokaurenoic acid (46) containing a trace of the 9-epimer. This *ent*-12-oxokaurenoic acid (46) was reduced with sodium borohydride in ethanol to a mixture of the required alcohols (3) and (4) which were separated by p.l.c. The stereochemistry of these alcohols was assigned from the ^{1}H-n.m.r. spectra in conjunction with the results reported by Jefferies and Retallack.[28] The synthesised *ent*-12β-hydroxykaurenoic acid (3) was identical to the hydrolysis product of an acetate, recently isolated[29] from *Helianthus decapetalus*.

Initial attempts to functionalise C-12 in grandiflorenic acid (5) were directed towards radical transannular reactions of the 17-ol (35). Selective hydroboronation of the 16,17-double bond in grandiflorenic acid (5) by diborane was shown earlier to be unselective. However, the bulkier 9-borabicyclo[3.3.1]nonane (9-BBN) was expected[30] to react faster with the exocyclic double bond from the less hindered face[31,32] and thereby sterically hinder further reaction from the β-face of the 9(11)-double bond which is also encumbered on the α-face by the 10-methyl group. In the event, treatment of potassium grandiflorenate with 9-BBN,[33] followed by work-up, gave the required 17-ol (35) which, after methylation, was converted into the 17-nitrite ester. This ester, in methylene dichloride, was irradiated with Pyrex-filtered u.v. light to give one product, identified as the ether (40) by comparison of the ^{1}H n.m.r. spectrum with that of the previously described[11] ether (41). Formation of an ether in a Barton reaction is not without precedent.[34] In another radical reaction, treatment of the 17-ol (34) with lead tetra-acetate in refluxing cyclohexane gave three isomeric ethers, one of which was (40); structures (42) and (43) for the other two ethers were suggested by the ^{1}H n.m.r. spectra. Formation of the ethers (42) and (43) are examples of the 10 ⟶ 9-methyl migration discussed in the following paper.

Hydride reduction of the enones (21) and (22)

Substrate	Solvent	Temp.	Hydride	% Yield of products [a] (24) or (23)	(22) or (21)	(28) or (27)
(22)	THF–ethanol (1 : 1)	R.T.	$NaBH_4$	33	60	7
(22)	Pyridine	R.T.	$NaBH_4$	53	45	2
(22)	Diglyme	R.T.	$NaBH_4$	77	23	
(22)	Propan-2-ol	R.T.	$NaBH_4$	15	82	3
(22)	THF	0 °C	L-Selectride		100	
(22)	THF–ethanol (1 : 1)	0 °C	$LiBH_4$	34	66	
(22) [b]	Methanol	R.T.	$NaBH_4$	78	22	
(21)	Ether	0 °C	$LiAlH_4$	65	32	3
(21)	1,2-Dimethoxyethane	Reflux	$NaBH_4$	85 [d]		
(21) [c]	THF	R.T.	$LiBH_4$	Several peaks		
(21) [c]	THF–ethanol (1 : 1)	R.T.	$NaBH_4$	Several peaks		

[a] Ratios of products were estimated from the g.l.c. traces of trimethylsilylated or methylated and trimethylsilylated products. [b] There were several other g.l.c. peaks with shorter retention times. [c] Reactions carried out overnight. [d] Isolated yield.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus, and are uncorrected. Unless otherwise stated, i.r. spectra were obtained for Nujol mulls on a Perkin-Elmer 257 instrument, u.v. spectra for methanolic solutions on a Unicam SP800A instrument, and n.m.r. spectra for deuteriochloroform solutions with tetramethylsilane as internal standard on a JEOL PS100 instrument. Probe and high-resolution mass spectra were recorded by an AEI MS902 spectrometer, and combined g.l.c.–m.s. analysis was performed on an AEI MS30 spectrometer coupled to a Pye–Unicam 104 chromatograph. G.l.c. data were obtained on a Pye 104 chromatograph fitted with a 5 ft × ¼ in o.d. column of 2% SE33 or 2% OV-17 on 80-100 mesh Gas Chrom Q, and a nitrogen flow rate of 60 ml/min. Light petroleum refers to the fraction with b.p. 60—80 °C. Silica gel (Hopkin and Williams M.F.C., 100—200 mesh) was used for column chromatography, and Merck Kieselgel HF silica was used for analytical (0.3 mm layers) and preparative (0.8 mm layers) t.l.c. Usual work-up refers to acidification with concentrated hydrochloric acid to pH 2 followed by extraction with ethyl acetate. The ethyl acetate was back-washed with water before evaporation *in vacuo*.

Mass-spectral Data.—Data for fully characterised compounds are available as Supplementary Publication No. SUP 22738 (8 pp.).

Extraction of Grandiflorenic Acid (5).—Crushed resin gall (126 g) from *Espeletia schultzii* was extracted with methanol (1.5 l) in a Soxhlet apparatus for 24 h. A solution of potassium hydroxide (95.5 g) in methanol (200 ml) was then added, and the resulting solution was refluxed for 24 h. The residue obtained by evaporation of the methanol *in vacuo* was partitioned between diethyl ether and water. The aqueous layer was acidified to pH 2 with concentrated hydrochloric acid and extracted with diethyl ether. Evaporation of the ether *in vacuo* gave the crude acid mixture (100.5 g) which was chromatographed on a column (115 × 5 cm; 1.25 kg) of silica gel, packed in light petroleum and eluted, stepwise, with light petroleum containing an increasing percentage of ethyl acetate (*i.e.* of each solvent system, collected in 250 ml

* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1979, Index issue.

fractions). A mixture (11.5 g) of grandiflorenic acid (5) and *ent*-kaurenoic acid (4), about 2 : 1 by g.l.c., was eluted with 20% ethyl acetate. Fractional crystallisation from methanol gave pure grandiflorenic acid (4.0 g), m.p. 154—156 °C (lit., 158—160 °C,[10] 155—157 °C [9]), identified from the published [10] i.r. and n.m.r. spectra; *m/e* values were similar to those in ref. 35 but with intensity differences below *m/e* 239.

