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A *ab Initio* Molecular Orbital Study of Molecular Interactions between Formic Acid and Ammonia

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A molecular orbital study of molecular interactions between formic acid and ammonia was performed using the *ab initio* LCAO-SCF-MO method. As primitive functions, the STO-3G basis set, in which valence properties are comparable to those of the STO set, was used. The interaction energies between NH_4^+ and $HCOO^-$, between NH_4^+ and HCOOH, between NH_3 and $HCOO^-$, and between NH_3 and HCOOH were calculated. For the NH_4^+–$HCOO^-$ complex, the structure containing two hydrogen bonds and in which the C_{2v} axis of NH_4^+ coincides with that of $HCOO^-$ was the most stable. For the complex NH_4^+–HCOOH, the structure in which the NH bond of NH_4^+ forms a hydrogen bond with the carbonyl oxygen was more stable. For the complex of NH_3 and $HCOO^-$, O of $HCOO^-$ and the NH bond of NH_3 form a linear hydrogen bond as the most stable structure. For the NH_3–HCOOH complex, the structure in which the nitrogen lone pair of NH_3 forms a linear hydrogen bond with the OH bond of HCOOH was the most stable. Those four structures are discussed in connection with the interaction between lysine and glutamate (or aspartate), and the hydrolysis of esters, taking account of the interaction energies between HCOOH and H_2O and between $HCOO^-$ and H_2O, and the stabilities in a vacuum and in nonpolar solvents.

Keywords——*ab initio*; complex; structure; interaction; molecular orbital; formate; ammonia; ammonia ion; formate ion; ion pair

Formic acid is dissociated into $HCOO^-$ and H^+ as follows,

$$HCOOH \rightleftarrows HCOO^- + H^+$$

and ammonia associates with H^+, to give the ammonium ion.

$$NH_3 + H^+ \rightleftarrows NH_4^+$$

HCOOH, $HCOO^-$, NH_3, and NH_4^+ are all important in biological systems. Moreover, derivatives of these molecules containing alkyl substituents are also biologically significant. $HCOO^-$ and HCOOH can be used as models of the side chains of glutamic acid and aspartic acid, and NH_4^+ and NH_3 as models of the side chain of lysine. Since interactions between glutamic or aspartic acid and lysine occur in many enzymes and proteins, these model interactions are worth studying. An amino acid zwitterion has $-NH_3^+$ and $-COO^-$ groups, and when one amino acid interacts with another, the interaction between $-NH_3^+$ and $-COO^-$ is significant. When an ester, RCOOR′, is hydrolyzed, the rate of alkaline hydrolysis is accelerated through the interaction between the carbonyl oxygen and $\equiv N^+-H$ group;[2] thus, knowledge of the interaction between HCOOH and $-NH_3^+$ should aid in elucidating the mechanism of the acceleration. The fact that DNA interacts with both histone and nonhistone proteins is well known. Since the bases of DNA contain $-NH_2$ groups, the model interaction between $-NH_2$ and $-COO^-$ groups may also cast light on these interactions.

HCOOH and NH_3 may be more stable in the gas phase than as ionic structures. A study of the HCOOH–NH_3 complex should also contribute to the elucidation of the reaction between HCOOH and NH_3 in the gas phase.

$$HCOOH + NH_3 \rightleftarrows HCONH_2 + H_2O$$

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[1] Location: *9–1, Shirokane 5-chome, Minato-ku, Tokyo 108, Japan.*

[2] H.J. Smith and H. Williams, *J. Pharm. Pharmacol.*, **17**, 529 (1965).

If HCOOH, NH_3, and $HCONH_2$ in this reaction are considered as models of –COOH and –NH_2 groups of amino acids and peptides, respectively, some information on the behavior of the gas phase or in lipophilic solvents may be derived.

Thus, the origin of the molecular interactions mentioned above is of great interest. We therefore studied the interaction energies between HCOOH or $HCOO^-$ and NH_3 or NH_4^+ by energy decomposition analysis using *ab initio* calculations.

