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MO 理論에 依한 反應性의 決定 (第15報). 아세트아미드류의 형태와 산촉매반응에 관한 이론적 연구

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Determination of Reactivities by MO Theory (XV). Theoretical Studies on Conformations and Acid Catalysis of Acetamides

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요 약. 아세트아미드, 디아세트아미드 및 그들의 양성자 부가물들에 대한 형태 결정을 목적으로 EHT 및 CNDO/2 계산을 실시하였다. 계산 결과에 따르면 H^+와 N간의 인력으로 인하여 양성자는 항상 N에 대하여 *cis* 위치에 첨가되는 것이 유리하며, 양성자 부가가 안되었을 때는 *cis-trans* 형이 가장 안정하지만 양성자 부가물은 오히려 *trans-trans* 형이 가장 안정하였다. 양성자 첨가는 첨가된 카르보닐기의 탄소의 陽하전을 증가시키고 또 π-LUMO의 AO 계수를 증대시키므로 charge-controlled 및 orbital controlled 친핵 반응을 모두 촉진시킬 것이 예상되었다.

그러므로 디아세트아마이드의 酸촉매 가수분해 반응에서는 친핵체인 물 分子가 양성자화된 카르보닐탄소를 공격할 것이며 그 탄소와 질소간의 결합이 끊어지게 될 것이다. 이 메카니즘은 묽은 酸속에서의 아미드류의 가수분해 메카니즘으로 알려진 것과 일치하며 N-아세틸 락탐의 산촉매 가수분해 메카니즘으로 제안된 Laurent[3] 등의 것과는 다르다.

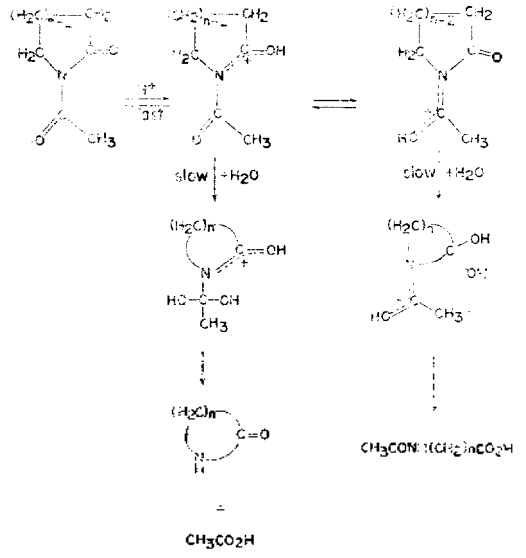
ABSTRACT. EHT and CNDO/2 calculations have been performed to determine conformations of acetamides and diacetamides, and of their protonated forms. Results show that: protonation is always favored on the *cis* position with respect to N due to greater attractive potential between H^+ and N; the *trans-trans* conformer of diacetamides gives the most preferred protonated form although the *cis-trans* conformer is the most stable one for the uprotonated diacetamides. Protonation on a carbonyl oxygen is predicted to increase both charge and orbital controlled S_N reactivities of the protonated carbonyl carbon due to increases in positive charge and AO coefficient of π-LUMO of the carbon atom.

In the acid catalyzed hydorlysis of diacetamides therefore it appears highly probable that the rate determining attack by a water molecule occurs at the carbon of the protonated carbonyl group

and the carbonyl carbon-nitrogen bond scission follows subsequently. This mechanism is consistent with that generally accepted for the hydrolysis of amides in dilute acid solution but disagrees with that proposed by Laureut *et al.*, for acid hydrolysis of N-acety-lactams.

