Heteroatom Chemistry
Volume 7, Number 4, 1996

Ab Initio MO Study of the Solvent Effect on the S_N2 Reaction of the Trimethylsulfonium Cation with Chloride Anion

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Received 26 January 1996; revised 13 March 1996

ABSTRACT

A recently developed ab initio MO theory including solvent effects has been applied to a typical cation-anion reaction, the S_N2 reaction of the trimethylsulfonium cation with the chloride anion. In the gas phase, the trimethylsulfonium and chloride ions are unstabilized, and the reaction is expected to proceed rapidly. In aqueous solution, the reactant ions are largely stabilized, and the reaction has been predicted to be endothermic, with an activation energy of 30–40 kcal/mol. This potential energy profile, which agrees with experimental results, has been well elucidated by differential solvation at several stages of the reaction path. At the transition state of this reaction, the C and H atoms in the transferring CH_3 group are almost in a plane that is perpendicular to the Cl–C–S line, reflecting the concerted nature of the reaction. The population analysis has shown that the electrons in the C–S bond are mostly withdrawn by the sulfur atom at the transition state and that the electron transfer from Cl to CH_3 occurs after the transition state. The calculated activation energy for the reaction in ethanol is smaller than that in water. This agrees with experiments. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

The S_N2 decomposition of trimethylsulfonium halides is an excellent model for demonstrating some features of bimolecular cation-anion reactions in solution, and many experimental studies have been reported [1–6].

$$S^+(CH_3)_3 + X^- \rightarrow S(CH_3)_2 + CH_3X \qquad (1)$$

The apparent reactivity of the various halide ions in this reaction follows the order $I^- > Br^- > Cl^-$ [3,4]. For the bromide ion, the reaction is endothermic by 20.4 kcal/mol with the activation energy being 32.0 kcal/mol in dimethylacetamide [4]. The S_N2 reaction of a three-membered cyclic sulfonium ion and a nucleophile is involved in the toxic action of mustard gas [7,8]. Methyl transfers from the sulfonium center to various acceptors are widespread processes in biological systems [9]. These reactions involve a heterolytic C–S bond cleavage and proceed in aqueous solution or in polar organic solvents, and theoretical studies of these reactions should include the important role of solvent polarity.

We recently developed a method for incorporation of solvent effects into ab initio SCF calculations using the generalized Born formula [10]. The method reproduces well the hydration free energies of cations and anions. Also, the method has been applied successfully to ionic reactions in solution. In the present study, the method was applied to the S_N2 reaction of the trimethylsulfonium cation with the chloride anion,

$$S^+(CH_3)_3 + Cl^- \rightarrow S(CH_3)_2 + CH_3Cl \qquad (2)$$

which is a typical S_N2 reaction of an alkylsulfonium cation with a nucleophile, and the solvent effects on the potential energy curve along the predicted reac-

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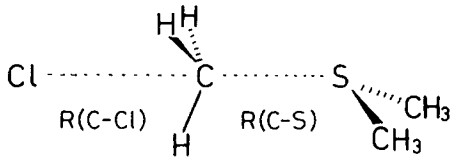