Method

All the calculations were performed within the framework of closed-shell single-determinant *ab initio* LCAO-SCF-MO theory using the Gaussian 70 program.[3] As primitive functions, the STO-3G basis set in which valence properties are comparable to the STO set was used.[4]

Monomer Geometries——For HCOOH, r(CO) = 1.202 Å and 1.343 Å, r(CH) = 1.097 Å, r(OH) = 0.972 Å, $\angle$OCO = 124.9°, $\angle$HCO = 124.1° and $\angle$COH = 106.3°.[5] For $HCOO^-$, r(CH) = 1.1494 Å, r(CO) = 1.26693 Å, and $\angle$OCO = 130.1972°; the geometry of $HCOO^-$ was optimized by using the STO-3G basis set.[6] For NH_3, r(NH) = 1.0124 Å and $\angle$HNH = 106.67°.[5] For NH_4^+, r(NH) = 1.032 A, and $\angle$HNH = 109°28′.[7]

Energy Decomposition——In order to elucidate the origin of the molecular complexes, energy decomposition analysis was performed.[8] If E_A and E_B are the total energies of the isolated molecules, and E_{AB} is the total energy of the molecular complex, the interaction energy ΔE is as follows;

$$\Delta E = E_{AB} - (E_A + E_B)$$

ΔE was broken up into five terms,

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

where ES is the electrostatic interaction energy. A° and B° are respectively, the wave functions for isolated fragments A and B. The MO's of A° and B° are in general nonorthogonal, *i.e.* $\langle \phi_i^A | \phi_j^B \rangle \neq 0$, where ϕ_i is an MO. The exchange interaction EX is the sum of two energy terms. One is obtained from the wave function allowing the exchange of electrons between A° and B° without consideration of the nonorthogonality of MO's. The other is obtained from the repulsion due to the MO overlap $\langle \phi_i^A | \phi_j^B \rangle \neq 0$ with consideration of the orthogonality of MO's. PL is the polarization energy, which is the interaction energy between the occupied and vacant MO's of one molecule due to the perturbation of the other molecule without the MO overlap $\langle \phi_i^A | \phi_j^B \rangle$. The charge transfer energy (CT) arises from the interaction between the occupied and vacant MO sets. MIX is the coupling energy.

Calculations were performed using a HITAC 8700-8800 computer at the Tokyo University Computer Center.

Results

Interaction between NH_4^+ and $HCOO^-$

The four structures shown in Fig. 1 were calculated for the interaction between NH_4^+ and $HCOO^-$. In structure I, the distance between N in NH_4^+ and C in $HCOO^-$ was varied. The intermolecular interaction energy was most stable at a distance of 2.51 Å. The total energy is shown in Table I. The interaction energy originated from ES (66%) and CT (26%), as shown in Table II. In this structure two hydrogen bonds are present. I was the most stable structure of the four.

Next the structure II, forming a linear hydrogen bond between N and O, was calculated at various hydrogen bond distances. The optimum distance was 2.25 Å, and the optimum CON angle was 104.8 degrees. The contribution to the stabilization energy was due to ES

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[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, 1974.

