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화학반응성의 분자궤도론적 연구(제10보). 카르보닐 탄소에서의 S_N2-보존형 메카니즘

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Determination of Reactivities by Molecular Orbital Theory(X). S_N2 Retention Mechanism at a Carbonyl Carbon

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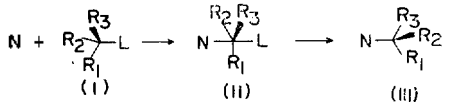
요 약. CH_3COCl의 카르보닐 탄소에서의 Cl^-의 2분자 치환반응을 여러 거리에서 전방 및 후방 공격할 때의 에너지 변화(EHT)와 전자분포(CNDO/2)를 계산함으로서 분자궤도론적으로 연구하였다. 다른 실험 및 MO결과들과 함께 검토하여 본 결과 이 치환반응은 S_N2-보존형 메카니즘임을 알았다.

ABSTRACT. Bimolecular substitution of Cl^- at carbonyl carbon of CH_3COCl has been investigated MO theoretically by calculating energy profiles (EHT) and electronic distribution (CNDO/2) for frontsdie and backside attacks at several distances of approach. Considerations of other experimental and MO data together with these calculations support the S_N2-retention mechanism for the substitution at carbonyl carbon.

INTRODUCTION

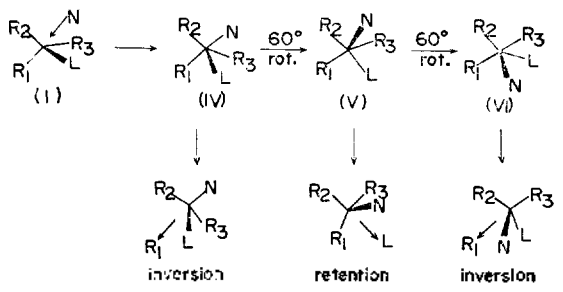
It has beea generally accepted that the bimole cular substitution at a saturated carbon (S_N2) proceeds norumally with inversion. In this mechanism the backside attack of nucleophile N and leaving of L is concerted and therefore the



(I) (II) (III)

trigonal-bipyramid (II) is the transition state. This has been confirmed both by experiment and molecular orbital (MO) calculation.[1]

However recently bimolecular substitutions with retention were found to occur at a saturated carbon forming small ring compounds including double bond as a two membered ring[2]. Ugi has suggested[2] a retention mechanism involving frontside attack of nucleophile to give a trigonal-bipyramid intermediate (IV), which can subsequently undergo rotation (turnstile-rotation) resulting in either inversion or retention product.



Stohrer[3] has recently presented an elegant MO theoretical model for the S_N2 reaction with retention. In this model the frontside attack of nucleophile produces retention produtct exclusively, since here the formation of the trigonal-bipyramid transition state(IV), which undergoes rotation, and the bond-breaking of the leaving group are concerted. The results of their MO calculation show that this type of mechanism is favorable for small ring compounds on electronic and steric grounds. The formation of trigonal-bipyramid transition state by backside attack of small ring compounds is energetically more costly due to the I-strain[3]. Kelsey and Bergman[4] have also shown using extented Hückel type (EHT) calculations that direct backside S_N2 displacement at vinyl carbon is unfavorable. Recently Lipscomb *et al*[5]., investigated the orientational requirements of nucleophilic attack on a carbonyl system using an approximate MO theory and found a rather wide "reaction funnel" for the attacking nucleophile. This implies that the nucleophile is not very restricted in its path of approach and there is no "orbital steering" effect[6] in this type of reaction. Their results also showed the formation of tetrahedral* intermediate through frontside attack of a nucleophile at a carbonyl system with no energy for activation.

In this work we have attempted to confirm the S_N2-retention mechanism of Stohrer for substitution at a carbonyl carbon atom of acyl chloride. As a model reaction we have used chlorine exchange reaction of acetyl chloride.

CALCULATIONS

We have used both EHT[7] and the complete neglect of differential overlap (CNDO/2)[8] methods in our calculations. The former has been proved the best semiempirical method in simulating ab initio SCF calculations for conformational problems[9], while the latter is more realistic in showing electronic charge distributions. We therefore restricted applications of EHT results to energetics and CNDO/2 to population analy sis. *Table* 1 shows geometric parameters used in the calculation.[10] The planar geometry of skeletal atoms of acetyl chloride was held rigid

Table 1. Geometrical parameters for CH_3COCl and C_6C_5COCl.

