

Terpenoids. Part IV.¹ The Nuclear Magnetic Resonance Properties of the Stereoisomeric *ent*-Kauran-15-ols and 13 β -Kauran-15-ols

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The $J_{15,16}$ values for the stereoisomeric *ent*-kauran- and 13 β -kauran-15-ols indicate a twist envelope conformation for ring D in all except the (16*S*)-15 β -ols. The chemical shifts of the C-15 protons confirm the stereochemical assignments. Calculations of the difference in chemical shift of the C-15 protons in isomeric pairs of these alcohols are not sufficiently accurate to distinguish between envelope and twist envelope conformations of ring D.

THE conformation of ring D in derivatives of *ent*-kaurene (1) and 13 β -kaurene (phytylcladene) (2) has previously been investigated by studies on the 15,16-hydride shift in the allylic alcohols (3) and (4),² on the photo-oxygenation of *ent*-kaurene (1) and 13 β -kaurene (2),³ and on the o.r.d. properties¹ and rates of enolisation¹ of the 16*R*- [(5) and (7)] and 16*S*- [(6) and (8)] ketones. The present paper discusses the n.m.r. spectra of all four isomers of *ent*-kauran-15-ol (9) and of 13 β -kauran-15-ol (10) in relation to their ring D conformations.

TABLE 1

Chemical shifts (τ) and coupling constants (Hz) of the 15-, 16-, and 17-protons in the *ent*-kauran-15-ols and 13 β -kauran-15-ols

Compound	Chemical shift				Calc. ^a
	17-H	15-H	$J_{16,17}$	$J_{15,16}$	$\theta_{15,16}$
(9a)	9.08	6.48	7.0	11.0	0°
(9b)	8.95	7.07	7.5	4.5	130
(9c)	8.92	6.84	7.0	4.5	130
(9d)	9.09	6.47	7.5	8.0	30
(10a)	9.12	6.14	7.5	11.0	0
(10b)	8.98	6.76	7.0	5.5	135
(10c)	8.96	6.27	6.5	4.0	130
(10d)	9.10	5.84	7.5	8.0	30

^a Appropriate values obtained from $J = J_0 \cos^2 \theta$ where J_0 was assumed to be 11 Hz.

The preparation of the isomers of *ent*-kauran-15-ol (9)¹ and 13 β -kauran-15-ol (10)³ has been described. The relevant n.m.r. data are shown in Table 1. With the exception of isomers (9a) and (10a), the values of $J_{15,16}$ and the derived dihedral angles for C(15)-H and C(16)-H indicate twist envelope conformations. In the two exceptions (9a) and (10a) both the 15-hydroxy- and 16-methyl groups are β -oriented, and any twisting

of the 15,16-bridge would relieve eclipsing only at the expense of severe *endo*-steric interaction.

The chemical shifts for the 15-protons are consistent with the assigned stereochemistries. As expected, the 15-proton is shielded by a *cis*-16-methyl group. This shielding is caused by the magnetic anisotropies of the C-C and C-H bonds of the 16-methyl substituent and may be calculated for epimeric pairs by the method of ApSimon *et al.*⁴ To evaluate the use of such calculations in the study of the conformation of ring D in the alcohols listed in Table 1, the chemical shift differences between the C-16 epimers (9a) and (9b) were computed. The parameters were measured from Dreiding models and the calculations were made with a PDP8/L computer by use of D.E.C.s 'Focal conversational language'. The results are shown in Table 2 for three conformations of ring D: (a) an envelope with C-15 and C-16 substituents eclipsed; (b) a twist envelope with C-16 moved in the α -direction to give a 10° dihedral angle between C-15 and C-16 substituents; and (c) a similar twist envelope where C-16 is moved in the β -direction to the same extent. The agreement between the calculated and observed differences in chemical shift is good, particularly for the non-twist envelope; however in view of the errors involved in the calculation (see later), this agreement may be fortuitous.

