A Theoretical Comparison of S_N1 and S_N2 Reactions of Saturated Alkyl Chlorides

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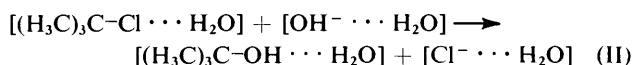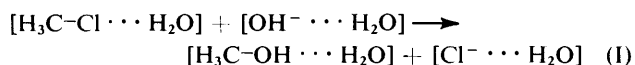*Department of Chemistry, Nara University of Education, Takabatake-cho, Nara 630, Japan*

The mechanistic difference between bimolecular (S_N2) and unimolecular (S_N1) nucleophilic substitutions of saturated alkyl chlorides is investigated with *ab initio* molecular orbital (MO) calculations. The t-butyl substrate undergoes early (almost spontaneous) C–Cl bond scission, which may give double OH^- (reagent) co-ordination on the carbonium cation. However, the symmetrically solvated ion, which has been accepted as a stable intermediate for racemization, is found to be located at the energy maximum of the OH^- exchange reaction. The origin of racemization in nucleophilic substitution is discussed on the basis of the calculated potential surface.

In solvolysis in neutral solutions, the reactivity of saturated alkyl halides is in the order tertiary > secondary > primary. If a powerful nucleophile (*e.g.* OH^-) is added to the solution, the reverse order appears: primary > secondary > tertiary. The former mechanism is S_N1 and the latter is S_N2. While S_N2 brings about the inversion of the geometric configuration, S_N1 causes racemization. S_N1 is thought to proceed *via* a symmetrically solvated carbonium ion intermediate, which may give either an inverted or a retained product.[1]

It is difficult to fit the solvolysis of the secondary substrate into a simple S_N1–S_N2 framework. Competition between S_N1 and S_N2 processes, which leads to partial racemization, cannot be justified easily. Bentley and co-workers put forward an intermediate mechanism in the S_N1–S_N2 spectrum to remove such problems.[2] This new mechanism involves a weakly nucleophilically solvated ion-pair formed in the rate-determining step, followed by relatively rapid substitution to give the products. Traditionally, t-butyl chloride is believed to be a typical S_N1 substrate and to be insensitive to the nucleophilicity of the solvent. The solvolysis of highly hindered 2-adamantyl halide in weakly nucleophilic media is faster than that of the butyl halide, but in more nucleophilic solvents the butyl halide solvolysis is faster.[2f] Experimental results have questioned the above assignment and have indicated that the solvolysis of butyl chloride is susceptible to nucleophilic assistance during heterolysis of the carbon–chlorine bond. Thus, a systematic and uniform interpretation of the S_N1–S_N2 spectrum is desirable.
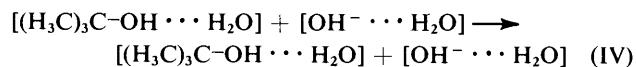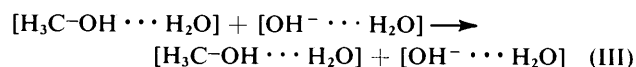
Method

Method of Calculation and Models Adopted.—The mechanistic difference between S_N1 and S_N2 was investigated with *ab initio* MO calculations.[3] The 4-31G basis set was used for neutral and cationic species, and on the oxygen atom of OH^- a diffuse *p* GTO (exponent = 0.059) was augmented. Two model reactions, (I) and (II), were adopted.

$$[H_3C-Cl \cdots H_2O] + [OH^- \cdots H_2O] \longrightarrow$$
$$[H_3C-OH \cdots H_2O] + [Cl^- \cdots H_2O] \quad (I)$$

$$[(H_3C)_3C-Cl \cdots H_2O] + [OH^- \cdots H_2O] \longrightarrow$$
$$[(H_3C)_3C-OH \cdots H_2O] + [Cl^- \cdots H_2O] \quad (II)$$