Molecule	Bond distance (Å) (AB)	Bond angle (deg.) (ABC)
CH_3COCl		
d=5, 4, 3Å	1.171 (CO)	109.5 (HCH)
	1.096 (CH)	120.0 (CCO) = (OCCl) = (CCCl)
	1.770 (CCl)	
	1.503 (CC)	
d=2.45Å	1.23 (CO)	117 (CCO)
	1.86 (CCl)	117 (OCCl)
	2.45 (CCl^-)	103 ($OCCl^-$)
d=2.05Å	1.30 (CO)	all angles=109.5.
	2.05 (CCl) = (CCl^-)	(For backside attack, linear form was assumed.)
C_6H_5COCl	All parameters are the same as for CH_3COCl except for benzene ring for which standard values are adopted.	

* Note that for unsaturated center the species is tetrahedral whereas for saturated center it is trigonal-bipyramid.

for d, the distance of Cl^- from the carbonyl from 5 to 3Å. The d value at the transition state was assumed to be 2.05Å.[1] For d value of 2.45 Å the geometry was partially optimized by varying angles. For frontside attack the turnstile rotation leading to the tetrahedral transition state (VIII) was assumed, whereas for backside attack a linear symmetrical transition state (VII) wasassumed from the reasons discussed below. The nucleophile approaches from directly above (or below) the carbonyl carbon i.e., above the molecular plane in the frontside attack, whereas in the backside attack the nucleophile approaches from rear of the leaving group (Cl) and within the molecular plane.

RESULTS AND DISCUSSION

Although substitution at unsaturated carbon is known to proceed with retention[2], we have nevertheless calculated energy profiles both for the frontside attack assuming the turnstile rotation mechanism of Stohrer and for backside attack of

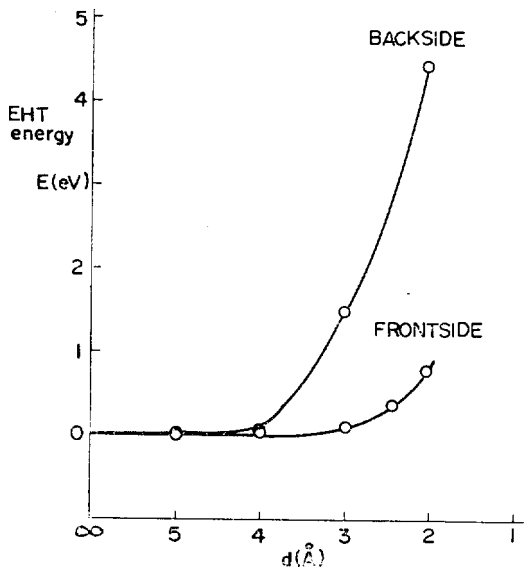


Fig. 1. Energy profiles for frontside and backside attacks of Cl^- on the carbonyl carbon atom of CH_3COCl, calculated by EHT.

Table 2. Population analysis for CH_3COCl—Cl^- system at several values of the reaction coordinates, d.

2-A

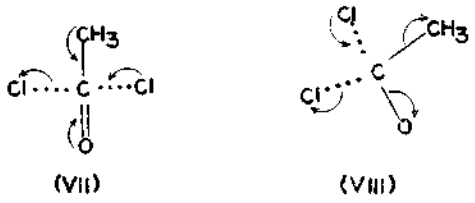
	Atomic charges (electronic charge unit)					
Frontside attack	d(Å)	(CH_3)	C	O	Cl	Cl^-
	∞	+0.060	+0.327	−0.199	−0.187	−1.000
	5	+0.057	+0.338	−0.201	−0.194	−1.000
	3	+0.039	+0.372	−0.219	−0.223	−0,970
Backside attack	∞	+0.060	+0.327	−0.199	−0.187	−1.000
	5	+0.084	+0.334	−0.182	−0.235	−1.000
	3	+0.097	+0.347	−0.165	−0.303	−0.975

2-B

	Bond indicies				
	C—Cl	C—O	C—(CH_3)	C—Cl^-	d(Å)
Frontside attack	0.951	1.939	1.030	0.000	∞
	0.949	1.940	1.029	0.000	5
	0.932	1.922	1.027	0.027	3
Backside attack	0.930	1.953	1.031	0.000	5
	0.893	1.964	1.037	0.008	3

Cl^- at carbonyl carbon of acetyl chloride. The profile constructed from energies calculated is shown in *Fig.* 1. Relative energies are always less for the frontside attack and therefore reaction path leading to retention is favorable. The energies of the reacting systems should not be taken as quantitative but only as relative.

