The Amino-Imino Tautomerization of the 2-Aminopyridine-Acetic Acid System in Isooctane

Kozo INUZUKA* and Akira FUJIMOTO
Department of Applied Science, Faculty of Engineering, Tokyo Denki University, Kanda, Chiyoda-ku, Tokyo 101
(Received September 19, 1989)

The UV absorption spectra of 2-aminopyridine were measured in isooctane (2,2,4-trimethylpentane) containing various amounts of acetic acid at room temperature; the temperature dependence (20 — −80 °C), of the spectra was also determined, while the concentration of acetic acid was maintained constant. An additional shoulder band appeared around 335 nm in the spectra obtained when the acetic acid concentration was higher than 1×10^{-2} mol dm^{-3}. The band corresponding to the 335 nm band was observed for monomethyl-substituted 2-aminopyridine. The 335 nm band was assigned to the π-π^* transition of the (*E*)-2(1*H*)-pyridinimine moiety in the 2-aminopyridine-acetic acid complex. The proton transfer from acetic acid to 2-aminopyridine in the complex may be difficult energetically in the ground state.

Numerous papers have been published on lactam-lactim tautomerizations of 2-hydroxypyridine and its related compounds,[1-6] while only a limited number of papers have reported on the amino-imino tautomerizations involving 2-aminopyridine and its related compounds.

In a previous paper,[7] from the UV absorption and the fluorescence spectral data concerning the 2-aminopyridine-acetic acid system in isooctane (2,2,4-trimethylpentane), it has been found that the formation of 2(1*H*)-pyridinimine (tautomer) and 2-aminopyridinium (monocation) occurs in the lowest π,π^* excited singlet state by means of interaction with acetic acid. Similarly, an amino-imino tautomerization in the lowest excited π,π^* singlet state was observed for the 4-amino-2-methyl-5*H*-chromeno[3,4-*c*]pyridin-5-one (CPD : abbrev.)-acetic acid system,[8] because CPD has 2-aminopyridine as a partial structure in the molecule. However, it is difficult to form 2(1*H*)-pyridinimine directly from 2-aminopyridine in the ground state due to the large stability of the amino form. It was pointed out that an additional weak band appeared around 335 nm on the addition of acetic acid, whose concentration is higher than 10^{-2} mol dm^{-3}, to an isooctane solution of 2-aminopyridine. The nature of the additional band was not, however clarified in the previous paper.[7] The band corresponding to the 335 nm band was not observed in the 2-aminopyridine-ethanol system. On the other hand, in the case of the 2,6-diaminopyridine-ethanol system, an additional band was observed around 345 nm as a shoulder; it was assigned to the π,π^* transition of 6-amino-2[1*H*]-pyridinimine.[9]

This paper aims to clarify the nature and the origin of the additional 335 nm band in the 2-aminopyridine-acetic acid system based on the concentration and temperature dependences of the absorption spectra and on MO theories.

Experimental

The purification of 2-aminopyridine and isooctane was described in a previous paper.[7] The 3-methyl- and 6-methyl-2-aminopyridine were purified by vacuum distillation to give samples with boiling points of 106.0—106.5 °C/2.2 kPa and 80.4—80.6 °C/0.93 kPa respectively. The 4-methyl- and 5-methyl-2-aminopyridine were recrystallized several times from benzene and hexane respectively. 2-Dimethylaminopyridine was distilled at 119.0—119.5°C/1.3 kPa prior to use. Acetic acid of an ultra-pure grade (Kanto Chemical Co., Inc.) was used without further purification. The apparatus of UV absorption measurements was used as has been described elsewhere.[7] The absorption measurements for various temperatures were carried out on the samples in a 10-mm-square quartz cell placed in a metallic Dewar vessel with two quartz windows. The temperature-regulation of the samples was carried out by using liquid nitrogen.

