Theoretical study on the nature of the hydrogen bonds in an α-helical polymer and its model systems

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The semi-empirical CNDO/2 SCF (self-consistent field) MO (molecular orbital) method using the tight-binding approximation for polymers was applied to polyglycine. The CNDO/2 calculations were also performed on model systems of this polymer. From the calculated results, the characteristics of the hydrogen bond in the α-helix were derived by comparison with those in the model systems. It was found that the hydrogen bond in the α-helix is very stable against proton transfer whereas the hydrogen bond in the model system is not so stable; this characteristic difference between the two systems is due to the coupling of two π-electron systems through hydrogen bonding in the α-helix.

Keywords Hydrogen bond; proton transfer; CNDO/2; α-helix; polyglycine

INTRODUCTION

It is well known that an α-helix plays an important role in the determination of the molecular conformation of protein, since this helix constitutes the backbone of the protein[1]. The structure of the α-helix is very well known[2] and is shown in *Figure 1*. The α-helix has many hydrogen bonds in its inner part and these hydrogen bonds stabilize the α-helix. In the present article, the nature of the hydrogen bonding in the α-helix was studied by using a molecular orbital (MO) method in comparison with the usual hydrogen bonding in the model systems.

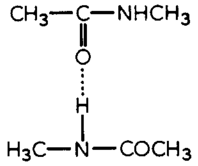
The molecular orbital approach to the study of the electronic structures of polymers has been followed extensively by using the tight-binding approximation[3] with various types of molecular orbital methods, such as extended Hückel[4] CNDO/2[5], MNDO[6] and *ab initio* methods[7]. We have also studied the electronic structure of various poly(amino acid)s[5,8–10] using the tight-binding approximation with the CNDO/2 method[11]. In the present paper, the properties of the hydrogen bond in the α-helix were discovered from the theoretical point of view.

METHODS OF CALCULATION

The potential curve for proton transfer was calculated to obtain a measure of the stability of the system. It should be mentioned that the potential curve for proton transfer is not always a good and quantitative measure for the stability of various chemical processes. However, this curve gives qualitatively the stability for the hydrogen bond systems.

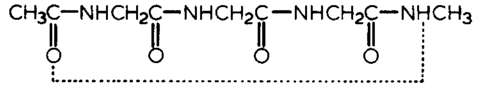
For the MO calculations, the CNDO/2 method was used[11]. We tried to show the characteristic feature of the hydrogen bond in the α-helix by comparing the potential curve for proton transfer in the hydrogen bond system in the α-helix with that in the usual hydrogen bond system. The hydrogen bond system of an oligomer and a dimer of *N*-methyl acetamide was calculated as a model for the usual hydrogen bond system.

By comparing the hydrogen bond system in the oligomer with that in the dimer, the effect of environmental atoms which surround the hydrogen bonds in the α-helix on the potential curve for proton transfer can be evaluated. Next, the polymer effect of the hydrogen bond system on the potential curve can be assessed in comparison with the energy of polyglycine in the α-helical form with that in the oligomer. In the following calculations, two molecules of *N*-methyl acetamide were used as the model system for the dimer as shown below:



$$\begin{array}{c} CH_3-C-NHCH_3 \\ \| \\ O \\ \vdots \\ H \\ | \\ H_3C-N-COCH_3 \end{array}$$

As mentioned in the previous paragraph, the positions of these molecules coincide with those of glycyl residue in a polymer with α-helical conformation. The following model system was used for the calculation of the oligomer:



$$CH_3\underset{\overset{\|}{O}}{C}-NHCH_2\underset{\overset{\|}{O}}{C}-NHCH_2\underset{\overset{\|}{O}}{C}-NHCH_2\underset{\overset{\|}{O}}{C}-NHCH_3$$

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In these cases the positions of atoms concerned are coincident with those of glycyl residue in a polymer with α-helical conformation, and the hydrogen bond part N–H…O was assumed to be linear. All other geometric parameters are the same as those in the previous paper[5] and numerical calculations were performed according to the procedure described in the previous papers[5,12].

