Terpenoids. Part VI.[1] Preparation of *ent*-[13,14α-$^2H_2$]Kaur-16-ene and Some Derivatives; Bridgehead Enolisation of *ent*-17-Nor[13,14α-$^2H_2$]-kauran-16-one

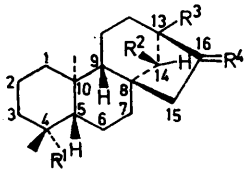
By **David H. Bowen, Christopher Cloke, and Jake MacMillan,*** The School of Chemistry, The University, Bristol BS8 1TS

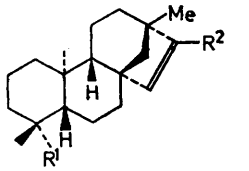
Rearrangement of the phenylsulphonylhydrazone of *ent*-beyeran-16-one (*ent*-13-methyl-17-nor-8β,13β-kauran-16-one) (17) with sodium methoxide in methan[^{2}H]ol yielded *ent*-[16-^{2}H]beyer-15-ene (11), *ent*-[13,14α-$^2H_2$]kaur-16-ene (5), *ent*-[13,14α-$^2H_2$]kaur-15-ene (20), and three methoxy-substituted isomers of which *ent*-16-methoxy[$^2H_2$]kaurane was the main component. Bridgehead enolisation of *ent*-17-nor[13,14α-$^2H_2$]kauran-16-one (6) was demonstrated by oxidation of the ketone, before and after heating with potassium t-butoxide, to the lactones (23) and (25), respectively, in which the absence or presence of the 13-hydrogen atom was shown by the presence or otherwise of a one-proton multiplet at τ 5·22 in the n.m.r. spectra.

The mass spectra of some of the [$^2H_2$]diterpenes, and the n.m.r. spectra of the *ent*-beyeran-15- and 16-ones (16) and (17) in the presence of the shift reagent Eu(dpm)$_3$, are discussed.

PRECEDENTS [2-4] for the formation or intermediacy of bridgehead olefins encouraged us to examine 13-bridgehead enolisation of *ent*-17-norkauran-16-one (1) as a basis for an auto-oxidative route to *ent*-13-hydroxykauranes, required for metabolic studies. Since the completion of this study numerous additional examples of the intermediacy of bridgehead olefins in normal-sized rings have appeared.[5] A particularly relevant example is the bridgehead enolisation in the bicyclo[3.2.1]octanones copacamphor and longicamphor, reported by Turnbull *et al.*[6] prior to our preliminary note.[7]

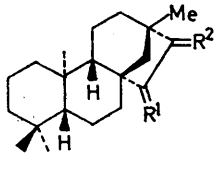
Direct base-catalysed deuteriation of the nor-ketone (1) with potassium t-butoxide in t-butyl alcohol was examined first. Mass spectrometry of the recovered ketone showed the following distribution of label: 6% $^2H_0$, 34·5% $^2H_1$, 58% $^2H_2$, 1·5% $^2H_3$. After treatment with 0·05N-sodium hydroxide, the ^{2}H distribution was 96·5% $^2H_0$, 3·5% $^2H_1$. The low percentage of trideuteriated material precluded the unambiguous assignment of the third ^{2}H atom to the bridgehead position, and the known [8] stereospecificity of ^{2}H–^{1}H exchange at the 15-position in the nor-ketone (1) made interpretation of these results difficult. Moreover, deuteriation at C-12 *via* the homoenolate anion [9] could not be excluded. Accordingly, definitive evidence for bridgehead enolisation was sought by studying ^{2}H–^{1}H exchange in the [13-^{2}H]nor-ketone (2), derived from *ent*-[13-^{2}H]kaur-16-ene (3), the latter being rationally synthesised by rearrangement of *ent*-beyeran-16-one phenylsulphonylhydrazone (13) in a deuteriated alcohol. The starting point was *ent*-kaur-16-ene (4), which was isolated [10] from *Cryptomeria japonica* var. elegans. It was isomerised by iodine in boiling xylene to give a mixture containing 70% *ent*-beyer-15-ene (10), 15% *ent*-kaur-16-ene (4), and 15% *ent*-kaur-15-ene (18) (*cf.* ref. 11), which was separated by preparative layer chromatography (p.l.c.) with difficulty. Hydroboronation of *ent*-beyer-15-ene (10) [12] provided the 15- and 16-alcohols (14) and (15), which were oxidised to the respective ketones (16) and (17). Since the hydrocarbons (10) and (18) and the alcohols (14) and (15) were difficult to separate it was more economical to convert *ent*-kaur-16-ene (4) directly into the readily separable ketones (16) and (17) and *ent*-kauran-15-one without