Close look at the electronic charge distribution reveals several interesting features. *Table* 2 shows



(VII) (VIII)

atomic charges and bond indicies calculated with CNDO/2 results for Cl^- placed at 5 and 3 A each from the carbonyl carbon of acetyl chloride.

The population analysis shows that in both cases the carbonyl carbon becomes polarized and C—Cl bond weakens as Cl^- approaches. However in backside attack the bond-weakening is greater while the bond-formation is less than those in frontside attack. This indicates that the former has some S_N1 character. The essential differences however are in bond index changes of C—O and C—CH_3 bonds. During the frontside attack these bonds weaken while they strengthen in the backside attack. These are in good accord with the accepted retention and inversion mechanisms. The population analysis from EHT calculations also showed essentially the same general trends in atom and bond population changes as the nucleophile was made to approach. In the frontside attack, the approaching nucleophile induces the formation of tetrahedral, or trigonal-bipyramid, transition state(VIII) while in the backside attack it induces the linear acylium ion, $H_3C—C=O$, of an S_N1-like transition state (VII).

We therefore conclude that chlorine substitution at the carbonyl carbon of acetyl chloride proceeds by frontside attack followed by turnstile rotation leading to retention product. Main characteristic features of the mechanism are:

1. Nucleophile approaches the π system of the carbonyl carbon from above or below probably within the "reaction funnel" of Lipscomb.[5]
2. The concerted bond weakening of C—Cl (and C=O) and bond-formation of C—Cl^- induces "turnstile" rotation of C—Cl bonds.
3. The tetrahedral transition state(or inter mediate) is formed by breaking π bond of C=O into C—O^- and rotating C—Cl bonds.
4. Further rotation concerted with complete dissociation leads to retention product.

Naturally in the carbonyl substitution there is no distinction between retention and inversion products. Here we are concerned only with the steric course or path leading to the retention and inversion.

S_N2 VERSUS S_AN

Bimolecular nucleophilic substitution can be either concerted(S_N2) or multistage (S_AN) process depending on the lifetime of the tetrahedral species (VIII). If the lifetime is sufficiently long the tetrahedral species becomes an intermediate and the reaction proceeds via S_AN mechanism. Thus it is rather a difficult problem to decide whether mechanism is S_N2 or S_AN. In what follows we present arguments in favor of concerted mechanism for bimolecular substitution at carbonyl systems.

(i) Oxygen exchange during hydrolysis of benzoyl chlorides shows very large k_h/k_x values where k_h and k_x are the rate constants for hydrolysis and oxygen exchange respectively[11]. This indicates that concerted process is dominant.

(ii) Bunton and coworkers[12] have calculated values of the solvent isotope effect for various assumed models of the transition state of the

hydrolysis of acyl halides. For S_N2-like reactions, their estimate of k_H/k_D is 1.5, which is of the same order as the experimentally determined values.

(iii) Elliott and Mason[13] obtained k_H/k_D= 0.86, where k_H and k_D are the rate constants for reactions between benzoyl chloride with aniline and with *N, N*-dideuteroaniline respectively. Hence breaking of a nitrogen-hydrogen bond cannot be rate-determining.

(iv) Majority of the reported rate ratios,[14] k_{RCOF}/k_{RCOCl} and k_{RCOCl}/k_{RCOBr}, are much smaller than unity, 10^{-2}~10^{-4}. Here k values are for hydrolyses of R=CH_3 or C_6H_5. This may be interpreted as indicating an S_N2 type mechanism where varying degrees of carbon hydrogen bond stretching is involved in the transition state. The situation will be however more complicated if there is an intermediate on the reaction path, since the elimination step could be the rate determining. Howerver the results of Elliott and Mason, (iii), preclude this possibility.

(v) The reversal of rate sequence for RCOCl and ROCOCl as R was varied from CH_3 to C_6H_5, as can be seen from *Table* 3 and 4; for RCOCl rates are in the order of $CH_3>C_6H_5$, while for ROCOCl it is $CH_3<C_6H_5$ except reactions with I^- for which the order of k is again $CH_3>C_6H_5$. Comparison of MO properties together with these rate data provides some illumination on the mechanism involved. The CNDO /2 MO quantites are summarized in *Table* 5. The lowest unoccupied (LU) MOs of all four compounds were antibonding with respect to C—Cl bond. *Table* 5 shows that the first three MO quantities, which are related to the easiness of bond-formation, will give the rate order as $CH_3>C_6H_5$, since numerically large values in all cases are considered to favor easy bond-formation and hence larger k values. The rate order is consistent with that obtained from *Tables* 3 and 4 for RCOCl, but is reverse of rate results for ROCOCl. On the other hand, the last two MO quantities, bond index, W_{C-Cl}, and partial bond index of LUMO, W^{LU}_{C-Cl}, are considered to indicate easiness of bond breaking. Bond breaking of C—Cl bond will be easier, the smaller the value of W_{C-Cl} and the larger the value of W^{LU}_{C-Cl}, since the former is a measure of bond strength and the latter is a measure of antibonding strength of C—Cl bond in the LUMO. These two will give the order of k as $C_6H_5>CH_3$ if the bond breaking were the rate determining. This is con-