INTRODUCTION

Acetamides have recently attracted much interest due to their possible role as intermediates of acyl transfer reactions in biological synthesis of peptide and proteins.[1] Laurent *et. al.*, studied conformations as well as acid catalyed hydrolysis of N-methyldiacetamide[2] and N-acetyllc tams,[3] and showed that the hydrolysis proceeded *via* the A_2 mechanism, being specifically hydrogen ion catalyzed. Furthermore they reported that protonation occurred on the carbonyl oxygen while attack by a water molecule occurred on the carbon atom of the unprotonated carbonyl group. They concluded that in the case of N-acetyllactams, the smaller is the ring, the more negative is the carbonyl carbon due to greater, S character; hence decreases the delocalization of carbon toward oxygen which becomes accordingly less basic. Thus the protonation occurs more preferentially at the ring carbonyl oxygen as the ring size increases and therefore the acyl cleavage tends to increase as the ring size increases since the nucleophile, H_2O, attacks the unprotonated carbonyl carbon, where the C–N bond cleavage occurs subsepuently (*Scheme* 1).



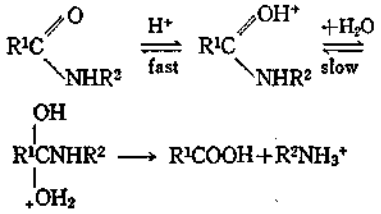
Scheme 1.

In contrast with this view of Laureut *et al.*,[3] however, our molecular orbital studies[4] have shown that the electron density (basicity) of ring carbonyl oxygen increases as the ring size decreases and nucleophile should attack the protonated carbonyl carbon. This is consistent with the mechanism generally accepted for the hydrolysis of amides in dilute acid solution (*Scheme* 2), which involves nucleophilic attack by a water molecule on the protonated amide as the rate determining step.[5]

In this report we will examine further MO theoretically the structures and acid catalyzed S_N reactivities of acetamide, N-methylacetamide, diacetamide, N-methyldiacetamide and N-methylsuccinimide in order to gain additional insight into the mechanism of acid catalyzed reactions of acetamides, and hopefully generalize the mechanism involved.

CALCULATIONS

Both the EHT[6] and CNDO/2[7] methods have been used for eigenvalue problems, while for the derivation of eigenvector properties the latter



Scheme 2.

only was employed. In the calculations for diacetamides the optimized geometries of Capparelli[8] were used. The geometrical parameters are given in *Table* 1. Standard values[9] of bond lengths and angles were used for the calculations on acetamides and N-methyl succinimide.

Although there have been some controversies regarding the position of protonation of amides, results of experimental as well as theoretical studies now seem to support the predominant O-protonation over a small degree of N-protonation in weak acid solutions.[5] Hence we considered only the O-protonated forms. The proton was placed at 0.99 Å from O with 120° angle in the same plane with C=O group throughout these calculations.[10]

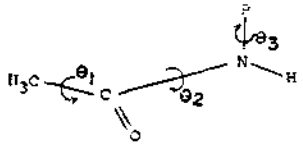
All the atoms in molecules investigated in this work were considered to be coplanar except hydrogens in methyl group, since the nitrogen is known to take planar form, *i.e.*, sp^2 hybrid, when strong electron withdrawing groups such as *p*-$NO_2C_6H_5$-, CHO and $-COCH_3$ are attached to it.[11] This coplanarity was confirmed by calculation for acetamides.

RESULTS AND DISCUSSION

Acetamides. Preferred conformations were determined by examining EHT energies as

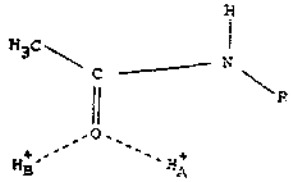
Table 1. Structural parameters used for diacetamides.

Geometrical parameters	
d_{C-N}	1.405 Å
$d_{C=O}$	1.283 Å
d_{C-C}	1.460 Å
d_{C-H}	1.110 Å
d_{N-H}	1.050 Å
∠NCO	119.5°
∠CNH	117°
∠CNC	126°



angles θ_1, θ_2 and θ_3 were varied. For acetamide R is H and therefore θ_3 needs not be considered. All angles are taken as zero degree when one of H atoms is on the plane of the coplanar non-hydrogen skeleton. The results are summarized in *Table* 2.

