Energy Inequivalence of Peptide Enantiomers from Parity Non-conservation

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L-Alanine and L-peptides in the α-helix and β-sheet conformation are stabilized relative to the corresponding enantiomer by the weak parity-violating interaction.

Owing to connections with the electromagnetic interaction, the weak parity-violating interactions give rise to a small difference in electronic binding energy between a chiral molecule and its enantiomer.[1-3] The weak interactions mix electronic states of opposite parity in an atom or molecule. The electronic states of a chiral molecule, lacking secondary (S_p) stereochemical symmetry elements, are necessarily of mixed parity, and small electronic-energy shifts, of equal magnitude and opposite sign for the two enantiomers, result from the weak interactions represented by equation (1).

$$E_L - E_D = 2\Delta E_{pv} \quad (1)$$

The more significant of the connections refers to the weak neutral current (W.N.C.) interaction, mediated by the exchange of massive neutral bosons. The W.N.C. interaction has two principal components, the electron–nucleon potential (V_{pv}^{eN}), confined to the nucleus of an atom, and the less-important electron–electron potential (V_{pv}^{ee}), effective in the region of the atomic K-shell.[3,4] Recent calculations, based upon the V_{pv}^{eN} component of the W.N.C. interaction, give the (R)-isomer of

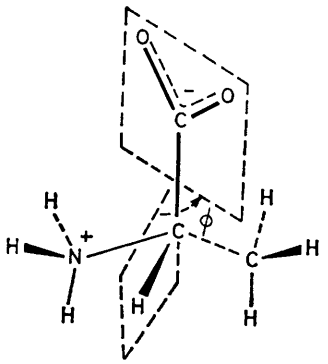

Figure 1. The dihedral torsion angle, ϕ, of the carboxylate-group plane about the bond to the α-carbon atom in L-alanine.

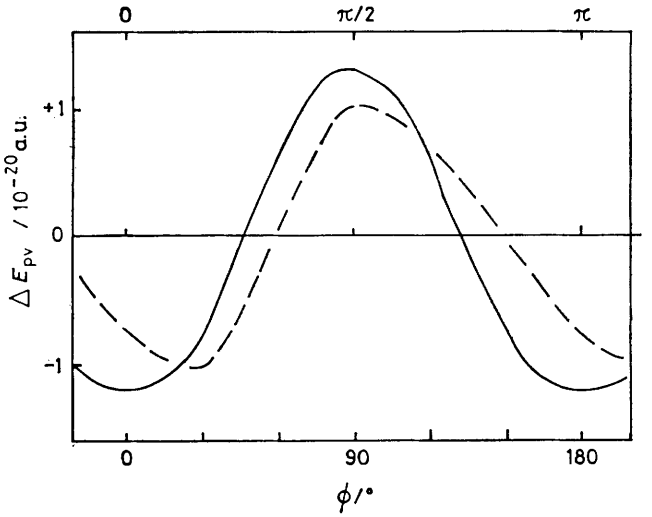

Figure 2. The relation between the parity-violation energy shift, ΔE_{pv} (10^{-20} a.u.), and the torsion angle, ϕ, of the carboxylate-group plane about the bond to the α-carbon atom in L-alanine (full line) and in glycine (broken line).

a D_2 ethylene molecule with a 10° dihedral angle between the planes of the two CH_2 groups an energy higher by 4×10^{-20} a.u. (1×10^{-13} J mol^{-1}) than the (*S*)-enantiomer.[3] The valence-shell M.O.s of the (*R*)-isomer[5] and the inner-shell M.O.s of planar ethylene[6] provided the orbital basis for the calculations.[3]

An intrinsic energy difference between optical stereoisomers provides a possible basis for the particular selection of L-amino acids and related substances, as opposed to the corresponding antimers, in the homochiral biochemistry of terrestrial organisms. Calculations of the energy shift (ΔE_{pv}) arising from the V_{pv}^{eN} component of the W.N.C. interaction are reported for L-alanine and chiral conformations of glycine (Figures 1 and 2), together with ΔE_{pv} for the α-helix and the β-sheet conformation of a glycyl peptide twist unit[7,8] (Figure 3) in an L-amino acid polypeptide chain.

