other hand, delocalization can occur without similar electrostatic destabilization, for here the reaction partners are no longer together and the opposite charges are not in close proximity. Thus, this effect raises the free energy of the transition state without having a corresponding influence on the free energy of reaction.

Phosphoric acid also shows a positive deviation despite the fact that it resembles the neutral carboxylic acids in being uncharged and having a charge-delocalized anion. The rate acceleration here may be the result of a particularly favorable disposition of solvent molecules about the hydroxylic H_3PO_4 species, which reduces the amount of solvent reorganization that must take place upon proton transfer. A similar argument has been advanced to explain the positive deviations generally observed for bisulfate ion in reactions of this kind.[14] It is not at all clear, however, that the catalytic effectiveness of bisulfate ion cannot be accounted for in terms of the electrostatic influence of the negative charge alone.

It is interesting that sulfamic acid gives a negative deviation. This is consistent with a zwitterionic structure, $SO_3^-NH_3^+$, for this substance, which makes its acidic end positive and puts it into the category of positively charged catalysts. Sulfamic acid is known to exist in this and not the neutral form, HSO_3NH_2, in the crystal,[15] but there has been some uncertainty about its structure in solution.[16]

The sulfamic acid deviation is smaller than expected for a catalyst with its positive charge so near the seat of reaction, but this is undoubtedly due to the close proximity of the negatively charged sulfonate group. The structural situation is not unlike that in the bisulfate ion, and approximating the effect of the negative charge by the positive deviation shown by bisulfate gives 1.1 log units as the negative deviation of $-NH_3^+$ alone; this comes to within a factor of 2 in rate to the strong negative deviation shown by the structurally similar hydronium ion. The hydronium ion is consistently a very poor catalyst in reactions such as this,[11b,17] and it has been suggested that this may be the result of an improperly assessed acidity constant.[18] The present results indicate that a good portion of the effect could be electrostatic in origin.

Apart from being interesting in their own right, these electrostatic effects on acid catalysis illustrate rather dramatically the dangers inherent in basing Brønsted correlations on structurally inhomogeneous groups of catalysts. For example, the present data for phosphoric and cyanoacetic acids give a Brønsted exponent of -2.7, whereas the data for bisulfate ion and sulfamic acid provide a value of nearly $+15$! On the other hand, the seven neutral carboxylic acids and the seven amino acids, taken as two separate groups, give exponents which are very similar: $\alpha = 0.70 \pm 0.03$ and 0.65 ± 0.04, respectively. This suggests that Brønsted exponents based upon different homogeneous groups of catalysts which cover the same pK_a range may in general be similar and therefore independent of the structure of the catalysts.

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(14) M. M. Kreevoy, T. S. Straub, W. V. Kayser, and J. L. Melquist, *J. Amer. Chem. Soc.*, **89**, 1201 (1967).

(15) F. A. Kanada and A. J. King, *ibid.*, 73, 2315 (1951).; K. Osaki, H. Tadokoro, and I. Nitta, *Bull. Chem. Soc. Jap.*, **28**, 529 (1955).

(16) P. Baumgarten, *Ber.*, **62B**, 820 (1929); E, J. King and G. W. King, *J. Amer. Chem. Soc.*, **74**, 1212 (1952); M. K. Hargreaves, E. A. Stevenson, and J. Evans, *J. Chem. Soc.*, 4582 (1965); H. P. Hopkins, Jr., C. H. Wu, and L. G. Hepler, *J. Phys. Chem.*, **69**, 2344 (1965).

(17) J. M. Williams, Jr., and M. M. Kreevoy, *Advan. Phys. Org. Chem.*, **6**, 63 (1968).

(18) R. P. Bell, *Trans. Faraday Soc.*, **39**, 253 (1943).

Determination of Intermediate Ion Structure in the Mass Spectrometry of Heteroaromatic Compounds[1]

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Abstract: A quantum chemical method for the determination of ion structure in the course of the fragmentation of cyclic compounds is proposed. Using this method, the fragmentation mechanisms of pyridine and pyrimidine are examined. Electronic structures of some ions are calculated by the open-shell CNDO/2 method to give bases for their organic chemical expressions. It is shown that the first bond scission of a heteroaromatic ring generally occurs at the bond β to the heteroatom with an unpaired electron.