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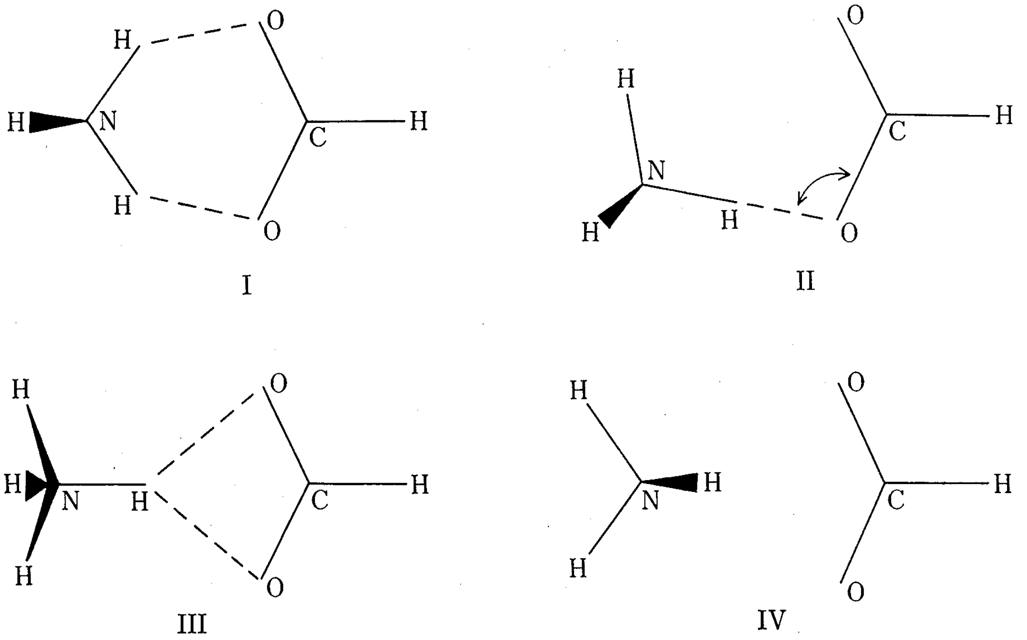


Fig. 1. Interacting Structures of NH_4^+ and $HCOO^-$

TABLE I. Total Energies for Various Interaction Structures between NH_4^+ or NH_3 and $HCOO^-$ or HCOOH Using the STO-3G Basis Set (kcal/mol)

Structure	Total energy (a.u.)[a]	Distance (Å)	Angle (degrees)
I	−241.61345	2.50732(N-C)	
II	−241.60746	2.24640(N-O)	104.769(NOC)
III	−241.55128	2.84040(N-C)	
IV	−241.51939	2.75610(N-C)	
V	−242.13001	2.43760(N-O)	118.623(NOC)
VI	−242.12092	2.46730(N-O)	130.273(NOC)
VII	−240.94154	2.57160(N-O)	114.105(NOC)
VIII	−240.93490	2.99010(N-C)	
IX	−240.92781	3.24700(N-C)	
X	−241.68699	2.70220(N-O)	105.178(NOC)[b]
XI	−241.67363	2.96710(N-O)	115.766(NOC)
XII	−241.67248	3.03040(N-O)	140.611(NOC)
XIII	−241.67109	3.03738(N-O)	

a) For the structures II, V, VI, VII, XI, and XII the dihedral angles corresponding to the changed angles were calculated to be zero.
Total energies of NH_3, NH_4^+, HCOOH and $HCOO^-$ were −55.45409, −55.86833, −186.21520 and −185.45626 a.u., respectively.

b) The HCO angle of HCOOH does not change.

(65%) and *CT* (19%), and it was less stable than the structure I by 3.8 kcal/mol due to the difference in *ΔCT* and *ΔES*.

Thirdly a bifurcated structure III was calculated. The NH bond, which is on the $HCOO^-$ plane, approaches the mid-point between both oxygens in $HCOO^-$. When the distance between N and C was 2.84 Å, the interaction energy was optimum. The interaction energy was dominantly due to *ES* (79%) and *CT* (15%). It was smaller in III than in the structure I by 39 kcal/mol due to *ΔCT* and *ΔES*. The structure II, which includes a linear hydrogen bond, was more stable than the structure III which contains a bifurcated hydrogen bond by 35.3 kcal/mol due to *ΔES* (30.9 kcal/mol) and *ΔCT* (22.7 kcal/mol).

Lastly, the structure IV in which the C_{2v} axis in NH_4^+ is aligned with the CH bond axis corresponds to that in which NH_4^+ in structure I is rotated about the N–C axis by 90 degrees.

