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Exciton Optical Activity of Molecules Containing Three and Six Coupled Oscillators Belonging to C₃ and D₃ Point Groups: Applications to Cyclotrivenatrylenes and Cryptophanes

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The exciton model of optical activity has been applied to C₃ cyclotrivenatrylenes and D₃ cryptophanes, molecules containing three and six coupled oscillators, respectively. Using this model, in conjunction with Platt's spectroscopic moment approach, very good agreement has been established between experimental and calculated spectra. These results point to the importance of the exciton model in explaining the CD spectra of molecules containing more than two oscillators.

In the thirties Kuhn realized that the coupling of two electric vectors devoid from inverse symmetry elements gives rise to the collinear electric and magnetic moments necessary to generate optical activity.^{1a} This idea was subsequently elaborated and generalized by Kirkwood.^{1b} The Kuhn-Kirkwood coupled-oscillator model is particularly attractive and useful for several reasons: (i) It is based on physical concepts that are simple and can easily be applied by nonspecialists. (ii) Its scope is well-defined and limited to molecules containing a few chromophoric units interacting through their electric transition dipoles induced by a radiation field. (iii) It normally gives rise to strong and characteristic Cotton effects (exciton optical activity) whose signs and magnitude are, in many instances, unambiguously predictable, thus leading to safe configurational or conformational assignments.

In 1959, Moffitt² successfully applied the model to the optical activity of the peptide α -helix.

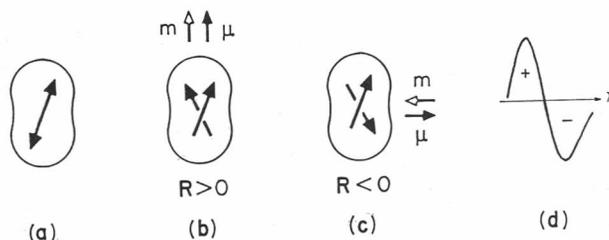
With the pioneering work by Mason in the 1960s³ and with the development of molecular spectroscopy and the subsequent better knowledge of the polarization direction of electronic transitions in a variety of chromophores, the model became increasingly used by organic as well as inorganic chemists, as illustrated by the large number of applications recently quoted by Harada and Nakanishi.⁴

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Until recently, the Kuhn-Kirkwood mechanism has mainly been observed and used for stereochemical applications in the case of molecules containing two coupled oscillators, for instance diol dibenzoates,⁴ trans-stilbene oxide,⁵ biaryl derivatives,⁶ etc. There are several studies dealing with compounds containing three oscillators in the field of coordination metal complexes,⁶ and very few among organic molecules.⁴ In this paper we report applications of the exciton model to cyclotrimeratrylenes and cryptophanes, molecules which contain three and six coupled aromatic chromophores, respectively.

The Exciton Model

In this theory, a single electric transition moment is represented by a double-headed arrow, which suggests its oscillatory nature (Scheme 1). In a molecule containing two such oscillators, their relative phase has to be considered, and the system is best represented by using pairs of single-headed arrows. For two transition moments, there are thus only two relative phases of motion, (b) and (c) (Scheme 1). In (b), which here is equivalent to a right-handed helix, the coupling of the transition dipoles generates, overall electric (μ) and magnetic (m) moments along the C2 axis, hence a positive rotational strength R .



Scheme 1.

Conversely, the coupling (c) defines a left-handed helix in which anti-parallel electric and magnetic moments create a negative rotational strength. The exciton mechanism therefore generates, for each electronic transition, a pair of oppositely signed circular dichroism (CD) bands. In order to establish whichever band will appear at higher or lower energy in the actual CD spectrum, the sign of the interaction energy (V) in each of the coupling modes (b) and (c) must be determined. In Scheme 1, the dipoles are arranged in such a way that the result is obvious: the head-to-head situation (b) is clearly repulsive ($V > 0$), and should therefore be found at higher energy than the attractive head-to-tail coupling (c) ($V < 0$). The CD spectrum will show a positive-negative sequence, from high to low energy, as shown in (d). Such a clear-cut situation is often encountered in real molecules, for instance in vicinal diol dibenzoates.⁴ Ambiguous cases also exist, where the determination of the energy sequence of the two CD bands requires the calculation of the interaction potential V , as a function of the geometry of the system. Such calculations are usually effected by the point-dipole approximation.

