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Parity-Violating Energy Shift of Glycine, Alanine, and Serine in the Zwitterionic Forms: Calculation Using HFO-NG Basis Sets

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The parity-violating energy shift, E_{pv}, was calculated for glycine, alanine, and serine using the HFO-5G and -6G minimal basis sets, which were determined so as to well reproduce the behavior of an atomic orbital near the nucleus. A clear basis set dependence was observed in both the sign and magnitude of E_{pv}. For the zwitterionic form of glycine, the HFO-5G and -6G calculations gave an E_{pv} similar to that obtained by the (14,14/10) minimal basis set. For the most stable conformation of L-alanine, these basis set gave a negative E_{pv}, indicating that L-alanine is more stable than D-alanine, while the split-valence basis sets gave positive values. It was shown that L-serine is lower in energy than D-serine due to the parity-violating interaction for almost the entire range of the C–C rotation angle.

The parity-violating weak neutral current interaction between an electron and a nucleus causes an energy difference between mirror-image molecules.[1] This parity-violating energy difference can be the origin of the ubiquity of the L-amino acids and D-sugers in the biochemistry of living organisms.[2] Although this energy difference is very small, ca. 10^{-20} au, non-equilibrium thermodynamics considerations have shown that such a small energy difference is sufficient to reproduce the observable effect of chiral selection.[3] It is, thus, very interesting and important to evaluate this energy difference for biologically important molecules. In this respect, Hegstrom et al.[4] developed a method of evaluation for the parity-violating energy shift, E_{pv}, and gave formula which can be used along the molecular orbital theory:

$$E_{pv}=2\sum_{T}\frac{<\psi_0|H_{pv}|\psi_T><\psi_T|H_{so}|\psi_0>}{E_0-E_T}, \tag{1}$$

$$H_{pv}=-\Gamma\sum_{A}\sum_{i}Q_A\{\boldsymbol{p}_i\cdot\boldsymbol{s}_i,\ \delta^3(\boldsymbol{r}_i-\boldsymbol{r}_A)\}_+ \tag{2}$$

and

$$H_{so}=\sum_{A}\sum_{i}\zeta_A\boldsymbol{l}_{Ai}\cdot\boldsymbol{s}_i, \tag{3}$$

where T indicates the excited triplet state which mixes with the singlet ground state, ψ_0, through the spin-orbit coupling, H_{so}. Γ is a constant and Q_A is the Salam-Weinberg parameter[5] of atom A. This theory has been applied to biological molecules by Mason and Tranter.[6-8] They used ab initio MO methods with the 4-31G and 6-31G basis sets, and calculated E_{pv} for several amino acids[6] and the transition states for chirality producing step in chemical reactions.[7]

E_{pv} has a small magnitude and is expressed by the sum of terms which have similar magnitudes with different signs; a profound examination is necessary for any practical calculation of E_{pv}. Among the points to be considered, the basis set employed may be the most important, since each term appearing in the E_{pv} calculation is proportional to the function value of the s-type atomic orbital at each nucleus in the molecule,[4,6] $\chi_{ns}(0)$, which varies largely from one basis set to another. It has been pointed out[9] that a popular small basis set, such as STO-6G and 6-31G, may not properly be used for the E_{pv} calculation, since the function values of these basis sets at the nucleus are significantly different from those of Hartree-Fock atomic orbitals (Table 1). We have developed new minimal basis sets, HFO-NG (N=3—6), which give better bahavior near the nucleus than do other basis sets of comparable size.[10] This study reports the E_{pv} values of the zwitterionic forms of amino acids calculated by using new basis sets. The calculation was carried out according to the procedure given by Mason and Tranter.[6,9] The only exception is a calculation of the denominator in Eq. 1; Mason and Tranter used an approximate formula, while the correct formula was used in this study.

Table 1. Function Values of Radial Part of Oxygen Core(1s) and Valence(2s) Atomic Functions at the Nucleus[10]

Basis set	$R_{1s}(r=0)$	$R_{2s}(r=0)$
HFAO[a]	43.17	−9.80
(14,14/10)[b]	42.94	−9.74
HFO-5G	39.01	−8.23
HFO-6G	40.17	−8.04
STO-6G	39.84	0.36
6-31G[c]	41.99	0.37
4-31G[c]	40.11	0.29

a) Hartree-Fock orbitals given in Ref. 15. b) Gaussian functions given in Ref. 14. The 1s and 2s orbitals of an oxygen atom are expressed by 14 s-type primitive GTOs, while the 2p orbital is expressed by 10 p-type primitive GTOs. c) In the split-valence basis sets, the atomic orbital cannot be defined for the valence shell; the core function was assigned to the 1s orbital and the valence (2s) orbital was obtained by equivalent mixing of two valence functions.