SCHEME 1

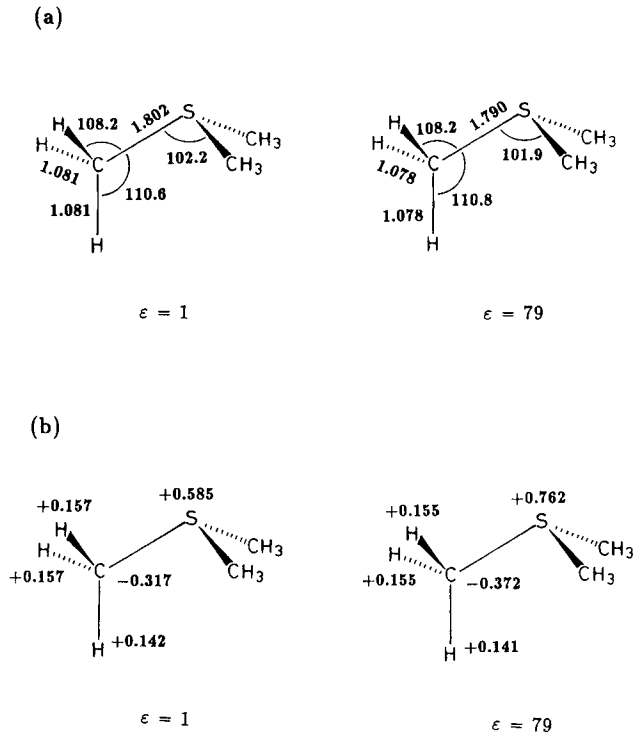

FIGURE 1 Molecular structure (a) and Löwdin population (b) of the trimethylsulfonium cation in the gas phase ($\varepsilon = 1$) and in aqueous solution ($\varepsilon = 79$) calculated with the 3-21G(*) basis set.

tion path have been elucidated. The electronic structure and solvation energy at each stage of the reaction path also were elucidated.

METHOD

Ab initio SCF calculations with the generalized Born formula have been described in a previous article [10]. In this model, the solvation free energy of a molecule is expressed as

$$\Delta G_{\text{sol}} = -\frac{1}{2}\left(1 - \frac{1}{\varepsilon}\right)\sum_A \sum_B Q_A Q_B \Gamma_{AB} \qquad (3)$$

where ε is the dielecric constant of the solvent, A and B are atoms in the molecule, and Q_A and Q_B are fractional charges. Γ_{AB} values are calculated by atomic radii for one-center terms and by an Ohno-Klopman–type formula for two-center terms. If Q_A is calculated from the nuclear charge and Löwdin population analysis, the Fock matrix elements, including solvent effects, become

$$F_{\mu\nu} = F^0_{\mu\nu} + F^{\text{sol}}_{\mu\nu} \qquad (4)$$

$$F^{\text{sol}}_{\mu\nu} = -\sum_\lambda \frac{\partial \Delta G_{\text{sol}}}{\partial Q_\lambda} (\mathbf{S}^{1/2})_{\mu\lambda}(\mathbf{S}^{1/2})_{\nu\lambda} \qquad (5)$$

where $F^0_{\mu\nu}$ is the Fock matrix element for an isolated molecule and $F^{\text{sol}}_{\mu\nu}$ describes the contribution of the solvent. Q_λ is the charge of the atom to which the basis function λ belongs, and $\mathbf{S}$ is the overlap integral matrix. According to the conventional SCF procedure using Equation 4 instead of $F^0_{\mu\nu}$, the SCF MO including solvent effects are obtained.

The reaction profile of Reaction 2 was understood to be a two-dimensional potential energy surface that was calculated as a function of two atomic distances, $R_{C\text{-}Cl}$ and $R_{C\text{-}S}$, with reference to the carbon atom in the methyl group being transferred; the three atoms Cl, C, and S were constrained to be collinear (Scheme 1). Although the hydrogen atoms in the methyl groups are not equivalent, a local C_3 symmetry was assumed for all methyl groups in the calculations of the two-dimensional energy maps; the energies of the trimethylsulfonium cation with and without this restriction differ by 0.3 kcal/mol.

The 3-21G(*) basis set [11] was used in the two-dimensional potential surface calculations, while 6-31G* [12] and MIDI-4(d) [13] basis sets also were used for the calculations of molecular and electronic structures and energetic properties. All calculations were carried out using our ABINIT program on the HP-735 workstations.