Table II. Interaction Energies between NH_4^+ and $HCOO^-$ or HCOOH for Various Structures and Energy DecompositionTerms Using the STO-3G Basis Set (kcal/mol)

	I	Ⅱ	Ⅲ	IV	V	VI
ΔE	−181.3	−177.5	−142.3	−122.3	−29.2	−23.5
ES	−179.8	−164.7	−133.8	−126.7	−26.5	−21.8
EX	93.1	77.0	27.6	16.0	35.6	30.1
PL	−4.8	−5.5	−3.3	−2.4	−3.6	−3.2
CT	−72.2	−48.3	−25.6	−8.3	−26.6	−23.5
MIX	−17.5	−36.1	−7.2	−0.9	−8.1	−5.1
$\Delta\Delta E$	0	3.8	39.0	59.0	0	5.7
ΔES	0	15.2	46.1	53.1	0	4.7
ΔEX	0	−16.1	−65.5	−77.1	0	−5.4
ΔPL	0	−0.7	1.5	2.4	0	0.3
ΔCT	0	23.9	46.6	64.0	0	3.1
ΔMIX	0	−18.6	10.3	16.6	0	3.0

Calculations were performed at various distances between N and C. At a distance of 2.76 Å the structure was most stable. In comparison with the structure I, structure IV was less stable by 59.0 kcal/mol due to ΔCT and ΔES. When the ammonium ion in the structure I was rotated around the N–C axis by 90 degrees, the N–C distance increased by 0.25 Å with a decrease of CT and ES.

Interaction between NH_4^+ and HCOOH

The structures in which NH_4^+ interacts with HCOOH were calculated as shown in Fig. 2. First the NH bond in NH_4^+ interacts with the carbonyl oxygen of HCOOH (V). Total energies were calculated against distance between N and the carbonyl oxygen, and against angles of CON. The most stable geometry was obtained with values of 2.44 Å for r(NO) and 118.6 degrees for $\angle$CON. The interaction energy was due to ES (41%) and CT (41%).

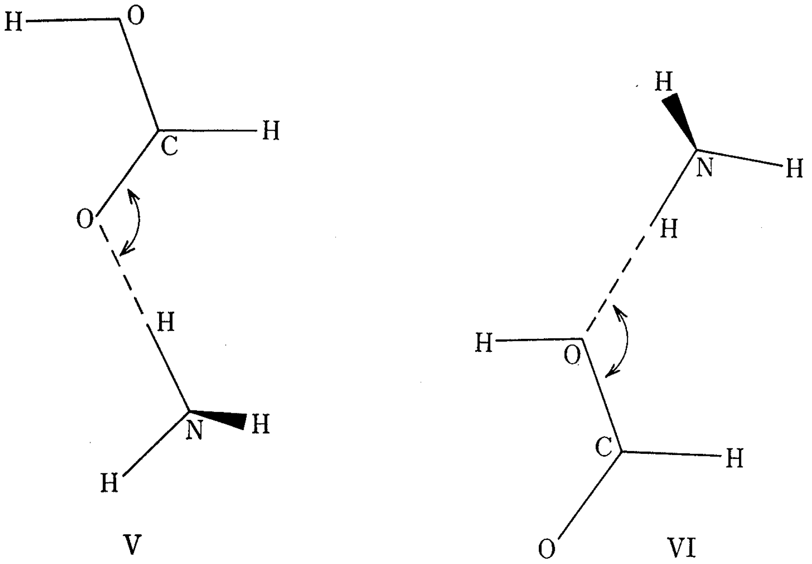


Fig. 2. Interacting Structures of NH_4^+ and HCOOH

Secondly, the structure VI in which the NH bond in NH_4^+ interacts with the hydroxyl oxygen of HCOOH, was calculated. The optimum distance and angle were 2.47 Å and 130.3 degrees, respectively. The dominant contributors were CT (44%) and ES (41%). This structure was less stable than the structure V by 5.7 kcal/mol due to ΔES and ΔCT.

