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Absolute Configuration of 1,4-Dialkyl-2,5-dioxabicyclo[2.2.1]heptane-3,6-dione Enantiomers

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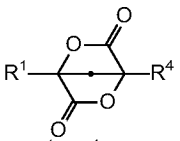
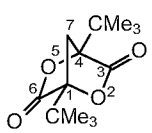
The correlation of the Cotton effect sign of the $n \rightarrow \pi^*$ transition with the cage structure chirality and the absolute configuration of 1,4-dialkyl-2,5-dioxabicyclo[2.2.1]heptane-3,6-diones has been established.

Optically active γ-lactones are widely used as synthetic building blocks[1] and their chiroptical properties have been studied extensively.[2–6] However, investigations of norbornane cage structure bridged dilactones of symmetry C_2 by means of chiroptical methods are absent, and only 1,4-di-*tert*-butyl-2,5-dioxabicyclo[2.2.1]heptane-3,6-diones (+)-**2a** and (−)-**2b** have been obtained[7] in optically active form.

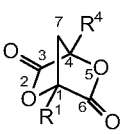
Earlier several sector[2,3] and other[4–6] rules have been proposed which connect the Cotton effect (CE) sign of the $n \rightarrow \pi^*$ transition of the lactone chromophore with its chiral environment. In the present work, the relationship between the CE sign of the lactone $n \rightarrow \pi^*$ transition and the cage



1 $R^1 = R^4 = Me$
2 $R^1 = R^4 = Bu^t$



(+)-(1*R*,4*R*)-**2a**



(1*R*,4*R*)-**1b**
(−)-(1*S*,4*S*)-**2b**

structure chirality of symmetrical 1,4-dialkyl dilactones is established on the basis of an experimental study of the chiroptical properties of the antipodes **2a**, **2b** and optical activity calculation data of dilactones **1b**, **2b** using *ab initio* methods[8] [Gaussian 92 (G92)[8a], PCI[8b]] with the 6-31G* (geometry) and 6-31+G* (optical activity) basis sets.

The enantiomers **2a** ($[\alpha]_{20}^{D} + 86.3^{\circ}$ (*c* 0.93, $CHCl_3$)) and **2b**, ($[\alpha]_{20}^{D} - 84.5^{\circ}$ (*c* 1.01, $CHCl_3$)) were obtained by the reaction of dilactone **2** with (*S*)-α-phenylethylamine ($[\alpha]_{20}^{D} - 38.8^{\circ}$, neat) followed by diastereomeric lactonoamides (d.e. ≥94–96%, according to ^{1}H NMR spectroscopic measurements) separation[9] by means of fractional crystallization and column chromatography, and further by acid-catalysed cyclization[7] to antipodes **2a**,**b**. The absolute configuration of the high-melting diastereomer has been determined[9] by X-ray analysis.

In the CD spectra of enantiomeric dilactones **2a** and **2b** (Fig. 1), both the long-wavelength dichroic bands (almost mirror and near Gaussian shape) at 232.5 nm ($\Delta\varepsilon = 5.791$ and -5.603, respectively) and intense short-wavelength bands at <200 nm (without extremum) are observed. The assignment of the long-wavelength CE to the $n \rightarrow \pi^*$ transition has been made by using MO analysis and the calculated values of the oscillator strengths of the first two electronic transitions for dilactones **1b**, **2b**. According to the calculations (G92), the long-wavelength dichroic absorption band of the dilactone chromophore is caused by two near degenerate $n \rightarrow \pi^*$ transitions to excited singlet states of B and A symmetry: $\Delta E_B = 6.60$ eV, $f_B = 0.0009$ CGSE for **1b**, $\Delta E_B = 6.58$ eV, $f_B = 0.0007$ CGSE for **2b**; $\Delta E_A = 6.61$ eV, $f_A = 0.0044$ CGSE for **1b**, $\Delta E_A = 6.59$ eV, $f_A = 0.0034$ CGSE for **2b**. The $n\pi^*$ orbital origin for the first dichroic band is confirmed by both the hypsochromic shift of the long-wavelength band in the UV spectra of dilactone **2** with increasing polarity of the medium and the comparatively small magnitude of the extinction coefficient (ε = 278, Fig. 1). The last indicates the "forbidden" character of this transition.

The $n \rightarrow \pi^*$ transition band at 233–236 nm was also observed earlier in the ORD and CD spectra of bridged monolactones **3**[3] and dilactone **4**,[10] as distinct from monocyclic γ-lactones **5**[4] and dilactones **6**, **7**[11] ($\lambda_{max} = 216$–221 nm).

The calculated rotational strengths of the near degenerate $n \rightarrow \pi^*$ transitions have opposite signs for both dilactones **1b** and **2b**. However, the values (G92) of the negative B components are rather greater than the values of the positive A components: $[R]^r_B = -22.9$ and $[R]^r_A = +21.8$ for **1b**; $[R]^r_B = -20.0$ and $[R]^r_A = +18.8$ for **2b**. Thus, the observed negative sign of the first CE in the CD spectrum of dilactone **2b** agrees with the calculated data. The very slight difference between the excitation energies of the negative B and positive A components (*vide infra*) does not permit the observation of a bisignate form of the first dichroic absorption band in the experimental CD spectrum of dilactone **2b**.