Methyl ent-11α,17-*Dihydroxy*-16βH-*kauran*-19-*oate* (10).—Grandiflorenic acid (5) (50 mg) was methylated with excess of ethereal diazomethane, and the product, in tetrahydrofuran (20 ml), was treated with sodium borohydride (800 mg), and boron trifluoride–diethyl ether (1.2 ml). After 24 h at 3 °C, the reaction was worked up by cautiously adding water (6 ml) and 2M-sodium hydroxide (3 ml), followed by 30% hydrogen peroxide (3 ml). The tetrahydrofuran was removed *in vacuo*, and the usual work-up gave *methyl* ent-11α,17-*dihydroxy*-16βH-*kauran*-19-*oate* (10) (25 mg) as a gum (Found: M^+ 350.247. $C_{21}H_{34}O_4$ requires *M*, 350.246); $\nu_{max.}$ ($CHCl_3$) 3 400 (OH) and 1 720 (CO_2Me) cm^{-1}; δ 0.70 (s, 20-H_3), 1.18 (s, 18-H_3), 3.64 (s, CO_2Me), and 3.80—3.96 (m, 11-H and 17-H_2).

Attempted Bromination of Methyl ent-11α,17-*Dihydroxy*-16βH-*kauran*-19-*oate* (10).—The diol (10) (5 mg), in methylene dichloride (1 ml), was stirred at room temperature with carbon tetrabromide (36 mg) and triphenylphosphine (26 mg) until no starting material remained [t.l.c. with ethyl acetate–light petroleum (2 : 3)]. The solvent was evaporated off and the residue was partitioned between ethyl acetate and water. The product from the organic layer had the same t.l.c., g.l.c., and g.l.c.–mass spectroscopic properties as authentic [11] methyl *ent*-11β,17β-oxidokauran-19-oate (11), m.p. 153—155.5 °C, prepared [36] by lead tetra-acetate oxidation of methyl *ent*-17-hydroxy-16βH-kauran-19-oate.

ent-16-*Oxo*-17-*norkaur*-9(11)-*en*-19-*oic Acid* (14).—Grandiflorenic acid (5) (1 g), in tetrahydrofuran–water (1 : 1; 70 ml), sodium metaperiodate (2.5 g), and one crystal of osmium tetraoxide were stirred at room temperature overnight. The reaction was worked-up by adding water, evaporating the solvent *in vacuo*, and partitioning the product between ethyl acetate and water. Evaporation of the organic phase gave the crude norketone (14) in quantitative yield. This product was chromatographed on a column (2.5 × 35 cm) of silica gel (100 g), eluted with light petroleum containing an increasing percentage of ethyl acetate, m.p. 185—186 °C (from ethyl acetate) (lit.,[9] 195—196 °C) (Found: C, 75.5; H, 8.8. Calc. for $C_{19}H_{26}O_3$: C, 75.5; H, 8.7%); $\nu_{max.}$ 3 200 (CO_2H), 1 728 (CO_2H), 1 713 (C=O), 1 141, 1 128, and 820 (C=C) cm^{-1}; δ 1.07 (s, 20-H_3), 1.26 (s, 18-H_3), and 5.31 (t, *J* 3 Hz, 11-H); $\lambda_{max.}$ 254 nm (ε, 500); Δε (λ/nm) 0 (330), +2.13 (298), +0.70 (265), +4.06 (226), 0 (208), −5.99 (200), and 0 (195); *m/e* values were similar to the literature [24] values but intensities were double the published [24] values below M^+.

ent-16α-*Hydroxy*-17-*norkaur*-9(11)-*en*-19-*oic Acid* (15).—Grandiflorenic acid norketone (14) (500 mg), in tetrahydrofuran–ethanol (1 : 1, 50 ml), was stirred at room temperature for 1.5 h with sodium borohydride (300 mg). The tetrahydrofuran was evaporated *in vacuo*, and the usual work-up gave ent-16β-*hydroxy*-17-*norgrandiflorenic acid* (15) (500 mg), decomposing above 203 °C with change in crystal form above 190 °C (from acetone) (Found: C, 75.0; H, 9.4. $C_{19}H_{28}O_3$ requires: C, 74.8; H, 9.3%); $\nu_{max.}$ 3 425 (OH) and 1 692 (CO_2H) cm^{-1}; δ(CD_3COCD_3) 1.04 (s, 20-H_3), 1.21 (s, 18-H_3), 4.36—4.60 (m, 16-H), and 5.30 (t, *J* 3 Hz, 11-H).

