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NMR STUDIES OF KAURANE DERIVATIVES

Masayuki Kitadani, Hisashi Uda, and Akira Yoshikoshi
Chemical Research Institute of Non-Aqueous Solutions,
Tohoku University
Sendai, Japan

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Recently the anisotropic long-range shielding effect of a three-membered ring on neighboring protons has been of much interest. Particularly in bridged ring systems, the nmr signal arising from the methylene-bridge proton anti to an exo-cyclopropane (1), -epoxide (2), or -aziridine ring (2d) is significantly shifted upfield by this shielding effect. We report here the results on the chemical shifts and the additional shift values of anti (β) bridge proton Ha at C-14 in 15,16β(exo)-epoxy (or cyclopropo)-14α-hydroxy (or acetoxy)-kaurane derivatives (I~IV) (Table 1) or of syn (α) bridge proton Hs in the corresponding 14β-hydroxy (or acetoxy) derivatives (V~VIII) (Table 2), having a bicyclo[3.2.1]octane ring system*[1,2].

Signals of the anti proton Ha, except in the cases of I (R=H) (a comparatively sharp singlet) and IV (R=Ac) (a doublet, J=2 cps),

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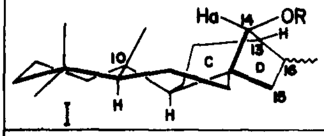
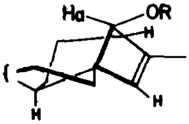
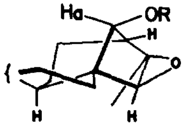
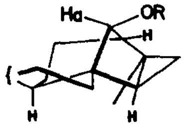
*1 The compounds used in this investigation were prepared from 14α-hydroxyisokaurene (II, R=H) (3) by introduction of an epoxide or a cyclopropane ring with the required orientation. Satisfactory analytical and infrared spectral data were obtained for all the new compounds. Detailed preparative experiments will be reported in a subsequent paper.

*2 Nmr data were obtained at 60 Mc with a Varian A-60 Spectrometer using carbon tetrachloride solutions and tetramethylsilane as an internal standard.

TABLE 1

Chemical Shifts and Additional Shift Values of 14β-Proton in 14α-Hydroxy (Acetoxy)-kaurane Derivatives

	14α-Hydroxy Derivative R=H		14α-Acetoxy Derivative R=Ac	
	Ha τ	$\Delta\tau$ [a]	Ha τ	$\Delta\tau$ [a]
 I	5.91	0	4.79[b] (4.69)	0
 II	5.97	+0.06	4.68	-0.11 (-0.01)
 III	6.34[c]	+0.43	4.94	+0.15 (+0.25)
 IV	6.03	+0.12	4.85	+0.06 (+0.16)

a Additional shift values in comparison with the signal of Ha of I. Positive sign represents an upfield shift.

b Two peaks, both assignable to the C-14 Ha proton, with intensity ratio of about 3:1 were observed in the spectrum of this compound; the chemical shift value in parenthesis is the weaker one. The values in parentheses in the $\Delta\tau$ column indicate the additional shift values from this weaker peak. The reason for the appearance of these two peaks is not understood. The sample used in the nmr measurements was proved to be essentially homogeneous by gas or thin-layer chromatography.

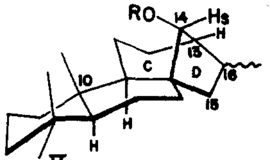
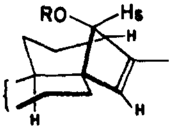
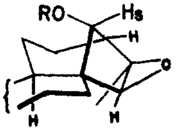
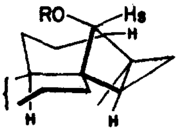
c In this compound the Ha peak was observed as a broad doublet with a coupling constant of 11.5 cps. Addition of a small amount of deuterium oxide changed this doublet to a broad singlet and the sharp doublet (J=11.5 cps) at 2.51 τ (OH proton) disappeared, which confirms the existence of coupling between Ha and the hydroxyl proton.

appear as broad singlets due to long-range spin coupling with the C-15 proton olefinic or *endo* (α) proton ; no coupling with the C-13 bridgehead proton is observed, which is in accord with the stereochemistry of all the substituents. The effect of the C-15,16 double bond is small but in opposite directions in the case of the pair of compounds (II), Ha being shifted upfield in the alcohol (II, R=H) and downfield in its acetate (II, R=Ac). A significantly large upfield shift of about 0.43 ppm is observed for the epoxy-alcohol (III, R=H) consistent with the previous finding (2b); this shift is apparently due to the long-range shielding effect of the epoxide. However, the effect is weak (0.15∼0.25 ppm) in the case of its acetate (III, R=Ac). Similarly the *anti* proton Ha is also shifted upfield by introduction of an *exo* cyclopropane ring but the magnitude is comparatively small as shown in Table 1.

