# Biomolecular Homochirality and Electroweak Interactions. I. The Yamagata Hypothesis

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*Received: December 9, 2002; In Final Form: May 28, 2003*

In 1966, Y.Yamagata proposed that neutral weak currents between electrons and nucleons could be responsible for specific biomolecular homochirality in life. We critically evaluate this hypothesis by applying relativistic parity nonconserving calculations for amino acids. The results reveal no clear evidence that the naturally occurring L-amino acids are stabilized by parity violation effects.

## 1. Introduction

In the first picoseconds of our universe (*the cosmic stage*), the electroweak forces underwent a distinct phase transition that separated the electromagnetic from the weak force. The carrier of the neutral weak current, the $Z^0$-particle, is well-known to cause parity symmetry[1,2] to be broken[3] thus leading to a very small and still undetected energy difference between the two enantiomers of chiral molecules. For atoms, these parity nonconserving (PNC) effects have been confirmed by experiment to a relatively high accuracy.[4] For molecules, however, the search for PNC effects has just begun.[5−9]

The first molecules were formed about 10 billion years ago in diffuse and dense interstellar clouds (*the chemical stage*). Life in the universe is a fairly recent development and began after formation of the first planets (*the biological stage*). Since Pasteur's fundamental discovery of chirality in 1860, we know that living systems on earth exhibit a distinct asymmetry, the so-called *biomolecular homochirality*. Nearly all organisms use (with a few exceptions) exclusively L-amino acids for protein formation and D-sugars for their DNA and RNA. Here L and D refer to specific spatial conformations of these chiral molecules. This asymmetry at the microscopic level is possibly responsible for most asymmetries observed at the macroscopic level in living systems.[10,11] Yet the origin of specific biomolecular homochirality remains a mystery and is still a subject of intense debate.[12−15] Homochirality is an accepted tenet for the structure of biomolecules; however, the origin of the exclusive use of L-amino acids and D-sugars remains a mystery.

Not long after the first experimental observation of PNC by Wu et al. in 1957,[16] it was suggested that what is now known as the neutral weak current between electrons and nuclear particles might be responsible for specific biomolecular homochirality on earth. This is the *Yamagata hypothesis*:[17] "The asymmetric appearance of biomolecules is most naturally explained by supposing a slight breakdown of parity in electromagnetic interaction and an "accumulation" of it in a series of chemical reactions. Conversely, it seems that the asymmetric existence of biomolecules verifies a parity nonconservation in electromagnetic interaction. This universality, if true, would promise similar results on other planets than the earth." From the early work by Hegstrom et al.,[18] Rein,[19] Letokhov,[20] Tranter,[21,22] Mason[23] and others[24] on PNC effects in chiral molecules, it was previously assumed (or even accepted) that L-amino acids and D-sugars are more stable than their enantiomeric forms.[25,26] Together with an autocatalytic process for the synthesis of amino acids, this PNC stabilization is assumed to have led to a small excess of one enantiomeric species, the *Kondepudi−Nelson hypothesis*.[27] The preferential stability of L-amino acids has, however, been questioned very recently by a number of groups.[28−31]

The energy difference between two enantiomers, the parity nonconserving energy difference, $\Delta E_{\mathrm{PNC}}$, scales approximately as the fifth power of the nuclear charge $Z$ of the heaviest atom in the chiral molecule.[18,32,33] For the amino acids studied so far, $\Delta E_{\mathrm{PNC}}$ is therefore small and on the order of $10^{-16}$ kJ $\mathrm{mol}^{-1}$.[28,29,34] This corresponds to an excess of only $10^7$ molecules per mole of the more stable enantiomer in a nominally racemic mixture at room temperature. There are however a number of serious points of criticism concerning previous PNC calculations. First, the PNC operator is intrinsically relativistic. Although we do not expect any significant scalar-relativistic effects for natural amino acids here, the preferable treatment of PNC effects is within a relativistic framework because of the simplicity of the parity violation operator in the relativistic framework and to avoid picture change effects arising from the unitary transformation of the Dirac operator, which may become important for heavier elements.[33] Second, the PNC operator requires an accurate description of the wave function in both the core and valence regions,[33] and most of the basis sets used so far were of rather low quality. In addition to these methodological points, even more fundamental criticism of PNC calculations for amino acids and their relevance for biomolecular homochirality can be raised. For example, it is an open question whether the first amino acids on earth at the prebiotic stage came from outer space, for example, by meteoric impact,[35] whether their formation occurred in a reducing earth atmosphere, or whether the synthesis occurred in aqueous solution possibly adsorbed on some catalytic surface like clay, quartz, metal oxide, or sulfide.[36,37] For each scenario, the molecular environment of a specific amino acid and the resulting geometry considered for PNC calculations would be quite different. To date, there are more than 120 interstellar molecules known and a list can be found on the Internet.[38] However, none of the amino acids have been discovered yet in interstellar space. Furthermore, even if all amino acids would show a preference for left-handedness,