Hydroboration of Methyl ent-16α-*Hydroxy*-17-*norkaur*-9(11)-*en*-19-*oate* (15).—The acid (15) (326 mg) was methylated with excess of ethereal diazomethane; the product in tetrahydrofuran (120 ml) at 0 °C was treated with sodium borohydride (3.6 g) and boron trifluoride–diethyl ether (7.2 ml), and left at 3 °C for 96 h. During this time sodium borohydride (500 mg) and boron trifluoride–diethyl ether (0.6 ml) were added in three equal portions. The reaction was worked-up by cooling the mixture to 0 °C and cautiously treating with water (40 ml) and 2M-sodium hydroxide (20 ml), followed by 30% hydrogen peroxide (20 ml). After effervescence had ceased the tetrahydrofuran was removed *in vacuo*, and the usual work-up gave a gum which was purified by p.l.c. with ethyl acetate–light petroleum (65 : 35). The band at R_F 0.3 gave *methyl* ent-11β,16α-*dihydroxy*-9βH-17-*norkauran*-19-*oate* (16) (290 mg), m.p. 235—236 °C, with change in crystal form above 180 °C (from methanol) (Found: C, 71.4; H, 9.3. $C_{20}H_{32}O_4$ requires: C, 71.4; H, 9.6%); $\nu_{max.}$ 3 300 (OH), 1 733 (CO_2Me) cm^{-1}; δ(C_5D_5N) 1.18 (s, 18-H_3), 1.26 (s, 20-H_3), 3.64 (s, CO_2Me), and 4.54—5.00 (m, 11-H and 16-H).

Jones Oxidation of the 11α,16β-*Diol* (16).—The diol (16) (223 mg), in acetone, was treated with 8N-chromic acid for 1 h at room temperature, then methanol, followed by water. After removal of the organic phase *in vacuo* the product was partitioned between ethyl acetate and water. The residue, obtained from the ethyl acetate, was dissolved in 10% methanolic potassium hydroxide and refluxed for 1 h. The usual work-up gave a gum (200 mg) which by g.l.c.–mass spectrometry gave a mass spectrum consistent with the desired diketone (18); δ 0.92 (s, 20-H_3), 1.24 (s, 18-H_3), and 3.70 (s, CO_2Me). This product was demethylated without further characterisation.

Demethylation of the Methyl Ester (18).—The methyl ester (18) (200 mg), in dry collidine (40 ml), was treated with triphenylphosphine (500 mg) and anhydrous lithium iodide (1 g), and refluxed for 1 h under nitrogen. The cooled mixture was added to water which was acidified to pH 2 with concentrated hydrochloric acid, and extracted with ethyl acetate. The ethyl acetate was washed with saturated sodium thiosulphate solution followed by water, before extraction with 2M-sodium hydroxide. Usual work-up of the alkaline extract gave a gum which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (60 : 40 : 1). The band at R_F 0.5 gave ent-11,16-*dioxo*-17-*norkauran*-19-*oic acid* (19) (70 mg), m.p. 297—302 °C (decomp.) (from acetone) (Found: C, 71.4; H, 8.3. $C_{19}H_{26}O_4$ requires: C, 71.7; H, 8.2%); $\nu_{max.}$ 3 300 (CO_2H), 1 730br (6-ring C=O +5-ring C=O), and 1 694 (CO_2H) cm^{-1}, $\nu_{max.}$ (CH_2Cl_2) 1 744 (5-ring C=O) and 1 694br (6-ring C=O and CO_2H); δ 1.04 (s, 20-H_3) and 1.30 (s, 18-H_3).

ent-11-*Oxokaur*-16-*en*-19-*oic Acid* (20).—Sodium hydride (1.78 g; 60% suspension in oil) was washed twice with light petroleum then added, under nitrogen, to a suspension of methyltriphenylphosphonium bromide (4.8 g) in dry tetrahydrofuran (80 ml). The mixture was stirred at room temperature for 24 h, and the sodium bromide was then allowed to settle. The diketone (19) (60 mg) in pyridine (0.5 ml) was converted into its trimethylsilyl ester by warming for 0.5 h with hexamethyldisilazane (0.3 ml) and trichloromethylsilane (0.3 ml). The residue, after filtration and removal of the solvent, was treated with the supernatant solution (5.0 ml) of the ylide and stirred for

15 min. Acetone, then water, were added to the reaction mixture which was acidified to pH 2 with concentrated hydrochloric acid and stirred at room temperature for 1 h. The product was extracted into ethyl acetate followed by extraction into 2M-sodium hydroxide; the usual work-up of the aqueous layer gave the crude product which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (55. : 45 : 1). The band at R_F 0.7 gave ent-11-*oxokaurenoic acid* (20) (23 mg) as a gum (Found: M^+ 316.203. $C_{20}H_{28}O_3$ Requires M, 316.204); $\nu_{max.}$ (CH_2Cl_2) 1 730sh, 1 693br (6-4ing C=O and CO_2H), 1 660 (C=C), and 883 (C=CH_2) cm^{-1}; δ 0.96 (s, 20-H_3), 1.27 (s, 18-H_3), 2.93 (m, 13-H), and 4.84 and 4.94 (s, 17-H_2).