The total intensity of the bisignate band system sums to zero, following the classic sum rule.⁷ More generally, the coupling of n vectors gives rise to n exciton components some of which may be degenerated according to the symmetry of the system. In all cases the sum rule must be followed, *i. e.* the total intensity of the CD bands over the whole energy interval of the exciton system must be zero.

Cyclotrimeratrylenes and Cryptophanes

First described in 1915 as a cyclic dimer⁸ (dihydroanthracene) and later as a cyclic hexamer^{9,10} the major product of the reaction of veratrole and formaldehyde in the presence of acid was shown by Lindsey^{11,12} in 1963—65 to have the trimer structure 1a, and was then called cyclotrimeratrylene for convenience. At about the same time, several other researchers¹³⁻¹⁵ reached the same conclusion independently, and were able to establish that the compound adopted the locked crown conformation depicted on the stereoformula 1, and later evidenced by single crystal X-ray crystallography.¹⁶

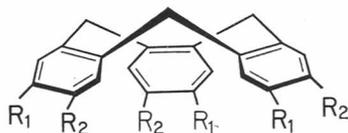
As a consequence of the high inversion barrier of the crown (ca. 26—28 kcal/mol), suitably substituted derivatives of 1a may be chiral. Since the first observation of a weak rotatory power in such a molecule¹⁷ (1966), many optically active cyclotrimeratrylenes have been described, most of them at the Collège de France in Paris. Some of these compounds, which belong to the C₃ point group, are listed in Table I, together with the data on their optical rotation and absolute configuration. The absolute configurations of these molecules, which are atropoisomers, can be specified by means of the P- and M-helicity descriptors. To this end, appropriate torsional angles are defined using the Cahn-Ingold-Prelog rules, along the lines described in ref. 18.

The cryptophanes¹⁹ are made of two C₃ cyclotrimeratrylene units linked in front of one another by three bridges. These hollow molecules are probably the most powerful complexing agents known to date for neutral, lipophilic molecules.

Cryptophanes in which the two C₃ units have the same structure and the same configuration (M or P) belong to the D₃ point group and hence are chiral, and stereoformula 2 represents one of the two enantiomeric forms. On the contrary, assembly of two C₃ units of opposite configurations leads to cryptophanes which are achiral (C_{3h}, meso), except in cases where the substituents of the two caps are different.^{19,20,22} Only the D₃ cryptophanes will be considered here. Table II lists the specimens of this family that have been described thus far, and indicates the rotation of the enantiomers having the absolute configuration of stereoformula 2.

Because of the presence in these molecules of 3 or 6 equivalent aromatic units arranged in a well defined geometry, C₃ cyclotrimeratrylenes and D₃ cryptophanes are beautiful models for studying the chiroptical properties of

highly symmetrical molecules, and their optical activity actually represents what is perhaps one of the most impressive illustrations of the Kuhn-Kirwood coupled oscillator mechanism.



1a $R_1 = R_2 = \text{OCH}_3$

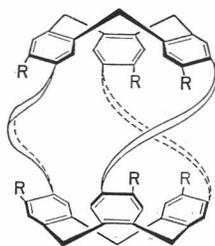
1b-q $R_1 \neq R_2$: Table 1

TABLE I

Structure and Optical Rotation of C3 Cyclotrivena-Trylenes for the Absolute Configuration of Stereoformula 1.

No	R ₁	R ₂	absolute configuration	[α] _D ^a	refs.
1b	OCH ₃	OH	P	-272	23
1c	OCH ₃	OCD ₃	M	-3.4	23
1d	OC ₂ H ₅	OH	P	-293	23
1e	OC ₂ H ₅	OCH ₃	P	-20	23
1f	OC ₂ H ₅	OiC ₃ H ₇	M	-47	23
1g	OCH ₃	OiC ₃ H ₇	M	-14.1	23
1h	OCH ₃	OCOCH ₃	M	-169	23
1i	OC ₂ H ₅	OCOCH ₃	M	-218	23
1j	Br	OCH ₃	P	-10	30
1k	Br	OH	P	-174 ^b	30
1l	Br	OCOCH ₃	P	-122	30
1m	OCH ₃	CH ₂ OH	P	-221	31
1n	OH	H	P	-199	23
1o	OCH ₃	H	P	-165	23
1p	OCOCH ₃	H	P	-190	23
1q	H	D	M	-2.3	29

^a Rotations in CHCl₃ at 25 °C unless stated otherwise; ^b in dioxane.