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10.1021/jp022568v CCC: $25.00 
Published on Web 07/31/2003

it is still questionable whether a small energy difference on the order of $10^{-16}$ kJ mol$^{-1}$ can lead to biomolecular homochirality.[12] Nevertheless, Wang et al. recently claimed to have found first evidence for the so-called *Salam hypothesis*,[39] which propose that at a certain critical temperature, $T_c$, a phase transition into the more stable enantiomeric form occurs (the L-form for amino acids).[40] However, in our opinion the effects found by differential scanning calorimetry, by superconducting quantum interference device (SQUID) magnetic measurements, and by laser Raman spectroscopy are simply too large to be due to tiny PNC effects. In part II of this contribution, we have reexamined the experimental evidence for support of the Salam hypothesis. Most of the experimental results reported cannot be repeated, or the features observed become smaller upon purification.

Notwithstanding all of these problems, we have begun a systematic study of fully relativistic PNC calculations using high-quality basis sets for biologically relevant molecules. Preliminary results were published recently for alanine.[28] In the current paper, the first part of a series, we present the first comparative study on PNC effects of the four amino acids glycine, alanine, serine, and cysteine to gain insight into the Yamagata hypothesis. The following paper will cover the experimental investigations of weak interactions as possible cause for phase transitions of amino acids, which is an important part of the Salam hypothesis. The systematic variation of the α-substituent, −H for glycine, −$CH_3$ for alanine, −OH for serine, and −SH for cysteine, allows us to study the $Z^5$ dependence of $\Delta E_{PNC}$. Sulfur is the heaviest element that occurs in natural amino acids. Therefore, the largest $\Delta E_{PNC}$ would be expected for cysteine. Note that glycine does not contain an asymmetric carbon atom, in contrast to all other natural amino acids. However, several of its minimum energy conformations are chiral and therefore exhibit a nonzero $\Delta E_{PNC}$.

## 2. Theory

We briefly outline the theory for the nuclear spin-independent PNC interactions between electrons and nucleons. For virtual $Z^0$-bosons in the low-energy limit, the approximate electron−nucleon PNC interaction is (timelike component of the vector nucleus−axial electron coupling)[41]

$$H_{eN}^{odd} = \frac{G}{2\sqrt{2}} Q_w \gamma_5 \rho(x) \tag{1}$$

and the superscript odd indicates a parity-odd operator. $\rho(x)$ is the normalized nucleon density. $G$ is the Fermi coupling constant with $G = (1.166\,37 \pm 0.000\,02) \times 10^{-11}$ MeV$^{-2}$ or $(2.222\,55 \pm 0.000\,04) \times 10^{-14}$ au, and the Dirac matrix $\gamma_5$ is the $4 \times 4$ pseudoscalar chirality operator

$$\gamma_5 = \gamma^5 = \begin{pmatrix} 0 & \mathbf{I} \\ \mathbf{I} & 0 \end{pmatrix} = i\gamma^1\gamma^2\gamma^3\gamma^0 \tag{2}$$

$\mathbf{I}$ is the $2 \times 2$ unit matrix, and the $4 \times 4$ matrices $\gamma^i$ are the Dirac matrices.[41] The weak charge is

$$Q_w = (1 - 4\sin^2\theta_w)Z - N \tag{3}$$

$\theta_w$ is the Weinberg angle with $\sin^2\theta_w = 0.2259 \pm 0.0046$, $Z$ is the number of protons (equal to the nuclear charge), and $N$ is the number of neutrons. The corresponding electron−electron interaction PNC term is small and can be neglected.[42]