RESULTS AND DISCUSSION

Molecular Structure and Charge Population of the Trimethylsulfonium Cation

The molecular structure of the trimethylsulfonium cation in its isolated state has been reported [14–16]. It has a C_{3v} pyramidal conformation in which the tortional angle of the methyl groups is $\tau = 0°$, as illustrated in Figure 1. This C_{3v} conformation also was found to be the most stable in water; another C_{3v} conformation with $\tau = 180°$ lies 8.8 kcal/mol (3-21G(*)) above the $\tau = 0$ conformation. The 3-21G(*) structures and Löwdin populations in the gas phase and in water are shown in Figure 1, while the 6-31G* results are depicted in Figure 2. The 3-21G(*) and 6-31G* structures agree with each other within 0.006 Å with regard to bond lengths and 0.9° for angles. Figures 1 and 2 show that the solvent polarity affects the structure of the trimethylsulfonium cation. How-

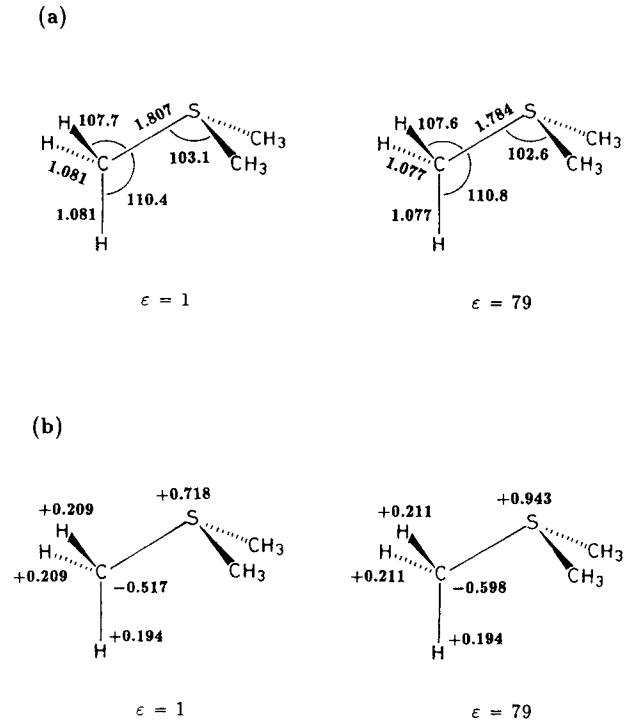

FIGURE 2 Molecular structure (a) and Löwdin population (b) of the trimethylsulfonium cation in the gas phase (ε = 1) and in aqueous solution (ε = 79) calculated with the 6-31G* basis set.

ever, the effect is small; bond lengths being shortened by 0.01–0.02 Å, with the bond angles remaining almost constant. The calculated C–S–C angle agrees well with the experimental value of 103.4° that has been determined by evaluation of NMR spectra of the trimethylsulfonium cation in the solid state [17]. The Löwdin populations (Figures 1 and 2) show that the polarization of the S–C bond is enhanced in polar solvents.

Potential Surface in the Gas Phase

The 3-21G(*) energy contours for Reaction 2 in the gas phase are shown in Figure 3. The lower right side of the map corresponds to the reactants of Reaction 2 and the upper left side to the products. The energies cited are in kcal/mol with respect to the reactants, $S^+(CH_3)_3 + Cl^-$. The overall feature of Figure 3 resembles the AM1 energy contour map for the S_N2 Menshutkin reaction between NH_3 and CH_3Cl [18]. Since the potential energy of the reaction product is much lower than that of the reactant, Reaction 2 is expected to proceed rapidly in the gas phase when the sulfonium cation and the chloride anion approach each other from the predicted direction.

Potential Surface in Solution

Figure 4 shows the 3-21G(*) potential surface of Reaction 2 in water that was calculated with ε = 79.