Qualitatively, the calculations readily distinguish between the two epimers. The calculations show that the shielding of the 15-proton by a *cis*-16-methyl group is due mainly to the anisotropy of the C-H bonds of the methyl group. However the calculations are too inaccurate to provide conformational information in the present case. A major inaccuracy lies in the measurement of angles and distances, particularly in

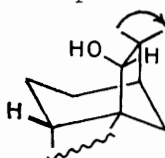
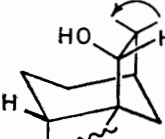
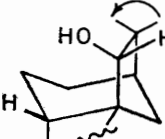
¹ Part III, J. MacMillan and E. R. H. Walker, *J.C.S. Perkin I*, 1972, 986.

² M. F. Barnes and J. MacMillan, *J. Chem. Soc. (C)*, 1967, 361.

³ J. MacMillan and E. R. H. Walker, *J.C.S. Perkin I*, 1972, 981.

⁴ J. W. ApSimon, W. G. Craig, P. V. Demarco, D. W. Mathieson, L. Saunders, and W. B. Whalley, *Tetrahedron*, 1967, **23**, 2339 and 2357.

TABLE 2
Calculated shielding (p.p.m.) of the 15-proton in the alcohols (9a) and (9b)

Conformation Eclipsed	16 <i>S</i> -Epimer				16 <i>R</i> -Epimer				Total ($\Delta\sigma_{16S} - \Delta\sigma_{16R}$)
	C-C ^a	C-H ^b	CH ₃ ^c	$\Delta\sigma_{16S}$	C-C ^a	C-H ^b	CH ₃ ^c	$\Delta\sigma_{16R}$	
	0.52	-0.13	1.04	1.43	-0.16	0.33	0.48	0.65	0.78
	0.41	-0.05	1.18	1.54	-0.06	0.27	0.38	0.59	0.95
	0.31	-0.18	1.08	1.21	-0.23	0.20	0.24	0.21	1.00

^a Terms I + II. ^b Terms IV + V. ^c Term III (see Experimental section).

calculations involving the methyl group where the limit of ± 0.1 Å in the measurement of distance produces an error of ± 0.25 p.p.m. Since the methyl calculations

occur twice the total errors are estimated to be ± 0.4 p.p.m.

TABLE 3
Chemical shift (τ) of the 10-methyl protons in 13 β -kaur-16-ene (2) and some derivatives

13 β -Kaur-16-ene (2)	9.1
13 β -Kaur-15-ene	9.29
13 β -Kaur-16-en-15 α -ol	9.09
13 β -Kaur-16-en-15-one	9.25
13 β -Kaur-15-en-17-ol	9.28
(16 <i>R</i>)-13 β -Kaur-15-one (7)	9.18
(16 <i>S</i>)-13 β -Kaur-15-one (8)	9.22
(16 <i>R</i>)-13 β -Kauran-15 β -ol (10a)	9.06
(d, $J \leq 1$ Hz)	
(16 <i>S</i>)-13 β -Kauran-15 β -ol (10b)	9.03
(16 <i>R</i>)-13 β -Kauran-15 α -ol (10c)	9.10
(16 <i>S</i>)-13 β -Kauran-15 α -ol (10d)	9.10