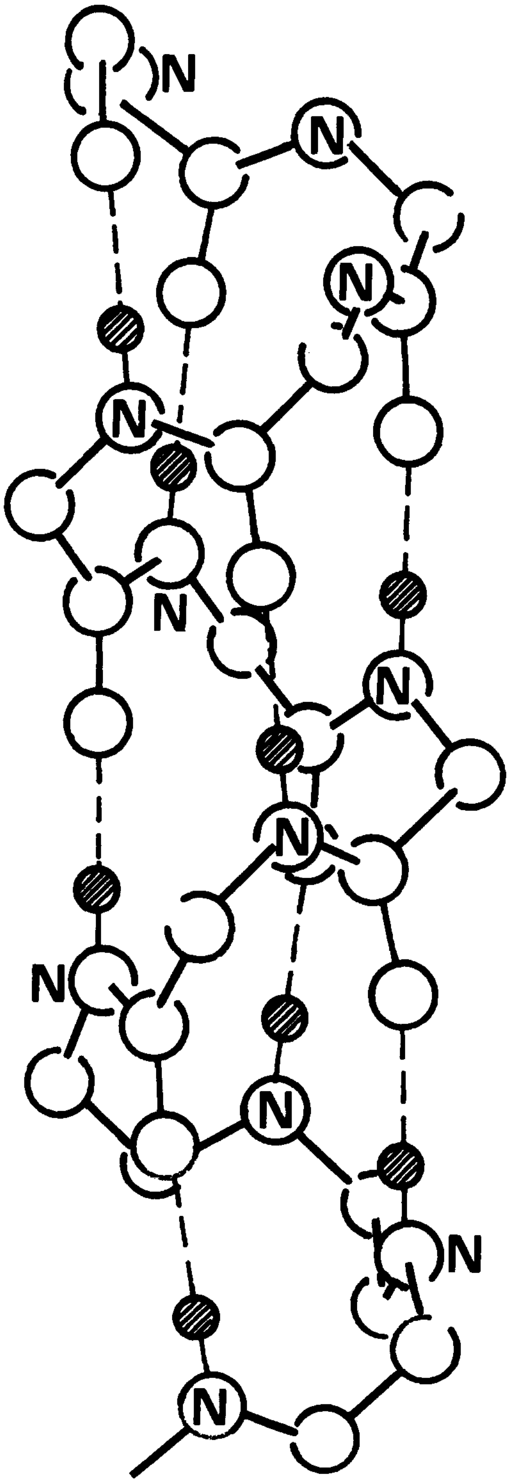


Figure 1 Schematic structure of α-helix: polyglycine. ▨, hydrogen

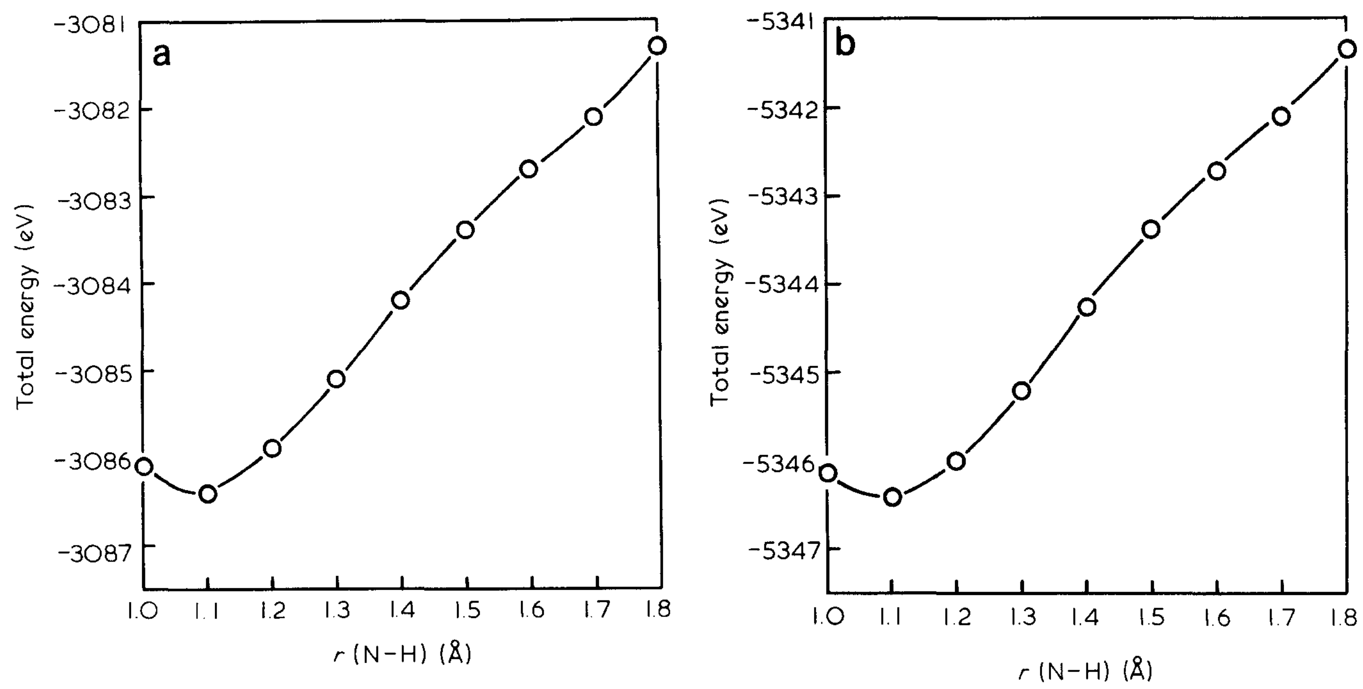
RESULTS AND DISCUSSION

First of all, we performed calculations on the electronic structure of the hydrogen bonds in the dimer and oligomer. In the present study, we have tried to pick out the properties of the hydrogen bond system from the potential curve for proton transfer. The obtained potential curves of the dimer, oligomer and the polymer are given in *Figure 2.* The estimated bond length *r*(N–H) in N–H…O hydrogen bonding is around 1.1 Å and this is in a good agreement with *ab initio* calculations[13] for hydrogen bonding and with the experimental value[2]. From *Figure 2* it is clear that the polymer has a double minimum while the dimer and oligomer have no double minimum in the curves. It is obvious that the potential curve for the dimer is similar to that for the oligomer. This result indicates that atoms surrounding the hydrogen bond have little effect on the potential curve for proton transfer. On the other hand, the remarkable difference in the shape of the potential curve between the oligomer and the polymer can be attributed to the interaction between hydrogen bonding systems in the polymer. This problem will be discussed later. However, in the polymer, all of the protons in the hydrogen bond system were transferred simultaneously. Thus, the above-mentioned proton transfer required much energy and it probably would not be of frequent occurrence.

