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DISSYMMETRIC CHROMOPHORES. II.[1] CIRCULAR DICHROISM OF (2*R*)-BICYCLO[3·1·0]HEXAN-2-ONE AND (2*S*)-6,6-DIMETHYLBICYCLO[3·1·0]HEXANE-2-ONE.

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The success of the "reversed" Octant Rule[2] for α,β-cyclopropylketones, which may be viewed as inherently dissymmetric chromophores,[3] depends critically on the relative geometries of the cyclopropane and carbonyl chromophores.[1] The rule has been extended to[4] and investigated for[1] β,γ-cyclopropylketones, and even a redefined rule has been elaborated for α,β-cyclopropyl ketones based on front octant work.[5] However, failures of the rule[2] have been noted in some cases for both β,γ-cyclopropylketones[1] and α,β-cyclopropyl ketones, *e.g.* i-steroids[2,6] and (+)-carvone.[2,7] For the latter, the "reversed" Octant Rule predicts a (-)-Cotton effect (CE), but a (+) CE is observed. In order to account for the discrepancy, it was suggested[2] that the normal Octant Rule contributions (+) of the *gem*-dimethyl group of (+)-carvone overweighed the "reversed" Octant contributions (-) of the cyclopropyl ketone. The reasonableness of this argument was supported by the work of Hill and Morgan,[7] who prepared (-)-bicyclo[4·1·0]heptan-2-one, which has the same absolute configuration as (+)-carvone, but exhibits a (-) CE. Alternatively, since it is expected that the sign and magnitude of the CE of inherently dissymmetric cyclopropyl ketones will vary with the relative geometries of the two chromophores,[1,2] another explanation for the observed CE sign differences is that conformations resulting in different relative orientations of the cyclopropyl and carbonyl groups play an important sign determining role. In order to examine this rationale, we prepared the related, structurally rigid (2*R*)-bicyclo[3·1·0]hexan-2-one (**1**) and (2*S*)-6,6-dimethyl[3·1·0]hexan-2-one (**2**) of known absolute configuration and examined their CE's.

The syntheses of **1** and **2** were accomplished from cyclopentadiene and (-)-β-pinene respectively Cyclopentadiene underwent HCl addition at -78° to give 3-chlorocyclopentene[8] which was not isolated, but hydrolyzed (aq. $NaHCO_3$) to give 2-cyclopentenol. A Simmons-Smith reaction[9] of the latter gave the cyclopropyl derivative, *syn*-bicyclo[3·1·0]hexan-2-ol, which was resolved *via* its half-acid phthalate salt with ℓ-ephedrine. Cleavage of the salt afforded the (-)-alcohol which gave (+)-1 upon oxidation with CrO_3·pyridine in CH_2Cl_2. The starting material for the preparation of 2, (-)-β-pinene, was isomerized[10] to (+)-α-pinene and converted to 3-isopropenylcyclopentanone as previously described.[11] Reaction of the latter with gaseous HCl in the cold followed by treatment with KH in THF gave 2.[12] The absolute configuration and optical purity of 1 was ascertained by its Li/NH_3[7,13] conversion to the known 3-methylcyclopentanone[14] with a (+) CE. The optical purity of 2 was based on the optical purity of the (+)-α-pinene used to prepare it, and the absolute configuration of 2 was additionally confirmed by the (+) CE of 3-isopropylcyclopentanone obtained from catalytic hydrogenation of 3-isopropenylcyclopentanone.

Application of the Octant Rule[3,15] to both 1 and 2 leads to the prediction of (-) CE's in the region of the n-π* absorption for both isomers. However, both are observed (Figure 1) to have (+) CE's: 1, $\Delta\varepsilon_{298}$ + 1.83 and 2, $\Delta\varepsilon_{307}$ + 1.35 in their circular dichroism (CD) spectra as predicted by the "reversed" Octant Rule.[2] Octant projection diagrams[15] reveal that the static dissymmetric perturber methyl groups (present in 2 but absent in 1) are essentially (-) contributors to the CE sign according to the Octant Rule; hence, it is reasonable to expect that 2 would have a smaller (+) Δε than 1 -- as is observed. In related systems, Schuster and Resnick[16] determined the absolute configurations of (2*S*)-*syn*-propyl-*anti*-methyl- and (2*R*)-*syn*-methyl-*anti*-propylbicycol[3·1·0]hexane-2-one [(+) and (-) CE's respectively] from the "reversed" Octant Rule.

The same-signed n-π* CE's in the CD spectra of 1 and 2 may be contrasted with the CE's of their enantiomeric homologs: (-)-bicyclo[4·1·0]heptan-2-one (3) [(-) CE] and (+)-carvone (4) [(+) CE] respectively with the same absolute configuration. The former (3) obeys the "reversed" Octant Rule, but 4 obeys the original Octant Rule.[3,15] Since the "addition" of the *gem*-dimethyl group of 2 does not cause a change in CE sign of 2 relative to 1, it is clearly insufficient to explain the CE sign differences of 3 and 4 by this rationale (*vide supra*). We believe that the difference in CE signs of 3 and 4 is due rather to a conformational difference imposed by the presence of the *gem*-dimethyl group, and one which could not arise in structurally rigid 1 and 2.