2a-h

R and Bridges : Table 2

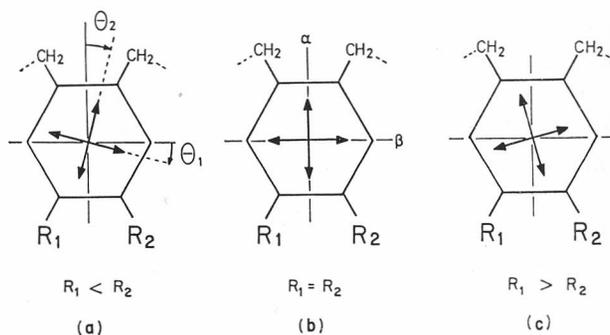
TABLE II

Structure and Rotation of D₃ Cryptophanes for the Absolute Configuration of Stereoformula 2.

No	Bridges	R	$[\alpha]_D^a$	refs
2a	—O—(CH ₂) ₂ —O—	OCH ₃	—254	26
2b	—O—(CH ₂) ₃ —O—	OCH ₃	—49	26
2c	—O—CH ₂ —=—CH ₂ —O—	OCH ₃	—154	32
2d	—O—CH ₂ —=—CH ₂ —O—	OCH ₃	—71	32
2e	—O—CH ₂ —C≡C—CH ₂ —O—	OCH ₃	—201	26
2f	—O—(CH ₂) ₂ —O—	OH	—172 ^b	26
2g	—O—(CH ₂) ₂ —O—	OCOCH ₃	—24	26
2h	—O—(CH ₂) ₂ —O—	OCH ₂ CO ₂ CH ₃	—116	26

The Benzene Chromophore

In order to use exciton model, it is necessary to know which transitions are involved and how they are polarized. The chromophoric unit in cyclotri-*veratrylenes*^{23,24,25} and cryptophanes²⁶ is a 1,2,4,5-tetrasubstituted benzene (Scheme 2). The two lowest energy transitions that are accessible in the UV



and CD spectra occur at 280–290 nm and 240–250 nm. These transitions will be thereafter designated as B_{2u} and B_{1u} , respectively, as in the parent benzene molecule. The higher energy (E_{1u}) transitions below ca. 220 nm are generally not considered in the coupled oscillator model, because their energy and polarization are not experimentally known nor easily predictable.

In achiral cyclotrimeratriylenes (where $R_1 = R_2$), the B_{2u} and B_{1u} transitions are polarized along the short (α) and long (β) axes of the benzene ring as shown in Scheme 2b. The presence of two different substituents causes a rotation of these transition moments, from the α and β axes; the sign and magnitude of the rotation depend on the relative magnitude of the spectroscopic moments (SM) of the R_1 and R_2 substituents. The SMs are empirical parameters which have been introduced as a way to quantify the influence of the substituents on the absorption intensities of forbidden transitions in aromatic compounds.²⁷ It is classically assumed that Θ_2 , the rotation angle of the B_{2u} transition dipole, can be evaluated by vector addition of the substituent spectroscopic moments, and that $\Theta_1 = \Theta_2$ (which is equivalent to saying that the transitions are polarized at 90). In Scheme 2, when the SM of R_2 is greater than that of R_1 ($R_2 > R_1$), one obtains a clockwise rotation (Θ_2 and $\Theta_1 > 0$), which is inverted when $R_2 < R_1$.

