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A Cluster Model Study of Contact Ion Pair Formation of *t*-BuCl in Aqueous Solution: Calculational Evidence for Nucleophilic Solvent Assistance in S_N1 Reaction

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To achieve an understanding of the solvent effects on the contact ion pair formation of *t*-BuCl in aqueous solution from a microscopic point of view, we carried out ab initio molecular-orbital calculations for a cluster system consisting of *t*-BuCl and four water molecules. Each of the most stable contact ion pair and the relevant transition state was found to have a ten-membered ring structure in which one edge of a hydrogen-bonded chain consisting of four water molecules solvates nucleophilically on the back side of the central carbon of the *t*-Bu group and the other edge of the water chain hangs electrophilically on the chlorine. This finding suggested that the contact ion pair formation for the cluster system is assisted not only by electrophilic solvation but also by nucleophilic solvation of the water on *t*-BuCl. The calculated energy barrier for the contact ion pair formation was comparable with the experimental data for the corresponding solution reaction when the influence of bulk water is taken into account by means of a continuum solvation model. The calculated solvent kinetic isotope effects for the cluster system were in good accord with the experimental data for the solution reaction. The contact ion pair and the relevant transition state structures for the cluster system were therefore suggested to have some relevance in the solution reaction. We concluded that the contact ion pair formation of *t*-BuCl in aqueous solution proceeds via the nucleophilically (and electrophilically) solvated transition state, followed by the formation of the nucleophilically (and electrophilically) solvated contact ion pair.

Introduction

The kinetics and stereochemistry of the S_N1 reactions such as the hydrolysis of *t*-BuCl in aqueous solution have been rationalized by the ion pair mechanism[1] represented as

$$RX \rightleftarrows R^+X^- \rightleftarrows R^+//X^- \rightleftarrows R^+ + X^- \qquad (1)$$

where RX is a reactant. R^+X^-, $R^+//X^-$, and $R^+ + X^-$ are a contact ion pair, a solvent-separated ion pair, and dissociated ions, respectively, which can all react with a nucleophile and then lead to nucleophilic substitution products. The nature of this process has been the subject of much experimental and theoretical scrutiny because of the critical role of the solvent.[1−7] Nevertheless, relatively little is known about the details of the microscopic participation of the solvent in this process. For example, for hydroxylic solvents such as water and alcohols, although the specific electrophilic solvation on the solute ionic state via hydrogen bonds has been widely known to play a significant role in determining the activation free energy, there is no consensus about the role of nucleophilic solvent assistance.[2−7]

On one hand, Bentley et al.[2] proposed a borderline mechanism between the S_N1 and S_N2 mechanisms, i.e., an "S_N2(intermediate)" mechanism, to rationalize the gradation of reactivities of solvolysis, caused by variation in the extent of nucleophilic solvent assistance to ionic dissociation of the bond between the carbon and the leaving group. In the S_N2(intermediate) mechanism, a reaction is postulated to proceed via a nucleophilically solvated transition state, leading to a nucleophilically solvated contact ion pair (Figure 1). As stated by Bentley and Schleyer,[2f,h] the portion "S_N2" of the term "S_N2(intermediate)" stems from Ingold's theoretical definition in which the requirement for an S_N2 reaction is that two molecules necessarily undergo covalency change during the rate-determining step and the S_N2 reaction need not necessarily proceed by attack by nucleophile on covalent substrate leading directly to product. The difficulty of fitting some solvolysis into a simple S_N1-S_N2 framework was explained in terms of the S_N2(intermediate) mechanism. The other groups[3] also demonstrated some experimental evidence of nucleophilic solvent assistance to several S_N1 reactions.

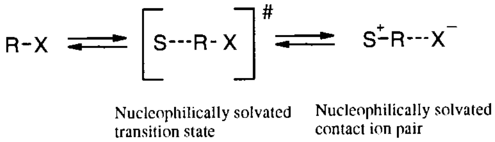

Figure 1. Schematic representation of the S_N2(intermediate) mechanism, in which the reaction proceeds via a nucleophilically solvated transition state leading to a nucleophilically solvated contact ion pair. Substrate is RX and solvent is S.