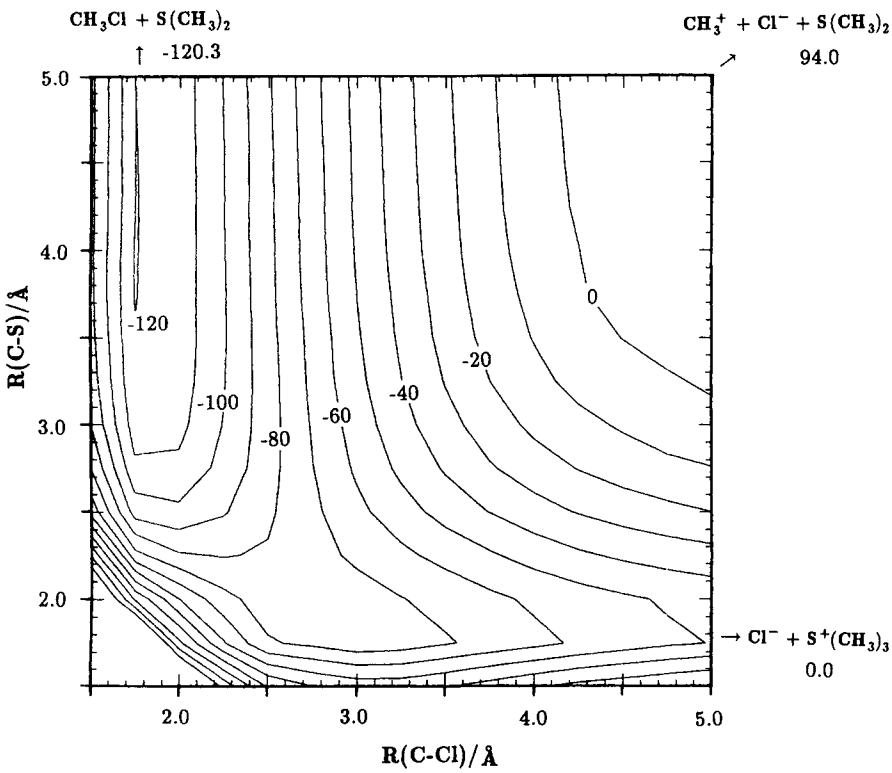

FIGURE 3 Two-dimensional potential energy surface of the S_N2 reaction of $S^+(CH_3)_3$ and Cl^- in the gas phase calculated with the 3-21G(*) basis set. Energies cited are in kcal/mol and are relative to the separated reactant.

