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STUDIES ON VITAMIN D AND RELATED COMPOUNDS XX.
THE CONFORMATION OF TACHYSTEROL; N.O.E. AND 220 MHz N.M.R.

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Although many stereochemical features of vitamin D and its isomeric precursors may be considered rather well established (1,2) by now, there remain a few intriguing questions. One of the problems that asked for further study, is concerned with the conformational analysis of tachysterol (Fig. I). The first suggestion made upon the

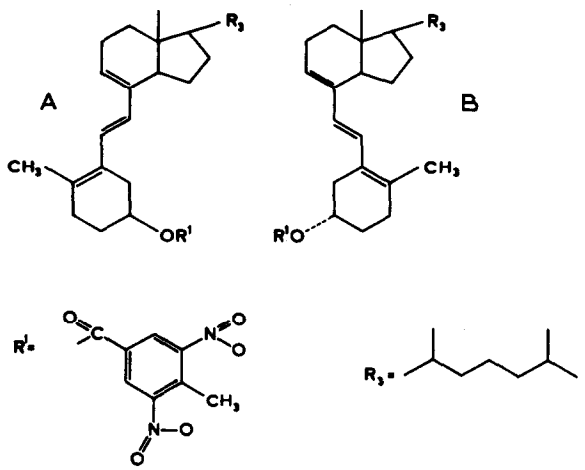

Fig.I: Planar representation of two conformations of the tachysterol molecule; R_3 is the side chain of the vitamin D_3 series.

structural and configurational elucidation of tachysterol based on consideration of molecular models (minimum crowding) was that a conformation, approximately represented by Formula I_A ($S_{5,6}$ trans, $S_{7,8}$ cis) would be the most favoured one (3,4). This view has been questionned (5) on the basis of the UV absorption data that were considered to agree better with the ($S_{7,8}$ trans) form I_B, the only alternative to I_A that would not suffer from severe steric strain when approximately planar. However, a reexamination (2,6) indicated that a definite conclusion from the spectral data could not be drawn. It recently occurred to us that the Nuclear Overhauser Effect (N.O.E.) could give information with respect to this problem and allow a decision to be made whether I_A or I_B represents the

preferred conformation of tachysterol.

60 mg of tachysterol-3.5-dinitro-4-methylbenzoate* were dissolved in 0.5 ml $CDCl_3$ and a few drops of hexamethyl disiloxane (δ = 0.05 ppm T.M.S.), degassed and sealed. The 100 MHz N.M.R. data obtained from this solution are summarized in Table I.

Table I

δ ppm(H.M.D.S)	structure	intensity	assignment	area increase on $19CH_3$ saturation
6.67	A_1	1	6H	45%
	A_2			35%
5.92	B_1	1	7H	18%
	B_2			15%
5.64	broad singlet	1	9H	0%
5.29	multiplet	1	3H	35%
1.78	broad singlet	3	$19CH_3$	---

Table I. NMR data of tachysterol-3.5-dinitro-4-methylbenzoate in $CDCl_3$; 100 MHz; H.M.D.S. as internal reference.

The increase in area of the 3H signal is due to partial saturation of the 2H signal; the increase in area of the 7H signal may be of similar origin or may be an effect related to that found by R.A. Bell and J.K. Saunders (7).

Saturating the 9H signal resulted in a 10% increase in area of the 6H signals; the signals of 7H and 3H were unaffected.

Of the two conformations under consideration only conformation I_A is in agreement with the N.O.E.'s observed.

The same sample (solution of tachysterol-3.5-dinitro-4-methylbenzoate in $CDCl_3$) was used to obtain the 220 MHz N.M.R. spectrum (Fig. II).

In Table II data and assignments from the 220 Hz spectra are collected.

Attention is drawn to the splitting (~1Hz) observed in the peaks of $26CH_3$ + $27CH_3$; we are inclined to attribute this to a chemical shift difference between the $26CH_3$ and $27CH_3$ resonances, connected with the chirality of the molecule. This, as far as we know, would constitute the first instance where the non-equivalence of the 26 and $27CH_3$ groups in steroid molecules is observed. Further assignment of peaks in the 220 MHz spectrum has to await the application of double resonance.

* prepared by Mr. A.E.C. Snoeren.