On the other hand, many researchers[4−7] claimed that the rationalization for the existing data of the S_N1 reactions does not necessarily require the concept of nucleophilic solvent assistance. For example, it was suggested that the gradation of reactivities of the S_N1 reactions may be explained in terms of the degrees of electrophilic assistance of the solvent in the reactions.[4] In the other studies, the gradation was demonstrated to be possibly explained in terms of internal return[5] or the variation in the solvent effects on the reactant species.[6] Some experimental evidence for the absence of the nucleophilic solvent assistant was also presented.[7]

In this way, although this subject is of general and broad interest, the academic controversy on this subject has involved

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much confusion for a long time. These mutually contradictory conclusions reflect the lack of information on interpreting experimental findings. Therefore, a theoretical study should be desired.

Some theoreticians[8−10] have addressed the investigation of a prototype S_N1 reaction, the hydrolysis of *t*-BuCl in aqueous solution. Jorgensen et al.[8] determined the free energy profile of the ion pair region during the hydrolysis, conducting Monte Carlo simulations. They demonstrated that the free energy barrier between a contact ion pair and a solvent-separated ion pair is ca. 2 kcal/mol and the solvent-separated ion pair is lower in free energy than the contact ion pair. Their radial distribution function analysis showed one water molecule to be on the back side of the carbocation at the contact ion pair; this fact may suggest the existence of nucleophilic solvent assistance. However, their attention was confined to the ion pair region, and the contact ion pair formation step was not investigated in more detail. In addition, because the potential energy surface represented by the two-body potential functions employed is obviously a significant approximation (e.g., polarization effects have not been explicitly included),[11] their results must all be taken as quantitatively preliminary.

Keirstead et al.[9] carried out molecular dynamics simulations for the contact ion pair formation step. The height of the free energy barrier was found from calculation to be in good agreement with the corresponding experimental value. However, as they themselves pointed out, this agreement should be regarded as fortuitous because of the very approximate nature of their model (e.g., the united atom treatment of the *t*-Bu group and the employment of the two-body potential functions).

Hartsough and Merz[10] also executed qauntum mechanical/molecular mechanical coupled potential simulations. They found that the calculated free energy barrier for the contact ion pair formation is in good agreement with the experimental estimate only if long-range electrostatic interactions are additionally taken into account using a Born correction or a reaction field. They demonstrated that, at the contact ion pair, a clear solvent structure is observed about the chloride anion but not the back side of the carbocation, in contrast to the calculational finding of Jorgensen et al.;[8] this demonstration may suggest that the nucleophilic solvent assistance is unimportant for the contact ion pair formation. However, the calculational method of Hartsough and Merz[10] seems to be associated with large uncertainties because they employed the semiempirical PM3 Hamiltonian for the solute potential and the molecular mechanical potential for the solute−solvent and solvent−solvent interactions, both of which seem to be unacceptable for quantitative discussion.

In addition, the other researchers[12−14] have examined the S_N1 reactions by a continuum model. Hynes et al.[12] extensively studied the nonequilibrium solvent effects on the S_N1 ionic dissociation of alkyl halides in several solvents. Ford and Wang[13] and Takahashi et al.[14] determined the free energy profile of the ionic dissociation of *t*-BuCl in aqueous solution by semiempirical and ab initio calculations equipped with the continuum model, respectively. However, since the specific solvent molecules which directly interact with the solute are expected to be essential for the S_N1 reaction, it must be doubtful whether the continuum model is appropriate.

In this way, although these studies provided an understanding of some characteristic aspects of the S_N1 reaction, the uncertainties associated with these studies result in some confusion. Several solvent molecules within the first solvation shell are expected to be inextricably involved in the reaction coordinate motion; thus, the interaction between the solute and these solvent molecules should be more accurately represented. In the previous studies,[15,16] certain characteristic trends of condensed-phase solvation of several S_N2 reactions were shown to be reproduced by means of a cluster model study in which the reactions within the cluster system consisting of a solute and a handful of solvent molecules are quantitatively examined. The other studies[17−19] also demonstrated that a few solvent molecules significantly stabilize some ion pairs and thus the free energy profile of the ion pair formation in solution is reproduced by means of a cluster model. Therefore, cluster structures consisting of a solute and a handful of solvent molecules are expected to have some relevance in the process of reaction in the bulk solvent.

In the present paper, we report ab inito molecular-orbital calculations for the contact ion pair formation within the cluster system composed of *t*-BuCl and four water molecules. Because a contact ion pair formation corresponds to the rate-determining step for most of the S_N1 reactions, the kinetics of the S_N1 reactions will be understood by the clarification of the process of the contact ion pair formation that is the hallmark of the S_N1 reactions. The prime object of the present study is to clarify whether or not the nucleophilic solvent assistance is essential for the contact ion pair formation of *t*-BuCl in aqueous solution.

