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A NEW SENSITIVE METHOD FOR DETERMINING ABSOLUTE CONFIGURATION OF α-SUBSTITUTED CYCLIC IMINES BY CD SPECTRA OF CHROMOPHORIC DERIVATIVES

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In the course of studies on CD spectra of N-2,4-dinitrophenyl(=DNP)-amino acids[1),2)], it was found that DNP-proline shows a characteristic pattern of CD spectrum which is much different from those of other common DNP-amino acids. Thus, a series of cyclic α-imino acids were converted to the DNP derivatives and their CD spectra were measured in MeOH. All the CD spectra so far examined exhibited similar pattern and their sign of ellipticity reflected well the absolute configuration at the α-position: i.e. $[\theta]_{400}<0$ for L-series compounds and $[\theta]_{400}>0$ for D-series compounds (Fig. 1).

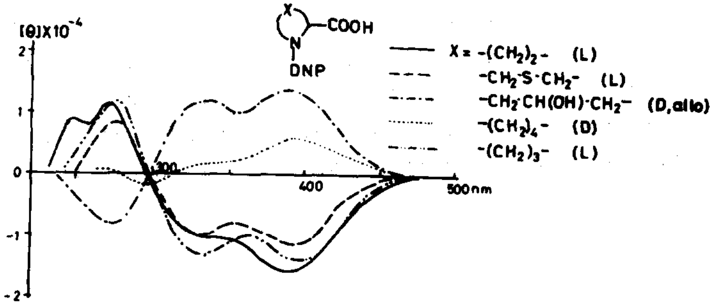

Fig. 1 CD spectra of DNP derivatives of various cyclic α-imino acids.

The reason why their CD pattern differ from those of DNP-α-amino acids and why such clear relation between their sign and the absolute configuration is observed can be considered as below. Inspection of CPK molecular model revealed that the dimethylamino group of o-nitrodimethylaniline cannot be coplanar with the benzene ring but twisted due to steric hindrance with the o-nitro group. By analogy to o-nitrobenzoates[3)], conformational equilibrium as shown in Fig. 2 is proposed as the origin of the observed CD behaviour of these compounds. Fig. 2 illustrates the following points: (i) the two o-situated bulky sp^2 substituents favour to be twisted in the same direction in order to relieve the steric overcrowdedness, (ii) when an alkyl group on the amino nitrogene is chiral the twistmer have different energy and so different population of molecules would exist in the two conformational states, and (iii) the conformer (right) having the α-carboxyl group nearer the o-nitro group would be less populated.

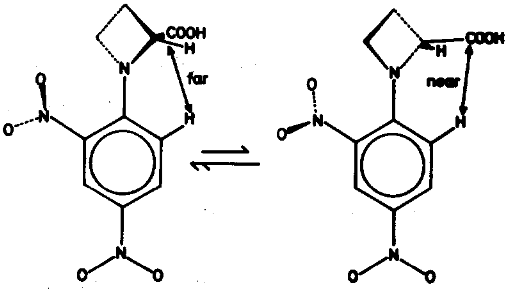

Fig. 2 Conformational equilibrium proposed as the origin of the characteristic CD pattern of DNP-L-azetidine carboxylic acid as an example.

Experiments to confirm these concepts by X-ray crystallography and by low temperature CD measurements are in progress.

On the basis of these considerations it is suggested that replacement of the α-carboxyl group by some other groups or substituents on farther ring carbon atoms (including stereochemistry) would not affect the validity of the rule. Thus, DNP-derivatives of D-coniin, L-prolinol, L-α-kainic acid and L-α-allo-kainic acid were prepared and their CD spectra were measured in MeOH (Fig. 3). All of their spectra have very similar pattern to that of DNP-proline and their signs agreed with those expected from the known absolute configurations of each compound and the above rule. Therefore, the rule affords a very useful and sensitive (micromoles) method for determining absolute configuration of α-substituted cyclic imines, in general. The authors express their gratitude to Prof. Takemoto and Prof. Yamada for generous gift of samples of kainic acids and coniin, respectively.

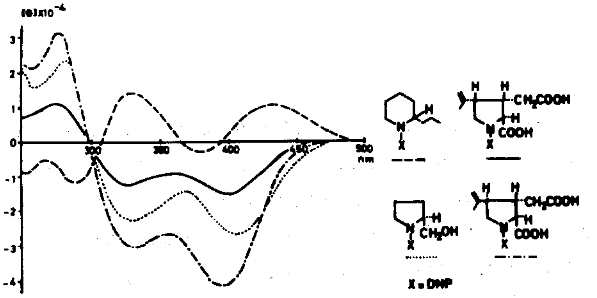

Fig. 3 CD spectra of DNP-derivatives of various α-substituted cyclic imines.

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