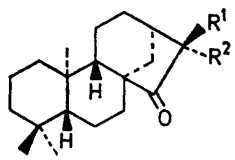
Terpenoids. Part III.[1] The Enolisation–Ketonisation and Optical Rotatory Dispersion of the *ent*-Kauran-15-ones and 13β-Kauran-15-ones

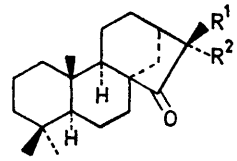
By J. MacMillan * and E. R. H. Walker, School of Chemistry, The University, Bristol BS8 1TS

At temperatures below 100° the rates of enolisation of the 16*R*-epimers of *ent*-kauran-15-one and 13β-kauran-15-one are much greater than those of the 16*S*-epimers, and the enols are exclusively ketonised to the 16*R*-epimers. Reasons for this kinetic control are discussed in terms of steric hindrance, torsional strain, and stereoelectronic factors. The conformation of these ketones is also discussed in terms of their o.r.d. and c.d. properties.

CONTINUING our studies on the chemistry and conformation of ring D derivatives of *ent*-kaurane and 13β-kaurane, we have investigated the acid-catalysed epimerisation of the *ent*-kauran-15-ones (1)—(3) and of the 13β-kauran-15-ones (5) and (6). This study was

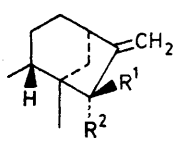


(1) R^1 = Me, R^2 = H
(2) R^1 = H, R^2 = Me
(3) R^1 = Me, R^2 = ^{2}H
(4) R^1 = Me, R^2 = Br

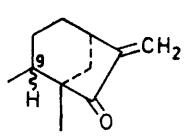


(5) R^1 = Me, R^2 = H
(6) R^1 = H, R^2 = Me
(7) R^1 = Me, R^2 = Br

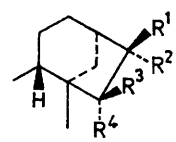
prompted by the observation [2] that *ent*-(16*S*)-[16-^{2}H]-kauran-15-one (3), prepared [3] by rearrangement of *ent*-[15-^{2}H]-kaur-16-en-15α-ol (10), slowly exchanged its deuterium in acidic media to yield the ketone (1) with complete retention of configuration. The conformation of ring D in these ketones is discussed in terms of their rates of enolisation and of their o.r.d. and c.d. spectra.



(8) R^1 = OH, R^2 = H
(9) R^1 = H, R^2 = OH
(10) R^1 = OH, R^2 = ^{2}H



(11) 9βH
(12) 9αH



	R^1	R^2	R^3	R^4
(13)	Me	H	OH	H
(14)	H	Me	OH	H
(15)	Me	H	H	OH
(16)	H	Me	H	OH

The 13β-kauran-15-ones (5) and (6) were prepared as described in Part II.[1] The 16-epimers (1) and (2) of *ent*-kauran-15-one were prepared in the following similar manner. The 16-en-15α-ol (9), obtained [3] by photo-oxygenation of *ent*-kaur-15-ene, was oxidised to *ent*-kaur-16-en-15-one (11). The latter compound was stereospecifically hydrogenated to a saturated ketone, identical with the 16*R*-epimer (1) of *ent*-kauran-15-one, previously prepared [3] with unambiguous stereochemistry by 15,16-hydride shift in the 16-carbonium ion derived from the 16-en-15β-ol (8). The physical constants for the (16*R*)-ketone (1) differ from those reported by Briggs *et al.*[4] (see Table). Also, in contrast to the findings of Briggs *et al.*,[4] base-epimerisation of the (16*R*)-ketone (1) gave a mixture of the 16*R*- and 16*S*- (2) epimers which contained 65% of the latter (g.l.c.) and which could not be separated by crystallisation, t.l.c., or column chromatography. The epimeric mixture was directly reduced by lithium aluminium hydride to a mixture of the (16*R*)- and (16*S*)-15β-ols (13) and (14), which was readily separated by t.l.c. Each epimeric alcohol was separately oxidised by chromium trioxide to the (16*R*)- and (16*S*)-ketones (1) and (2), which were shown to be free from each other by g.l.c. As in the case of the (16*R*)-ketone (1), the physical constants for the (16*S*)-ketone (2) differed from those previously reported [4] (see Table). The o.r.d. and c.d. data in the Table are discussed later.