Method of Calculations

Ab initio molecular-orbital calculations were carried out for the cluster system consisting of *t*-BuCl and four water molecules. The Gaussian 94 program package[20] was employed on an NEC high-performance computing server SX-4B/e for all calculations.

First, preliminary calculations were conducted to discover the most stable contact ion pair structure among many stable conformers, because it is expected that there are many stable states and transition states for the cluster system. All the geometries of the various contact ion pairs were fully optimized with the 6-31+G* basis set at the Hartree−Fock (HF) level of theory.[20] The single-point energies were then calculated for all the optimized species with the same basis set at the Møller−Plesset second-order perturbation (MP2) level of theory[20] (MP2/6-31+G*//HF/6-31+G*). Inner shells were excluded from the electron correlation calculations. From these calculations, the most stable contact ion pair structure was determined.

Secondly, the reoptimization of the most stable contact ion pair structure determined above and the optimizations of its probable precursers (the relevant reactant and transition state) were executed with the 6-31+G* basis set at the MP2 level of theory (MP2/6-31+G*).[20] A tight convergence criterion was adopted for the optimizations because the potential energy surface was relatively flat around each mimimum of the stationary states; in the tight convergence criterion, thresholds are to 10^{-5} a.u. for the root-mean-square gradient and to 1.5×10^{-5} a.u. for the maximum gradient component, and the corresponding thresholds for the displacements are 4 times the gradient thresholds.[20] The contact ion pair, the relevant transition state and reactant species were characterized by means of harmonic-frequency calculations. The correspondence of the reactant through the transition state to the contact ion pair was confirmed by means of the intrinsic reaction coordinate (IRC) analysis;[21] the IRC calculations were performed with a step length of ca. 0.05 $\text{amu}^{1/2}\cdot\text{bohr}$. The single-point energies for the optimized species were then calculated with the same basis set at the quadratic configuration interaction calculation level of theory, which includes single and double substitution with a triple contribution to the energy added (QCISD(T)/6-31+G*//MP2/6-31+G*).[20] Inner shells were again excluded from all

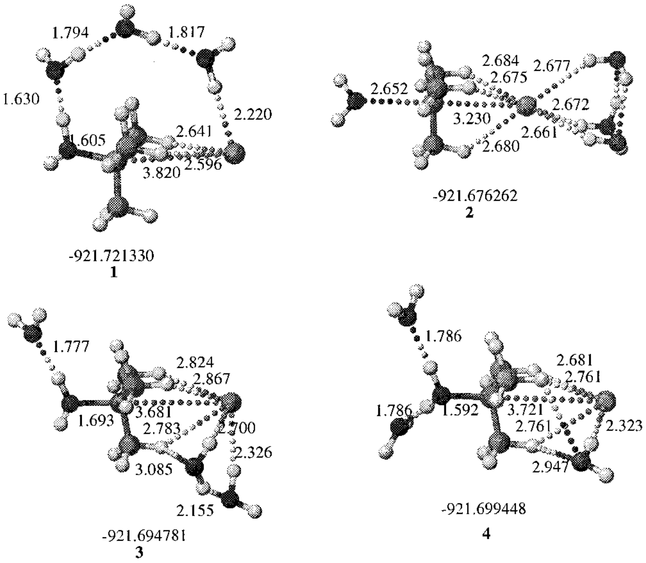


Figure 2. Optimized structures and energies of the contact ion pair at MP2/6-31+G*//HF/6-31+G* level. Bond lengths in Å and energies in Eh. The structures of this figure and Figures 3−5 were drawn using the CAChe3.1 program package of Oxford Molecular, Ltd.

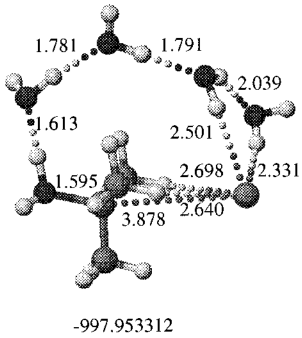


Figure 3. Optimized structure and energy (Eh) of the contact ion pair for the cluster system consisting of *t*-BuCl and five water molecules at the MP2/6-31+G*//HF/6-31+G* level.

these electron correlation calculations. The harmonic frequencies at the MP2/6-31+G* level were employed to estimate the zero-point energies.

