Chapter 3

Application to the ionic fragmentation of *t*–BuCl in aqueous solution

According to the current view for the S_N1 type dissociation of *t*–BuCl in aqueous solution,[55,56] *t*–BuCl dissociates to free ions via a contact ion pair(CIP), and then a solvent–separated ion pair (SSIP).

$$\begin{array}{ccccccc} t\text{–BuCl} & \rightleftharpoons & t\text{–Bu}^+\ \text{Cl}^- & \rightleftharpoons & t\text{–Bu}^+\ //\ \text{Cl}^- & \rightleftharpoons & t\text{–Bu}^+ + \text{Cl}^- \\ & & \text{CIP} & & \text{SSIP} & & \text{free ions} \end{array}$$

The activation free energy for this hydrolysis of *t*–BuCl was reported to be 19.6 kcal/mol.[29] The CIP and fully separated ions were considered to have same free energy, 14.5 kcal/mol above the reactant, though the uncertainty was at least ±5 kcal/mol.[57]

Jorgensen *et al.*[27] investigated the potential energy profile for the ion pair region in the hydrolysis of *t*–BuCl by MC simulation. They showed a well-defined minimum for a CIP at a C-Cl distance of about 2.9 Å, and a minimum for an SSIP at 5.75 Å, though they suggested that free ions and SSIP are not energetically distinct species. Their calculation was confined to the ion pair region.

Keirstead *et al.*[28] carried out the empirical valence bond simulation for the CIP formation step. Their method can treat the non-equilibrium solvation by including

the coupling between an ionic state and a covalent state explicitly. They obtained a reasonable value for the free energy barrier which separates *t*–BuCl and CIP, although the CIP was predicted to be lower in energy than *t*–BuCl.

More recently, Hartsough and Merz[29] carried out a quantum mechanical/molecular mechanical (QM/MM) coupled potential simulation of the S_N1 heterolysis of *t*–BuCl in water using the semiempirical PM3 Hamiltonian for the solute. Their approach can treat the system over the whole range of the reaction coordinate since the solute electronic structure is calculated in the presence of the solvent. They obtained a reasonable potential energy curve only when the correction was taken into account in the long-range solute–solvent electrostatic interaction; a deep minimum corresponding to a CIP and a shallow minimum corresponding to an SSIP appeared at 2.9 and 6.4 Å, respectively.

This study has examined the same reaction system by the present method. The heterolysis of *t*–BuCl does not occur in the gas phase because the electron affinity of *t*–Bu^+, i.e. the first ionization potential of the *t*–Bu group, is larger than the electron affinity of Cl when the C-Cl distance is long. However, the *ab initio* GB method describes appropriately the heterolysis reaction. On the basis of *ab initio* GB calculations, the EPPF between *t*–BuCl and a water molecule which covers whole region of the C-Cl distance was determined. By using this EPPF, the Monte Carlo simulation and statistical perturbation theory were carried out to calculate the free energy profile of the reaction.

3.1 Calculation

At first, the EPPF between t–BuCl and a water molecule was determined. The geometry of t–BuCl was optimized within C_3 symmetry and local C_3 symmetry for the methyl groups for 12 different C-Cl distances (R_{C-Cl}) using the *ab initio* GB 6-31G* method with the dielectric constants of ε=1 and 79 for the gas phase and aqueous solution, respectively. For each of 12 structures of t–BuCl in the range of 1.76 Å $\leq R_{C-Cl} \leq$ 9.00 Å, the interaction energies, E^{int}, were calculated for 126 orientations of the t–BuCl– H_2O system. The electron correlation plays important role in this system,[45] and the energy of the isolated solute molecule was corrected using the MP2/6-31+G* calculation for the structure optimized by the HF/6-31G* calculation.

In Eqn. 2.10, the methyl groups were treated as united atoms. The Jorgensen's Lenard–Jones parameters[27] were used for the central carbon atom in t–Bu^+. From the PF parameters determined for the 12 different structures of t–BuCl, the EPPF which covers the whole range of the reaction coordinate was determined by interpolation. The PF of water was newly determined in order to reproduce the dipole moment of *ab initio* GB 6-31G* calculation, density (0.997 g/cm^3), and the pair correlation functions for water. The procedure followed the WK model[41] in which the water EPPF model was determined using a mean field approximation. The parameters and properties of the EPPF were listed in Table 3.1 and in Figure 3.1. The TIP4P[38] and WK[41] models for water were also employed.