In the exciton model, the chiroptical properties of cyclotrimeratriylenes and cryptophanes in the near UV entirely depend on the signs and magnitudes of the polarization angles Θ_2 and Θ_1 .^{23,26}

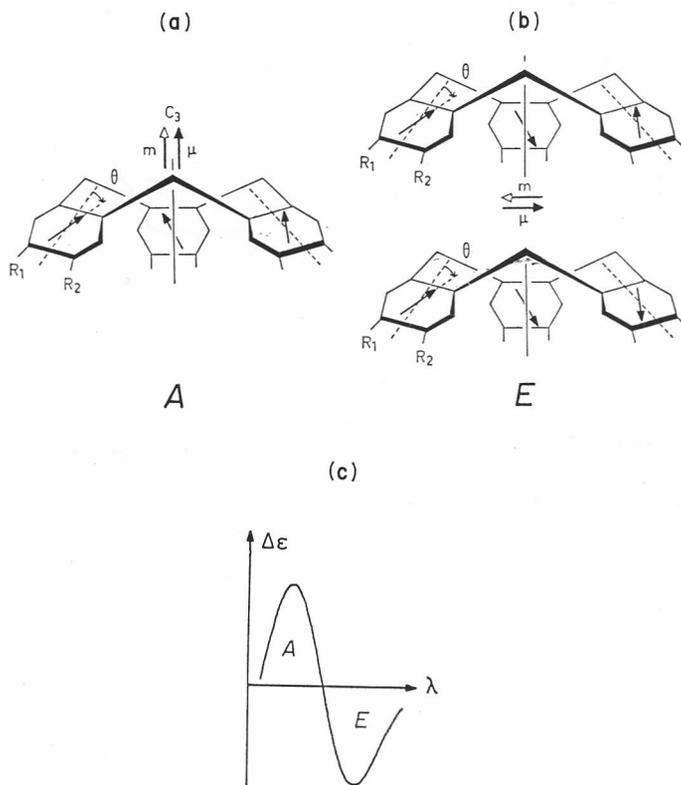
C3-Cyclotrimeratriylenes

In these compounds, there are three identical chromophores, and three coupling modes for each of the B_{2u} and B_{1u} transitions. The symmetrical A-coupling (Scheme 3) gives rise to overall electric and magnetic moments along the C3 axis of the molecule, while the two degenerate E-coupling modes are polarized perpendicularly to this axis.²³

As in the classical case of two oscillators, the exciton CD of cyclotrimeratriylenes consists of two oppositely signed bands for each transition. As a pictorial example, it can be easily seen that the A-coupling of the B_{2u} transition dipoles depicted in Scheme 3 (a) generates, for a small positive value of Θ_2 , a positive rotational strength ($m\mu > 0$) at high energy ($V > 0$), whereas the E-couplings (b) give a negative component at low energy. By a similar reasoning for a small positive value of Θ_1 , the A-coupling of the B_{1u} transition is also positive, but the interaction of the transition dipoles being attractive ($V < 0$), this component is at low energy. Accordingly, the overall CD spectrum for the $B_{1u} - B_{2u}$ region has the shape shown in Scheme 4.

The dependence of the CD spectrum on variations of Θ is shown in Scheme 5.

There are four critical values of Θ , 0° , 45° , 90° and 135° , which correspond to the total inversion of the exciton pattern, by changing the sign of either m , V , μ , and V (respectively). These angles thus define the four sectors I–IV, each being characterized by a particular sequence of the A and E components, as sketched in the Scheme.