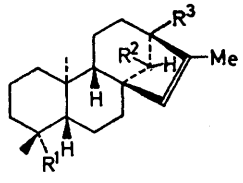




	R^1	R^2	R^3	R^4
(1)	Me	H	H	O
(2)	Me	H	D	O
(3)	Me	H	D	CH_2
(4)	Me	H	H	CH_2
(5)	Me	D	D	CH_2
(6)	Me	D	D	O
(7)	Me	D	H	O
(8)	Me	D	D	Me,OMe
(9)	CO_2Me	H	H	CH_2

(10) R^1 = Me, R^2 = H
(11) R^1 = Me, R^2 = D
(12) R^1 = CO_2Me, R^2 = H





(13) R^1 = H_2, R^2 = N·NH·SO_2Ph
(14) R^1 = H, β – OH, R^2 = H_2
(15) R^1 = H_2, R^2 = H, β – OH
(16) R^1 = O, R^2 = H_2
(17) R^1 = H_2, R^2 = O

(18) R^1 = Me, R^2 = R^3 = H
(19) R^1 = CO_2Me, R^2 = R^3 = H
(20) R^1 = Me, R^2 = R^3 = D

[1] PartV, J. MacMillan and E. R. H. Walker, *J.C.S. Perkin I*, 1972, 1274.
[2] W. Carruthers and M. J. Qureshi, *Chem. Comm.*, 1969, 832.
[3] R. Keese and J. P. Chen, *Angew. Chem. Internat. Edn.*, 1971, **10**, 262.
[4] J. R. Wiseman and W. A. Pletcher, *J. Amer. Chem. Soc.*, 1970, **92**, 956.
[5] J. Mellor, *Ann. Reports (B)*, 1972, **69**, 408.
[6] K. W. Turnbull, S. J. Gould, and D. Arigoni, *J.C.S. Chem. Comm.*, 1972, 597.
[7] D. H. Bowen and J. MacMillan, *Tetrahedron Letters*, 1972, 4111.
[8] R. Evans and J. R. Hanson, *J.C.S. Perkin I*, 1972, 2382.
[9] A. Nickon and J. L. Lambert, *J. Amer. Chem. Soc.*, 1966, **88**, 1905.
[10] J. MacMillan and E. R. H. Walker, *J.C.S. Perkin I*, 1972, 981.
[11] A. Yoshikoshi, M. Kitadami, and Y. Kitahara, *Tetrahedron*, 1967, **23**, 1175.
[12] P. R. Sobti and S. Dev, *Tetrahedron Letters*, 1966, 3939.

intermediate separations. Like their enantiomers,[13] the ketones (16) and (17) were distinguished by the non-reactivity of the less polar and more hindered 15-oxo-group (16) to carbonyl reagents. They were also distinguished by their n.m.r. spectra run in the presence of the shift reagent $Eu(dpm)_3$.

The gradient of the least squares plot of the observed shift (δ_0) against $Eu(dpm)_3$ concentration (L_0) was obtained for the methyl and CH_2CO protons in the 15- and 16-ketones (16) and (17). In the 16-ketone one of the 15-methylene protons was located by INDOR. For $\delta_0 \ll \delta_c$ (shift for the substrate–reagent complex), the gradient of a plot of δ_0 against the ratio $L_0 : S_0$ (substrate concentration) is given by $S_0[\delta_c/(S_0 + 1/K)]$ where K is the equilibrium constant for the formation of the complex. Since measurements are usually made at similar concentrations (S_0 *ca.* 0·1 mM), the shift gradients can be usefully compared.[14] If K is large, the gradient simplifies to δ_c. However, some recently determined [15] values of K are not sufficiently large for $1/K$ to be neglected. We therefore elected to normalise the gradients relative to the smallest gradient, which was taken as unity. The term $S_0/(S_0 + 1/K)$ cancels out for all proton gradients and the normalised gradients are independent of the concentration S_0. Relative gradients calculated from the McConnell equation by using reiterative computation, were compared with the observed relative gradients for a series of parameters. The best fits, shown in Table 1, are not intended to indicate the

TABLE 1

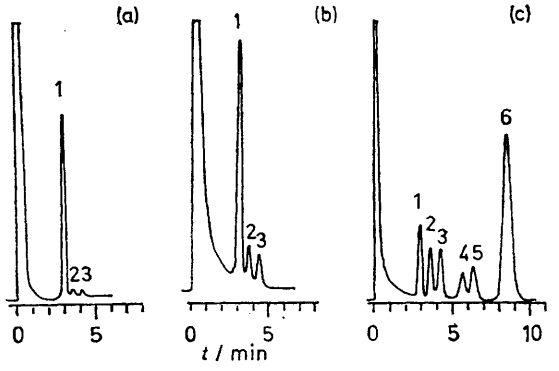
Relative shift gradients for *ent*-beyeran-15- and 16-ones

	15-Ketone (16)		16-Ketone (17)	
Proton	Obs.	Calc.[a]	Obs.	Calc.[b]
15-H_A	8·4	6·7	57·0	40·0
15-H_B	8·3	6·7	60·0	48·0
20-H_3	6·1	5·1	6·6	9·9
18-H_3	1·0	1·0	1·0	1·0
19-H_3	1·2	1·4	3·1	1·6
17-H_3	1·1	1·6	48·0	44·0

[a] Eu–$\widehat{O}$–C 140°; Eu–O 2 Å; ring A in boat conformation. [b] Eu–$\widehat{O}$–C 180°; Eu–O 2·7 Å; ring A in chair conformation.