Using Dreiding models, we examined four reasonable conformations for 3 and 4 involving boat (A and D) and twist (B and C) conformers (Figure 2). The Octant Rule predicts a (+) CE for each

Figure 1

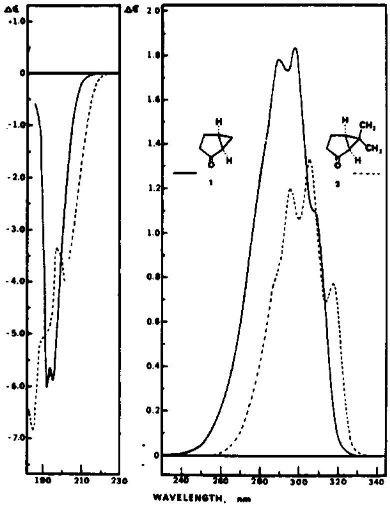

Figure 2

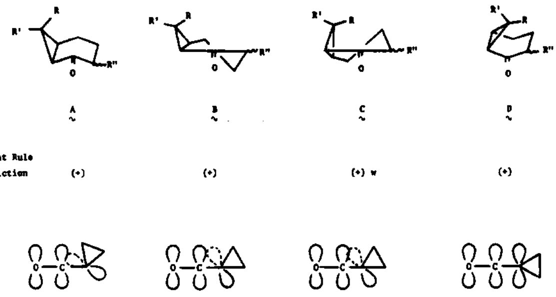

Fig. 1: The CD spectra of $\underset{\sim}{1}$ and 2 in isopentane at 20° C, measured on a JASCO J40-A-CD Spectrometer. Corrections are made to 100% optical purity.

Fig. 2: Conformational diagrams of $\underset{\sim}{3}$ (R=R'=R"=H) and $\underset{\sim}{4}$ (R=R'=R"=CH_3) involving boat ($\underset{\sim}{A}$ & $\underset{\sim}{D}$) and twist ($\underset{\sim}{B}$ & $\underset{\sim}{C}$) forms with the associated Octant Rule predicted CE signs (line 2). Orbital diagrams (C=O π & cyclopropane p) for the conformations are on the third line.

conformer. However, the usually more important consideration is the treatment of α,β-cyclopropyl ketones as inherently dissymmetric chromophores[3] with the result that the CE sign is determined by the geometric relationship of the two chromophores, expressed here in terms of the carbonyl π and cyclopropyl p-orbitals.[1,2] The orbital representations from Dreiding models (Figure 2) reveal that the orbital angular relationships for the two twist conformations, $\underset{\sim}{B}$ and $\underset{\sim}{C}$ are essentially identical. Moreover, the orbital relationships expressed by the twist conformers are essentially the same as those found in geometrically rigid $\underset{\sim}{1}$ and $\underset{\sim}{2}$. Since $\underset{\sim}{1}$ and $\underset{\sim}{2}$ have the same interchromophoric geometry as expressed by the mirror images of $\underset{\sim}{B}$ or $\underset{\sim}{C}$ and since both $\underset{\sim}{1}$ and $\underset{\sim}{2}$ exhibit a (+) CE, we suggest that $\underset{\sim}{B}$ and $\underset{\sim}{C}$ are the preferred conformations for $\underset{\sim}{3}$, (-) CE. Furthermore, since $\underset{\sim}{A}$ and $\underset{\sim}{B}$ exhibit fewer unfavorable non-bonded interactions than $\underset{\sim}{C}$ and $\underset{\sim}{D}$, $\underset{\sim}{B}$ becomes the reasonable conformational representation for $\underset{\sim}{3}$. Turning to the conformation of (+) carvone ($\underset{\sim}{4}$), because $\underset{\sim}{4}$ has the same absolute configuration as $\underset{\sim}{3}$ but the opposite (+) CE, $\underset{\sim}{B}$ can be excluded as the major conformational representation for $\underset{\sim}{4}$. Since non-bonded steric interactions are even more severe in $\underset{\sim}{C}$ and $\underset{\sim}{D}$ with the presence of a *gem*-dimethyl group, neither $\underset{\sim}{C}$ nor $\underset{\sim}{D}$ (especially) can be expected to be major contributing conformers. Conformation $\underset{\sim}{A}$, however, minimizes the non-bonded interactions between the *syn*-CH_3 and ring atoms $\underset{\sim}{5}$ and $\underset{\sim}{6}$, and we assume it to be the most favorable representation for **4**. However, since the carbonyl π and nearest cyclopropane p-orbital are nearly orthogonal in **A**, the cyclopropylketone may no longer exhibit the properties of a dissymmetric chromophore[3] and the observed (+) CE sign would thus be determined largely by the sum of the normal octant-like contributions of the C-6 CH_3 group and the *gem*-dimethyl group. In **A**, all components of the *gem*-dimethyl group lie nominally in a (+) back octant, but the configuration of the C-6 CH_3 group (and thus its signed octant contribution) is uncertain.

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