In order to see in more detail the nature of the hydrogen bonding system, the change in the charge distribution upon proton transfer is very helpful and is listed in *Table 1* for the oligomer. The charge on the oxygen atom in the proton acceptor decreases due to hydrogen bond formation through the transferred proton. The characteristic feature is the remarkable increase in the negative charge on the oxygen and nitrogen atoms in the proton donating group. This indicates that the leaving proton has positive charge and thus nitrogen has negative charge in the proton donating group. This tendency should increase the potential energy in the proton transferred state. On the other hand, α-helical polymer has a periodicity in its helical chain. Thus such a charge separation cannot occur in the α-helical polymer as shown in *Table 2.* Thus, this tendency may probably give the double well potential in the polymer for proton transfer.

We are now in a position to investigate the hydrogen bond in the α-helical polymer in more detail. For this purpose, we consider the following model. That is, at first, the proton in every alternate segment is allowed to transfer, while the proton in the other alternate segment is not allowed to transfer as is shown in *Figure 3.* After transferring every alternate proton, the remaining protons are allowed to move. The potential map for proton transfer in the α-helical polymer is shown in *Figure 4.* In this map, the total energy of the polymer with various N—H bond distances is shown. From this result, it can be shown that simultaneous movement of the two sets of protons is energetically unfavourable. Therefore, proton transfer should occur along the dotted line.