Equation 1 can easily be extended to a multiparticle system to give the parity nonconserving energy shift, $E_{PNC}$, in first order

$$\Delta E_{PNC} = 2E_{PNC} = 2\sum_n {E_{PNC}}^n = 2\langle \Psi_{DHF} | H_{eN}^{odd} | \Psi_{DHF} \rangle = \frac{G_F}{\sqrt{2}} \sum_n Q_{w,n} \sum_i \langle \psi_i | {\gamma_i}^5 \rho_n(\mathbf{r}_i) | \psi_i \rangle \tag{4}$$

within the Dirac picture. Here $\Psi_{DHF}$ is the Dirac−Hartree−Fock wave function, composed of the four-component, one-electron spinors $\psi_i$. The summation is over all electrons, $i$, and nuclei, $n$. It is easy to show that operator 1 leads to parity violation. The parity operator can be derived in matrix representation as an improper Lorentz transformation

$$P = e^{i\varphi}\, \gamma^0 P_R \tag{5}$$

and we see that $PP^{-1} = 1$ (in this case the $4 \times 4$ unit matrix) and $[\gamma^\mu, \gamma_5]_+ = 0$ ($[\ ,\ ]_+$ denotes the anticommutator and $P_R$ represents space inversion in three-dimensional space). We therefore have

$$P{:}\psi(x) \rightarrow P\psi(x) = \psi(-x)$$
$$\psi^* P^{-1} \gamma_5 P \psi = -\psi^* P^{-1} P \gamma_5 \psi = -\psi^* \gamma_5 \psi \tag{6}$$

and a change of the parity of the wave function leads to a negative sign in the expectation value over $H_{eN}^{odd}$. As a result, the total Hamiltonian consisting of a parity even and odd parts

$$H = H^{even} + H^{odd} \tag{7}$$

transforms as

$$P^{-1} H P = H^{even} - H^{odd} = H - 2H^{odd} \neq H \tag{8}$$

Consequently, if one enantiomer becomes stabilized by $E_{PNC}$, its mirror image then becomes destabilized by the same amount, and we obtain the difference between both enantiomeric forms

$$\Delta E_{PNC} = \Delta E_{L-D} = E_{PNC,L} - E_{PNC,D} = 2E_{PNC,L} \tag{9}$$

## 3. Details of Calculations

To the best of our knowledge, the precise gas-phase structures of amino acids are not accurately known from experiment, and only few data are available for glycine or alanine.[43−46] Therefore, we have optimized the geometries for the global and all local minima of glycine and alanine. Because of the additional α-substituent, the number of conformational minima becomes very large for serine and cysteine. Consequently, we only investigated some selected conformations for these two amino acids. Numerical frequency calculations were routinely employed to exclude saddle points. The calculations were performed using the gradient-corrected BLYP density functional as implemented in the ADF program package,[47] together with doubly polarized triple-ζ Slater-type basis sets. For each minimum structure, we carried out a four-component Dirac−Hartree−Fock calculation of the PNC energy shift, $E_{PNC}$, as shown in eq 4 using uncontracted cc-pVDZ+3p basis sets[28,48,49] with the DIRAC program package.[50] A more detailed description of the computational methods applied has previously been given by the authors.[48]

## 4. Results and Discussion

The gas-phase optimized global energy minimum structures for the amino acids are shown in Figure 1. All important

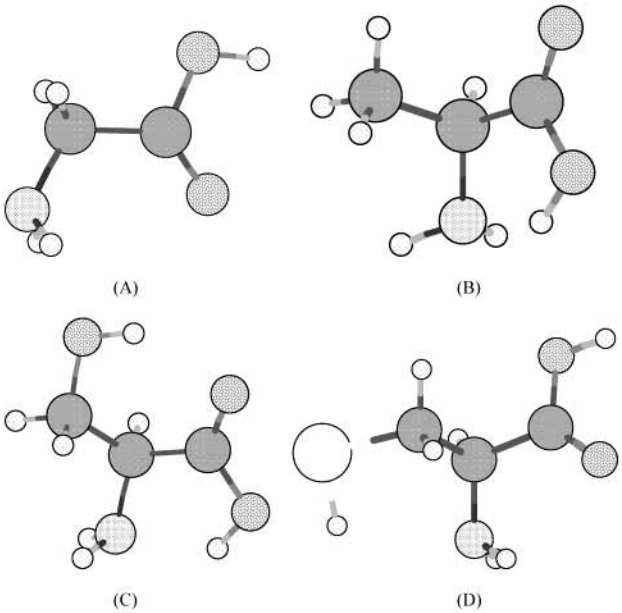


**Figure 1.** Global minima on the potential energy surface for (A) glycine, (B) alanine, (C) serine, and (D) cysteine in the gas phase. For atom labels, see Figure 3.