The solvent kinetic isotope effects were also determined at 298 K without tunneling contribution on the basis of the conventional transition state theory.[22] For this determination, the influence of the bulk water was neglected. The origin of the solvent kinetic isotope effects was scrutinized by means of the factorization analysis previously[23] introduced. That is, the rate ratio k_{H_2O}/k_{D_2O} for the deuteration of all the waters was factorized as

$$k_{H_2O}/k_{D_2O} = \eta_{trans}\eta_{rot}\eta_{vib}{}^{low}\eta_{vib}{}^{mid}\eta_{vib}{}^{high} \qquad (2)$$

where the factors η_{trans}, η_{rot}, $\eta_{vib}{}^{low}$, $\eta_{vib}{}^{mid}$, and $\eta_{vib}{}^{high}$ refer respectively to contributions from translational and rotational and from vibrational modes with frequencies below 600 cm^{-1}, between 600 and 2000 cm^{-1}, and above 2000 cm^{-1}. The definition of these factors is available.[23]

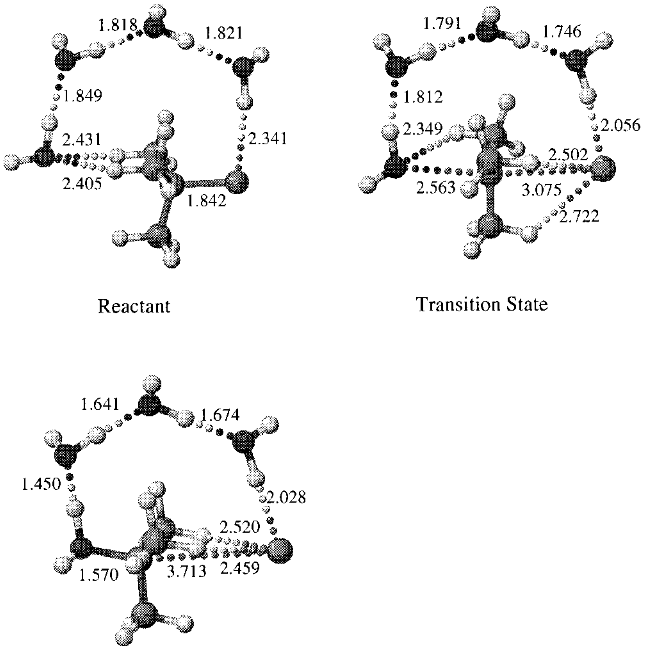
The influence not only of several active solvent molecules neighbor to the solute but also of the bulk solvent must be taken into account for a complete treatment of solvation effects. The calculations with the isodensity surface polarizable continuum model (IPCM)[24] method were therefore executed at the MP2/6-31+G* level using the experimental value of the dielectric constant $\epsilon = 78.3$. In the IPCM method, the bulk solvent is simply regarded as a continuous unstructured dielectric with a given dielectric constant surrounding a relevant solute embedded in a cavity that is determined from an isodensity surface of the solute. The single-point IPCM energies were calculated at the reactant, the transition state, and the contact ion pair, and at $s = -1.5, -1.0, -0.5, 0.5, 1.0$, and 1.5 amu$^{1/2}$·bohr along the IRC, and the influence of the bulk water was roughly estimated.

Results and Discussion

Most Stable Contact Ion Pair. No stable contact ion pair structure without the nucleophilic solvation on the backside of the carbocation was found in the preliminary calculations at the MP2/6-31+G*//HF/6-31+G* level (Figure 2). The most stable contact ion pair is a ten-membered ring structure in which one edge of a hydrogen-bonded chain consisting of four water molecules solvates nucleophilically on the backside of the carbocation and the other edge of the water chain solvates electrophilically on the chloride anion (**1** in Figure 2). The most stable contact ion pair might be described as a contact ion pair between protonated *tert*-butyl alcohol and the chloride anion. This contact ion pair is more than 13 kcal/mol more stable compared with the other contact ion pairs. The most stable contact ion pair structure was hardly changed by the reoptimization at the MP2/6-31+G* level (Figure 3). Therefore, the preliminary calculations at the MP2/6-31+G*//HF/6-31+G* level would provide reliable results.