For N-methylacetamide the *trans* form is more stable by about 18 kcal/mole than the *cis* form. Comparison of charge densities and overlap population indicates that π-electron densities delocalized from the N atom to the O is greater for the trans form (*Fig.* 1).



Two protonated forms, H_A^+ and H_B^+, are considered for both systems: R=H and R=CH_3. In both cases *cis*-protonation (with respect to N), H_A^+, was preferred. Energy component analysis[12] in *Table* 3 shows that the preference of *cis* protonation to *trans* protonation is mainly due to the larger attractive potential V_{ne} for the *cis* protonation. This attractive potential is predominantly of the electrostatic nature between H^+ and N as can be seen from ΔQ.[13] Note that repulsion terms V_{ee} and V_{nn} are also larger for

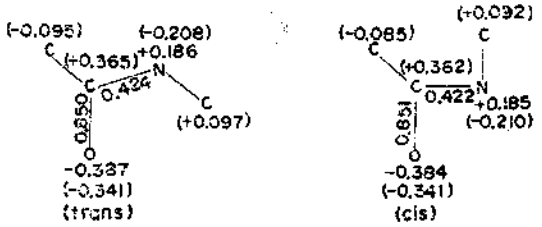


Fig. 1. CNDO/2 gross (in parenthesis) and π charges, and π overlap populations for N-methylacetamide.

Table 2. EHT energy changes with torsional angles for acetamide and N-methylacetamide.

	Acetamide, R=H						N-Methylacetamide, R=CH_3							
θ_1	30	60	90	30	30	30	60	60	60	60	60	60	60	60
θ_2	0	0	0	90	60	30	0	60	120	180	240	300	0	0
θ_3							60	60	60	60	60	60	90	0
ΔE (kcal)	0.5	0.0	0.4	116.5	49.1	171.0	18.4 (*cis*)	15.7	11.7	0.0 (*trans*)	11.7	15.4	12.9	7.8

the *cis* protonation.

Furthermore it was found that the protonation of O caused increase in positive charge on the carbonyl carbon by about 0.110 electronic charge unit in both cases; for R=H and R=CH_3. Owing to the delocalization of the nitrogen lone pair toward carbonyl oxygen, N-C-O forms a pseudopropenyl π system. These π orbitals are summarized in *Table* 4.

Topologically three π MOs for N···C···O systems of two acetamides are equivalent to those for the propenyl system, C···C···C, but replacement of two carbons with heteroatoms, N and O, considerably distorts the actual nodal properties and the relative magnitude of the AO coefficients. The lowest unoccupied orbitals (LUMO), π_3, are perturbed due to the O-protonation: energy levels are lowered and the AO coefficient of the carboyl carbon becomes larger increasing the antibonding character of C-N bond. This suggests that the orbital controlled S_N reactivity[14] of the carbonyl carbon increases and the C-N bond cleavage becomes easier when protonated. The charge controlled S_N reactivity should increase since the positive charge of the carbonyl carbon increases as the oxygen is protonated.

Increase in AO coefficient of the carbonyl carbon in the perturbed (protonated) LUMO, π_3', is primarilly effected by in-phase mixing of the HOMO, π_2, into the LUMO, π_3, as shown in *Table* 4.[15]

Diacetamides. Various experimental studies[2a,11b] have shown that only three planar conofrmers are possible for these compounds: *cis-trans*, *trans-trans* and *cis-cis* (*Fig.* 2). Moreover it is generally agreed that the *cis-trans* conformer is the most stable one.