**TABLE 1: The Most Important Torsion Angles (in deg), Distances for Weak H-bonding within the Carboxyl Group, OH···O, or from the Carboxyl Group to the N Atom, OH···N (in Å), Energy Differences, $\Delta E$, Relative to the Global Minimum (in kJ mol$^{-1}$ at the BLYP Level), and the Parity Nonconserving Energy Shift, $E_{PNC}$ (in 10$^{-17}$ kJ mol$^{-1}$), for All Minima of Glycine[a]**

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| $C_1C_2NH$ | −58.2 | −139.7 | −61.6 | −177.0 | −67.6 |
| $C_1C_2NH'$ | 58.2 | 99.3 | 56.6 | −58.2 | 67.6 |
| $NC_2C_1$═O | 0 | −170.6 | 171.6 | −167.2 | 180 |
| $NC_2C_1$−O(H) | 180 | 10.6 | −9.4 | 15.1 | 0 |
| $C_2C_1OH$ | 0 | −2.1 | −178.6 | 178.2 | 0 |
| OH···N | 4.436 | 1.935 | 3.790 | 3.671 | 2.259 |
| OH···O | 2.319 | 3.014 | 2.304 | 2.305 | 3.024 |
| $\Delta E$ | 0 | 0.76 | 6.27 | 11.90 | 20.81 |
| $E_{PNC}$ | 0.00 | +0.17 | −3.91 | +5.36 | 0.0 |

[a] A negative sign of $E_{PNC}$ indicates a preferred stability of the given conformation with respect to its mirror image.

geometric parameters and the energy differences with respect to the global minimum for the local minima optimized structures are listed in Tables 1−4. The global and local minima obtained for glycine and alanine compare favorably with other studies,[51,52] for example, with Cao et al. using 6-311G** basis sets at the second-order Møller−Plesset level of theory.[53] For each structure, we carried out relativistic calculations of the PNC energy shift, $E_{PNC}$, which is also shown in the tables. For all global minima, we have $E_{PNC,L} \geq 0$. For alanine, serine, and cysteine, this implies that the D-structure is preferred energetically.

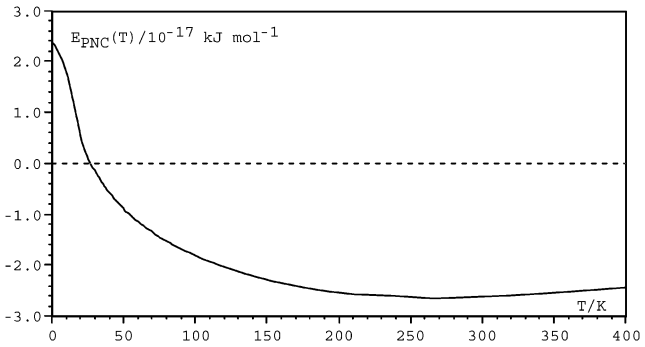


**Figure 2.** Parity nonconserving energy shift, $E_{PNC}$, for L-alanine as a function of the temperature $T$ obtained from a Boltzman distribution using the $\Delta E$ values given in Table 2.

Perhaps more important is that the preference for one enantiomeric form is critically dependent on the conformation chosen, especially that of the carboxylic acid group, which contains two of the heavier oxygen atoms, and there is no clear overall preference for one chiral form. That is, the chiral carbon center does not determine the overall stability of one enantiomer. The energy differences between L- and D-enantiomers for amino acids studied here are $|\Delta E_{L-D}| = |2E_{PNC,L}| = 10^{-17}-10^{-15}$ kJ mol$^{-1}$, which is more than 1 order of magnitude larger than the values previously published by Mason and Tranter.[21,22] This has been pointed out before.[28,29,54,55]

Another important point is that at certain conformations $E_{PNC} = 0$. This fact is well-known; for example, $E_{PNC}$ changes sign at a torsion angle close to 90° $H_2O_2$.[33] Hence, *nonzero* $E_{PNC}$ *implies chirality, but zero* $E_{PNC}$ *does not imply nonchirality.*

