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DISSYMMETRIC CHROMOPHORES. III.[1] CIRCULAR DICHROISM OF β,γ-UNSATURATED KETONES AND THE GENERALIZED OCTANT RULE

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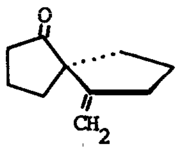
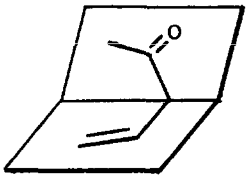
The notion of the extended Octant Rule[2] or Generalized Octant Rule[2,3] (GOR), which is an incompletely explored chirality rule[4], is related in a fundamental way to the useful concept of classifying optically active chromophores into two limiting types: (i) inherently dissymmetric chromophores and (iii) inherently symmetric, but dissymmetrically perturbed chromophores.[5] The former may be recognized by rotational strengths (R) of the order 10^{-38} cgs ($\Delta\varepsilon > 10$), which are typically of sufficient magnitude to outweigh extrachromophoric dissymmetric perturbations (as happens in the GOR). They may also be recognized by inspection of the molecular structure and/or by structural similarity to "confirmed" inherently dissymmetric chromophores, e.g. hexahelicine[6] and dehydronorcamphor.[2,7] However, as has been explained already,[2,3,5] the *magnitude* of the Cotton effect (CE) depends critically on the interchromophoric geometry and the nature of the locally excited transitions, hence their coupled transition moment dipoles. Consequently, "unfavorable" geometries will lead to small rotational strengths ($R < 10^{-38}$ cgs) emanating from the coupled, chiral chromophore -- rotational strengths which may be comparable in magnitude to those derived from extrachromophoric perturbations by the dissymmetric environment (ii above). We refer particularly to those conformations, already succinctly described,[8] which result in no enhancement of R, *viz.* in the orbital formalism,[8] those with: (a) no significant overlap of the C=C and C=O π-system, (b) no significant overlap of the C=O n-system with the extended π-system, and (c) the induced electric dipole moment of the C=C perpendicular (or nearly so) to the induced magnetic moment of the C=O. In those cases, unless the signed CE contributions from the chiral chromophore are consignate with those emanating from static dissymmetric perturbers (ordinary Octant Rule)[5,9,10] the observed CE sign may be opposite to that predicted by the GOR, and the rule will appear to break down.

To illustrate this point and the need for caution in applying the GOR, we refer to the recent work of Shingu et al.[11] They reinvestigated chiral β,γ-unsaturated ketones on the spiro-

[4.4]nonane skeleton and found that whereas (+)-(5*R*)-6-methylenespiro[4.4]nonan-1-one (1) exhibits a long wavelength circular dichroism (CD) CE, $\Delta\varepsilon_{310} = +1.50$, in agreement with that predicted by the GOR,[2,3] the CE ($\Delta\varepsilon_{306} = -3.14$) of the related (-)-(5*R*)-spiro[4.4]non-6-en-1-one (2) does not seem to agree in sign. To explain the discrepancy, the authors noted that whereas the carbon-carbon double bonds of both 1 and 2 always lie in a (+) back octant, they point in different directions in the octant. Although 1 exhibits the cisoid geometry of the C=O and C=C groups for which the GOR was pictured,[2] 2 exhibits a transoid relationship. On the basis of this difference and example, one should not assume that the CE sign of β,γ-unsaturated ketones is based simply on the cisoid or transoid interchromophoric geometries depicted in the Figure of reference 11 and repeated again below. Rather, the observations may be understood more clearly by recognizing that the GOR does not apply to either 1 or 2 because criterion (c),[8] *vide ante*, is being met. Indeed, 1 and 2, with their *ca.* 90° geometries, constitute new examples which complete the various conformations previously discussed[2] in delineating the constraints on the GOR, for their UV and CD data show that there can be relative geometries which will give an enhanced electric dipole intensity but no enhancement of R.