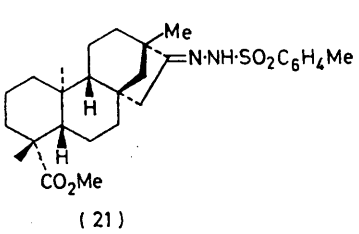
best conformations but to illustrate that sufficient agreement was obtained to assign the methyl signals for both ketones. In the spectra of the uncomplexed ketones the 17-proton signals were at higher field for the 16-ketone, indicating that ring D in this ketone is twisted to place the 17-protons in the shielding zone of the 16-carbonyl group. This twisting would relieve steric interaction between the 20- and the 15-protons.

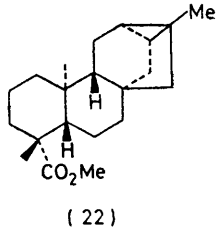
A close analogy for the rearrangement of the phenylsulphonylhydrazone (13) to *ent*-kaur-16-ene (4) is provided by Coates and Bertram,[16] who obtained methyl *ent*-kaur-16-en-18-oate (9) and the epimeric 15-ene together with methyl *ent*-beyer-15-en-18-oate (12) and methyl *ent*-13,16-cycloatisan-18-oate (22) by decomposition of the sodium salt of the *p*-tolylsulphonylhydrazone (21). We examined the decomposition of the phenylsulphonylhydrazone (13) under a variety of conditions, analysing the products by g.l.c. and g.l.c.–mass spectrometry

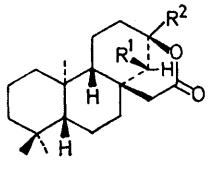


G.l.c. of products from decomposition of the phenylsulphonylhydrazone (13) with sodium methoxide in: (a) 3,6-dioxaoctan-1-ol at 190°; (b) 3,6-dioxaoctan-1-ol at 90°; and (c) methanol. Products: 1, *ent*-beyer-15-ene; 2, *ent*-kaur-15-ene; 3, *ent*-kaur-16-ene; 4 and 5, unknown isomers of 6; and 6, *ent*-16-methoxykaurane

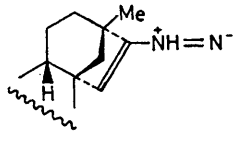
(Figure). With sodium methoxide in 3,6-dioxaoctan-1-[^{2}H]ol at 190° for 1 h the main product (35%) was non-deuteriated *ent*-beyer-15-ene (10), obtained in conjunction with *ent*-[^{2}H]kaur-15- and 16-enes (each 4%) [Figure (a)] containing *ca.* 20% ^{2}H. At 90° for 2 h with

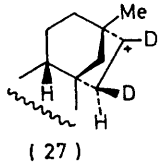


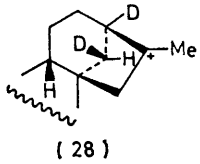




(23) $R^1 = R^2 = D$
(24) $R^1 = R^2 = H$
(25) $R^1 = D, R^2 = H$







another preparation of the same solvent the total yield of hydrocarbons was 75% [Figure (b)] of which 17% was *ent*-kaur-16-ene containing 50% $^2H_1$. However, at both

[13] Y. Kitahara and A. Yoshikoshi, *Tetrahedron Letters*, 1964, 1771.
[14] J. K. M. Saunders and D. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 641.
[15] I. Armitage, G. Dunsmore, L. D. Hall, and A. G. Marshall, *Canad. J. Chem.*, 1972, **50**, 2119.
[16] R. M. Coates and E. F. Bertram, *J. Org. Chem.*, 1971, **36**, 3722.

temperatures the yield of *ent*-kaur-16-ene varied from 0 to 20%; the ^2H incorporations were also low and variable owing to difficulty in the preparation of the deuteriated solvent. As expected [17,18] the use of less acidic alcohols such as propan-2-ol and t-butyl alcohol yielded almost entirely *ent*-beyer-15-ene (10), presumably *via* the carbene. With sodium methoxide in methan-[^2H]ol [Figure (c)] nearly equal amounts of the hydrocarbons were obtained together with three isomeric methoxy-compounds of which *ent*-16-methoxy[$^2H_2$]-kaurane (8) was the major product. The ^2H content of these products is shown in Table 2; the incorporation of

TABLE 2

^2H Content (%) [a] of *ent*-[13,14α-$^2H_2$]kaur-16-ene and related compounds

Compound	$^2H_0$	$^2H_1$	$^2H_2$
(5)	5	38	57
(20)	6	37	56
(11)	19	79	2
(6)	5	38	57
(6) [b]	5	36	59
(23)	5	36	59
(6) [c]	4	51	45
(7)	43	52	5
(25)	42	51	7

[a] Average of 10 mass spectral scans; corrected for ^{13}C. [b] After treatment with aqueous sodium hydroxide. [c] Second preparation.

two deuterium atoms in the *ent*-kauranes was unexpected and is discussed later. The positions of the ^2H atoms in the products were determined from the following data.