In *Figure 5,* three potential curves are given corresponding to proton transfer in all segments, in every alternate segment, and in the other remaining segment. From this result, it is clear that proton transfer in every alternate segment hardly ever occurs. In other words, the α-helix is very stable for proton transfer in every alternate segment. On the other hand, proton transfer in all segments should not realistically occur. As a result, it can



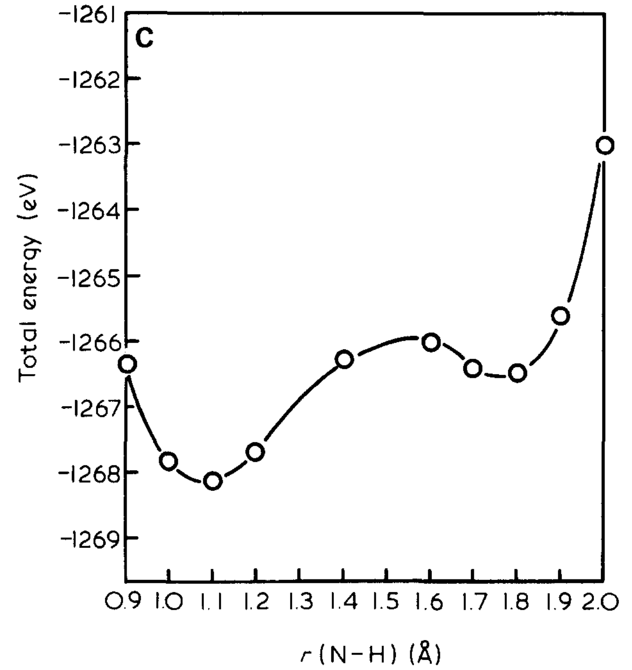


Figure 2 Total energy (eV) as a function of N–H distance (Å) in the N–H...O hydrogen bonding system in (a) dimer, (b) oligomer, and (c) polymer, polyglycine. N...O distance was fixed as 2.824 Å

Table 1 Change in the charge distribution as a function of the N–H distance (A) upon proton transfer in the case of oligomer

	1.1	1.2	1.4	1.6	1.8
C[a]	0.369	0.372	0.391	0.428	0.467
O[a]	–0.371	–0.368	–0.361	–0.336	–0.289
N[a]	–0.187	–0.187	–0.183	–0.172	–0.153
H[a]	0.105	0.107	0.114	0.129	0.148
C[b]	0.356	0.356	0.356	0.354	0.346
O[b]	–0.360	–0.362	–0.376	–0.408	–0.448
N[b]	–0.208	–0.218	–0.268	–0.367	–0.469
H[b]	0.152	0.161	0.205	0.284	0.349

[a] Proton accepting group
[b] Proton donating group

Table 2 Change in the charge distribution as a function of the N–H distance (A) upon proton transfer in the case of polymer

	1,1	1.2	1.4	1.6	1.8
C	0.371	0.376	0.399	0.406	0.393
O	–0.382	–0.387	–0.400	–0.354	–0.308
N	–0.214	–0.226	–0.294	–0.378	–0.372
H	0.159	0.175	0.251	0.299	0.261

be said that the hydrogen bonds in the α-helical polymer should be stable for proton transfer.

In order to see why proton transfer in every alternate segment is difficult, the change in the charge distribution on the atoms upon proton transfer is shown in *Table 3*. This result shows that the charge distribution changes remarkably not only for the proton transferred hydrogen bond but also for the hydrogen bond whose proton does not transfer. In other words, two hydrogen bonding systems are coupled with each other to protect the proton transfer, leading to the stabilizing character of the hydrogen bond in the α-helix. The change in the charge distribution for the remaining proton transfer is given in *Table 4*. As can be easily understood by comparing *Tables 3* and *4*, the remaining proton is quite ready to transfer, that is, proton accepting carbonyl oxygen has remarkable negative charge at the beginning of proton transfer. This result corresponds well with the lowering of the potential barrier for proton transfer. From these calculations, it was found that the coupling of the two hydrogen bonding systems through a π-electron system, that is, a peptide group, plays a very important role in stabilizing the α-helix of the peptide.

CONCLUDING REMARKS

The adiabatic potential energy in proton transfer in the dimer is slightly different from that in the oligomer due to the polarization energy of the surrounding backbone and is remarkably different from that in the polymer due to the polarization energy of the surrounding backbone and the interaction between hydrogen bonds. These effects can also be shown in the charge distribution on the atoms as shown in *Tables 1* and *2*.