Results and Discussion

The E_{pv} value was evaluated for glycine, alanine, and serine in the zwitterionic form. The E_{pv} values for these molecules have been reported by Mason and

Tranter.⁶⁾ The molecular structures employed here are the same as those used by them. The conformational change was considered only for rotation about the C–C bond, other molecular parameters being fixed at the assumed values. Figure 1 shows the E_{pv} values of glycine obtained with the STO-6G, 4-31G, 6-31G, HFO-5G, HFO-6G, and (14,14/10) basis set; the basis set dependence of E_{pv} was clearly observed. The (14,14/10) basis set comprises well-tempered Gaussian-type functions given by Huzinaga and Klobukowski.¹⁴⁾ We used this as a minimal basis set. For the sign of E_{pv} and the conformational dependence of E_{pv}, HFO-5G and HFO-6G gave results parallel to those of the (14,14/10) minimal basis set. The 4-31G and 6-31G basis set gave E_{pv} having a sign opposite to the (14,14/10) value for $-40<\theta<40$, where the moststable conformation of glycine is involved.¹⁶⁾

In the LCAO-MO expansion of Eq. 1, the nonvanishing terms involve one s-type atomic orbital;⁶⁾ in the present case, E_{pv} can be divided into two components (core (1s) and valence (2s) components) according to the s-orbital involved in the matrix element. Figure 2 shows the two components for glycine. The two components have opposite signs and the magnitude of the valence component is larger than the core component. As may be expected from Table 1, the N-31G calculation gives a very small 2s contribution; for the case of 6-31G, the contribution of the valence

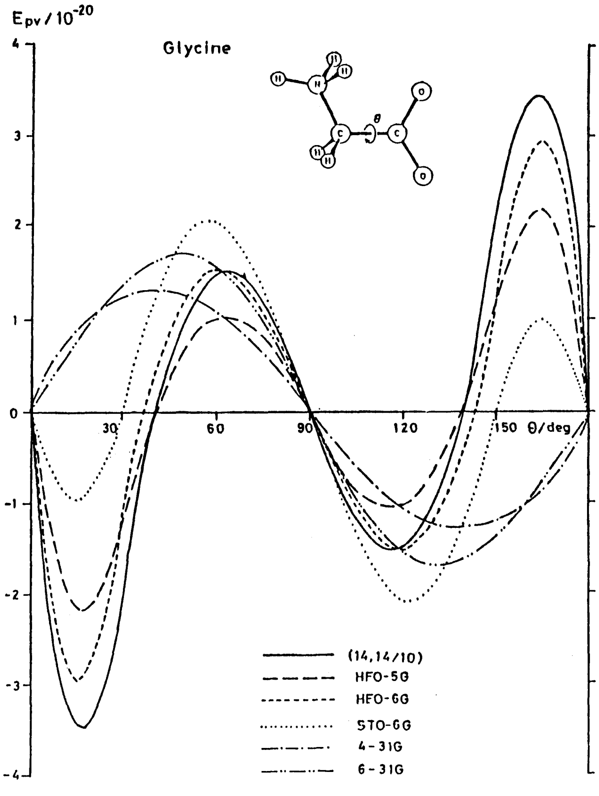

Fig. 1. The parity-violating energy shift, $E_{\mathrm{pv}}/10^{-20}$ au, of glycine as a function of rotation angle θ. The angle θ indicates the rotation of the CO$_2$ group and the cited conformation corresponds to θ=0. The molecular parameters used are same as those reported in Ref. 6. The 6-31G result is slightly different from that reported previously,⁶⁾ since the energy difference E_0-E_T in Eq. 1 was correctly evaluated in this study. If the approximate formula is used, the 6-31G values reported in Ref. 6 are obtained.