Methods of Calculation and Molecular Models

The molecular models of 2-aminopyridine, (*E*)- and (*Z*)-2(1*H*)-pyridinimine, and 2-aminopyridinium which were obtained by the MINDO/3 method with full geometry optimization were used.[7] For the sake of simplicity, the formic acid model was used for the acetic acid model in the present calculations. The following experimental values were used for the model of formic acid:[10]

C-H: 1.085 Å; C-O: 1.312 Å; C=O: 1.245 Å;
O-H: 0.95 Å; ∠OCO: 124.3°; ∠COH: 107.8°.

The molecular model of formate which was obtained by the 4-31G method was used.[11]

Figure 1 shows the three kinds of complex models. Model (1) corresponds to the 2-aminopyridine-acetic acid complex; Model (2), to the (*E*)-2(1*H*)-pyridinimine-acetic acid complex (tautomer model), and Model (3), to the 2-aminopyridinium-formate (proton-transferred model). The present complex models have three kinds of parameters-R, α, and β, and they are all planar, as is also shown in Fig. 1. The geometry of each complex model was optimized with respect to the distance, R, and the angles, α and β. The total energies (E_T) of the complex models

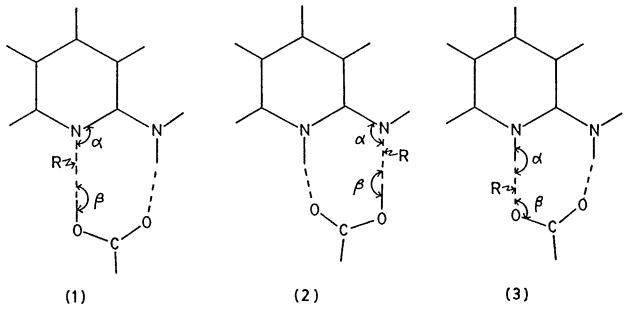


Fig. 1. The molecular models of three complexes used in the present calculation. The Model (1) corresponds to the 2-aminopyridine-acetic acid complex, the Model (2) to the (*E*)-2(1*H*)-pyridinimine-acetic acid complex, and the Model (3) to the 2-aminopyridinium-acetoxide anion.

were calculated under the assumption that the composite parts of the complex are invariant on complex formation. The total energy of each complex model was calculated by changing R, α, and β until it reached a minimum, by means of the ab initio STO-3G method.[12]

Results and Discussion

The addition of a small amount of acetic acid perturbs the absorption spectrum of 2-aminopyridine in isooctane, as is shown in Fig. 2. The large band shift to the longer wavelength, the enhancement of the band intensity, and the presence of the isosbestic point at 293 nm were attributed to the formation of a hydrogen-bonded 1:1 complex like Model (1), as is shown in Fig. 1.[7] An additional band appears around 335 nm in the spectrum of the 2-aminopyridine-acetic acid system in isooctane when the concentration of acetic acid is higher than 10^{-2} mol dm^{-3} (Fig. 2); then, the isosbestic point shifts to the longer wavelength. This experimental result indicates the appearance of

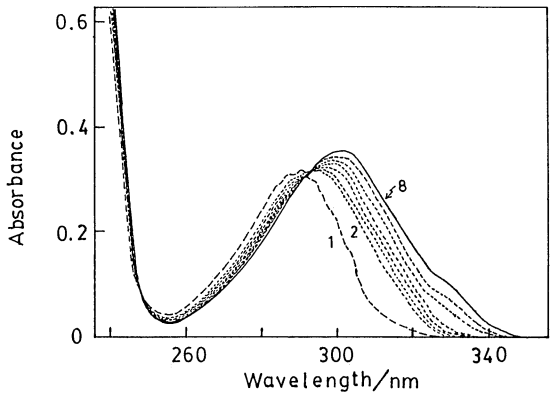


Fig. 2. The UV absorption spectra of the 2-aminopyridine-acetic acid system in isooctane at 20 °C. Concentration of 2-aminopyridine: 1.0×10^{-4} mol dm^{-3}; concentrations of acetic acid (mol dm^{-3}): (1) 0, (2) 5×10^{-4}, (3) 1×10^{-3}, (4) 2×10^{-3}, (5) 5×10^{-3}, (6) 1×10^{-2}, (7) 5×10^{-2}, (8) 1×10^{-1}.