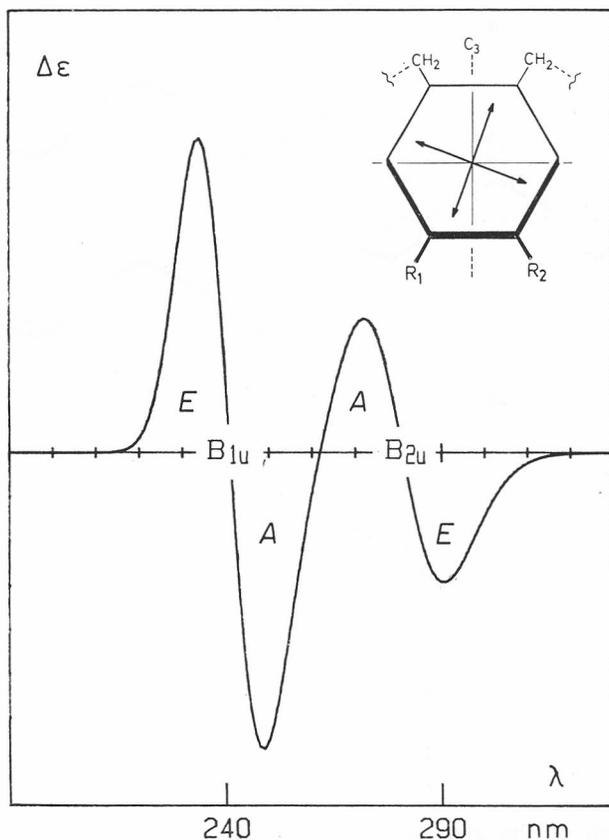


Scheme 3. Sketch of the symmetrical A-coupling (a) and of the two degenerate antisymmetrical E-couplings (b) in C₃ cyclotrimeratrylenes. The case specifically corresponds to the B_{2u} transition, with a small, positive value of θ_2 . The resulting exciton couplet is depicted in (c). (After A. Collet, *Tetrahedron*, 43 (1987) 5725, by permission of Pergamon Journals, Ltd.).

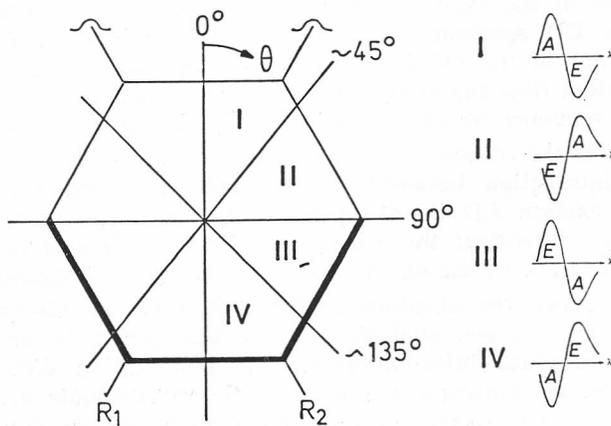
The validity of the exciton model in C₃-cyclotrimeratrylenes can be illustrated by the CD spectrum of P-(—)-cyclotrianiisylene 10 (Figure 1). In this case, the SM of the OCH₃ group (R₁) being much larger than that of the hydrogen atom (R₂), angles θ_2 and θ_1 are unambiguously negative ($\sim -38^\circ$), and the entire sequence of CD bands is exactly that predicted by the theory.

Furthermore, the crude exciton model can be improved by allowing configuration interaction between the B_{2u} and B_{1u} band systems. In this way, the two exciton CD bands of a single electronic transition have no longer the same intensity; the theory predicts²³ variations of intensity in excellent agreement with the experimental spectra (see for example Figure 1).

Conversely, since the absolute configurations of the C₃-cyclotrimeratrylenes are generally known, analysis of their CD spectra in the light of the exciton model provides information on the polarization directions of the transitions, when spectroscopic moments of the substituents are not known. More precisely, the CD spectra of these compounds can be employed for the determination of the relative magnitude of the SMs of R₁ and R₂ substituents



Scheme 4. Theoretical sequence of exciton bands for the B_{2u} and B_{1u} transitions in C_3 cyclotrimeratrylenes, for small ($<45^\circ$) positive values of θ_2 and θ_1 .



Scheme 5.