Reduction of ent-11-*Oxokaurenoic Acid* (20).—The acid (20) (17 mg), in diethyl ether (4 ml), was stirred with lithium aluminium hydride (10 mg) for 26 h at room temperature. The usual work-up gave a product which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (50 : 50 : 1). The band at R_F 0.8 gave ent-11β-*hydroxykaur*-16-*en*-19-*oic acid* (2) (11 mg), m.p. 201—202 °C, with change in crystal form above 150 °C (from ethyl acetate) (Found: M^+ 318.221. $C_{20}H_{30}O_3$ requires M, 318.219); $\nu_{max.}$ ($CHCl_3$) 3 500—3 100 (OH and CO_2H), 1 694 (CO_2H), 1 660 (C=C), and 882 (C=CH_2) cm^{-1}; δ 1.14 (s, 20-H_3), 1.24 (s, 18-H_3), 4.35 (dt, J_d 12 Hz, J_t 10 Hz, 11-H), and 4.74 and 4.89 (s, 17-H_2).

ent-12-*Oxokaura*-9(11),16-*dien*-19-*oic Acid* (21).—To a solution of chromium trioxide (8.568 g) in t-butyl alcohol (21.8 ml) was added dry benzene (58.8 ml), glacial acetic acid (2.8 ml), and acetic anhydride (3.6 ml). To this dried solution (Na_2SO_4) was added grandiflorenic acid (5) (2 g) in benzene (4.2 ml). The mixture was stirred at 60 °C for 5 h, then at room temperature overnight. The reaction was worked up by adding a little water followed cautiously by oxalic acid (8.4 g). The mixture was stirred for 3 h and diluted with water, and the product extracted with ethyl acetate. Evaporation of the ethyl acetate gave a gum (2.11 g) which was purified by column chromatography (3.5 × 33 cm; 200 g of silica gel) using light petroleum with an increasing percentage of ethyl acetate. Fractions containing about 35% ethyl acetate gave ent-12-*oxokaur*-9(11)-*en*-19-*oic acid* (21) (1.01 g), m.p. 258—260 °C (from acetone) (Found: C, 76.4; H, 8.7. $C_{20}H_{26}O_3$ requires: C, 76.4; H, 8.3%); $\nu_{max.}$ 3 120 (CO_2H), 1 722 (CO_2H), 1 644 (C=O), and 1 598 (C=C) cm^{-1}; δ 1.16 (s, 20-H_3), 1.30 (s, 18-H_3), 3.43 (d, J 4 Hz, 13-H), 5.02 and 5.26 (s, 17-H_2), and 5.78 (s, 11-H); $\lambda_{max.}$ 250 nm (ε 15 300); $\Delta\varepsilon$ (λ/nm) 0 (385), +2.87 (328), 0 (268), −11.16 (245), 0 (224), +1.49 (216), 0 (210), −3.47 (203), and 0 (195).

Hydride Reductions on ent-12-*Oxokaur*-9(11)-*en*-19-*oic Acid* (21).—A series of hydride reductions were carried out on the acid (21) (5 mg). The reactions were worked-up in the usual way and the products analysed by g.l.c. on 2% SE33 as the methyl trimethylsilyl derivatives. The following reagents were used: sodium borohydride (5 mg) in tetrahydrofuran–ethanol (1 : 1; 1 ml), pyridine (1 ml), diglyme (bismethoxymethyl ether) (1 ml), propan-2-ol (1 ml), or methanol (1 ml) for 2 h at room temperature; L-Selectride [lithium tri-s-butylborohydride; 1M solution in tetrahydrofuran (THF); 10 μl] in THF (1 ml) at 0 °C for 1 h; sodium borohydride (5 mg) and lithium borohydride (11 mg) in THF–ethanol (1 : 1; 1 ml) at 0 °C for 1 h; lithium aluminium hydride (5 mg) in diethyl ether (1 ml) at 0 °C for 2 h; sodium borohydride (10 mg) in THF–ethanol (1 : 1; 1 ml) overnight at room temperature; sodium borohydride (10 mg) and lithium bromide (20 mg) in THF (1 ml) overnight at room temperature. The results are in the Table.

ent-12α-*Hydroxykaura*-9(11),16-*dien*-19-*oic Acid* (23).—*ent*-12-Oxokaur-9(11)en-19-oic acid (21) (90 mg), in 1,2-dimethoxyethane (30 ml), was refluxed for 2 h under nitrogen with sodium borohydride (200 mg). Water was then added, and the solvent removed *in vacuo*. Dilution with water followed by the usual work-up gave a gum which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (50 : 50 : 1). The band with R_F 0.6 gave ent-12α-*hydroxykaura*-9(11),16-*dien*-19-*oic acid* (23) (76 mg), m.p. 143—154 °C, recrystallising and remelting at 164—169 °C (from ethyl acetate) (Found: C, 76.0; H, 9.0. $C_{20}H_{28}O_3$ requires: C, 75.9; H, 8.9%); $\nu_{max.}$ 3 513 (OH), 3 120 (CO_2H), 1 724 (CO_2H), and 1 646 and 906 (C=CH_2) cm^{-1}; δ 1.04 (s, 20-H_3), 1.24 (s, 18-H_3), 2.73 (m, 13-H), 4.36 (dd, J 6 and 2 Hz, 12-H), 5.02 and 5.06br (s, 17-H_2), and 5.21br, (s, 11-H).