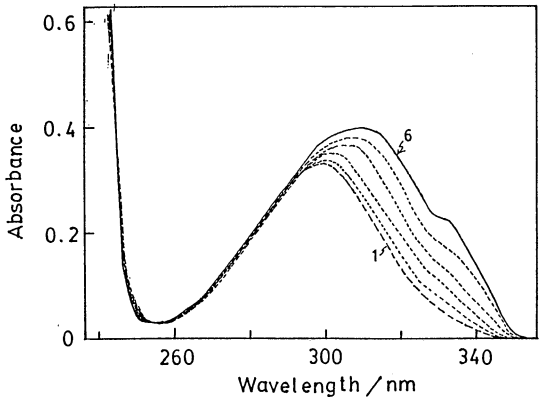


Fig. 3. The temperature effect on the UV absorption spectra of the 2-aminopyridine (1×10^{-4} mol dm^{-3})-acetic acid (1×10^{-2} mol dm^{-3}) system in isooctane: (1) 20 °C, (2) 0 °C, (3) −20 °C, (4) −40 °C, (5) −60 °C, (6) −80 °C.

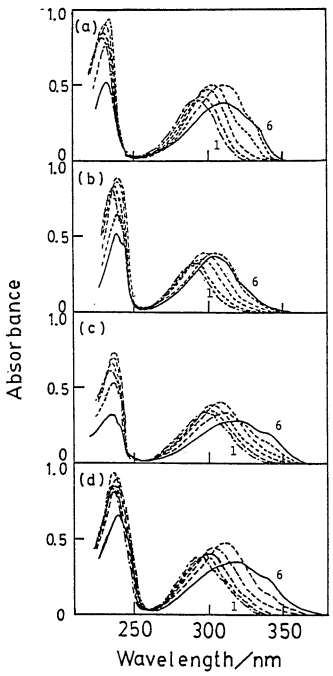


Fig. 4. The temperature effect on the UV absorption spectra of the monomethyl-substituted 2-aminopyridine (1×10^{-4} mol dm^{-3})-acetic acid (1×10^{-2} mol dm^{-3}) system in isooctane: (1) 20 °C, (2) 0 °C, (3) −25 °C, (4) −50 °C, (5) −75 °C, (6) −95 °C.
(a): 3-methyl-2-aminopyridine, (b): 4-methyl-2-aminopyridine, (c): 5-methyl-2-aminopyridine, (d): 6-methyl-2-aminopyridine.

the other complex in the 2-aminopyridine-acetic acid system. Figure 3 shows the temperature dependences of the absorption spectra of the 2-aminopyridine-acetic acid system in isooctane, the concentration of acetic acid being kept 10^{-2} mol dm^{-3}. The intensity of the additional 335 nm band increases with the decrease in the temperature. The UV absorption spectra of monomethyl-substituted 2-aminopyridines at a constant concentration of acetic acid under var-

ious temperatures are measured in order to ascertain the effect of methyl substitution on the 335 nm band of 2-aminopyridine. As is shown in Fig. 4, the bands corresponding to the 335 nm bands were observed for 3-methyl-, 4-methyl-, 5-methyl-, and 6-methyl-2-aminopyridines at low temperatures; however, the relationship between the band intensity (or the maximum wavelength) and the methyl-substituted position could not be clarified because of some uncertainty in the measurement. Further, in order to elucidate the relation of the 335 nm band with the NH_2 group at the 2-position, the UV absorption spectrum of the 2-dimethylaminopyridine-acetic acid system was measured, as is shown in Fig. 5. The similar shoulder band observed in Fig. 2 was not found for the 2-dimethylaminopyridine-acetic acid system. Accordingly, this result suggests that the appearance of the shoulder band may be connected with the NH_2 group.

