Autoassembling of the cage structures

11.* Absolute configuration and chiroptical properties of 1,4-di-*tert*-butyl-2,5-dioxabicyclo[2.2.1]heptane-3,6-dione enantiomers

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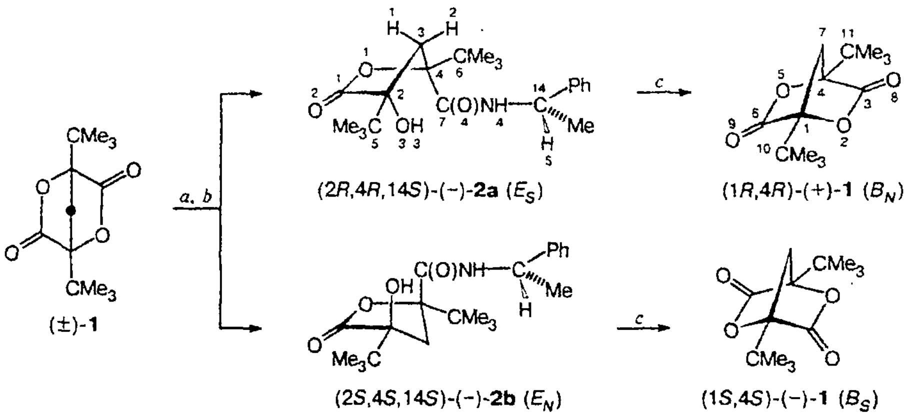
Enantiomeric dilactones ((1*R*,4*R*)-(+)-**1** and (1*S*,4*S*)-(−)-**1**) of α,α′-dihydroxy-α,α′-di-*tert*-butylglutaric acid have been prepared. The Cotton effect sign of the n→π*-transition of the lactone chromophore in enantiomers **1** is determined by the contribution of the uncompensated bonds of the δ-dilactone ring, but not by that of the γ-monolactone ring of **1**. The correlation of the Cotton effect sign of the n→π*-transition with the chirality of the cage structure and the absolute configuration for the series of 1,4-dialkyldilactones of type **1** has been suggested. The contribution of the pseudo-*a*-oriented amide group to the Cotton effect sign of the lactone n→π*-transition (the effect of the third chiral sphere) in diastereomeric lactonamides **2a,b** predominates over that of the nonplanar bonds of the heterocycle (over the effect of the second chiral sphere).

Key words: 2,5-dioxanorbornane derivatives, absolute configuration; enantiomeric dilactones, diastereomeric lactonamides, circular dichroism spectra.

Optically active γ-lactones[3] and α-hydroxycarboxylic acids[4] are widely used as synthons in asymmetric synthesis. Chiral bridged dilactones with the cage norbornane structure with the C_2 symmetry are promising synthons for organic synthesis.

We have previously developed[5] a method for the stereoselective synthesis of dilactone of (±)-α,α′-dihydroxy-α,α′-di-*tert*-butylglutaric acid (**1**). Diastereomerically pure lactonamides **2a,b** (Scheme 1) were prepared from the latter, and the absolute configuration was determined for high-melting diastereomer **2a** by X-ray diffraction analysis.[6] In this work, we synthesized enantiomers of dilactone **1** from compounds **2a,b** (see Scheme 1) and studied their chiroptical properties to

Scheme 1



Reagents and conditions: *a.* (*S*)-α-PEA ($[\alpha]_D^{20}$ −38.8° (pure)), toluene, Δ, 15 h; *b.* neutral Al_2O_3 (II Brockmann activity), $CHCl_3$ (60.9% yield of **2a**, m.p. 172 °C; 64.6% yield of **2b**, m.p. 108 °C);[6] *c.* TsOH, toluene, Δ, 30 h.

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* For Part 10, see Ref. 1. For preliminary report, see Ref. 2.

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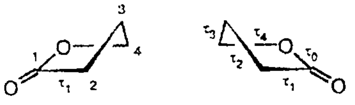
establish correlations of the Cotton effect (CE) sign of the n→π*-transition of the lactonic chromophore with the chiral environment of the latter in molecules of optically active compounds **1** and **2a,b** and the absolute configuration of other 1,4-dialkyl analogs of **1**.

Results and Discussion

Published data on the chiroptical properties of γ- and δ-lactones are very ample.[7—19] For example, different sector[8—11] and other chirality rules,[16—19] which related the CE sign of the n→π*-transition of the intrasymmetrical lactonic chromophore with its chiral environment and the absolute configuration of the lactones, have been suggested.

In the case of monocyclic γ- and δ-lactones, the n→π*-CE sign correlates with the chirality of the enantiomeric envelope (*E*) and boat (*B*) conformations of the γ-lactone (**3**)[18] and δ-lactone (**4**)[16] rings, respectively, and is opposite to the sign of the endocyclic torsion O—C(=O)—C—C angle in molecules of γ- (τ_1) or δ-lactones (τ_1')[17] (for the determination of the conformations of the *N* and *S* types, see in detail Ref. 1).