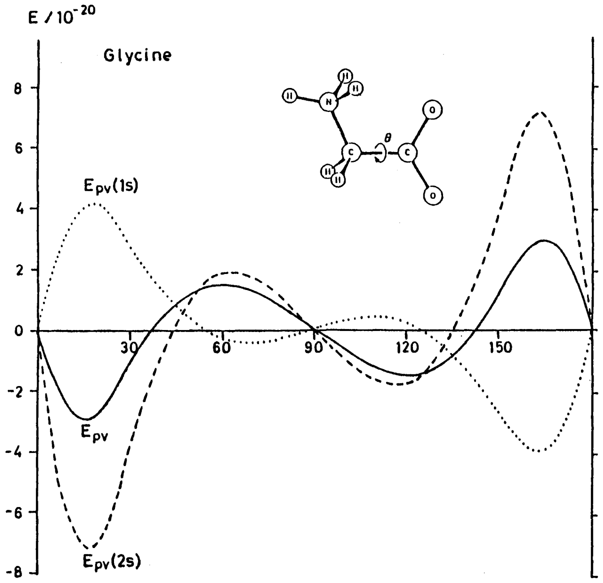

Fig. 2. The core (1s) and valence (2s) components of E_{pv} of glycine as a function of rotation angle θ. The HFO-6G results are presented.

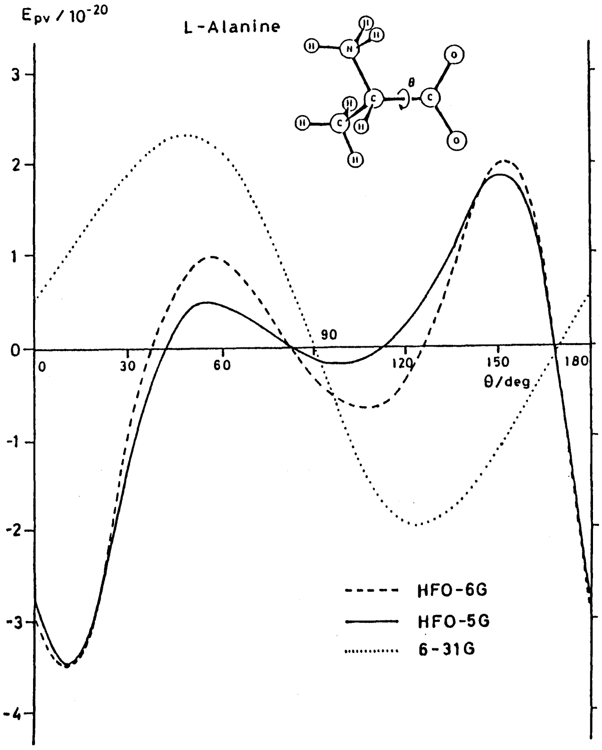

Fig. 3. The parity-violating energy shift, $E_{\mathrm{pv}}/10^{-20}$ au, of L-alanine as a function of rotation angle θ. See the caption of Fig. 1 for the definition of θ and for the 6-31G results.

(2s) functions was 1/4 of the core (1s) contribution. This is the reason why the drastic basis set dependence is observed in Fig. 2. Both HFO-5G and HFO-6G are better than the other basis sets of comparable size, provided that the (14,14/10) minimal basis set gives a correct E_{pv}.

The E_{pv} value of L-alanine is shown as a function of θ in Fig. 3. Both HFO-5G and HFO-6G gave similar E_{pv} values, while 6-31G gave a θ-dependence different from the HFO-NG one. The negative E_{pv} value indicates that L-alanine has a lower energy than does D-alanine by $2|E_{pv}|$. Since the sign of the calculated E_{pv} value depends on the θ angle, the preference of one enantiomer to the other can not be determined. However, if the conformational preference is taken into account, the L-alanine can be said to be more stable by a parity-violating neutral-current interaction, since E_{pv} is negative for $\theta=0$, where alanine is the most stable (Fig. 4). The conformation of amino acids in water is important for estimating the sign of E_{pv} for amino acids. There have been a few theoretical studies which address the conformation of zwitterionic amino acids in vacuo[17–19] and in water.[18,19] All of these have shown that the conformation with $\theta=0$ is the most stable in water as well as in vacuo for glycine, alanine, and serine. Thus, the present results indicate that the zwitterionic form of L-alanine has a lower energy than does the D-alanine in its most stable conformation.

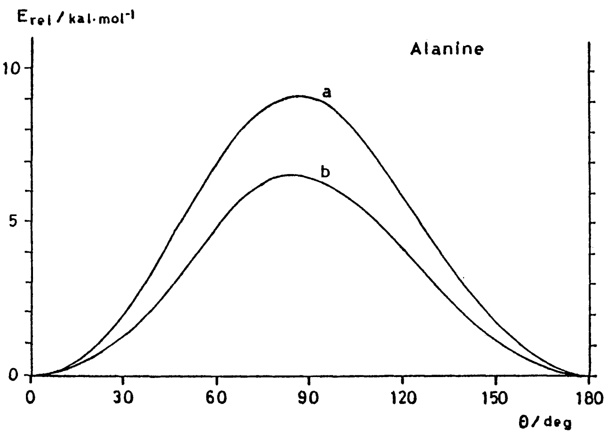

Fig. 4. Energy variation of L-alanine as a function of θ. a: 6-31G, b: HFO-6G.