The MC simulation was carried out by NPT ensemble according to the standard Metropolis method[52] for one t–BuCl solute and 506 water molecules in a periodic rectangular cubic cell which had the dimension of ca. 22 × 22 × 30 Å. The pressure and temperature of the system were 1.0 atm and 298K, respectively. The interaction energies calculated by the PF were truncated at 10.0 Å. The solvation free-energy change was determined by using statistical perturbation theory (SPT[63,64]) along the

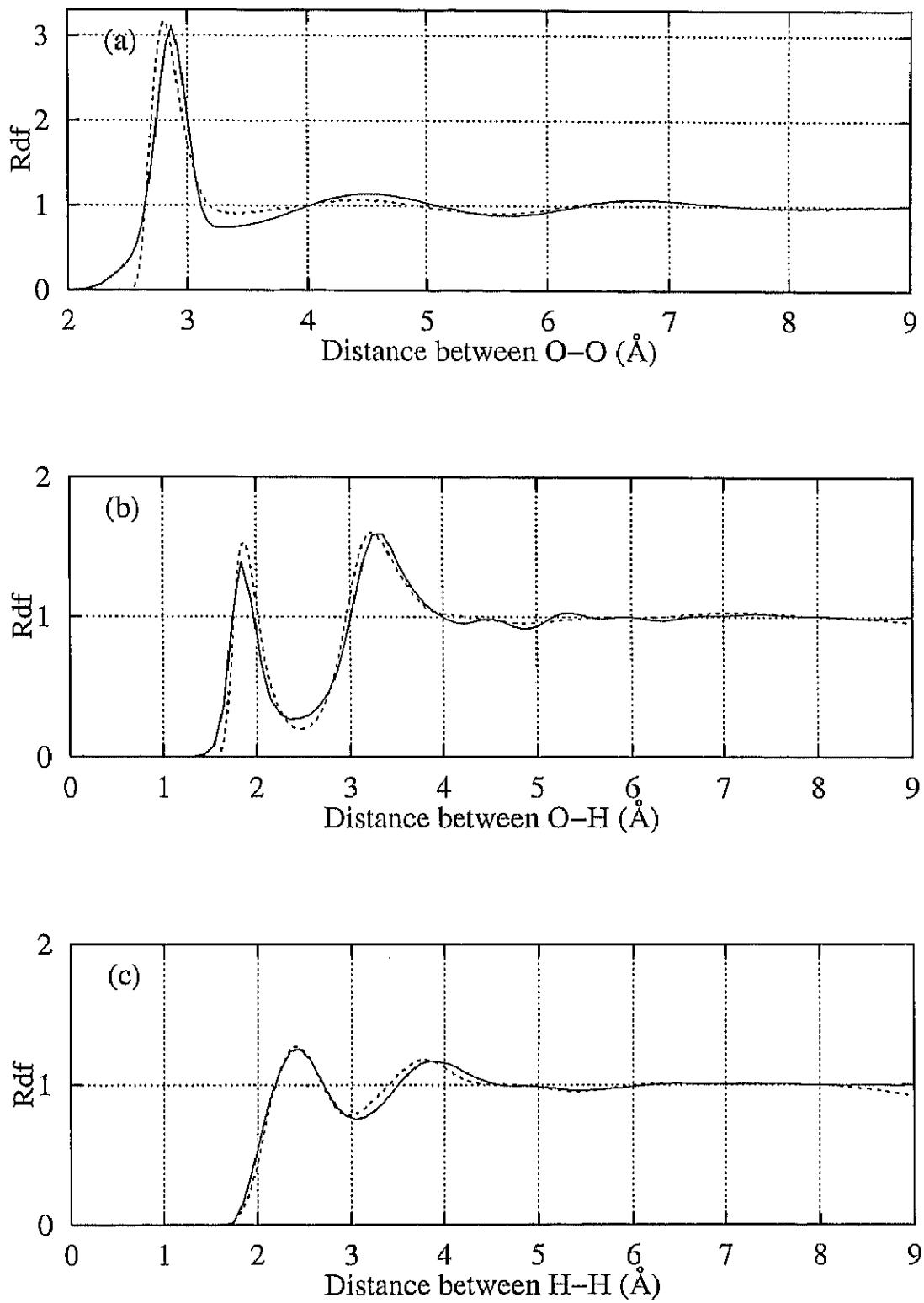

Figure 3.1: Calculated (a) oxygen-oxygen, (b) oxygen-hydrogen, and (c) hydrogen-hydrogen radial distribution functions of water (dotted curves) obtained by using the potential function determined in present work for water. The experimental data (solid curves) are from ref. 60–62.

R_{C-Cl} stretching in steps of 0.05 Å. Double-wide sampling[64] was used and 0.10 Å of the C-Cl distance could be covered in each MC simulation.

All MO calculations were carried out using our ABINIT program and MC simulations using our SIMPLS program on HP J282 workstations and GAIA-300 personal supercomputers.

