Tetrahedron Letters No.13, pp. 1561-1564, 1968. Pergamon Press. Printed in Great Britain.

THE CONFORMATION OF PRIMARY HYDROXYL GROUPS IN TERPENOIDS* +

C.R. Narayanan, N.R. Bhadane and M.R. Sarma
National Chemical Laboratory, Poona 8

(Received in UK 12 December 1967)

One of the gem dimethyl groups or an angular methyl group in terpenoids are often oxidised to a primary hydroxyl group. In their PMR spectra the two protons of this methylene group often show different chemical shifts and a coupling constant of ~ 11 cps, (1) showing thereby that they are not freely rotating but have a preferred conformation. But there is no clear idea about these conformations.

It is well known that a methyl signal is deshielded by an adjacent eclipsing hydroxyl group (2). We have now found that in such cases, the methyl signal is further deshielded, when the spectra is taken in pyridine solution (see Table 1).

Models show that the most stable conformation for an axial C_4-CH_2-OH in a normal terpenoid with a C_{10}-CH_3, will be that in which the hydroxyl C-O bond nearly eclipses the C_4-equatorial methyl group. This is fully supported by the data from a number of diterpenoids given in Table 2, when viewed in the light of the observations in Table 1.

It will be seen from VI, XI and XIII that the C_4-axial and equatorial methyl protons in a compound resonate at about the same place. But when an axial C_4-CH_3 is oxidised to a -CH_2-OH the equatorial C_4-CH_3 resonates ~ 10 cps downfield (compare VI & VII or XI & XII or XIII & XIV), which is further deshielded by over 10 cps in pyridine, thus showing that the hydroxyl on the axial group has an eclipsed or nearly eclipsed position with the equatorial C_4-CH_3. Consistent with this, the C_{10}-CH_3 in VI or VII, XI or XII, and XIII or XIV, resonate at the same place in the two compounds in each pair, showing thereby that the hydroxyl group is far away from the C_{10}-CH_3 in these cases. By analogy, the conformation of a C_{10}-CH_2-OH in such compounds should be the one in which the OH group points equally away from the A/B rings.

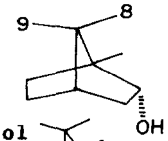
The axial C_4-CH_3 in VIII, X and XVI resonate ~ 10 cps higher field than the equatorial methyl groups in the corresponding axial hydroxymethylene

---

*Communication No.1159 from the National Chemical Laboratory, Poona 8.

+Stereochemical studies by PMR spectroscopy X.

TABLE 1

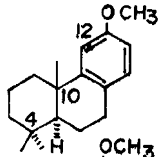
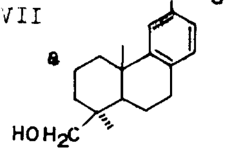
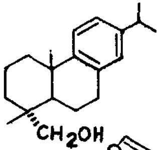
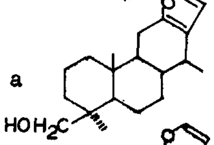
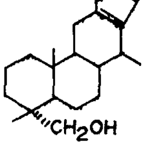
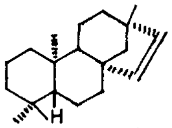
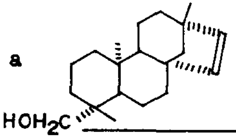
Compound	Chemical shift in cps at 60 Mc of the				Shift in pyridine solution	
	18-H in $CDCl_3$	19-H in $CDCl_3$	18-H in pyridine	19-H in pyridine	18-H	19-H
I 11α-hydroxy-progesterone	42.5	79.5	43.5	79.5	-1	0
II 11β-hydroxy-progesterone	55	87	68	95	-13	-8
III 11β-hydroxy-5α-pregnane	47	62	63	78	-16	-16
IV Borneol 	8H	9H	8H	9H	8H	9H
	52	52	52	52	0	0
V Isoborneol 	61	51	77	51	-16	0

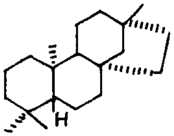
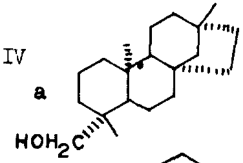
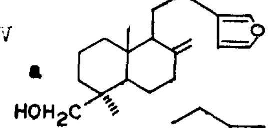
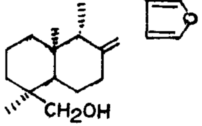
III, m.o.124°, $(\alpha)_D$ +38° IV, V, K.Tori, Y. Hamashima and K.Takamizama Chem.& Pharm. Bull. Japan, 12, 924 (1964). All spectra given in this paper were taken on a Varian A-60 spectrometer, using TMS as internal standard.

