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CONFORMATION AND NMR OF LACTONE-BRIDGED CYCLOHEXANES

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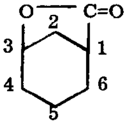
A γ-lactone ring, bridging the 1 and 3 positions in cyclohexane, introduces considerable strain into the molecule by drawing the axial atoms at these positions into a much closer distance than in the undistorted six membered ring. This strain is relieved partly by distortion of other neighboring bonds and should reflect itself in the coupling constants between the hydrogens on the carbons vicinal to the lactone ring.

We have measured the NMR spectra of such bridged γ-lactones I having additional various substituents on the cyclohexane ring. In Table 1 are recorded the positions of the absorption bands, coupling constants and multiplicity of the hydrogens on the carbon α to the oxygen of the lactone and of the hydrogen on the carbons vicinal to this α carbon. The coupling constants are compared with constants found from the curve (2) drawn according to the Karplus equation (3) that relates the dihedral angle between vicinal carbon-hydrogen bonds and the coupling constants. The dihedral angles were measured on Dreiding models with the cyclohexane in the chair conformation with the aid of a protractor. These measurements are necessarily crude and a margin of error has to be assumed. They proved themselves however by their agreement with the experimental J values. The lactones and halolactones are of known configuration, that was previously established chemically (4, 5, 6, 7).

The hydrogens on the α-carbons (Ha) in the lactones IIa and IIb having no substituents on the vicinal carbons, show as triplets with coupling constants of 4.5 c.p.s. This fact indicates that two hydrogens on the vicinal carbons have dihedral angles close to normal ones (Ha is equatorial), but two other hydrogens are not coupled to Ha and their dihedral angles with Ha are close to 90°. The position and conformation of the latter two hydrogens is found from the NMR spectra of the halo-lactones. The <u>cis</u> bromo-lactones IIIa; IIIb and IIIc having the halogen disposed equatorially on the C_4 carbon vicinal to the lactone ring, show Ha as a doublet (Fig. 1), thus proving that one of the hydrogens that couple with Ha is the equatorial one on C_4. The axial hydrogen on C_4 does not couple with Ha since the <u>trans</u> bromo- and iodo-lactones IVa; IVb and IVc with an axial halogen show Ha as a triplet (Fig. 2). The second hydrogen that couples with Ha is placed therefore on C_2. This hydrogen is the one that is disposed equatorially in the undistorted molecule. This is seen in the spectrum of the bromolactones V and VI having a phenyl group at position 2 <u>cis</u> to the lactone ring. These lactones show Ha as a doublet, when the bromine is axially disposed and as a singlet, when the halogen is equatorial. The benzylic hydrogen appears as a singlet in both lactones. This hydrogen is shifted considerably (by 0.8 p.p.m.) to lower field when the bromine is axial, thus proving independently diaxial disposition of this hydrogen and the bromine atom. The hydrogen α to the halogen atom (H_b) confirms the conformation of the molecule. It shows as a doublet of doublets when <u>trans</u> to the lactone ring (H axial) and as a multiplet when <u>cis</u> to the lactone ring (H equatorial).



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The experimental coupling constants are almost identical to those found from the theoretical curve in the case of the unsubstituted lactones and very close, but somewhat on the higher side, (this is rather unexpected) for the halogenated lactones. The similar coupling constants between Ha and the two equatorial hydrogens on the vicinal carbons prove the distorted chair conformation for the cyclohexane ring. A boat conformer should show different coupling constants. The six-membered ring is therefore a distorted chair conformer, having the equatorial-equatorial dihedral angles smaller and the equatorial-axial ones higher than normal.

