The Optical Rotatory Dispersion and Conformation of Some Optically Active ϵ-Caprolactones

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Abstract: The optical rotatory dispersion properties of a series of methyl-substituted ϵ-caprolactones of known absolute configuration have been determined and $n-\pi^*$ Cotton effects assigned. By correlating the signs of these $n-\pi^*$ Cotton effects with that for iridomyrmecin, a slightly deformed chair containing a planar lactone group is thought to be the conformation of the ϵ-caprolactone ring system. This conclusion is in agreement with the predictions of the sector rule.

The optical rotatory dispersion[2–9] and conformation[8,10–12] of γ- and δ-lactones has recently attracted considerable attention.

With the availability[13] of a series of monocyclic optically active ϵ-caprolactones with known absolute configurations it was of interest to us to determine their optical rotatory dispersion properties in order to utilize this information in a study of the conformation of their corresponding polyesters.[14]

Furthermore, it was of academic interest to determine the conformation of the ϵ-caprolactone ring system as such information to our knowledge was not available.

Optical Rotatory Dispersion

The optical rotatory dispersion curve of (*R*)-(−)-β-methyl-ϵ-caprolactone in heptane indicated a pseudo-negative Cotton effect at 275 mμ with a maximum at 250 mμ which then went very negative as seen in Figure 1.

Because the ultraviolet spectrum showed an $n-\pi^*$[15] transition at 222 mμ (ϵ 62.8) and an intense transition which had a maximum below 179 mμ (ϵ 3020), thought to be a $\pi-\pi^*$ transition, the maximum in the optical rotatory dispersion curve at 250 mμ was assigned to be a positive $n-\pi^*$ Cotton effect superimposed on a strong negative $\pi-\pi^*$ or other Cotton effect. The overlapping of these two Cotton effects of opposite sign therefore resulted in the appearance of a pseudo-negative Cotton effect at 275 mμ.

The position of the presumed $\pi-\pi^*$ ultraviolet maximum in heptane was below the limit of the instrument used. In trifluoroethanol however, the $n-\pi^*$ ultraviolet absorption underwent a hypsochromic shift to 209 mμ with an increase of intensity (ϵ_{209} 107.5) and the presumed $\pi-\pi^*$ transition exhibited a bathochromic shift to 181.5 mμ (ϵ 3718), making the maximum detectable. This phenomenon is quite general and characteristic for $n-\pi^*$ and $\pi-\pi^*$ transitions.[15,16]

Overlapping of the two ultraviolet absorption bands as they move closer together may be partly responsible for the $n-\pi^*$ intensity increase, but a solvation effect is probably also important.[17a] This is analogous to the effect of solvent on the rotational strength observed for ketones[17b] and the Cotton effect peak of an alicyclic diester.[14]

The ultraviolet absorption characteristics of both (*R*)-(+)-γ-methyl-ϵ-caprolactone and (*R*)-(−)-δ-methyl-ϵ-caprolactone were essentially the same as described above for (*R*)-(−)-β-methyl-ϵ-caprolactone.

(*R*)-(+)-γ-Methyl-ϵ-caprolactone in heptane showed a strong positive $n-\pi^*$ Cotton effect with a peak at 242 mμ and a trough at 200 mμ[18] (see Figure 2). It appears that the $n-\pi^*$ Cotton effect is predominant over the background Cotton effect in the γ-methyl lactone with the largest rotation of any of the other ϵ-caprolactones described.

(*R*)-(−)-δ-Methyl-ϵ-caprolactone in heptane exhibited a weak negative $n-\pi^*$[19a,b] Cotton effect with a trough at 230 mμ superimposed on a stronger negative background Cotton effect[19a,b] (see Figure 3).

The optical rotatory dispersion curve of (*R*)-(−)-α-bromo-δ-methyl-ϵ-caprolactone in heptane shown in Figure 4 shows a positive $n-\pi^*$ Cotton effect with a

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(1) Taken from the dissertation of H. Kaye submitted to the faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1965.

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(17) (a) In trifluoroethanol the positive $n-\pi^*$ Cotton effect extremum shifted down to 227 mμ for (*R*)-(−)-β-methyl-ϵ-caprolactone and increased the molar rotation to +130°. (b) K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 66 (1965).

(18) In trifluoroethanol the $n-\pi^*$ Cotton effect for (*R*)-(+)-γ-methyl-ϵ-caprolactone shifted down to 226 mμ and increased the molar rotation to +1880°.