Interaction between NH_3 and $HCOO^-$

For the interaction between NH_3 and $HCOO^-$, three structures were calculated as shown in Fig. 3. The first structure VII contains a linear hydrogen bond between N and O. The optimum distance and angle were 2.57 Å and 114.1 degrees, respectively. *CT* (45%) and *ES* (39%) were the dominant contributors, as shown in Table III.

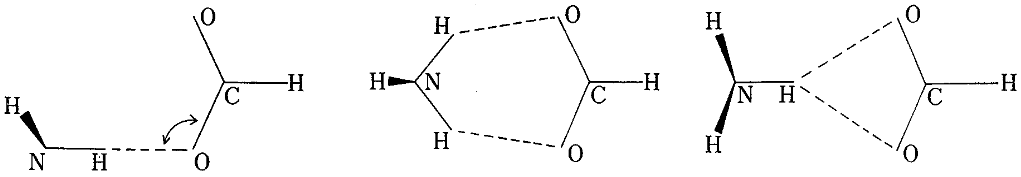

VII VIII IX

Fig. 3. Interacting Structures of NH_3 and $HCOO^-$

Table III. Interaction Energies between NH_3 and $HCOO^-$ or HCOOH for Various Structures and Energy Decomposition Terms Using the STO-3G Basis Set (kcal/mol)

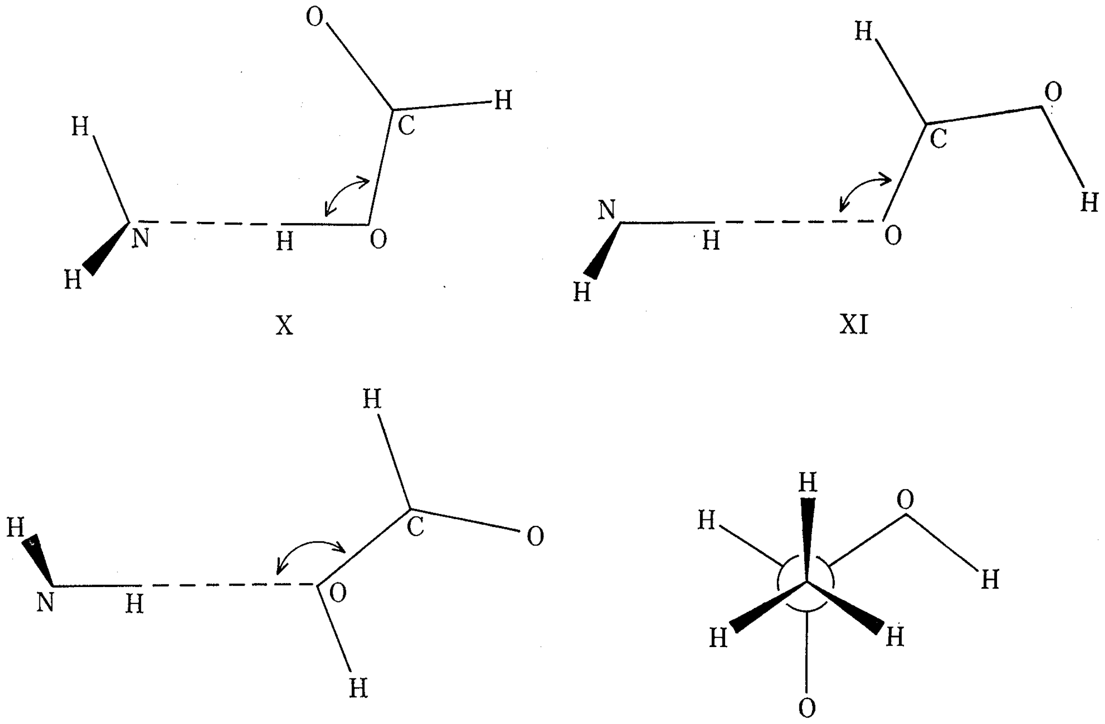
	VII	VIII	IX	X	XI	XII	XIII
ΔE	−19.6	−15.4	−11.0	−11.1	−2.7	−2.0	−1.1
ES	−18.5	−15.2	−8.5	−15.6	−3.6	−2.6	−1.5
EX	28.1	19.1	8.8	19.1	5.8	4.2	0.9
PL	−2.0	−1.5	−1.7	−0.8	−0.1	−0.1	−0.1
CT	−21.5	−17.4	−8.4	−11.9	−4.9	−3.6	−0.5
MIX	−5.6	−0.4	−1.1	−2.0	0.1	0.1	0.0
$\Delta\Delta E$	0	4.2	8.6	0	8.4	9.1	10.0
ΔES	0	3.3	10.0	0	11.9	12.9	14.1
ΔEX	0	−9.0	−19.3	0	−13.3	−14.9	−18.2
ΔPL	0	0.6	0.3	0	0.6	0.7	0.7
ΔCT	0	4.1	13.0	0	7.1	8.3	11.5
ΔMIX	0	5.2	4.6	0	2.0	2.1	2.0