Table 3. Energy (CNDO/2) component analysis for the protonated *trans*-N-methylacetamide (kcal/mole)

Position	ΔE_T[a]	$-\Delta V_{nn}$[b]	ΔV_{ee}[c]	ΔV_{nn}[d]	ΔQ[e]
A	0.0	0.0	0.0	0.0	0.0
B	2.8	−537.3	−233.8	−297.9	3.6

[a]Total energy difference. [b]Negative value of the difference in nuclear-electron attraction potential. Thus if $-\Delta V_{ne}<0$, the attraction decreases and causes destabilization, and if $-\Delta V_{ne}>0$, the attraction increases. [c]Difference in electron-electron repulsion. [d]Difference in nuclear-nuclear repulsion. [e]Difference in Coulomb energy calculated based on the point charge approximation using $0.5292\Sigma q_i q_j/r_{ij}$ (a.u)[13] where q_i and q_j are formal charges of atoms i and j, and r_{ij} is the internuclear distance between atoms i and j. Positive value of this term indicates less attractive or more repulsive interaction and hence destabilizing by that amount.

Capparelli *et al.*, reported on the conformational studies of diacetamide (R=H) using CNDO/2 method. They have found from the calculated total energies that the *trans-trans* conformer was 3.0 kcal/mole over the *cis-trans* and the *cis-cis* form was the least stable. Using their optimized geometrical parameters, we have calculated stabilities of various conformers for diacetamide and N-methyldiacetamide and results are shown in *Table* 5 together with energy component analysis. For both diacetamides,

Table 4. Pseudopropenyl π MOs (CNDO/2) for acetamide and N-methylacetamide.

MO	Acetamide				N-methylacetamide			
	AO Coefficient			E(a. u)	AO Coefficient			E(a. u)
	O	C	N		O	C	N	
π_1	0.331	0.297	0.540	−0.659	0.509	0.383	0.295	−0.602
π_2	0.680	0.220	−0.689	−0.495	0.572	0.125	−0.722	−0.466
π_3	−0.518	0.683	−0.254	0.187	−0.519	0.683	−0.244	−0.183
$\pi_3'(H_A^+)$	−0.367	0.791	−0.372	−0.153	−0.362	0.783	−0.379	−0.143
$\pi_3' = -0.087\pi_1 + 0.181\pi_2 + 0.825\pi_3$					$\pi_3' = -0.004\pi_1 + 0.164\pi_2 + 0.980\pi_3$			

R=H and R=CH_3, the *cis-trans* form (I) is the most stable. This is in good agreement with experimental results.[2,11] The energy component analysis of *Table* 5 shows that the dominant destabilizing factor is the decrease in attractive potential, $-\Delta V_{ne}<0$, for the *trans-trans* form while it is the increase in repulsive potential, $(\Delta V_{ee}+V_{nn})>0$, for the *cis-cis* form as compared with the *cis-trans* conformer respectively.

Energies of nine possible protonated forms were then analyzed as given in *Table* 6. *Fig.* 3 shows the positions of protonation and the numbering scheme for major skeletal atoms.

Results of energy analysis in *Table* 6 show that, except I (D) form, *cis* protonation with respect to N is always preferred to trans protonation as we found for acetamides. The energy component analysis clearly indicates that this general trend of *cis* stability is due to increase in the attractive potential rather than due to decrease in the repulsive potential. Rough esti-

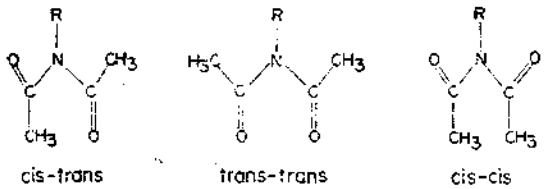


Fig. 2. Three planar conformers of diacetamides: R=H diacetamide; R=CH_3 N-methyldiacetamide.

Table 5. Energy component analysis of diacetamide and N-methyldiacetamide.

	Conformer[a]	ΔE_T	$-\Delta V_{ne}$	ΔV_{ee}	ΔV_{nn}[b]
R=H	I	0.0	0.0	0.0	0.0
	II	3.0	−1189.1	−571.9	−611.2
	III	10.0	1368.6	588.9	799.6
R=CH_3	I	0.0	0.0	0.0	0.0
	II	6.7	−815.1	−408.1	−393.6
	III	11.5	995.6	438.8	579.7

[a]The designation of conformers are as shown in *Fig.* 2. [b]All the terms have the same significances as defined in *Table* 3.

