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Proton Migration in Proton Cryptate: A Molecular Orbital Study on a Proton Cryptate Model

HIDEAKI UMEYAMA

School of Pharmaceutical Sciences, Kitasato University[1)]

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Proton migration in a model of the proton cryptate was studied from a quantum chemical point of view. The barrier to proton transfer in the model is 13 kcal/mol. This result is consistent with experimental findings which suggest that the proton is jumping back and forwards in the proton cryptate. Since the barrier height for proton transfer is 41 kcal/mol in the absence of the three ether groups, the three oxygen lone pairs play a significant role in lowering the barrier to proton transfer. A migration map of the proton transfer is presented, and the paths of migration are shown. Moreover, the migration paths are analyzed by the energy decomposition method.

Keywords——quantum chemistry; *ab initio*; structure; molecular orbital; MO; proton transfer; cryptate; proton cryptate; inclusion compound; 1,6-diazabicyclo-[5,5,5] type

Cheny and Lehn synthesized compounds of the 1,6-diazabicyclo[5,5,5] type, and the tertiary mono- and di-ammonium salts have been obtained in which the protons are "cryptated," *i.e.* located inside the molecular cavity.[2)] The structure in which a single proton is shielded in the cryptate is shown in Fig. 1. The two nitrogens are separated by *ca.* 3.5 Å, and NMR experiments suggest that the proton is probably not located symmetrically between the two nitrogens but jumps rapidly from one to the other.[2)] In this paper the transfer path of the single proton is studied from a quantum chemical point of view.

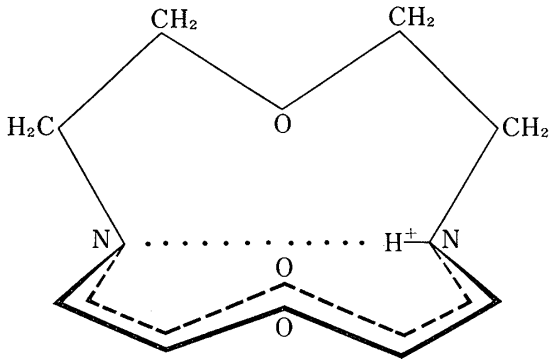


Fig. 1. Structure of the Proton Cryptate

Method

All the calculations were performed within the framework of the closed-shell single determinant LCAO-SCF-MO theory. The GAUSSIAN 70 program was used as a nonempirical method.[3)] A 4-31G basis set was used.[4)] Calculations were carried out using a HITAC M-180 computer at the Institute for Molecular Science. The method of energy decomposition analyses of the proton affinity was the same as that described in another paper.[5)] The energy of the proton affinity, ΔE, can be decomposed into four terms as follows.

$$\Delta E = ES + CT + PL + MIX$$

where ES is electrostatic energy, CT is charge transfer energy, PL is polarization energy, and MIX is coupling energy.

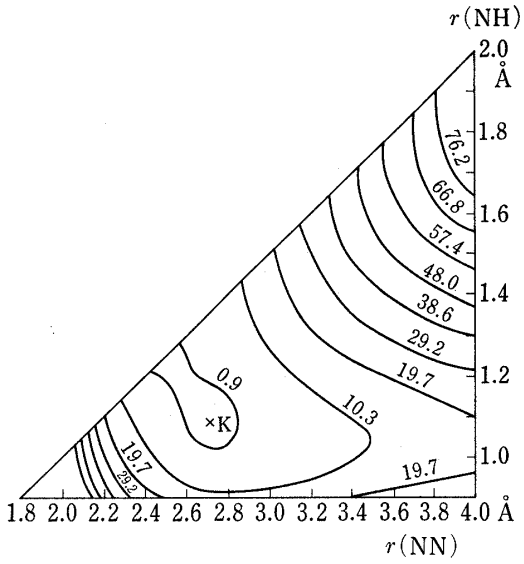
1) Location: *9-1, Shirokane 5-chome, Minato-ku, Tokyo 108, Japan.*
2) J. Cheny and J.M. Lehn, *J.C.S. Chem. Comm.*, **1972**, 487.
3) W.J. Hehre, W.A. Lathan, R. Ditchfield, M.D. Newton, and J.A. Pople, GAUSSIAN 70 Program 236, Quantum Chemistry Program Exchange, Indiana University, 1973.
4) R. Ditchfield, W.J. Hehre, and J.A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).
5) H. Umeyama and K. Morokuma, *J. Am. Chem. Soc.*, **98**, 4400 (1976).