The hydrocarbon mixture [Figure (c)], separated from the methoxy-compounds by p.l.c., was further fractionated on silica gel–silver nitrate layers to give *ent*-[$^2H_2$]-kaur-16-ene and a 2 : 1 mixture of *ent*-[$^2H_1$]beyer-15-ene and *ent*-[$^2H_2$]kaur-15-ene. The latter mixture was hydroboronated, then oxidised to give a mixture of ketones which was analysed by g.l.c.–mass spectrometry. The ^2H atom was retained in the 15-ketone (16) but not in the 16-ketone (17), showing that the *ent*-beyer-15-ene contained a 16-^2H atom. Moreover the n.m.r. spectrum of the mixture of *ent*-[16-^2H]beyer-15-ene (11) and *ent*-[$^2H_2$]kaur-15-ene did not show the higher field proton (τ 4·60) of the AB-vinylic proton signal of *ent*-beyer-15-ene (10), and the lower field proton (τ 4·33, *J* 6 Hz) of (10) was present in the case of (11) as a broad singlet (τ 4·32). Thus the higher field vinylic doublet in the spectrum of (10) is due to the 16-proton. Comparison of the n.m.r. spectrum of *ent*-kaur-15-ene (18) with that of *ent*-[$^2H_2$]-kaur-15-ene admixed with *ent*-[16-$^2H_1$]beyer-15-ene (11) showed the following significant differences. The multiplet at τ 7·63, assigned to the 13-proton, was absent from the spectrum of the $^2H_2$ compound. Also the doublet (τ 7·82, *J* 11 Hz) which was assigned to the *ent*-14α-proton in *ent*-kaur-15-ene (18) since there was no further coupling to the 13-proton (θ *ca.* 90°) occurred in the spectrum of the $^2H_2$ compound as a broad singlet. From these facts *ent*-[13,14α-$^2H_2$]kaur-15-ene (20) was identified as one of the products.

The presence of a 13-^2H atom in the *ent*-[$^2H_2$]kaur-16-ene was established as follows. Oxidation with osmium tetroxide–sodium periodate gave the [$^2H_2$]nor-ketone (6) without change in the ^2H content (Table 2) either before or after treatment with dilute sodium hydroxide, showing the absence of 15- and 17-^2H in *ent*-[$^2H_2$]kaur-16-ene. Oxidation of the nor-ketone (6) to the lactone (23) also occurred without change in the ^2H content (Table 2). The n.m.r. spectrum of the lactone (23) showed that the 13-H multiplet occurring at τ 5·22 in the spectrum of the undeuteriated lactone (24) was absent.

The formation of *ent*-[16-^2H]beyer-15-ene (11), *ent*-[13,14α-$^2H_2$]kaur-16-ene (5), and *ent*-[13,14α-$^2H_2$]kaur-15-ene (20) from the rearrangement of the hydrazone (13) with sodium methoxide in methan[^2H]ol may be explained by the intermediary of the 15-ene (26). Stereospecific 15-deuteriation of this enamine followed by acid-catalysed decomposition [17] would provide the ion (27). The latter ion can either give *ent*-[16-^2H]beyerene (11) by stereospecific loss of the 15-^2H or undergo rearrangement to the ion (28) and hence the *ent*-[13,14α-$^2H_2$]kaurenes (5) and (20). Capture of the ion (28) by methanol would explain the formation of *ent*-16-methoxy-[$^2H_2$]kaurane (8). However similar capture of the ion (27) by methanol does not account for the formation of either of the two isomers of *ent*-methoxy[$^2H_2$]kaurane. Both showed different mass spectral fragmentations from those of the two products obtained by treatment of *ent*-beyer-15-ene (10) with methanol and sulphuric acid, and their structures are unknown.

Bridgehead enolisation in *ent*-17-nor[13,14α-$^2H_2$]-kauran-16-one (6) was demonstrated by heating with potassium t-butoxide in t-butyl alcohol. The nor-ketone used in this experiment was obtained from a rearrangement of the phenylsulphonylhydrazone (13) with the following label distribution: 4% $^2H_0$, 51% $^2H_1$, and 45% $^2H_2$ (Table 2). After treatment with base, the nor-ketone (7) had clearly exchanged one ^2H atom (Table 2). This exchange was shown to be at the 13-position by oxidation to the lactone (25), the n.m.r. spectrum of which showed the one-proton multiplet at τ 5·22 for the 13-hydrogen atom.

