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# OPTICAL PROPERTIES OF $C_\alpha$ OXY-SUBSTITUTED $\delta$-LACTONES

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Abstract - The CD curves of steroidal and terpenoid $\delta$-lactones, deoxyandrololactone, and its C-16 epimeric acetoxy and hydroxy derivatives, and ambreinolide and its C-12 epimeric acetoxy derivatives, have been measured by conventional technique. The spectra are analyzed in terms of earlier investigations in the steroid and terpene series using empirical correlations.

Studies concerning the structure, conformation and configuration of saturated $\delta$-lactones are a subject of continuing interest. Circular dichroism (CD) studies have been used frequently to study $\delta$-lactones in solution. Our earlier interest in $\delta$-lactones[1,2] resulted in the preparation of number of related optically active compounds, the structure of which provides an opportunity to obtain basic information on the factors effecting the sign, shift and magnitude of the $n-\pi^*$ Cotton effect (CE).

Several studies of substituted and unsubstituted $\gamma$- and $\delta$- lactones[3] by CD were carried out in an attempt to correlate the geometry of the lactone ring and the sign of the CE. Some of the rules which resulted from these studies could accurately be applied to specific structures only, particulary those not containing a second chiral sphere. Further attempts were made taking into account both the substitution pattern and chirality of the lactone ring[4]. According to Legrand and Bucourt[5] the sign of the CE is opposite to the sign of the torsional angle between the ethereal oxygen --cabonyl carbon bond and the $C_\alpha$ -- $C_\beta$ bond when a

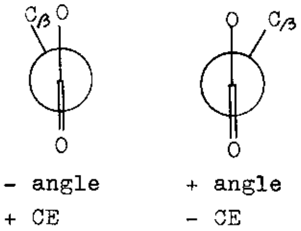


Figure 1.

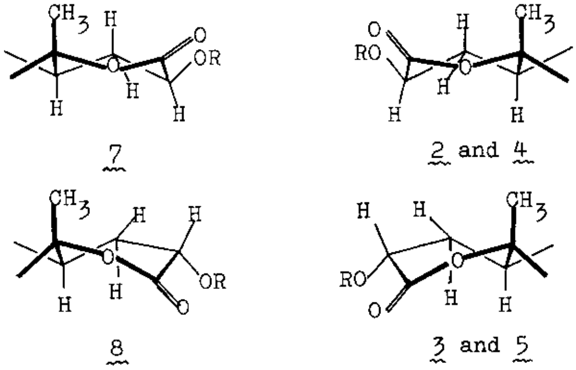
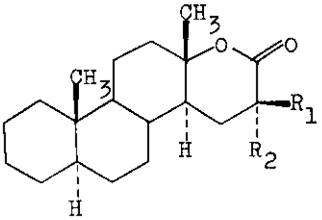
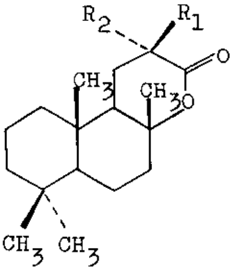


Figure 2.





