A Molecular Orbital Theory of Saturated Compounds. II. Chemical Reactivity in Nucleophilic Substitution

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(Received February 26, 1960)

It is well known that a nucleophilic substitution of aliphatic compounds has available two reaction mechanisms, one being the unimolecular (S_N1) and the other the bimolecular mechanism (S_N2)¹⁾. The explanation of reactivity in aliphatic substitution has hitherto been carried out only by means of empirical electronic theory. No quantum-mechanical treatment of chemical reactivity in nucleophilic aliphatic substitution has ever been put into practice though some theoretical studies have been made with regard to the Walden inversion by Jaffé²⁾ and others³,⁴⁾.

In Part I⁵⁾ of this series of papers the ionization potential and the bond dissociation energy of several aliphatic compounds were calculated by the use of the C–C skeleton method proposed by Yoshizumi⁶⁾, resulting in a good agreement with the experiments.

In the present paper, an attempt is made to elucidate the reactivity in nucleophilic substitution of some alkyl halides, following the same quantum-mechanical procedure as used in Part I⁵⁾. Also by the use of the procedure of simple LCAO MO method of conjugated molecules the stability of some aliphatic ions is discussed, in which the hyperconjugative effect is thought to be prevailing.

S_N2 Reaction

The reaction of this type is expressed by the equation¹⁾

$$A^- + R-X \rightarrow [A\cdots R\cdots X]^- \rightarrow A-R + X^-$$

where A^- is a nucleophilic reagent, R is an alkyl group, X is the group to be expelled, and the compound in brackets, stands for the activated complex.

The structure of activated complex is schematically written in Fig. 1. In this state, R′, R″, R‴ and C-atom lie all in one plane, and also A, C-atom and X lie on one straight line perpendicular to the plane. Four sp^3 orbitals of the central carbon atom may change to three sp^2 orbitals and one p orbital which binds both A and X to C-atom. However, for the sake of simplicity, we neglect the influence of altered hybridization at the central C-atom and adopt the same values for Coulomb and exchange integrals as sp^3 hybridization. The overlap integral between sp^2 orbital and p orbital is put equal to zero. The contribution of the reagent A to the energy of the total system is regarded as the same in all the reactions of the same type. We assume that in the transition state two σ electrons in the C–X bond to be broken are localized at X-atom*. According to the present model, the difference in the energy between the transition state and the initial state, ΔE, is calculated as

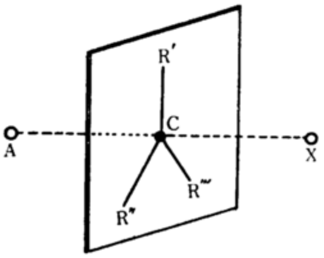

Fig. 1. Transition state in S_N2 reaction.

$$\Delta E = \{E[R^+] + E[X^-]\} - E[R-X] \qquad (1)$$

where $E[A]$ is the calculated total energy of the molecule or ion A. This procedure corresponds to the localization method in the theory of aromatic substitution. This energy, ΔE, is considered to be a measure of the activation energy of the reaction.

Calculations are made with respect to some alkyl bromides, chlorides and iodides. The second order reactions of ethoxide anion and

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1) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, N. Y. (1953), Chapter VII.

2) H. H. Jaffé, *J. Chem. Phys.*, **22**, 1618 (1953).

3) I. Dostrovsky, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1946**, 173.

4) S. Glasstone K. J. Laidlar and H. Eyring, "The Theory of Rate Processes", McGraw-Hill Book Co., New York, London (1941), pp. 135, 400.

5) U. Fukui, H. Kato and T. Yonezawa, This Bulletin, **33**, 1197 (1960).

6) H. Yoshizumi, *Trans. Faraday Soc.*, **53**, 123 (1957).

* Two alternative models may be possible. The one is the model in which the two σ electrons are localized in the C-X bond, and the other is that in which the two electrons move in A···C and C···X bonds. Whichever of these two models one may adopt, only a constant term will be added to the energy difference obtained in the present treatment and no serious alteration arises with regard to the results.

chloride anion with alkyl bromides are investigated and the calculated results are compared with the ovserved activation energy and reaction rate in Table I. The agreement with this experiment is found satisfactory. In the present calculation, the energetic contribution of the attacking anion is not taken into account, since the anion is regarded as having the same energy in all the reactions of the same type.

In Table I, ΔE values of several alkyl bromides are listed for two types of nucleophilic reaction. In Table II, the experimental activation energies of alkyl iodides in the Menschutkin type reaction and in the substitution with the chloride anion are compared with the calculated values of ΔE. Table III indicates the results of calculation with regard to the reaction of alkyl chloride with iodide anion. It is observed that the value of ΔE increases according as the reaction rate decreases.