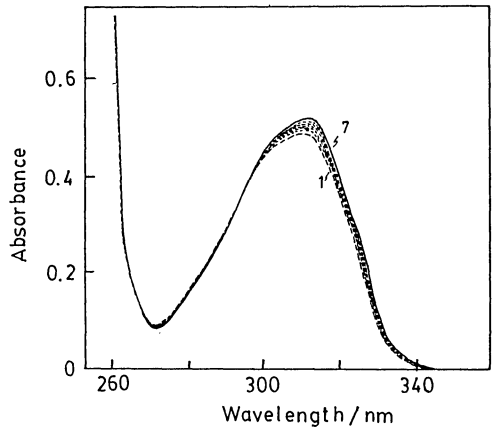
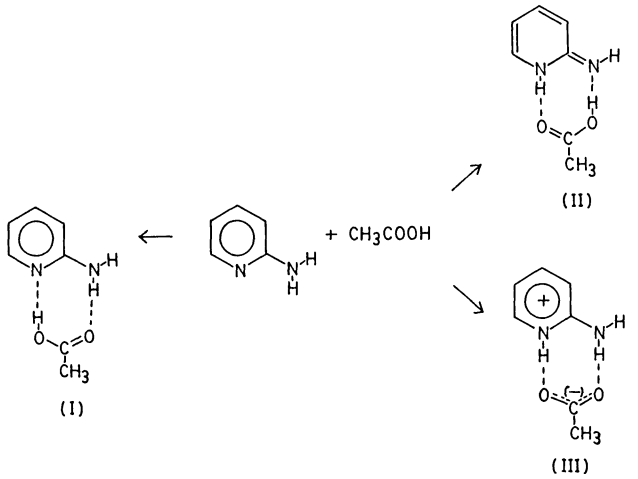


Fig. 5. The UV absorption spectra of the 2-dimethylaminopyridine-acetic acid system in isooctane at 20 °C.
Concentration of 2-dimethylaminopyridine: 1.9×10^{-4} mol dm^{-3}; concentrations of acetic acid (mol dm^{-3}): (1) 0, (2) 1×10^{-3}, (3) 2×10^{-3}, (4) 5×10^{-3}, (5) 1×10^{-2}, (6) 5×10^{-2}, (7) 1×10^{-1}.

Table 1 shows the total energies and dipole moments of the 2-aminopyridine and its related compounds, as calculated by the ab initio STO-3G method. The present calculations show that 2-aminopyridine is more stable than (*E*)- and (*Z*)-2(1*H*)-pyridinimine by 88.3 and 101.9 kJ mol^{-1} respectively in the ground state.

2-Aminopyridine in isooctane may be expected to form the following three complexes in the presence of acetic acid:



In the present calculations, Complexes **I**, **II**, and **III** correspond to Models (1), (2), and (3) respectively (cf. Fig. 1).

The total energies, E_T, and the equilibrium distances, R_e, and angles, α_e and β_e, of the three complex models were obtained after the optimization of the parameters, R, α, and β, which are shown in Fig. 1, by

Table 1. The Total Energies (E_T), Energy Differences (ΔE_T), and Dipole Moments (μ) of the Optimized MINDO/3 Models of 2-Aminopyridine and Its Related Compounds, as Calculated by the Ab Initio STO-3G Method

Compound	E_T/a.u.	ΔE_T/kJ mol^{-1}	μ_{calc}/D	μ_{obs}/D
2-Aminopyridine	−297.94762	0	1.763	2.04[a]
(*E*)-2(1*H*)-Pyridinimine	−297.91398	88.3	2.118	
(*Z*)-2(1*H*)-Pyridinimine	−297.90879	101.9	3.380	
2-Aminopyridinium	−298.41252	−1220		

a) M. T. Rogers, *J. Phys. Chem.*, **60**, 125 (1956).