To address the problem as to whether one enantiomeric species is preferred over the other, the complete $3N - 6$ dimensional potential energy surface, $V(\vec{R})$, together with the PNC surface, $E_{PNC}(\vec{R})$, has to be known or simulated in molecular dynamics calculations to obtain the temperature-dependent function $E_{PNC}(T)$ through a Boltzman distribution. The data in both tables show that at least five or more torsion angles are needed to describe the important part of $E_{PNC}(\vec{R})$.[56] It is presently not feasible to calculate the complete hypersurface. We therefore decided to treat all minima for alanine within a Boltzman distribution, $f_j(\Delta E_i)$, with the $\Delta E_i$ values given in Table 2. From this, we obtain the dependence of $E_{PNC}(T)$ on the temperature $T$, which is shown in Figure 2. The Boltzman curve shows that the L-form of alanine is indeed preferred at temperatures $T > 28$ K. However, we note that this result is only of approximate nature and will critically depend on the accurate determination of the amino acid gas-phase structures. Also, it does not contain dynamic or quantum effects. We also

**TABLE 2: The Most Important Torsion Angles (in deg), Distances for Weak H-bonding within the Carboxyl Group, OH···O, or from the Carboxyl Group to the N Atom, OH···N (in Å), Energy Differences, $\Delta E$, Relative to the Global Minimum (in kJ mol$^{-1}$ at the BLYP Level), and the Parity Nonconserving Energy Shift, $E_{PNC}$ (in 10$^{-17}$ kJ mol$^{-1}$), for All Minima of L-Alanine[a]**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $C_1C_2NH$ | −95.0 | 94.9 | −58.3 | −58.5 | 43.7 | −34.5 | −52.3 | −57.7 | 65.6 | 56.3 | −60.2 | 42.0 | −30.4 |
| $C_1C_2NH'$ | 144.5 | −145.8 | 57.6 | 59.7 | 162.6 | −154.5 | 65.6 | −176.0 | −176.2 | −59.4 | 75.2 | 160.8 | −150.8 |
| $NC_2C_1$═O | 167.7 | −167.8 | −12.6 | 142.4 | −29.6 | 15.6 | −133.8 | −137.0 | 136.6 | −20.4 | 170.8 | −38.0 | 16.5 |
| $NC_2C_1$−O(H) | −13.4 | 14.3 | 167.4 | −38.8 | 152.7 | −167.0 | 47.0 | 45.6 | −46.2 | 160.5 | −9.0 | 144.8 | −166.7 |
| $C_2C_1OH$ | 2.7 | −3.7 | 179.2 | −177.9 | 176.8 | −177.0 | 179.5 | 178.8 | −178.7 | −2.4 | 1.0 | −6.9 | 6.0 |
| OH···N | 1.907 | 1.898 | 4.408 | 3.793 | 4.293 | 4.327 | 3.774 | 3.661 | 3.679 | 3.840 | 2.220 | 3.698 | 3.833 |
| OH···O | 3.011 | 3.010 | 2.309 | 2.303 | 2.310 | 2.300 | 2.300 | 2.303 | 2.310 | 3.038 | 3.021 | 3.033 | 3.033 |
| $\Delta E$ | 0.00 | 0.21 | 1.38 | 5.45 | 5.79 | 7.05 | 7.21 | 9.69 | 10.35 | 21.33 | 21.51 | 25.63 | 26.34 |
| $E_{PNC}$ | +2.5 | −5.9 | −6.7 | −8.9 | −14.9 | +12.1 | +20.0 | +13.8 | −12.8 | −15.8 | +1.3 | −33.3 | +24.6 |

[a] A negative sign of $E_{PNC}$ indicates a preferred stability of the L-enantiomer.

