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CIRCULAR DICHROISM IN LACTONES

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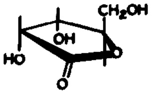
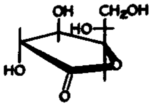
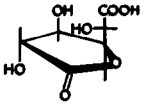
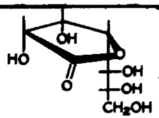
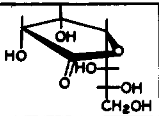
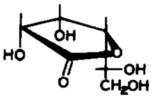
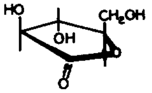
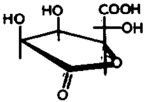
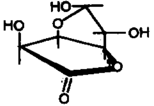
Recent interest in the lactone group as an optically-active chromophore (1-7) has prompted a C.D. study of seven γ-lactones of aldonic and related acids. The results are shown in Table 1, which also contains data from an O.R.D. study of a similar series of compounds (1). Two δ-lactones have also been examined.

In both the C.D. and U.V. spectra of these compounds the n → π* absorption band (8) at 214-219mμ is clearly defined. There is no evidence that the sign or magnitude of the C.D. in this band is influenced by the lactone ring substituents at C_β or C_γ (or C_δ), but, in the γ-lactones, the sign appears to relate to the substitution pattern at C_α, as has already been noted by Okuda et. al. (1). The same apparent relationship exists in the two δ-lactones, but here it seems doubtful that the sign is determined by the disposition of the C_α substituents since, in the δ-lactone whose molecular geometry is accurately known (9), the C_α substituent lies in the plane (10) of the lactone system and this is a nodal plane of the antibonding π orbital. However, there is evidence, both in γ- and in δ-lactones (9, 11-13) that the disposition of C_β relative to the lactone plane is related to the substitution pattern at C_α, which suggests that the location of C_β may be the sign-determining factor. This, in turn, suggests that the sign of the Cotton effect associated with the lactone n → π* transition may depend on the chirality of the lactone ring itself rather than on the asymmetric disposition of substituents. Wolf (6) has already concluded that the sign is related to ring-chirality in δ-lactones. A more detailed discussion follows.

From Table 1 it would appear that the sign of the observed Cotton effect depends upon the configuration of C_α since, when the hydroxyl group at C_α lies below (↓) the plane of the lactone system, oriented as shown, the sign is negative and when above (↑) it is positive. All the

TABLE 1

	Compound		Substituent Orientation			U.V.†		C.D.†		$\left\|\frac{\Delta\varepsilon}{\varepsilon}\right\|$
			C_α	C_β	C_γ	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\Delta\varepsilon_{max.}$	
I*	D-Galacto-γ-lactone		↓	↑	↓	219mμ	98	220mμ	-5.52	0.056
II*	D-Ribono-γ-lactone		↓	↓	↑	217mμ	79	220mμ	-4.23	0.054
III*	D-Glucono-γ-lactone		↓	↑	↑				-ve	
IV*	D-Glucosaccharo-1, 4-lactone		↓	↑	↑				-ve	
V	D-*glycero*-D-*gulo*-Heptono-γ-lactone		↓	↓	↓	215mμ	91	219mμ	-3.84	0.042
VI	D-*glycero*-L-*manno*-Heptono-γ-lactone		↓	↓	↓	215mμ	98	219mμ	-4.04	0.041
VII	D-Gulono-γ-lactone		↓	↓	↓	215mμ	90	219	-3.77	0.042
VIII*	D-Arabono-γ-lactone		↑	↓	↑	217mμ	89	219	+5.05	0.057
IX*	D-Glucosaccharo-3,6-lactone		↑	↑	↑				+ve	
X*	β-D-Glucurono-γ-lactone		↑	↑	↑	217mμ	72	219	+4.00	0.056

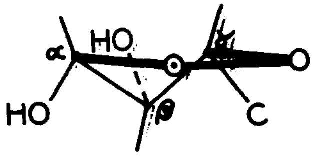
* O.R.D. determined by Okuda et. al. (1).