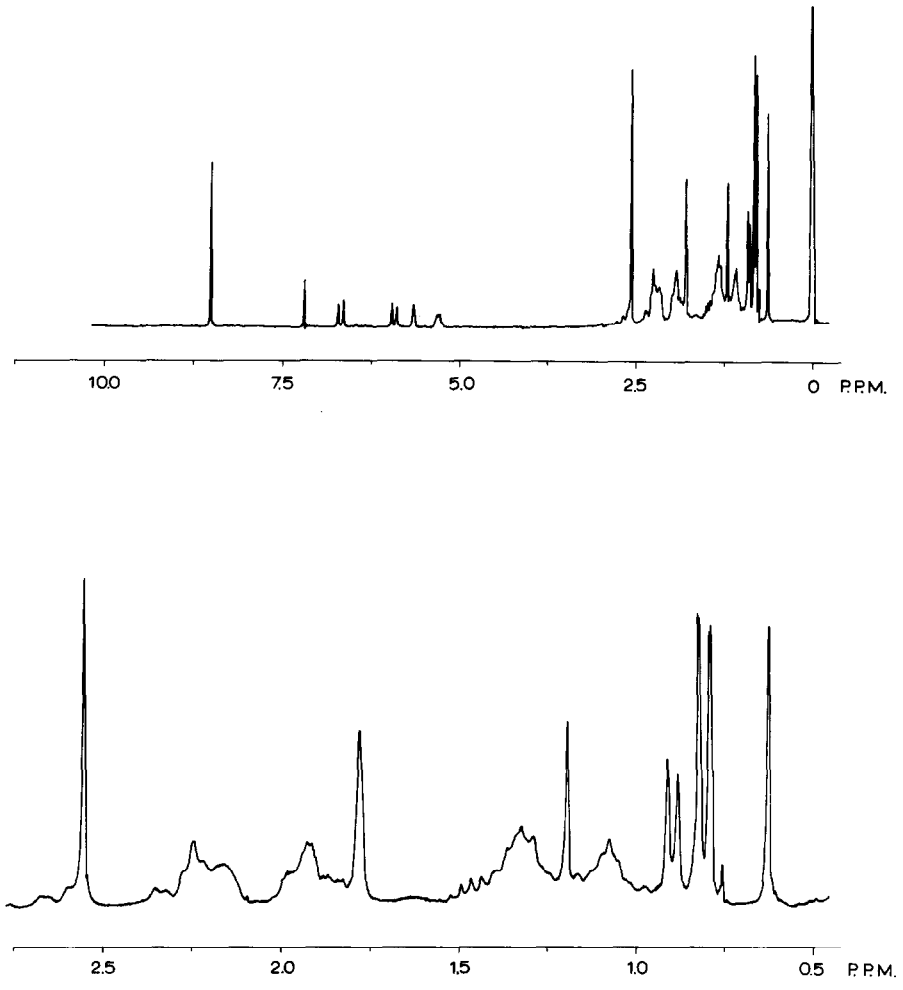

Fig. II. 220 MHz spectra of tachysterol-3.5-dinitro-4-methylbenzoate in $CDCl_3$, H.M.D.S. as internal reference.

Table II

δH.M.D.S.	intensity	assignment	δH.M.D.S.	intensity	assignment
8.491	2	aromatic protons of acid residues	2.551	3	CH_3 of acid residue
			2.31	1	4βH
7.191		$CHCl_3$	1.778	3	$19CH_3$
6.672	1	6H } J_{6-7} = 16.0Hz	1.449	1	20H J=6.2Hz
5.923	1	7H }	1.191		impurity (H_2O)
5.645	1	9H	0.895	3	$21CH_3$ J=6.2Hz
5.29	1	3αH	0.806	6	$26CH_3$+$27CH_3$ J=6.6Hz
2.64	1	4αH $J_{4\alpha-4\beta}$=15.5Hz	0.624	3	$18CH_3$

Table II. Data from 220 MHz spectra (cf. Table I and Fig. II).

The 100 MHz double resonance spectra have been recorded with a Varian HA 100 N.M.R. spectrometer with H.M.D.S. as internal lock; a Muirhead D 890 B decade oscillator was used.

The 220 MHz NMR spectrum was obtained using a Varian H.R. 220.

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