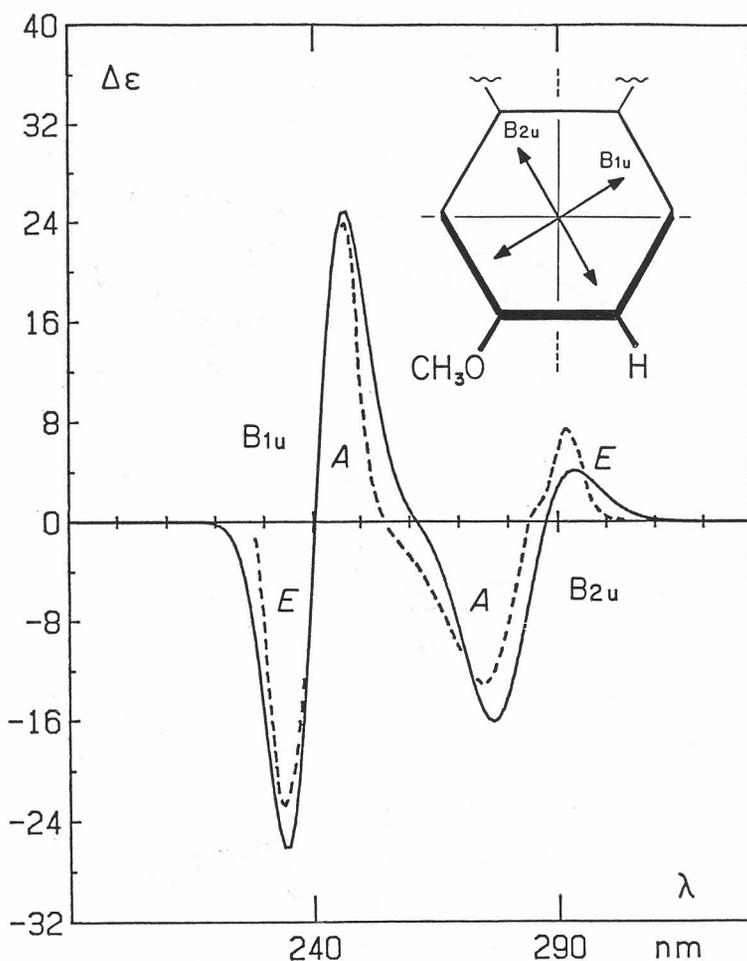


Figure 1. Calculated (—) and experimental (---) CD spectra of P-(−)-10. (After Canceill et al., *J. Amer. Chem. Soc.* **107** (1985) 1299, by permission of The American Chemical Society).

attached to the CTV structure. For instance, the CD spectrum of cyclotriguacylene (1b) displays inversion of all bands with respect to those of cyclo-trianisylene (Fig. 1) clearly showing that the OH group must be given a SM larger than the OCH₃ group,²⁴ and, in general, it has been found by this method that the SM of alkoxy substituent decreases as their size increases. Actually, direct SM measurements (based on UV absorption intensities), are not accurate enough to reveal such weak differences between alkoxy substituents in most cases. Even very small rotations generate observable exciton CD patterns, and the system easily evidences SM differences due to isotopic substitution. In M-(−)-cyclotrimeratrylene-d₉ (1c), the sequence of signs of the exciton couplet (Figure 2) indicates that the SM of OCD₃ is larger than that of OCH₃ which may be explained by conformational effects.²⁸ In C3-cyclo-tribenzylylene-d₃ (1q), which exhibits an exciton pattern in the 270 nm region,

the rotation of the B_{2u} transition dipole is consistently explained by vibronic effects.²⁹ The effect of ionization of a phenol group on the polarization direction of the transitions has also been studied by this CD method.²⁵

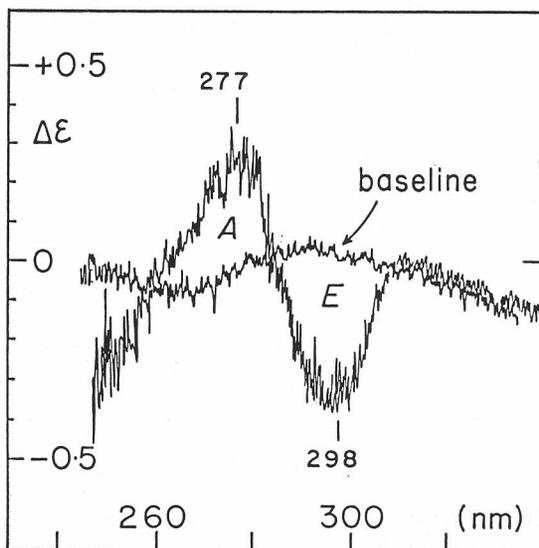
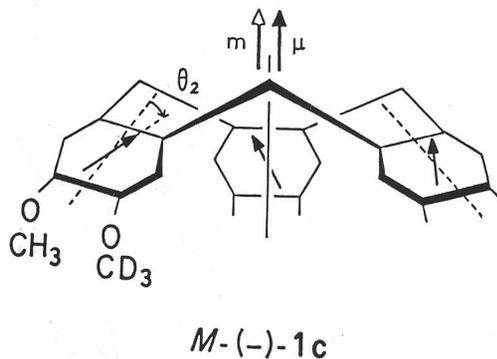


Figure 2. CD spectrum of isotopically chiral $M-(-)-1c$ in the B_{2u} region (After A. Collet and G. Gottarelli, *J. Amer. Chem. Soc.* 103 (1981) 5912, by permission of the American Chemical Society).

