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STERIC EFFECTS ON THE CONFORMATION OF VALEROLACTONES

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Apart from incidental observations, the conformation of δ-lactones has, as far as we are aware, been the subject of three generalisations (1,2,3). Although Mathieson (1) inferred generally the boat conformation, more recently "normal" carbonyl-stretching frequencies near 1740 cm^{-1} in solution have been correlated with half-chair conformations in the solid state by X-ray analysis, and "high" values near 1760 cm^{-1} in solution have been correlated with boat conformations in the solid state by X-ray analysis, or geometrical requirements in bridged systems (2). Most recently optical rotatory dispersion measurements on optically active δ-lactones derived from natural products of known configuration have been correlated on the basis that the δ-lactone ring adopts a boat conformation unless certain steric interactions are relieved in a half-chair conformation (3).

We have examined the proton magnetic resonance (p.m.r.) spectra of all twelve isomeric *gem*-dimethylphenylvalerolactones and of 3,3-dimethyl-5-*tert*-butylvalerolactone. Vicinal coupling constants or pair sums readily extracted from the spectra by appropriate analyses are shown in Table 1, where for consistency, we refer to the 2-, 3-, 4-, and 5-methylene groups as *AB*, *KL*, *MN*, and *XY*, respectively, *A*, *K*, *M*, and *X* being the downfield

Table 1

COUPLING CONSTANTS FOR *GEM*-DIMETHYLPHENYLVALEROLACTONES
in $CDCl_3$ at 30°

	Substituents		Coupling constants (c/s)			ϕ_{ij} (*J*° in c/s)
	Me_2	Ph	Vicinal		Long-range	or ΔG° (cal/mole)
I	2,2	4	*MX* 5.0	*MY* 11.0		ϕ_{45} 49° (11.6)
			KM 12.8	*LM* 3.5	*LX* 2.2	ϕ_{34} 58° (12.5)
II	5,5	3	*AK* 4.3	*BK* 12.7		ϕ_{23} 55° (13.1)
			KM 3.5	*KN* 12.6	*AM* 2.0	ϕ_{34} 58° (12.5)
III	3,3	5	*MX* 3.1	*NX* 12.7	*AM* 1.7	ϕ_{45} 60° (12.4)
IV	4,4	2	*AK* 6.5	*AL* 13.1	*KX* 1.5	ϕ_{23} 46° (13.5)
V	3,3	4	*MX* 10.9	*MY* 5.0		$\Delta G^\circ > 1760$
VI	4,4	3	*AK* 11.5[a]	*BK* 5.5[a]		
VII	2,2	3	(*MX* + *NX*)[b] 14.3			
			(*MY* + *NY*)[b] 8.7			$\Delta G^\circ \sim 680$
			KM 11.2	*KN* 3.0		
VIII	3,3	2	*MX* 5.6	*NX* 9.0		
			MY 5.5	*NY* 5.4		$\Delta G^\circ \sim 340$
IX	4,4	5	(*AK* + *BK*)[c] 16.0			
			(*AL* + *BL*)[c] 13.1			$\Delta G^\circ \sim 240$

[a] Approx. values to fit calculated *ABC* spectrum to observed 8-line spectrum

[b] *X* and *Y* assignments are arbitrary

[c] *K* and *L* assignments are arbitrary

or only members of the respective pairs. Lactones I-IV each have the phenyl group in a *cis*-1,3 relation to one of the geminal methyl pair, and may be expected to exist preferentially in a conformation that avoids diaxial opposition of these groups and probably eclipsing interaction of especially the *gem*-dimethyl pair with an adjacent methylene group. First approximations, probably a little high (*cf.* 4), to vicinal *cis*-dihedral angles as given by solution of

$$J^{cis}/J^{trans} = J^{0}\cos^{2}\phi/J^{0}\cos^{2}(120+\phi)$$

are consistent with existence of these four in fixed half-chair conformations in deuterochloroform at 30°, the phenyl group being equatorial (or *pseudo*-equatorial at the 2- or 5- positions). More diagnostic is the occurrence for all four of marked long-range coupling between the more weakly vicinally coupled (equatorial) proton of an appropriate methylene group and one of the protons of the other methylene group, and of unresolved long-range coupling (detected by spin-decoupling) of one of the methyl groups and the adjacent more strongly vicinally coupled (axial) methylene proton. The near-planar W-arrangement of bonds usually required for such long-range coupling (5) is present in the half-chair but not in the boat conformation. The efficacy of the phenyl-methyl interaction in fixing conformation in these cases is attested by the values, $J_{MX} = 3.0$, $J_{NX} = 12.5$, $J_{AM} = 1.7$ c/s for 3,3-dimethyl-5-tert-butylvalerolactone (*cf.* III, Table 1).

All other lactones in Table 1 have adjacent phenyl and *gem*-dimethyl substituents which are unlikely to be eclipsed in a stable conformation. This implies half-chair conformations for V and VI. All thirteen valerolactones reported on here show in carbon tetrachloride solution "normal" carbonyl frequencies in the infrared (1730-1740 cm^{-1} if the *gem*-dimethyl group is 2- or 5-, 1740-1750 cm^{-1} if it is 3- or 4-), so there is probably no significant incursion of boat forms. The p.m.r. spectrum of III is little affected by increase of temperature in the range, 30-150°, but that of V shows marked changes probably as a result of increasing residence times in a less stable inverted conformation. Vicinal coupling constants in comparison with those for I suggest the phenyl group in V is $>95\%$ equatorial in $CDCl_3$ at 30° (whence $\Delta G^{0} > 1760$ cal/mole). The *ABC* spectrum of VI is more difficult to analyze but a similar conclusion probably applies. Lactones VII-IX each contains a vicinal pair of methylene groups and application of the approximation previously suggested (6) for rapid symmetrical inversion gives the ΔG^{0} values shown. If, as is clearly so for lactones I-VII, the equatorial-phenyl conformer is the more stable, the ΔG^{o} values imply that interaction of a *pseudo*-axial phenyl group at the 2- or 5- positions with an axial 4- or 3- hydrogen atom, respectively, and the lone pair or pi-electrons of the lactone group is less energetic than the corresponding interactions of a more nearly axial phenyl group at the 3- or 4- positions.

The remaining isomeric *gem*-dimethylphenylvalerolactones show closely coupled 5-spin spectra we have not yet analyzed unambiguously.

Synthesis and characterisation of new compounds will be reported elsewhere. P.m.r. spectra were measured on a Varian HA-60-IL spectrometer purchased with a grant from the Australian Research Grants Committee. Earlier measurements were kindly made for us on an A-60 spectrometer by Mr. D.C. Dahlsen and Mr. W.D. Davidson under the supervision of Dr. A.V. Robertson and Dr. S. Sternhell at the University of Sydney.

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