**TABLE 3: The Most Important Torsion Angles (in deg), Energy Differences, $\Delta E$, Relative to the Global Minimum (in kJ mol$^{-1}$ at the BLYP Level), and the Parity Nonconserving Energy Shift, $E_{PNC}$ (in $10^{-17}$ kJ mol$^{-1}$), for Selected Minima of L-Serine[a]**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $C_1C_2NH$ | −144.3 | −83.9 | −76.5 | −68.2 | −164.1 | −44.9 | −76.3 | −40.7 | 42.0 | −70.6 | −73.7 | −46.7 | −45.4 | −151.8 | 54.4 | −36.4 |
| $C_1C_2NH'$ | 95.5 | 33.5 | 42.6 | 50.6 | 78.8 | 70.9 | 40.1 | 75.7 | 161.4 | 47.2 | 44.0 | 71.2 | −166.0 | 90.2 | 174.0 | −155.1 |
| $NC_2C_1$=O | −167.0 | −13.7 | 163.6 | −152.2 | −78.2 | 3.0 | −7.8 | 5.0 | −24.1 | −56.8 | −46.4 | −176.6 | 23.8 | 108.8 | −50.9 | 33.7 |
| $NC_2C_1$−O(H) | 13.5 | 168.0 | −18.7 | 29.0 | 102.1 | 179.8 | 174.1 | −176.8 | 157.8 | 121.0 | 132.5 | 6.3 | −159.2 | −71.7 | 129.4 | −147.6 |
| $C_2C_1OH$ | −2.9 | 177.7 | −177.0 | 177.7 | −178.2 | −178.3 | 177.8 | −176.6 | 177.6 | −179.2 | 178.3 | 178.1 | −176.7 | 178.4 | 178.0 | −177.6 |
| $NC_2C_3O$ | −173.5 | −53.7 | −54.4 | −56.5 | 53.5 | 64.2 | −161.8 | 61.3 | −58.7 | 178.5 | −178.8 | 60.7 | −64.0 | 48.5 | −175.9 | −156.5 |
| $C_2C_3OH$ | −50.2 | 44.0 | 43.1 | 43.2 | 55.5 | −177.6 | −56.2 | 79.5 | 172.4 | 72.1 | −169.7 | 178.6 | 167.9 | 61.9 | −171.3 | −165.2 |
| $\Delta E$ | 0.0 | 0.54 | 7.14 | 9.91 | 11.52 | 11.91 | 12.74 | 13.04 | 14.35 | 14.72 | 15.05 | 15.43 | 16.17 | 18.39 | 19.67 | 25.61 |
| $E_{PNC}$ | +2.6 | −0.5 | −3.0 | +9.5 | −4.3 | −2.7 | −7.0 | +7.1 | −1.3 | −7.9 | −20.6 | +1.2 | +17.8 | −22.6 | −17.0 | +20.8 |

[a] Anegative sign of $E_{PNC}$ indicates a preferred stability of the L-enantiomer.

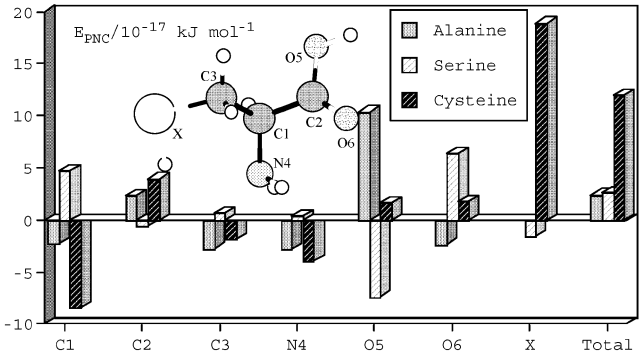


**Figure 3.** Individual atomic contributions to $E_{PNC}$ for L-alanine, L-serine, and L-cysteine. The very small contributions from the hydrogen atoms are not shown.

**TABLE 4: The Most Important Torsion Angles (in deg), Energy Differences, $\Delta E$, Relative to the Global Minimum (in kJ mol$^{-1}$ at the BLYP Level), and the Parity Nonconserving Energy Shift, $E_{PNC}$ (in $10^{-17}$ kJ mol$^{-1}$), for Selected Minima of L-Cysteine[a]**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| $C_1C_2NH$ | −78.2 | −49.0 | −51.8 | −74.8 | −94.0 | −71.3 | −71.8 |
| $C_1C_2NH'$ | 39.0 | 67.7 | 63.2 | 42.9 | 146.0 | 45.8 | 43.0 |
| $NC_2C_1$=O | −20.8 | −6.3 | 3.4 | −20.3 | 166.9 | −46.0 | −6.5 |
| $NC_2C_1$−O(H) | 160.5 | 172.2 | −179.6 | 160.7 | −14.5 | 132.5 | 172.0 |
| $C_2C_1OH$ | 178.0 | −179.0 | −178.0 | 178.5 | 3.5 | 178.7 | 10.3 |
| $NC_2C_3S$ | −63.8 | 60.9 | 62.3 | −59.6 | −167.2 | −174.0 | −168.7 |
| $C_2C_3SH$ | 50.4 | 71.7 | −82.5 | −143.0 | −49.4 | 179.0 | −99.9 |
| $\Delta E$ | 0.0 | 2.55 | 3.30 | 7.72 | 8.64 | 10.38 | 14.58 |
| $E_{PNC}$ | +11.9 | +1.5 | +24.8 | +5.6 | −3.1 | −21.2 | −43.6 |