These findings suggest that the hydrogen-bonding network forming the ring structure is responsible for the significant stabilization of the solute ionic state. This situation somewhat resembles the results of Jensen et al.[17] and Tao,[18] in which each of some contact and solvent-separated ion pairs has been found to have a ring structure bridged by a hydrogen-bonded chain consisting of several water molecules. As discussed by Nguyen et al.,[25] because the water plays both the roles of a donor and an acceptor, one water among a water chain will polarize the electron clouds of the second water and then the third and fourth molecules and so forth, and this mutual polarization will result in a greater attraction between those waters. The mutual polarization of the associated waters will clearly increase by means of the formation of a ring structure. The most stable contact ion pair structure for the cluster system, the ten-membered ring structure, is therefore most advantageous for the stabilization due to such mutual polarization. Although ring strain is also another important factor determining a stable structure, the present findings indicate that the cooperative stabilization of hydrogen bonds by means of the formation of the ten-membered ring structure surpasses the unstabilization due to the ring strain.

In the most stable contact ion pair, only one water molecule solvates the chloride anion (**1** in Figure 2). In actual solution, the chloride anion must be solvated by more water molecules. To have some qualitative indication as to how sensitive the structure of the contact ion pair is to the inclusion of additional water molecules, we newly carried out at the MP2/6-31+G*//HF/6-31+G* level the optimization of the contact ion pair structure for the cluster system consisting of *t*-BuCl and five water molecules in which two water molecules solvate the chloride anion. The optimized structure is shown in Figure 3. It was found that inclusion of an additional water molecule into the cluster system consisting of *t*-BuCl and four water molecules lengthens the C−Cl distance of the contact ion pair only by ca. 0.06 Å, although the hydrogen bond between the additional water and the chloride anion is moderately strong. This finding



Reactant

Transition State

Contact Ion Pair

Figure 4. Optimized structures of the reactant, the transition state, and the contact ion pair. The MP2/6-31+G* level was employed for the optimization. Bond lengths in Å.

suggests that while additional water molecules contribute moderately to the energy stabilization of the contact ion pair, the qualitative characteristics of the structure of the contact ion pair is hardly changed by the presence of the additional water molecules. Therefore, the main reason for the long C−Cl distance calculated for the contact ion pair will not be the lack of water molecules around the chloride anion.

Nucleophilic Solvent Assistance. Figure 4 shows the optimized geometries of the reactant, the transition state, and the contact ion pair at the MP2/6-31+G* level. The respective C−Cl distances at the transition state and the contact ion pair, 3.075 Å and 3.713 Å (Figure 4), are larger than the values previously estimated at the transition state by Keirstead et al.,[9] Ford and Wang,[13] and Takahashi et al.,[14] 2.28−3.0 Å, and the value estimated at the contact ion pair by each of Jorgensen et al.,[8] Keirstead et al.,[9] Hartsough and Merz,[10] Ford and Wang,[13] and Takahashi et al,[14] 2.9−3.3 Å. The IPCM calculations at several points along the IRC showed that the influence of the bulk water on the C−Cl distance at the transition state is small (Table 2). Therefore, the large discrepancy between our results and the others cannot be accounted for by the defect due to the disregard of the bulk water for our cluster model. The discrepancy will be primarily attributed to the flaw in the potential functions employed in the previous studies, as discussed in the Introduction. As a result, we can safely say that the C−Cl ionic dissociation is already well advanced in the transition state.

The analysis of the IRC (Figure 5) demonstrated that the C−Cl ionic dissociation in the contact ion pair formation step is accompanied by umbrella inversion of the configuration and rotation of each of the methyl groups around the relevant C−C axis. This conformational change in passing from the reactant through the transition state to the contact ion pair obviously decreases the steric hindrance of the backside of the central carbon of the *t*-Bu group. As a result, the *t*-Bu group at each of the transition state and the contact ion pair seems not to be large enough to block the backside completely to nucleophilic attack.