compounds, viz. VII, IX and XV respectively, i.e. at about the same place, had there been a gem-dimethyl group at C_4. Besides, in pyridine solution, the axial methyl groups of the equatorial $-CH_2-OH$ compounds (see VIII and X) do not show any significant downfield shift. These results indicate that the hydroxyl group of the equatorial $-CH_2-OH$, is far removed from the axial C_4-CH_3, and hence should be nearly perpendicular to the plane of the ring. This is fully supported by the data in Table 3, which show that this hydroxyl group has a 1,3-diaxial relationship with the C_3-axial proton in the normal A/B-trans terpenoids.(3)

Acknowledgement - We are indebted to Dr.L.M. Kogan for samples of I & II, to Glaxo Laboratories for 3β-acetoxy-16-pregnene-11,20-dione, to make III, to Prof. T.J. King for the acids of IX and X, to Dr.Sukh Dev for XII, to Dr.I.K. Walker for the acid of VII and to Dr.J.W.W. Morgan for XIX and XX.

TABLE 2

Compd.		Chemical shift of the C_4-CH_3 in $CDCl_3$	Chemical shift of the C_4-CH_3 in Pyri.	Shift in pyridine
VI		55	53	-2
VII a		63	74	-11
VIII e		53	55	-2
IX a		60	73	-13
X e		49	52	-3
XI		49, 51		
XII a		57	72	-15

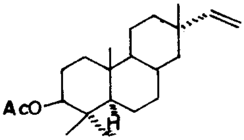
Compd.		Chemical shift of the C_4-CH_3 in $CDCl_3$	Chemical shift of the C_4-CH_3 in Pyridine	Shift in pyridine
XIII		50		
XIV a		58	71	-13
XV a		55		
XVI e		44		

'a' indicates axial and 'e' equatorial C_4-CH_3. VI, Podocarpane-12-methyl ether; VII, podocarpanol-12-methyl ether; VIII, dehydroabietanol; IX, voucapenol, X, vinhaticol, F.E.King, T.J. King and J.M. Uprichard, J.Chem.Soc. 3428 (1958) and previous papers; XII, monogynol, XIV, dihydromonogynol, XI and XIII, hydrocarbons related to them, A.H.Kapadi and Sukh Dev, Tet. Letters 1171, 2751 (1964), A.H.Kapadi Ph.D thesis, Poona University (1965); XV, lamertianic alcohol, W.G. Dauben and V.F.German, Tetrahedron 22, 679 (1965); XVI, polyalthyl alcohol, C.A.Henrick and P.R. Jefferies, Aust. J.Chem. 17, 915 (1964).

TABLE 3

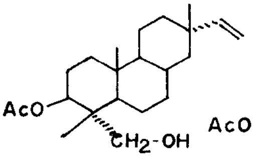
Chemical shift of the C_3-H, in $CDCl_3$ at 60 Mc

XVII	Cholestane 3β-ol methyl ether ..	187 cps
XVIII	Cholestane 3β, 5α-diol, 3-methyl ether	217 cps
Shift of the C_3α-axial proton, due to the 5α-axial hydroxyl group		-30 cps



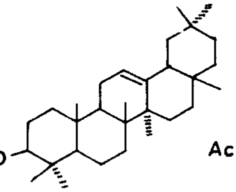
XIX

C_3-H at 268 cps



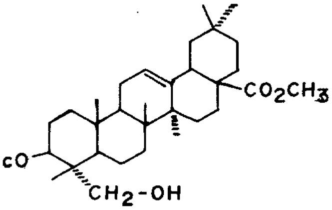
XX

301 cps



XXI

271 cps



XXII

296 cps

XIX and XX sandacopimaradiene derivatives, R.A. Laidlaw and J.W.W. Morgan, J. Chem. Soc. 644 (1963); XXI, β-amyrin acetate; XXII hederagenin methyl ester-3-acetate, m.p. 160° $(\alpha)_D$ 43·25 prepared by the hydrogenolysis of hederagenin methyl ester-3-acetate-tritytl ether, m.p. 225°, $(\alpha)_D$ +67° .

REFERENCES

1 See e.g. A.Gaudemer, M^{me} J. Polonsky and E. Wenkert, Bull.Soc.(France) 407 (1964).

2 Y. Kamazo, Y. Sato, M. Matsume, H. Hasegawa, T. Okamoto and K. Tsuda, Chem. & Pharm. Bull. Japan, 10, 338 (1962).

3 It may be added that these conformations of the hydroxymethylene group may be vitiated by interfering substituents in the A/B rings.