[a] A negative sign of $E_{PNC}$ indicates a preferred stability of the L-enantiomer.

mention that electron correlation in the evaluation of eq 4 has to be taken into account for more precise PNC effects. It is currently not well-known how important such effects are for chiral molecules,[29] although for $H_2O_2$ and $H_2S_2$ they seem to be small at torsion angles where $E_{PNC}$ is large.[57,55]

Another important fact is that all heavy atoms in the amino acid contribute significantly to $E_{PNC}$ and not only the carbon chirality center as mentioned above, see Figure 3. This explains the sensitivity to the conformational structure. Moreover, our calculations reveal that the $E_{PNC}$ contribution to the carbon at the chirality center can change sign with varying torsion angles of the ligands. It is now evident that in the free amino acids secondary effects (ligand conformation) play an important role for the total $E_{PNC}$ contribution. The $Z^5$ scaling of PNC effects is illustrated in Figure 3, in which the largest single atomic contribution is from the heaviest nucleus, that is, that of sulfur in cystein. However, this sulfur contribution is not sufficient to make the cysteine $E_{PNC}$ values (Table 4) significantly larger than those for the other amino acids (Tables 2 and 3).

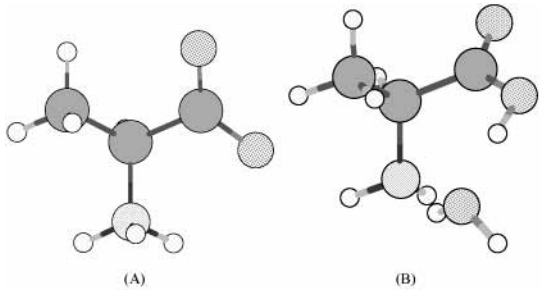


**Figure 4.** (A) Zwitterionic and (B) $H_2O$-coordinated form of L-alanine.

Prebiotic amino acid formation occurred most likely in aqueous solution, and water molecules coordinated to the amino acid can have a substantial influence on the PNC energy differences both directly and through the preferred amino acid conformations (see also the work by Berger and Quack[29]). Moreover, in early Precambrian time, surface water and oceans may have been slightly acidic (Freeland et al., 1999).[58] Hence, amino acids would also appear in the zwitterionic or protonated form. For the zwitterionic form (Figure 4A) of alanine, we used the structure published earlier by Tranter[22] because a complete geometry optimization reveals that such a structure is not stable toward H-shift from the protonated amine to the carboxylic acid group. This is in line with the findings of Jensen et al.,[59] who found that at least two water molecules are necessary to stabilize the zwitterionic form of glycine. Nevertheless, at torsion angles of 0°, 30°, 60°, and 90° (between the carboxylate and the C−($C_{CO_2}$)−H plane), we obtain $E_{PNC} = -28.9 \times 10^{-17}$, $-25.1 \times 10^{-17}$, $+7.9 \times 10^{-17}$, and $+34.4 \times 10^{-17}$ kJ mol$^{-1}$, which again are an order of magnitude larger than Tranter's results.[21,22] If we follow Tranter's argument that the preferred torsion angle in aqueous solution is 0°, then the L-structure is indeed preferred. However, this analysis does not include the influence of the solvent, which can be substantial. For example, if we attach just a single water molecule (of the whole hydratization sphere) to L-alanine (the optimized structure is shown in Figure 4B), the PNC contribution $E_{PNC}$ changes by $-1.7 \times 10^{-17}$ kJ mol$^{-1}$ (approximately 10%) upon coordination. Kikuchi and Wang[34] have also pointed out that the torsion angle employed by Tranter is without experimental support, although there is some theoretical evidence that for the zwitterionic species the optimal torsion angle in $\theta_{NCCO} = 0°$.[56,60] In a more recent paper, Kikuchi and co-workers explored the two-dimensional ($\theta$,$\phi$) hypersurface for zwitterionic alanine with $\theta$ being the NCOO and $\phi$ the HNCC torsion angle. Again, a Boltzman distribution over 96 conformations gave preference for D-alanine at 300 K.[31]