Reaction of Thionyl Chloride with Methyl ent-12α-*Hydroxykaura*-9(11),16-*dien*-19-*oate* (24).—The allylic alcohol (23) (35 mg) was methylated with ethereal diazomethane, and a solution of the product in diethyl ether (3 ml) was stirred overnight at room temperature with thionyl chloride (20 μl). The reaction was worked-up by adding a little calcium carbonate and evaporating the solvent. The product was then partitioned between ethyl acetate and water. The residue obtained after evaporation of the ethyl acetate was purified by p.l.c. with ethyl acetate–light petroleum (5 : 6). The band at R_F 0.9 gave a gum (10 mg), tentatively identified as the dimeric ether (29) (Found: M^+ 642.426. $C_{42}H_{58}O_5$ requires M 642.428); $\nu_{max.}$ (CH_2Cl_2) 1 724 (CO_2Me), 1 663 (C=C), and 1 148 (C–O) cm^{-1}; δ 0.98 (s, 20-H_3), 1.18 (s, 18-H_3), 2.84br. (s, 13-H), 3.66 (s, CO_2Me and 12-H), 4.90 and 5.00 (s, 17-H_2), and 5.30 (dd, J 4 and 2 Hz, 11-H). The band at R_F 0.5 gave *methyl* ent-12β-*hydroxykaura*-9(11),16-*dien*-19-*oate* (25) (7 mg) as a gum (Found: M^+ 330.218. $C_{21}H_{30}O_3$ requires M 330.219), $\nu_{max.}$ (CH_2Cl_2) 3 604 (OH), 1 722 (CO_2Me), 1 660 (C=C), and 1 150 (C–O) cm^{-1}; δ 0.98 (s, 20-H_3), 1.20 (s, 18-H_3), 2.84br. (s, 13-H), 3.67 (s, CO_2Me), 3.96 (m, 12-H), 4.92 and 5.06 (s, 17-H_2), and 5.38 (d, J 4 Hz, 11-H).

Dissolving Metal Reductions of ent-12-*Oxokaura*-9(11),16-*dien*-19-*oic Acid* (21).—(a) *Lithium in ethylamine*. Lithium shot (*ca.* 20 mg) was added to ethylamine (1.5 ml) under nitrogen, and the mixture was stirred at 0 °C until a dark blue colour appeared. After a further 15 min. the acid (21) (15 mg) was added and the mixture was stirred for 3 h at 0 °C. Sufficient lithium shot was added, during this time, to retain the blue colour. The blue colour was then discharged by the addition of t-butyl alcohol. The reaction mixture was diluted with water and worked-up in the usual way. The product was analysed by g.l.c.–mass spectrometry as the trimethylsilyl derivative on 2% SE33. One major peak was observed which was consistent with the derivative of 12-oxo-16ξH-kauran-19-oic acid (30); *m/e* (%) 390 (M^+, 10), 375 (21), 300 (26), 273 (100), 258 (16), 203 (7), 159 (11), 143 (14), 123 (17), 109 (17), 107 (20), 95 (11), and 93 (11).

(b) *Sodium in naphthalene*. Naphthalene (700 mg) was added to 1,2-dimethoxyethane (10 ml), and treated with freshly cut sodium (250 mg). This mixture was stirred under nitrogen for 2 h after a dark green colour had appeared. A solution of the acid (21) (5 mg) in t-butyl alcohol (0.1 ml) and 1,2-dimethoxyethane (0.4 ml) was

treated with the above reagent until the green colour persisted. The mixture was stirred for 1 h at room temperature, and quenched by adding water. The product obtained by the usual work-up was analysed by g.l.c.–mass spectrometry as the methyl trimethylsilyl derivative and shown to contain unchanged starting material and two products, tentatively identified as the methyl trimethylsilyl derivatives of *ent*-12β-hydroxykaura-9(11),15-dien-19-oic acid (33) [*m/e* (%) 402 (M^+, 33), 397 (7), 273 (20), 258 (60), 220 (18), 154 (31), 153 (37), 141 (27), 130 (31), and 104 (100)] and the methyl ester of *ent*-12-oxokaur-16-en-19-oic acid (32) [*m/e* (%) 330 (M^+, 41), 315 (5), 302 (6), 271 (36), 233 (15), 147 (17), 143 (16), 135 (16), 121 (27), 119 (27), 107 (34), 105 (100), and 92 (48)].

(c) *Birch reduction.* The acid (21) (25 mg), in tetrahydrofuran (5 ml) and t-butyl alcohol (7 μl), was treated with freshly redistilled ammonia (25 ml) at −67 °C. Sufficient lithium shot was added to retain the dark blue colour for 15 min at −67 °C. Methanol was then added to discharge the blue colour, and the resulting mixture was left overnight at room temperature. The product was diluted with water, and the usual work-up gave a gum which was subjected to p.l.c. with ethyl acetate–light petroleum–acetic acid (40 : 60 : 1). The band at R_F 0.45 gave *ent*-12-oxo-16ξ*H*-kaur-9(11)-en-19-oic acid (34, 16ξH) (10 mg) (Found: M^+ 316.204. $C_{20}H_{28}O_3$ requires *M* 316.204); $\nu_{max.}$ (CH_2Cl_2) 3 070 (CO_2H), 1 693 (CO_2H), 1 666 (C=O), and 1 593 (C=C) cm^{-1}; δ 1.12, 1.20, and 1.31 (3 × Me), and 5.88 (s, 11-H); $\lambda_{max.}$ 247 nm (ε 10 180).

This product (5 mg) was reduced with lithium and liquid ammonia at −33 °C for 0.5 h with no co-solvent. The reaction was worked-up as described earlier, and after p.l.c. with ethyl acetate–light petroleum–acetic acid (40 : 60 : 1) the products were analysed by mass spectrometry. The band at R_F 0.8 gave methyl *ent*-12-oxo-16ξ*H*-kauran-19-oate (31) (1.3 mg), and the band at R_F 0.65 gave a mixture of starting material (34, 16ξH) and 12-oxokauranoic acid (30) (3.1 mg).