Some physical constants for the 16*R*- and 16*S*-epimers of *ent*-kauran-15-one and of 13β-kauran-15-one

Compound	M.p. (°C)	$[\alpha]_D^{22}$ (°)	O.r.d. (*a*)	C.d. (Δε)	Lit. m.p. (°C)	Lit. $[\alpha]_D$ (°)
(1)	147—148	−101	−26	−0·51	138 [a]	−5 [a]
(2)	119—120	−89	+47	+0·79	145 [a]	−50 [a]
(5)	103—104	−64	−135	−2·82	101—102 [b]	−62 [b]
(6)	128·5—129·5	−64	−97	−2·05	127·5—129 [b]	−50 [b]

[a] Ref. 4. [b] Ref. 17.

Although the 16*R*- and 16*S*-epimers of *ent*-kaur-15-one and of 13β-kauran-15-one were readily epimerised by base to give equilibrium mixtures, they were not epimerised by hydrochloric acid in refluxing methanol or t-butyl alcohol. The observation by Barnes [2] that the (16*R*)-[16-^{2}H]-ketone (3) exchanged deuterium for protium on treatment with acid without epimerisation was confirmed, and indicated that the (16*R*)-ketone (1) was enolised under these conditions. Enolisation of the (16*R*)-ketone (1) was also observed at 80° in glacial acetic acid containing bromine: the 16α-bromo-ketone (4) was formed quantitatively. Also the latter product, whose 16α-bromo-configuration was determined on the basis of the o.r.d. data discussed later, was debrominated exclusively to the 16*R*-epimer (1) by hydriodic acid, a process shown [5] to proceed by enol formation. Under identical conditions the 16*S*-epimer (2) was not brominated. The same results were obtained in the 13β-kaurane series. The 16*R*-epimer (5) was enolised at 60° in the presence of acetic acid and bromine to give the

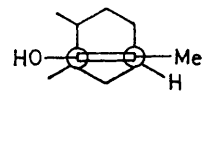
[1] Part II, J. MacMillan and E. R. H. Walker, preceding paper.
[2] M. F. Barnes, Ph.D. Thesis, University of Bristol, 1965.
[3] M. F. Barnes and J. McMillan, *J. Chem. Soc.* (*C*), 1967, 361.
[4] L. H. Briggs, R. C. Cambie, and P. S. Rutledge, *J. Chem. Soc.*, 1963, 5374.
[5] H. E. Zimmerman, *J. Amer. Chem. Soc.*, 1957, **79**, 6554.

16α-bromo-derivative (7). Under identical conditions the 16*S*-epimer (6) was recovered unchanged.

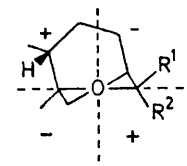
Clearly the 16*R*-epimers (1) and (5) are enolised much faster than the 16*S*-epimers (2) and (6), and the enols are ketonised exclusively to the 16*R*-epimers at the temperatures of boiling methanol or t-butyl alcohol. Slow epimerisation of the 16*R*- and 16*S*-epimers in both the *ent*-kauran-15-ones and the 13β-kauran-15-ones was observed in boiling n-propanol containing concentrated hydrochloric acid. The rate was greater in boiling dioxan but still *ca.* ten times less than the base-catalysed process. Prolonged treatment of the 16*R*- [(1) and (5)] and 16*S*- [(2) and (6)] epimers with acid in boiling dioxan gave the same mixture ratios as did the base-catalysed equilibration. Thus kinetic control of enolisation and ketonisation is replaced by thermodynamic control at higher temperatures.