Many papers on the mass spectrometry of heteroaromatic compounds have been published.[2] In spite of the efforts of many authors, the mechanism of the fragmentation has not been so systematically established as with aliphatic compounds. The difficulty is considered to be caused by the uncertainty of our knowledge of the ion structures in the course of fragmentation. Besides, there seems to be no direct experimental technique available for determination of structures. In this paper we will deal with general cyclic ions and will propose a quantum chemical method based on three hypotheses: (1) the fracture of a ring proceeds stepwise; (2) the velocity of the first

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(1) A Molecular Orbital Approach to the Interpretation of Organic Mass Spectra. III. Part II: H. Ichikawa and M. Ogata, *Bull. Chem. Soc. Jap.*, submitted for publication.

(2) See, *e.g.*, Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds," Wiley-Interscience, New York, N. Y., 1971.

bond scission is related to the rate constant, which can be obtained by the quasi-equilibrium theory of mass spectra (QET);[3] and (3) the Bell–Evans–Polanyi (BEP) principle[4] holds in the mass spectral reactions.

When QET is applied to the interpretation of organic mass spectra, it is usually assumed that contributions to reactivity from excited electronic states all cancel and/or that radiationless transitions occur such that unimolecular decomposition occurs mostly on the surface of the ground electronic state. This is not of course always the case, but may be an important one judging from the wide validity of the theory.[3] In the present theory, we consider the case of the doublet molecule ion in the ground electronic state as a reactive electronic state. Such ions may electronically correspond to those which give class I reactions according to the classification by Dougherty.[5]

Theory

It is widely known that the bond strength in the (closed-shell) normal state is not applicable to the prediction of the position of bond rupture in organic mass spectrometry. It is also shown[6] that the calculated bond index of doublet ions in the ground electronic state does not still represent the possibility of bond fracture; this suggests that the assumption of noncrossing of the potential energy curves between the perturbational and the transition states is not applicable to the mass spectral reactions. Therefore, the activation energy involved in the reaction should be estimated in order to predict the position of the first bond scission.

According to the generally accepted QET, the relationship between the rate constant (k) of bond fracture and the activation energy (ΔE) is expressed in several forms.[3] Among them, for the model composed wholly of harmonic oscillators, the general expression in the rate constant is simply

$$k = \nu((E - \Delta E)/E)^{s-1} \qquad (1)$$

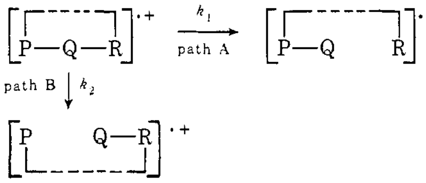
where E is the internal energy, ν is a constant with the dimension of cm^{-1}, and s is the effective number of degrees of freedom which is determined empirically. Although eq 1 is a very poor approximation, it may be adequate for the purpose in this paper.

The activation energy, ΔE, may depend critically on the detailed geometry of the transition state. The structure and the total energy of such a transition state can be deduced by MO methods in general. However, one must repeat the calculations until the most stable structure is obtained. An alternative method, which has proved extremely valuable in a variety of chemical reactions,[7] depends on a general treatment of the problem of reactivity which was introduced by Bell,[4a] Evans and Polanyi[4b] (BEP principle). The activation energy for a given reaction may be written in a linear form

$$E = X + Y\Delta H \qquad (2)$$

where X and Y are constants in the same system and ΔH is the heat of reaction. If this relation holds in the mass spectral reactions,[8] then the ratio of the rate constants, k_1/k_2, for any two of the fragmentation paths A and B will be given by eq 3, where $E' = (E - X)/Y$.

$$\frac{k_1}{k_2} = \left(\frac{E' - \Delta H_1}{E' - \Delta H_2}\right)^{s-1} \qquad (3)$$



Equation 3 indicates that the fracture occurs predominantly on the position which gives the lowest value of ΔH; one can predict the most probable position of bond scission by simply comparing the total energies of the possible intermediate ion structures.

The more the MO method for the calculation of total energy is rigorous, the better results would be obtained. But even the crude Hückel-type theory would be applicable, if it is for all valence electrons and the following cautions are taken into account. Here we take the extended Hückel (EH) theory.[9]

The Hartree–Fock molecular energy (E) for a closed-shell system may be written as

$$E = 2\sum E_i + \sum E_{nn'} - \sum E_{ee'} \qquad (4)$$

where E_i's are one-electron energies and $\Sigma E_{nn'}$ and $\Sigma E_{ee'}$ are the sums of nuclear–nuclear and electron–electron repulsions, respectively. The Hückel theory stands on approximate cancellation of the second and the third terms. The theory runs into difficulties for charged species, since there are fewer electronic repulsions. However, the present method requires the differences of the total energy of the same system, in which

$$\sum E_{nn'} - \sum E_{ee'} \simeq \text{constant} \qquad (5)$$

may hold unless the bond lengths are substantially changed. For some extremely polar compounds to which the EH theory is not applicable, the iterative EH (IEH)[10] method may be effective. Besides, the converged Coulomb integrals which are obtained from the calculation of IEH MO's for small molecules are shown[11] to be successfully applicable as parameters to large molecules.