(19) (a) For (*R*)-(−)-δ-methyl-ϵ-caprolactone in trifluoroethanol the $n-\pi^*$ Cotton effect shifted down as the presumed $\pi-\pi^*$ Cotton effect shifted up, resulting in almost complete overlap, thereby making the $n-\pi^*$ trough barely visible. (b) The optical rotatory dispersion curve of this lactone in hexane recorded with a Cary spectropolarimeter indicated an 8% more negative Cotton effect at 230 mμ than with a Bendix-Ericcson spectropolarimeter. (c) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 115.

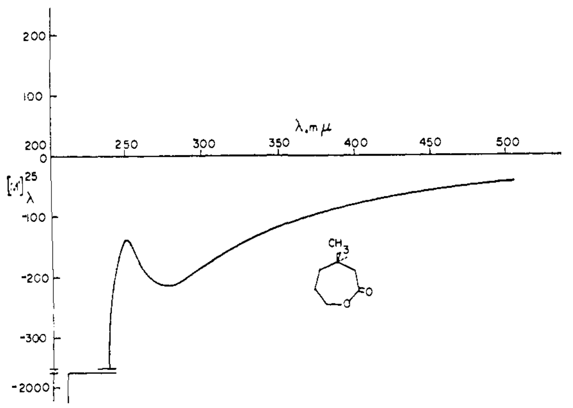

Figure 1. Optical rotatory dispersion curve of (*R*)-(−)-β-methyl-ε-caprolactone in heptane.

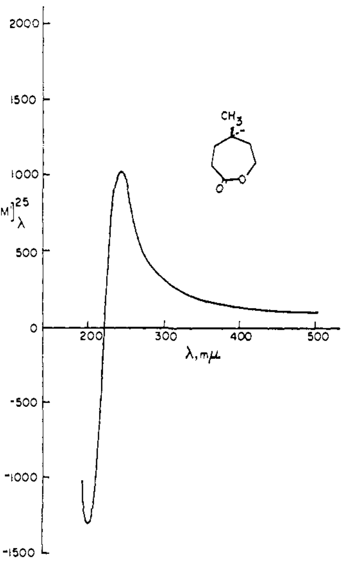

Figure 2. Optical rotatory dispersion curve of (*R*)-(+)-γ-methyl-ε-caprolactone in heptane.

peak at 274 mμ, while in trifluoroethanol the peak shifted down to 256 mμ. Thus placement of an α-bromine on (*R*)-(−)-δ-methyl-ε-caprolactone caused an inversion of sign of the n−π* Cotton effect indicating the predominant effect of the bromine atom. This predominance is also well known in axial α-bromo ketones[19c] and α-hydroxy sugars.[2]

Conformation

Examination of Dreiding models indicated that the only two possible conformations for ε-caprolactone are the boat and chair forms containing a planar lactone group (see Figure 5, a and b). Evidence for this planarity is known[10,12,20–25] from dipole moment studies[26,27] and X-ray crystallography.

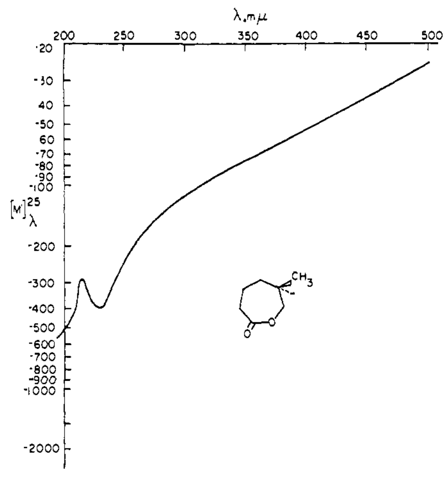

Figure 3. Optical rotatory dispersion curve of (*R*)-(−)-δ-methyl-ε-caprolactone in heptane.

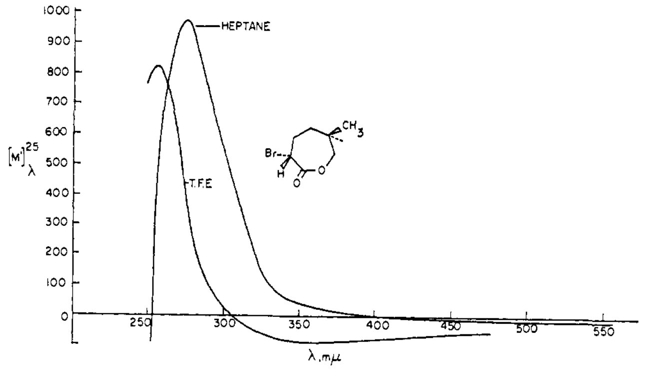

Figure 4. Optical rotatory dispersion curves of *trans*-(*R*)-(−)-α-bromo-δ-methyl-ε-caprolactone in heptane and TFE.