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(E_S, $\tau_1 > 0$) (−)-n→π*-CE

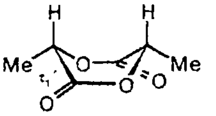
(E_N, $\tau_1 < 0$) (+)-n→π*-CE

4

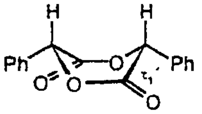
(B_S, $\tau_1' > 0$) (−)-n→π*-CE

(B_N, $\tau_1' < 0$) (+)-n→π*-CE

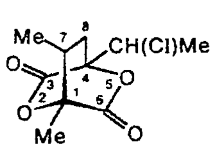
However, using the empirical rules suggested[8—11,16—19] or comparing the CD spectra of monocyclic dilactones **5** and **6** (see Ref. 20) and bridged dilactone **7** (see Ref. 21), which are close in structure to compound **1**, we cannot predict unambiguously the absolute configurations of enantiomers **1** from the CE sign of the lactone n→π*-transition. Therefore, the chiroptical properties of enantiomers **1** were analyzed using the known absolute configuration (see Scheme 1).



(*S,S*)-**5** (B_S)
(−)-n→π*-CE



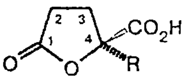
(*R,R*)-**6** (B_N)
(+)-n→π*-CE



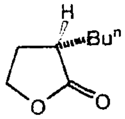
(1*R*,4*R*,7*R*,9*R*)-**7**
(+)-n→π*-CE

Chiroptical properties of enantiomeric dilactones (+)-1 and (−)-1

In the CD spectra of dilactones (+)-**1** and (−)-**1** (Table 1, Fig. 1), the long-wave dichroic bands at 232.5 nm ($\Delta\varepsilon$ = 5.791 and −5.603) and intense short-wave bands (with λ_{max} < 200 nm) were assigned to the lactone n→π*- (n→π_3*) and π→π*-transitions (π_2→π_3*), respectively, based on the following facts: (1) it is known that for the lactone chromophore, these transitions are lowest in energy[22] and opposite in sign in the CD spectra;[20] (2) the CD spectrum of bridged dilactone **7** contains the long-wave shift of the dichroic band of the n→π*-transition (236 nm in EtOH)[21] as compared to monocyclic dilactones **5** and **6** and γ-lactones **8**, **9**,[13] and **10** [14] in polar solvents (213—218 nm); (3) the intense dichroic band with λ_{max} < 200 nm in the CD spectrum of compound **5** was assigned to the π→π*-transition;[20] and (4) in the UV spectra of racemate (±)-**1** (see Table 1), the hypsochromic shift of the long-wave band is observed as the solvent polarity increases, which indicates that this band has the nπ*-orbital nature.[22] The relatively low value of the extinction coefficients ε of this band indicates the symmetry-"forbidden" character of the transition.[22]



(4*S*)-**8**: R = H,
(4*S*)-**9**: R = Me
(+)-n→π*-CE



(2*S*)-**10**
(+)-n→π*-CE

(*R,R*)-**11**
(−)-n→π*-CE

The low value of the bathochromic shift of the extreme of the n→π* band in the UV spectra of racemate (±)-**1** is likely caused by the restricted solvation of the lone electron pair of the n_y-orbital of the O atom of the carbonyl group due to shielding by the Bu^t groups. The maxima of the bands of the n→π*-transition in the CD and UV spectra of dilactones **1** in EtOH do not coincide, probably due to the different superpositions[9] of the bands of the n→π*- and π→π*-transitions with the different (CD) and the same (UV) signs.

Let us consider the effect of the chiral environment of the identical lactone chromophores of (+)-**1** on the CE sign of the n→π*-transition in the projections of the lactone Klyne rule.[9] They were plotted taking into account the geometric parameters of the calculated structure of (+)-**1** with the C_2 symmetry (Fig. 2, Table 2).

According to the octant projection of molecule (+)-**1** (Fig. 3, *a*), the n→π*-CE sign is determined by two

Table 1. Parameters of CD spectra and specific rotation of enantiomeric dilactones **1**[a] and diastereomeric lactonamides **2a,b** [b]