The iteration was carried out according to the following equation

$$H_{rr}(n + 1) = H_{rr}(0) - (Z_X - M_X(n))(I_{pr} - A_r) \qquad (6)$$

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(3) (a) H. M. Rosenstock, M. B. Wallenstein, A. L. Wahrhaftig, and H. Eyring, *Proc. Nat. Acad. Sci. U. S.*, **38**, 667 (1952); (b) H. M. Rosenstock and M. Krauss, *Advan. Mass Spectrom.*, **2**, 251 (1963); (c) H. M. Rosenstock, *ibid.*, **4**, 523 (1968).

(4) (a) R. P. Bell, *Proc. Roy. Soc.*, *Ser. A*, **154**, 414 (1936); (b) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1340 (1936).

(5) R. C. Dougherty, *J. Amer. Chem. Soc.*, **90**, 5780 (1968).

(6) Part II of this series: see ref 1.

(7) M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry," McGraw-Hill, New York, N. Y., 1969, Chapter 8.

(8) Budziwiewicz, *et al.*, have pointed out that the stability of the final products must be taken into account in the consideration of the fragmentation mechanism: H. Budzikiewicz, C. Fenselau, and C. Djerassi, *Tetrahedron*, **22**, 1391 (1966). Actually, it should be reminded that in the establishment of the fragmentation rules of organic mass spectra (see, *e.g.*, ref 18) the stabilities of the produced fragments should always be taken into account. Those facts indicate that the BEP principle mostly holds in the mass spectral reactions.

(9) R. Hoffmann, *J. Chem. Phys.*, **39**, 1397 (1963).

(10) (a) L. C. Cusachs and J. W. Reynolds, *ibid.*, **43**, S160 (1965); (b) D. G. Carroll, A. T. Armstrong, and S. P. McGlynn, *ibid.*, **44**, 1865 (1966); (c) R. Rein, N. Fukuda, H. Win, and G. A. Clarke, *ibid.*, **45**, 4743 (1966).

(11) T. Yonezawa, K. Shimizu, H. Morimoto, and H. Kato, *Nippon Kagaku Zasshi*, **90**, 1196 (1969).

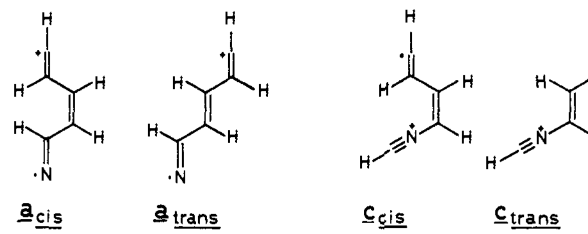


Figure 1. Configurations and conformations of ions a and c.

Here, A_r and I_{pr} are the electron affinity and the ionization potential of the atomic orbital ψ_r, respectively, $H_{rr}(i)$ is the Coulomb integral for ψ_r at the ith turn, and $H_{rr}(0)$ is set to be equal to $-I_{pr}$. X indicates the atom to which ψ_r belongs, Z_X is the number of the valence electrons, and $M_X(i)$ is the atomic population at the ith turn.

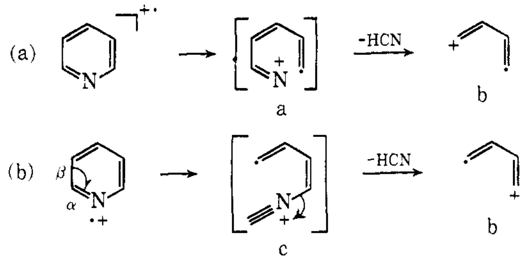
In the ASMO-SCF calculation, the total energy may be critically dependent on the bond lengths. It is generally impossible to know the bond lengths of ions. In this regard, the Hückel-type MO method has an advantage due to neglect of explicit consideration of nuclear-nuclear repulsions. In the present calculation, bond lengths in ångströms are assumed as follows: C—H, 1.09; C=C(sp), 1.30; C=N, 1.35; C—C(conj), 1.45; C=C(conj), 1.35; C—C(sp), 1.50; C≡N, 1.15; C—N(sp), 1.40. For the relative comparison of total energy, the results are not very sensitive to the assumed values of the parameters, unless they are changed in the calculation of the same system.