According to Klyne's sector rule[3] applied to either of the lactone groups, the $n \rightarrow \pi^*$ CE sign of dilactones **1b**, **2b** is determined by two opposing effects, the dominant negative contribution of the other (rear) lactone group, and a weaker positive contribution of the CH_2 bridge. The two *tert*-butyl contributions are expected to cancel. Thus, the δ-dilactonic ring contribution predominates over that of the γ-lactonic ring in the case of **1b**, **2a**,**b**. These have contrary perturbing effects due to the second type, two chiral spheres (according to Snatzke's spheres doctrine[12]). In contrast, the δ-pentanolide ring contribution plays a dominant role in the case of dilactone **4**. Therefore, the long-wavelength CE sign of the type **1**, **2** enantiomeric dilactones may be directly connected with their cage structure chirality.

In accordance with this correlation the *positive* CE sign of the lactone $n \rightarrow \pi^*$ transition of optically active 1,4-dialkyl dilactones corresponds to the N-type [(−)-τ_1, Θ ($O^5C^6C^1O^2$)] of the boat enantiomeric form of the δ-dilactonic ring and the *negative* $n \rightarrow \pi^*$ CE to the S-type [(+)-τ_1]. The correlation is confirmed by ORD[11] spectra of monocyclic dilactones **6**, **7** as well as Wolf's[5] and Legrand's[6] chirality rules for δ-lactones, in contradistinction to Legrand's[6] rule for γ-lactones.

The rigid frame of 1,4-dialkyl dilactones **1**, **2** also enables one to connect the CE sign of the $n \rightarrow \pi^*$ transition with their absolute configuration. The latter, however, depends upon the 1,4-substituent type, as seen from an example of homochiral dilactones (1*R*,4*R*)-**1b**, and (1*S*,4*S*)-**2b**.

Hence, the *positive* $n \rightarrow \pi^*$ CE sign corresponds to (*R*)-configuration, and the *negative* $n \rightarrow \pi^*$ CE sign to (*S*)-configuration in the case of $R^1 = R^4 = Pr^i$, Bu^t, *etc.* The dependence of absolute configuration from the CE sign of the $n \rightarrow \pi^*$ transition is opposite in the case of $R^1 = R^4 = Me$, Et, Pr^n, *etc.*

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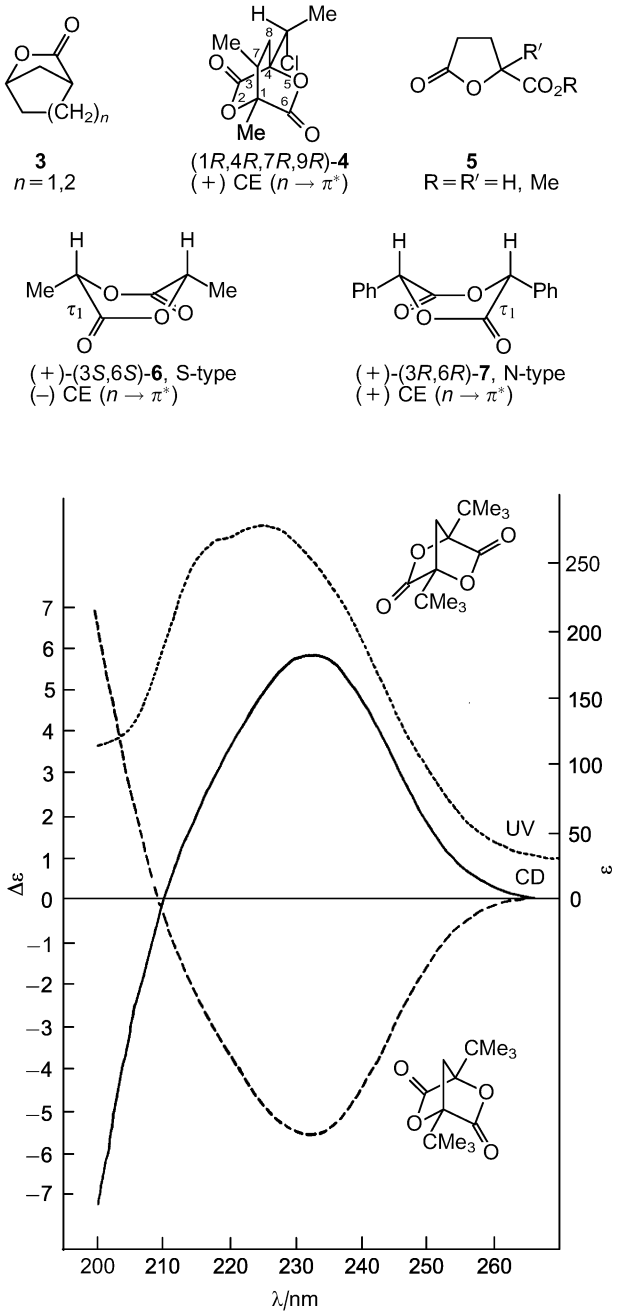

Fig. 1 CD spectra of enantiomers **2a** (—) and **2b** (– – –) in EtOH and UV spectrum of **2** in *n*-heptane (---).

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