The preferential adsorption of one enantiomer on a chiral crystal surface is now well documented.[61−63] Here, we address a different problem, how PNC effects are influenced if amino acids are coordinated to metal ions or are adsorbed on surfaces. For example, in a recent paper by Strasdeit et al.,[64] it was argued

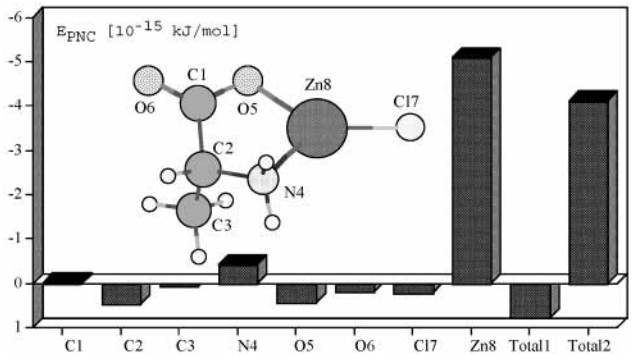


**Figure 5.** Individual atomic contributions to $E_{PNC}$ for deprotonated L-alanine, $CH_3CHNH_2CO_2^-$, coordinated to a $ZnCl^+$ unit. The very small contributions from the hydrogen atoms are not shown. Total1 denotes the total PNC contribution of the amino acid excluding Zn and Cl; Total2 contains all atomic PNC contributions.

that under prebiotic conditions amino acids might have been coordinated to metal ions such as $Ca^{2+}$ or $Zn^{2+}$ to form zinc and calcium acidates. To investigate how this might influence PNC effects, we modeled one of Strasdeit's compounds—alanine acidate coordinated to $ZnCl^+$—as shown in the optimized structure in Figure 5. The subsequent PNC calculations were quite CPU intensive because large uncontracted basis sets for Zn and Cl extended by additional high exponent s- and p-functions were used. The results are summarized in Figure 5, and we comment on the most important findings. First, the major PNC contribution now comes from the heaviest element involved, zinc. Second, while the amino acid unit gives a positive value for $E_{PNC}$ (preference for the D-form), coordination to the $ZnCl^+$ unit reverses the sign. This shows that PNC effects are very sensitive toward influence from the environment.

## 5. Conclusion

The most important conclusions for the amino acids studied here are as follows: (1) The chiral carbon center does not determine the sign of $\Delta E_{PNC}$, that is, the preference of one enantiomeric species. (2) Because the ligands attached to the chiral center contain heavier atoms such as oxygen or sulfur, they give larger PNC contributions and slight changes in the geometry may alter the sign of $\Delta E_{PNC}$.[34] (3) For the global minima investigated for alanine, serine, and cysteine, the D-form is stabilized due to PNC effects. (4) Environmental effects through coordination to heavier atoms such as zinc, copper, or calcium[64,65] or by adsorption on surfaces containing metals such as iron or nickel often found in thermal vents on the ocean floor[36,66] can completely determine which chiral form is to be preferred.

We conclude that because the exact prebiotic conditions when amino acids and peptides were formed are not known and can only be guessed,[67] the Yamagata hypothesis can neither be proved nor disproved and should be taken with great care when discussing experimental results such as the ones by Wang et al.[40] or in connection with other theories, such as the Salam hypothesis.[39] We will reexamine the Wang et al.[40] results and its connections to the Salam hypothesis in part II of our contribution. Moreover, the chronological sequence in early synthesis of biologically active molecules is less than clear, that is, we do not know which of the molecules came first, RNA, DNA, or proteins.[58,68] There is some evidence that RNA came first[69] and the Yamagata hypothesis should be applied to sugars rather than amino acids. Finally, we agree with Bonner's thesis[70] that there is currently no clear evidence for a causal connection between PNC and biomolecular homochirality. There are other more likely and more plausible scenarios for the origin of biomolecular homochirality on Earth involving, for example, propagation and evolutionary competition,[71,72] and it is questionable that symmetry breaking[73] occurred at the chemical and not at the biological stage of evolution.[74] The Yamagata hypothesis remains to be nothing more than pure speculation.

**Acknowledgment.** This work was supported through a James Cook fellowship by the Royal Society of New Zealand. R.N.C. thanks the National Science Foundation (U.S.A.) for support.

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