Two substrates, methyl chloride and t-butyl chloride, and a reagent, OH^-, were assumed to be mono-hydrated ($\cdots H_2O$). This comes, of course, from computational restrictions (maximum size of the present system is 107 basis functions). Although the assumption evidently does not reproduce the

solvent effect, energetics may be somewhat more reliable than the solvent-free data. To check for the possibility of a solvated carbonium ion, model reactions (III) and (IV) were also examined. The minimum-energy paths of the model reactions

$$[H_3C-OH \cdots H_2O] + [OH^- \cdots H_2O] \longrightarrow$$
$$[H_3C-OH \cdots H_2O] + [OH^- \cdots H_2O] \quad (III)$$

$$[(H_3C)_3C-OH \cdots H_2O] + [OH^- \cdots H_2O] \longrightarrow$$
$$[(H_3C)_3C-OH \cdots H_2O] + [OH^- \cdots H_2O] \quad (IV)$$

were calculated by optimization of the parameters at a given *R*. The potential-energy profiles obtained are shown in Figure 1 together with the parameters.

To simulate solvolysis in a neutral media, two models of methyl and t-butyl cations, solvated symmetrically and unsymmetrically, by two water molecules were adopted [(V) and (VI)]. Their geometries are calculated and displayed in Figure 4.

$$H_2O \cdots CH_3^+ \cdots OH_2 \quad (V)$$

$$H_2O \cdots t\text{-}Bu^+ \cdots OH_2 \quad (VI)$$
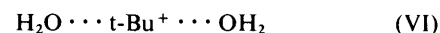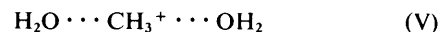
Results and Discussion

The results obtained from calculations on models (I)—(IV), shown in Figures 1 and 2, are discussed first.

1. Figure 2 shows that as OH^- approaches the substrate, the butyl group pushes out Cl^- more readily than the methyl group. If the Cl^- ion radius is considered (1.88 Å), the ion is regarded as completely separated at $R = 2.25$ Å ($l = 2.77$ Å) in (II). Since at this point OH^- interacts only weakly with the butyl carbon, the C–Cl bond is broken almost 'spontaneously.' This early bond scission arises from charge accumulation (which repels the Cl^- electronic cloud) on the central carbon of the butyl group through the hyperconjugation. In fact, the C–Me bond is shortened ($r = 1.523$ Å at $R = \infty$, and $r = 1.500$ Å at $R = 2.25$ Å) as the reaction proceeds.

2. The potential energy of (I) is almost flat at $R = 2.75$—2.25 Å, without a noticeable activation-energy barrier. Comparison of the energy in (I) and (II) indicates a larger reactivity of methyl chloride in the solution with the strong nucleophile.