Table 3.1: Parameters of MC simulation of water

	this study[a]	TIP4P[b]	WK	Experiment
R_{OH} ($\AA$)	0.9572	0.9572	0.9572	0.9572[c]
R_{OM} ($\AA$)	0.15	0.15	0.15	
$\angle$HOH (deg)	104.52	104.52	104.52	104.52[c]
A (kcal $\AA^{12}$) mol^{-1}	960.0	774.6	1093.2	
C (kcal $\AA^{6}$) mol^{-1}	30.3	24.7	34.05	
Q_M	-1.156	-1.04	-1.24	
Q_H (e)	0.578	0.52	0.62	
$E^{eff-sol}$ (kcal mol^{-1})	-12.45	—	-14.46	
E_{pol} (kcal mol^{-1})	2.74	—	3.97[d]	
$E^{tot-sol}$ (kcal mol^{-1})	-9.71	-10.07	-10.49	-9.9[e]
μ (g cm^{-3})	1.011	0.999	1.000	0.997[e]
dipole moment (Debye)	2.424[f]	2.177	2.596	1.85[e]

[a] The MC simulation carried out for the NPT ensemble (216 molecules, 1.0 atm and 298K). [b] Ref.41. [c] Ref.58. [d] Ref.38. [e] Ref.59. [f] This value is equal to the dipole moment calculated using *ab initio* GB method with 6-31G* basis set.

3.2 Molecular and electronic structures of t–BuCl

The optimized molecular structures, relative energies, and charges of t–BuCl along the reaction coordinate are listed in Table 3.2. The energy minimum structure in the gas phase was found at R_{C-Cl}= 1.83 Å. The heterolytic C-C bond dissociation energy in the gas phase, which is largely method-dependent,[45] was evaluated as 150.58 kcal/mol, which was compared with the experimental value of 160 ± 6 kcal/mol.[59] The energy calculated by MP2/6-31+G**//HF/6-31G* level was 167.17 kcal/mol, showing that the electron correlation effect stabilizes the covalent electronic state more than the ion-pair state.

Charge separation between the t–Bu group and chlorine almost completed at R_{C-Cl}= 3.5 Å, and the charges of the t–Bu^+ and Cl^- fragments become +1.0 and -1.0, respectively, for $R_{C-Cl} > 3.5$ Å. The structural changes also almost completed at R_{C-Cl}= 3.5 Å, and the hybridization of the central carbon in the t–Bu group changed from sp^3 to sp^2; R_{C-C} became shorter by 0.05 Å and ∠ClCC became smaller by 17.3 degrees. The effect of solvation on the solute energy was the largest at R_{C-Cl}= 2.8 Å, where E_{pol} was 4.05 kcal/mol. At this structure, destabilization of the solute molecule caused by polarization is large, because the solvation effect stabilizes the ionic electronic state more than the covalent one and then accelerates the ionic dissociation of t–BuCl. Inclusion of the electron correlation effect enlarges the E_{pol}, because the stabilization by the electron correlation is relatively small for the ionic electronic state which has larger contribution in solution than in the gas phase.

Table 3.2: Relative nergies, polarization self–energies (kcal/mol), bond lengths (Å), bond angles (degree), and Löwdin charges of t–BuCl calculated by *ab initio* GB method[a]

R_{C-Cl}	ΔE	E_{pol}	R_{C-C}	R_{C-H}	$\angle$ClCC	Q_{Cl}
1.70	4.10(3.11)	0.27(-0.42)	1.534	1.085	109.1	-0.008
	4.37(2.69)		1.533	1.085	109.1	-0.012
1.80	0.19(0.00)	0.32(-0.33)	1.527	1.084	107.7	-0.082
	0.51(-0.33)		1.527	1.085	107.8	-0.094
1.83	0.00(0.01)	0.34(-0.28)	1.526	1.084	107.3	-0.103
	0.34(-0.27)		1.525	1.085	107.4	-0.119
1.90	0.76(1.21)	0.42(-0.08)	1.522	1.084	106.4	-0.155
	1.18(1.13)		1.521	1.084	106.4	-0.180
2.00	3.81(4.92)	0.62(0.47)	1.516	1.084	105.0	-0.229
	4.44(5.38)		1.515	1.084	105.0	-0.270
2.20	12.88(15.82)	1.46(2.86)	1.507	1.083	102.2	-0.378
	14.34(18.68)		1.505	1.083	102.2	-0.459
2.50	26.88(33.99)	3.29(7.91)	1.496	1.083	98.4	-0.585
	30.17(41.90)		1.492	1.082	98.3	-0.709
2.80	38.60(49.85)	4.05(9.41)	1.489	1.083	95.2	-0.744
	42.65(59.26)		1.483	1.081	95.6	-0.861
3.00	45.10(58.66)	3.78(8.38)	1.484	1.083	93.3	-0.832
	48.88(67.04)		1.479	1.081	94.3	-0.917
3.50	55.95(73.37)	3.31(5.32)	1.476	1.085	90.0	-0.946
	59.26(78.69)		1.474	1.082	91.9	-0.974
4.00	66.55(83.79)	1.88(4.20)	1.475	1.086	90.0	-0.976
	68.43(88.00)		1.474	1.082	90.0	-0.990
5.00	84.44(100.78)	1.22(2.21)	1.475	1.086	90.0	-0.997
	85.67(102.99)		1.474	1.082	90.0	-0.999
6.00	95.73(112.38)	0.86(1.05)	1.475	1.086	90.0	-1.000
	96.59(113.43)		1.475	1.082	90.0	-1.000
7.00	103.52(120.36)	0.73(0.70)	1.476	1.086	90.0	-1.000
	104.25(121.06)		1.475	1.082	90.0	-1.000
8.00	109.35(126.27)	0.69(0.62)	1.476	1.086	90.0	-1.000
	110.05(126.89)		1.475	1.082	90.0	-1.000
9.00	113.90(130.83)	0.68(0.61)	1.476	1.086	90.0	-1.000
	114.57(131.44)		1.475	1.082	90.0	-1.000
∞	150.58(167.17)	0.66(1.13)	1.476	1.086	—	-1.000
	151.24(168.30)		1.475	1.082	—	-1.000

