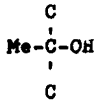
Tetrahedron Letters No. 48, pp 4865 - 4866, 1972. Pergamon Press. Printed in Great Britain.

FORMYLATION PMR-SHIFT FOR THE DETECTION OF METHYLS ON CARBONS LINKED TO HYDROXYL

R. Misra and Sukh Dev
National Chemical Laboratory, Poona, INDIA

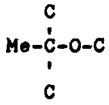
(Received in UK 17 October 1972; accepted for publication 26 October 1972)

IT is well known[1] that the effect of a substituent on the chemical shift of protons on β -carbon ($H\text{-}\underset{\beta}{C}\text{-}\underset{\alpha}{C}\text{-}X$) is relatively small and essentially the same for several different types of substituents. Thus, for example, the usual range for methyl resonance in structures, such as a - d, is δ (ppm) 1.00 - 1.25[1] and hence, it is difficult to differentiate between these possibilities in a multifunctional



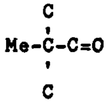
$\mathrm{Me{-}\overset{C}{\underset{C}{C}}{-}OH}$

a



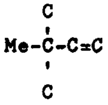
$\mathrm{Me{-}\overset{C}{\underset{C}{C}}{-}O{-}C}$

b



$\mathrm{Me{-}\overset{C}{\underset{C}{C}}{-}C{=}O}$

c



$\mathrm{Me{-}\overset{C}{\underset{C}{C}}{-}C{=}C}$

d

molecule, on the basis of chemical shifts alone. In actual practice, one is often faced with such situations when investigating the structures of complex natural products, especially terpenoids.

Though it has been recorded[1] that acetylation of a tertiary alcohol causes a downfield shift of the resonance of the protons on the β -carbon (e.g. $\delta^{Me}_{CDCl_3}$: ^{t}BuOH 1.28 ppm; ^{t}BuOAc 1.45 ppm)[2], the available data is very meagre and, this property does not appear to have been exploited for structural investigations (cf."acylation shift" of protons α to primary and secondary hydroxyls)[1], possibly because, it is usually difficult to acetylate tertiary alcohols. We now find that formylation of tertiary alcohols with the part structure a results in a downfield shift of the tertiary Me signal by 0.25 - 0.35 ppm; other methyl signals of the molecule remain essentially unchanged. Fig.1 gives some representative cases; the original chemical shift (δ) of the concerned tertiary Me as well as its value after formylation (in parenthesis) is shown. Thus, the "formylation shift" can serve as a useful aid in detecting grouping a, by PMR, in complex molecules.

Formylation was conveniently carried out by acetic-formic anhydride[3] and PMR spectral measurements were made on the reaction product directly, without any further purification. A typical procedure is given below:

Acetic-formic anhydride (2 ml) is cooled to 0°, a small drop of anhydrous pyridine is added and then, the compound (50 mg) is introduced. The mixture is well-shaken and the clear soln left aside at 10-15° for 48 to 96 hr, under anhydrous conditions. After completion of the reaction, as ascertained by TLC, the excess reagent etc. is removed at room temp. (25-30°) under vacuum (0.5 - 1.0 mm) during several hrs.

The residue is taken up in a suitable solvent (usually CCl_4) and its PMR spectrum taken.

In the present work all spectra were measured in CCl_4 soln. on a Varian T-60 NMR spectrometer, using TMS as internal standard.

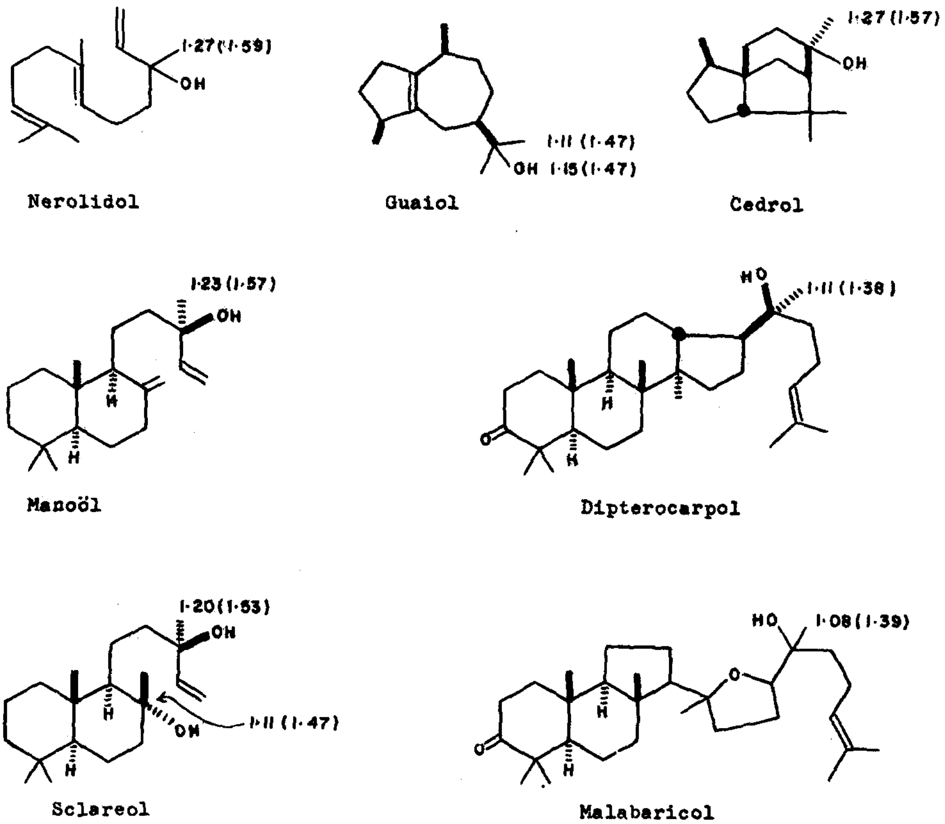


Fig.1 "Formylation shift" of methyl in tertiary alcohols.

REFERENCES

1 L.M. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry pp.163-183. Pergamon Press, London (1969).

2 Varian NMR SPECTRA Catalog, spectra Nos.141, 423. Varian Associates, Palo Alto (1962,1963).

3 E. Guenther, The Essential Oils Vol.1, p.276. D van Nostrand, New York (1948). Also see: L. Muramatsu, M. Murakami, T. Yoneda and A. Hagitani, Bull Chem. Soc. Japan 38, 244 (1965).