TABLE I

(1) $RBr+C_2H_5O^- \rightarrow C_2H_5OR+Br^-$ 1)

RBr	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Rate constant obs. 10^3k at 55°C ($sec^{-1}mol^{-1}l.$)
C-Br	0.7420	20.0	34.4
C-C-Br	0.8156	21.0	1.95
C-C-C-Br	0.8174	—	0.55
C | C-C-C-Br	0.8215	22.8	0.05
C | C-C-C-Br | C	0.9215	26.2	0.000008

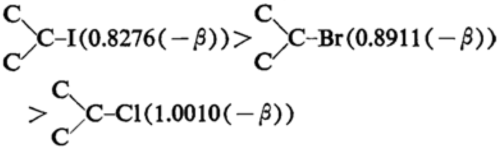
(2) $RBr+Cl^- \rightarrow RCl+Br^-$ 1)

RBr	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Relative rate obs.
C-Br	0.7420	15.8	100
C-C-Br	0.8156	17.9	1.97
C-C-C-Br	0.8174	18.1	1.29
C-C-C-C-Br	0.8174	—	1.29
C C-Br C	0.8911	18.7	0.040
C | C-C-Br | C	0.9580	21.2	0.009

The calculated results in these tables indicate that the rate of S_N2 reaction decreases in the order methyl>ethyl>higher *n*-alkyl>*i*-propyl >*t*-butyl, in accordance with experience.

The absolute rate of S_N2 substitution is strongly affected by an exchange of the group to be displaced. The observed rate of hydrolysis or alcoholysis decreases in the order R–I >R–Br>R–Cl. Calculated values in brackets exhibit a similar tendency as follows:

C–C–I (0.7494($-\beta$))>C–C–Br(0.8156($-\beta$))
>C–C–Cl(0.9288($-\beta$)).
C–C–C–I (0.7524($-\beta$))
>C–C–C–Br(0.8174($-\beta$))
>C–C–C–Cl(0.9305($-\beta$))



C–I(0.8276($-\beta$))>C–Br(0.8911($-\beta$))
>C–Cl(1.0010($-\beta$))

TABLE II

(3) $RI+Cl^- \rightarrow RCl+I^-$ 1)

RI	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Relative rate Obs.
C-I	0.6880	16.0	100
C-C-I	0.7494	17.3	8.9
C-C-C-I	0.7524	17.3	5.2
C-C-C-C-I	0.7520	—	—
C C-I C	0.8276	18.0	0.26

(4) $RI+(CH_3)_3N \rightarrow (CH_3)_3N^+R+I^-$ 1)

RI	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Relative rate obs.
C-I	0.6880	9.7	100
C-C-I	0.7494	11.4	0.58
C C-I C	0.8276	17.1	0.003

$RI+Et_3N \rightarrow RN^+Et_3+I^-$ a)

RI	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Relative rate obs.
C-I	0.6880	9.7	100
C-C-I	0.7494	12.5	8.8
C-C-C-I	0.7524	—	1.7
C-C-C-C-I	0.7520	16.0	1.2
C C-I C	0.8276	—	0.18

a) M. S. Newman, "Steric Effects in Organic Chemistry", John Wiley & Sons, Inc., New York (1956), p. 75.

TABLE III

$RCl+I^- \rightarrow RI+Cl^-$ 1)

RCl	ΔE calc. $(-\beta)$	Activation energy obs. (kcal./mol.)	Relative rate obs.
C-Cl	0.8480	—	93
C-C-Cl	0.9288	—	1.0
C-C-C-Cl	0.9305	—	0.37
C-C-C-C-Cl	0.9324	—	0.57
C C-Cl C	1.0010	—	0.0076
C | C-C-Cl | C	1.0942	—	—

S_N1 Reaction

The rate determining step in this type of reaction is the ionic dissociation represented by the formula $RX \rightarrow R^+ + X^-$. Dewar[7] proposed a model for this transition state which may be written as S···R···X···S, where S stands for a solvent molecule, R is the alkyl group, and X is the group to be expelled. The factors affecting the rate of S_N1 reactions are considered to be (1) the rate of ionic dissociation of the molecule R–X, (2) the solvent effect, and so on. Refering to this we adopt as reactivity indexes the electron densities at the central C-atom (q_C) and at the X-atom (q_X) in the C–X bond. The larger q_C is, the faster is the rate of ionic dissociation of the molecule R–X. Furthermore, the larger q_X is, the stronger is the X···S binding.