[a]The upper values are for the gas phase ($\varepsilon = 1$), and the lower values are for aqueous solution ($\varepsilon = 79$). The values were calculated at HF/6-31G*//HF/6-31G* level, and the values in parentheses were calculated at MP2/6-31+G*//HF/6-31G* level.

3.3 EPPF between t–BuCl and water

The effective interaction energy in Eqn. 2.9 which used to determine the EPPF was examined. The effective interaction energies of Cl^--water are plotted for the distance between the Cl^- and the oxygen atom in water in Figure 3.2. As discussed in subsection 2.1.3, the electronic state of Cl^- is not polarized by the present method but that of water is polarized, and the effective interaction energy in aqueous solution is larger than in the gas phase by 0.5 kcal/mol.

The effective interaction energies of t–Bu^+-water are plotted for the distance between the central carbon atom in t–Bu^+ and the oxygen atom in water in Figure 3.3. The effective interaction energy in aqueous solution is larger than in the gas phase by 1.1 kcal/mol. In the t–Bu^+-water system, the polarization occurs both in water and t–Bu^+, and the change of the effective interaction energy of t–Bu^+-water is larger than that of the Cl^--water system.

The EPPF parameters of t–BuCl determined for the new water PF are shown in Figure 3.4. The charge of the chlorine atom at 9.0 Å is almost unit value, -0.988. This was obtained without any restriction except the total charge of the t–BuCl system which was set to be zero, because the charges in the PF of water were determined to reproduce the dipole moment calculated by *ab initio* GB method using 6-31G* basis set. The corresponding values determined for the TIP4P and WK water models were 1.098 and 0.921, respectively; they are not unit charge because the charges in the PF for these models do not reproduce the dipole moment obtained by the *ab initio* calculation. Discrepancy of the charge from the unit value causes a significant error in evaluation of the solvation energy of the ionic species in the dissociation limit.

In order to apply the EPPF to the SPT calculation, the charges were expressed

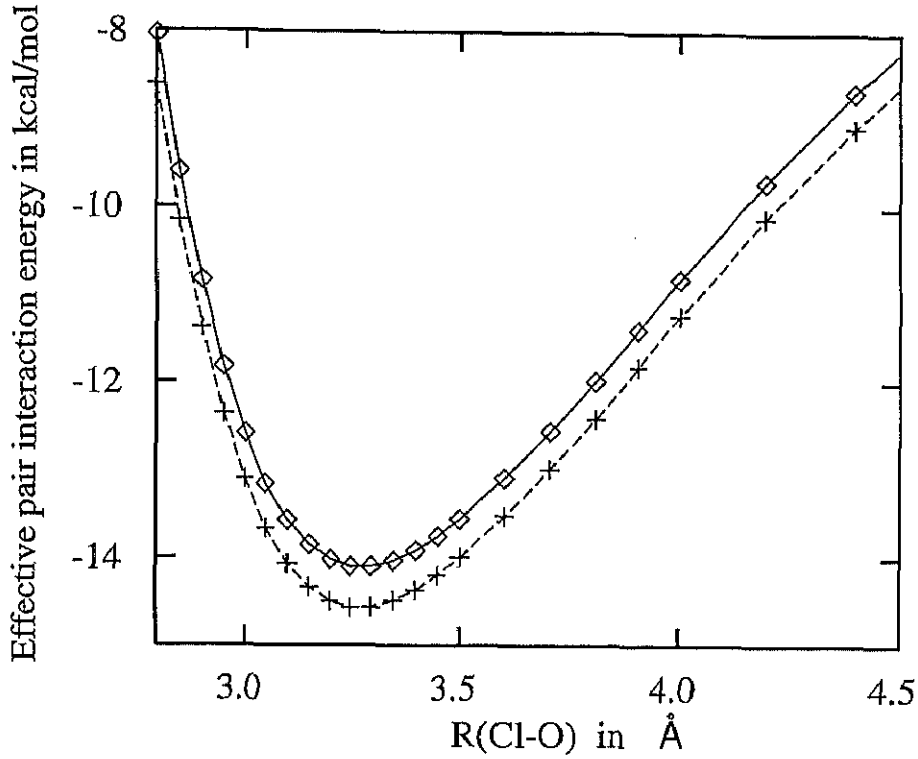

Figure 3.2: The effective pair interaction energy for Cl^--H_2O. The solid line and open squares are calculated in the gas phase ($\varepsilon = 1$), and the broken line and crosses are calculated in aqueous solution ($\varepsilon = 79$).