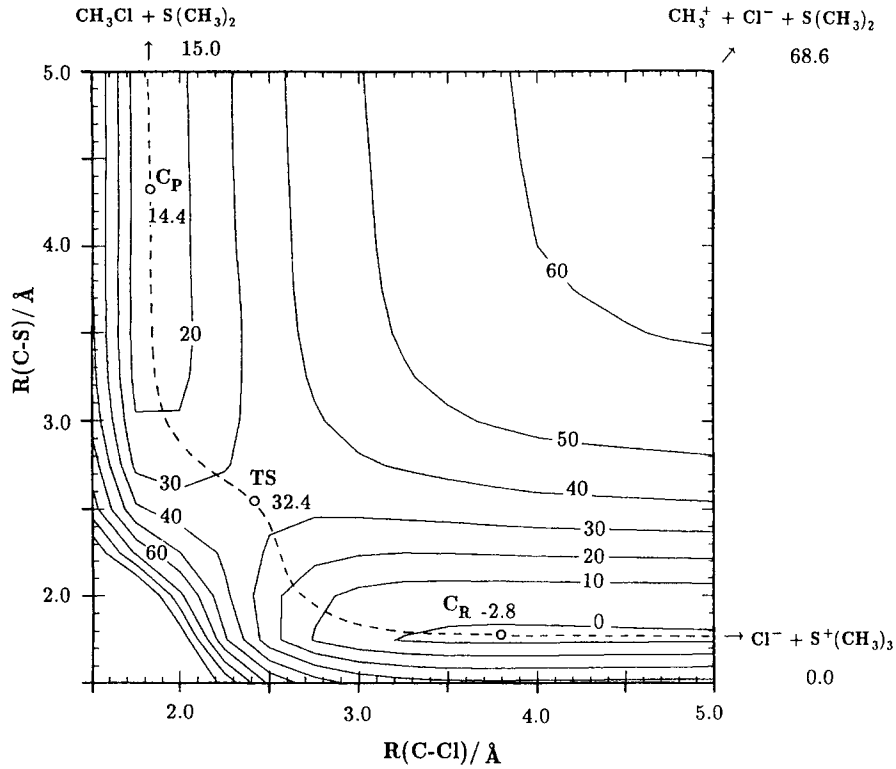

FIGURE 4 Two-dimensional potential energy surface of the S_N2 reaction of $S^+(CH_3)_3$ and Cl^- in aqueous solution (ε = 79) calculated with the 3-21G(*) basis set. Energies cited are in kcal/mol and are relative to the separated reactant.

TABLE 1 Solvation Energies[a] (kcal/mol) at Different Stages[b] in the Reaction of the Trimethysulfonium Cation with the Chloride Ion in Water

S_R	C_R	TS	C_P	S_P
−139.2	−75.0	−21.2	−3.5	−3.7

[a]Difference between energies for ε = 1 and ε = 79 calculated using the same geometry that was determined for ε = 79.
[b]S_R, C_R, TS, C_P, and S_P are the separated reactant, association complex on the reactant side, transition state, association complex on the product side, and separated product, respectively. C_R, TS, and C_P are indicated by open circles in Figure 4.

The reactant ions, $S^+(CH_3)_3$ and Cl^-, are largely stabilized in water, and stable association complexes and transition state are observed. A minimum energy path, which is shown by a broken line, was determined by energy minimization at different values of the reaction coordinate, r_C, defined by

$$r_C = R_{C-S} - R_{C-Cl} \tag{6}$$

where R_{C-S} and R_{C-Cl} are, respectively, the distances of S and Cl from C. The open circles in Figure 4 indicate the association complexes on the reactant side, C_R, and product side, C_P, and the transition state, TS. The association energy of C_R is 2.8 kcal/mol. A more stable ion pair was obtained when the chloride ion was allowed to approach on the C_3 axis of the trimethylsulfonium cation from the direction opposite to the lone pair orbital of the sulfur atom, although the association energy is not very large, viz., 5.6 kcal/mol. The transition state lies 35.2 kcal/mol [19] above the association complex, C_R. The reaction is calculated to be endothermic, as shown experimentally for the reaction of the trimethysulfonium cation with the bromide ion [4]. When the reaction proceeds, the positive and negative charges compensate each other, and the solvation energy decreases. This differential solvation along the reaction path is shown clearly in Table 1.

The reaction of the *t*-butyldimethylsulfonium cation and a nucleophile proceeds via the S_N1 mechanism, in which the sulfonium ion decomposes to the *t*-butyl cation and dimethylsulfide [20–23]. This S_N1 reaction path corresponds to the geometrical change from the lower to the upper parts on the right-hand side of the two-dimensional energy map. In the case of the trimethylsulfonium cation, the present calculations suggest that the S_N1 process in water requires an activation energy of about 70 kcal/mol and therefore is not expected to occur, as was confirmed by experiment [1–6]. A similar potential surface was obtained for the reaction in ethanol (ε = 25), as shown in Figure 5. The potential barrier in ethanol is slightly smaller than that in water.