ent-17-*Acetoxy*-16βH-*kaur*-9(11)-*en*-19-*oic Acid* (36).—*ent*-17-Hydroxykauranoic acid (35) (1.5 g), prepared as described later, in pyridine (15 ml), and acetic anhydride (6 ml), was stirred overnight at room temperature. The product, recovered in the usual way, was purified by column chromatography (3.5 × 33 cm; 200 g of silica gel) using stepped elution with light petroleum containing an increasing percentage of ethyl acetate. Fractions containing about 20% ethyl acetate gave the 17-*acetate* (36) (1.5 g), m.p. 158—160 °C (from ethyl acetate) (Found: C, 73.4; H, 9.5. $C_{22}H_{32}O_4$ requires: C, 73.3; H, 9.0%); $\nu_{max.}$ 1 739 (OCOMe) and 1 694 (CO_2H) cm^{-1}; δ 1.02 (s, 20-H_3), 1.26 (s, 18-H_3), 2.08 (s, OCOMe), 4.07 (dd, *J* 8 and 3 Hz, 17-H_2), and 5.26 (t, *J* 3 Hz, 11-H).

ent-17-*Acetoxy*-12-*oxo*-16βH-*kaur*-9(11)-*en*-19-*oic Acid* (37).—The acetate (36) (1 g) in dry benzene (3.6 ml), was treated with a solution of t-butyl chromate, prepared as described earlier. Quantities used were: chromium trioxide (4.62 g), t-butyl alcohol (12.6 ml), dry benzene (33.6 ml), glacial acetic acid (1.47 ml), acetic anhydride (1.92 ml), and oxalic acid (4.65 g). The product obtained after work-up was purified by column chromatography (2.5 × 33 cm; 100 g of silica gel). Stepped elution with light petroleum containing an increasing percentage of ethyl acetate gave, at about 50% ethyl acetate, the 12-*ketone* (37) (550 mg), m.p. 168—171 °C (from ethyl acetate) (Found: C, 70.6; H, 8.3. $C_{22}H_{30}O_5$ requires: C, 70.6; H, 8.1%); $\nu_{max.}$ 3 300 (CO_2H), 1 724 (OCOMe), 1 700 (CO_2H), 1 673 (C=O), 1 597 and 886 (C=C) cm^{-1}; δ 1.16 (s, 20-H_3), 1.31 (s, 18-H_3), 2.06 (s, OCOMe), 2.98br. (d, *J* 4 Hz, 13-H), 3.70 (d, *J* 7 Hz, 17-H_2), and 5.90 (s, 11-H); $\lambda_{max.}$ 248 nm (ε 11 970).

Birch Reduction of ent-17-*Acetoxy*-12-*oxo*-16βH-*kaur*-9(11)-*en*-19-*oic Acid* (37).—The keto-acid (37) (100 mg) was subjected to Birch reduction, using the method described earlier, for 2.5 h at −33 °C, and stopped by the addition of solid ammonium chloride. After work-up a gum was obtained which was purified by p.l.c. with ethyl acetate–light petroleum–glacial acetic acid (50 : 50 : 1). The main band at R_F 0.2 gave a solid (66 mg) which, by g.l.c.–mass spectrometry on 2% SE33 as the trimethylsilyl derivative, contained two components with mass spectra consistent with the derivative of *ent*-12β,17-dihydroxykauranoic acid (38) [*m/e* (%) 552 (M^+, <1), 537 (10), 462 (14), 372 (9), 333 (25), 331 (16), 255 (25), 215 (22), 147 (16), 129 (21), 123 (20), 109 (16), 105 (15), 93 (11), 81 (14), 75 (29), and 73 (100)] and *ent*-12-oxo-17-hydroxykauranoic acid (39) [*m/e* (%) 478 (M^+, 21), 463 (26), 388 (13), 361 (13), 291 (8), 271 (20), 231 (7), 157 (11), 136 (13), 129 (13), 107 (14), 93 (11), 81 (10), 75 (22), and 73 (100)]. Unsuccessful attempts were made to separate these two components.

ent-12,16-*Dioxo*-17-*norkaur*-9(11)-*en*-19-*oic Acid* (44).—*ent*-12-Oxokaur-9(11)-en-19-oic acid (21) (500 mg), in tetrahydrofuran–water (1 : 1; 15 ml) was treated with sodium metaperiodate (1 g) and one crystal of osmium tetraoxide, and stirred at room temperature overnight. The reaction mixture was diluted with water and worked-up in the usual way to give the nor-ketone (44) (500 mg), m.p. 255—258 °C (from ethyl acetate) (Found: C, 71.7; H, 8.1. $C_{19}H_{24}O_4$ requires: C, 72.1; H, 7.7%); $\nu_{max.}$ 3 100 (CO_2H), 1 754 (5 ring C=O), 1 707 (CO_2H), 1 694 (C=O), 1 594 (C=C), 1 162 cm^{-1}; δ 1.20 (s, 20-H_3), 1.28 (s, 18-H_3), 3.43 (d, *J* 6 Hz, 13-H), and 5.80 (s, 11-H); $\lambda_{max.}$ 257 nm (ε 9 100).

ent-12,16-*Dioxo*-17-*norkaur*-9(11)-*en*-19-*oic Acid Ethylene Acetal.*—*ent*-12,16-Dioxo-17-norkaur-9(11)-en-19-oic acid (44) (470 mg) in dry benzene (30 ml) was refluxed in a Dean–Stark water separator for 24 h with ethylene glycol (3.25 ml) and toluene-*p*-sulphonic acid (70 mg). The reaction was worked-up by removing the benzene *in vacuo*, neutralising the acid with ammonium hydroxide, and extracting with ethyl acetate. Removal of the ethyl acetate gave a gum which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (50 : 50 : 1). The band at R_F 0.5 gave the *acetal* (76 mg), m.p. 284—286 °C, changing form above 240 °C (from acetone) (Found: C, 70.2; H, 7.9. $C_{21}H_{28}O_5$ requires: C, 70.0; H, 7.8%); $\nu_{max.}$ 3 050 (CO_2H), 1 727 (CO_2H), 1 644 (C=O), 1 596 (C=C), and 1 143 (acetal C–O) cm^{-1}; δ 1.15 (s, 20-H_3), 1.27 (s, 18-H_3), 2.67br. (s, 13-H), 3.93 (m, acetal CH_2), and 5.82 (s, 11-H); $\lambda_{max.}$ 248 nm (ε 10 170).