† Concentrations were ≃ 0.01M in water; 10, 2 and 1 mm path lengths.

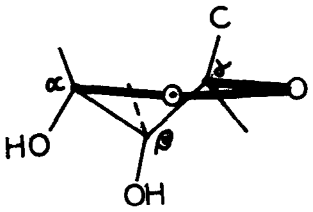
possible configurations at C_β and C_γ (.↑↑, .↑↓, .↓↑, .↓↓) are represented in the compounds listed but none of these appears to influence the sign. Application of the octant rule (14) to the lactone carbonyl group (1) correctly predicts the substituent orientation at C_α and the configuration here is also compatible with Klyne's lactone sector rule (3) and with Snatzke's formulation (7). However, none of these three rules would predict the absence of detectable contributions from the groups attached to C_β and C_γ.

The dissymmetry factors (15), i.e. the ratios $|\frac{\Delta\varepsilon}{\varepsilon}|$, for the lactones in Table 1 fall into two groups whose numerical values are approximately 0.042 and 0.056. In each compound the ratio persists within the $n \rightarrow \pi^*$ band on the longer wavelength side of the maximum where, presumably, contributions from transitions of higher energy are negligible. Within each of the two groups, therefore, the difference between the transition probabilities for left- and right-circularly polarized light is nearly identically related to the transition probability for unpolarized light. The dissymmetry factors, in effect, are normalized rotational strengths. Unless the constancy of $|\frac{\Delta\varepsilon}{\varepsilon}|$ within each group is to be looked on as fortuitous, it must imply near-identity in the asymmetric molecular features upon which the circular dichroism depends.

X-ray structure analyses have established the co-planarity of the five atoms, C-CO-O-C, of the lactone group (10). The plane is both a symmetry plane for the group and a nodal plane for the antibonding π orbital. With respect to the C.D. associated with the lactone $n \rightarrow \pi^*$ transition, therefore, one might reasonably assume that the asymmetric perturbation from a group or atom would be unchanged in magnitude but inverted in sign by reflection of that group or atom through the plane. The location, relative to the plane, of the fifth ring atom, C_β, and of the ring substituents is precisely known in the two γ-lactones, I and II. In I, structure analysis (11) has shown that C_β lies below the plane as depicted and, in II, the results of a P.M.R. study are consistent only with the same location (13). In I, the hydroxyl group attached to C_β is almost co-planar with the lactone system (11) whereas in II it must project below this plane. Yet the two compounds are both members of the group with $|\frac{\Delta\varepsilon}{\varepsilon}| \simeq 0.056$; that is their normalized rotational



I



II

strengths are equal. Evidently, if I and II exist largely in the conformations depicted, the C_β substituents have no detectable influence on the Cotton effect of the $n \to \pi^*$ transition.* Similarly the C_γ substituents, although respectively above and below the lactone plane, appear to be without effect.

I and II have opposite configurations at C_β, hence the location of C_β above or below the lactone plane is independent of its own substitution pattern. It lies, however, on the same side of the plane as the hydroxyl group at C_α.

Of the remaining compounds with $|\frac{\Delta\varepsilon}{\varepsilon}| \approx 0.056$, in VIII the substitution pattern, ↑↓↑, is the mirror image of that in I, but in X, structure analysis (12) has shown that the three ring substituents and also C_β are all above the lactone plane. The presence of the second ring imposes additional constraints in X, since C_γ is also slightly above the plane of the remaining four atoms of the lactone group. It is interesting that the dissymmetry factor in X is not changed despite the differences in molecular structure from other members of the group.

In each of the three compounds, V, VI and VII, comprising the group with $|\frac{\Delta\varepsilon}{\varepsilon}| \approx 0.042$, all the ring substituents lie on the same side of the lactone plane. Some distortion of "normal" ring geometry may therefore exist, but there is no X-ray or other structural information bearing on this point.