Compound	$[\alpha]_D^{20}$/deg (c, $CHCl_3$)	CD spectrum	
		λ_{max}/nm ($\Delta\varepsilon$/deg L mol^{-1} cm^{-1})	Solvent ($c\cdot10^2$/mol L^{-1})
(1*R*,4*R*)-**1**	+86.3 (0.93)	232.5 (+5.791), 210 (0), 200 (−7.377)[c]	EtOH (0.191)
(1*S*,4*S*)-**1**	−84.5 (1.01)	232.5 (−5.603), 210 (0), 200 (−6.866)[c]	EtOH (0.192)
(2*R*,4*R*,14*S*)-**2a**	−2.7 (1.01)	267 (+0.339), 260 (+0.379), 253 (+0.403), 228 (+2.772), 220 (0), 216 (−5.932), 213 (−6.125), 205 (−7.994)[c]	MeOH (0.94)
(2*S*,4*S*,14*S*)-**2b**	−38.0 (2.86)	267 (+0.297), 260 (+0.208), 258 (0), 215 (−12.767), 205 (−12.346)[c]	MeOH (1.08)
(2*S*,4*S*,14*S*)-**2b**		267 (+0.048), 265.5 (0), 260.5 (−0.024), 218 (−5.760), 205 (−3.00)[c]	Heptane (1.01)

[a] UV spectra of racemate (±)-**1**, λ_{max}/nm (ε/L mol^{-1} cm^{-1}): 222 (324.21, EtOH); 224 (277.66, heptane); 224 (275.17, pentane).

[b] Correspond to the diastereomeric purity of **2a** and **2b** ≥96% (by the ^{1}H NMR spectrum).[6]

[c] Without a maximum.

effects of the second chiral spheres (see Snatzke's determination of types of chiral spheres[23]): by the predominant effect of another (rear) lactone group under the opposite disturbing effect of the nonplanar bridge. According to the sector projection (Fig. 3, *b*), the O—C(=O) bond of the disturbing lactone group mainly falls in the sector of the maximum contribution of the positive sign, while the nonplanar bridging bonds fall in the negative sign sector. Nevertheless, the n→π*-CE sign for enantiomer (+)-**1** is determined by the chiral perturbation of the nonplanar bonds of the δ-dilactone ring rather than the γ-lactone ring (unlike dilactone **7**, where the contribution of the nonplanar bridging bonds of the δ-pentanolide cycle in n→π*-CE predominates over the contribution of the nonplanar bonds of the dilactone cycle[21]). This can be explained by the different absolute values of the torsion angles τ_1 (35.5°) of the γ-monolactone and τ_1' (−66.9°, see Fig. 2) of the dilactone cycles of enantiomer (+)-**1**, *i.e.*, by the differ-

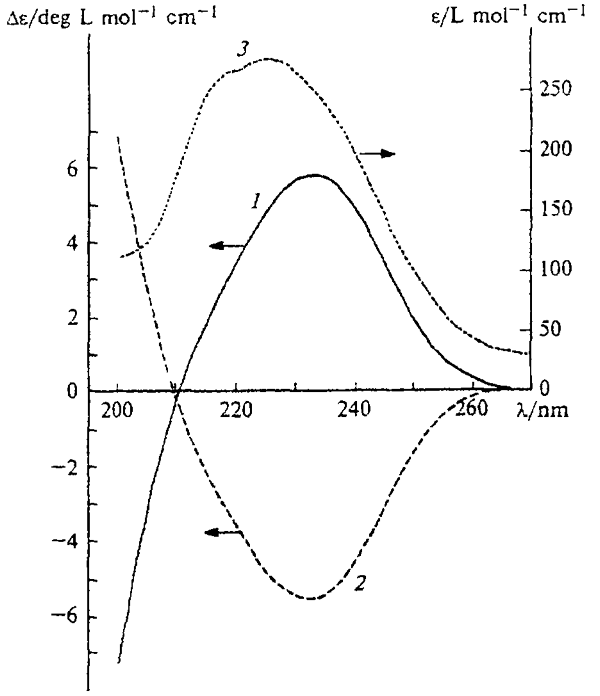


Fig. 1. CD spectra of enantiomers (+)-**1** (*1*) and (−)-**1** (*2*) in EtOH and UV spectrum of (±)-**1** in heptane (*3*).

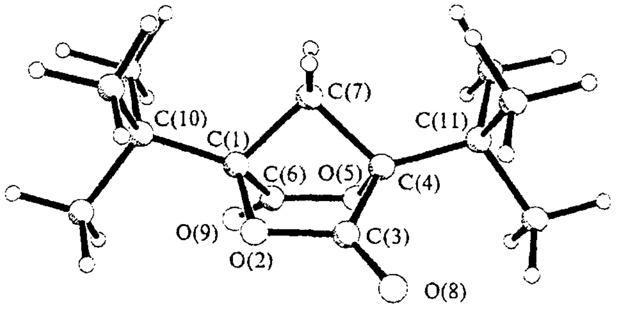


Fig. 2. Structure of molecule (+)-**1** (calculated by the MMX method).

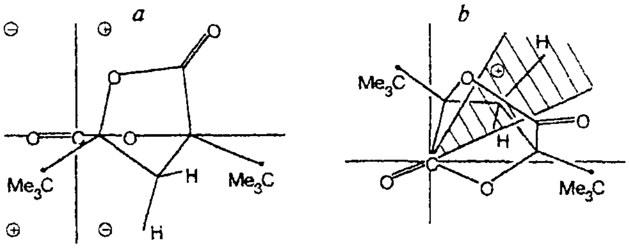


Fig. 3. Octant (*a*) and sector (*b*) projections of lactone Klyne's rule[9] for enantiomer (+)-**1** (signs are presented for remote octants).