Geometris——For NH_3, r(NH) is 1.0124 Å, and $\angle XNH = 112.14°$, where X is positioned in the direction of the lone pair orbital.[6] For H_2O, r(OH) is 0.956 Å, and $\angle HOH$ is 105.2°.[6]

Results and Discussion

Structure of $H_3N\cdots H^+\cdots NH_3$

A single proton is thought to jump between two nitrogens in the proton cryptate.[2] Calculations of the proton affinity of the two nitrogen lone pairs alone were performed in connection with the proton jump in the proton cryptate. The structure, $H_3N\cdots NH_3$, is composed of two ammonia molecules which are assumed to be rigid in the calculations. Figure 2 shows the potential energy map for the total energy of the structure, $H_3N\cdots H^+\cdots NH_3$. The structure is most stable at the K position, where r (NN) and r (NH) are 2.71 and 1.094 Å, respectively. The energies relative to that at the K position are shown in Fig. 2. Next, the geometries of the ammonia molecules, which were assumed to be rigid in the above calculations, were changed in the optimization process. The structure obtained is shown in Fig. 3. The optimized structure was calculated to be asymmetric. Electrons transfer from N^1H_3 to $N^2H_4^+$, and the value is 0.112. r (N^2H) is longer than r (N^1H) by 0.076 Å. Experimentally, r (NH) in isolated NH_4^+ is longer than that in isolated NH_3 by 0.02 Å.[7] In order to calculate the barrier to proton transfer, the symmetric structure with $r(N^1H)=r(N^2H)$ was optimized. The geometries and the total electron densities are shown in Fig. 4. The distance $r(N^1N^2)$ is 2.59 Å, and is shorter by 0.16 Å than that in the asymmetric structure. The symmetric structure was less stable than the asymmetric one by 1.82 kcal/mol. Marlet *et al.* calculated the barrier height to be 3.5 kcal/mol in the case of fixed equilibrium positions of the two nitrogens.[8] The barrier height of proton transfer in the optimized structure is smaller by 1.7 kcal/mol than that in the fixed geometry.



Total energy of K: −112.6114 hartrees
K: (2.71, 1.094)

Fig. 2. Potential Energy Map in kcal/mol of the Structure, $H_3N..H^+..NH_3$, Relative to the Total Energy at the K Position

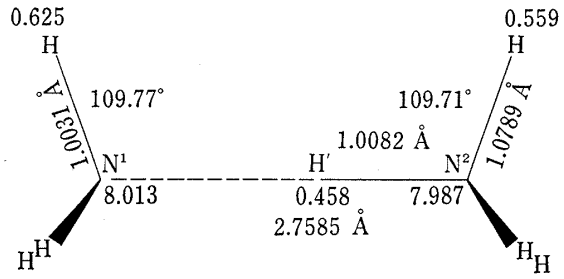


Fig. 3. Optimized Structure of $H_3N..H^+..NH_3$ and the Total Electron Densities

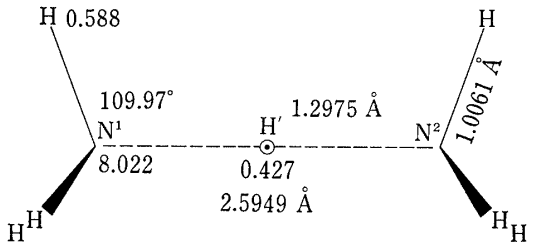


Fig. 4. Optimized Structure of $H_3N..H^+..NH_3$ with the Symmetric Structure and the Total Electron Densities

6) G. Herzberg, "Electronic Spectra of Polyatomic Molecules," Van Nostrand, New York, N.Y., 1966.
7) L.E. Sutton, "Tables of Interatomic Distances and Configurations in Molecules and Ions," The Chemical Society, London, 1958.
8) P. Marlet, S.D. Peyerimhoff, and R.J. Buenker, *J. Am. Chem. Soc.*, **94**, 8301 (1972).