ent-12,16-*Dioxo*-17-*norkauran*-19-*oic Acid* (45).—The 12,-16-dione (44) (359 mg) was treated with 10% palladium on calcium carbonate (350 mg) in ethyl acetate, and stirred at room temperature with hydrogen gas until g.l.c. analysis of the methyl ester on 2% SE33 indicated no starting material. Analysis of the product by g.l.c.–mass spectrometry indicated conversion into ent-12,16-dioxo-17-norkauranoic acid (45) (91%) and an isomer presumed to be the 9-epimer. This mixture (335 mg) crystallised from ethyl acetate–light petroleum, m.p.: crystals changed form above 200 °C then melted at 236—238 °C (Found: C, 71.9; H, 8.5.

$C_{19}H_{26}O_4$ requires: C, 71.7; H, 8.2%); $\nu_{max.}$ 3 180 (CO_2H), 1 752 (5 ring C=O), 1 723 (6 ring C=O), and 1 693 (CO_2H) cm^{-1}; δ 0.86 (s, 20-H_3), 1.28 (s, 18-H_3), 3.28 (d, *J* 5 Hz, 13-H).

ent-12-*Oxokaur*-16-*en*-19-*oic Acid* (46).—The diketone (45) (335 mg), in dry pyridine (4.5 ml), was treated with hexamethyldisilazane (1.3 ml) and trichloromethylsilane (1.3 ml) for 0.5 h with warming. The residue, obtained after filtration and evaporation of the solvent, was stirred with a solution of methylenetriphenylphosphorane (20 ml), prepared as described earlier. The reaction was stopped after 5 min by adding acetone and worked-up as before. The residue, obtained after extraction with ethyl acetate followed by evaporation of the solvent, was chromatographed on a column (2.5 × 30 cm) of silica gel (80 g) and eluted using light petroleum containing an increasing percentage of ethyl acetate to give ent-12-*oxokaurenoic acid* (46) (185 mg), sublimes above 190 °C (from ethyl acetate) (Found: C, 75.8; H, 9.0. $C_{20}H_{28}O_3$ requires: C, 75.9; H, 8.9%); $\nu_{max.}$ 1 704 (C=O), 1 693 (CO_2H), 1 657 and 893 ($C=CH_2$) cm^{-1}; δ 0.81 (s, 20-H_3), 1.27 (s, 18-H_3), 3.26 (d, *J* 5 Hz, 13-H), 4.92 and 5.04 (s, 17-H_2).

Sodium Borohydride Reduction of ent-12-*Oxokaurenoic Acid* (46).—The acid (46) (20 mg), in ethanol (2 ml), and sodium borohydride (40 mg) were stirred for 4 h at room temperature. After the addition of water, the usual work-up gave a gum which was purified by p.l.c. with ethyl acetate–light petroleum–acetic acid (35 : 65 : 1). The band at R_F 0.45 gave ent-12β-*hydroxykaur*-16-*en*-19-*oic acid* (3) (10 mg), m.p. 224.5—226.5 °C (from ethyl acetate) (Found: C, 75.0; H, 9.8. $C_{20}H_{30}O_3$ requires: C, 75.4; H, 9.5%); $\nu_{max.}$ 3 400 (OH), 1 703 (CO_2H), and 893 ($C=CH_2$) cm^{-1}; δ 1.08 (s, 20-H_3), 1.22 (s, 18-H_3), 2.72 (m, 13-H), 3.93 (m, 12-H), 4.81 and 4.88 (s, 17-H_2). The band at R_F 0.3 gave ent-12α-*hydroxykaur*-16-*en*-19-*oic acid* (4) (4 mg), m.p. 207—208.5 °C (from methanol–water) (Found: M^+ 318.220. $C_{20}H_{30}O_3$ requires *M* 318.219); $\nu_{max.}$ (CH_2Cl_2) 3 500 (OH), 1 693 (CO_2H), and 893 ($C=CH_2$) cm^{-1}; δ 0.92 (s, 20-H_3), 1.23 (s, 18-H_3), 2.64 (m, 13-H), 3.80 (m, 12-H), and 4.89 (s, 17-H_2).