Table 2. Main bond lengths (d) and bond (ω) and torsion (τ) angles in molecule **1** (calculated by the MMX method)

Bond	d/Å	Angle	ω/deg	Angle	τ/deg	Angle	τ/deg
C(1)—O(2)	1.420	C(1)—O(2)—C(3)	111.2	C(1)—O(2)—C(3)—C(4) (τ_0)	1.3	C(3)—C(4)—C(7)—C(1) (τ_2)	−53.9
C(1)—C(7)	1.543	C(1)—C(7)—C(4)	91.0	C(1)—O(2)—C(3)—O(8)	−179.2	C(4)—C(7)—C(1)—O(2) (τ_3)	54.6
O(2)—C(3)	1.351	O(2)—C(3)—C(4)	102.5	O(2)—C(3)—C(4)—C(7) (τ_1)	35.5	C(7)—C(1)—O(2)—C(3) (τ_4)	−37.5
C(3)—C(4)	1.530	O(2)—C(3)—O(8)	126.0	O(2)—C(3)—C(4)—O(5) (τ_1')	−66.9		
C(3)—O(8)	1.209						

Note. Steric energy E = 37.47 kcal mol^{-1}; μ_D = 3.731 D.

ent extents of convergence of the nonplanar bonds of the cage structure and the lactone group plane, unlike molecule **7** in which $\tau_1 \approx \tau_1'$.

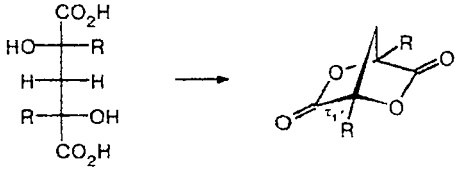
The contribution of the Bu^t groups of dilactone (+)-**1** (the third chiral sphere effect[23]) to the rotational bond of the n→π*-transition can be neglected, since each of the C(1)—C(10) and C(4)—C(11) bonds falls in octants with the opposite sign (see Fig. 3, *b*) and is arranged almost in the chromophore plane (see Fig. 3, *a*) (the O(8)—C(3)—C(4)—C(11) angle is equal to −14.2°, see Fig. 2) and, in addition, the C—C bonds of the Bu^t groups compensate each other due to the rotation of the Me groups.

Thus, the relative arrangement of the lactone groups is the main factor controlling the CE sign of the n→π*-transition in enantiomers **1**, and the other fragments of the molecule (nonplanar bridging groups and Bu^t groups) make a minor contribution to the rotational force of the n→π*-transition. Since the molecule (+)-**1** possesses the C_2 symmetry (see Fig. 2) and the conformationally rigid cage structure,[1] the chiral perturbation of the homotopic lactone chromophores is additive, which explains the sufficiently intense CE of the n→π*-transition and assigns the molecule **1** to the dynamically bound system of achiral chromophores.[24] This is confirmed by an increase in the intensity of the lactone n→π*-CE of enantiomers **1** as compared to dilactone **7** ($\Delta\varepsilon_{236}$ = +1.31, EtOH)[21], lactonic acids **8** ($\Delta\varepsilon_{213}$ = +1.727, EtOH), **9** ($\Delta\varepsilon_{215}$ = +1.803, EtOH),[13] and γ-lactone **10** ($\Delta\varepsilon_{218}$ = +0.555, MeCN, enantiomeric purity 70%).[14] However, an increase in folding (see Ref. 1) of the δ-dilactone cycle in molecule **1** as compared to monocyclic dilactones **5** and **6** does not result in a noticeable difference in intensities of n→π*-CE in the CD spectra of compounds **1** (see Table 1) and **5** ($\Delta\varepsilon_{218}$ = −5.939, $(CF_3)_2CHOH$), **6** ($\Delta\varepsilon_{218}$ = +6.970, $(CF_3)_2CHOH$),[20] since the contribution of the bridging bonds decreases CE of the n→π*-transition in molecule **1** (the ^1L_a band (π→π*) of the phenyl chromophore is also observed in the region of the n→π* band of dilactone **6**, see below).

As already mentioned, the contributions of the Bu^t groups are mutually extinguished; therefore, the sign of the long-wave CE for the 1,4-dialkyl analogs of **1** can be directly related to the chirality of their cage structure. According to this correlation, the *positive* CE sign of the lactone n→π*-transition in the CD spectra of the 1,4-dialkyl dilactones (analogs of **1**) should be observed for the N type ($\tau_1' < 0$, O(2)—C(3)—C(4)—O(5) angle, see Fig. 2) of the enantiomeric form of the δ-dilactone cycle (B_N), while the *negative* n→π*-CE is observed for the S type ($\tau_1' > 0$, B_S). This correlation is confirmed by the CD spectra of dilactones **5** and **6** and Wolf's[16] and Legrand's[17] chirality rules for δ-lactones, unlike Beecham's[18] and Legrand's[17] rules for γ-lactones. In addition, the correspondence of the signs of the lactone n→π*-CE for enantiomer (+)-**1** and ketone n→π*-CE for bicyclic diketone (R,R)-**11** [25] with the same chirality of their cage structures also can support this correlation (taking into account that the signs of the ketone[8] and lactone[9] rules are opposite).