Table 3.3: Coulomb parameters[a] in EPPF

	a_1	a_2	a_3	a_4	a_5	a_6
for chlorine	-0.988	0.264	0.358	-0.0736	0.250	-0.0935
for methyl group	0.217	-3.56	-0.150	-0.000942	2.86	-0.139

[a] The charge for carbon at the center of t–Bu^+ was decided by $Q_C = -3Q_{Me} - Q_{Cl}$.

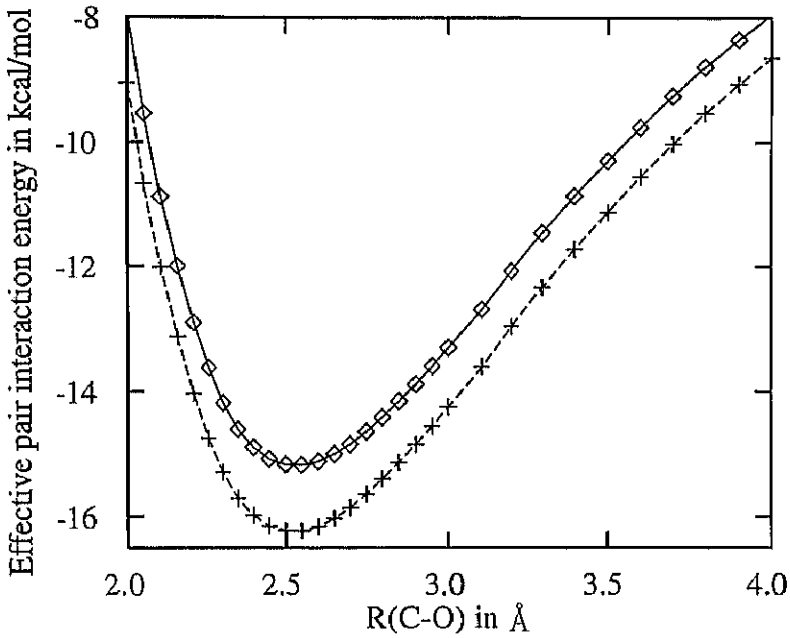

Figure 3.3: The effective pair interaction energy for t–Bu^+-H_2O. The solid line and open squares are calculated in the gas phase ($\varepsilon = 1$), and the broken line and crosses are calculated in aqueous solution ($\varepsilon = 79$).