1, $R_1=R_2=H$

2, $R_1=OAc$, $R_2=H$

3, $R_1=H$, $R_2=OAc$

4, $R_1=OH$, $R_2=H$

5, $R_1=H$, $R_2=OH$

6, $R_1=R_2=H$

7, $R_1=OAc$, $R_2=H$

8, $R_1=H$, $R_2=OAc$

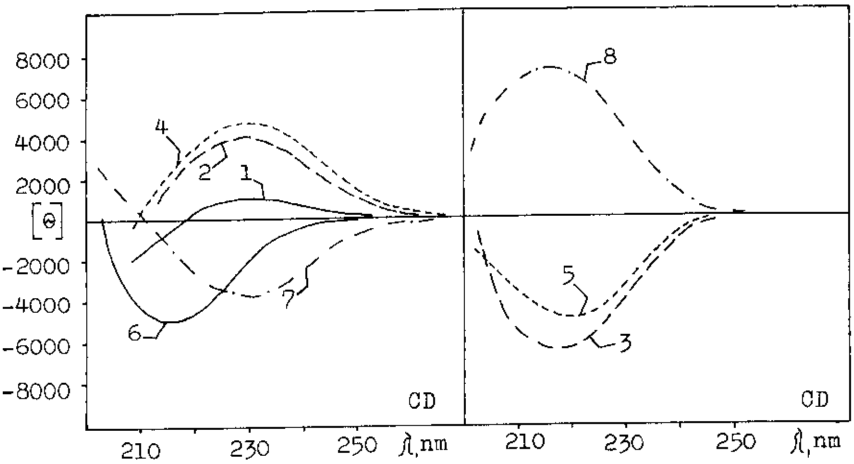


Figure 3. CD spectra of compounds 1 - 8; CD were measured at ambient temperature on a Cary 60 with the 6001 unit spectropolarimetar (calibrated with d-10-camphorsulfonic acid) in 0.01 M methanolic solutions using a 10-mm cell.

Newman projection is viewed along the carbonyl carbon -- $C_\alpha$ bond (Fig. 1). However, the structural features of most of the $\delta$-lactones examined did not allow a complete rationalization of the all effects which determine the CE sign. This is particulary true for epimeric $\alpha$-heterosubstituted $\delta$-lactones which may exist in different conformations. The results of our $^{13}C$ nmr study of terpenoid and steroidal $\delta$-lactones and their $\alpha$-substituted derivatives[6] pointed to conformations as depicted on Fig.2: a half-chair for both unsubstituted and quasi-equatorially substituted $\delta$-lactones 1, 2, 4, 6 and 7 and twist boat conformations for their quasi-axial counterparts 3, 5 and 8.

As can be seen, the lactone ring in 1 has two asymmetrical carbons C(13)(S) and C(14)(S), similarly as the lactone ring in 6, C(8)(R) and C(9)(R), but the two corresponding configurations are opposite, namely the lactone ring pattern of 1 and 6 are related as mirror images. Since for each of the $\alpha$-substituted lactones both epimers were available, it was possible to estimate the effect of the substitution pattern on $C_\alpha$, as well as the effect of the disposition of $C_\beta$ relative to the lactone chromophore on the CE sign and magnitude.

The CD curves (Fig.3) for 1 (weak positive) and 6 (negative) reflect the conformational difference of the steroid and terpenoid lactone rings; it is quite possible, however, that the two half-chair conformations, due to conformational mobility of the lactone ring, are slightly different, leading to difference in magnitude and shift. The $\alpha$-substituted lactones 2, 4 and 7 show CD curves of the same sign as the unsubstituted lactones 1 and 6 from which they are derived, and with which they have the same half-chair conformations. For the corresponding epimers 3, 5 and 8 which are in a twist-boat conformation, opposite CE signs were found. Furthermore, the CD maximum for 2 ( $[\theta] = +3750$ at 229 nm) and 7 ( $[\theta] = -3750$ at 230 nm) as well as for the epimers 3 ( $[\theta] = -6740$ at 218 nm) and 8 ( $[\theta] = +7000$ at 218 nm) are in excellent agreement with the mirror image relation. The position of the CD extremum for 2 and 7 on one hand, and 3 and 8 on the other is in accord with Wolf's finding that the CD maximum of a half-chair conformation usually lies at longer wavelengths than those of the corresponding half-boat[3a].

Conformations of lactones 1, 2, 4, 6 and 7 as depicted in Fig. 2 also indicate coplanarity of the $C_\alpha$-heterosubstituent and the lactone group. Hence, in such spatial orientation, even strongly perturbing substituents do not seem to effect the sign of CD curves. On the other hand, in the epimeric $\alpha$-substituted $\delta$-lactones **3**, **5** and **8**, the substitution pattern at $C_\alpha$ invokes ring inversion to a twist boat conformation. In this conformation the relative disposition of $C_\beta$ is opposite to that found in the parent lactones **1** and **6**, while the heterosubstituent and the lactone group are again nearly coplanar. Thus, the result of this study of $\alpha$-oxysubstituted $\delta$-lactones confirm suggestions by Wolf[4a,b] and Beecham[4c,d] that the overall ring chirality determines the CE sign in $\delta$-lactones, and that the CE signs, positive for lactones **1**, **2**, **4** and **8** and negative for **3**, **5**, **6** and **7** are in full agreement with the Legrand-Bucourt rules.

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