Table 2. The Total Energies (E_T), Equilibrium Distance R_e[a], and Angles α_e and β_e[a] of 2-Aminopyridine-Formic Acid Complexes, the Energy Differences (ΔE_T) between the Complexes and Initial State, and the Dipole Moments (μ), as Calculated by the Ab Initio STO-3G Method

Complex	E_T/a.u.	R_e/Å	α_e/deg	β_e/deg	ΔE_T/kJ mol^{-1}	μ/D
Model (1)	−484.18352	1.702	120.0	191.2	−74.5	1.389
Model (2)	−484.15616	1.835	130.5	180.0	−2.84	1.199
Model (3)	−484.14035	1.349	172.0	122.6	38.6	6.337

a) The equilibrium distances and angles of the models correspond to the R, α, and β parameters of the three models shown in Fig. 1.

means of the ab initio STO-3G method. The calculated results are shown in Table 2. Each of the total energies of the complex models was compared with that of the initial state, that is, the sum of the total energies of 2-aminopyridine and formic acid. In Table 2, Model (1) is of the most stable among the three models. The ΔE_T of Model (1) corresponds to the hydrogen-bond energy of the 2-aminopyridine-acetic acid system. The calculated value of 74.5 kJ mol^{-1} is larger than the experimental value of 47.3 kJ mol^{-1} for the 2-aminopyridine-acetic acid system.[7] However, it is noteworthy that Model (2) is more stable than the initial state, although the energy difference between Model (2) and the initial state is small. This calculated result suggests that the indirect formation of a tautomer may be possible energetically in the ground state through the complex-formation with acetic acid, although the direct formation of a tautomer is difficult. However, judging from the ΔE_T value of Model (3), the proton transfer from acetic acid to 2-aminopyridine may be difficult in the ground state.

The charge densities of Models (1) and (2) are shown in Fig. 6. 2-Aminopyridine and formic acid have dual characters, such as a proton donor and a proton acceptor, in the present models. In Model (1), the electron-charge transfer occurs from 2-aminopyridine to formic acid by 0.005 electron units, while there is no electron transfer in the π-electron system. However, in Model (2) the electron transfer occurs from formic acid to 2(1*H*)-pyridinimine by 0.017 electron units, while there is no electron transfer in the π-electron system. In both models, the charge transfer occurs in the σ-electron system through the hydrogen bonds.

The first π-π^* absorption band of 2-aminopyridine in a strong acidic aqueous solution and that of the 2-aminopyridine trichloroacetate salt appear at 305 nm; they are attributed to the first π-π^* absorption band of 2-aminopyridinium.[7] The first π-π^* absorption band of 2-aminopyridinium appears at a shorter wavelength than the present shoulder band at about 335 nm. Therefore, it may be unreasonable to attribute the shoulder band near 335 nm to Complex **III**. In Fig. 2 if it is assumed that the 335 nm shoulder band is to be assigned to (*E*)-2(1*H*)-pyridinimine, the energy difference between the first π-π^* bands of 2-aminopyridine and (*E*)-2(1*H*)-pyridinimine is about 4600 cm^{-1}. The corresponding value as calculated by the CNDO/CI method is 4620 cm^{-1}.[7]