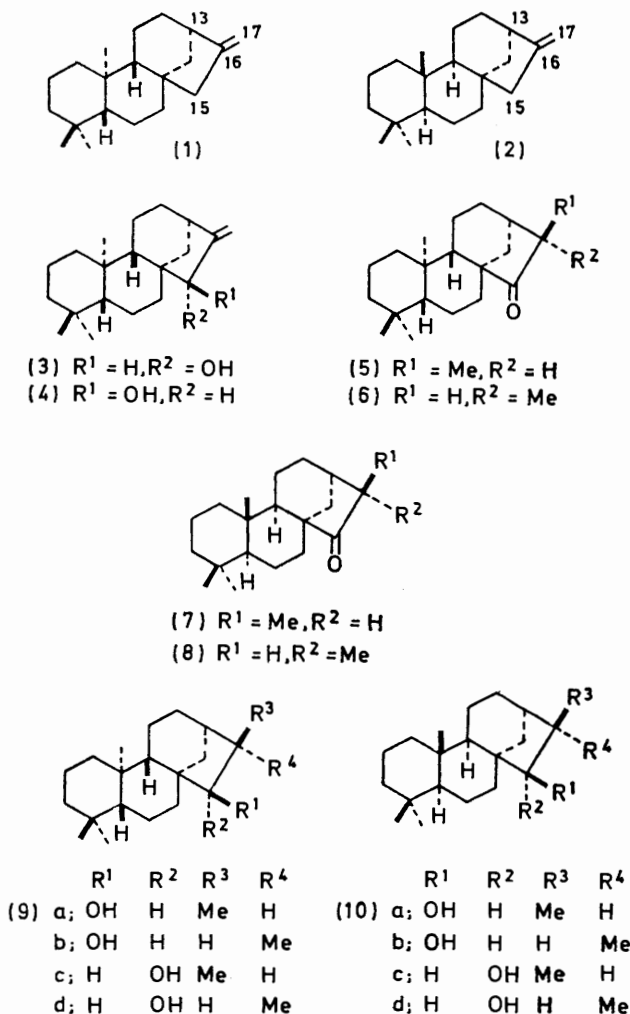
The effect of some ring D substituents on the chemical shift of the 10-methyl group in 13 β -kaurane derivatives is shown in Table 3. The anisotropic shielding by the 15,16-double bond, previously⁵ noted in 13 β -kaur-15-ene, also occurs in 13 β -kaur-15-en-17-ol. A 15-oxo-function exerts a similar anisotropic shielding which is most pronounced in the case of the enone, 13 β -kaur-16-en-15-one. The 10-methyl group is deshielded by a 15 β -hydroxy-substituent. The 10-methyl group in (16*R*)-13 β -kauran-15 β -ol (10a) gives rise to a doublet with J ca. 1.0 Hz which collapsed to a broad singlet on irradiation at τ 8.46. In the spectra of all other derivatives of 13 β -kaurane and *ent*-kaurane examined the 10-methyl signal was a singlet.

EXPERIMENTAL

N.m.r. spectra were determined with a Varian HA100 instrument for deuteriochloroform solutions, with tetramethylsilane as internal standard. Calculations were performed on a PDP8/L computer by use of 'Focal' conversational programming language, supplied by Digital Equipment Corporation.

The method is illustrated for the 16*S*- and 16*R*-epimers (9a) and (9b) with the five-membered ring in an envelope

⁵ Y. Kitahara and A. Yoshikoshi, *Bull. Chem. Soc. Japan*, 1964, **37**, 890.



conformation and the substituents at C-15 and C-16 eclipsed. The following relationship, derived by ApSimon *et al.*,⁴ was used (see ref. 4 for definition of parameters):

$$\Delta\sigma = \Delta\chi^{\text{CC}} \cdot f[\theta_1, R_1] \quad \text{Term I} \\ + \chi_L^{\text{CO}}, \chi_T^{\text{CO}} f[\theta_1, R_1, S_1] \quad \text{Term II} \\ + \Delta\chi^{\text{CH}} f[R_2, a, b, l, r] \quad \text{Term III} \\ - \{\chi^{\text{CH}} \cdot f[\theta_3, R_3] \quad \text{Term IV} \\ + \chi_L^{\text{OH}}, \chi_T^{\text{OH}} f[\theta_3, R_3, S_3]\} \quad \text{Term V}$$

Constants.— $\chi_L^{\text{CO}} = +3.15$; $\chi_T^{\text{CO}} = -10.83$; $\chi_L^{\text{OH}} = +0.92$; $\chi_T^{\text{OH}} = 10.08$ (all in $\text{cm}^3 \text{ molecule}^{-1} \times 10^{30}$); $b = 0.77 \times 10^{-8} \text{ cm}$; $r = 0.7 \times 10^{-8} \text{ cm}^{-1}$.