3. In Figure 1, the symmetrically solvated ions are found to be at energy maxima in both (III) and (IV). This result conflicts with the well accepted view that a stable intermediate is present. The instability of ($HO^- \cdots t\text{-}Bu^+ \cdots OH^-$) is
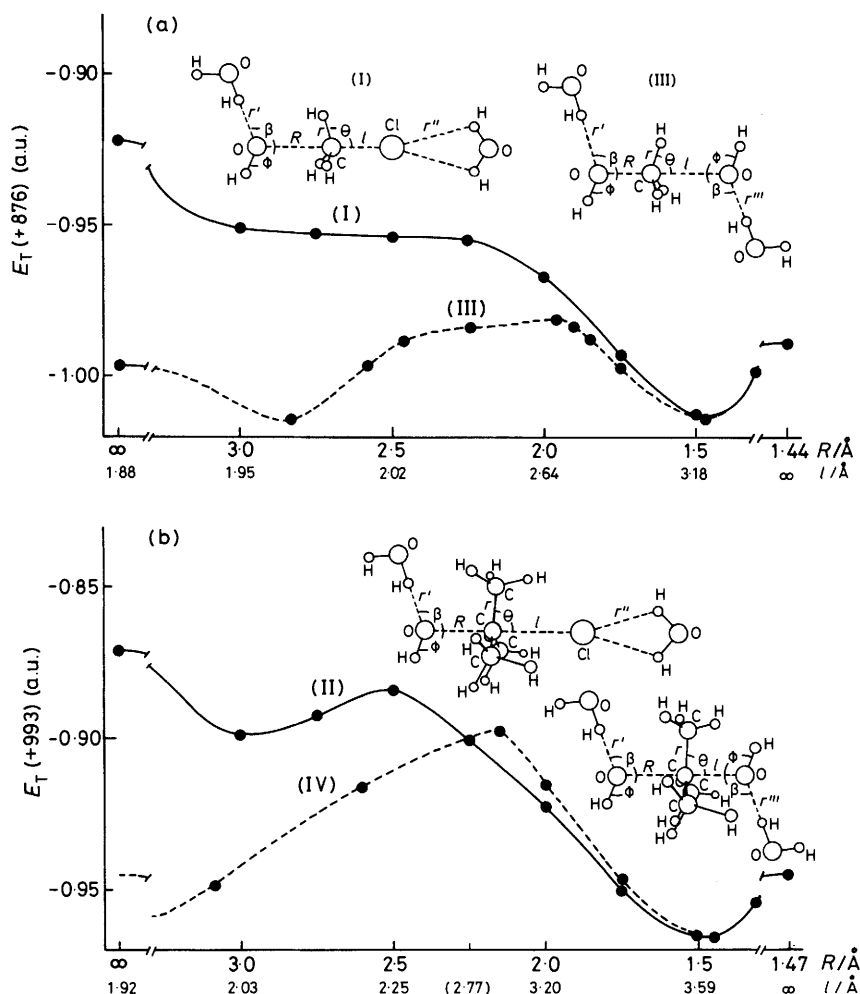
Figure 1. The geometric parameters of (I) (S_N2 type) and (II) (S_N1 type) for seeking the minimum-energy paths. The frozen parameters during the reactions are C–H bond length (1.08 Å), the methyl sp^3 hybridization angle (109.5°) in the butyl group, HÔH (107°), and the O–H distance (0.97 Å) of the solvent water. $\Phi = \beta = 110°$ is also fixed. This restriction gives only a slight (<1 kcal mol^{-1}) error in the energy. (a) The methyl substrate and (b) the t-butyl substrate. The full and broken lines are for nucleophilic substitution and for the OH$^-$ exchange reaction, respectively

quite significant relative to that of (butanol · · · OH$^-$). This is, however, somewhat artificial due to the simple model of mono-hydration.

4. Whereas the potential energy of (I) does not cross that of (III), the curve of (II) does cross that of (IV). The presence or the absence of this ' surface touch ' seems to be related to the possibility of racemization. (I) proceeds independently of (III). However, at R ca. 2.25 Å the ' switch-over ' from (II) to (IV) is likely and the point is almost at the energy maximum of (IV). This leads to the appearance of the product with a retained configuration. The facile (II) —→ (IV) switch-over is caused by the early heterolysis of the butyl substrate. The Cl$^-$ may be readily replaced by OH$^-$ at the right side of the butyl group. This process is schematically illustrated in Figure 3 together with that of the methyl substrate. The broken lines stand for the switch-over paths, (I) —→ (III) and (II) —→ (IV). The energetic barrier for the latter is smaller than that for the former. This demonstrates that the substitution of butyl chloride may readily proceed in two directions. The leader arrows attached to curves indicate these processes. Thus, one route of (b) may give the product with the retained configuration.

5. Since the switch-over stated in 4 takes place at R ca.

2.25 Å, the energy barrier of (II) corresponding to the transition state is almost certainly due to the C–Cl bond scission. This reflects the S_N1 kinetic data, $i.e.$, the rate depends only on the concentration of the substrate, t-butyl chloride. According to our calculations, therefore, the rate-determining step is independent of the junction for racemization.

6. Although the C–Cl bond of t-butyl chloride is broken at the early stage of substitution as is described in 5, it does not necessarily mean the self-cleavage of the substrate. According to the analysis of the lowest-unoccupied MO of t-butyl chloride, it is eager to accept the electronic charge of OH$^-$. The reaction is initiated by the charge-transfer interaction. In this respect, the (II) —→ (IV) process is regarded as an intermediate mechanism in the S_N1–S_N2 spectrum. Bentley et $al.$ pointed out that nucleophilic assistance to the substitution of the bulky substrate has been underestimated so far in aqueous or alcoholic solvents.[2f] The present result would support their proposal.