The total energy may vary with the conformation and the configurations. The most stable intermediate structure will be given according to the following considerations: (1) there should be appropriate distance between any two atoms to avoid nuclear-nuclear repulsion; (2) conjugation of double and/or triple bonds would lead to a more stable state (the question whether conjugation takes place or not will be discussed in the later section); (3) the positive charge should predominantly reside on the atom with the lower ionization potential in its valence state;[12] and (4) the configurations of cationic and radical centers should be changed to those of appropriate form (*e.g.*, $sp^3 \rightarrow sp^2$).

Results and Discussions

Pyridine. Pyridine, under electron impact, loses a HCN molecule to give mainly the ion of m/e 52. Williams and Ronayne[13] have studied the fragmentation of pyridine-*2,6-d*$_2$. From the intensities of the metastable ions, these workers show that the hydrogens of pyridine are completely randomized prior to the expulsion of hydrogen cyanide even at 14 eV. This randomization may be analogous to that which occurs with the hydrogen atoms of benzene. For benzene the isomerization to prismane and benzvalene structures has been suggested[14] as one possibility and for pyridine that of aza analogs;[15] such tautomerism implies the expulsion of hydrogen cyanide from one of the tautomers. However, such processes would be most improbable, since the expulsion requires at least four sequential bond scissions. Therefore, it is assumed that the fragmentation occurs without formation of (a) new σ bond(s) in the process; there are two possible pathways for the elimination of a HCN molecule.

Scheme I



In the conventional mechanism[16] shown in Scheme I(a), the first step from the molecular ion to the intermediate ion a might stand on the fact that the bond energy of C–N is weaker than that of C–C in the normal molecule. As already mentioned, such a bond index in the normal molecule is not applicable to the ionic state; we have another mechanism as shown in Scheme I(b). The problem is which intermediate ion (a or c) has lower total energy. On calculation of the total energies, the most stable conformations and the configurations of a and c are assigned to be $\mathrm{a_{cis}}$ and $\mathrm{c_{cis}}$, respectively (Figure 1); those like $\mathrm{a_{trans}}$ are not taken into account, since transformation from the molecular ion to $\mathrm{a_{trans}}$ requires rotation of a double bond. It is not of course impossible to know whether the ions have cis structures. However, even if the ions actually have trans structures, the differences of total energy between $\mathrm{a_{trans}}$ and $\mathrm{c_{trans}}$ may be almost the same as that between $\mathrm{a_{cis}}$ and $\mathrm{c_{cis}}$. The case that one ion is cis and the other is trans may be a small possibility and is not taken into account at present.

The results for cis structures are as follows

Method	a_{cis}	$\mathrm{c_{cis}}$	$\Delta(E_a - E_c)$
EH	−531.6452	−532.5726	0.9274
IEH	−523.6802	−529.2255	5.5453

where the values are in terms of eV. In both MO methods the ion $\mathrm{c_{cis}}$ is more stable than that of $\mathrm{a_{cis}}$; the β bond is more inclined to cleave under electron impact. Therefore, the intermediate is c; the mechanism shown in Scheme I(b) should be given for pyridine.

Pyrimidine. Rice, *et al.*,[17] already reported the spectra and a fragmentation mechanism of pyrimidine. Pyrimidine itself yields a molecular ion at m/e 80, which loses HCN to give an ion at m/e 53 (d). The molecular ion and the ion radical d lose a hydrogen atom to give ions e and f at m/e 79 and 52, respectively. Though the metastable transition is not observed, HCN is probably lost from d to give ionized acetylene g at m/e 26. They also showed from comparison of spectra recorded at 70, 20, and 16 eV that sequential loss of two HCN molecules from the pyrimidine molecular ion is the major fragmentation path.

For elimination of a HCN molecule from pyrimidine, there are three possible intermediate ions which correspond to the bond scissions of C_2–N_3, C_5–C_6, and C_6–N_1. The total energies of the three possible intermediate structures in the ionic states are

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[12] This principle is based on Stevenson's rule: D. P. Stevenson, *Discuss. Faraday Soc.*, **10**, 35 (1951).

[13] D. H. Williams and J. Ronayne, *Chem. Commun.*, 1129 (1967).

[14] K. Jennings, *Z. Naturforsch.*, **22a**, 454 (1967).

[15] See ref 2, p 376.

[16] "Catalog of Mass Spectral Data," API Research Project 44.