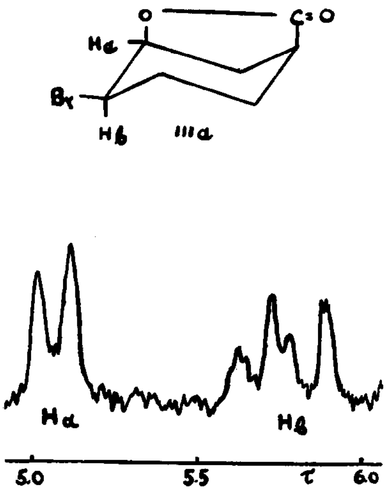


FIG 1

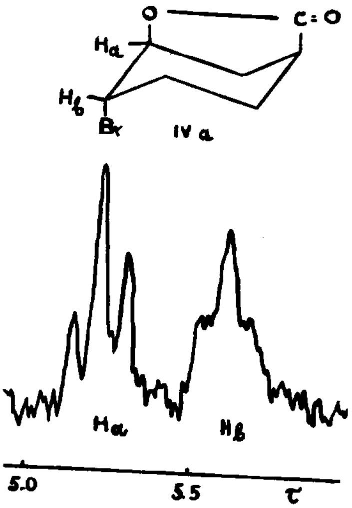
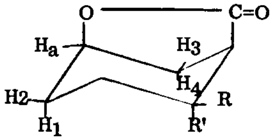
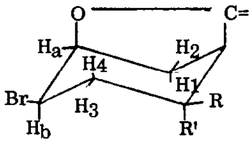
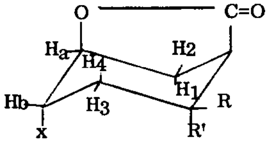
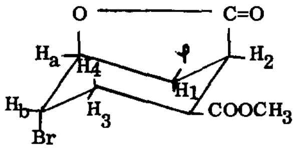
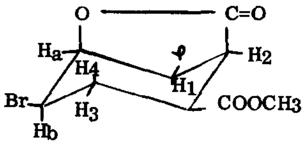


FIG 2

TABLE 1

N.M.R. of Lactone-Bridged Cyclohexanes[a]

Compound	τ	Coupling constants J exp. in c.p.s.	Dihedral angles α°	J cal.[b] in c.p.s.	Reference[c]
			$H_aC - CH_1$ 75	~ 0	4
			$H_aC - CH_2$ 50	4	
	H_a 5.12	4.5 (t)[d]	$H_aC - CH_3$ 45	4.3	
II_a R = $COOCH_3$; R' = H			$H_aC - CH_4$ 80	~ 0	
II_b R = H; R' = $COOCH_3$	H_a 5.12	4.5 (t)	"	"	4
			$H_aC - CH_1$ 80	~ 0	5
	H_a 5.08	6 (d)	$H_aC - CH_2$ 45	4.3	
			$H_aC - CH_b$ 75	~ 0	
			$H_bC - CH_a$ 75	~ 0	
III_a R = H; R' = H	H_b 5.75	11;6(d;d)	$H_bC - CH_3$ 50	4	
			$H_bC - CH_4$ 170	9	
III_b R = $COOCH_3$; R' = H	H_a 5.02	6 (d)	"	"	6,7
	H_b 5.68	11;6(d;d)			
III_c R = H; R' = $COOCH_3$	H_a 5.00	6 (d)	"	"	7
	H_b 5.60	11;6(d;d)			
			$H_aC - CH_1$ 80	~ 0	5
	H_a 5.20	4.5 (t)	$H_aC - CH_2$ 45	4.3	
			$H_aC - CH_b$ 50	4	
			$H_bC - CH_a$ 50	4	
IV_a x = Br; R = H; R' = H	H_b 5.58	10 w/2(m)	$H_bC - CH_3$ 65	1	
			$H_bC - CH_4$ 50	4	

IVb x = I; R = H; R' = H	H_a	5.15	5 (t)	"		"	5
	H_b	5.50	10 w/2 (m)				
IVc x = Br; R = $COOCH_3$; R' = H	H_a	5.12	4.5 (t)	"		"	6, 7
	H_b	5.43	10 w/2 (m)				
	H_1	5.92	(s)	$H_1C - CH_a$	80	~ 0	7
				$H_1C - CH_2$	80	~ 0	
	H_a	5.17	4(d)	$H_aC - CH_1$	80	~ 0	
				$H_aC - CH_b$	50	4	
				$H_bC - CH_a$	50	4	
V	H_b	5.40	10 w/2 (m)	$H_bC - CH_3$	65	1	
				$H_bC - CH_4$	50	4	
	H_1	6.70	(s)	$H_1C - CH_a$	80	~ 0	7
				$H_1C - CH_2$	80	~ 0	
	H_a	4.99	(s)	$H_aC - CH_1$	80	~ 0	
				$H_aC - CH_b$	75	~ 0	
				$H_bC - CH_a$	75	~ 0	
VI	H_b	5.60	11;6(d;d)	$H_bC - CH_3$	50	4	
				$H_bC - CH_4$	170	9	

a) Measurements were carried out in deutochloroform with T.M.S. as internal reference on a Varian A-60.

b) Found from dihedral angles in Dreiding models (2).

c) Reference where the structure was determined.

d) (s) = singlet; (d) = doublet; (d;d) = doublet of doublets; (t) = triplet; (m) = multiplet; $w/_2$ width at mid-height.

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