The observed kinetic control of enolisation and ketonisation in these ketones can be explained by steric,[6-10] torsional,[11] and stereoelectronic [12,13] factors. On steric grounds it would be expected that the loss of a 16-proton from the ketones and addition of a 16-proton to the enols would occur more rapidly from the less hindered α-face. Torsional strain would act in the same direction. Ketonisation of the enol (17) from the α-face moves the 16-methyl group in the β-direction, increasing the dihedral angle between it and the 13-hydrogen atom and decreasing torsional strain. Ketonisation from the β-face decreases the dihedral angle between the 16-methyl group and the 13-hydrogen atom and increases torsional strain. By the principle of microscopic reversibility torsional strain should also favour enolisation of the 16*R*-epimers (1) and (5) over the 16*S*-epimers (2) and (6). For stereoelectronic effects to operate in the observed direction, the 16α-hydrogen atom is required to be pseudo-axial and the 16β-hydrogen atom to be pseudo-equatorial. If it is assumed that no conformational change takes place in forming the 16α-bromo-ketones (4) and (7), both the i.r. and the u.v. data for these bromo-ketones indicate that the 15,16-bridge is skewed such that the 16α-bond is pseudo-axial in character. Compared to the parent ketones, the 16α-bromo-ketones (4) and (7) respectively show Δν +5 and +8 cm^{-1} in the i.r. spectrum and Δλ +24 and +20 nm in the u.v. spectrum. The i.r. shifts are slightly greater [14,15] and the u.v. shifts slightly less [16] than those observed for axial bromocyclohexanones and indicate a partial axial character in the 16α-bonds. This evidence thus indicates that stereoelectronic factors, as well as steric and torsional effects, may control enolisation–ketonisation of the ketones (1) and (2) and (5) and (6).

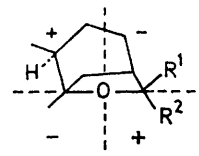
The o.r.d. and c.d. data for the 16*R*- and 16*S*-epimers (1) and (2) of *ent*-kauran-15-one differed from those previously reported; [4] the o.r.d. of (16*S*)-13β-kauran-15-one (6) has been described [17] as more negative than that of the 16*R*-epimer (5) without further details. In each pair the o.r.d. and c.d., the 16*R*-epimers are more negative than those of the 16*S*-epimers in accord with the assigned configurations [see (18), (19), (21), and (22)]. Both epimers of 13β-kauran-15-one show strong negative Cotton effects, suggesting that C-13 and C-14 are severely skewed into negative quadrants [see (18 ≡ 1) and (19 ≡ 2)]. The *ent*-kauran-15-ones show much smaller amplitudes in the negative sense, suggesting the much less skewed conformation [see (21 ≡ 5) and (22 ≡ 6)]. Indeed, the positive Cotton effect of the 16*S*-epimer (2) of *ent*-kauran-15-one is another exception to the generalisation [18] that bicyclo[3,2,1]octanones (24) have negative Cotton effects.



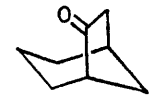
(17)



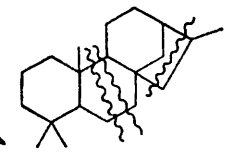
(18) R^1 = Me, R^2 = H
(19) R^1 = H, R^2 = Me
(20) R^1 = Me, R^2 = Br



(21) R^1 = Me, R^2 = H
(22) R^1 = H, R^2 = Me
(23) R^1 = Me, R^2 = Br



(24)



(25)

In the o.r.d. and c.d. spectra of the αβ-unsaturated ketones (11) and (12) the enone chromophores show *R*-bands ($n \longrightarrow \pi^*$) at 350 nm and *K*-bands ($\pi \longrightarrow \pi^*$) at about 215 nm. However, the rules which have been proposed correlating chirality of non-planar enone systems with the signs of the first-sphere [19] Cotton effect of the *K*-band [20] and *R*-band [19] cannot be reliably applied to cyclopentenones.[19] The chirality of the enones (11) and (12) cannot therefore be deduced from the data. The sign of the Cotton effects in the 16α-bromo-ketones (4) and (7) is much more positive than in

[6] H. E. Zimmerman, *J. Org. Chem.*, 1955, **20**, 559.
[7] H. E. Zimmerman, *J. Amer. Chem. Soc.*, 1956, **78**, 1168.
[8] H. E. Zimmerman, 'Molecular Rearrangement,' ed. P. de Mayo, Wiley, New York, 1963, Part I, p. 345.
[9] H. E. Zimmerman and P. S. Mariano, *J. Amer. Chem. Soc.*, 1968, **90**, 6091.
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[14] R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828.
[15] E. J. Corey and H. J. Burke, *J. Amer. Chem. Soc.*, 1955, **77**, 5418.
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[17] R. Henderson and R. Hodges, *Tetrahedron*, 1960, **11**, 226.
[18] W. Klyne, *Tetrahedron*, 1961, **13**, 29.
[19] G. Snatzke, 'Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry,' ed. G. Snatzke, Heyden and Son, London, 1967, p. 208.
[20] C. Djerassi, R. Records, E. Bunnenberg, K. Mislow, and A. Moscowitz, *J. Amer. Chem. Soc.*, 1962, **84**, 870.

the unbrominated ketones; this confirms the 16α-bromo-configuration in which the bromine atom is placed in a positive octant as in (20) and (23).

