Tetrahedron Letters No.50, pp. 5113–5117, 1967. Pergamon Press Ltd. Printed in Great Britain.

STERIC AND POLAR EFFECTS ON THE CONFORMATION OF BUTYROLACTONES

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(Received in UK 21 July 1967)

Some observations on coupling constants extracted from the proton magnetic resonance (p.m.r.) spectra of γ-lactones have been previously reported (1). In the assumption that vicinal coupling constants were related to dihedral angle by Karplus-type equations (2) it was concluded that several 2,2-disubstituted butyrolactones were undergoing inversion in solution at 40° between two "envelope" conformations of the type found in crystalline γ-lactones (3).

Table 1 shows vicinal coupling constants extracted from the p.m.r. spectra of a selected series of substituted butyrolactones. We interpret these values in terms of an envelope conformation, possibly slightly distorted (4), in which ϕ, the cis-dihedral angle for vicinal protons (2,3- or 3,4-), is 35–40°, arrived at as follows: in first approximation, we take all projected geminal angles as 120° and the proportionality constants (J^{0}) of modified Karplus equations (2) for a given pair of vicinal positions as equal for dihedral angles greater than or less than

Table 1

VICINAL COUPLING CONSTANTS FOR SOME BUTYROLACTONES[a]

	Substituents[b]	Vicinal Coupling Constants[c] (c/s) AM	AN	BM	XM	XN	YM
I	2,2'-Me_2-4-Ph	.	.	.	6.3	9.9	.
II	2-Ph-4,4'-Me_2	8.6	12.2	.	.	.	.
III	4'-Me-2,4-Ph_2	8.6	12.1	.	.	.	.
IV	4-Me-2,4'-Ph_2	7.6	13.1	.	.	.	.
V	2,4-Ph_2	8.2	13.0	.	5.5	10.9	.
VI	4-Me-2-Ph	8.4	12.7	.	5.2	10.3	.
VII	2,4'-Ph_2	7.3	9.7	.	7.6	5.5	.
VIII	4'-Me-2-Ph	6.7	9.7	.	6.9	5.6	.
IX	3-OH[d,f]	5.5	.	1.8	4.1	.	1.6
X	3-OAc[f]	6.6	.	1.6	4.6	.	1.5
XI	3-Ph[f]	7.5	.	9.4	7.6	.	7.4
XII	4,4'-Me_2-3-Ph	7.2	.	10.9	.	.	.
XIII	2-OH-2'-Me-3-Ph[e]	.	.	.	6.9	.	10.0
XIV	2-OH-2'-Me-3'-Ph	.	.	.	8.3	.	9.3
XV	2-Ac	6.5[g]	8.9[g]	.	?	?	?
XVI	2-CO_2Me	7.6[g]	9.1[g]	.	?	?	?
XVII	2-Ph[e]	8.7[g]	10.4[g]	.	?	?	?
XVIII	2-Br[e]	3.8[g]	6.7[g]	.	?	?	?

[a] Solvent: $CDCl_3$ at $35 \pm 5^{\circ}$ except d and e.

[b] A prime indicates that the substituent is trans to substituents at unprimed positions; the first-named 2-substituent is arbitrary reference.

[g] The 2-, 3-, and 4-methylene groups are labelled AB, MM, and XY, respectively; A, M, and X are the downfield or only members of the respective pairs.

[d] Mixture with equal volume of $CDCl_3$ made homogeneous with C_5H_5N at 30°.

[g] Solvent : C_5H_5N at 40°.

[f] Long-range couplings (c/s) as follows: IX, $J_{BY} \sim 0.9$; X, $J_{BY} \sim 0.9$; XI, $J_{AY} \sim 0.3$, $J_{BX} \sim 0.5$.

[g] These values are splittings in the A quartet; the smaller value is arbitrarily assigned to J_{AM}.

? Analyses of the 5-spin spectra to give these values have not been completed.

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a right angle (and neglect the small additive constant). Then

$$J^{cis}/J^{trans} \sim J^{o}\cos^2\phi/J^{o}\cos^2(120 + \phi)$$

For lactones I-VI, $J^{o}_{23} \sim 14.2$-14.6, $J^{o}_{34} \sim 10.8$-11.4,

and $\phi \sim 39$-$46°$ if the smaller vicinal coupling is J^{cis}

or $\phi \sim 21$-$14°$ if the smaller vicinal coupling is J^{trans}.