Finally, the CD spectra of several cyclotriveratrylenes in which $R_1 = Br$ and $R_2 = OCH_3, OH,$ or $OCOH_3$ (Figure 3) provide evidence that the B_{2u} and B_{1u} transitions in these compounds are not polarized at 90° , a result which may have a general bearing, and which emphasizes the risk of using B_{1u} transitions for configurational assignments based on chiroptical methods in CTV and in systems where the exact value of the polarisation angle is critical.³⁰

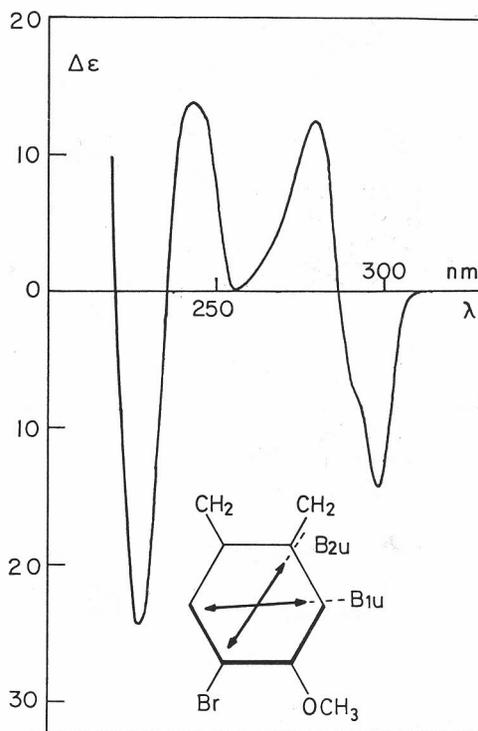


Figure 3. CD spectrum of (—)-1j and sketch of a set of polarization directions of the B_{2u} and B_{1u} transitions that is compatible with this spectrum.

D3-Cryptophanes

In these molecules, the optical activity originates from the coupling of six identical chromophores in a D_3 arrangement. The treatment has been accomplished mathematically, by using the formalism of the group theory, in order to extend the exciton model to a D_3 array of six oscillators.²⁶

The main conclusions of this analysis are as follows: (i) the coupling of the six transition dipoles generates for each transition six exciton components: one (forbidden) with A_1 symmetry, one with A_2 symmetry, and two degenerate pairs with E symmetry, one (A_2 symmetry) being polarized along the C_3 axis of the molecule, and two (E symmetry) in the equatorial plane; (ii) the two E levels have opposite signs and different intensities, the stronger one having a sign opposite to the A_2 component (see Figure 4); (iii) variations of the twist angle of two CTV caps only slightly modulate the CD intensities and the interaction energies, without affecting neither the sign nor the sequence of the components; (iv) as in the C_3 -cyclotrimeratrylenes, the chirality of the oscillator array in D_3 -cryptophanes is entirely governed by the signs and magnitudes of the polarization angles θ_1 and θ_2 of the benzene subunit.