Secondly, the structure VIII in which the HNH plane coincides with the $HCOO^-$ plane was calculated. The optimum distance was 2.99 Å between N and C. This structure contains two hydrogen bonds. The contributions of *CT* (50%) and *ES* (44%) were large. The interaction energy was smaller than that of structure VII by 4.2 kcal/mol due to ΔMIX, ΔCT, and ΔES.

Thirdly the bifurcated hydrogen bond structure IX was calculated. The structure was most stable at a distance of 3.25 Å between N and C. The stabilization was due to *CT* (43%) and *ES* (43%). In comparison with the structure VII, structure IX was less stable by 8.6 kcal/mol due to ΔCT and ΔES.

Interaction between NH_3 and HCOOH

Four structures were calculated, as shown in Fig. 4. In the structures X and XIII, NH_3 was an electron donor. In the structure X, the optimum values were 2.70 Å and 105.2 degrees for the N–O distance and ∠CON, respectively, with the NH bond of NH_3 on the COC plane. The interaction energy was due to *ES* (51%) and *CT* (40%). In the structure XIII, the optimum distance between N and C was 3.04 Å. The interaction energy was due to *ES* (73%) and *CT* (22%). This structure was less stable than the structure X by 10.0 kcal/mol due to ΔES and ΔCT.



X XI

XII XIII

Fig. 4. Interacting Structures of NH_3 and HCOOH

In the structures XI and XII, NH_3 is an electron acceptor. In structure XI, a linear hydrogen bond between N and the carbonyl oxygen is formed. The optimum values were 2.97 Å and 115.8 degrees for the N–O distance and ∠CON, respectively. The interaction energy was due to *CT* (57%) and *ES* (42%). This structure was less stable than the structure X by 8.4 kcal/mol due to *ΔES* and *ΔCT*. In the structure XII, the NH bond interacts with the hydroxyl oxygen. The optimum values were 3.03 Å and 140.6 degrees for the distance between N and O and the CON angle, respectively. The interaction energy was due to *CT* (57%) and *ES* (41%). Moreover, the interaction energy in the structure XII was smaller than that in the structure XI by 0.7 kcal/mol due to *ΔCT* and *ΔES*. With such a small difference, however, it is difficult to determine which structure is more stable.