TABLE IV

$RBr + OH^- \rightarrow ROH + Br^-$ [1]

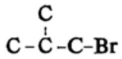
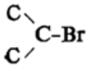
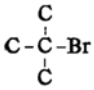
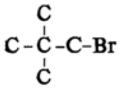
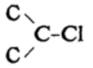
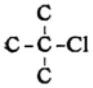
RBr	Calc. total density q_C	q_{Br}	Relative rate obs.
C-Br	0.5768	1.4231	1.00
C-C-Br	0.5979	1.4359	1.71
C-C-C-Br	0.6000	1.4401	—
 C C-C-C-Br	0.6005	1.4437	—
 C C-Br C	0.6063	1.4511	44.7
 C C-C-Br C	0.6056	1.4667	10^8
 C C-C-C-Br C	0.6091	1.4874	—

TABLE V

(1) $R-X\ aq \rightarrow R^+\ aq + X^-\ aq$[7]

R-Cl	Calc. total density q_C	q_{Cl}	Heat of reaction by Evans, Q (kcal./mol.)
C-Cl	0.6076	1.3924	89
C-C-Cl	0.6219	1.4085	59
 C C-Cl C	0.6289	1.4223	37
 C C-C-Cl C	0.6257	1.4358	26

(2)

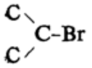
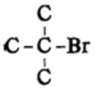
R-Br	Calc. total density q_C	q_{Br}	Heat of reaction by Evans, Q (kcal./mol.)
C-Br	0.5768	1.4231	86.5
C-C-Br	0.5979	1.4359	56.5
 C C-Br C	0.6063	1.4511	34.5
 C C-C-Br C	0.6056	1.4667	23.5

TABLE VI

Ions	Resonance energy calc. ($-\beta_0$)	Stabilization energy[10] obs. (kcal./mol.)
CH_3^+	0	0
$C_2H_5^+$	0.3350	36
n-$C_3H_7^+$	0.5081	—
i-$C_3H_7^+$	0.6462	66
t-$C_4H_9^+$	0.9043	84

Calculated values of q_C and q_{Br} are listed together with the rate of hydrolysis of alkyl bromide in Table IV in which a parallelism between them is found. Since there exist, however, no sufficient data available for comparison, the heat of reaction, Q, i. e. the approximate activation energy in S_N1 solvolysis of alkyl halides, computed by Evans[8,9] is used in Table V for this purpose. The magnitudes of q_C and q_X are seen to be parallel with the value of Q. Therefore, we conclude that q_C and q_X are useful reactivity indexes in S_N1 reaction.

Furthermore, it has been shown that the rates of some S_N1 reactions can be connected with stabilites of alkyl ions formed by dissociation[10,12]. These stabilities can be represented by the resonance energy. In order to calculate the resonance energy in these saturated molecules, we may apply the simple LCAO MO treatment of conjugated molecules[10]. The following parameters are adopted in this calculation:

Coulomb integrals:

$$\alpha_{H_3} = \alpha_0 - 0.3\,\beta_0, \quad \alpha_{H_2} = \alpha_0 - 0.5\,\beta_0,$$

Resonance integrals:

$$\beta_{H_3\equiv C} = 2.5\beta_0, \quad \beta_{H_2=C} = 2.0\beta_0,$$

$\beta_{C-C} = 0.88\beta_0$ (in a C–C bond adjacent to the central C-atom),

$\beta_{C-C} = 0.50\beta_0$ (in other C–C bonds),

where α_0 and β_0 are the Coulomb and resonance integrals in benzene, respectively. The latter two parameters β_{C-C} are evaluated by considering the degree of localization in hyperconjugation[11].

The result of calculation with respect to several alkyl ions is indicated in Table VI. In S_N1 reaction the rate decreases along the series methyl < ethyl < higher n-alkyl < i-propyl < t-butyl, and the extremely large stability of the

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[7] M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Clarendon Press, Oxford (1949), p. 64.

[8] A. G. Evans, *Trans. Faraday Soc.*, **42**, 719 (1946).

[9] J. L. Franklin, ibid., **48**, 443 (1952).

[10] N. Muller and R. S. Mulliken, *J. Am. Chem. Soc.*, **80**, 3489 (1958).

[11] Y. I'haya, This Bulletin, **28**, 369, 376 (1955).

[12] A. Stretwieser, *Chem. Revs.*, **56**, 570 (1956).

tertiary carbonium ion was also reflected in the solvolysis rates of alkyl halides[12]. These facts are explained by our results.

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