Mason[13] measured the absorption spectrum of 2-imino-1-methyl-1,2-dihydropyridone, which can be regarded as a model compound of 2(1*H*)-pyridinimine. The model compound shows two absorption bands at 317 and 251 nm in water and at 362 and 255 nm in cyclohexane. The first band at a longer wavelength is very broad in comparison with that of 2-aminopyridine, and its band maximum, as observed in water, shifts by 3900 cm^{-1} in cyclohexane. The band maximum of the first band depends on the polarity of the solvent. From the methyl-substitution effect and dependence of the first band on the polarity of the solvent of 2-imino-1-methyl-1,2-dihydropyridone, the 335 nm band position is in good agreement with that of 2-imino-1-methyl-1,2-dihydropyridone. Therefore, the present assignment may be reasonable in view of both calculated and experimental results. It is interesting that the fluorescence spectrum resulting from excitation at 330 nm was observed at 360 nm. The fluorescence spectrum at 360 nm was assigned to 2-aminopyridinium in a previous paper.[7] No fluorescence spectrum which corresponds to 2(1H)-pyridinimine was observed near 420 nm.[7] These experimental results suggest that the (*E*)-2(1*H*)-pyridinimine-acetic acid complex is converted rapidly into the cation complex, as is shown in Model (3) in the lowest excited π,π^* singlet state.

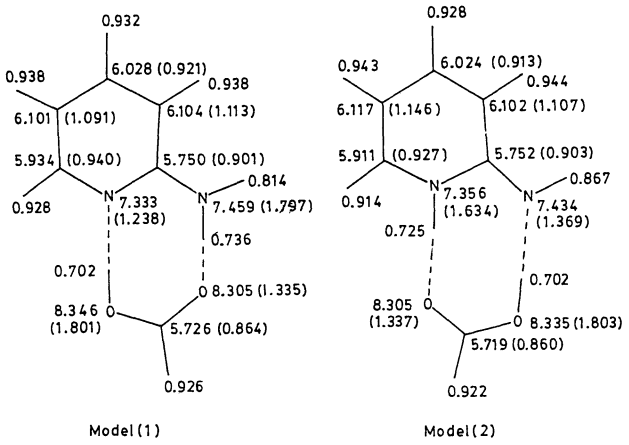


Fig. 6. The charge densities of the Models (1) and (2) for the 2-aminopyridine-formic acid complexes calculated by the ab initio STO-3G method. The values of π-charge densities are shown in parentheses.

This work was supported by grants from the Research and Development Center of Engineering of Tokyo Denki University. One of the authors (K.I.) also acknowledges his gratitude for the assistance of Mr. Shinichi Dohi of the T.D.U. Computer Center.

References

1) P. Beak, F. S. Fry, Jr., J. Lee, and F. Steele, *J. Am. Chem. Soc.*, **98**, 171 (1976).
2) P. Beak, *Acc. Chem. Res.*, **10**, 186 (1977).
3) P.Beak, J. B. Convington, and J. M. White, *J. Org. Chem.*, **45**, 1347 (1980).
4) M. J. Scanlan, L. H. Hillier, and R. H. Davies, *J. Chem. Soc., Chem. Commun.*, **1982**, 685.
5) H. B. Schlegel, P. Gund, and E. M. Fluder, *J. Am. Chem. Soc.*, **104**, 5347 (1982).
6) M. Kuzuya, A. Noguchi, and T. Okuda, *Bull. Chem. Soc. Jpn.*, **57**, 3454 (1984).
7) K. Inuzuka and A. Fujimoto, *Spectrochim. Acta, Part*

A, **42**, 929 (1986).
8) A. Fujimoto and K. Inuzuka, *Spectrochim. Acta, Part A*, **38**, 1035 (1982).
9) K. Inuzuka and A. Fujimoto, *Bull. Chem. Soc. Jpn.*, **63**, 216 (1990).
10) R. G.Lerner, B. P. Dailey, and J. P. Friend, *J. Chem. Phys.*, **26**, 680 (1957).
11) L. Radom, *Aust. J. Chem.*, **29**, 1635 (1976).
12) W. J.Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, and J. A. Pople, GAUSSIAN70, QCPE#236, University of Indiana, Bloomington, Indiana 47401, U.S.A.
13) S. F. Mason, *J. Chem. Soc.*, **1960**, 219.