The potential energy map of the proton affinity of $H_3N\cdots NH_3$ for various r(NN) and r(NH) is shown in Fig. 5. The energy of the proton affinity is greatest at a distance of about 2.4 Å for r(NN). At a distance of 3.5 Å for r(NN), the barrier to proton transfer was calculated to be 40.8 kcal/mol. Since the barrier is very large, the proton in the proton crytate will not jump rapidly back and forth between two nitrogens without a catalyst. The potential energy maps of the ES and CT terms are shown in Figs. 6 and 7. In Fig. 6 ES is greatest at a distance of about 2.6 Å for r(NN), and the proton is placed in a symmetric position. At r(NN) distances less than 2.8 Å, the symmetric structure for the proton is more stable. In Fig. 7, as the distance r(NH) decreases at a given distance of r(NN), the CT value increases. The potential energy map of the proton affinity can be considered as the sum of the two potential energy maps in Figs. 6 and 7, because the values of the *PL* and *MIX* terms are small in comparison with those of *CT* and *ES*.

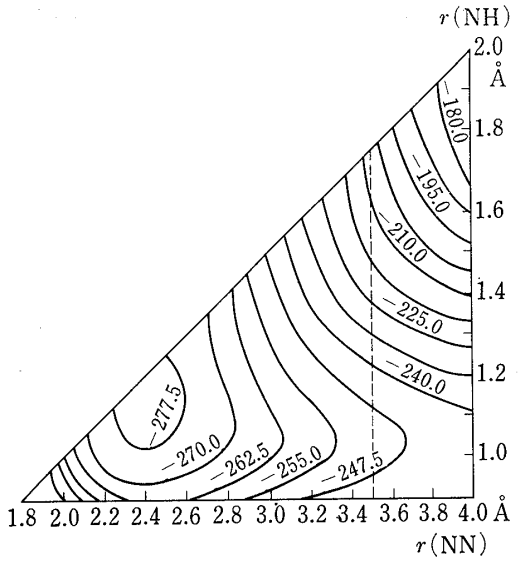


Fig. 5. Potential Energy Map in kcal/mol of the Proton Affinity of $H_3N\cdot\cdot NH_3$

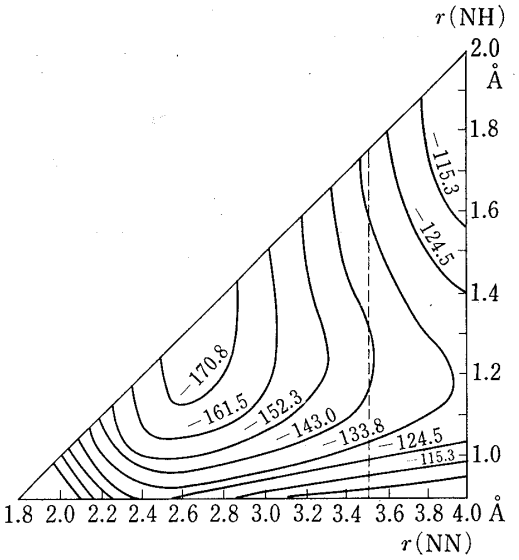


Fig. 6. Potential Energy Map in kcal/mol of ES in the Proton Affinity of $H_3N\cdot\cdot NH_3$

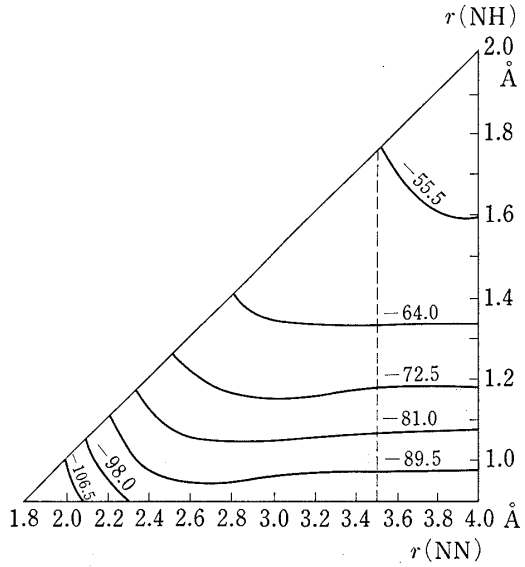


Fig. 7. Potential Energy Map in kcal/mol of CT in the Proton Affinity of $H_3N\cdot\cdot NH_3$