The preparation of the (16*R*)- and (16*S*)-15β-ols (13) and (14) has already been described. The remaining two epimers (15) and (16), required for n.m.r. studies, were prepared by hydrogenation of the 16-en-15α-ol (9), which gave both isomers (15) and (16) and not exclusively the 16*R*-epimer (15) as previously reported.[3,4] The major epimer (70%) was assigned the 16*R*-configuration because it could be oxidised quantitatively to the (16*R*)-ketone (1). The minor (30%) hydrogenation product (16) was likewise oxidised to the (16*S*)-ketone (2).

The mass spectra of the *ent*-kaurane and *ent*-13β-kauranes described in this paper and in Part II [1] indicate the three basic fragmentations shown in (25). The fragmentation patterns of Δ^{15} and Δ^{16} isomers and those of epimers were usually identical. However, the spectra of the *ent*-kauranes were always different from those of the corresponding diastereoisomeric 13β-kauranes.

EXPERIMENTAL

General experimental procedures are given in Part II.[1]

ent-*Kaur*-15-*ene*.—*ent*-Kaurene (1 g) was heated under reflux for 7 h in benzene (100 ml) with iodine (*ca.* 40 mg). The cooled mixture was washed with aqueous sodium thiosulphate (2 × 25 ml) and water (2 × 25 ml), dried, and evaporated to give a yellow solid (950 mg) shown by g.l.c. to contain 73% *ent*-kaur-15-ene. Preparative t.l.c. on eight silica gel plates (0·5 mm × 50 × 20 cm) impregnated with silver nitrate (25%) and developed with light petroleum–chloroform (3 : 1) gave *ent*-kaur-15-ene (560 mg), as plates, m.p. 65—67° (from ethanol); $[\alpha]_D^{22}$ −18° (*c* 2·6); $\nu_{max.}$ 3045, 1650, and 810 cm^{-1}; τ 9·18, 9·16, and 8·95 (each 3H, s), 8·50br (3H, s), and 5·0br (1H, s).

ent-*Kaur*-16-*en*-15β-*ol*.—*ent*-Kaur-15-ene (1·2 g) and haematoporphyrin (30 mg) in pyridine (25 ml) were irradiated and oxygenated for 96 h. The solution was evaporated at 40° and the crude product dissolved in ethanol (150 ml). Glacial acetic acid (15 drops) and sodium iodide (2·5 g) were added, and the solution was stirred at room temperature overnight. The ethanol was evaporated off and the dark residue washed with ether (3 × 20 ml). The combined ethereal solution was washed with aqueous sodium thiosulphate and water, dried, and evaporated to give a brown paste (1·25 g) which was chromatographed on silica gel (30 g). Elution with light petroleum gave a mixture of *ent*-kaur-15-ene and *ent*-kaur-16-ene (460 mg): 10% ether in benzene eluted *ent*-kaur-16-en-15β-ol (9) (680 mg), which crystallised from methanol as needles, m.p. 91—95°; $[\alpha]_D^{22}$ −30° (*c* 0·2); $\nu_{max.}$ 3380, 3050, 1660, and 898 cm^{-1}; τ 9·20, 9·15, and 8·98 (each 3H, s), 6·25br (1H, s), and 4·98br and 4·82br (each 1H, s).