ent-17-*Hydroxy*-16βH-*kaur*-9(11)-*en*-19-*oic Acid* (35).—Grandiflorenic acid (5) (2 g) was dissolved in a solution of potassium hydroxide in methanol (37.5 ml; 10 mg KOH/ml) and the solution stirred for 0.5 h. The methanol was evaporated *in vacuo*. The residue, after drying, was treated with 0.5M 9-BBN in tetrahydrofuran [33] (40 ml). After being stirred at room temperature for two days, the solution was cooled to 0 °C, then water (20 ml), 2M-sodium hydroxide (70 ml), and 30% hydrogen peroxide (60 ml) were added. The mixture was allowed to warm up to room temperature and left to stand for 24 h. The usual work-up gave a clear oil (6.6 g) which was purified by chromatography on a column (4.5 × 45 cm) containing silica gel (300 g) and eluted with light petroleum containing an increasing percentage of ethyl acetate. The fractions containing about 60% ethyl acetate gave ent-17-*hydroxy*-16βH-*kaur*-9(11)-*en*-19-*oic acid* (35) (2.2 g), m.p. 154—156 °C (from ethyl acetate) (Found: C, 75.0; H, 9.6. $C_{20}H_{30}O_3$ requires: C, 75.4; H, 9.5%); $\nu_{max.}$ 3 400 (OH) and 1 700 (CO_2H) cm^{-1}; δ 1.00 (s, 20-H_3), 1.22 (s, 18-H_3), 3.61 (d, *J* 8 Hz, 17-H_2), and 5.21 (t, *J* 3 Hz, 11-H).

Methyl ent-17-*Nitrosyloxy*-16βH-*kaur*-9(11)-*en*-19-*oate*.—The 17-alcohol (35) (600 mg) was methylated using excess of ethereal diazomethane. The residue, dissolved in dry pyridine (8.5 ml), was cooled to −20 to −30 °C and rapidly stirred. Nitrosyl chloride was condensed into the flask until the solution remained orange-brown. Water (48 ml) was then added, and the mixture was extracted with ethyl acetate. Evaporation of the organic phase gave the unstable nitrite ester (597 mg), identified by its i.r. spectrum; $\nu_{max.}$ (CH_2Cl_2) 1 720 (CO_2Me), 1 640 and 1 600 (ONO) cm^{-1}.

Photolysis of the Nitrite Ester.—The nitrite ester from the previous preparation (300 mg) dissolved in methylene dichloride (5 ml) was irradiated for 3.5 h by a medium-pressure Hanovia u.v. lamp, using a Pyrex filter. The mixture was then left at room temperature overnight. Removal of the solvent *in vacuo* gave a gum (410 mg) which was subjected to p.l.c. using ethyl acetate–light petroleum (2 : 3). Removal of the main band at R_F 0.7 gave *methyl* ent-12α,17-*epoxy*-16βH-*kaur*-9(11)-*en*-19-*oate* (40) (65 mg) as a gummy solid (Found: M^+ 330.218. $C_{21}H_{30}O_3$ requires *M* 330.219); $\nu_{max.}$ (CH_2Cl_2) 1 620 (CO_2Me), 1 635 (C=C), and 1 150 (C–O) cm^{-1}; δ 0.98 (s, 20-H_3), 1.18 (s, 18-H_3), 3.34 (dd, *J* 9 and 4 Hz, 17β-H), 3.66 (s, CO_2Me), 4.08 (t, *J* 9 Hz, 17α-H), 4.68 (dd, *J* 6 and 4 Hz, 12-H), and 5.20 (d, *J* 4 Hz, 11-H).

Reaction of Methyl ent-17-*Hydroxykaur*-9(11)-*en*-19-*oate with Lead Tetra-acetate*.—Lead tetra-acetate (7.5 g) and calcium carbonate (5 g) were stirred in dry cyclohexane (60 ml) overnight. Methyl *ent*-17-hydroxykaur-9(11)-en-19-oate (280 mg) in cyclohexane (50 ml) was added. The mixture was refluxed for 8 h in the dark. A few drops of ethylene glycol were added, the mixture was filtered, and the filtrate was partitioned between ethyl acetate and water. The organic phase was evaporated *in vacuo* to give a gum (297 mg) which was subjected to p.l.c. using ethyl acetate–light petroleum (1 : 4). The band at R_F 0.6 gave the unstable *methyl* ent-9β-*methyl*-11α,17-*epoxy*-16βH-20-*norkaur*-5(10)-en-19-*oate* (42) (28 mg) as a gummy solid (Found: M^+ 330.219. $C_{21}H_{30}O_3$ requires *M* 330.219); $\nu_{max.}$ (CH_2Cl_2) 1 720 (CO_2Me) cm^{-1}; δ 1.04 (s, 20-H_3), 1.26 (s, 18-H_3), 3.64 (s, CO_2Me), and 3.34—4.00 (several peaks, 11-H and 17-H_2); 360 MHz n.m.r. shows δ 3.423 (dd, *J* 10 and 2.5 Hz, 17β-H), 3.787 (d, *J* 10 Hz, 17α-H), and 3.927 (t, *J* 2—3 Hz, 11-H). The band at R_F 0.5 gave the ether (11) (61 mg), and the band at R_F 0.4 gave the unstable *methyl* ent-9β-*methyl*-11α,17-*epoxy*-16βH-20-*norkaur*-1(10)-*en*-19-*oate* (43) (39 mg) as a gummy solid (Found: M^+ 330.219. $C_{21}H_{30}O_3$ requires *M* 330.219); $\nu_{max.}$ (CH_2Cl_2) 1 723 (CO_2Me) and 840 (C=C) cm^{-1}; δ 1.11 (s, 20-H_3), 1.27 (s, 18-H_3), 3.61 (s, CO_2Me), 3.35—3.99 (several peaks, 11-H and 17-H_2), and 5.26br. (d, *J* 4 Hz, 1-H), 360 MHz n.m.r. shows δ 3.437 (dd, *J* 9.5 and 2.5 Hz, 17β-H), 3.744 (d, *J* 9.5 Hz, 17α-H), 3.967 (t, *J* 2 Hz, 11-H), and 5.469 (dt, *J* 4.5 and 2 Hz, 1-H).

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