The signal of the *syn* bridge proton Hs always appears as a clean doublet (J=4∼5 cps), without further splitting, due to coupling with the C-13 bridgehead proton. The values of additional shift of the proton Hs in each pair of compounds, alcohol and its acetate (VI, VII, VIII), are almost equal. In compound VI, the double bond appreciably deshields the proton Hs with the shift value of 0.16∼0.17 ppm similar to the recent observation on norbornene (2e,4). Almost no difference in the chemical shifts of the proton Hs is observed in the case of the epoxy derivatives (VII) and the parent compounds (V), which can be ascribed to mutual compensation of the shielding effect of an epoxide ring and the deshielding effect of the oxygen atom of the epoxide. Proton Hs in VIII, which is located almost right above the plane of the cyclopropane ring, would be expected to be more

TABLE 2

Chemical Shifts and Additional Shift Values of 14α-Proton in 14β-Hydroxy (Acetoxy)-kaurane Derivatives

	14β-Hydroxy Derivative R=H		14β-Acetoxy Derivative R=Ac	
	Hs τ	$\Delta\tau^{a}$	Hs τ	$\Delta\tau^{a}$
 V	6.54	0	5.58	0
 VI	6.37	-0.17	5.42	-0.16
 VII	6.52^{b}	-0.02	5.61	+0.03
 VIII	6.86^{b}	+0.32	5.93	+0.35

a Additional shift values in comparison with the signal of Hs of V.

b This signal originally appeared as a very broad peak by being superimposed on the hydroxyl proton signal. Addition of a small amount of deuterium oxide resulted in the clear appearance of this signal as a doublet.

strongly shielded than the anti proton Ha in IV by the shielding effect of the cyclopropane ring. The observed large shift value of 0.32∼0.35 ppm clearly supports this expectation and, in this case, the diamagnetic anisotropy of a β-C-H bond of the cyclopropane methylene probably also takes part in the above shielding.

It should be noted that the C-ring has the chair form in the

14α-hydroxy (or acetoxy) derivatives and the boat form in the 14β-hydroxy (or acetoxy) derivatives[*3] (see Tables) , and that this conformational difference prevents a precise comparison of the magnitude of the long-range shielding effects of the epoxide or cyclopropane ring upon the anti and syn bridge protons in the simple bicyclo[3.2.1]octane ring system. As a rule it seems, however, to be probable that the syn proton Hs suffers the shielding effect of an exo cyclopropane ring more strongly than the anti proton Ha and that an exo epoxide ring does exert a stronger shielding effect upon the anti proton Ha than the corresponding cyclopropane ring in the same bridged ring system.

Existence of strong hydrogen bonding in III (R=H)[*4] might effectively cause a change in the molecular geometry of III (R=H) leading to the D-ring being in a more puckered form in contrast with the corresponding acetate (III, R=Ac), in which the conformation of the D-ring would be rather flat owing to steric repulsion between the acetoxy group and the ethereal oxygen atom. Such a peculiar difference in molecular geometry including the relative spatial disposition, distance and perpendicularity, of the anti proton Ha to the plane of the epoxide ring in III (R=H

[*3] Conformation of the C-ring in the former has been established to be a chair form (3), but in the latter the C-ring must have a boat form because of large steric repulsion between a β-substituent (OH and OAc) and an angular methyl group at C-10.

[*4] The existence of hydrogen bonding, which rigidly fixes the hydroxyl proton to the ethereal oxygen atom, is proved by the observation of a coupling between this proton and the anti proton Ha (see the footnote c in Table 1). A larger coupling constant (11.5 cps) than the reported coupling constant of 4~8 cps (5) for HO-$\overset{|}{\underset{|}{C}}$H grouping is of interest since the geometry of these two protons has a dihedral angle of 180° or a trans olefinic relation in III (R=H).

or Ac) would be sensitively reflected in the shielding strength of the proton Ha by the epoxide ring, causing a much larger shift value in the alcohol (III, R=H) than that in its acetate (III, R=Ac) as observed. The fact that almost no difference in the additional shift values of the *syn* proton Hs of a pair of compounds, alcohol and acetate, (VII and VIII), in which there would not be an extra factor for changing molecular geometry, and a small difference in IV are observed would support this argument.

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