The molecular structures and Löwdin charges at

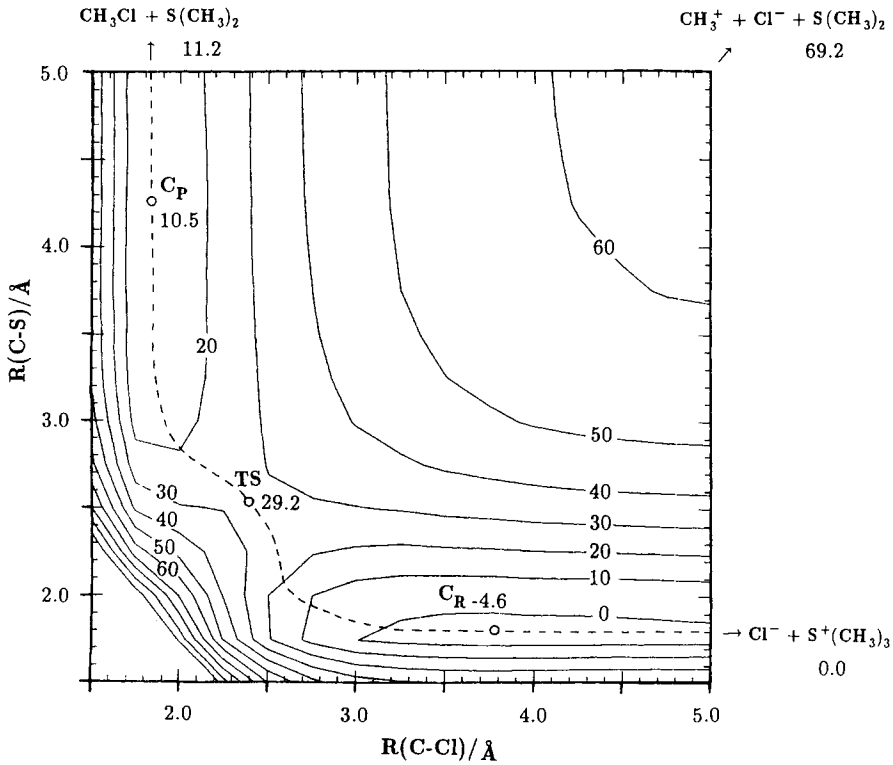

FIGURE 5 Two-dimensional potential energy surface of the S_N2 reaction of $S^+(CH_3)_3$ and Cl^- in ethanol (ε = 25) calculated with the 3-21G(*) basis set. Energies cited are in kcal/mol and are relative to the separated reactant.

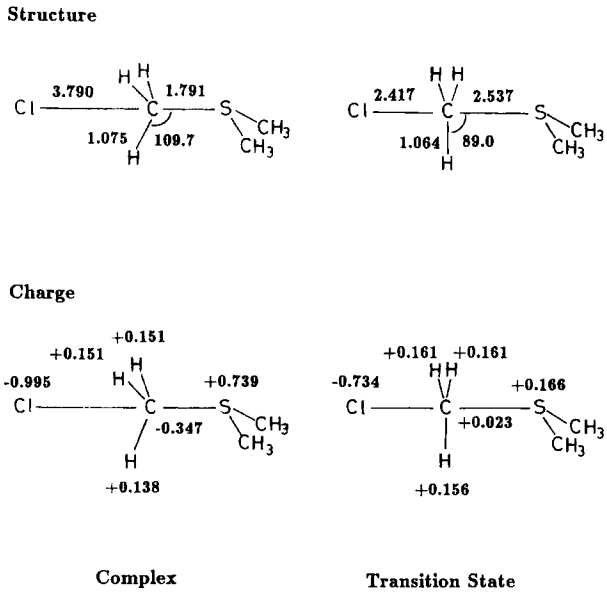

FIGURE 6 Molecular structure and Löwdin population of the association complex of the trimethylsulfonium cation and the chloride ion, C_R, and the transition state, TS, in aqueous solution (ε = 79) calculated with the 3-21G(*) basis set.

C_R and the TS in water are shown in Figure 6. In the association complex, C_R, the structure and charge distribution of the trimethylsulfonium cation resemble those in its separated state, S_R, in water. At the transition state, the C–S distance is slightly longer than the C–Cl one; this parallels the standard lengths for these bonds. The transferring CH_3 group is almost in a plane that is perpendicular to the Cl–C–S line, indicating the concerted nature of the reaction. The calculated charges at the C and S atoms indicate that the electrons in the C–S bond are mostly withdrawn by the sulfur atom at the transition state, and the leaving group, $S(CH_3)_2$, is almost neutral at the transition state; the electron transfer from Cl to the CH_3 group occurs after the transition state.