Table 3. Rate constants k_1 (sec^{-1}) for hydrolysis in acetone containing 10.9 vol. % water at 25° and k_2 (M^{-1}) for acylation of *m*-nitroaniline in benzene at 25°.

R in RCOCl	10^4k_1 [15]	10^2k_2 [15]
CH_3	10.9	1.231
C_6H_5	0.0417	0.0324
$C_6H_5CH_2$	3.60	2.079
$ClCH_2$	203	41.64

Table 4. Rate constants k_1 for hydrolysis in water (10±0.2°) and k_2 (25°) values with various nucleophiles for ROCOCl.

R in ROCOCl	$k_1\times10^4$ (sec^{-1}) [17]	$k_2\times10^3$ (M^{-1})			
		NO_3^- [18]	Anilion [19]	Cl^{-*} [19]	I^- [19]
CH_3	1.23	0.20	8.27	15.1	30.3
C_6H_5	34.6	6.70	366	123	0.175
C_2H_5	0.76	0.106	5.36	7.29	2.67
i-C_3H_7	2.36	0.035	3.47	0.489	0.267

*at 0 °C.

Table 5. MO quantities related to nucleophilic reactivities of RCOCl and ROCOCl.

	MO quantities	RCOCl		ROCOCl	
		R $=CH_3$	C_6H_5	CH_3	C_6H_5
(1)	Z_C	+0.327	+0.315	+0.490	+0.455
(2)	f_C^{LU}	0.622	0.359	0.946	0.600
(3)	$\frac{f_C^{LU}}{\varepsilon^{LU}-\varepsilon_{Cl^-}^{HO}}$	0.104	0.066	0.138	0.103
(4)	ε^{LU}(eV)	2.2	1.7	3.1	2.1
(5)	W_{C-Cl}	0.951	0.946	0.887	0.843
(6)	W_{C-Cl}^{LU}	0.0030	0.0361	0.660	0.705

(1) Charge density of the carbonyl carbon.
(2) Frontier electron density of the carbonyl carbon.
(3) Reactivity parameter from perturbation theory.[20] $\varepsilon_{HO}^{Cl^-}$ was taken as -3.7 eV.[21]
(4) Energy levels of LUMO
(5) and (6) are explained in the text.

sistent with k values of ROCOCl but is reverse of the order for RCOCl. This may be due to the large antibonding nature of σ^*_{C-Cl} for ROCOCl compared to relatively small values for RCOCl. Energy levels of LUMO are always lower for C_6H_5 than for CH_3, and this is also favorable for large k values of C_6H_5. It seems therefore that bond breaking is important in the transition state with ROCOCl while bond-formation is important with RCOCl. Results of *Table* 5 considered in conjunction with those of *Tables* 3 and 4 can be summarized as follows.

(a) Bond-formation is always easier with CH_3 than with C_6H_5, for both RCOCl and ROCOCl.

(b) Bond breaking is always easier with C_6H_5 than with CH_3, for both RCOCl and ROCOCl.

(c) Energy levels of LUMO indicate bimolecular S_N reaction is favorable with C_6H_5 compared with CH_3

(d) Bond breaking is likely to be more important at the transition state with ROCOCl, since W_{C-Cl}^{LU} values are larger with ROCOCl than with RCOCl. This implies that the transition state will be of the "late" type with ROCOCl. However with poor nucleophile like I^- it becomes "early" type.

(e) For relatively "early" type of transition state with RCOCl, bond breaking will be insignificant although some degree of bond loosening always occurs.

In conclusion we prefer concerted retention mechanism for S_N reactions of carbonyl halides to multistage process by invoking the "late" and "early" types of transition state for reactions in which bond breaking and bond-formation are important. This mechanism is similar to the S_N2-inversion mechanism which has a spectrum of transition state between the two limiting cases. The present mechanism differs only in that concerted bond-formation and bond breaking induces rotation of bonds leading to a tetrahedral transition state.

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