Discussion

The interaction energy and each component of the energy decomposition terms for the structure I were compared with those between the guanidinium ion and formic acid ion.[9]

Table IV. Comparisons between the Interaction Energies of the Guanidinium Ion–Formic Acid Ion Complex and the Ammonium Ion–Formic Acid Ion Complex, and between the Energy Decomposition Terms (kcal/mol)

	With guanidinium Ion	With ammonium Ion	Difference
ΔE	−169.4	−181.3	11.9
ES	−158.5	−179.8	21.3
EX	96.7	93.1	3.6
PL	−7.4	−4.8	−2.6
CT	−72.4	−72.2	−0.2
MIX	−27.7	−17.5	−10.2

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[9] S. Nakagawa and H. Umeyama, *J. Am. Chem. Soc.*, **100**, 7716 (1978).

The former was larger than the latter by 11.9 kcal/mol due to ΔES, as shown in Table IV. This result indicates that in proteins the interaction energy between lysine and aspartate or glutamate may be significant in maintaining the protein structure.

The total energy of the structure I was smaller than that of structure X by 46.2 kcal/mol. The types of interactions in the structures X and I were neutral–neutral and cation–anion, respectively. In polar solutions or proteins, however, the effects of neighboring molecules on the ion pair structure I should be considered. Since molecules with a large dipole moment stabilize an ion pair, the ion pair between NH_4^+ and $HCOO^-$ may exist in polar solutions or proteins.

Since HCOOH can be used as a model of an ester, the electronic effects of ammonia or its cation on the carbonyl carbon are of interest in connection with mechanism of accelerated attack by nucleophiles. Table V shows the results. The interaction in structure V corresponds to perturbation by NH_4^+ of the carbonyl carbon. The frontier electron density of the carbonyl carbon in LUMO (lowest unoccupied molecular orbital) increases greatly. From calculations including $CT+ES$ or $PL+ES$, the origin of the frontier electron-density change was found to be PL. The energy level of LUMO decreases markedly, and hence, the attack of the nucleophile becomes easy. This is due to $ES+CT+PL$. The electron density of the $2\,p_\pi$ orbital of the carbonyl carbon and the total electron densities decrease; the result is mainly due to PL. In the structure VI, NH_4^+ interacts with the hydroxyl oxygen corresponding to the ether oxygen of the ester. The frontier electron density decreases, and the energy level of LUMO decreases. The frontier electron density changes have an unfavorable effect on reactivity. The decrease of the energy level of LUMO was also smaller than that of structure V. The NH bond of NH_4^+ in XI and XII binds with the carbonyl oxygen and the oxygen of OH, respectively. The frontier electron densities and the LUMO level changes are much smaller than those of the structures V and VI. Therefore, protonation of the amine significantly increases the reactivity of the carbonyl carbon.

Table V. Effects of NH_4^+ or NH_3 on Frontier Electron Density, Electron Density of $2p_\pi$ AO, and Total Electron Density of Carbonyl Carbon in HCOOH, and Energy Level of LUMO in HCOOH

(1)		(2)	(3)	(4)	(5)
Isolated HCOOH		0.723	0.3073	0.908	5.732
V	Total	0.774	0.0919	0.808	5.670
	$CT+ES$	0.723	0.0900	0.908	5.725
	$PL+ES$	0.752	0.1304	0.853	5.705
VI	Total	0.705	0.1325	0.938	5.718
	$CT+ES$	0.723	0.1482	0.908	5.726
	$PL+ES$	0.707	0.1556	0.937	5.729
XI	Total	0.732	0.2943	0.891	5.722
	$CT+ES$	0.723	0.2940	0.908	5.731
	$PL+ES$	0.728	0.3008	0.899	5.728
XII	Total	0.721	0.2969	0.911	5.730
	$CT+ES$	0.723	0.2985	0.908	5.731
	$PL+ES$	0.721	0.3002	0.911	5.731

(1) Structure.
(2) Frontier electron density of carbonyl carbon in LUMO.
(3) Energy level of LUMO (a.u.).
(4) Electron density of the $2p_\pi$ atomic orbital of carbonyl carbon.
(5) Total electron density of carbonyl carbon.