7. The classical assignment of (S_N1, racemization) and (S_N2, inversion) is not always correct. In fact, the S_N2 reaction, reaction (1), has been reported to give products of partial racemization.[4] This result may be interpreted by the pattern of (II) —→ (IV) switch-over.
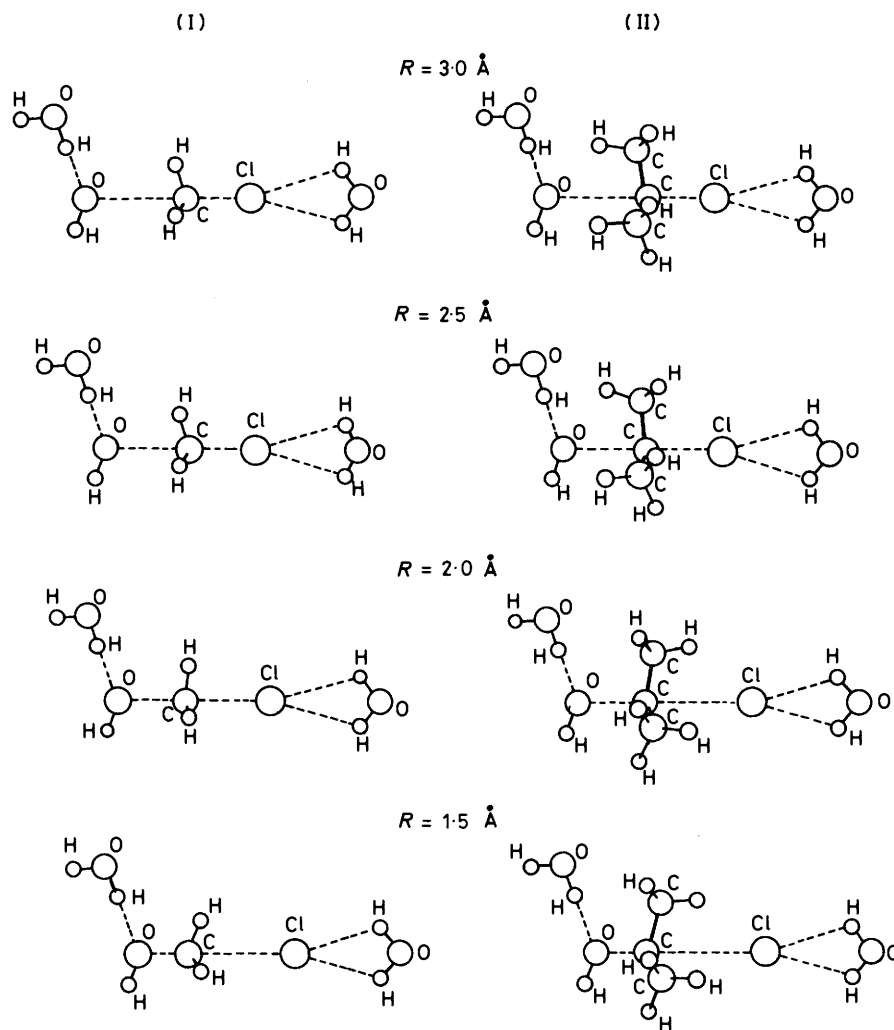
(I)   (II)

$R = 3.0$ Å

$R = 2.5$ Å

$R = 2.0$ Å

$R = 1.5$ Å

Figure 2. The sequence stages of reactions (I) and (II)

(a)
R
$(HO^-\text{---}Me\text{--}Cl)\ (HO^-\text{--}Me\overset{R}{\underset{}{\text{--}}}\overset{-OH}{)}\ (HO^-\text{--}Me\text{---}OH)$
^-OH
R
∞
R
(I)   (III)
1.44 Å
α   β   γ
No   ret
inv   inv
MeOH
OH$^-$
Cl$^-$