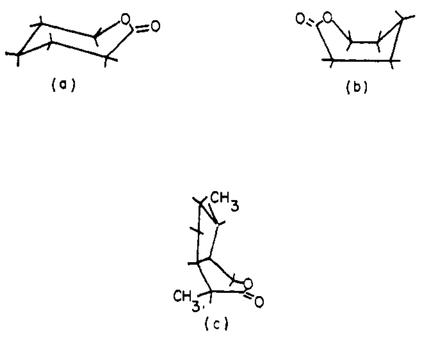

Figure 5. a, chair ε-caprolactone; b, boat ε-caprolactone; c, iridomyrmecin.

In both these forms the distance between the α-axial proton and ε-axial proton is only 1.2 A, a very severe interaction. It thus seems likely that the rings must be deformed slightly to relieve this interaction while the lactone group remains planar. The high dipole moment,[26,27] 4.45 D., for ε-caprolactones supports this planarity.

By carrying out a crude hydrogen–hydrogen repulsion energy calculation[28,29] using Dreiding models for the interatomic distances it was found that the chair form

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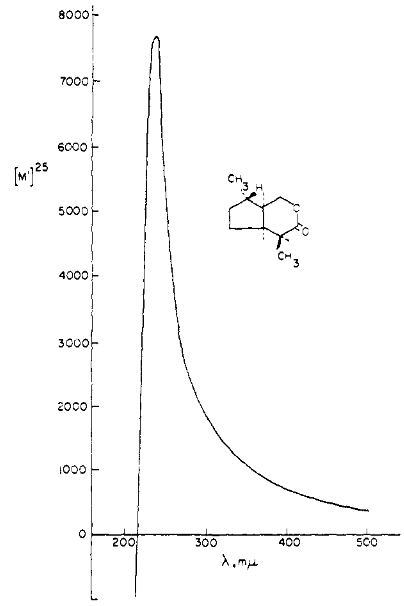


Figure 6. Optical rotatory dispersion curve of iridomyrmecin in heptane.

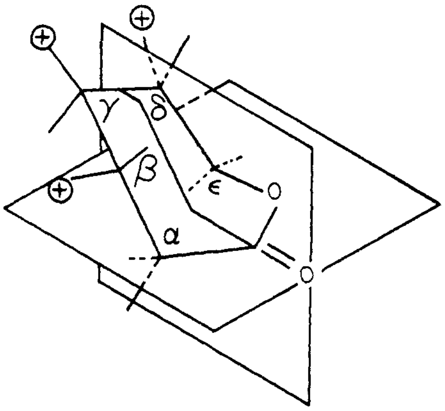


Figure 7. Isometric projection and signs of n–π* Cotton effects for chair ε-caprolactones.

was about 3 kcal/mole more stable than the boat. This result suggested a small qualitative energy difference and further evidence was therefore needed to support this conclusion.

One seldom-used approach to this problem short of a total crystallographic analysis was to determine the unit cell dimensions, the number of molecules per unit cell, and the space group for crystalline (*R*)-(−)-δ-methyl-ε-caprolactone,[13,30] and then attempt to pack Dreiding models of this lactone into a scaled-up model of the unit cell to see which conformation packed best. This seemed like a worthwhile attempt as there must be a very unique arrangement of (*R*)-(−)-δ-methyl-ε caprolactone as none of the other two optically active ε-caprolactones crystallize.[13] Unfortunately, no decision could be made by this method as either conformation could comfortably pack in a variety of ways.

Additional evidence regarding the preferred conformation of the ε-caprolactone system could be obtained by correlating the optical rotatory dispersions of the

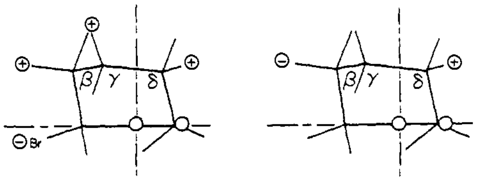
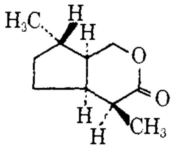


Figure 8. (a, left) Planar projection and n–π* Cotton effects for chair ε-caprolactones. (b, right) Planar projection and background Cotton effects for chair ε-caprolactones.

lactones with the optical rotatory properties of iridomyrmecin (I), a compound whose conformation has been determined by X-ray crystallography (see Figure 5c).