[17] J. Rice, G. Dudek, and M. Barber, *J. Amer. Chem. Soc.*, **87**, 4569 (1965).

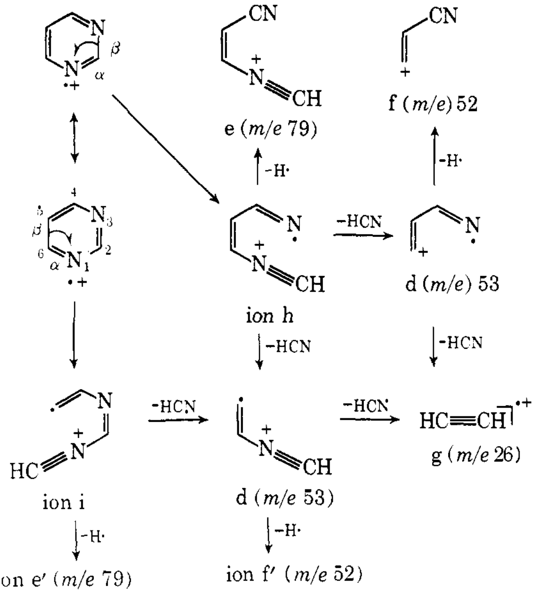
Table I. Total Energies of Three Possible Intermediate Ions in Pyrimidine

Position of cleavage	MO method: EH Total energy[a]	EH Dif[b]	IEH Total energy	IEH Dif
C_2–N_3	−549.8671	−2.103	−541.9656	−4.713
C_5–C_6	−548.7567	−0.993	−542.6834	−5.431
C_6–N_1	−547.7637	0	−537.2524	0

[a] In terms of eV. [b] The difference of total energy; the energy with the largest value is set to be zero.

listed in Table I. From the comparison of the total energies, the position of bond cleavage is easily determined; the possibility of the bond scissions of C_2–N_3 and C_5–C_6 is large while that of C_6–N_1 is the least. In spite of the results by Rice, *et al.*,[17] adoption of the intermediate ions h and i will lead the mechanism as shown in Scheme II, which can also explain the peaks of the mass spectrum of pyrimidine without discrepancy with the experimental facts.

Scheme II



Electronic Structures of Ions. As shown above, the intermediate ion structures formed by the β bond cleavage may be mostly assigned as the most stable one. Following the fragmentation rule proposed by McLafferty,[18] the stability may be caused by the unpaired electron at the nitrogen atom to produce a triple CN bond. In order to generalize this principle in N-heteroaromatic compounds, however, it should be investigated whether such electronic structures as shown by c, h, and i really occur.

As is well known, neglect of explicit consideration of electron–electron interactions in the MO theory often gives inappropriate electronic structures; the open-shell CNDO/2 method[19] was adopted for this study. In this theory, the total energy (E) of a given system can be written as the sum of one- and two-center terms

$$E = \sum E_A + \sum E_{AB} \qquad (7)$$

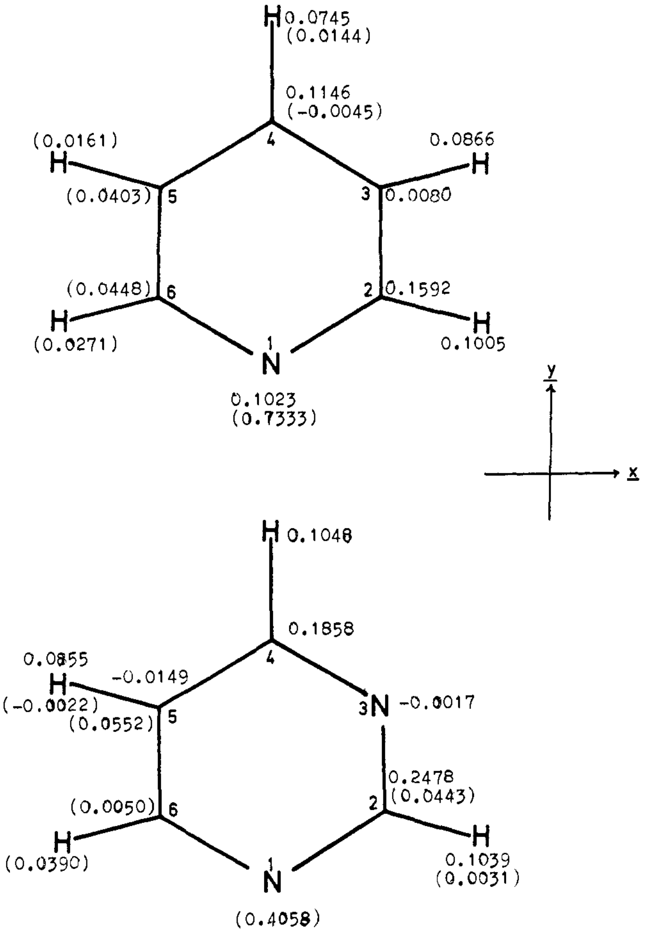


Figure 2. The net charge densities and the spin densities of the pyridine and pyrimidine ions. The values in parentheses represent the spin densities.