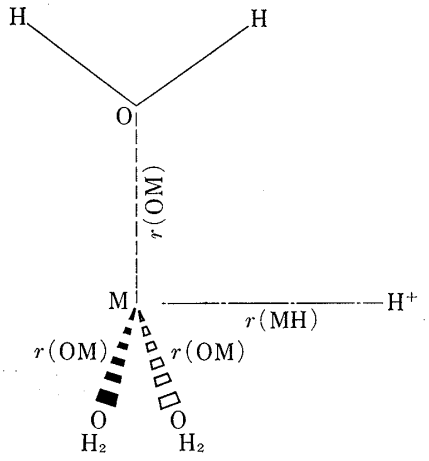
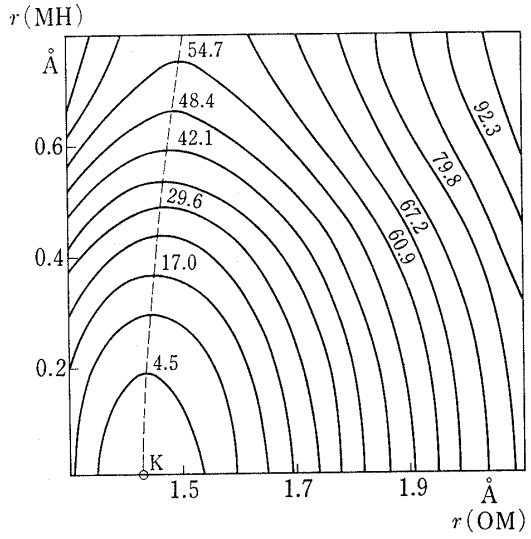


Fig. 8. D_{3h} Structure of $(H_2O)_3$

Structure of $(H_2O)_3H^+$

Three ether oxygens are included in the proton cryptate structure. Judging from a CPK model, the three oxygens come inside the van der Waals distance. Three water molecules are used in place of the three ethers in Fig. 8. The position M is the midpoint of the three oxygens. The conformation of the three water molecules is assumed to have D_{3h} symmetry. In the proton cryptate model, the proton passes through regions near the three water molecules. In order to determine the geometry under the assumed D_{3h} symmetry, energies of $(H_2O)_3H^+$ were calculated for the various forms. Figure 9 shows the potential energy map of $(H_2O)_3H^+$. The energies of the various forms relative to that at K position, where the values of r(OM) and r(MH) are 1.43 and 0.0 Å, respectively, are shown. The K position was obtained as a result of the calculations. When the proton approaches the M position, the value of r(OM) where the total energy is more stable at a given value of r(MH) changes from about 1.5 to 1.43 Å, as shown by the broken line. The structure at the K position is shown in Fig. 10. Next, the proton in the structure in Fig. 10 is moved from the M position towards one of the three oxygens, changing the distance r(OM); the optimized structure is shown in Fig. 11. The distances r(OH) and r(OM) are 1.0 and 1.53 Å, respectively. The structure shown in Fig. 11 is more stable than that shown in Fig. 10 by 7.7 kcal/mol. Therefore, in investigating the proton transfer in the proton cryptate, a value of 1.5 Å for r(OM) was used.