(b)
R
$(HO^-\text{---}Bu^t\text{--}Cl)\ (HO^-\text{---}Bu^t\overset{R}{\underset{}{\text{--}}}\overset{-OH}{)}\ (HO^-\text{---}Bu^t\text{--}OH)$
^-OH
R
∞
R
(II)   (IV)
1.47 Å
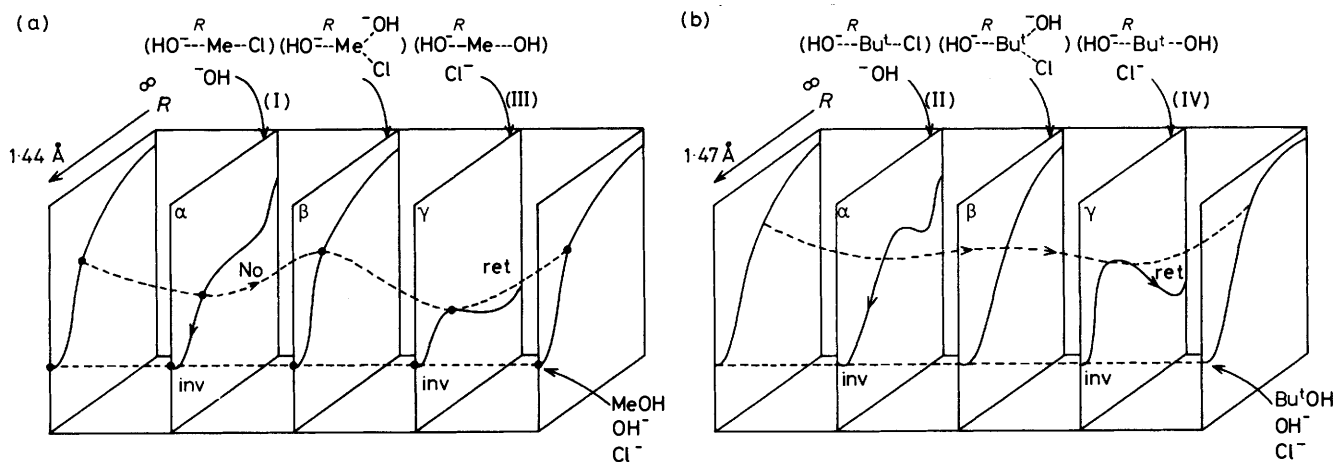α   β   γ
ret
inv   inv
Bu^{t}OH
OH$^-$
Cl$^-$

Figure 3. Schematic presentation of the potential-energy surfaces for nucleophilic substitution of (a) methyl chloride and (b) t-butyl chloride. α, β, and γ are used to distinguish the planes. Inv and ret mean inversion and retention, respectively

Secondly, the results for models (V) and (VI), shown in Figure 4, are discussed.

8. Vibrational analysis shows that the symmetrically solvated methyl cation is located at the transition state (one negative eigenvalue of the force constant matrix). Compared with the serious instability of $HO^- \cdots t\text{-}Bu^+ \cdots OH^-$, the energy difference of $H_2O \cdots t\text{-}Bu^+ \cdots OH_2$ is only a few kcal mol^{-1}. This slight energy difference demonstrates that
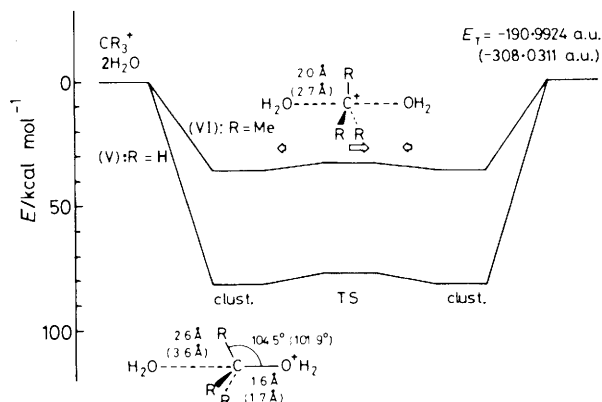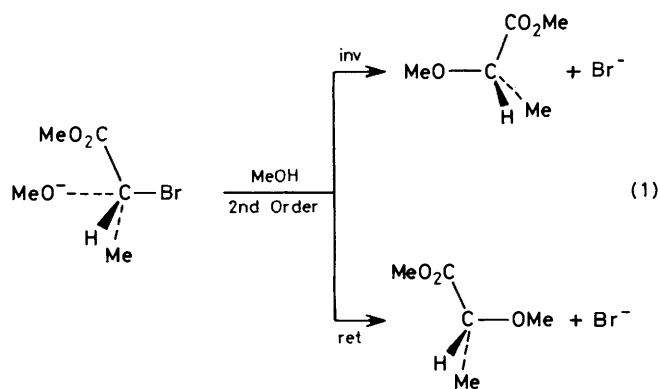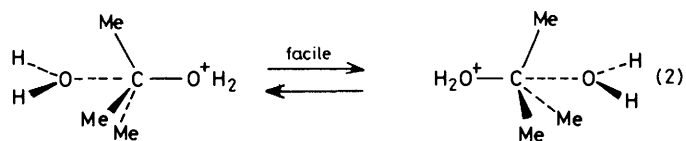
(1)