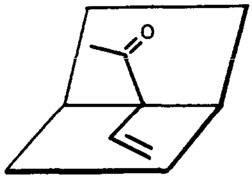


1



Cisoid

2



Transoid

A further case in point is the stereochemically more rigid β,γ-unsaturated ketone (1*R*)-2-methylenebicyclo[2.2.1]heptan-7-one (3)[12] (Figure), which also has a transoid interchromophoric geometrical relationship with the olefinic double bond in a positive octant; yet, it gives a positive CD CE ($\Delta\varepsilon_{298} = +2.0$) -- opposite to that of 2 and seemingly in agreement with the GOR.[2] The inherent chirality of the extended chromophore in 3 contributes in a significant, but not overwhelming way to the observed CE sign and magnitude. However, even if it made zero contribution, the CE would probably have the same sign and same order of magnitude, for the corresponding (+)-(1*R*)-*endo*-2-methylbicyclo[2.2.1]heptan-7-one, whose principal static dissymmetric perturber lies in roughly the same octant region as the methylene group of 3, has $\Delta\varepsilon = +0.6$.[13]

Similarly, even with the cisoid interchromophoric geometry expressed in 1, CE sign agreement with the GOR appears to be an accident of temperature, not of principle, and it depends (again) on a fortuitous mix of the signed contributions from the extrachromophoric perturbers and from interchromophoric interaction. The data of the Table (A is the enantiomer of 1) clearly show a crossing of the relative importance of these two types of contributions to the CE's of A. With B (or C) serving as an indicator of the CE contributions in A due to extrachromophoric perturbers, at 25°C that contribution is clearly dominated by the (albeit weak) contributions from interchromophoric interaction. At -160°C, on the other hand, the B-type contributions dominate. Unfortunately, a detailed analysis of the strucure-chiroptical relationships among these spiro-[4.4]nonane derivatives is complicated by conformational mobility of the skeleton, as previously recognized and discussed.[1,14]

A few words of caution are therefore advised in applying the GOR to make configurational assignments in β,γ-unsaturated ketones: the rule should best be applied to ketones with large Δε values (> 10), and the rule may *appear* to break down (or even be supported) in ketones with small Δε values (~3) where dissymmetric vicinal action can make oppositely signed CE contributions of the same order of magnitude as those derived from the chirality of the chromophore.

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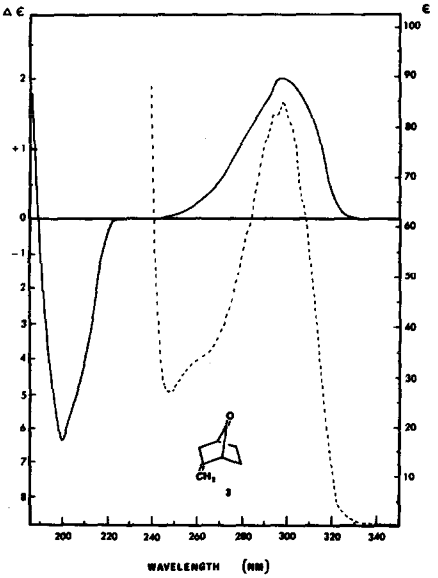

FIGURE Circular dichroism (————) and ultraviolet (- - - - -) spectra of (+)-(1*R*)-2-methylenebicyclo[2.2.1]heptan-7-one (3) measured in isopentane at 20°C on a JASCO model J-20 ORD-CD instrument equipped with a photoelastic modulator and on a Cary 14 UV spectrophotometer. Correction is made to 100% enantiomeric purity.

TABLE Temperature-Dependent Reduced Rotational Strengths for the Long Wavelength Cotton Effects of (-)-(5*S*)-6-Methylenespiro[4.4]nonan-1-one (A), (-)-(5*S*)-*cis*-6-Methylspiro[4.4]nonan-1-one (B) and (-)-(5*S*)-*trans*-6-Methylspiro[4.4]nonan-1-one (C) in Isopentane-Methylcyclohexane (5:1). Data are corrected for solvent contraction.

		$[R_0^T]$	
Temperature, °C	**A**	**B**	**C**
+25°	-2.93	-1.01	-1.17
-25°	-2.28	-1.25	-1.41
-125°	-	-1.97	-1.75
-160°	-1.81	-2.76	-1.75

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