Total energy of K: −228.0671 hartrees
K: (0.0, 1.43)

Fig. 9. Potential Energy Map in kcal/mol of $(H_2O)_3H^+$ Relative to the Total Energy at the K Position

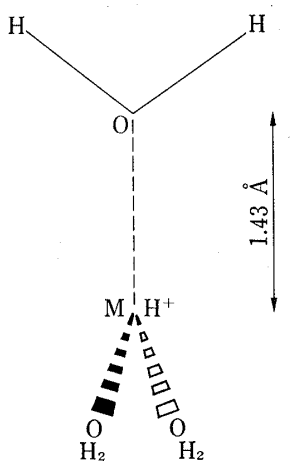


Fig. 10. Structure at the K Position

Proton Transfer in the Model of the Proton Cryptate

In order to obtain a potential energy map for proton transfer in the proton cryptate, the model shown in Fig. 12 was used. The distances r(OM) and r(NM) were taken as 1.5 and 1.75 Å, respectively, on the basis of experiments[2] and the calculations of the preceding section. Figure 13 shows the potential energy surface for the proton affinity in the model of the proton cryptate. The potential energy surface is described on the NON plane. Values are given relative to that at the Z position mentioned later. The position of the origin is "M". The position where the potential energy was most stable was (0.6855, 0.0) in the map. This position is labelled "Z". The energy of the proton affinity at the Z position is 314 kcal/mol, as shown in Table I, and the ES term is the dominant contributor. The CT and PL terms are also

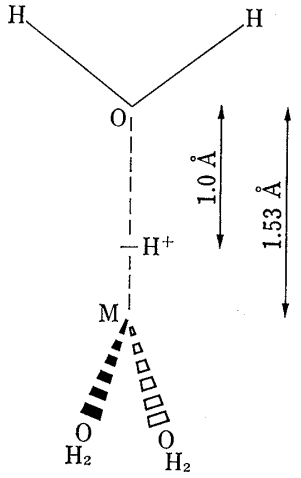


Fig. 11. Optimized Structure of $(H_2O)_3H^+$ in the D_{3h} Form of $(H_2O)_3$

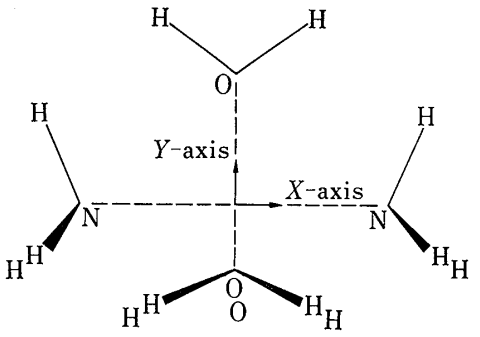


Fig. 12. Model of the Proton Cryptate

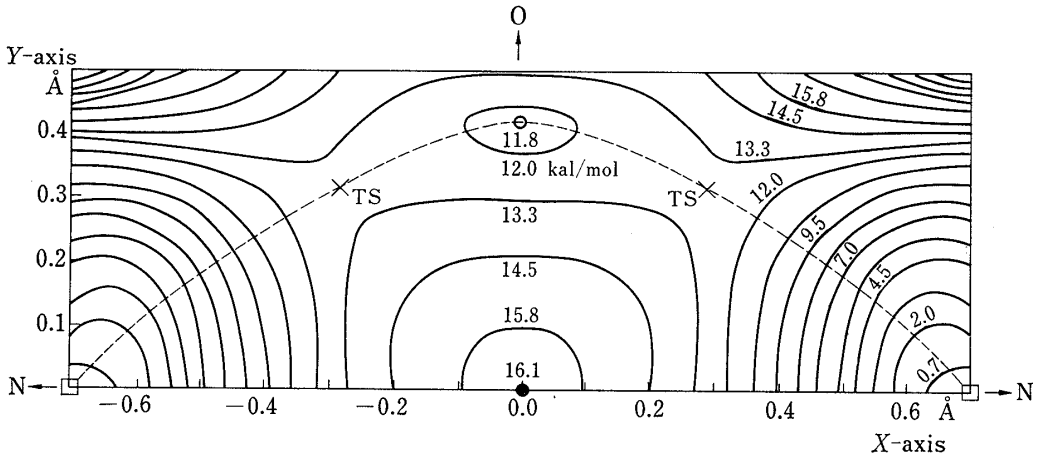


Fig. 13. Potential Energy Map in kcal/mol of the Proton Affinity of the Proton Cryptate Model Relative to That at the Z Position