The two-center terms (E_{AB}) for an open-shell system is given in eq 8 where P_{rs}^{α} is the partial charge density

$$E_{AB} = \sum_{r}^{A}\sum_{s}^{B}\{2\beta_{AB}^{0}P_{rs}S_{rs} - [(P_{rs}^{\alpha})^2 + (P_{rs}^{\beta})^2]\gamma_{AB}\} + Z_A Z_B R_{AB}^{-1} - P_{AA}V_{AB} - P_{BB}V_{BA} + P_{AA}P_{BB}\gamma_{AB} \qquad (8)$$

(when $r = s$) and the bond-order matrix (when $r \neq s$) between the atomic orbitals, ψ_r and ψ_s, for α spin. The total charge density and the bond-order matrix, P_{rs}, is given by

$$P_{rs} = P_{rs}^{\alpha} + P_{rs}^{\beta} \qquad (9)$$

P_{AA} is the total charge on atom A

$$P_{AA} = \sum_{r}^{A} P_{rr} \qquad (10)$$

Z_A is the number of valence electrons of A, γ_{AB} is an average interaction energy between an electron in any valence atomic orbital of A with another in an orbital of B, β_{AB}^{0} is a bonding parameter given by

$$\beta_{AB}^{0} = (\beta_A^{0} + \beta_B^{0})/2 \qquad (11)$$

where β_A^{0} is chosen empirically, and S_{rs} is the overlap integral between atomic orbitals, ψ_r and ψ_s. The parameter V_{AB} which represents the interaction between a valence electron on atom A with the core of another atom B is also given empirically by

$$V_{AB} = Z_B\gamma_{AB} \qquad (12)$$

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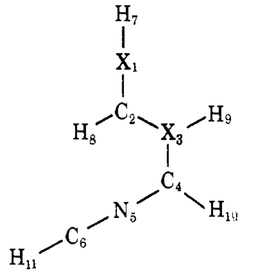
(18) F. W. McLafferty, Ed., "Mass Spectrometry of Organic Ions," Academic Press, New York, N. Y., 1963, pp 313–317.

(19) J. A. Pople and G. A. Segal, *J. Chem. Phys.*, **44**, 3289 (1966).

Table II. Bond Indices, Net Charge Densities, and Spin Densities of Ions c, h, and i



		Bond Indices[a]	
Bond	Ion c ($X_1 = X_3 = C$)	Ion h ($X_1 = N$; $X_3 = C$)	Ion i ($X_1 = C_1$; $X_3 = N$)
X_1–C_2	−1.7418	−1.5906	−1.7553
X_1–H_7	−0.7799		−0.7791
C_2–X_3	−1.1475	−1.1820	−1.0999
C_2–H_8	−0.7047	−0.7378	−0.7090
X_3–C_4	−1.5723	−1.5750	−1.5225
X_3–H_9	−0.7446	−0.7428	
C_4–N_5	−1.0961	−1.0944	−1.0884
C_4–H_{10}	−0.7500	−0.7491	−0.7553
N_5–C_6	−2.1670	−2.1656	−2.1629
C_6–H_{11}	−0.7504	−0.7480	−0.7476

			Net Charge and Spin Densities			
	Ion c ($X_1 = X_3 = C$)		Ion h ($X_1 = N$; $X_3 = C$)		Ion i ($X_1 = C$; $X_3 = N$)	
Atom	Net charge	Spin	Net charge	Spin	Net charge	Spin
X_1	−0.0119	0.8408	0.0036	0.9119	−0.0062	0.8443
C_2	−0.0042	−0.0780	0.0408	−0.0514	0.0643	−0.0852
X_3	0.1203	0.0805	0.0998	0.0494	0.0250	0.0894
C_4	−0.0064	0.0018	0.0223	0.0006	0.0771	0.0010
N_5	0.2177	0.0003	0.2182	0.0003	0.1986	0.0001
C_6	0.1826	0.0011	0.1890	0.0004	0.2049	0.0015
H_7	0.1147	−0.0003			0.1210	−0.0008
H_8	0.0227	0.1518	0.0412	0.0870	0.0140	0.1449
H_9	0.0773	−0.0032	0.0887	−0.0017		
H_{10}	0.0899	0.0053	0.0953	0.0032	0.1017	0.0046
H_{11}	0.1974	0.0000	0.2010	0.0000	0.1998	0.0000

[a] In terms of au.