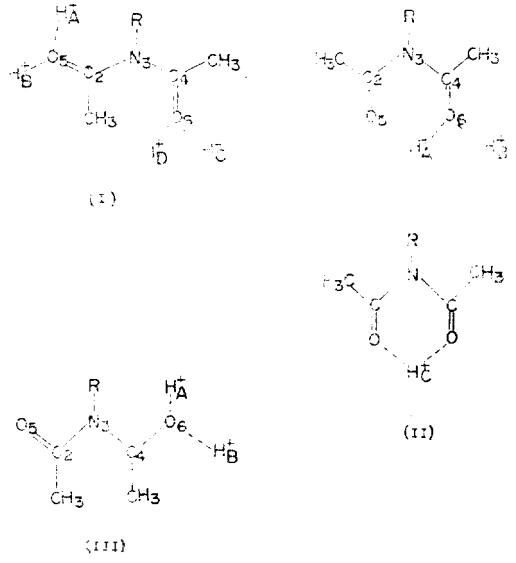
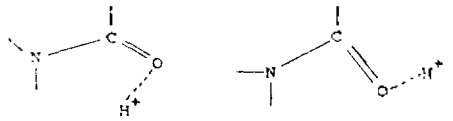


Fig. 3. Protonated forms of diacetamide, R=H, and N-methyldiacetamide, R=CH_3, and numbering schemes for major skeletal atoms.

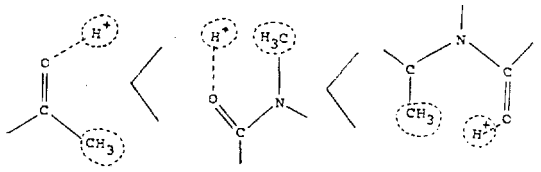
Table 6. Energy (CNDO/2) component analysis for protonated diacetamides (kcal/mole).

		ΔE	$-\Delta V_{nn}$	ΔV_{ee}	ΔV_{nn}	ΔQ
R=H	I(A)	2.1	−504.3	−245.6	−254.4	22.3
	I(B)	3.3	−738.7	−345.7	−386.3	29.0
	I(C)	10.1	−312.8	−183.7	−108.9	28.4
	I(D)	5.6	1284.2	513.9	763.4	20.6
	II(A)	0.0	0.0	0.0	0.0	0.0
	II(B)	9.0	−1510.9	−708.6	−784.3	28.3
	II(C)	55.6	−1121.1	−199.7	−810.2	11.8
	III(A)	30.9	1250.3	519.8	792.2	23.0
	III(B)	32.3	1036.9	422.9	678.6	28.2
R=CH_3	I(A)	2.7	−163.0	−76.9	−80.6	17.6
	I(B)	4.0	−988.8	−439.0	−541.8	26.0
	I(C)	8.9	−733.3	−353.4	−362.0	25.6
	I(D)	22.7	984.7	436.2	594.0	19.8
	II(A)	0.0	0.0	0.0	0.0	0.0
	II(B)	9.5	−1575.9	−737.3	−819.6	25.4
	II(C)	70.2	−1200.8	−222.8	−837.6	12.0
	II(A)	18.6	778.9	316.0	500.3	18.0
	II(B)	20.4	−31.3	−46.8	56.5	25.3



cis-protonation trans-protonation

mates of coulomb energies based on the point charge approximation, ΔQ, also confirm this view. In the case of I(D) form, the situation reverses; now the steric repulsion of the neighboring CH_3 group exceeds over the increase in the attractive potential. Another interesting feature is that the steric repulsion of the CH_3 group attached to N in I (A) form for N-methyldiacetamide is comparatively small. On the whole, the steric repulsion between H^+ and CH_3 increases as the following order.



