^{13}C-NMR AND ^{1}H-NMR SPECTROSCOPY OF PHORBOL AND DEOXYPHORBOL ESTERS

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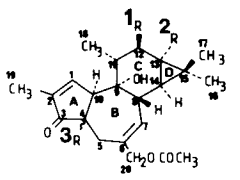
Primary carcinogens are not thought to be the sole causitive agent of human cancers. Some cancers may result from exposure to primary carcinogens and tumour-promoters, a process known as co-carcinogenesis (Hecker 1977). The 12,13-diesters of phorbol have been of major importance in furthering the understanding of tumour-growth and are classified as second order carcinogenic risk factors. The structure of analogues of phorbol have been obtained by comparisons of ^{1}H-NMR spectra to that of phorbol triacetate (Evans & Soper 1978). This communication describes the comparison of the ^{13}C-NMR spectra of four related tigliane diterpenes (Fig. 1) together with their ^{1}H-NMR spectra for assessment of the usefulness of the former method for phorbol analogue structure elucidation. Off resonance decoupled ^{13}C-NMR spectra were obtained on a Bruker WH-400 and ^{1}H-NMR spectra on a WH-250 instrument using $CDCl_3$ as solvent in both cases. Although the ^{13}C-NMR spectrum of (1) has been recorded (Neeman & Simmons 1979) the signals for the C-4 and C-9 positions were tentatively assigned. We have been able to assign the C-4 signal of (1) as 73.5 ppm and of C-9 as 78.0 ppm by comparison of the spectra of (1) and (3). In the ^{13}C-NMR spectrum of (2) the C-12 and C-13 signals occur about 5 ppm further downfield than would be expected from theoretical calculations. This may be explained by the deshielding effect of the C-13 phenylacetate of (2). The C-16 and C-17 signals are not affected because the rotation of the C-13 acyl group is sterically hindered. Compound (3) is a 4-deoxy-analogue of (1). In the ^{13}C-NMR spectrum of (3) the signal for the C-5 behaves as would be predicted theoretically, but the C-4 and C-10 signals have moved upfield by about half the amount predicted for a simple alkane model to 42.6 ppm and 54.0 ppm respectively. The vinylic and carbonyl functions of ring A of (3) may induce a delocalisation of π-electrons thereby explaining the anomaly. Compound (4) is the AB cis-analogue of (3). Because both the H-4 and the H-10 are in the α-configuration a fold is formed at the junctions of rings A and B. The interactions of these two rings causes a degree of steric strain in the molecule which is exhibited in its ^{13}C-NMR spectrum by an upfield shift for the signals of C-5, C-6, C-7, C-8 and C-10 of about 5 ppm. These effects are only noted for ring B carbons and not for the substituents in the pentacyclic ring A which has a more rigid structure.

FIGURE 1



		R^1	R^2	R^3
Phorbol-triacetate	(1)	acetate	acetate	β-OH
12-deoxyphorbol-phenyl-acetate-acetate	(2)	H	phenylacetate	β-OH
Sapintoxin-A-acetate	(3)	anthranilate	acetate	β-H
α-Sapintoxin-A-acetate	(4)	anthranilate	acetate	α-H

^{1}H-NMR assignments were made for compounds (1) to (4) on the basis of extensive decoupling experiments. From this study we can conclude that ^{13}C-NMR spectroscopy will form a useful adjunct to ^{1}H-NMR spectroscopy for the structure elucidation of tumour-promoting phorbol analogues.

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