The variations of the Cl–C–H angle and the charge at Cl along the reaction coordinate are shown in Figure 7. Figure 7 shows that the changes in the molecular and electronic structures occur in the region $-1 < r_C < 1$. It also suggests that the electron transfer from Cl^- occurs after the structural change.

Solvent Effect on the Potential Energy Curve

The potential energy curves in water and in ethanol along the reaction path are compared in Figure 8. The association energy at C_R is larger in ethanol (-4.6 kcal/mol) than in water. This is due to the fact that the electrostatic stabilization energy between a

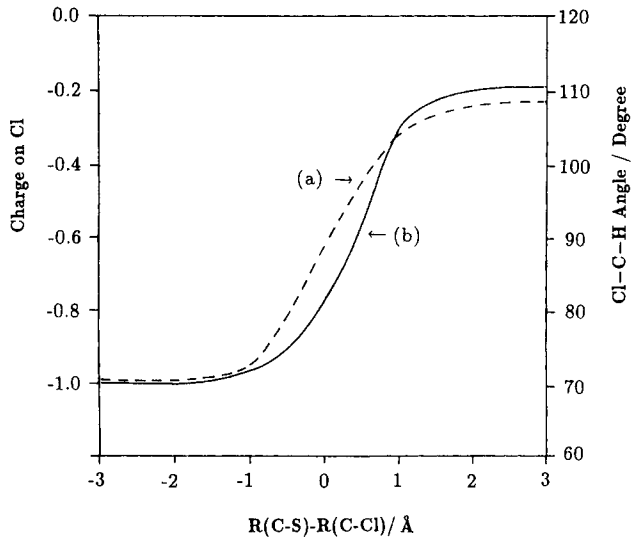

FIGURE 7 Variations in the Cl–C–H angle (a) and the charge on Cl (b) along the S_N2 reaction path of the trimethylsulfonium cation and the chloride ion.

TABLE 2 Relative Energies (kcal/mol) at Different Stages in the Reaction of the Trimethylsulfonium Cation with the Chloride Ion in Water

Basis sets	S_R	C_R	*TS*	C_P	S_P
3-21G(*)	0.0	−2.8	32.4	14.4	15.0
6-31G*	0.0	−2.1	40.6	19.2	19.7
MIDI-4(d)	0.0	−3.4	31.0	4.0	4.6

TABLE 3 Heats of Reaction (kcal/mol) for Three Reactions in the Gas Phase

	Reaction 7	*Reaction 8*	*Reaction 2*
3-21G(*)	−214	94	−120
6-31G*	−211	91	−120
MIDI-4(d)	−226	90	−136
Exp.[a]	−225	113	−112

[a]Experimental values were estimated from heats of formations [16,24] of $S^+(CH_3)_3$, $S(CH_3)_2$, CH_3^+, CH_3Cl, Cl, and electron affinity of the Cl atom [25].