The II (C) form has C_{2v} symmetry. Although this form has often been thought of the most stable protonated form[2b,16], it corresponds to the barrier when proton switches over from one oxygen to another in the *trans-trans* form, II (A), which is the most stable form. The II (A) form is actually more stable by 2~3 kcal/mole than I(A) form due to the greater attractive potential; II(A) form has also the largest coulomb attraction, Q. The fact that the protonated *trans-trans* form, II (A), has the greatest stability is quite noteworthy, since for unprotonated diacetamides it was the *cis-trans* form which was the most stable. Thus it is reasonable to assume that in the acid catalysis of diacetamides the protonated form is maialy that of the *trans-trans* conformers. This is in good agreement with the kinetic results of Laureut *et al.*,[2b,3] who found that the acid catalyzed hydrolysis rate was considerably slower for N-methylsuccimide for which protonation is not possible on a *trans-trans* form; the second

order rate constant for N-methylsuccimide was smaller by more than 10^{-3} compared to that for N-acetylpyrrolidone for which the the protonation on *trans-trans* form is possible.

Table 7 shows formal charges of carbonyl carbons for diacetamide and N-methyldiacetamide. It is quite clear from this table that the protonation always causes increase in the formal positive charge of the protonated carbonyl carbon atom and the largest increase is found for the most preferred protonation; for both diacetamide and N-methyldiacetamide II(A) form have the greasest increase of positive charge on the protonated carbonyl carbon atom.

Let us now examine some of the orbital characteristics. The nitrogen lone-pair can delocalize into two carbonyl groups in diacetamides forming a pseudo-pentadienyl π system, O···C···N···C···O. It should be noted that the *trans-trans* and *cis-cis* forms are symmetric as can be seen from *Table* 8, where we have shown π MO's of interst for discussion. We have given complete π MO's only for diacetamide (R=H), as MO features were exactly the same for N-methyldiacetamide ($R=CH_3$).

Table 7. Formal charges of carbonyl carbons for diacetamide and N-methyldiacetamide

	Protonated carbonyl carbon	Formal charge	
		C_2	C_4
Diacetamide: *cis-trans*		0.351	0.344
I(A)	C_2	0.476	0.355
I(B)	C_2	0.473	0.354
I(C)	C_4	0.342	0.468
I(D)	C_4	0.340	0.470
trans-tsans		0.344	0.344
II(A)	C_4	0.363	0.480
II(B)	C_4	0.349	0.473
cis-cis		0.342	0.342
III(A)	C_4	0.345	0.471
III(B)	C_4	0.345	0.468
N-Methyldiacetamide: *cis-trans*		0.348	0.340
I(A)	C_2	0.463	0.348
I(B)	C_2	0.459	0.348
I(C)	C_4	0.337	0.447
I(D)	C_4	0.335	0.453
trans-trans		0.342	0.342
II(A)	C_4	0.355	0.463
II(B)	C_4	0.341	0.455
cis-cis		0.338	0.338
III(A)	C_4	0.338	0.454
III(B)	C_4	0.336	0.450

First of all we notice from the table that π MO's are practically independent of the change in conformation and the position of protonation; thus comparison of MO I-π_4 with those of II-π_4 and III-π_4 reveals the essential similarity; and again MO's I-π_4' (A) and (B), II-π_4' (A) and III-π_4' (A) are not much different.

Secondly the protonation invariably leads to the increase in the AO coefficient of carbonyl carbon and antibonding character of the bond between carbonyl carbon and nitrogen; the carbonyl carbon involved being specifically that of the protonated carbonyl group. This is consistent with our previous results.[4]

Finally the orbital mixing analysis[15] show that perturbed LUMO, π_4' is effected mainly by mixing in the next to the lowest unoccupied orbital (NLUMO) π_5 (*Table* 9). This is also in accord with our results on N-acetyllactams.[4]

In the acid catalyzed hydrolysis of diacetamides therefore it is highly probable that the nucleophilic attack of H_2O occurs at the carbon of protonated carbonyl group and the carbonyl carbon-nitrogen bond scission follows subsequently.