Not only the contact ion pair but also the transition state were found to have the ten-membered ring structure (Figure 4). This finding indicates that the stabilization of the solute ionic state by the formation of the hydrogen-bonded ring structure is essential for the contact ion pair formation. The distance between

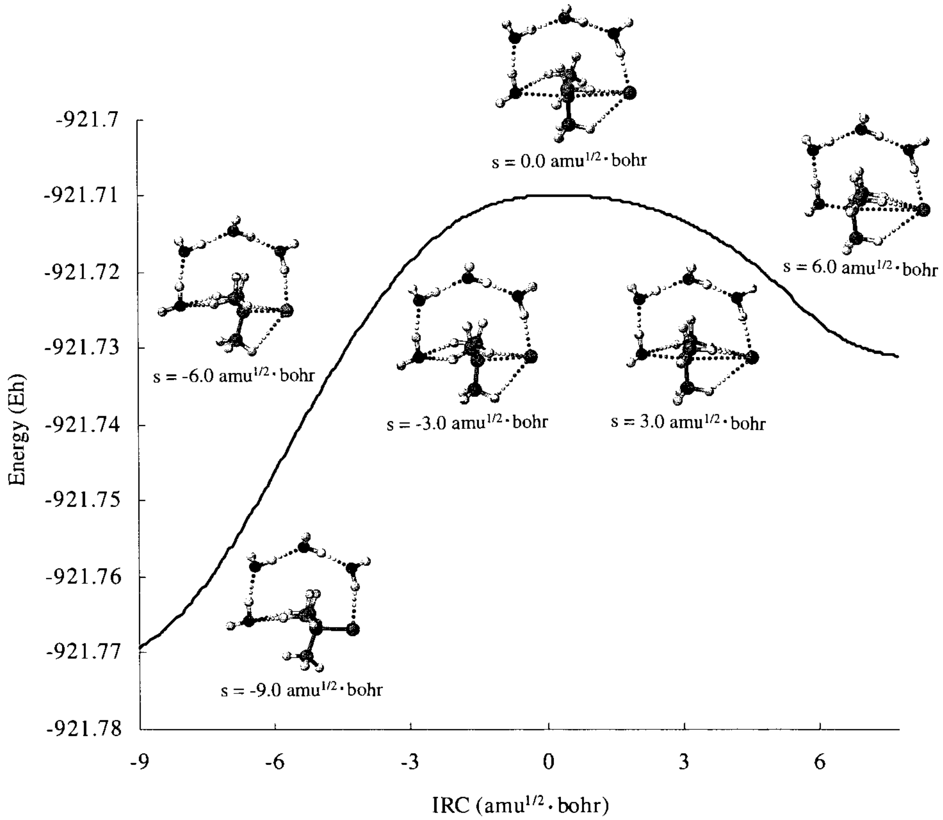


Figure 5. Potential energy profile along the IRC for the cluster system consisting of *t*-BuCl and four water molecules. Structures at $s = -9.0$, -6.0, -3.0, 0.0, 3.0, and 6.0 amu$^{1/2}$·bohr are also shown.

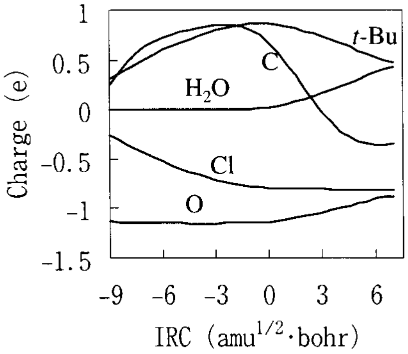


Figure 6. Change in the Mulliken charges along the IRC. The labels C, H_2O, and O indicate the central carbon of the *t*-Bu group, the water attached to the rearside of the *t*-Bu group, and the oxygen of the water, respectively.

TABLE 1: Total Electron Energies, Zero-Point Energies, and Relative Energies at the QCISD(T)/6-31+G*//MP2/6-31+G* Level for Stationary States

species	reactant	transition state	contact ion pair
energy (Eh)	−921.899 443 (−921.773 715)[a]	−921.839 023 (−921.709 766)	−921.856 386 (−921.731 772)
zero-point energy (Eh)	0.224 493	0.220 577	0.226 721
ΔE^b (kcal/mol)	0.0	35.46	28.42

[a] The values in parentheses are the energies calculated at the MP2/6-31+G* level. [b] Relative energies including zero-point correction.

the central carbon and the oxygen of the water neighboring the central carbon was found to decrease as the contact ion pair formation proceeds; namely, the C−O distance changes from 3.710 Å at the reactant through 2.563 Å at the transition state to 1.570 Å at the contact ion pair. This finding indicates that both the transition state and the contact ion pair are susceptible to nucleophilic solvent assistance, although the nucleophilic solvent assistance is relatively weak at the transition state. In other words, the stabilization due to the nucleophilic solvent assistance increases dramatically as the contact ion pair formation proceeds. The influence of electrophilic solvent assistance is also similar to that of the nucleophilic solvent assistance; namely, the extent of the electrophilic solvent assistance, the extent which is reflected by the distance between the chlorine and the hydrogen of the water neighboring the chlorine, increases as the contact ion pair formation proceeds. Therefore, not only the electrophilic but also the nucleophilic solvent assistance is essential for the contact ion pair formation.

