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APPLICATION IN THE USE OF A SHIFT REAGENT IN PROTON MAGNETIC RESONANCE SPECTROSCOPY FOR THE ELUCIDATION OF STRUCTURES AND STEREOCHEMISTRY OF EPIMERIC METHYL 4,9-DIMETHYL-7, 8-BENZOBICYCLO (3.3.1)NON-7-ENE-4-CARBOXYLATES

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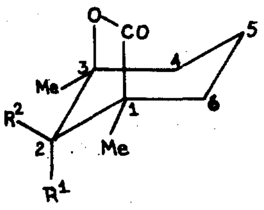
In the course of an investigation on the acid-catalysed cyclialkylation of substituted benzylcyclohexanol derivatives, we reported[1,2] cyclisations of the epimeric lactones (1) and (2). While $AlCl_3$-HCl catalysed cyclisation of (1) affords acid (3), the epimeric lactone (2) on the other hand, under similar reaction conditions, yields acid (4) and (5)[2] in a ratio of about 3:1. The stereochemistry of the bicyclo(3.3.1)nonene derivatives (3) and (4) were based[1] on the saponification rates of the corresponding methyl esters (6) and (7) and also in intramolecular participation[3] by the oxo group in facile alkaline hydrolysis of the oxo-ester (8) relative to (9). The possibility that the acids (3) and (4), both or either of them have the structure, such as (10), arising from cyclisation at C-6 in the incipient carbonium ions from (1) and (2) could not be discarded, however, from the evidences available then[1].

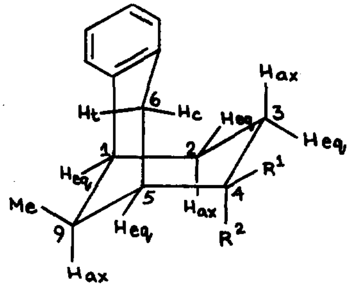
In this communication we wish to present unequivocal structural and stereochemical assignments** of these compounds based on a novel application of a recently disclosed[4] ^{1}H n.m.r. shift reagent tris-(dipivalomethanato) europium [Eu(DPM)$_3$].

** An axial stereochemistry of the C-9 methyl group in (4) originally assigned[1,3] from the resistance showed by its methyl ester (7) towards saponification should be actually represented by an equatorial configuration. Our subsequent investigations (cf. U.R. Ghatak, N.R. Chatterjee, A.K. Banerjee, J. Chakravarty and R.E. Moore, J. Org. Chem., 34, 3739 (1969)) have shown that



(1) $R^1 = H$; $R^2 = CH_2Ph$

(2) $R^1 = CH_2Ph$; $R^2 = H$

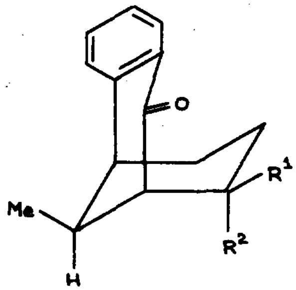


(3) $R^1 = CO_2H$; $R^2 = Me$

(4) $R^1 = Me$; $R^2 = CO_2H$

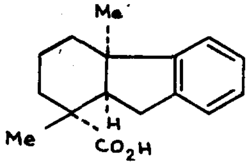
(6) $R^1 = CO_2Me$; $R^2 = Me$

(7) $R^1 = Me$; $R^2 = CO_2Me$

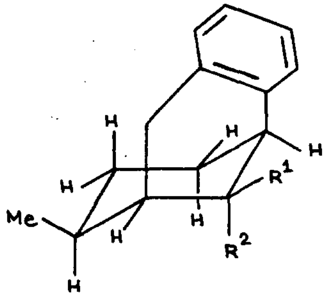


(8) $R^1 = CO_2Me$; $R^2 = Me$

(9) $R^1 = Me$; $R^2 = CO_2Me$



(5)



(10) $R^1 = Me$; $R^2 = CO_2H$
$R^1 = CO_2H$; $R^2 = Me$

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even the presence of an axial hydrogen in such cases induce comparable resistance in saponification. Similarly, the tentative axial assignment[1,3] of C-9 methyl group in (3) and its derivatives be amended in favour of equatorial orientation. The mechanistic interpretation[1] on the cyclisations of (1) and (2) in the light of the established stereochemistry of corresponding cyclisation products will be discussed in the detailed paper.