Evans and Hanson [8] have shown that the $M^+ - 43$ ions in the mass spectrum of *ent*-kaur-16-ene (4) and *ent*-17-norkauran-16-one (1) are formed by loss of ring D. They suggested that this fragmentation also involves the transfer of the 9-hydrogen atom together with the transfer of one of the 14-hydrogen atoms in the case of the hydrocarbon (4) or, in the case of the ketone (1) with the transfer of an unspecified hydrogen atom. Comparison (Table 3) of the ^2H content of the M^+ and $M^+ - 43$ ions for the $^2H_2$ derivatives indicates partial loss of the *ent*-14α-^2H in both the *ent*-kaur-16-ene and the nor-ketone, and also some loss of the 13-^2H in the *ent*-kaur-16-ene. The data also show that the $M^+ - 43$ ion in *ent*-[13,14α-$^2H_2$]kauran-15-one does not involve loss of the deuterium; on the other hand the $M^+ - 58$ ion in the fragmentation of this compound appears to involve the stereospecific loss of one ^2H atom, probably that at position 14.

[17] J. W. Powell and M. C. Whiting, *Tetrahedron*, 1959, **7**, 305.
[18] J. M. Coxon, M. P. Hartshorn, D. M. Kirk, and M. A. Wilson, *Tetrahedron*, 1969, **25**, 3017.

TABLE 3

^2H Content [a] of some fragment ions from *ent*-[13,14α-$2H_2$]kaur-16-ene and related compounds

Compound	Ion	$^2H_0$	$^2H_1$	$^2H_2$
(5)	M^+	6	36	57
	$M^+ - 15$	4	39	57
	$M^+ - 43$	25	50	25
(6)	M^+	3	37	59
	$M^+ - 15$	3	42	55
	$M^+ - 43$	9	53	35
(7)	M^+	43	52	5
	$M^+ - 15$	46	51	3
	$M^+ - 43$	62	32	6
ent-Kauran-15-one	M^+	10	37	53
	$M^+ - 15$	17	36	48
	$M^+ - 43$	17	34	49
	$M^+ - 58$	10	83	7

[a] Data from a single mass spectral scan of each compound corrected for ^{13}C.

Significant ions at *m/e* 246, 245, and 244 occur in the spectrum of both the *ent*-beyeran-15-one (16) and the 16-^2H derivative with the same relative abundance, and clearly represent the loss of ring D with the transfer of none, one, and two hydrogen atoms.

EXPERIMENTAL

For general experimental details see Part II.[10] G.l.c.–mass spectrometry was carried out as described in ref. 19. For g.l.c. and g.l.c.–mass spectrometry a 2% SE-33 column was routinely used isothermally at 181°.

Calculation of Relative Shift Gradients.—For a distant proton (H_d), the measured distance $H_d \cdots O$ (*a*), the relative shift gradient (= 1), and trial values for the $Eu \cdots H_d$ distance (*r*) and $Eu \cdots O$ distance (*b*) were used to calculate *K* from the expression (i). The *s* and *a* values for the

$$\text{Shift } (s) = \frac{K[3(r^2 + b^2 - a^2)^2 - 4b^2r^2]}{4b^2r^5} \qquad \text{(i)}$$

remaining protons were considered in turn. For the values *r* between a lower limit and rising by increments to a higher limit the values *s* were calculated. If the observed values for *s* lay between two successive calculated values for *s*, one of the calculated *s* values was printed out together with the appropriate value *r*. Thus a set of *r* values were obtained which best fitted the observed data for the trial values of *b* and *r* for the proton H_d. If an observed value of *s* lay on a turning point it might be missed; to avoid this the relevant turning points were printed out by using the expression (ii).

$$r \text{ (at turning point)} = \pm[b^2 + 3a^2 \pm 2(a^4 - a^2b^2 + b^4)^{\frac{1}{2}}]^{\frac{1}{2}} \qquad \text{(ii)}$$

Direct Deuteriation of ent-17-*Norkauran*-16-*one* (1).—The nor-ketone (45 mg), t-butyl [^2H]alcohol (1 g), and potassium t-butoxide (1 g) were heated at 140° for 6 days in a sealed tube. After addition of deuterium oxide (0·9 ml) the product was recovered in ethyl acetate and purified by p.l.c. on silica gel with light petroleum–acetone (4 : 1). Extraction of the band at R_F 0·5—0·7 gave the [^2H]nor-ketone (1), which crystallised from methanol in needles (40 mg), m.p. 117—118°, with isotope distribution 6% $^2H_0$, 34·5% $^2H_1$, 58% $^2H_2$, 1·5% $^2H_3$; *m/e* 277 (7·5%), 276 (36), 275 (20), 274 (3), 262 (9), 261 (49), 260 (25), 231 (17), 123 (93), and 43 (100).