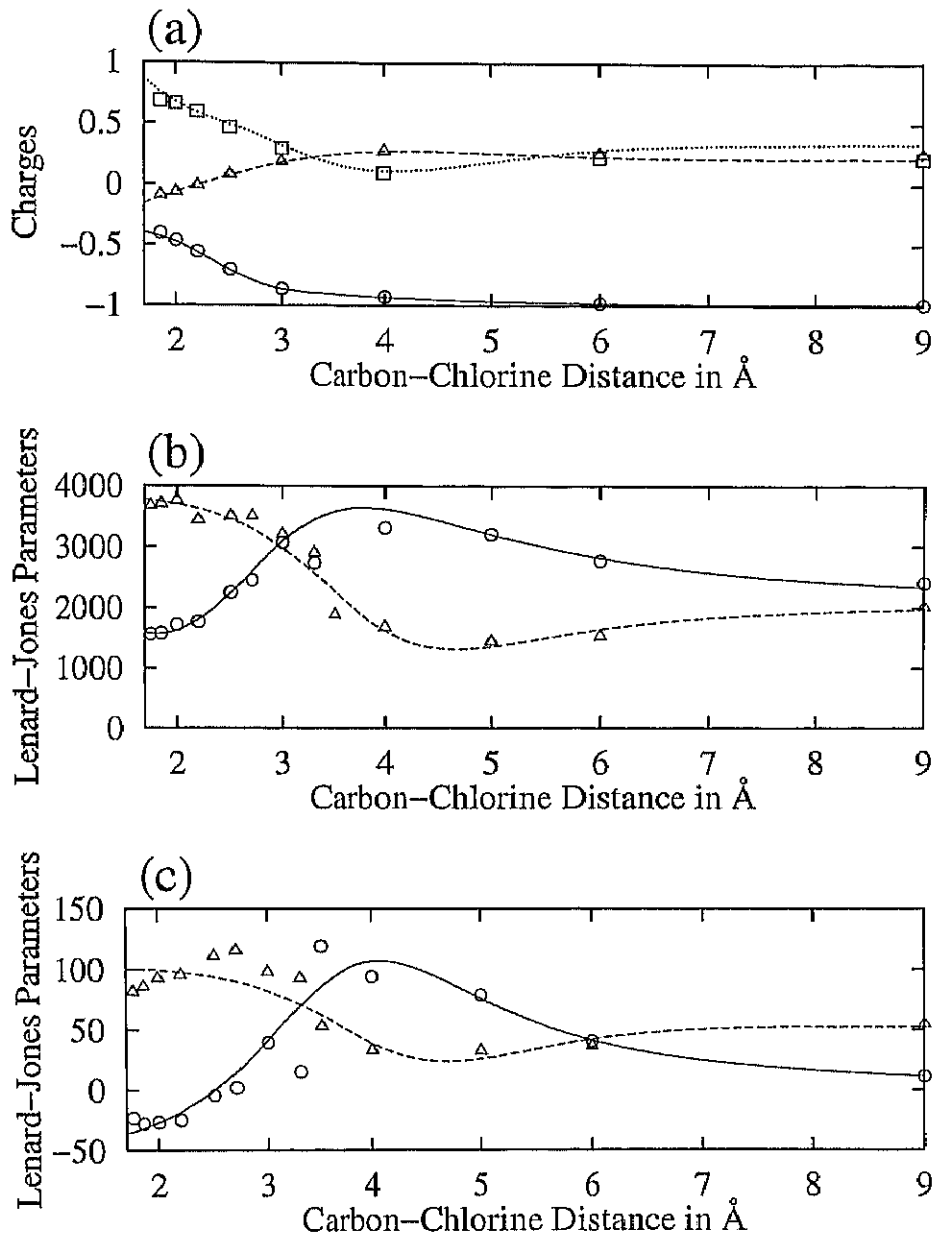

Figure 3.4: Parameters in the potential functions. (a)The coulomb parameters Q_i for carbon at the center of t–Bu$^+$(dotted line, squares), methyl groups(broken line, triangles) and chlorine(solid line, circles). (b) The Lenard-Jones repulsion parameters A_{ij} for methyl groups(broken line, triangles) and chlorine(solid line, circles). For carbon at the center of t–Bu$^+$, the fixed value of 66.8 $kcal^6 \cdot mol^{-6} \cdot \mathring{A}^{-6}$ was used.[27] (c) The Lenard-Jones dispersion parameters C_{ij} for methyl groups(broken line, triangles) and chlorine(solid line, circles). For carbon at the center of t–Bu$^+$, the fixed value of 5.76 $kcal^3 \cdot mol^{-3} \cdot \mathring{A}^{-3}$ was used.[27]

analytically as a function of R_{C-Cl}, $Q(R_{C-Cl})$, using the following equation,

$$Q(r) = a_1 + a_2\, exp\left(a_3\, r^2 + a_4\, r^4\right) + a_5\, exp\left(a_6\, r^2\right) \tag{3.1}$$

where a_i were fitting parameters, listed in Table 3.3. The parameters of the Lenard-Jones terms have a minimum or a maximum near the R_{C-Cl}= 4 Å. This characteristic feature comes from the bonding property of t–BuCl which changes from covalent to ionic near this region. In order to represent these complex variations in the Lenard-Jones parameters, P_{LJ}, the following functions were employed.

$$P_{LJ}(r) = (a_1 + a_2\, r^{n_1})\; f(r : a_3) + (a_4 + a_5\, r^{n_2})\,(1 - f(r : a_3)) \tag{3.2}$$

$$f(r : a_3) = \frac{1}{2}\,(tanh\,(r - a_3)\; +\; 1) \tag{3.3}$$

where a_i and n_i were fitting parameters, listed in Table 3.4.

The correlation between the energies calculated by the *ab initio* GB method and the EPPF determined in this work is shown in Figure 3.5. The standard deviation of these interaction energies was 0.73 kcal/mol, suggesting that the EPPF reproduce well the *ab initio* GB energies.

Table 3.4: Lenard-Jones parameters[a] in EPPF

	a_1	a_2	a_3	a_4	a_5	n_1	n_2
for chlorine							
A	2130	155000	-486	2.69	-1460	3	2
C	-4.75	1310	0.846	3.67	-52.7	2	4
for methyl group							
A	2070	-70200	-1.39	3.79	4040	3	5
C	48.1	337	-0.0814	4.19	101	2	5

[a] The Lenard-Jones parameters for carbon at the center of t–Bu^+ were taken from literature.[27]