ent-*Kaur*-16-*en*-15-*one* (11).—*ent*-Kaur-16-en-15β-ol (9) (100 mg) in pyridine (2 ml) was added to a stirred suspension of chromium trioxide (150 mg) in pyridine (2 ml) at 0°. After 4·5 h at room temperature the mixture was poured into ether (10 ml) and the ethereal solution was washed with aqueous sodium carbonate (2 × 2 ml), 3N-hydrochloric acid (2 × 2 ml), brine (2 × 2 ml), and water (2 × 2 ml). Recovery from the dried ether solution gave *ent*-kaur-16-en-15-one (11) (93 mg), as plates, m.p. 98—100° (from acetone); c.d. $\Delta\varepsilon_{400}$ 0, $\Delta\varepsilon_{348}$ −0·52, $\Delta\varepsilon_{290}$ 0, $\Delta\varepsilon_{250}$ 0, $\Delta\varepsilon_{212}$ −7·03, $\Delta\varepsilon_{200}$ 0; $\lambda_{max.}$ 236 nm (ε 7400); $\nu_{max.}$ 1720, 1640, and 935 cm^{-1}.

ent-(16S)-*Kauran*-15-*one* (1).—*ent*-Kaur-16-en-15-one (9) (98 mg) in ethanol (7 ml) was added to 10% palladium–charcoal (50 mg) and hydrogenated at room temperature for 45 min. After removal of the catalyst by filtration, evaporation yielded the ketone (1) which crystallised from acetone as needles (98 mg), m.p. 147—148° (Found: M^+, 288·241. Calc. for $C_{20}H_{32}O$: *M*, 288·245); $[\alpha]_D^{22}$ −101° (*c* 0·55), $[\alpha]_D^{22}$ −104° (*c* 0·55 in $CHCl_3$); o.r.d. $[\phi]_{322}$ −2240, $[\phi]_{295}$ +415, $[\phi]_{248}$ −2610, $[\phi]_{200}$ −9000; c.d. $\Delta\varepsilon_{330}$ 0, $\Delta\varepsilon_{310}$ −0·51, $\Delta\varepsilon_{292}$ 0, $\Delta\varepsilon_{280}$ +0·17, $\Delta\varepsilon_{250}$ 0, $\Delta\varepsilon_{208}$ −0·83; $\lambda_{max.}$ 297 nm (ε 55); $\nu_{max.}$ 1730 cm^{-1}; τ 9·22, 9·17, and 8·96 (each 3H, s), and 8·94 (3H, d, $J_{16.17}$ 6·5 Hz).

Epimerisation of ent-(16S)-*Kauran*-15-*one* (1).—*ent*-(16*S*)-Kauran-15-one (98 mg) was heated under reflux with methanolic 2% sodium hydroxide (20 ml) for 9 h. The methanol was removed and the residue taken up in water (10 ml) and extracted with ether (3 × 5 ml). The combined extracts were washed with water (3 × 3 ml), dried, and evaporated to yield a crystalline solid (93 mg); g.l.c. analysis on a 2% SE-33 column showed two components (%; retention index): *ent*-(16*S*)-kauran-15-one (1) (62; 2217), and *ent*-(16*R*)-kauran-15-one (2) (38; 2203). Further treat- under basic conditions did not change the composition of the epimeric mixture.

ent-(16S)-*Kauran*-15α-*ol* (13).—*ent*-(16*S*)-Kauran-15-one (10 mg) in sodium-dried ether (2 ml) was added to a stirred suspension of lithium aluminium hydride (10 mg) in sodium-dried ether (2 ml) at room temperature. After 40 min, water was added and the mixture was stirred for a further 5 min. 3N-Hydrochloric acid was added dropwise until a clear solution was obtained. This was extracted with ether (3 × 5 ml) and the combined extracts were washed with brine (2 × 5 ml) and water (2 × 5 ml), dried, and evaporated to yield ent-(16S)-*kauran*-15α-*ol* (9 mg) which crystallised from methanol as white prisms, m.p. 133—134° (Found: M^+ 290·258. $C_{20}H_{34}O$ requires *M*, 290·261); $[\alpha]_D^{22}$ −52° (*c* 0·4); $\nu_{max.}$ 3540 and 3350 cm^{-1}; τ 9·22, 9·18, and 9·00 (each 3H, s), 9·08 (3H, d, $J_{16.17}$ 7 Hz), and 6·48 (1H, d, $J_{15.16}$ 11 Hz).