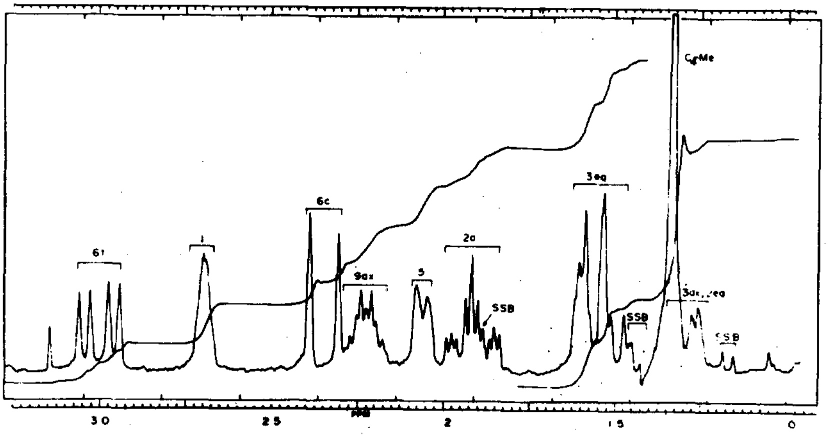

FIGURE 1a. A portion of 220 MHz ^1H n.m.r. spectrum of (6) in $CDCl_3$ (ca 20 mg in 0.5 ml). Chemical shifts in units (p.p.m.) relative to internal Me_4Si.

Fig. 1a shows a portion of the 220 MHz proton n.m.r. spectrum of (6) run in deuteriochloroform (approximately 20 mg in 0.5 ml). Signals from the two protons on C_6 are assigned to the doublets at 2.34 δ and the pair of doublets at 3.00 δ, where in each pattern $J_{6c,6t}$ is seen as 19 Hz. A Dreiding model shows that the dihedral angle between H_{6c} and H_5 is near 90° which is in accord with the lack of observable spin-coupling between H_{6c} and H_5 and permits the assignment of the two C_6 protons. The equatorial proton on C_1 is assigned to the ill-resolved multiplet at 2.70 δ. The lack of detail in this multiplet makes it impossible to determine the number of protons on adjacent carbon atoms and therefore rule out or prove the existence of structures such as (10). The multiplet at 2.22 δ is assigned to H_9 and this was confirmed by a spin decoupling experiment with irradiation of the C_9 methyl doublet at 0.87 δ, causing partial collapse of the multiplet at 2.22 δ. The doublet at 2.06 δ can be assigned to the proton on C_5 since it shows a splitting equal to that seen in the pair of doublets from H_{6t} and a tilt towards the H_{6t} pattern. Finally, the triplet of triplets seen at 1.92 δ is assigned to the axial proton on C_2 which has a large coupling to its geminal neighbour and the axial proton on C_3 and a small coupling to equatorial protons on C_1 and C_3. Fig. 1b shows the result of addition of 4 mg of $Eu(DPM)_3$ to the solution used for Fig. 1a. Shifts toward lower field are immediately apparent and are listed in Table I for those protons assigned above.

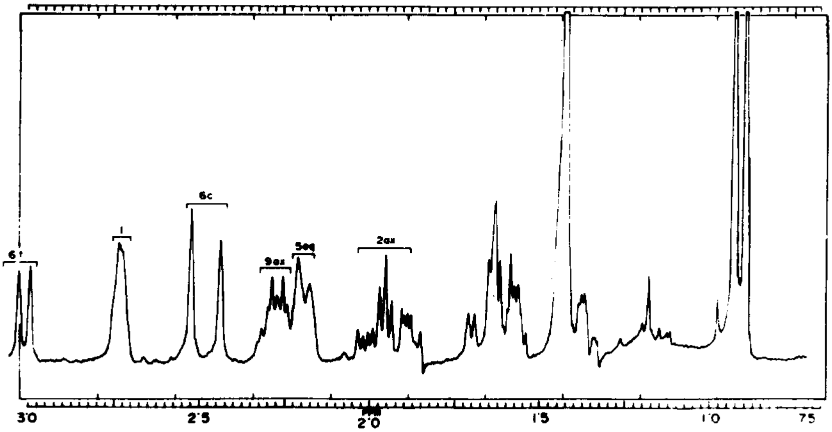

FIGURE 1b. A portion of the 220 MHz n.m.r. spectrum of (6) in $CDCl_3$ (the solution used for figure 1a) after the addition of 4 mg of $Eu(DPM)_3$.

It has been shown that $Eu(DPM)_3$ will complex with ester groups[4] and this is expected to be the site for complexing with (6). The amount of downfield shift of proton signals depends mainly on their average distance from the Europium nucleus which is complexed with the ester function. Thus, the observation of largest shifts for the signals H_{6c} and H_5 are in accord with an equatorial configuration of the carbomethoxy group on C_4.