Since the protonation on the *trans-trans* conformer (form II(A)) was the most preferred and the two carbonyl groups are equivalent in the *trans-trans* form, two indistinguishable C-N bonds should have equal chance of cleaving.

N-Methylsuccimide. Two coplanar protonat-

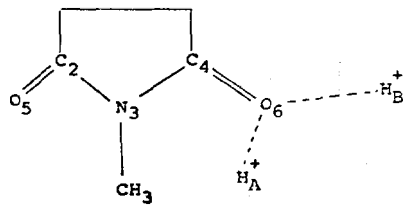
Table 8. Pseudo-pentadienyl MO's for OCNCO systems of diacetamide and N-methyldiacetamide.

	E(a. u.)	AO Coefficient				
		O_5	C_2	N_3	C_4	O_6
Diacetamide:						
cis-trans (I) π_1	−0.6542	0.143	0.151	0.572	0.198	0.164
π_2	−0.5646	−0.504	−0.321	−0.050	0.321	0.569
π_3	−0.4637	−0.582	−0.160	0.574	−0.127	−0.516
π_4	0.1153	−0.356	0.445	0.047	−0.563	0.444
π_5	0.1666	0.381	−0.535	0.326	−0.398	0.267
π_4' (A)	−0.1743	−0.328	0.772	−0.287	−0.186	0.231
π_4' (B)	−0.1726	−0.329	0.771	−0.282	−0.182	0.236
π_4' (D)	−0.1800	−0.236	0.199	0.282	−0.765	0.336
trans-trans (II) π_4	0.1206	−0.408	0.499	0.000	−0.499	0.408
π_5	0.1687	0.333	−0.463	0.322	−0.463	0.333
π_4' (A)	−0.1744	−0.223	0.209	0.271	−0.765	0.341
cis-cis (III) π_4	0.1114	−0.403	0.509	0.000	−0.509	0.403
π_5	0.1529	0.326	−0.448	0.323	−0.448	0.326
π_4' (A)	−0.1910	−0.226	0.183	0.297	−0.764	0.330
N-methyldiacetamide:						
cis-trans(I) π_4'	0.1131	−0.360	0.447	0.045	−0.558	0.440
π_5	0.1642	0.378	−0.526	0.317	−0.397	0.272
π_4' (A)	−0.1681	−0.325	0.761	−0.286	−0.204	0.240
π_4' (C)	−0.1716	−0.250	0.218	0.284	−0.751	0.331
trans-trans (II) π_4	0.1188	−0.409	0.496	0.000	−0.496	0.409
π_5	0.1667	0.332	−0.458	0.312	−0.458	0.332
π_4' (A)	−0.1689	−0.239	0.222	0.276	−0.753	0.335
cis-cis (III) π_4	0.1056	−0.404	0.499	0.000	−0.499	0.404
π_5	0.1604	0.331	−0.462	0.322	−0.462	0.331
π_4' (A)	−0.1788	−0.241	0.203	0.296	−0.755	0.326

Table 9. Orbital mixing analysis of perturbed (protonated) LUMO', π_4', for some protonated Diacetamide and N-methyldiacetamide.

Diacetamide :	I (A), $\pi_4' = -0.093\pi_1 + 0.004\pi_2 - 0.193\pi_3 + 0.654\pi_4 - 0.496\pi_5$
	I (D), $\pi_4' = 0.061\pi_1 - 0.013\pi_2 + 0.191\pi_3 + 0.766\pi_4 + 0.290\pi_5$
	II (A), $\pi_4' = 0.069\pi_1 - 0.021\pi_2 - 0.179\pi_3 + 0.716\pi_4 + 0.384\pi_5$
	III (A), $\pi_4' = -0.056\pi_1 + 0.016\pi_2 - 0.206\pi_3 + 0.706\pi_4 + 0.390\pi_5$
N-Methyldiacetamide :	I (A), $\pi_4' = -0.021\pi_1 + 0.009\pi_2 + 0.187\pi_3 + 0.664\pi_4 - 0.468\pi_5$
	I (C), $\pi_4' = -0.001\pi_1 - 0.001\pi_2 - 0.185\pi_3 + 0.765\pi_4 + 0.269\pi_5$
	II (A), $\pi_4' = -0.010\pi_1 - 0.019\pi_2 - 0.178\pi_3 + 0.718\pi_4 + 0.361\pi_5$
	III (A), $\pi_4' = 0.014\pi_1 + 0.001\pi_2 - 0.198\pi_3 + 0.707\pi_4 + 0.378\pi_5$