The δ-lactone, XI, which has been the subject of an X-ray structure analysis (9), had $\varepsilon_{\text{max.}(214\text{m}\mu)} = 84$, $\Delta\varepsilon_{\text{max.}(215\text{m}\mu)} = -4.95$ (0.01M in MeOH) and $|\frac{\Delta\varepsilon}{\varepsilon}| \approx 0.059$. The sign of the Cotton effect reflects the absolute configuration at C_α as in the γ-lactones of Table 1 and the dissymmetry factor relates XI to the group with $|\frac{\Delta\varepsilon}{\varepsilon}| \approx 0.056$. However, in XI, the methyl substituent at C_α is almost co-planar with the lactone system (9). This is quite unlike the situation in the γ-lactones, where the C_α substituents project above or below the lactone plane. In the δ-lactone, XII, which is unstable in solution, the $n \to \pi^*$ transition in the U.V. spectrum was largely masked by rising end absorption. However, the associated C.D. peak was well defined with $\Delta\varepsilon_{\text{max.}(219\text{m}\mu)} = -4.26$, extrapolated to zero time (0.01M in water). At zero time the ratio $|\frac{\Delta\varepsilon}{\varepsilon}|$ at 230mμ was 0.043. Again the sign of the Cotton effect reflects the configuration at C_α while the dissymmetry factor suggests a relationship to the γ-lactones with $|\frac{\Delta\varepsilon}{\varepsilon}| \approx 0.042$. According to a recent generalization (16) XII would preferentially adopt the half-chair conformation.

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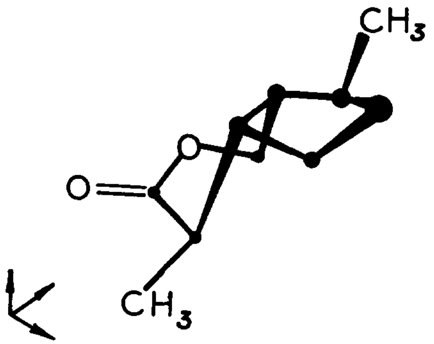
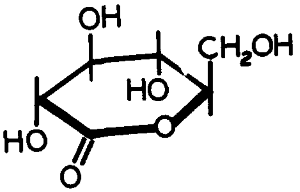
* Such evidence as is available (13) suggests that the alternative conformational state with C_β above the plane is unlikely to be appreciably populated at ambient temperatures. However, if it is assumed to be present in the appropriate proportions in both I and II, then it may be envisaged that the perturbations from out-of-plane atoms will cancel with the exception of those from the hydroxyl groups at C_α. But a conclusion that the $n \to \pi^*$ Cotton effect is determined in sign and magnitude by the C_α substituents cannot be reconciled with the known geometry of X and XI discussed below.



XI Isoiridomyrmecin



XII D-Glucono-δ-lactone.

In each of the compounds discussed the sign of the Cotton effect may be correlated with the absolute configuration at C_α. In the γ-lactones the hydroxyl substituents at C_α are either above or below the lactone plane, but in the δ-lactone, XI, the methyl group at C_α lies nearly *in* the plane, where it should produce no asymmetric perturbation. The sign of the Cotton effect is independent of the location of the substituents on C_β and C_γ. However, in the four examples, I, II, X and XI, where the molecular conformations are known, the location of C_β may be correlated both with the absolute configuration at C_α and with the sign of the Cotton effect, which suggests that the sign may be determined by the disposition of C_β relative to the lactone chromophore.

Wolf (6) found that the C.D. and O.R.D. of fourteen δ-lactones could be interpreted under the assumption that the sign of the n → π* Cotton effect is determined by the chirality of the boat or half-chair conformation of the δ-lactone ring. The results reported here accord with this finding and indicate that ring-chirality also determines the sign in γ-lactones. Further, they include nothing to suggest that the sign or magnitude of the Cotton effect may be influenced by molecular asymmetry other than that of the lactone ring itself.

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