significant. In the proton cryptate model, the proton moves along the broken line. First the proton moves to the transition state TS in Fig. 13, and passes to the metastable point "S"; the coordinates of the S position are (0.0, 0.4158). It then passes through the transition state TS, to the other most stable position. At the S position, the energy of the proton affinity is smaller than at the Z position by 11.8 kcal/mol, mainly due to ΔCT, as shown in Table I. The transition energy or the barrier height of the proton transfer is 13 kcal/mol from the results in Fig. 13. Therefore it is suggested that the proton probably jumps back and forwards between the two nitrogen lone pairs under the catalytic influence of the three oxygen lone pairs. The proton cryptate has three planes of N, O and N, as shown in Fig. 13, and hence the proton migrates along three paths in accord with the D_{3h} symmetry.

Table I shows the energy decomposition analyses relative to that at the Z position. If the proton moves from the Z position to the M position, the change of the potential energy is 16.1 kcal/mol, as shown in Fig. 13 and Table I. The ΔCT term is the dominant contributor to this. On the other hand, the ES term plays an important role in lowering the potential energy at the M position. Next, if the proton moves from the S position to the M position, the change of the potential energy is 4.3 kcal/mol, as shown in Fig. 13 and Table I. The ΔCT

term is again the dominant contributor. At this time, the ES term also plays a significant role in lowering the potential energy at the M position.

Energy decomposition analyses of the structure composed of only $H_3N\cdots NH_3$in the model of the proton cryptate are shown in Table II. Values are given relative to that of the most stable position. As the proton approaches from the Z position to the M position, the energy of the proton affinity becomes smaller, mainly due to the ΔCT term. The energy decomposition analyses of the structure composed of only $(H_2O)_3$ in the model of the proton cryptate are shown in Table III. As the proton approaches from the Z position to the M position, the energy of the proton affinity becomes larger due to the ΔES term. Therefore the form referring to the M position in Fig. 13 is stabilized by the ES term due to the interactions among H^+ and the three water molecules.

The permeation or movement of protons is important in biological systems. In the proton cryptate, a proton migrates under the catalytic influence of three ether oxygens, as

Table I. Proton Affinity in kcal/mol Relative to That of the Most Stable Position for the Cryptate Model (the Structure Composed of $(H_2O)_3$ and $(NH_3)_2$) and the Relative Energy Decomposition Analyses Using the 4-31G Basis Set

x	y	$\Delta\Delta E$	ΔES	ΔPL	ΔCT	ΔMIX
0.75	0.0	1.4	11.2	−1.4	−6.3	−2.1
0.70		0.1	2.1	−0.3	−1.4	−0.5
0.6855[a)]		0	0	0	0	0
		(−313.8)	(−196.4)	(−56.6)	(−69.2)	(8.4)
0.65		0.3	−4.4	0.5	3.2	1.0
0.60		1.6	−9.3	1.2	7.3	2.3
0.40		9.5	−19.0	3.1	20.1	5.3
0.20		14.6	−22.5	4.3	26.9	5.9
0.0	0.0	16.1	−23.5	4.7	29.0	5.9
	0.35	12.3	−12.4	−0.2	18.8	6.1
	0.40	11.8	−7.6	−1.7	15.4	6.0
	0.4158	11.8	−5.7	−2.2	14.2	5.5
	0.45	12.0	−1.2	−3.3	11.5	5.0
	0.50	13.4	7.4	−5.1	7.1	4.0

a) Parentheses show ΔE, ES, PL, CT and MIX terms.