I

By superimposing the lactone group of iridomyrmecin on the lactone group of the chair ε-caprolactones with Dreiding models, it can be seen that the geometric position of atoms in relation to the chromophore are very similar, whereas they are almost enantiomeric with the boat ε-caprolactones. It is a reasonable assumption that the methyl group in the ε-caprolactones will preferentially exist in the equatorial position in analogy to the more stable equatorial methyl group in methylcyclohexanone.[31]

Iridomyrmecin[32] in heptane exhibited a strong positive Cotton effect at 238 mμ, as shown in Figure 6. This result when compared with the positive Cotton effects of the lactones as summarized in Figure 7, where the chair conformation is drawn and where the δ-methyl-ε-caprolactone is shown as its enantiomer, indicates that the preferred conformation is the chair. Even though the strong α–ε proton repulsion probably distorts or skews the chair slightly, this correlation still remains valid as any distortion does not greatly alter the geometric position of atoms in relation to the chromophore.

Further support for the chair conformation has also been obtained by application of the sector rule.[4,5,9] Conformational analysis of α-bromocyclohexanone[33–35] has shown that in nonpolar solvents dipole repulsion between the bromine and carbonyl atoms tends to increase the concentration of axial α-bromo ketone in solution, whereas in polar solvents the equatorial conformation is stabilized by the high dielectric constant of the media. Although bromo lactones have not, to our knowledge, been studied in this respect before, it seems likely that similar solvent dependencies may also occur.

Thus, inspection of Dreiding models indicated that the chair conformation of *trans*-(*R*)-(−)-α-bromo-δ-methyl-ε-caprolactone (II) with the methyl group and

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(30) All X-ray analysis was carried out by Mr. Rubin Rudman of the Polytechnic Institute of Brooklyn and are reported in the ASTM X-Ray Powder Data File.

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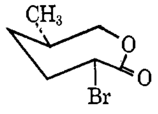
bromine atom both equatorial was the most stable conformer in trifluoroethanol. Here too, a small deformation of the ring is expected to relieve the α–ϵ proton repulsion. In heptane, the situation is more complicated because of repulsion between the α-bromine and the carbonyl group. Although this energy is only about 0.45 kcal/mole,[34] it is uncertain at this time whether in combination with the α–ϵ proton repulsion energy, the planarity of the lactone group will be broken.



II

The planar projection of chair ϵ-caprolactone looking down the carbonyl group shown in Figure 8a summarizes the signs of the n–π^* Cotton effects for substituents at the appropriate positions. The enantiomers of the δ-methyl- and α-bromo-δ-methyl lactones are drawn in this diagram. It can be seen that the α-bromine atom falls in the lower left quadrant below the plane of the lactone group. The conclusion which can be drawn from this diagram is that the atoms in the upper and lower left quadrants contribute most to the sign of the Cotton effect, in agreement with the rule of Okuda,[2] Klyne's sector rule,[4,5] and more recently with the modified sector rule.[9] Furthermore, the signs for the atoms in these quadrants are in accord with the theoretical calculations of Schellman[36,37] for the analogous amide group.

The signs of the background Cotton effects, most pronounced for the β- and δ-methyl lactones, Figures 1 and 3, can be summarized in Figure 8b. It is uncertain whether a π–π^* or another transition[38,39] is responsible. Diagram 8b is suggestive of a lactone rule for the higher energy transitions.

Experimental Section

Optical rotatory dispersion measurements were taken with a Bendix-Ericcson Polarimatic 62 automatic scanning spectropolarimeter.[40] Dispersions were carried out in 5-, 1-, and 0.1-mm jacketed quartz cells and optical rotations below 40% transmission were ignored. Below 200 mμ a nitrogen flush was used. Rotatory dispersion data are expressed as molar rotations for the lactones. Refractive index corrections were made on all dispersion measurements.[41] For trifluoroethanol the value of the refractive index, $n^{25}{}_{\mathrm{D}}$ 1.2895,[42] was used at all wavelengths. For n-heptane, the value $n^{25}{}_{434}$ 1.3938 was used at all wavelengths.[43] All ultraviolet spectra were taken on a Perkin-Elmer Model 350.

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The Optical Rotatory Dispersion and Conformation of Some Poly-ϵ- caprolactones in Solution

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Abstract: Optically active polymethyl-ϵ-caprolactones and their model compounds were prepared *via* the lactones. No special conformations were detected for these polyesters in solution as evidenced by the linear decrease in the ratio of the Cotton effect extrema for the β-methyl polymer and its model compound as a function of decreasing coil size and the absence of any n–π_3^* Cotton effects for the γ-methyl and δ-methyl polymers in good and poor solvents. The Drude equation was obeyed in all solvents studied and the λ_0 values corresponded to those ultraviolet bands which were optically active.

In solution under special conditions polypeptides[2–5] and polynucleotides[6] can exist as extended helices. Recently a great deal of experimental evidence has been presented supporting the existence of microhelical regions in solutions of isotactic polymers.[7,8]

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