Variables.—For the 16S-epimer (9a): $R_1 = 2.17 \times 10^{-8} \text{ cm}$; $\theta_1 = 78^\circ$; $S_1 = 0.6 \times 10^{-8} \text{ cm}$; $R_2 = 2.8 \times 10^{-8} \text{ cm}$; $a = 2.5 \times 10^{-8} \text{ cm}$; $l = 2.2 \times 10^{-8} \text{ cm}$; $k^2 = +0.18896$ hence $K = 1.6546$ and $E = 1.4933$; $R_3 = 2.65 \times 10^{-8} \text{ cm}$; $\theta_3 = 42^\circ$; $S_3 = 0.25 \times 10^{-8} \text{ cm}$.

For the 16R-epimer (9b): $R_1 = 2.65 \times 10^{-8} \text{ cm}$; $\theta_1 = 42^\circ$; $S_1 = 0.6 \times 10^{-8} \text{ cm}$; $R_2 = 3.5 \times 10^{-8} \text{ cm}$; $a = 3.25 \times 10^{-8} \text{ cm}$; $k^2 = +0.1387$ and hence $K = 1.6306$ and $E = 1.1543$; $R_3 = 2.17 \times 10^{-8} \text{ cm}$; $\theta_3 = 78^\circ$; $S_3 = 0.25 \times 10^{-8} \text{ cm}$.

Hence, for the 16S-epimer (9a):

$$\text{Term I} = [(1 - 3 \cos^2 \theta_1)/3R_1^3] \Delta\chi^{\text{CO}} = +0.40 \text{ p.p.m.}$$

$$\text{Term II} = \frac{S_1^2}{R_1^5} \left[\frac{-(\chi_L + 2\chi_T)}{2} + 5(\chi_L \cos^2 \theta_1 + \chi_T \sin^2 \theta_1) - \frac{35}{6} (\chi_L \cos^4 \theta_1 + \chi_T \sin^4 \theta_1) \right] = +0.12 \text{ p.p.m.}$$

$$\text{Term III} = \left[-3 \frac{2K}{4b^2 \pi p^{\frac{1}{2}}} + \frac{(3a^2 - b^2)}{2b^2} \cdot \frac{2E}{\pi p^{\frac{1}{2}} q} - \frac{3(a^2 - b^2)^2}{4b^2} \cdot \frac{2(4wE - qK)}{3\pi p^{\frac{3}{2}} q^2} \right] \Delta\chi^{\text{CH}} = +1.04 \text{ p.p.m.}$$

$$\text{Term IV} = [(1 - 3 \cos^2 \theta_3)/3R_3^3] \Delta\chi^{\text{OH}} = -0.13 \text{ p.p.m.}$$

$$\text{Term V} = \left[\frac{\Delta\chi}{3} \left(\frac{1 - 3 \cos^2 \theta_3}{R_3^3} \right) \right] + \frac{S_3^2}{R_3^5} \left[-\frac{(\chi_L + 2\chi_T)}{2} + 5(\chi_L \cos^2 \theta_3 + \chi_T \sin^2 \theta_3) - \frac{35}{6} (\chi_L \cos^4 \theta_3 + \chi_T \sin^4 \theta_3) \right] \\ = -0.12 \times 10^{-3} \text{ p.p.m.}$$

Similarly for the 16R-epimer (9b): Term I = -0.16 p.p.m.; Term II = +0.002 p.p.m.; Term III = +0.48 p.p.m.; Term IV = +0.31 p.p.m.; and Term V = +0.02 p.p.m.

We thank the Worshipful Company of Salters for a Research Scholarship (to E. R. H. W.).

[1/2300 Received, 3rd December, 1971]