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OPTICAL ACTIVITY AND LACTONE RING CONFIGURATIONS

A. F. Beecham

Division of Chemical Physics, C.S.I.R.O. Chemical Research Laboratories,
Melbourne, Australia

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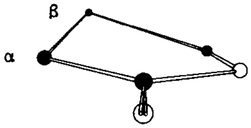
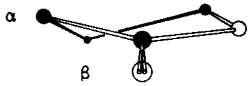
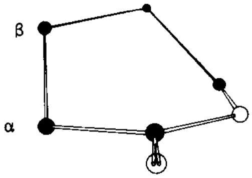
The preference for co-planarity (1) of the five atoms of the lactone group, C-CO-O-C, implies that the stable conformations of the γ-lactone ring are restricted to an enantiomeric pair, in which the fifth ring atom, C_β, is either above or below the lactone plane, oriented as shown in I and II. A study of the CD and UV spectra of some γ-lactones derived from sugars (2) suggested that the sign of the CD associated with the lactone n → π* transition (3) was determined by this fact, I and II being associated respectively with +ve and -ve Cotton



I (+)



II (-)



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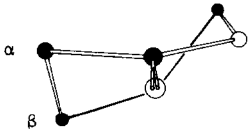

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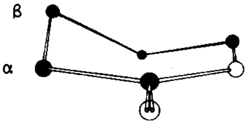
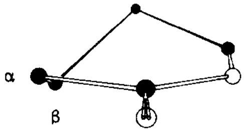


V (+)



VI (-)

effects. Wolf (4) has reached a similar conclusion in regard to δ-lactones, in which the boat, III, IV (1,5) and half-chair, V, VI (5) conformations are each enantiomeric. The proposed relationships between the sign of the n → π* Cotton effect and the location of C_β relative to the lactone plane are the same in both γ- and δ-lactones.

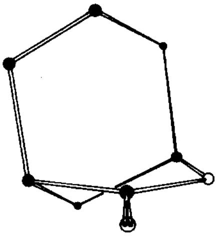
In the γ-lactones (2), the Cotton effect sign appeared to reflect the configuration at C_α. Okuda (6) had previously noted this in an ORD study of a similar series of compounds. Also a constancy was observed (2) in the dissymmetry factors, $|\frac{\Delta\varepsilon}{\varepsilon}|$ (7), which suggested a correspondingly constant source for the optical activity and this seemed consistent with the presence of a hydroxyl substituent on C_α in every case. Only reference to the δ-lactone, isoiridomyrmecin, in which the C_α methyl substituent is nearly co-planar with the lactone group (8) suggested that ring-chirality rather than the C_α configuration was the sign-determining factor. But to accept this required one to believe, firstly, that the location of C_β with respect to the lactone plane was related to the configuration at C_α in the γ-lactones studied and, secondly, that the ring-conformation was fixed as either I or II exclusively, even in the monocyclic lactones. For these reasons further evidence has been sought from the literature.

Klyne (9) has tabulated ORD data for thirty-four compounds in each of which a γ-lactone is *cis*- or *trans*-fused to a six-membered ring, in a polycyclic structure. Dreiding models of all of these compounds have been examined and it has been found that the relationship between sign and ring-chirality holds, without exception. Two eudesman 13 → 8 lactones[†], with the same 1-oxa-*trans*-hexahydroindan-2-one part-structure, are of particular interest. In both, the sign of the ORD curve is positive, as expected from the chirality of the γ-lactone ring, but the compounds are C_α epimers, with the methyl substituent at this centre above the lactone plane in one and below it in the other. In this case, then, the sign is necessarily independent of the configuration at C_α.

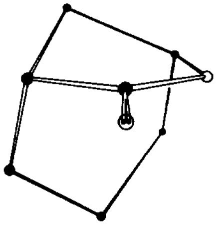
These results provide added evidence that the sign of the n → π* Cotton effect in γ-lactones depends upon the location of C_β relative to the planar lactone system. This is reminiscent of the situation in certain bi- and polycyclic cyclopentanones, where the out-of-plane C atoms of the cyclopentanone ring have a dominant influence on the ketone n → π* Cotton effect (10).

[†] Ref.9, diagrams XXIII, E XXIIIa, E XXIIIb.

In bridged ring lactones based on the bicyclo [3,2,1] octane skeleton the structure comprising the lactone group and its immediate environment has the enantiomeric forms represented by VII and VIII. Klyne (11) recorded the ORD of fourteen compounds of this type and concluded that the sign was determined by which of the two enantiomeric forms was present. The Cotton effect of rosenonolactone and seven related compounds (12) also observed this relationship, as did the γ-lactones of eight D-(-)-quinic acid derivatives (13). It is important to note that signs found to be associated with VII and VIII are opposite to those which would be expected from the incorporated γ-lactone ring.

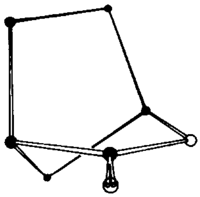


VII (+)

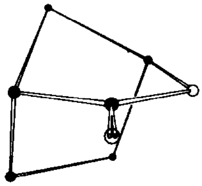


VIII (-)

The bridged ring system of lactones with the bicyclo [2,2,1] heptane skeleton is also enantiomeric, IX, X. The ORD of four such compounds, two of each type, was recorded by Klyne (11).



IX (?)



X (?)

The reported results showed no relationship between sign and the chirality in IX and X, possibly because in the region of the lactone n → π* absorption band the weak anomalous dispersion was superimposed on a strong background curve.

The purpose of this brief survey is to draw attention to the influence of ring geometry on the optical rotatory properties of lactones. At least in the γ-lactones (2) there is evidence that the Cotton effect associated with the n → π* transition is determined both in sign and magnitude by interactions within the asymmetric ring. Asymmetry elsewhere in the molecule appears to be of minor. even negligible, importance. If this is also the case in other lactone systems, as seems possible, the advantages for interpretation of results in terms of stereochemistry are obvious. Further experimental data from all classes of lactones, particularly from circular dichroism studies, would be of great interest.

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