TABLE I

Proton	Shift/4mg $Eu(DPM)_3$
6t	11Hz
1	8
6c	29
9	10
5	29
2a	8

TABLE II

Proton	Shift/8mg $Eu(DPM)_3$	Calculated shift/ 4mg $Eu(DPM)_3$
6t	14Hz	7
6c	18	9
1	15	7.5
5	57	28.5
2a	40	20

Fig. 2a shows a portion of the 220 MHz spectrum of (7) run in deuteriochloroform (approximately 20mg/0.5ml). Signals from the two protons on C_6 are assigned to the doublet at 2.78 δ and the pair of doublets at 2.96 δ where in each pattern $J_{6c,6t}$ is seen as 19 Hz.

The proton on C_1 can be assigned to the broad peak seen at 2.68 δ, H_5 to the doublet at 2.30 δ, and the axial proton on C_2 to the multiplet centered at 1.91δ, (overlapped with other signals on the right hand side).

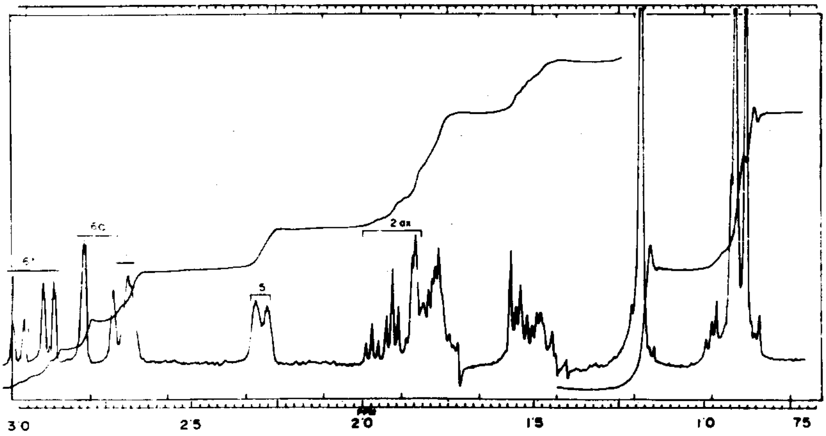

FIGURE 2a. 220 MHz ^1H n.m.r. spectrum of (7) in $CDCl_3$ (ca 20 mg in 0.5 ml). Chemical shifts in units (p.p.m.) relative to internal Me_4Si.

Fig. 2b shows the results of addition of 8mg of $Eu(DPM)_3$ to the solution used for fig. 2a. Again, shifts towards lower field are apparent and are summarized in Table II.

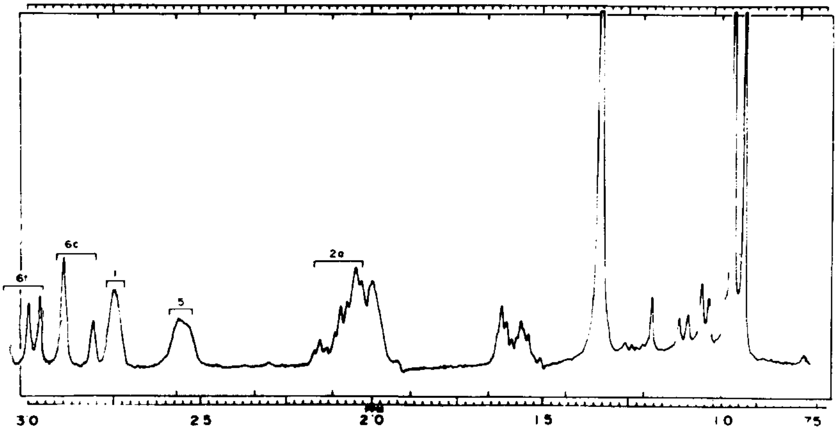

FIGURE 2b. 220 MHz ^1H n.m.r. spectrum of (7) in $CDCl_3$ (the solution used for fig. 1a) after the addition of 8mg of $Eu(DPM)_3$.

The observed shifts due to addition of 8mg of $Eu(DPM)_3$ can be halved in order to calculate shifts for 4mg addition of $Eu(DPM)_3$ for comparison with values listed in Table I. Thus the effect on the shift for H_5 is the same in both isomers which is to be expected due to the nearly equal interatomic distances involved. However, H_{2a} now shows a large shift while H_{6c} shows a small one and this is in accord with an axial configuration for the carbomethoxy group on C_4. Alternate structures such as (10) can be ruled out since $Eu(DPM)_3$ induced shifts for 6_c and 6_t would be reversed from that observed and H_1 and H_5 shifts would be similar in magnitude rather than quite different as observed. Thus, $Eu(DPM)_3$ induced shifts quite directly indicate molecular geometry in this study, and although 220 MHz spectra were used, the problem could probably have been solved at 100 MHz. In many cases where a sufficient number of assignments can be made, even 60 MHz spectra will be adequate for structural proofs using a shift reagent.

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