ent-(16R)-*Kauran*-15α-*ol* (14).—A mixture of *ent*-(16*S*)-kauran-15-one (65%) and *ent*-(16*R*)-kauran-15-one (35%) (93 mg) in sodium-dried ether (5 ml) was added to a stirred suspension of lithium aluminium hydride (90 mg) in sodium-dried ether (5 ml) at room temperature. After 40 min water was added and the mixture stirred for a further 5 min. Work-up as before yielded a mixture of *ent*-(16*S*)-kauran-15α-ol and *ent*-(16*R*)-kauran-15α-ol (90 mg) as a white semi-crystalline solid. Preparative t.l.c. on five silica plates (0·5 mm × 20 × 20 cm), developed in benzene–light petroleum (3 : 2), yielded *ent*-(16*S*)-kauran-15α-ol (51 mg) as prisms, m.p. 133—134° (from methanol), and ent-(16*R*)-*kauran*-15α-*ol* (25 mg), a clear non-crystalline oil shown to contain less than 0·5% of the 16*R*-epimer by g.l.c. (Found: M^+, 290·260. $C_{20}H_{34}O$ requires *M*, 290·261); $\nu_{max.}$ 3570 and 3350 cm^{-1}; τ 9·21, 9·17, and 8·98 (each 3H, s), 8·95 (3H, d, $J_{16.17}$ 7·5 Hz), and 7·07 (1H, d, $J_{15.16}$ 4·5 Hz).

Oxidation of ent-(16S)-*Kauran*-15α-*ol* (13).—*ent*-(16*S*)-Kauran-15α-ol (1 mg) in dry pyridine (2 ml) was added to a stirred suspension of chromium trioxide (5 mg) in dry pyridine (2 ml) at 0°. The mixture was allowed to warm to room temperature and stirred for 5 h. It was then poured into ether (3 ml), acidified with 3N-hydrochloric acid, and

extracted with ether (2 × 5 ml). The combined ethereal solution was washed with brine (2 × 5 ml) and water (2 × 5 ml), dried, and evaporated to yield a white crystalline solid (0·9 mg) which was shown by g.l.c. and t.l.c. to be pure *ent*-(16*S*)-kauran-15-one (1).

Oxidation of ent-(16R)-*Kauran*-15α-*ol* (14).—*ent*-(16*R*)-Kauran-15α-ol (20 mg) in dry pyridine (1 ml) was added to a stirred suspension of chromium trioxide (30 mg) in dry pyridine (1·5 ml) at 0°. The stirred mixture was allowed to warm to room temperature, and after 3 h was poured into ether (10 ml); the solution was washed with 3N-hydrochloric acid (2 × 2 ml), brine (2 × 2 ml), and water (2 × 2 ml), dried, and evaporated to yield ent-(16R)-*kauran*-15-*one* (2) (19·8 mg), which crystallised from acetone as needles, m.p. 119—120° (Found: M^+, 288·245. $C_{20}H_{32}O$ requires M, 288·245); $[\alpha]_D^{22}$ −89° (*c* 1·1); $[\alpha]_D^{22}$ −89° (*c* 1·1 in MeOH); o.r.d. $[\phi]_{400}$ −680, $[\phi]_{320}$ +340, $[\phi]_{276}$ −4420, $[\phi]_{205}$ −21,000; c.d. $\Delta\varepsilon_{330}$ 0, $\Delta\varepsilon_{304}$ +0·79, $\Delta\varepsilon_{250}$ 0, $\Delta\varepsilon_{209}$ −2·64; $\lambda_{max.}$ 300 nm (ε 21); $\nu_{max.}$ 1725 cm^{-1}.

Treatment of ent-(16S)-*Kauran*-15-*one* (1) *with Acid*.—(*a*) The following refluxing media did not effect epimerisation, and *ent*-(16*S*)-kauran-15-one was recovered quantitatively: 2% hydrochloric acid in methanol; 6% hydrochloric acid in t-butyl alcohol; and glacial acetic acid at 80°. In a typical experiment, *ent*-(16*S*)-kauran-15-one (1 mg) was dissolved in the acidic medium (2 ml) and refluxed for 3 h. The organic solvent was removed and the residue dissolved in ether (2 ml). The ethereal solution was washed with water (3 × 0·5 ml), dried, and evaporated to yield a solid which was shown by g.l.c. and t.l.c. to be pure starting material.