The change in the Mulliken charges along the IRC is shown in Figure 6. It was found that ionization completes at the transition state and the cationic charge accumulated on the central carbon in the neighborhood of the transition state disperses within the protonated *tert*-butyl alcohol in passing from the transition state to the contact ion pair intermediate. This finding indicates that the contact ion pair can be better described as a contact ion pair between the protonated *tert*-butyl alcohol and the chloride anion.

Energy Barrier and Solvent Kinetic Isotope Effects. The calculated energy barrier for the contact ion pair formation, 35.46 kcal/mol (Table 1), is larger than the experimental data for the corresponding solution reaction, the hydrolysis of *t*-BuCl in aqueous solution, $\Delta H^{\ddagger} = 22.58-23.22$ kcal/mol.[26] However, the difference is only 12−13 kcal/mol. We emphasize that the energy required for the gas phase heterolytic dissociation *t*-BuCl → $t\text{-Bu}^+ + \text{Cl}^-$, is ca. 156 kcal/mol and four water molecules reduces the energy barrier by ca. 120 kcal/mol. This means that the influence of the other water molecules on the contact ion pair formation is expected to be small compared with that of the four water molecules. During the contact ion pair formation, the dipole moment of the cluster system was found to vary dramatically from 2.00 D at the reactant through 8.35 D at the transition state to 12.73 D at the contact ion pair. Therefore, the discrepancy between the calculated energy barrier and the experimental value will be attributed to the neglect of the influence of bulk water, i.e., the disregard of the long-range electrostatic interaction. In fact, the IPCM calculations showed that the bulk water causes the reduction of the energy barrier of the cluster system by (21.42 − 11.26=) 10.16 kcal/mol (Table 2). Therefore, the energy barrier for the contact ion pair formation in aqueous solution is estimated from calculation to be (35.46 − 10.16=) 25.30 kcal/mol by rule of thumb. As a result, the estimated value is moderately comparable with experimental data for the solution reaction, 22.58−23.22 kcal/mol.[26]

TABLE 2: Solvation Energy Due to the Bulk Water

	C−Cl bond length (Å)	solvation energy[a] (kcal/mol)	total energy at MP2/6-31+G* level (Eh)
reactant	1.842	11.26	−921.791 651
$s = -1.5$ amu$^{1/2}$·bohr	2.874	20.95	−921.744 446
$s = -1.0$ amu$^{1/2}$·bohr	2.941	21.39	−921.744 359
$s = -0.5$ amu$^{1/2}$·bohr	3.008	21.52	−921.744 184
transition state	3.075	21.42	−921.743 899
$s = 0.5$ amu$^{1/2}$·bohr	3.135	21.23	−921.743 694
$s = 1.0$ amu$^{1/2}$·bohr	3.184	21.12	−921.743 793
$s = 1.5$ amu$^{1/2}$·bohr	3.227	21.16	−921.744 354
contact ion pair	3.713	31.86	−921.782 545

[a] Solvation energy computed by IPCM calculations.

TABLE 3: Factor Analysis of the Solvent Kinetic Isotope Effects at 298 K

k_{H_2O}/k_{D_2O}	η_{trans}	η_{rot}	η_{vib}^{low}	η_{vib}^{mid}	η_{vib}^{high}
1.20	1.00	1.00	1.26	0.95	1.00

The relative energy of the contact ion pair for the cluster system with respect to the reactant was found from calculation to be 28.42 kcal/mol. The corresponding relative energy in the presence of the bulk water was roughly estimated to be (28.42 − (21.42 − 11.26)=) 7.82 kcal/mol. Our findings suggest that solvent effects constitute a significant barrier (25.30 − 7.82 = 17.48 kcal/mol) to the reverse reaction and thus help to prevent internal return.

