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ROTATIONAL STRENGTH OF THE PEPTIDE n-π^* TRANSITIONS: EQUIVALENCE OF THE ++ AND -- QUADRANTS

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The purpose of this communication is to note the adequacy of a quadrant (or an octant) type geometric dependence for the peptide n-π^* transition, when utilizing relatively rigid model systems--4-and 5-substituted pyrrolid-2-ones--and when the vicinal group is the carboxylate or carboxyl moiety (see structure I). The rotational strength of the sodium pyrrolid-2-one-4-carboxylate can be calculated from the values for sodium pyrrolid-2-one-5-carboxylate, when the angular probability functions of the carboxylate anion at positions 4 and 5 in the ++ and -- quadrants are considered. In a manner consistent with the partial molar rotatory power approach[1-3] the carboxylate moiety is treated as charged perturber in which the contributions of the atoms are proportional to the sign and magnitude of the charge. Similarly the rotational strength for the 4-carboxylic acid may be calculated from the 5-carboxylic acid. Due to the very different angular probability functions for both substituents at the two positions and due to the decreased symmetry in the case of the carboxyl vicinal group, one might have expected a more apparent contribution from the magnetic-electric coupled oscillator term[4-5] which would have been expressed by non-adherence to the simple geometric dependence. These results are particularly significant since the quadrant (or octant) dependence has not been demonstrated so unambiguously for the peptide n-π^* transition which is to further note that the results provide no evidence for other regional dependencies[6] nor for ring chirality as a dominant factor[7]. Also the non-octant behavior exhibited in cyclic ketones with substituents in somewhat similar positions[8-10] is not seen.

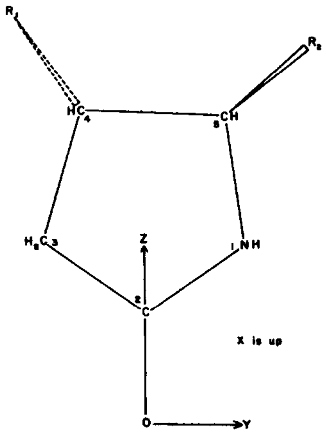
The absolute configuration of pyroglutamic acid (L-pyrrolid-2-one-5-carboxylic acid) is well known and is supported by x-ray diffraction studies on the derivative 5-iodomethyl-pyrrolid-2-one[11]. The absolute configuration of pyrrolid-2-one-4-carboxylic acid was determined by conversion to the R-hydroxymethyl succinic acid dihydrazide derivative[12].

The optical purity of the 4-carboxylic acid was verified using the method of an optically active nuclear magnetic resonance solvent[13]. Table 1 contains the molar ellipticities and rotational strengths for the four molecules. Energies for the angular distribution were calculated by taking a six-fold symmetric rotational barrier of 0.2 kcal/mole[14] and by calculating the coulombic interaction potentials between the atoms of the peptide group and those of the carboxyl and carboxylate groups. Atomic charges for the carboxylate, carboxyl and peptide groups were obtained from references 14, 15 and 16 respectively.

TABLE 1 OPTICAL ROTATION DATA ON 4-AND 5-SUBSTITUTED PYRROLID-2-ONES

Vicinal group	Molar ellipticity	R(exptl)x10^{40}	R(calc)x10^{40}
5-COO-	2.5x10^4	20	
4-COO-	1.5x10^4	11	12.9 (11)[a]
5-COOH	11x10^4	12	
4-COOH	7.6x10^4	7	6.9 (6.5)[a]

[a] Calculated with a 0.24 Å displacement of the 4C from the CON plane



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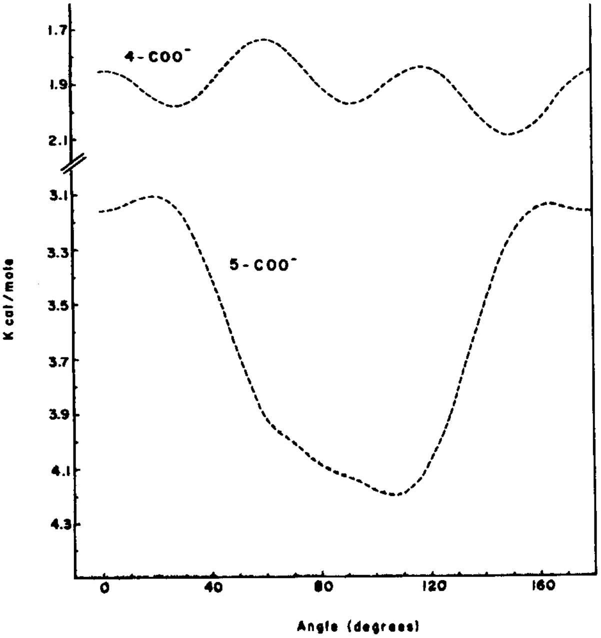

Figure 1. Plot of potential energy as a function rotation about the ring carbon-substituent carbon bond. (see text for discussion).

Potential energies as a function of rotational angle are given in Fig. 1 for the carboxylate substituent. The zero angle is taken when C=0 and the C-H are eclipsed. Direction of rotation is taken as positive when looking along the C–C bond and rotating the far carbon in a clockwise direction[17].

The expression used to calculate the contribution of the carboxylate and carboxyl vicinal groups to the rotational strength[18], R, is

$$R = \frac{\sum_{\theta} R_{\theta} \; e^{-\varepsilon_{\theta}/RT}}{\sum e^{-\varepsilon_{\theta}/RT}} \qquad \text{where} \qquad R_{\theta} = -A \sum_{i} \frac{x_{\theta i} \; y_{\theta i}}{r_{\theta i}^{3}} q_{i}$$

and where the summation is over the atoms in the vicinal group. x, y, and r are the coordinates and distance of the atom, and q_i is the charge on the atom. The coefficient A, determined on the 5-substituted pyrrolid-2-one, is used to calculate the 4-substituted pyrrolid-2-one. While there is evidence for two terms with differing distance dependence and sign[1-3,19], for our concerns here, using only the less steep term, as in Eq. 2, is adequate. This is justified on the basis that the vicinal groups at positions 4 and 5 are at a similar distance from the acyl moiety and also they are at a distance where the steeper term is much less significant. The atomic coordinates of the pyrrolid-2-ones are taken from the crystal structure of L-5 iodomethyl-pyrrolid-2-one and L-pyrrolid-2-one-5-carboxamide[9]. The pyrrolid-2-one ring is only slightly non-planar with the 4 carbon being about 0.2 Å out of the plane defined by the CON peptide atoms. The calculated rotational strengths included in Table 1, are seen to agree very satisfactorily with experimental values. Substitution at the four position is expected to move the 4 carbon somewhat further out of the plane as the substituent presses equatorially. When an anticipated greater mean displacement from the peptide plane of 0.24 Å is taken, the experimental result is exactly obtained for the carboxylate vicinal group.

In the calculations the angular dependence of rotational strength for sodium pyrrolid-2-one-5-carboxylate varies from 9×10^{-40} at an angle of 50° to 30×10^{-40} at 130° with an experimental value of 20×10^{-40} and for sodium pyrrolid-2-one-4 carboxylate from 2×10^{-40} at 40° to 16×10^{-40} at 140° with an experimental value of 11×10^{-40}. Thus the angular dependence is not inordinately steep and the experimental result lies neither near zero nor at an extreme on the calculated curve.

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