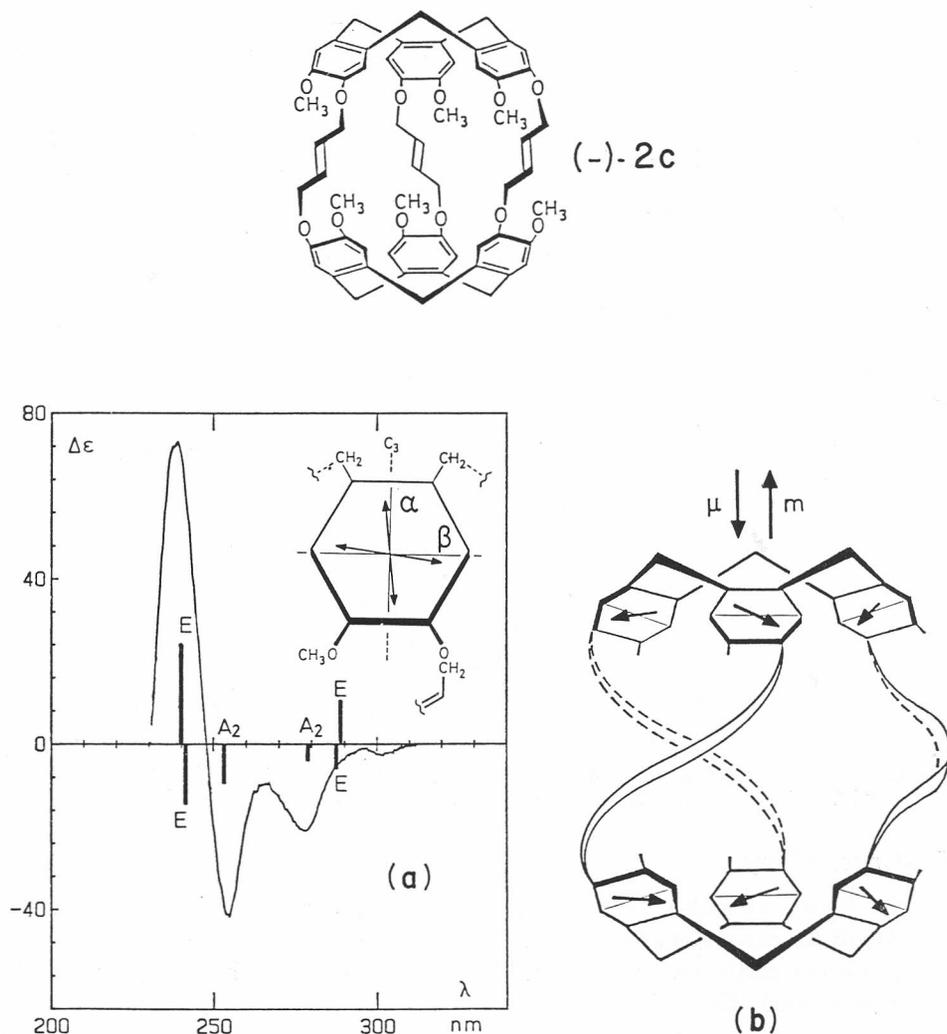


Figure 4. (a) CD spectrum of cryptophane (—)-2c; the bars represent the calculated CD components, and the insert shows the polarization directions of the B_{2u} (α) and B_{1u} (β) transitions (b) sketch of the A₂ coupling of the transition dipoles which generates a negative rotational strength at lower energy for the B_{1u} system.

The CD spectra of all the chiral D₃-cryptophanes known to date (Table II) have been satisfactorily analyzed in the light of this model. The presence of the three predicted CD components has been experimentally observed in the B_{2u} region for several of these compounds, although very often extensive band overlap and cancellation occur, as illustrated in Figure 4 (which also provides a pictorial representation of only the A₂ symmetry coupling as the

complete description would be too complex). These results demonstrate the general validity and usefulness of the Kuhn-Kirkwood model for explaining the optical activity of complex molecules of high symmetry.

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SAŽETAK

Ekscitonska optička aktivnost molekula koje sadrže tri i šest spregnutih oscilatora koji pripadaju C3 i D3 grupi točke: primjena na ciklotriveratrilene i kriptofane

Andre Collet i Giovanni Gottarelli

Ekscitonski model optičke aktivnosti primjenjen je na C3 ciklotriveratrilene i D3 kriptofane, molekule koje sadrže tri, odn. šest spregnutih oscilatora. Koristeći taj model, povezan Plattovim spektroskopskim momentima, postignuto je vrlo dobro slaganje eksperimentalnih i proračunanih spektara. Ti rezultati ističu važnost ekscitonskog modela u tumačenju CD spektara molekula koje sadrže više od dva oscilatora.