Since the cage of the type **1** dilactones is rigid,[1] the n→π*-CE sign can be related to their absolute configuration. However, the latter, according to the consecutive seniority rule,[26] depends on the type of alkyl substituents in positions 1 and 4, which follows, for example, from the comparison of the configurations of (R,R)-(+)-**1** and (S,S)-1,4-dimethylketone (Scheme 2).

Scheme 2



l-DDGA
(+)-n→π*-CE

l-configuration (B_N, $\tau_1' < 0$)
(+)-n→π*-CE

R = Me, Pr^n, Bu^n (S,S); R = Pr^i, Bu^t (R,R)

d-DDGA
(−)-n→π*-CE

d-configuration (B_S, $\tau_1' > 0$)
(−)-n→π*-CE

R = Me, Pr^n, Bu^n (R,R); R = Pr^i, Bu^t (S,S)

Therefore, the *positive* n→π*-CE sign should correspond to the (R)-configuration, and the *negative* n→π*-CE sign should correspond to the (*S*)-configuration when R = Pr^i, Bu^t, *etc.*, *i.e.*, in the case of tertiary or quaternary C(10) and C(11) atoms. This dependence of the absolute configuration of the optically active dilactones of type **1** on the CE sign of the n→π*-transition in the CD spectra is inverse when R = Me, Et, Pr^n, *etc.*, *i.e.*, in the case of primary and secondary C(10) and C(11) atoms.

For simplicity, it is reasonable to relate the positive and negative n→π*-CE of the 1,4-dialkylsubstituted dilactones of type **1** with their *l*- and *d*-configurations, respectively, for both bicyclic derivatives of *l*- and *d*-α,α′-dihydroxy-α,α′-dialkylglutaric acids (DDGA) (see Scheme 2).

It is known that α-hydroxylic acids (including tartaric acid) with the *l*-configuration are characterized by (+)-CE of the n→π*-transition in the region of 210—220 nm, and their *d*-enantiomers have (−)-n→π*-CE.[7,27] Therefore, the n→π*-CE sign of conformationally labile α-hydroxylic acids correlates with their absolute configurations. This dependence is likely appropriate for the DDGA enantiomers, whose absolute configuration is unknown due to spontaneous cyclization. Thus, the n→π*-CE sign is likely retained due to the intramolecular bicyclization of the DDGA enantiomers, while the n→π*-CE sign is inverse for the products of the intermolecular condensation of (*S*)-lactic ($\Delta\varepsilon_{208}$ = +1.030, CF_3CH_2OH [20]) and (*R*)-amygdalic acids ($\Delta\varepsilon_{220}$ = −12.727, CF_3CH_2OH [20]; $\Delta\varepsilon_{221}$ = −12.206, MeOH [28]), *i.e.*, (*S*,*S*)-lactide **5** and (*R*,*R*)-diphenylglycolide **6** (see above), respectively.

Chiroptical properties of diastereomeric lactonamides 2a,b

The analysis of the complicated CD spectra of diastereomers **2a** and **2b** (see Table 1, Fig. 4) is difficult due to the superposition of the bands of the electronic transitions of the lactone, amide, and aromatic chromophores. Therefore, to assign the dichroic band of the lactone n→π*-transition, the bands of the electronic transitions of the phenyl chromophore **2a** were determined at first.

It is known[7] that UV spectra of aromatic compounds contain in the 200—300 nm region two bands of the π→π* type transitions: an intense band at 200—220 nm (^1L_a- or $'A_{1g}\rightarrow'B_{1u}$-transition) and a weak band at 260—280 nm (^1L_b- or $'A_{1g}\rightarrow'B_{2u}$-transition).