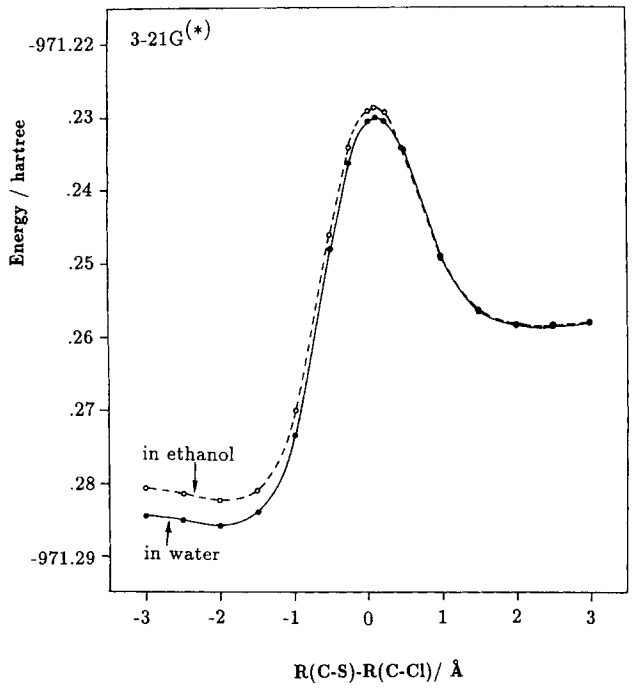

FIGURE 8 Solvent effect on the potential energy curve along the S_N2 reaction path of the trimethylsulfonium cation and the chloride ion. The energy of 0.01 hartree corresponds to 6.275 kcal/mol.

cation and an anion in solution is proportional to the reciprocal of the dielectric constant of the solvent. In the present model, the solvation energy of a charged species increases as the dielectric constant of the solvent increases. As shown in Figure 8, the potential energy in water is lower than that in ethanol. This energy difference is large at the separated reactant, S_R, where the cation and anion are separated. As the reaction proceeds, the positive and negative charges compensate each other, and the solvation energy decreases; the potential energies in water and in ethanol almost coincide with each other at the separated product, S_P, $S(CH_3)_2 + CH_3Cl$.

The energies at several stages along the reaction path in water were also calculated by 6-31G* and MIDI-4(d) basis sets and are compared in Table 2. The 6-31G* activation energy is larger than the 3-21G(*) value, while the MIDI-4(d) heat of reaction is much smaller than the other two values. The energy profile in Figure 8 appears to be reasonable, judging from the experimental results for Reaction 1 [3,4]. Thus, we examined the calculated gas phase heats of reactions for two reactions:

$$CH_3^+ + Cl^- \rightarrow CH_3Cl \quad (7)$$

$$S^+(CH_3)_3 \rightarrow S(CH_3)_2 + CH_3^+ \quad (8)$$

The calculated heats of reactions for these reactions are shown in Table 3 as well as the experimental values that were estimated from heats of formation of the species and the electron affinity of the Cl atom. The 3-21G(*) and 6-31G* calculations underestimate the exothermic change of Reaction 7 by about 10

kcal/mol, while three different methods underestimate the endothermic change of Reaction 8 by about 20 kcal/mol. As a result, the 3-21G(*) and 6-31G* methods are expected to overestimate the stabilization of Reaction 2 in the gas phase by about 10 kcal/mol, while the MIDI-4(d) method does so by about 20 kcal/mol. It should be noted that the reliability of the energy profile of an ionic reaction in solution depends primarily on the accuracy of ab initio calculations employed for the gas phase reaction. It is very important to examine whether or not the method reproduces well the energy change of ionic reactions in the gas phase.

CONCLUSION

Most cation-anion reactions proceed in aqueous solution or in polar organic solvents, and theoretical studies of their reaction paths should include solvent effects. The present study applied the ab initio MO theory, which includes the continuum model of the solvent effect, to the substitution reaction of the trimethylsulfonium cation, with the chloride ion in water and demonstrated how the dielectric constant of the solvent affects the potential energy profile. At the stage of the separated reactants, the trimethylsulfonium cation and the chloride anion are largely stabilized by polar solvents, while, at the transition state, the leaving group $S(CH_3)_2$ is almost neutral, and the stabilization is significantly diminished. This differential solvation determines the shape of the potential energy curve along the reaction path. Although several constraints were forced on the reaction path and structural changes, the present analysis suggested that the energy profile and the changes in the molecular and electronic structure with respect to cation-anion reactions can well be elucidated by our ab initio MO solvation model, if the basis set reproduces well the gas phase heats of reactions.

ACKNOWLEDGMENT

This research was supported by a Grant-in-Aid for Scientific Research (C) No. 08640633 from the Ministry of Education, Science, Sports and Culture and by a Tsukuba University Research Project A.

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