ent-*Beyer*-15-*ene* (ent-13-*Methyl*-17-*nor*-8β,13β-*kaur*-15-*ene*) (10).—ent-Kaur-16-ene (4) (500 mg), xylene (300 ml), and iodine (*ca.* 200 mg) were boiled for 20 h. The mixture was washed with aqueous sodium thiosulphate (3 × 50 ml) and water (3 × 50 ml), then dried and evaporated under reduced pressure to give a yellow oil. This product, shown by g.l.c. to contain 70% of *ent*-beyer-15-ene (10), 15% of *ent*-kaur-15-ene (18), and 15% of *ent*-kaur-16-ene (4), was fractionated by p.l.c. on silica gel–10% silver nitrate with benzene–light petroleum (3 : 2). Rechromatography of the material recovered from the lower portion of the elongated zone was repeated under the same conditions until *ent*-beyer-15-ene (10) (200 mg), m.p. *ca.* 30°, was obtained free from *ent*-kaur-15-ene (18) as judged by g.l.c. (Found: M^+, 272·250. Calc. for $C_{20}H_{32}$: *M*, 272·250); τ 9·26, 9·20, 9·17, and 9·02 (each 3H, s), 4·60 and 4·32 (d, *J* 6 Hz, 15- and 16-H).

ent-*Beyeran*-15- *and* 16-*ols* [(14) *and* (15)].—*ent*-Beyer-15-ene (200 mg) in tetrahydrofuran (50 ml) was treated with an excess of sodium borohydride and boron trifluoride–ether complex. After 16 h at room temperature, 3N-sodium hydroxide (1 ml) and hydrogen peroxide (5 ml; 30% v/v) were added and stirring was continued for 0·5 h. Recovery in ethyl acetate from the residue obtained by evaporation gave a gum which was separated by p.l.c. on silica gel HF with light petroleum–acetate (9 : 1) to give: (*a*) the more polar ent-*beyeran*-16-*ol* (15), crystallising from ethyl acetate in needles, m.p. 98—101° (Found: M^+, 290·261. $C_{20}H_{34}O$ requires *M*, 290·261); τ 9·20, 9·15, 9·11, and 9·07 (each 3H, s) and 6·30 (1H, d, *J* 6 Hz); and (*b*) the less polar 15-alcohol (14), τ 9·18, 9·14, 9·05, and 9·02 (each 3H, s) and 5·72 (4H, d, *J* 6 Hz), characterised by oxidation to the 15-one (16) (see later).

ent-*Beyeran*-16-*one* (17).—The 16-alcohol (15) (70 mg) was oxidised with an excess of Jones reagent at 0° for 15 min. The usual work-up gave the 16-*ketone* (17), crystallising from light petroleum in needles (70 mg), m.p. 103—104° (lit.[13] m.p. for enantiomer, 102—103°) (Found: C, 83·7; H, 11·0%; M^+, 288·245. $C_{20}H_{32}O$ requires C, 83·5; H, 11·1%; *M*, 288·245); $\nu_{max.}$ ($CHCl_3$) 1735 cm^{-1}; τ 9·19 (18-H_3), 9·14 (19- and 20-H_3), 9·04 (17-H_3), 8·34 (15-H_B, *J* 18 Hz), and 7·31 (15-H_A, *J* 3 and 18 Hz); *m/e* 288 (62%), 273 (68), 246 (12), 245 (38), 244 (24), and 123 (100).

ent-*Beyeran*-15-*one* (16).—The 15-alcohol (14) was oxidised as in the previous experiment to the 15-*ketone* (16), crystallising from methanol in needles, m.p. 88—89° (lit.[13] m.p. for enantiomer, 88—89°) (Found: C, 83·5; H, 11·4. $C_{20}H_{32}O$ requires C, 83·3; H, 11·1%); τ 9·22 (20-H_3), 9·18 (18-H_3), 9·16 (19-H_3), 8·96 (17-H_3), 8·14 (16-H_B, *J* 19 Hz), and 7·86 (16-H_A, *J* 3 and 19 Hz); *m/e* 288 (52%), 273 (31), 246 (16), 245 (20), 244 (23), and 123 (100).

Routine Preparation of ent-*Beyeran*-15- *and* 16-*ones from* ent-*Kaur*-16-*ene*.—The following typical procedure was routinely used. The reaction product (910 mg) from *ent*-kaur-16-ene (1·3 g) and iodine (1·0 g) in xylene (500 ml) was freed from unchanged *ent*-kaur-16-ene by p.l.c. on silica gel–10% silver nitrate (0·4 mm) with light petroleum–benzene (4 : 1). The lower band gave a mixture of *ent*-beyer-15-ene and *ent*-kaur-15-ene (536 mg; 2 : 1 by g.l.c.), which was directly hydroboronated in tetrahydrofuran (40 ml) with sodium borohydride (520 mg) and boron trifluoride–ether complex (5 ml). The resultant mixture (764 mg) of alcohols was oxidised in acetone (50 ml) with Jones reagent (2 ml) to give a product which was separated by p.l.c. on silica gel HF (0·3 mm) by multiple elution with light petroleum–acetone (99 : 1). From the lower band *ent*-beyeran-16-one

[19] J. R. Bearder, J. MacMillan, and B. O. Phinney, *Phytochemistry*, 1973, **12**, 2655.

