Tetrahedron Letters No.25, pp. 2825-2829, 1966. Pergamon Press Ltd.
Printed in Great Britain.

NMR SOLVENT INDUCED SHIFTS IN SOME δ LACTONES (+)

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(Received 4 April 1966)

The method of solvent induced shifts has been recently proposed as a tool for structural and stereochemical elucidation [1].

Nevertheless same care is necessary in interpreting the data from it because "it is not possible to say at present on which side" of a molecule "the benzene ring is located" [2,3]

(+) We thank CNR for a support

[1] - See for examples N.S.Bhacca and D.H.Williams "Application of NMR spectroscopy in Organic Chemistry" Holden-Day, S.Francisco 1964 and D.H.Williams, N.S.Bhacca, Tetrahedron, **21**, 2021 (1965).

[2] - J.E.Anderson, Tetrahedron Lett., 4713 (1965)

[3] - Very recently D.H.Williams and D.A.Wilson (J.Chem.Soc.(B), 144, (1966)) established the approximate geometry of the benzene collision complexes for 11-oxo-steroids.

particularly so when a flat molecule is at hand.

We believe that in the case we shall discuss here such a distinction can be made for trans lactones II and III of table I.

For this purpose we synthesized the hitherto unknown lactone I by reaction of CH_3MgCl in THF on 5-tBu cyclohexan-2-one 1-propionic acid methyl ester[4]. The cis junction and the t-Bu group strongly inhibit the approach of the benzene molecule from the concave face of I. Thus Δ_{CH_3} of I represents the solvent induced shift of an axial methyl group α to oxygen in a six membered lactone when the benzene molecule approaches from the same side of the methyl group[5].

If the Grignard reaction is conducted in ethyl ether and with CH_3MgI a greater amount of lactone trans II is produced as expected[4]. Its $\Delta_{CH_3} = + 0,39$ is quite close to that

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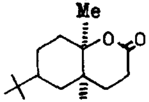
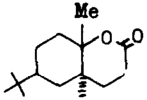
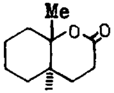
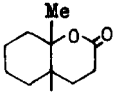
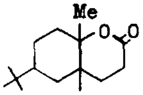
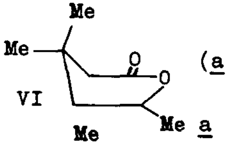
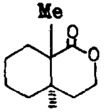
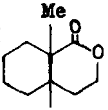
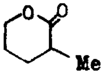
[4] - The conditions used are known to be those of best obedience to the Cram's rule (see W.J.Houlihan J.Org.Chem., **27**, 3860 (1962)).

[5] - It is not possible to predict the exact geometry of the collision complex, nevertheless it is hard to conceive a situation of parallelism and superimposition between the lactone ring and benzene because of steric repulsion of methyl group.

TABLE I

Solvent Effects on Methyl resonances (δ values in ppm ref. to $SiMe_4$)

lactones		$\delta CDCl_3$	δC_6H_6	Δ
I		1.36	0.98	+0.38
II		1.28	0.89	+0.39
III		1.30	0.94	+0.36
IV		1.41	1.04	+0.37
V		1.46	1.18	+0.28
VI		(a) 1.35	1.08	+0.27
VII		1.20	0.93	+0.27
VIII		1.33	1.11	+0.22
IX		1.22	1.08	+0.I4

Full experimental details for the preparation of some of the substsnces in this table will be published in a subsequent paper.

of I thus indicating that relative positions of lactone ring, methyl group and benzene are identical both in I and in II i.e. the benzene approaches to lactone II from the same side of the methyl group [5]. The same we can think about lactone III.

This result can now be used to establish the preferred conformation of cis lactone IV: the nearness of its Δ_{CH_3} to that of lactone III is not a mere coincidence but really means that benzene "sees" methyl group and lactone ring in the same perspective in III and in IV or in other words that the preferred conformation of lactone IV is that with the methyl group axially oriented with respect to the lactone ring. Confirmatorly lactone V which is formed in little amount in the Grignard reaction and possessing the methyl group equatorially oriented with respect to the lactone ring has $\Delta_{CH_3} = +0.28$.

Since these conclusions can be invalitated if the molecular compositions of collision complexes are not the same for trans compounds as for cis or if the equilibrium constants for complex formation are very different, we determined these two parameters for lactones III, IV and VI as representatives of the family.

The results obtained [6] indicate a 1 : 1 complex both for III, IV and VI. The equilibrium constants are also very close being .67± .03; .64± .03 and .65± .03 respectively.

Table I contains some more interesting data:

1) Δ_{CH_3} of V and Δ_a of VI are very close thus indicating that, at least in absence of other polar substituents, the solvent induced shifts are not influenced by further substitution on the methyl-bearing carbon atom but are uniquely related to conformations.

2) Δ_{CH_3} of compounds VII, VIII and IX can tentatively be interpreted in the sense that VIII is an equilibrium mixture (near 1 : 1) of the two possible cis conformations. This conclusion would be quite sure if one could demonstrate, as for II and III that benzene approaches to the trans compound VII from the methyl side.

3) Analogously to what is known for steroids, δ_{CDCl_3} of angular substituents are constantly at lower field if the ring junction is cis.

4) Δ are greater for substituents α to the hetero atom than for substituents α to the CO.

Acknowledgment - We are indebted with Dr.D.H.Williams who read the manuscript

[6] - The method employed is that described by J.Tyrrel, Can.J.Chem., 43, 783 (1965). We used a Varian A60 Spectrometer.