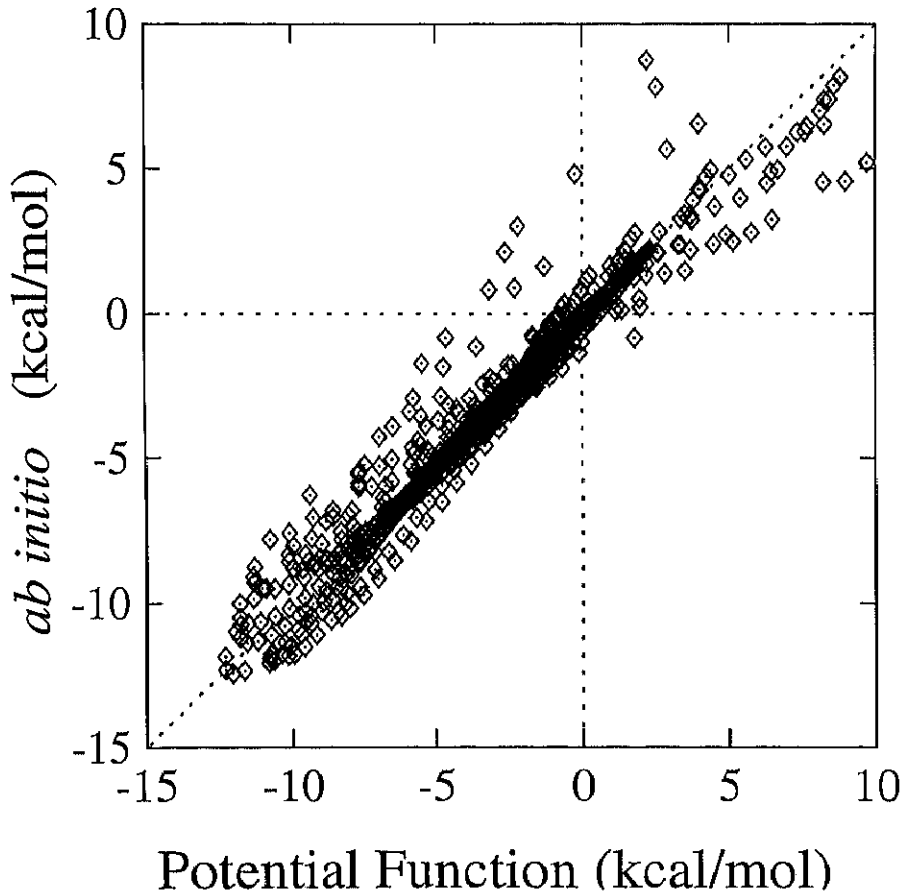

Figure 3.5: The comparison of interaction energies obtained by *ab initio* GB calculations and the EPPF for the t–BuCl– H_2O configurations.

3.4 Energy profile for the ionic fragmentation reaction of t–BuCl in aqueous solution

Energy profile for the ionic fragmentation reaction of t–BuCl in aqueous solution was calculated by Eqn. 2.13b in which $E^{eff-sol}$ and E_0^{sol} were calculated by using a MC simulation and *ab initio* GB calculation, respectively. The computed free energy profile is displayed in Figure 3.6, and the corresponding numerical datas are listed in Table 3.5. In Figure 3.6, the energy of the solute molecule, E_0^{sol} was calculated by HF/6-31G*//HF/6-31G*(dotted line) or MP2/6-31+G**//HF/6-31G*(solid lines) levels.

The energy minimum at the C-Cl distance of 1.85 Å corresponds to the t–BuCl molecule, and the second minimum, which appears at ca. 3.7 Å, corresponds to a CIP.

The result based on the HF calculation underestimated the dissociation energy largely. In this reaction system, the inclusion of electron correlation favors the covalent state[45] and the energy profile was corrected by the MP2 calculation.

The MP2 corrected relative energy of the free ions, 14.96 kcal/mol, agrees well with experiment, though activation energy, 28.52 kcal/mol, is slightly overestimated. This overestimation may be attributed to (1) the lack of the electron correlation in the fitting procedure of EPPF, (2) the disadvantage of the mean field approximation, and (3) the adoption for the simple forms of the potential functions.

With respect to the first point, the MP2 and the counterpoise calculations of the solute–solvent interaction energy were carried out at several points, and it was confirmed that 60-80% of the electron correlation were compensated by the basis set super position error (BSSE).

With respect to the disadvantage of the mean field approximation, the model of Keirstead *et al.*,[28] which is responsible to the change in solvation, may be appropriate to predict correctly the transition state between the reactant and CIP (TS_1). TS_1 in