For example, the CD spectra of (*S*)-α-phenylethylamine ((*S*)-α-PEA) contain the following CE of the weak dichroic ^1L_b band, λ_{max}/nm (Δε): in cyclohexane, 268 (+0.136), 262 (+0.173), 256 (+0.135); in MeOH, 268 (+0.106), 261 (+0.133), 257 (+0.091).[29] The sign of the longest-wave CE (at 268 nm) of the multiplet positive ^1L_b band of (*S*)-α-PEA depends only on the configuration of the benzyl asymmetrical center (AC), since it is caused by the contribution of the allowed ^1B_B-transition.[29] The second component of the π→π*-transition of the Ph chromophore of (*S*)-α-PEA appears as a negative multiplet dichroic ^1L_a band at wavelengths shorter than 220 nm.[29]

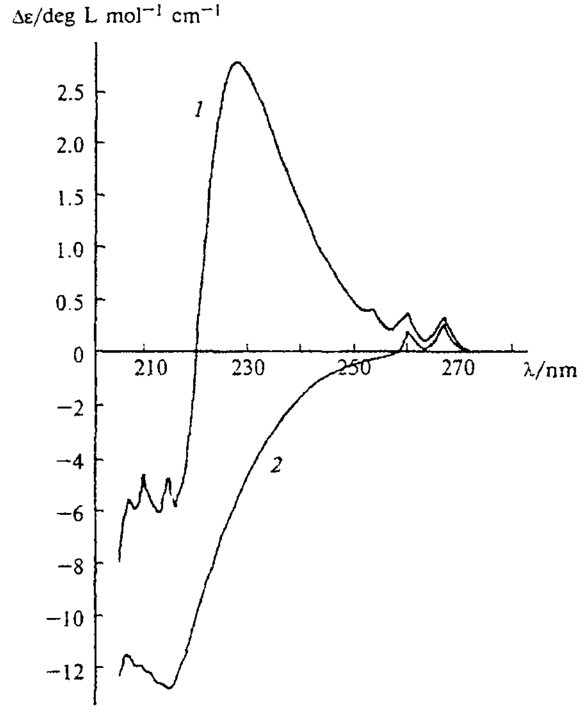


Fig. 4. CD spectra of diastereomers **2a** (*1*) and **2b** (*2*) in MeOH.

The configuration of the benzylic AC with the known conformation of the chiral group can be predicted from the ^1L_b-CE sign using the empirical rules,[30,31] which make it possible to summate the rotational contributions of the ligands at the benzylic AC. To assign reliably the long-wave dichroic band in the CD spectrum of diastereomer **2a** (see Table 1) to the ^1L_b-transition of the Ph chromophore, let us determine the CE sign of this transition in projections of the quadrant rule[30] for the preferable conformation[6] of the chiral group at the benzylic AC of the (*S*)-configuration of **2a** (Fig. 5).

According to the almost coinciding X-ray structural data (the torsion C(17)—C(16)—C(14)—H(5), C(17)—C(16)—C(14)—N, and C(17)—C(16)—C(14)—C(15) angles are equal to 16.8°, 133.5°, and −103°, respectively) and calculations by the MM method (PCMODEL; 24.4°, 148.1°, and −91.6°, respectively)[6] of lactonamide **2a**, the C(14)—C(15) bond in the quadrant projection (see Fig. 5, *b*) is almost coplanar to the *B* plane, and the C(14)—N and C(14)—H(5) bonds are arranged in quadrants with opposite signs and almost equally close to the *A* plane. Since the contribution of the Me group at the C(14) atom to the ^1L_b-transition of **2a** is almost zero, and the contribution of the H(5) atom is low (due to the low polarizability of the C—H bond),[24] the ^1L_b-CE sign is determined by the contribution of the —NHC(=O) group, which falls in the positive quadrant (see Fig. 5, *b*).

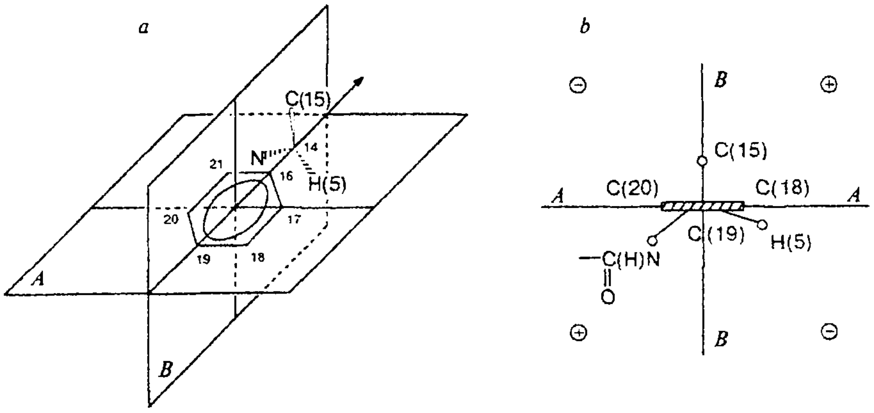


Fig. 5. Symmetry planes (*a*) and quadrant projection (*b*) of the aromatic chromophore of diastereomer **2a** (signs of quadrants are given for the ^1L_b-transition and correspond to the published data[30]).

This agrees with the observed positive CE (at 267 nm) of the multiplet dichroic ^1L_b band in the CD spectrum of diastereomer **2a** in MeOH (see Table 1 and Fig. 4).