From the calculations in the α-helical polymer, it can be said that occurrence of proton transfer in each segment is

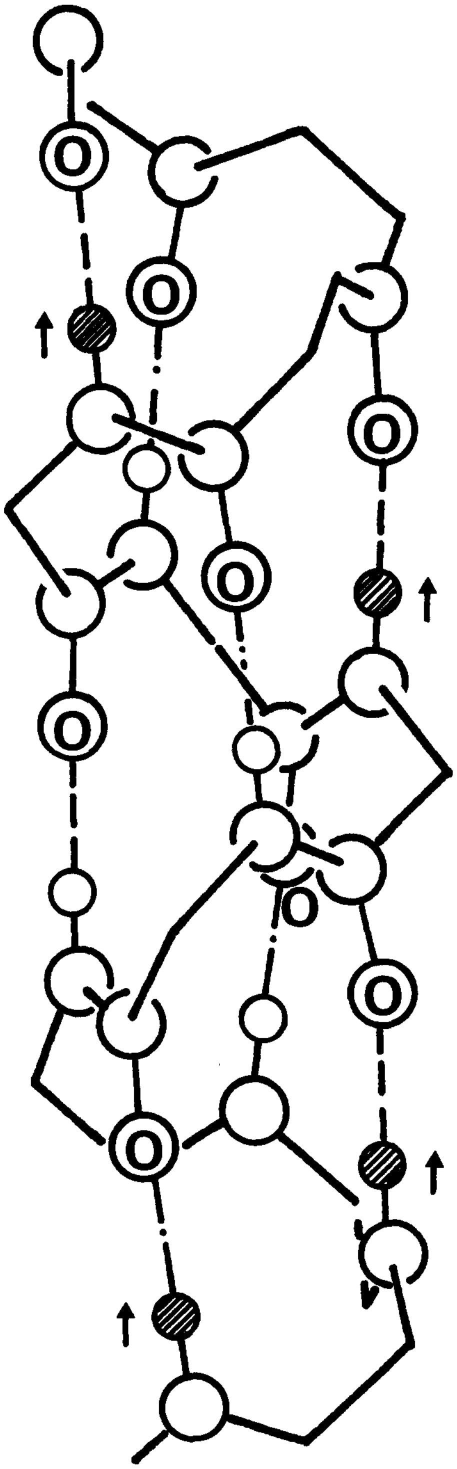


Figure 3 Proton transfer model in every alternate segment

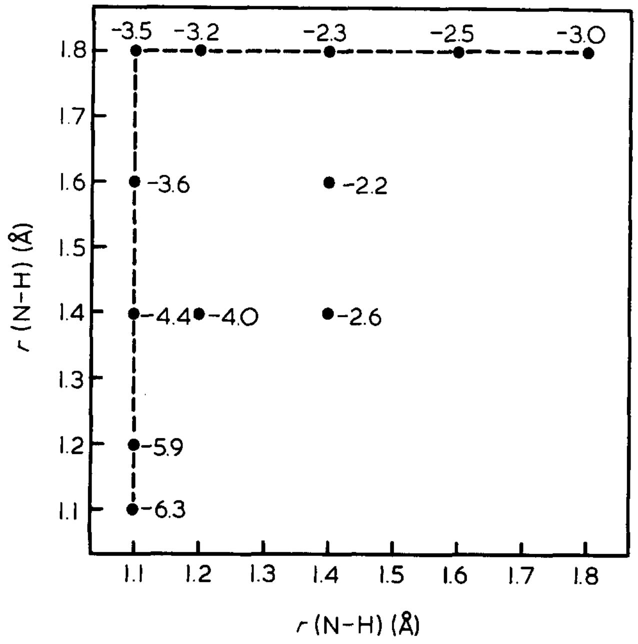


Figure 4 Two dimensional display of the total energy (eV) as a function of N–H distance (Å) in the N–H...O hydrogen bonding system in α-helix, polyglycine. N...O distance was fixed as 2.824 Å. Figures are the difference from the value of −2530.0 eV; here two monomer units are considered as a segment. See also text and *Figure 3*