(*b*) *ent*-(16*S*)-Kauran-15-one (1 mg) was heated under reflux in 5% hydrochloric acid in n-propanol and in 5% hydrochloric acid in dioxan. The work-up procedure was as in (*a*) and the ratio of the mixtures of the (16*R*)- (1) (retention index 2217) and (16*S*)- (2) (retention index 2203) ketones was determined by g.l.c. on a 2% SE-33 column. After 15 h under reflux in the first solvent the ratio of (1) to (2) was 94 : 6. In the second solvent ratios were 74 : 26 (15·5 h), 67 : 33 (30 h), and 65 : 35 (40 h).

Epimerisation of ent-(16R)-*Kauran*-15-*one* (2).—(a) *Base*. *ent*-(16*R*)-Kauran-15-one (1 mg) was heated under reflux with 2% sodium hydroxide in methanol. The products were analysed by g.l.c. after 6 and 20 h. The work-up procedure was similar to that described for base-catalysed epimerisation of *ent*-(16*S*)-kauran-15-one. The ratio of (1) to (2) was 50 : 50 after 6 h and 63·5 : 36·5 after 20 h.

(*b*) *Acid*. The following media did not effect epimerisation and *ent*-(16*R*)-kauran-15-one was recovered quantitatively: 2% hydrochloric acid in refluxing methanol; 6% hydrochloric acid in refluxing t-butyl alcohol; and glacial acetic acid at 80°. The experimental procedure was identical to that described for the attempted acid-epimerisation of *ent*-(16*S*)-kauran-15-one (1).

Bromination of ent-(16S)-*Kauran*-15-*one* (1).—The ketone (10 mg) was dissolved in glacial acetic acid (2 ml) and an excess of bromine was added. After 10 min at 80° the mixture was poured into an excess of sodium hydrogen carbonate solution containing sodium thiosulphate to discharge the remaining bromine; the product was extracted with ether (3 × 5 ml) and the combined ethereal solutions were washed with water (2 × 3 ml), dried, and evaporated to yield ent-16β-*bromokauran*-15-*one* (4) (9·3 mg), which crystallised from light petroleum as plates, m.p. 160—162° (Found: M^+, 368·151. $C_{20}H_{31}BrO$ requires M, 368·153); o.r.d. $[\phi]_{400}$ 0, $[\phi]_{350}$ +1690, $[\phi]_{310}$ −6100, $[\phi]_{286}$ −4750, $[\phi]_{237}$ −8110, $[\phi]_{210}$ +2710; c.d. $\Delta\varepsilon_{370}$ 0, $\Delta\varepsilon_{329}$ +1·73, $\Delta\varepsilon_{290}$ 0, $\Delta\varepsilon_{220}$ −3·05; $\lambda_{max.}$ 231 nm (ε 73); $\nu_{max.}$ 1735 cm^{-1}.

Attempted Bromination of ent-(16R)-*Kauran*-15-*one* (2).—The ketone was recovered quantitatively after treatment with excess of bromine in glacial acetic acid at 80° for 10 min.

Bromination of (16R)-13β-*Kauran*-15-*one* (5).—(16*R*)-13β-Kauran-15-one (5) (10 mg) was dissolved in glacial acetic acid (2 ml) and an excess of bromine was added. After 15 min at 80°, the mixture was poured into an excess of sodium hydrogen carbonate solution containing sodium thiosulphate to discharge the remaining bromine. Recovery of the organic material in ether and evaporation gave 16α-*bromo*-13β-*kauran*-15-*one* (7) (10·5 mg), which crystallised from light petroleum as needles, m.p. 100—105°; $[\alpha]_D^{22}$ +37° (*c* 0·43); o.r.d. $[\phi]_{400}$ 0, $[\phi]_{335}$ +680, $[\phi]_{237}$ −2220, $[\phi]_{216}$ +8040; c.d. $\Delta\varepsilon_{350}$ 0, $\Delta\varepsilon_{319}$ +0·26, $\Delta\varepsilon_{254}$ +0·29, $\Delta\varepsilon_{224}$ −2·13; $\lambda_{max.}$ 320 nm (ε 132); $\nu_{max.}$ 1735 cm^{-1}.

Attempted Bromination of (16S)-13β-*Kauran*-15-*one* (6).—The ketone was recovered quantitatively after treatment with excess of bromine in glacial acetic acid at 80° for 15 min.