It is noteworthy that the signs of the corresponding quadrants for the ^1L_b-transition are opposite in De Angelis' rule[30] and Smith's work,[31] because their evaluations of the rotational contributions of the ligands to the ^1L_b-CE sign differ. The following ratio of the group contributions to the ^1L_b-transition has been proposed:[31] Bu^t > Me > COOH, NH_2, OH. However, aromatic compounds were considered[31] to be in such predominant conformations of the chiral benzyl group in which the H atom at the benzylic AC was coplanar (or almost coplanar) to the benzene ring plane (according to the data of XDA, ^1H NMR, electron diffraction, and laser spectroscopy, see Ref. 31).

In fact, if the C(14)—H(5) bond in molecule **2a** in the projection in Fig. 5, *b* is arranged in the *A* plane, (+)-CE of the ^1L_b-transition should be observed according to Smith's rule. However, De Angelis' rule is more appropriate for the above considered conformation of the chiral group at the C(14) atom in molecule **2a**.[30]

Since the CE sign of the short-wave ^1L_a-transition of the aromatic chromophore should be opposite to the ^1L_b-CE sign (see Refs. 7 and 8), the intense negative multiplet band with the first extreme at 216 nm observed in the CD spectrum of diastereomer **2a** in MeOH (see Fig. 4) was assigned to the ^1L_a-transition.

The CD spectra of isomer **2b** in MeOH and heptane (see Table 1 and Fig. 4), like those of isomer **2a**, contain the long-wave ^1L_b-(+)-CE (λ_{max} = 267 nm) and the negative multiplet band of the ^1L_a-transition, which corresponds to the equivalent (*S*)-configurations of the benzyl AC in both diastereomers. Thus, the ^1L_b- and ^1L_a-CE signs for isomers **2a** and **2b** coincide with those expected from the quadrant rule[30] and correspond to the signs of (*S*)-α-PEA.[29]

The assignment of the dichroic ^1L_b and ^1L_a bands of the $\pi\to\pi^*$-type makes it possible to determine the CE signs of the $n\to\pi^*$-transitions of the lactone and amide chromophores of lactonamides **2a** and **2b** by the comparison of their CD spectra, taking into account the absorption of the given chromophores in the same region.[7,8]

For example, the CD spectrum of diastereomer **2a** in MeOH, unlike that of **2b**, exhibits the positive dichroic band at λ_{max} = 228 nm assigned to the $n\to\pi^*$-transitions. The bathochromic shift of this band, as compared to the dichroic bands of the $n\to\pi^*$-type of γ-lactones **8—10** (see above), is probably caused by the superposition[8] of the bands with the opposite signs of the ^1L_a- and $n\to\pi^*$-transitions for diastereomer **2a**.

Since, as already mentioned, the intensity of the common $n\to\pi^*$-CE for lactonamide **2a** is higher than those for lactonic acids **8** and **9**, the signs for the amide and lactone $n\to\pi^*$-CE of diastereomer **2a** probably coincide. In addition, the intensity of the amide $n\to\pi^*$-CE in the CD spectra of compound **2a** (or **2b**) is assumed to be lower than that of lactone due to the conformational mobility of the amide group, unlike the γ-lactone cycle of **2a** (or **2b**) fixed by the bulky Bu^t groups in the enantiomeric envelope conformation.[6]

For lactonamide **2b**, the signs of both lactone and amide $n\to\pi^*$-CE should be opposite to the signs of the corresponding transitions of diastereomer **2a** due to the different chiral environments of these chromophores in diastereomers **2a** and **2b**. In fact, the CD spectrum of compound **2b** in MeOH contains no positive bands in the region of 220—230 nm, and the negative dichroic band in the region of 205—220 nm has a greater intensity than that in the spectrum of **2a**, which is caused by the superposition of the bands with the same sign of the ^1L_a- and $n\to\pi^*$-transitions. The bathochromic shift of the first maximum (λ_{max} = 218 nm) of the short-wave band in the spectrum of lactonamide **2b** in heptane, as compared to the spectrum in MeOH (λ_{max} = 215 nm, see Table 1), is characteristic of the lactone $n\to\pi^*$-transition.[22]

To determine the ratio of the contributions of chiral spheres of the lactone chromophore of diastereomer **2a**

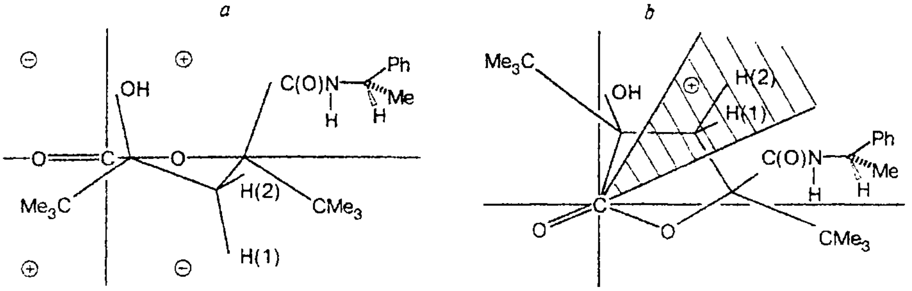


Fig. 6. Octant (*a*) and sector (*b*) projections of lactone Klyne's rule[9] for diastereomer **2a** (signs are presented for remote octants).