Table II. Proton Affinity in kcal/mol Relative to That of the Most Stable Position for the Structure Composed of $(NH_3)_2$ and the Relative Energy Decomposition Analyses Using the 4-31G Basis Set

x	y	$\Delta\Delta E$	ΔES	ΔPL	ΔCT	ΔMIX
0.85	0.0	9.8	35.6	−6.2	−16.6	−2.9
0.80		2.9	19.6	−3.4	−10.8	−2.4
0.75		−0.1	8.7	−1.6	−5.7	−1.4
0.70		−0.3	1.6	−0.3	−1.3	−0.3
0.6855[a)]		0	0	0	0	0
		(−250.6)	(−138.8)	(−29.0)	(−80.1)	(−2.8)
0.65		1.3	−2.7	0.6	2.7	0.7
0.60		4.3	−5.0	1.5	6.2	1.6
0.55		8.1	−5.9	2.3	9.4	2.3
0.45		16.8	−4.9	4.0	14.6	3.1
0.35		25.4	−2.2	5.6	18.4	3.5
0.25		32.6	0.8	7.1	21.2	3.6
0.15		37.8	3.1	8.3	22.8	3.6
0.0	0.0	40.8	4.6	8.9	23.8	3.5

a) Parentheses show ΔE, ES, PL, CT and MIX terms.

described above, and somewhat similar processes may occur in biological systems. Tetranactin accelerates the permeation of cations in biological membranes, and, for example, it can include an ammonium ion.[9] Four ether groups coordinate to the ammonium ion more strongly than four carbonyl groups, as elucidated by the author *et al.*[10] However, the ammonium ion does not migrate in the inclusion complex.[9,10]

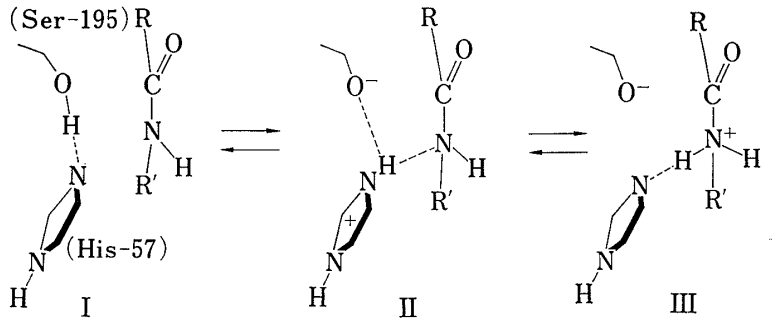


Fig. 14. Pretransition-state Protonation Proposed by Wang

TABLE III. Proton Affinity in kcal/mol Relative to That of the Most Stable Position for the Structure Composed of $(H_2O)_3$ and the Relative Energy Decomposition Analyses Using the 4-31G Basis Set

x	y	$\Delta\Delta E$	ΔES	ΔPL	ΔCT	ΔMIX
0.75	0.0	8.7	6.6	1.6	1.2	−0.7
0.6855[a]		0	0	0	0	0
		(−193.5)	(−131.8)	(−31.3)	(−39.0)	(8.6)
0.60		−10.7	−8.3	−1.9	−1.4	0.8
0.40		−32.6	−25.7	−5.4	−3.9	2.4
0.20		−47.1	−37.8	−7.3	−5.3	3.2
0.0	0.0	−52.2	−42.1	−7.9	−5.7	3.5
	0.3	−58.3	−38.6	−10.2	−12.5	3.1
	0.5	−61.8	−21.4	−13.7	−26.0	−0.7

a) Parentheses show ΔE, ES, PL, CT and MIX terms.

Proton transfer is well known as a fundamental function in enzymatic reactions. In serine proteases, for example, three amino acid residues of serine, histidine and aspartate in the active site form a hydrogen-bond structure. Wang proposed that a pretransition-state protonation treatment (Fig. 14) provides an adequate description of the catalytic process.[11] In Fig. 14, the proton of Ser 195 moves to the nitrogen lone pair of the substrate under the catalytic influence of the nitrogen lone pair of His 57. The catalytic effect of three oxygen lone pairs in the model of the proton cryptate seems similar in principle to that of the nitrogen lone pair of His 57 in serine proteases, even though the potential energy surfaces are different.

9) Y. Nawata, T. Sakamaki, and Y. Iitaka, *Acta Cryst.*, **B33**, 1201 (1977).
10) H. Umeyama, S. Nakagawa, T. Nomoto, and I. Moriguchi, *Chem. Pharm. Bull.*, **28**, 745 (1980).
11) J.H. Wang, *Science*, **161**, 328 (1968).