Conformation of the Inhibitor 1,5-Gluconolactone—an *X*-ray Determination

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Summary An *X*-ray structure investigation supports the hypothesis that enzyme-catalysed hydrolysis of pyranoside substrates involves intermediates with half-chair conformation.

THE conformations of substances which strongly inhibit enzymic processes provide insights into the nature of enzyme–substrate interactions. It has been found in studies[1,2] on the inhibition of glucosidases that the amount of inhibition was related to the configuration of the inhibitor. Heyworth and Walker[3] found that although glucose does inhibit glucosidase activity, the enzyme has a relatively low affinity for glucose as compared with gluconolactone, suggesting that glucose cannot interact with the enzyme as well as can a strong, competitive inhibitor such as gluconolactone. The results of this *X*-ray investigation support the suggestion by Leaback that intermediates with half-chair conformations are involved.

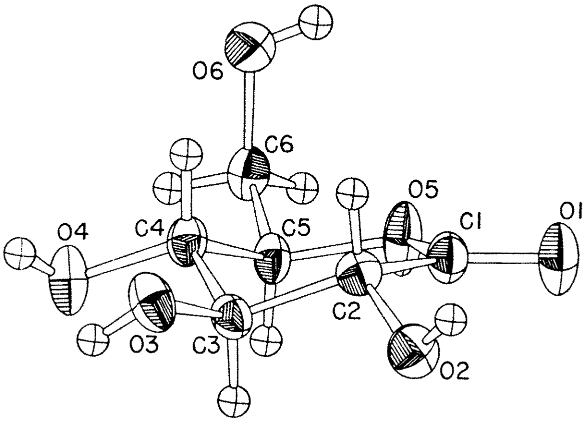
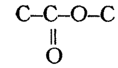
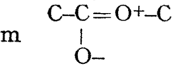


FIGURE. 1,5-D-*Gluconolactone*.

The crystals of 1,5-gluconolactone used belong to the orthorhombic space group $P2_12_12_1$ with $a = 7{\cdot}84$, $b = 12{\cdot}33$, and $c = 7{\cdot}54$ Å, $Z = 4$. The conformation of 1,5-gluconolactone as found in the solid state is shown[5] in the Figure. The CH_2OH and OH groups occupy the most "equatorial" positions possible, thus giving a half-chair conformation to the ring. Atom positions relative to the best least-squares plane through the ring carbonyl group are given in the Table. The average single bond C–C and C–O distances are 1·51 and 1·42 Å, respectively.

Also, the planarity of the lactone group in δ-lactones has been a subject of general interest.[6] Previous reports on δ-lactones have claimed that the  $\underset{\displaystyle O}{\overset{}{\text{C–C}}}\!\!\overset{}{\text{–O–C}}$ group is planar as expected from a simple valence-bond representation of the resonance from  $\mathrm{C{-}\underset{\displaystyle O^-}{C}{=}O^+{-}C}$ However, Jeffery[7] has shown that in certain γ-lactones the planarity does not extend beyond the bonds of the carbonyl atom. This is also the case in 1,5-gluconolactone with C-5 being 0·28 Å out of the plane formed by atoms C-1, C-2, O-1, and O-5; the C-1–O-5 distance is 1·32 Å, which is somewhat shorter than the 1·38 and 1·36 Å distances reported for other lactones.[8] This is believed to be another example in which the stereochemistry of the carbohydrate ring system is sensitive to steric requirements for minimum configuration energy.

TABLE

Distance from plane through ring carbonyl group.

C-1[a]	−0·02 Å	O-1[a]	0·01
C-2[a]	0·01	O-2	−0·69
C-3	−0·54	O-3	0·22
C-4	0·09	O-4	−0·41
C-5	−0·28	O-5[a]	0·01
C-6	0·46	O-6	1·86

[a] Indicates atoms used to form best least-squares plane.

Three-dimensional *X*-ray data for this analysis were taken with an automated Hilger–Watts four-circle diffractometer. Two equivalent octants of data were collected with Mo-K_α radiation within a θ sphere of 35°, resulting in 974 independent reflections whose intensities were judged significantly above background. All carbon and oxygen positions were determined by Patterson map–symmetry map superposition techniques.[9] The hydrogen atom positions were readily observable on the resulting difference electron density maps. Full-matrix least-squares refinement resulted in a conventional *R*-factor of 0·048.

The work was performed at the Ames Laboratory of the United States Atomic Energy Commission.

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