Umeyama and Matsuzaki reported the interaction energies between H_2O and $HCOO^-$, and between H_2O and HCOOH.⁶⁾ The interaction energies and energy decomponents between NH_3 and $HCOO^-$, and between NH_3 and HCOOH were compared with those between H_2O

TABLE VI. Differences of Interaction Energies between the H_2O–$HCOO^-$ or HCOOH Complex and the NH_3–$HCOO^-$ or HCOOH Complex, and between the Decomposition Terms of Both Complexes Using the STO-3G Basis Set (kcal/mol) (Primes indicate Complex with H_2O)

	(1) VII′—VII	(2) VIII′—VIII	(3) IX′—IX	(4) X′—X	(5) XI′—XI	(6) XII′—XII	(7) XIII′—XIII
$\Delta\Delta E$	−6.9	−9.0	−4.0	0.4	−1.4	−1.1	−0.1
ΔES	−6.6	−9.1	−3.5	2.7	−1.6	−1.5	−0.1
ΔEX	3.1	6.0	1.4	0.0	2.1	2.3	0.1
ΔPL	0.3	0.5	0.1	0.4	−0.1	0.0	0.0
ΔCT	−2.9	−6.5	−1.9	−3.1	−1.7	−1.9	−0.2
ΔMIX	−0.9	0.1	−0.2	0.5	−0.1	0.0	0.0

and $HCOO^-$, and between H_2O and HCOOH, as shown in Table VI. In columns (1), (2) and (3) for $HCOO^-$, the interaction energies between NH_3 and $HCOO^-$ are smaller than those between H_2O and $HCOO^-$, largely due to ΔES and ΔCT. In the interaction with HCOOH, columns (4) and (7) show the case where HCOOH is an electron acceptor. The interaction energies for NH_3 were comparable with those for H_2O. In columns (5) and (6), HCOOH is an electron donor. The interaction energies between NH_3 and HCOOH were smaller than those between H_2O and HCOOH due to ΔCT and ΔES.

Conclusion

1. For the $HCOO^-$–NH_4^+ complex, the most stable structure contains two hydrogen bonds, and the C_{2v} axis of NH_4^+ coincides with that of $HCOO^-$. Since the interaction energy was larger than that between a guanidinium ion and formic acid ion, it appears that in such biologocal systems as proteins the $RCOO^-$–$R'NH_3^+$ interaction is also significant.

2. For the HCOOH–NH_4^+ complex, the structure in which the NH bond of NH_4^+ interacts with the carbonyl oxygen of HCOOH was more stable. In the interaction through the hydrogen bond, a marked increase of the frontier electron density of the carbonyl carbon and decrease of the MO level of LUMO occurred. The former increase is due to *PL*, and the latter decrease is due to $PL+CT+ES$. These results explain why the approach of $\equiv N^+$–H to the carbonyl oxygen of the ester accelerates the attack of OH^-.

3. For the $HCOO^-$–NH_3 complex, the structure in which the NH of NH_3 and O of $HCOO^-$ form a linear hydrogen bond was the most stable. In the biological interaction between $RCOO^-$ and $R'NH_2$, the complex may be stabilized through a linear hydrogen bond between N and O.

4. For the HCOOH–NH_3 complex, the structure in which the lone pair orbital of N in NH_3 forms a linear hydrogen bond with OH of HCOOH was the most stable. The total energy of the most stable structure was greater than that of the $HCOO^-$–NH_4^+ complex containing two hydrogen bonds. In a nonpolar solvent or vacuum, therefore, the complex will be of neutral–neutral type. However, this result should be confirmed using a larger basis set.

5. The interaction energies involving the nitrogen lone pair in complexes between HCOOH and NH_3 were comparable with those in complexes between HCOOH and H_2O. However, the interaction energies between $HCOO^-$ and NH_3 and between HCOOH as an electron donor and NH_3 as an electron acceptor were smaller than those between $HCOO^-$ and H_2O and between HCOOH as an electron donor and H_2O.