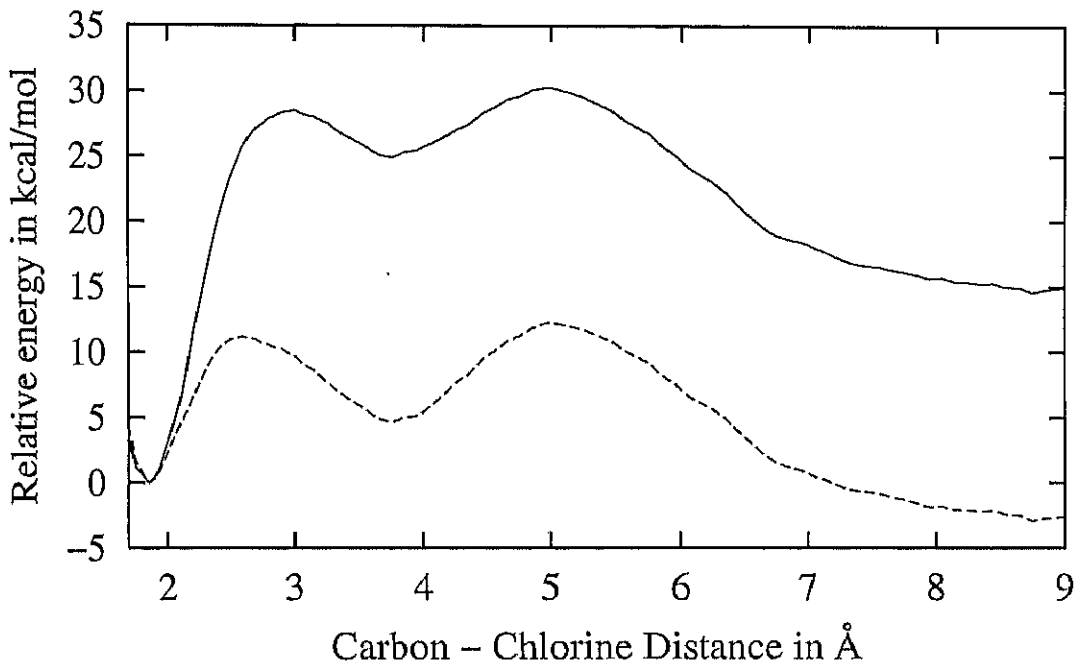

Figure 3.6: Free energy profile for the ionic fragmentation of t–BuCl plotted as a function of the carbon–chlorine distance: The energy is in kcal/mol and the distance is in $\AA$. Solid line was obtained by the MP2/6-31+G*//HF/6-31G* calculations, while dashed line was obtained by the HF/6-31G*//HF/6-31G* calculations.

Table 3.5: Relative energy (in kcal/mol) for the ionic fragmentation of t–BuCl

	This study[a]	Ref.27	Ref.28	Ref.29[b]	Ref.29[c]	Ref.29[d]	exptl.
ΔG_{React}	0.00	—	0	0	0.0	0.0	0.0
	(1.85Å)	(—)	(1.8Å)	(1.8Å)	(1.8Å)	(1.8Å)	(—)
$\Delta G_1^{\ddagger e}$	28.52	—	21	×	17.8	23.4	19.5
	(3.00Å)	(—)	(2.3Å)	(—)	(2.3Å)	(2.5Å)	(—)
ΔG_{CIP}	24.92	1.88	-1	×	9.1	22.9	14.5± 5.0
	(3.75Å)	(2.88Å)	(2.9Å)	(—)	(2.9Å)	(2.9Å)	(—)
$\Delta G_2^{\ddagger f}$	30.27	4.03	—	~57	20.5	23.9	—
	(5.00Å)	(4.13Å)	(—)	(5.5Å)	(5.2Å)	(3.5Å)	(—)
ΔG_{SSIP}	×	-2.12	—	~55	19.3	×	—
	(—)	(5.75Å)	(—)	(6.5Å)	(6.4Å)	(—)	(—)
ΔG_{FreeIP}	14.96	0.00	—	~58	20.6	10.0	18.5
	(9.00Å)	(10.00Å)	(—)	(—)	(—)	(9.0Å)	(—)

[a] The MP2/6-31+G**//HF/6-31*G calculation. [b] Without any correction. [c] With Born correction. [d] With charge correction. [e] The relative activation free energy between reactant and CIP. [f] The relative activation free energy between CIP and free IP.

the present study is located at a larger C-Cl distance, 3.00 Å, and then the CIP at 3.75 Å which is larger than the reported values.[27-29] The present method can adopt the empirical valence bond model like Keirstead *et al.*, and I am planning such an extension of the present model.

It may be difficult to describe the interaction near CIP region correctly by a simple form of the potential functions. In this area, the favorable molecular structure of the *t*–Bu group changes between C_{3v} and C_{3h} symmetries, and the united atom approximation of methyl groups could not reproduce the situation well. This is also the reason why the MP2 corrected result overestimates the energy in this area.

Hartsough and Merz[29] obtained the free energy profile of the reaction similar to those in Figure 3.6 by adopting the charge scaling correction; if the scaling correction was removed, the activation energy for the dissociation was vary large (~57 kcal/mol). This indicates that the evaluation of the electrostatic interaction between the ions at a long distance is not easy. When the TIP4P and WK models were used for the PFs of water in the simulation, the MP2 corrected relative energy at R_{C-Cl}= 9.0 Å were ca. 2 and 71 kcal/mol, respectively. These results are caused by the overestimation (TIP4P) and underestimation (WK) of the solvation energies of the ions, of which absolute charges, 1.098 for TIP4P and 0.921 for WK, are deviated from the unit value. So, the overestimation of the relative energy reported by Hartsough and Merz[29] is also caused by the discrepancy of the solute and solvent molecular charges. Their result with Born correction is not suitable for the *t*–BuCl system, because the long-range interaction is affected by dipole interaction. In the present simulation, no correction in the long-range interaction was considered, but the long-range interaction has an important role in the *t*–BuCl system.