The two-center term E_{AB} is considered to express the relative bond energy[20] between two arbitrary atoms, A and B, and is adopted here as an index of bond strength.

The first problem of electronic structure is where the unpaired electron and the positive charge are located in the molecular ion. The location of the net positive charge (which one may be allowed to regard as the positive charge) may not be clearly characterized because of redistribution of electrons on the positive site in an SCF manner. Suppose now that the unpaired electron has an α spin and the spin density (P_{AA}^{spin}; $P_{AA}^{spin} = P_{AA}^{\alpha} - P_{BB}^{\beta}$, where P_{AA}^{α} is the electron density for α spin on atom A) may represent the distribution of the unpaired electron. The net charge densities and the spin densities on the molecular ions of pyridine and pyrimidine are shown in Figure 2. The unpaired electrons are concentrated at the nitrogen atoms in both molecular ions (the density with a minus sign means that of the opposite spin to the considering unpaired electron). Those unpaired electrons do not contaminate the $2p_z$ atomic orbitals which make the π-electron systems; they occupy predominantly the $2p_y$ atomic orbitals of N_1 of the pyridine and pyrimidine ions and $2p_y$ and $2p_x$ of N_3 of the pyrimidine ion, which play the main part of the so-called lone pair orbitals of the neutral molecules. Accordingly, the structures of the molecular ions indicated in Schemes I(b) and II are well reproduced.

The results for ions c, h, and i are shown in Table II. In the ion c, the high spin density at C_1 supports the location of the unpaired electron at this site. The net charge densities are seen predominantly at N_5, C_6, and H_{11}. Further, the bond indices of C_1–C_2 and C_3–C_4 are larger than those of C_2–C_3 and C_4–N_5 and less than that of N_5–C_6 in their absolute values. The values for the single C—C, double C=C, and triple C≡N bonds are about 1.09, 1.70, and 2.24, respectively (the examples are respectively for ethane, ethylene, and hydrogen cyanide in their normal state). Therefore, as an organic chemical expression, ion c in Scheme I(b) is well-fitted for the purpose. The results for ions h and i also indicate that the expressions in Scheme II are suitable.

If one compares the cleavage of pyridine through its α and β bonds, it can be seen that the α bond cleavage does not produce any stabilization, while the β bond cleavage makes a new oxonium-type bond in place of the one destroyed. Thus, this principle of the β bond

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[20] The application of this index to an open-shell system has been discussed in part II; see also (a) M. S. Gordon, *J. Amer. Chem. Soc.*, **91**, 3122 (1969); (b) S. Ehrenson and S. Seltzer, *Theor. Chim. Acta*, **20**, 17 (1971); (c) H. Fischer and H. Kollmar, *ibid.*, **16**, 163 (1970).

cleavage is verified to be analogous to that in noncyclic compounds proposed by McLafferty.[18]

This technique of comparing the possible intermediate ions can be extended to other heteroaromatic compounds and will lead to meaningful results when it is applied to various compounds. We believe that the mechanism thus determined will be systematized to establish the generalized fragmentation rules of (hetero) aromatic compounds.

Acknowledgment. We acknowledge Y. Miyaji (Hoshi College of Pharmacy) for helpful discussions. The computations were carried out on a HITAC 5020E computer at the computation center of the Tokyo University.

Optically Active Amines. XIV.[1a] Circular Dichroism of 1-(2-, 3-, and 4-Pyridyl)ethylamine and Some Related Compounds[1b]