to the $n \to \pi^*$-CE sign, let us consider the molecule in the Klyne's rule projections.[9]

According to the octant projection of diastereomer **2a** (Fig. 6, *a*), functional substituents fall in the octant of the observed sign of the lactone $n \to \pi^*$-CE rather than the nonplanar bonds of the heterocycle. However, the C(2)—O(3) bond is close to the nodal surface (see Fig. 6, *a*), *i.e.*, its contribution is insignificant as that of the O—H bond (due to the low polarizability of the latter[24]). The contributions of the Bu^t groups are mutually extinguished (see above). This agrees with the chiroptical data for the series of γ-lactones,[13,14,18] according to which the OH group (at the C(2) atom) and alkyl substituents (at the C(2) and C(4) atoms) contribute insignificantly to the rotational force of the lactone $n \to \pi^*$-transition, unlike the nonplanar bonds of the heterocycle.

Thus, the CE sign of the lactone $n \to \pi^*$-transition in diastereomers **2a** and **2b** with the enantiomeric forms of the heterocycle (E_S and E_N, see Scheme 1) is mainly determined by the contribution of the pseudo-*a*-oriented amide group at the C(4) atom (the third chiral sphere effect[23]) with the opposite contribution of the nonplanar bonds of the lactone cycle (the second chiral sphere effect). This does not agree with the chirality rules for γ-lactones[17,18] and Cervinka's rule,[19] which relates the (+)- and (−)-signs of $n \to \pi^*$-CE for γ-butyrolactone-4-carboxylic acids of types **8** and **9**, respectively, to the absolute (4*S*)- and (4*R*)-configurations.

The similar effect of the predominant contribution of the third chiral sphere over the second sphere to the sign of the lactam $n \to \pi^*$-CE in the case of (*S*)-pyrrolid-2-one-5-carboxylic acid is explained by the electronegativity of the carboxyl group.[32]

The CD spectrum of diastereomer **2b** in heptane exhibits a lower intensity of the short-wave dichroic band in the region of 205—220 nm as compared to the spectrum in MeOH (see Table 1). This can be caused by the appearance in a nonpolar solvent, along with the predominant envelope conformer, of a noticeable fraction of conformer **2b** with the twist-form of the γ-lactone ring stabilized by intermolecular hydrogen bonds (shown for lactonamide **2a** by the comparison of the X-ray structural data and the calculation by the MM method).[6]

For twist conformer **2b**, the contribution of the amide group to the lactone $n \to \pi^*$-CE is lower (the pseudo-*a*-orientation of the amide group is less pronounced and, therefore, the latter is close to the nodal plane), and the contribution of the nonplanar bonds of the heterocycle is greater (they are strongly shifted from the lactone chromophore plane) than their contributions to envelope conformer, which results in a decrease in the intensity of $n \to \pi^*$-CE in the CD spectra of diastereomer **2b** in heptane.

Experimental

CD spectra were recorded on a Jasco J-500A dichrograph with a DP-500N processor. Optical rotational angles were measured on a Polamat A polarimeter at 546 and 578 nm. UV spectra were recorded on a Beckman DU-7 spectrometer.[20] Melting points were determined on a Boetius RNMK-05 table. The geometry and energy of dilactone (+)-**1** were calculated by the molecular mechanics (MM) method without symmetry restriction using the PCMODEL program in the force MMX field.[33]

Enantiomers of 1,4-di-*tert*-butyl-2,5-dioxabicyclo[2.2.1]-heptane-3,6-dione [(1*R*,4*R*)-(+)-1 and (1*S*,4*S*)-(−)-1]. TsOH · H_2O (170 mg, 0.89 mmol, 200% excess) was added to a boiling solution of lactonamide **2a** (110 mg, 0.30 mmol) in anhydrous toluene (12 mL), and the mixture was boiled for 30 h. The mixture was cooled to 20 °C, filtered 2 h after, and the residue was washed with benzene (30 mL). The combined solutions were evaporated to dryness *in vacuo*. The residue was washed with H_2O to pH 7, dried *in vacuo*, and sublimed at 120—130 °C (15 Torr). Dilactone (+)-**1** (45 mg, 61.5%) was isolated as white flocculent crystals, m.p. 164—166 °C (with decomp.). Under similar conditions, dilactone (−)-**1** (47 mg, 64.3%), m.p. 164—166 °C (with decomp.), was obtained from lactonamide **2b**. Enantiomers (+)-**1** and (−)-**1** were identified by ^1H NMR and IR spectroscopy (*cf.* Ref. 5 for (+)-**1**).

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