Debromination of ent-16β-*Bromokauran*-15-*one* (4).—Hydrogen iodide (60%; 0·1 ml) was added to a solution of *ent*-16β-bromokauran-15-one (1 mg) in acetone (0·5 ml). After 3 min at room temperature excess of sodium thiosulphate was added: the yellow solution was extracted with ether (2 × 1 ml) and the combined ethereal solution was washed with water (2 × 0·5 ml), dried, and evaporated to yield a yellow solid. G.l.c. and t.l.c. analyses showed the presence of pure *ent*-(16*S*)-kauran-15-one (1).

Debromination of 16α-*Bromo*-13β-*kauran*-15-*one* (7).—Treatment of 16α-bromo-13β-kauran-15-one (7) with 60% hydrogen iodide as just described yielded (16*R*)-13β-kauran-15-one (5) free from 16*S*-epimer.

Acid Epimerisation of (16R)- *and* (16S)-13β-*Kauran*-15-*ones* (5) *and* (6).—(*a*) (16*R*)- and (16*S*)-13β-Kauran-15-one (5 and 6) were recovered quantitatively from the following refluxing media: 2% hydrochloric acid in methanol; 6% hydrochloric acid in t-butyl alcohol; and glacial acetic acid at 80°.

(*b*) Prolonged treatment of both (16*R*)- and (16*S*)-13β-kauran-15-one (5) and (6) with refluxing 5% hydrochloric dioxan gave (g.l.c. analysis) an equilibrium mixture of (16*R*)- and (16*S*)-13β-kauran-15-one in the ratio of 4 : 6.

Hydrogenation of ent-*Kaur*-16-*en*-15β-*ol* (9).—*ent*-Kaur-16-en-15β-ol (39 mg) in ethanol (7 ml) was hydrogenated over 2% palladium–barium carbonate (40 mg) at room temperature and pressure for 3 h. After removal of the catalyst by filtration through sodium sulphate, evaporation gave a white crystalline solid (39 mg). Preparative t.l.c. on five silica plates (0·4 mm × 20 × 20 cm) developed with benzene–light petroleum (3 : 2) yielded ent-(16R)-*kauran*-15β-*ol* (16) (1·7 mg), R_F 0·3, crystallised from methanol as needles, m.p. 75—77° (Found: M^+, 290·259. $C_{20}H_{34}O$ requires M, 290·261); $\nu_{max.}$ 3570 and 3400 cm^{-1}; τ 9·22, 9·20, and 9·18 (each 3H, s), 9·09 (3H, d, $J_{16.17}$ 7·5 Hz), and 6·47 (1H, d, $J_{15.16}$ 8 Hz); and *ent*-(16*S*)-kauran-15β-ol (15) (25 mg),[3,4] R_F 0·18, which crystallised from light petroleum as needles, m.p. 138—139° (Found: M^+, 290·258. Calc. for $C_{20}H_{34}O$: M, 290·261); $[\alpha]_D^{22}$ −26°; $\nu_{max.}$ 3300, 3[illegible] and 1055 cm^{-1}; τ 9·22, 9·18, and 9·01 (each 3H, s), 8·92 (3H, d, $J_{16.17}$ 7·0 Hz), and 6·84 (1H, dd, $J_{15.16}$ 4·5 Hz, $J_{15.?}$ 1·5 Hz).

Oxidation of ent-(16S)-*Kauran*-15β-*ol* (15).—*ent*-(16*S*)-Kauran-15β-ol (15) (1 mg) in dry pyridine (0·5 ml) was added to a stirred suspension of chromium trioxide (1 mg)

in dry pyridine (0·5 ml) at 0°. The mixture was stirred at room temperature for 3 h. The usual work-up yielded pure *ent*-(16*S*)-kauran-15-one (1).

Oxidation of ent-(16R)-*Kauran*-15β-*ol* (16).—*ent*-(16*R*)-Kauran-15β-ol (10 mg) in dry pyridine (1 ml) was added to a stirred suspension of chromium trioxide (20 mg) in dry pyridine (1 ml) at 0°. The mixture was stirred at room temperature for 4 h. The usual work-up yielded *ent*-(16*R*)-kauran-15-one (2) (9 mg) containing 2% *ent*-(16*S*)-kauran-15-one (1) (analysed by g.l.c.).

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