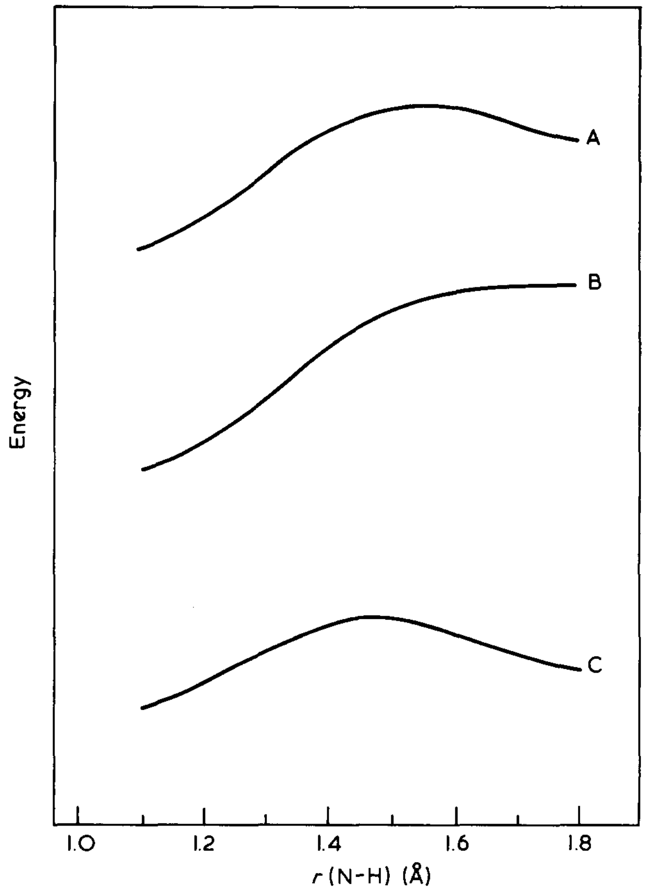


Figure 5 Schematic display of total energy as a function of N–H distance (Å) in the N–H...O hydrogen bonding system in polymer, polyglycine. N...O distance was fixed as 2.824 Å. Scale of energy is arbitrary. (a) Proton transfer in all segments. (b) Proton transfer in every alternate segment. (c) Proton transfer in all remaining segments

Table 3 Change in the charge distribution as a function of the N–H distance (Å) upon proton transfer in every alternate segment* in polymer

	1.1	1.2	1.4	1.6	1.8
N^a	–0.216	–0.218	–0.215	–0.204	–0.189
H^a	0.166	0.168	0.176	0.195	0.210
C^b	0.365	0.363	0.361	0.353	0.343
O^b	–0.389	–0.391	–0.411	–0.451	–0.477
N^b	–0.210	–0.226	–0.292	–0.403	–0.449
H^b	0.168	0.183	0.251	0.327	0.316
C^a	0.370	0.375	0.399	0.438	0.453
O^a	–0.387	–0.386	–0.386	–0.347	–0.290

* The other N–H bond in every alternate segment is fixed at 1.1 Å
[a] Proton accepting group
[b] Proton donating group

Table 4 Change in the charge distribution as a function of the N–H distance (Å) upon proton transfer in all remaining segments* in polymer

	1.1	1.2	1.4	1.6	1.8
N^a	–0.189	–0.207	–0.280	–0.354	–0.368
H^a	0.210	0.233	0.298	0.309	0.275
C^b	0.343	0.349	0.368	0.383	0.380
O^b	–0.477	–0.477	–0.457	–0.381	–0.327
N^b	–0.449	–0.445	–0.423	–0.383	–0.356
H^b	0.316	0.312	0.301	0.284	0.276
C^a	0.453	0.450	0.434	0.407	0.391
O^a	–0.290	–0.293	–0.304	–0.319	–0.325

* The other N–H bond in every alternate segment is fixed at 1.8 Å
[a] Proton donating group
[b] Proton accepting group

not easy, proton transfer in alternate segments is very difficult and proton transfer in the remaining group is easy. Therefore, a proton in the α-helical polymer is very stable. As a result, proton transfer in each segment simultaneously is not credible.

From the charge distribution on the atoms, we found that the neighbouring two hydrogen bonding systems couple with each other through the π-electron system of the peptide group when proton transfer occurs in every alternate segment. This first proton transfer makes it easy to move a proton in the other alternate hydrogen bonding system. This may be considered as a kind of cooperativity.

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