(200 mg) was obtained by extraction with ethyl acetate then crystallisation from methanol. From the upper band recovery in ethyl acetate gave a crystalline solid (232 mg) which was separated into *ent*-beyeran-15-one (113 mg) and *ent*-kauran-15-one (18 mg) by preparative g.l.c. (2% SE 30; 12 ft × ⅜ in; 230 ⟶ 250° at 2° min^{-1}).

ent-*Beyeran*-16-*one Phenylsulphonylhydrazone* (13).—The 16-ketone (17) (65 mg) in methanol (5 ml) was boiled for 6 h with phenylsulphonylhydrazine (120 mg). The product was purified by p.l.c. on silica gel HF (0·4 mm) with light petroleum–acetone (3 : 1) to give the *sulphonylhydrazone* (13) as needles (80 mg), m.p. 198—201° (decomp.) (Found: C, 70·1: H, 8·7. $C_{26}H_{38}N_2O_2S$ requires C, 70·5; H, 8·6%); $\nu_{max.}$ ($CHCl_3$) 1710, 1370, and 1170 cm^{-1}. Under the same conditions *ent*-beyeran-15-one (16) was unchanged.

Rearrangement of ent-*Beyeran*-16-*one Phenylsulphonylhydrazone* (13).—(a) *In* 3,6-*dioxaoctan*-1-[^{2}H]*ol at* 190°. The hydrazone (5 mg), sodium methoxide (5 mg), and 3,6-dioxaoctan-1-[^{2}H]ol (0·5 ml; prepared by distillation from a mixture of the sodio-derivative and deuterium oxide) were heated at 190° for 1 h. Water was added to the mixture, which was then extracted with ethyl acetate. Recovery from the extract gave a gum shown to contain *ent*-kaur-16-ene (4), *ent*-kaur-15-ene (18), and *ent*-beyer-15-ene (10) in the ratio 1 : 1 : 10 by g.l.c. [Figure (a)] and by g.l.c.–mass spectrometry. Fractionation of this mixture by p.l.c. on silica gel–25% silver nitrate with benzene–light petroleum (3 : 2) and recovery from the band at R_F 0·7 gave *ent*-kaur-16-ene (4); *m/e* 274 (4%), 273 (17·5), 272 (35·5), and 43 (100); 78·5% $^2H_0$, and 21·5% $^2H_1$. Recovery from the band at R_F 0·2 gave a mixture of *ent*-beyer-15-ene (10) and *ent*-kaur-15-ene (18).

(b) *In* 3,6-*dioxaoctan*-1-[^{2}H]*ol at* 90°. The hydrazone (5 mg), sodium methoxide (5 mg), and a new preparation of deuteriated dioxaoctanol (0·5 ml) were heated at 90° for 2 h. Work-up as in (a) gave *ent*-kaur-16-ene (4) (50% $^2H_0$, 50% $^2H_1$) admixed with *ent*-beyer-15-ene (10) and *ent*-kaur-15-ene (18) [Figure (b)].

(c) *In propan-2-ol.* The hydrazone (0·5 mg), sodium methoxide (0·5 mg), and propan-2-ol (0·4 ml) were heated at 95° for 12 h in a sealed tube. Addition of water and extraction with ethyl acetate gave a product which contained mainly *ent*-beyer-15-ene (10) (g.l.c. at 185°).

(d) *In t-butyl alcohol.* Replacing the propan-2-ol in the previous experiment by t-butyl alcohol gave a similar result.

(e) *In methan*[^{2}H]*ol.* The hydrazone (60 mg), sodium methoxide (80 mg), and methan[^{2}H]ol (2 ml) were heated at 95° for 16 h in a sealed tube. Work-up as in (a) gave a gum (50 mg) with a composition shown in Figure (c) (by g.l.c.). P.l.c. of this gum on silica gel with light petroleum–acetone (9 : 1) gave a hydrocarbon fraction (10 mg; R_F 0·7) and a fraction (25 mg; R_F 0·5—0·6) shown by g.l.c. (2% SE-33; 185°) and g.l.c.–mass spectrometry (2% OV-1; 188°) to contain three isomeric compounds (M^+ 396) of which the main component (80%) was identified as *ent*-16-methoxykaurane (8) (4% $^2H_0$, 41% $^2H_1$, 55% $^2H_2$) by comparison (n.m.r. and mass spectra) with an authentic specimen. The two other methoxy-containing isomers had a similar ^{2}H content, they showed similar fragmentation pathways with base peaks at *m/e* 245.