An *ab initio* calculation of the electronic M.O.s of the simplest α-amino-acid necessitates currently the use of a limited set of basis wavefunctions. The dependence of ΔE_{pv} upon the choice of basis set has been investigated for the enantiomers of a tetra-atomic system, hydrogen peroxide, containing the minimum number of atoms consistent with a chiral structure, employing the GAUSSIAN 76 *ab initio* M.O. program.[9] It is found[10] that the STO-*N*-31G bases, but not the STO-*N*G sets, give ΔE_{pv} values for hydrogen peroxide which converge as

Table 1. The mean dihedral torsion angles, ϕ and ψ (Figure 3) for an L-polypeptide chain in the α-helix and the β-sheet conformation, from ref. 7, and the energy-shift due to the weak parity-violating interaction, ΔE_{pv} (10^{-20} a.u.), for the total peptide twist fragment (P.T.F.) and the corresponding unit (P.T.U., square brackets, Figure 3), with R = H.

Conformation	ϕ/°	ψ/°	ΔE_{pv}^{PTF}	ΔE_{pv}^{PTU}
α-helix	−76	−36	−0.53	−0.33
β-sheet	−100	+130	−0.63	−0.33

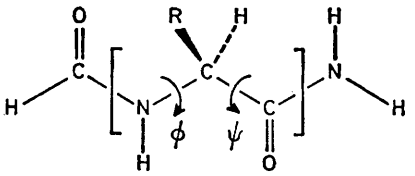

Figure 3. The dihedral angles, ϕ and ψ, in a polypeptide chain,[7,8] and the peptide twist fragment (P.T.F.) and the corresponding unit (P.T.U.), in square brackets. The calculations (Table 1) refer to a glycyl unit, R = H.

the number (*N*) of Gaussian functions (G) used to construct Slater-type-orbitals (STO) is increased over the standard bound, $4 \leqslant N \leqslant 6$, towards the corresponding value obtained with an extended basis set.[11]

Accordingly, the STO-6-31G basis set was employed to compute the ΔE_{pv} shifts of the amino-acid derivatives studied (Figures 1–3) by the previously described methods,[3] using the GAUSSIAN 76 program.[9] As in the case of hydrogen peroxide,[10] it is found that the parity-violating energy shift of L-alanine and of glycine is strongly dependent upon the molecular conformation (Figures 1 and 2). The preferred conformation of L-alanine in aqueous solution lies close to the minimum in the relation between the energy shift, ΔE_{pv}, and the torsion angle ϕ of the plane of the carboxylate group around the bond to the α-carbon atom (ϕ *ca.* 0, Figures 1 and 2). ΔE_{pv} for D-alanine has the same magnitude but the opposite sign for this conformation.

An analysis[7] of the main chain dihedral angles of some 2500 amino-acid residues in the structures of 13 proteins, determined by *X*-ray crystal diffractometry, gives the mean values listed (Table 1, Figure 3) for the α-helix and the β-sheet conformation of an L-polypeptide. For these particular values of the chain dihedral angles, the parity-violating energy-shift is negative, both for the right-handed α-helix and the β-sheet conformation, and for the central glycyl peptide twist unit (P.T.U.) and formylglycinamide, the total peptide twist fragment (P.T.F.) studied (Table 1, Figure 3).

The parity-violating stabilization of an L-peptide, relative to the corresponding D-peptide, in the α-helix or the β-helix conformation amounts to no more than *ca.* -2×10^{-14} J mol^{-1} per amino-acid residue, corresponding to an enantiomeric excess of some 10^6 L-peptide molecules per mole of racemate in thermodynamic equilibrium at ambient temperature. However small, the enantiomeric excess provides a determinate intrinsic bias which resolves the racemic metastability, otherwise subject to chance perturbations, in kinetic mechanisms for the time-evolution of L-peptide dominance, such as that of Frank,[12] even with the same corresponding catalytic and inhibitory rate constants for the two enantiomers. These kinetic mechanisms are thermal,[12] in contrast to the radiolytic or photomechanisms,[13] dependent upon the chiral discrimination between the enantiomers of a racemate by the spin-polarized electrons emitted during the β-decay of a

radionuclide, or by the circularly-polarized photons generated during the deceleration of the β-electrons.

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