The solvent kinetic isotope effects for the cluster system, $k_{H_2O}/k_{D_2O} = 1.20$, were found to be normal and to be in moderately good agreement with the experimental data for the corresponding solution reaction, $k_{H_2O}/k_{D_2O} = 1.30$.[27] The effect of the bulk solvent will be roughly ascribed to the discrepancy between our calculated value for the cluster system, $k_{H_2O}/k_{D_2O} = 1.20$, and the experimental value for the corresponding solution system, $k_{H_2O}/k_{D_2O} = 1.30$. Therefore, the solvent kinetic isotope effect due to the bulk water is possibly expected to be relatively small.[28] The factor analysis of the solvent kinetic isotope effects (Table 3) showed that the solvent kinetic isotope effects are determined by the low-frequency modes. This indicates that solvent structural stability as manifested in solvent librational degrees of freedom decreases significantly as the reaction proceeds from the reactant to the transition state, as discussed by Swain and Bader.[29]

The relatively good agreement in energy profile and solvent kinetic isotope effects between the present findings and the experimental data for the solution reaction suggests that the contact ion pair and the relevant transition state structure obtained for the cluster system have some relevance in the corresponding solution reaction.

S_N2(intermediate) Mechanism. On the basis of all these findings, the contact ion pair formation is concluded to proceed via a nucleophilically (though weakly) solvated transition state, leading to a nucleophilically solvated contact ion pair. That is, the hydrolysis of *t*-BuCl in aqueous solution will proceed via the S_N2(intermediate) mechanism previously proposed by Bentley et al.[2]

It should be noted that our conclusion does not necessarily contradict most of the previous findings of the absence of the nucleophilic solvent assistance in several S_N1 reactions.[4−7] We emphasize that the nucleophilic solvation at the transition state for the present system is rather weak. Because the extent of nucleophilic solvent assistance is possibly determined by the balance between the solvent nucleophilicity and the steric hindrance arising from the repulsive interaction between the solvent and the solute, such nucleophilic solvent assistance may disappear for the other S_N1 reactions, such as the S_N1 reaction in a weaker or bulkier nucleophilic solvent.

Now we briefly discuss the subsequent fate of the contact ion pair produced. The contact ion pair may undergo the displacement of the leaving Cl group by the hydroxy group of the nucleophilically solvated water in concert with simultaneous proton transfers, giving *t*-BuOH with an overall inversion of configuration. This possible pathway would provide the convenient explanation of the experimental findings[1] that the products with the predominant (5−20% net) configurational inversion are afforded by many S_N1 reactions. Otherwise, the contact ion pair may further dissociate into a solvent-separated ion pair. In fact, Yamabe et al.[30] have demonstrated that for the reaction of *t*-BuCl with OH^- in aqueous solution a nucleophile or a nucleophilic solvent feasibly wedges itself into the C−Cl weak bond of the *t*-BuCl by way of the contact ion pair formation. Jorgensen et al.[8] also demonstrated that the free energy barrier of the reaction of the contact ion pair to the solvent-separated ion pair is very small (2 kcal/mol). In addition, the convergion of the protonated *tert*-butyl alcohol with a nucleophilic water, $H_2O + t\text{-BuOH}_2^+ \rightleftarrows H_2Ot\text{-Bu}^+ + H_2O$, is expected to be facile, as demonstrated by Yamabe et al.[30] Therefore, the formation of the solvent-separated ion pair and the subsequent facile conversion gives the possibility of racemization before the proton attached to *tert*-butyl alcohol in the contact ion pair is taken off by the solvent water. It is also possible that some solvent-separated ion pairs may further dissociate into completely dissociated ions. The dissociated ions will then undergo nucleophilic attack on either side of the carbocation, leading to the substitution products with either retention or inversion of configuration.

Conclusions

We have revealed that each of the contact ion pair and the relevant transition state for the cluster system consisting of *t*-BuCl and four water molecules has a ten-membered ring structure in which one edge of a chain of four water molecules solvates nucleophilically on the backside of the central carbon of the *t*-Bu group and the other edge hangs electrophilically on the chlorine. The calculated energy barrier of the contact ion pair formation has been found to be comparable with the energy barrier for the corresponding solution reaction when taking into account the influence of the bulk water. The calculated solvent kinetic isotope effects for the cluster system have been also found to be in good agreement with the experimental data for the solution reaction. On the basis of these findings, we have concluded that the hydrolysis of *t*-BuCl in aqueous solution proceeds via the S_N2(intermediate) mechanism; namely, the hydrolysis of *t*-BuCl in aqueous solution preceeds via a nucleophilically solvated transition state and then a nucleophilically solvated contact ion pair intermediate, followed by the formation of the hydrolysis products.

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References and Notes

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