Each of these lactones has cis-2,4 substituents whose non-bonded interaction in the conformation with both pseudo-axial should lead to a fixed conformation with both pseudo-equatorial. For lactones V and VI, $\delta_{MM} = 0.68$ and 0.77 p.p.m., respectively, whereas for lactones VII and VIII, $\delta_{MM} = 0.14$ and 0.18 p.p.m., respectively. These values and the magnitudes of the vicinal coupling constants suggest that VII and VIII are inverting rapidly between the alternative envelope conformations with one pseudo-axial and one pseudo-equatorial substituent. Examination of models suggests that $\phi_{2,3} \sim \phi_{3,4}$ in either conformation, roughly in agreement with the above

results. With the assumptions already stated (5), we write time-averaged expressions for the vicinal coupling constants, J_{AM}, J_{AN}, J_{XM}, J_{XN} with $J^{o} = J^{\pi}$. Of the possible arrangements for lactone VII, if M is cis to X and N is cis to A, formal solution gives $\phi \sim 39^{\circ}$, $J^{o}_{23} = 16.0$, $J^{o}_{34} = 12.5$, whereas if M is cis to A and N is cis to X, the formal solution is $\phi \sim 50^{\circ}$, $J^{o}_{23} = 18.0$, $J^{o}_{34} = 13.6$. In either case, there are approximately equal ($\pm$ 2%) amounts of the two conformers present, which seems reasonable for this compound. Lactone VIII gives similar results. We therefore choose $\phi \sim 40^{\circ}$ rather than $\sim 20^{\circ}$ or 50° for all the above lactones. This angle is however to be adjusted downwards to allow for the observation that $J^{\pi} > J^{o}$. The ratio, J^{π}/J^{o}, is clearly not the same for the 2,3- and 3,4-positions but, with the reasonable average value, 1.25 (5), ϕ becomes 35-40°.

In lactones IX and X, long-range coupling between just one of the 2-protons and one of the 4- protons, presumably through bonds in the familiar near-planar W arrangement with both coupled protons equatorial (although they are the upfield members of their respective pairs) reveals that the conformation may be fixed by a single polar substituent at the 3- position. The magnitudes and ratio of the vicinal coupling constants are only consistent with an axial position for the polar-2-substituent and a cis-dihedral angle near 50°. This is also probably the case for 3-acetoxy-3-methylbutyrolactone in which the downfield 2- and 4- protons are long-range coupled ($J_{AX} \sim 0.8$ c/s); there are of course no vicinal couplings. The energy of interaction of the dipole of the substituent-C2 bond with dipoles in the plane of the lactone group will be lower in this conformation than in the alternative, and the earlier suggestion (1) that polar repulsion between trans- diaxial bromine atoms was responsible for the fixed conformation of 3,4-dibromo-γ-valerolactone appears not to be necessary.

The effect may not be attributed to absence of axially opposed substituents at C1 and the ring-O atom, because vicinal and long-range coupling constants in 3-phenylbutyrolactone (XI) show that it is a rapidly inverting system with equatorial Ph: axial Ph $\sim$ 1.6, (whence $\Delta G^{\circ} \sim 300$, probably $\pm$ 150 cal/mole). Its 2,2- and 4,4-disubstituted derivatives (XII-XIV) also appear to be inverting systems, as do the 2-monosubstituted lactones (XV-XVIII), but we are unable at present to assess the proportions of conformers. Both 2,2-dimethyl-3-phenyl- and 3,3-dimethyl-2-phenylbutyrolactone show $\delta_{XY} = 0$ so for the former we are able to observe only the average value of J_{XM} and J_{YM} (7.9 c/s); the latter shows no sign of 2,4-long-range coupling which may indicate that the 2-phenyl group is largely pseudo-equatorial.

Details of syntheses and characterization of new compounds will be reported in our full communication. Several spectra were kindly measured for us on a Varian A60 spectrometer by Mr. D.C. Dehlsen and Mr. W.J. Davidson under the supervision of Dr. A.V. Robertson and Dr. S. Sternhell at the University of Sydney. More recently we have measured spectra on a Varian HA-60-IL spectrometer purchased with a grant from the Australian Research Grants Committee.

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