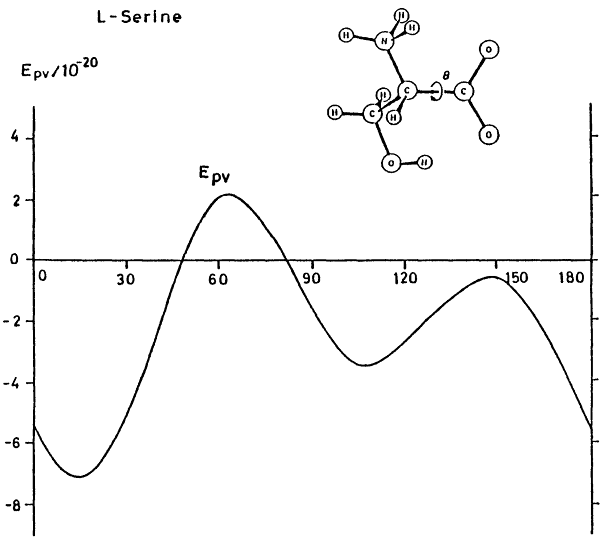

Fig. 5. The parity-violating energy shift, $E_{pv}/10^{-20}$ au, of L-serine as a function of rotation angle θ. See the caption of Fig. 1 for the definition of θ.

Mason and Tranter reported the same conclusion: "L-alanine is more stable than D-form in water by parity-violating interaction".[6] However, two points are different from the present results. They used the 6-31G basis set and obtained positive E_{pv} for $\theta=0$,[6] while the present calculation gave negative E_{pv} for $\theta=0$ (Fig. 3). Another point is the conformation of alanine adopted for the stable form. Mason and Tranter adopted a conformation with $\theta=120°$ ($\phi=0$ for their definition) as the conformation of alanine in water, which gives a negative E_{pv} value, but has no experimental or theoretical support. Thus, the present HFO-NG calculation is the first to show that L-alanine has a lower energy than D-alanine in its lowest-energy conformation.

Figure 5 shows E_{pv} of L-serine which was obtained by an HFO-5G calculation. The θ dependence of E_{pv} is similar to that observed in glycine and L-alanine. L-serine has the lowest energy in water when $\theta=0$, and is expected to have a slightly lower energy than the D-form due to the parity-violating interaction. Interestingly, E_{pv} of L-serine is negative for most θ. This may indicate that L-enantiomer has a lower energy than D-enantiomer in most parts of the conformational hypersurface. This conclusion, however, can be obtained after a more detailed examination of E_{pv} of L-serine, since the CH_2OH conformation must also be examined.

Although this study has shown the effect of the basis set on the parity-violating energy shift, it is not the main purpose of this study to generally discuss the efficiency of the basis sets for calculations of the molecular properties. The HFO-5G and -6G basis sets are small minimal basis sets and may be worse than the split-valence ones listed in Table 1 for the evaluation of the energy and molecular structures.[10] However, the HFO-5G and -6G basis sets represent the wavefunction well at the nuclei, which is essential for the E_{pv} calculation. The excitation energy and the spin-orbit coupling matrix in Eq. 1 are also important in the E_{pv} calculation, and a careful examination should be made for the evaluation of these quantities before any final quantitative E_{pv} values are determined.

It may be difficult to conclude which enantiomer of an amino acid is more stable by the parity-violating interaction, since the sign of E_{pv} depends on the conformation of the amino acid. Thus, a meaningful energy difference between enantiomers caused by the parity-violating interaction is obtained if E_{pv} has a definite sign over all of the conformational hypersurface of the molecule. The present results suggest that such a situation can not be encountered for small molecules in which the conformational change causes a change in the molecular skeleton and, then, a change in the E_{pv} sign. A meaningful energy difference can be obtained in the case of a large molecule with a rigid molecular skeleton.

As a more relaxed restriction, the E_{pv} value for the minimum-energy conformation can be used to determine a more stable enantiomer. In this case, the HFO-5G and HFO-6G calculations suggest that L-alanine and L-serine have a lower energy than do the corresponding D-forms by the varity-violating interaction, since the zwitterionic forms has negative E_{pv} values for the lowest-energy conformation at $\theta=0$.

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