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Abstract: Resolution with tartaric acid gave (*S*)-(−)-1-(2-, 3-, and 4-pyridyl)ethylamine and (*R*)-(+)-1-(3-pyridyl)ethylamine. As an extension of earlier work, the uv (isotropic absorption) and CD spectra of (*S*)-(+)-*N*-salicylidene-1-(2-pyridyl)ethylamine and (*S*)-(+)-*N*-(5-bromosalicylidene)-1-(4-pyridyl)ethylamine were examined. These are very similar to those of (*S*)-(+)-*N*-salicylidene-α-phenylethylamine, indicating that the CD spectra of such Schiff base derivatives may also be used for the establishment of the absolute configurations of chiral pyridyl-substituted alkylamines. 1-(4-Pyridyl)ethylamine on storage is unstable and forms *N*-[1-(4-pyridyl)ethylidene]-1-(4-pyridyl)ethylamine by way of a light-catalyzed oxidative process. For this reason, the racemic and optically active amines were converted to their respective dihydrochlorides. The uv spectrum of each amine in 0.1 *M* methanolic potassium hydroxide shows an absorption maximum near 260 nm flanked by shoulders near 255 and 265 nm. These extrema are assigned to the $\pi \rightarrow \pi^*$ (^1L_b) transition of the pyridyl chromophore. Corresponding to each of these uv extrema, a positive maximum is found in the CD spectra of (*S*)-(−)-1-(2-pyridyl)ethylamine and (*R*)-(+)-1-(3-pyridyl)ethylamine. For (*S*)-(−)-1-(3-pyridyl)ethylamine the corresponding CD maxima are negative. No CD maximum was found in the spectrum of (*S*)-(−)-1-(4-pyridyl)ethylamine from 240 to 300 nm. In each CD spectrum there is a maximum near 240 nm, negative for (*S*)-(−)-1-(2-pyridyl)ethylamine, (*R*)-(+)-1-(3-pyridyl)ethylamine, and (*S*)-(−)-1-(4-pyridyl)ethylamine and positive for (*S*)-(−)-1-(3-pyridyl)ethylamine. No corresponding absorption maximum near 240 nm was detected in any of the uv spectra. A first-order perturbation treatment of the CD spectra indicates that the $2B_2$ state at 180 nm makes a significant contribution to the rotational strength of the longer wavelength transitions. On the basis of this analysis we suggest that the CD maximum at 260 nm is due to the $1B_2 \leftarrow 1A_1$ ($\pi \rightarrow \pi^*$) transition, that the 240 nm maximum is due to the electric dipole forbidden $1A_2 \leftarrow 1A_1$ ($n \rightarrow \pi^*$) transition, and that the rotational strength of the allowed $1B_1 \leftarrow 1A_1$ ($n \rightarrow \pi^*$) transition near 288 nm is too weak to give an observable CD maximum. As expected, all CD maxima disappear when the pyridine nitrogen lone pair is protonated in strong acid.

Our continuing interest in the chiroptical properties of aromatic chromophores[3–5] and a recent note concerning the preparation and absolute configurations of the optically active isomers of 1-(2-, 3-, and 4-pyridyl)ethylamine[6] prompt us to report our work dealing with the preparation and spectral properties of (*S*)-(−)-1-(2-pyridyl)ethylamine[7] [(*S*)-**1a**], (*S*)-(−)- and (*R*)-(+)-1-(3-pyridyl)ethylamine [(*S*)- and (*R*)-**2a**], and (*S*)-(−)-1-(4-pyridyl)ethylamine [(*S*)-**3a**], the absolute configuration of each established by ozonolysis of the respective (*S*)-*N*-acetyl derivatives to *N*-acetyl-L-alanine.[6] In addition, we report the preparation of the racemic dihydrochlorides [(±)-**1b**–**3b**] and the preparation and spectral properties of the respective optically active dihydrochlorides [(*S*)-**1b**–**3b** and (*R*)-**2b**]. We have also examined the chiroptical properties of the Schiff base derivatives (*S*)-**1c** and (*S*)-**3c** to evaluate the use of such derivatives for the establishment of the absolute configurations of chiral pyridyl-substituted alkylamines.[8]

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(3) H. E. Smith, M. E. Warren, Jr., and L. I. Katzin, *Tetrahedron*, **24**, 1327 (1968); erratum, *ibid.*, **25**, 4648 (1969).

(4) H. E. Smith and A. A. Hicks, *J. Chem. Soc. D*, 1112 (1970).

(5) H. E. Smith and T. C. Willis, *J. Amer. Chem. Soc.*, **93**, 2282 (1971).

(6) O. Cervinka, O. Belovsky, and P. Rejmanova, *Z. Chem.*, **10**, 69 (1970).

(7) Except as noted otherwise, signs in parentheses refer to rotatory powers observed with the sodium D-light for the amines in absolute ethanol, for the amine dihydrochlorides in water, and for the Schiff bases in methanol or absolute ethanol.

(8) H. E. Smith and T. C. Willis, *Tetrahedron*, **26**, 107 (1970); erratum, *ibid.*, **26**, 2258 (1970).