ed forms were considered. Again the *cis* protonation, A form, was more stable and the extra stability was due to the greater attractive potential as can be seen from *Table* 10. In this case



the total energy difference of $\Delta E=4.0$ kcal/mole is almost completely accounted for by the electrostatic energy difference of $\Delta Q=3.9$ kcal/mole. The π-LUMO and its perturbed form are shown in *Table* 11. The protonation of a carbonyl oxygen again causes similar activation of the carbonyl carbon as for other acetamides discussed above; π-LUMO coefficient of the protonated carbonyl carbon becomes larger and hence antibonding character of C–N bond increases. The positive charge of the carbonyl carbon which is protonated on its O was also found to increase by 0.110 electronic charge unit.

CONCLUSIONS.

Our semi-empirical MO studies support the following conclusions.

1. Protonation on *cis* position with respect to N is always preferred due to greater attractive potential between H^+ and N.

2. For diacetamides the *cis-trans* conformer is the most stable, whereas the *trans-trans* conformer becomes the most stable form when the diacetamides are protonated.

3. Protonation leads to the increase in positive charge of the protonated carbonyl carbon; this will increase charge controlled S_N reactivity of the carbon atom.

4. Protonation also leads to increase in AO coefficient of π-LUMO and the antibonding character of the LUMO at the protonated carbonyl carbon; this will increase orbital controlled S_N reactivity of the of the carbon atom.

5. The perturbed LUMO is mainly effected by mxing in of the nearest MO; the nearest being NLUMO for diacetamides and HOMO for acetamides.

6. We therefore support the general mechanism of scheme 3 for the hydrolysis of acetamides and diacetamides, which is consistent with *Scheme* 2. but differs from the mechanism proposed by Laureut, *Schem* 1.

Table 10. Energy (CNDO/2) compnent analysis as protonated N-methylsuccinimide (kcal/mole)

Position	ΔE	$-\Delta V_{nn}$	ΔV_{ee}	ΔV_{en}	ΔQ
A	0.0	0.0	0.0	0.0	0.0
B	4.0	−540.7	−229.4	−303.0	3.9

Table 11. π-LUMO's for *N*-methylsuccinimide and its protonated form.

	E(a.u)	AO Coefficient				
		O_5	C_2	N_3	C_4	O_6
π_4	0.1375	−0.441	0.568	0.00	−0.568	0.441
π_4'(A)	−0.1503	−0.291	0.264	0.310	−0.738	0.314

$\pi_4'=-0.021\pi_1+0.041\pi_2+0.204\pi_3+0.741\pi_4+0.385\pi_5$

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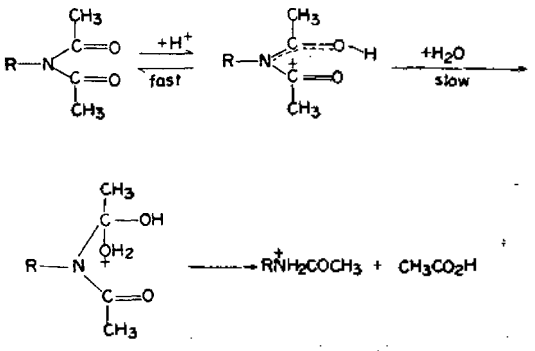

Scheme 3.

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