The hydrocarbon fraction was further fractionated on silica gel–10% silver nitrate layers, developed with benzene–light petroleum. The upper band (R_F *ca.* 0·6) gave *ent*-[13,14α-$^2H_2$]kaur-16-ene (5) (3 mg). The lower band (R_F *ca.* 0·2) gave a mixture (3 mg) shown by g.l.c., g.l.c.–mass spectrometry, and n.m.r. to contain 33% of *ent*-13,14α-[$^2H_2$]kaur-15-ene (20) and 67% of *ent*-[16-^{2}H]beyer-15-ene (11). Hydroboronation of this mixture (2·3 mg) with an excess of sodium borohydride and boron trifluoride–ether complex followed by Jones oxidation gave a product shown by g.l.c.–mass spectrometry to contain equal amounts of *ent*-beyeran-15-one (19% $^2H_0$, 81% $^2H_1$), *ent*-beyeran-16-one (100% $^2H_0$), and *ent*-kauran-15-one (10% $^2H_0$, 36% $^2H_1$, 53% $^2H_2$).

ent-17-*Nor*[13,14α-$^2H_2$]*kauran*-16-*one* (6).—*ent*-Kaur-16-ene (2 mg; 38% $^2H_2$) was stirred at 20° for 16 h in tetrahydrofuran (0·5 ml) and water (0·5 ml) with osmium tetraoxide (2 mg) and sodium periodate (50 mg). Recovery in ethyl acetate gave the nor-ketone (6), m.p. 116—117° (lit.,[20] 117°); 39% $^2H_1$, 57% $^2H_2$; *m/e* 277 (12%), 276 (65), 275 (41), 262 (12), 261 (65), 260 (44), 234 (4), 233 (14), 232 (16), and 123 (100). The undeuteriated ketone showed *m/e* 274 (100%), 259 (86), 231 (23), and 123 (88).

After refluxing in methanol (5 ml) and 0·1N-sodium hydroxide (5 ml), the [$^2H_2$]nor-ketone (2 mg) was recovered quantitatively and with unchanged ^{2}H content.

Bayer-Villiger Oxidation of ent-17-*Norkauran*-16-*one.*—(*a*) The undeuteriated nor-ketone (15 mg) in chloroform (2 ml) containing toluene-*p*-sulphonic acid (1 mg) with perbenzoic acid was oxidised as described by Hanson [21] to give the lactone (24) (15 mg), m.p. 146—147° (lit.,[21] 147—148°); τ 9·18, 9·14, 8·94 (each 3H, s), 7·80 (15-H_2), and 5·22 (m, 13-H); *m/e* 290 (23%), 285 (11), 234 (17), 231 (11), 123 (36), and 41 (100).

(*b*) The nor-ketone (2 mg; 39% $^2H_1$, 57% $^2H_2$) in dichloromethane (10 ml) was oxidised with trifluoroacetic anhydride and 90% hydrogen peroxide (0·17 ml) as described by Briggs *et al.*[22] Separation of the product by p.l.c. on silica gel with light petroleum–acetone (9 : 1) to give unchanged nor-ketone (20%; R_F 0·4) and the lactone (23) (80%; R_F 0·2), with unchanged ^{2}H content (g.l.c.–mass spectrometry) and showing no signal below τ 7·76 in an accumulated (× 20) n.m.r. spectrum.

(*c*) The nor-ketone (2 mg; 43% $^2H_0$, 52% $^2H_1$, 5% $^2H_2$) was oxidised and purified as in (*b*) to give the lactone (25) with unchanged ^{2}H content (g.l.c.–mass spectrometry) and showing a one-proton multiplet at τ 5·22 (13-H) in an accumulated (× 40) n.m.r. spectrum.

Treatment of ent-17-*Nor*[13,14α-$^2H_2$]*kauran*-16-*one with Base.*—The nor-ketone (3 mg; 51% $^2H_1$, 45% $^2H_2$) was heated at 100° for 48 h in a sealed tube with t-butyl alcohol (3 ml) and potassium t-butoxide (100 mg). After addition of water, the nor-ketone was recovered in ethyl acetate and purified by p.l.c. as described earlier. G.l.c.–mass spectrometry showed the isotope distribution: 43% $^2H_0$, 52% $^2H_1$, 5% $^2H_2$.

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[20] L. H. Briggs, R. C. Cambie, B. R. Davis, P. S. Rutledge, and J. K. Wilmhurst, *J. Chem. Soc.*, 1963, 1345.

[21] J. R. Hanson, *J. Chem. Soc.*, 1963, 5061.

[22] L. H. Briggs, R. C. Cambie, and P. S. Rutledge, *J. Chem. Soc.*, 1963, 5374.