(2)

Figure 4. Models of methyl (V) and t-butyl (VI) cations solvated by two water molecules. They are optimized with the MO of the 4-31G basis set. TS is the transition state of the symmetrical configuration. For methyl, one negative eigenvalue of the force constant matrix is obtained (-322.4 cm^{-1}) by the vibrational analysis. The unsymmetrical geometry is defined as clust. (cluster). The relative monomer energies (CH$_3$$^+$ + 2H$_2$O or t-Bu$^+$ + 2H$_2$O) are displayed at both edges. Values without and with parentheses are for methyl and butyl cations, respectively. Bold empty arrows at TS denote the distortion mode corresponding to the sole negative eigenvalue

isomerization, reaction (2), takes place readily under thermal conditions. The facile conversion gives the possibility of racemization before the proton attached to t-butanol is taken off by solvent water. Thus, the reagent H$_2$O would give a larger possibility of racemization than the reagent OH$^-$. This is consistent with the fact that the increase in the nucleophilicity of the solvent causes a decrease in racemization.[4]

Conclusions

It has been found that a symmetrically solvated carbocation is located at the transition state. Except when the rear side is sterically congested, such as in 2-adamantyl and 1-bicyclo-[2.2.2]octyl groups,[2c] even the bulky substrate is susceptible to nucleophilic assistance to some extent. The position of a substitution in the S_N1–S_N2 spectrum depends on the nucleophilicity of solvent, the stability of the carbocation, and the bond strength of C$^-$leaving group. The probability of the (II) $\longrightarrow$ (IV) switch-over automatically involving these three factors may be a criterion for the assignment.

References

1 D. J. Cram and G. S. Hammond, ' Organic Chemistry,' McGraw-Hill, New York, 1964, ch. 14, 2nd. edn.
2 (a) T. W. Bentley and P. v. R. Schleyer, *J. Am. Chem. Soc.*, 1976, **98**, 7658; (b) F. L. Schadt, T. W. Bentley, and P. v. R. Schleyer, *ibid.*, p. 7667; (c) T. W. Bentley, C. T. Bowen, D. H. Morten, and P. v. R. Schleyer, *ibid.*, 1981, **103**, 5466; (d) T. W. Bentley, C. T. Bowen, W. Parker, and C. I. F. Watt, *ibid.*, 1979, **101**, 2486; (e) T. W. Bentley, C. T. Bowen, W. Parker, and C. I. F. Watt, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1244; (f) T. W. Bentley and G. E. Carter, *J. Am. Chem. Soc.*, 1982, **104**, 5741.
3 GAUSSIAN 127 program extended from GAUSSIAN 70 by K. Kitaura and K. Morokuma at IMS is used; GAUSSIAN 70: W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, program #236, Quantum Chemistry Program Exchange, Indiana University, Bloomington, Idn., USA, 1973.
4 P. Sykes, ' The Search for Organic Reaction Pathways,' Longmans, London, ch. 4.