Spectroscopic Study of the Conformational Dependence on Acid Dissociation of Phenoxypyridinium Cations

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Synopsis. Thermodynamic constants for acid dissociation of the 2-, 3-, and 4-phenoxypyridinium, and 2-(2,6-xylyloxy)pyridinium cations were estimated by the spectroscopic method, and are extensively discussed in relation to the conformations around the bridging oxygen atom and the electronic states.

The conformations of two aromatic rings bridged by the oxygen atom, like diphenyl ethers and phenoxypyridines, have been a subject of continuing interest to both experimental and theoretical chemists,[1—7] being traditionally classified into four groups, that is, planar, skew, butterfly, and twist.[1,6] Recently, much attention has been focused on the internal barrier of rotation around C–O bonds in diphenyl ether.[1—5] Shaefer et al. have proposed the so-called one-ring flip mechanism for the internal motion of diphenyl ether,[2] and we have identified the conformation as nonrigid with a dihedral angle, about 90°, of the two phenyl rings at room temperature.[1] Phenoxypyridines are an isoelectronic system with diphenyl ether, and involve critical torsion angles with regard to the conjugation between phenyl and pyridyl rings through the bridging oxygen atom. The preferable conformation of 2-phenoxypyridine (**1a**) heve been identified as a skew form of $\theta_1=0°$ and $\theta_2=90°$ (definitions of θ_1 and θ_2 are given in the caption of Fig. 1) in our previous paper.[1] The smaller nuclear repulson in **1a** allows it to be rigid in the skew form. It is therefore of interest and importance in structural chemistry to find what difference occurs in the conformations of phenoxypyridines and the phenoxypyridinium cations brought about by the balance between the electronic stabilization (conjugation) and the steric crowding. In this paper thermodynamic constants for acid dissociation of the 2-, 3-, and 4-phenoxypyridinium cations have been spectroscopically evaluated, and are discussed in view of the current interest in the conformational preference of bridged aromatic rings.

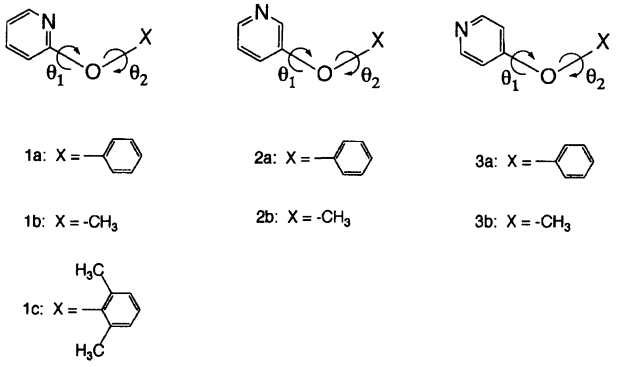

Fig. 1. Molecules employed here. In the figures of phenoxypyridines θ_1 and θ_2 denote the angles of twist about the C–O bonds, and defined as zero when the pyridyl and phenyl rings are in the COC plane just as shown above. The increases in the angles cause clockwise rotations of the pyridyl and phenyl rings around their O–C bonds.

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Experimental

Chemicals. Samples used here are **1a**, 2-methoxypyridine (**1b**), 2-(2,6-xylyloxy)pyridine (**1c**), 3-phenoxypyridine (**2a**), 3-methoxypyridine (**2b**), 4-phenoxypyridine (**3a**), and 4-methoxypyridine (**3b**) as illustrated in Fig. 1. Compounds **1a**—**c** are the same as those used for our previous work.[1] The method of Ullman was adopted to synthesize **2a** and **3a**.[7] Sample **2b** was synthesized by methylation of 3-pyridinol with diazomethane. Reduction of 4-methoxypyridine *N*-oxide by phosphorus trichloride derived to **3b**. Upon distillation under reduced pressure the purified **2a**, **b** and **3a**, **b** were obtained. The structure and purity of all the samples were checked by thin-layer chromatography, elemental analyses, and mass spectrometry.

Spectral Measurements. Absorption spectra of all the samples were recorded in the usual manner with a Hitachi spectrophotometer, Model 323, at various temperatures maintained by circulating constant-temperature water throughout the cell compartment. Solvents used for the measurements were 0.1 mol dm^{-3} acetate buffers and 0.1 mol dm^{-3} phosphate buffers in the pH regions of 3—6 and 6—8.5, respectively. HCl solution alone was used for pHs below 3. The ionic strength of all the buffer solutions was adjusted to 0.5 with NaCl.

Molecular Orbital Calculations. CNDO/S-CI calculations were done to interpret the experimental absorption spectra, the parameters being taken from the literature of Jaffé's group and the others.[8] Two-center repulsion integrals were evaluated using Nishimoto–Mataga's equation.[9] Only the one-electron transition was taken into account for the calculations of configuration interaction (CI). Molecular geometries were same as those identified in our previous work.[1] Ab initio SCF MO calculations were done to assign the minimum energy conformations of the **1a** pyridinium cation with STO-3G minimum basis sets. The conformational energies were computed in the counter rotations (θ_1 and θ_2 in Fig. 1) to each other at every 15° angle.

Results and Discussion

pK_a Values of Phenoxypyridinium Cations.

The electronic spectra of *N*-heterocyclic compounds investigated here are very sensitive to pH as shown in Fig. 2, showing clear isosbestic points that allow easy calculations of pK_a values by the application of the usual equation, $pH=pK_a+\log[(E-E_{BH^+})/(E_B-E)]$ for the system $BH^+ \rightleftharpoons B+H^+$, where E_B and E_{BH^+} are optical densities corresponding to B and BH^+ species alone, respectively, E being that in the intermediate pH range. The pK_a values obtained are collected in Table 1. The electron-donating effect of *p*-OCH_3 and *p*-OC_6H_5 groups on electronic states of the pyridyl ring allows an increase of the basicity of the pyridyl nitrogen atom.[11] The *m*-substituents (**2a**, **b**), however, have weaker basicity than pyridine. These are well-known substituent effects on the pK_a values of pyridine.[11] In fact we can see a good correlation between the Hammett substituent constants (σ)[12] and the pK_a values of *m*- and *p*-substituted pyridines (cited from Ref. 11) involving those of **2a**, **b** and **3a**, **b** evaluated in this work, the regression equation being $pK_a=-5.15\sigma(\sigma_p$ or $\sigma_m)+5.32$ with a correlation coefficient of 0.989 (sample number=40). On the other hand, the steric hindrance of the OCH_3 and OC_6H_5 groups and the electronegativity of the oxygen atom adjacent to the *o*-position make proton-addition to the pyridyl nitrogen atom of **1a**—**c** difficult. The smaller pK_a values of **1a** and **1c** than that of **1b** is considered to be owing to large steric crowding around the pyridyl nitrogen atom of **1a** and **1c**, which prefer a skew conformation.[1]

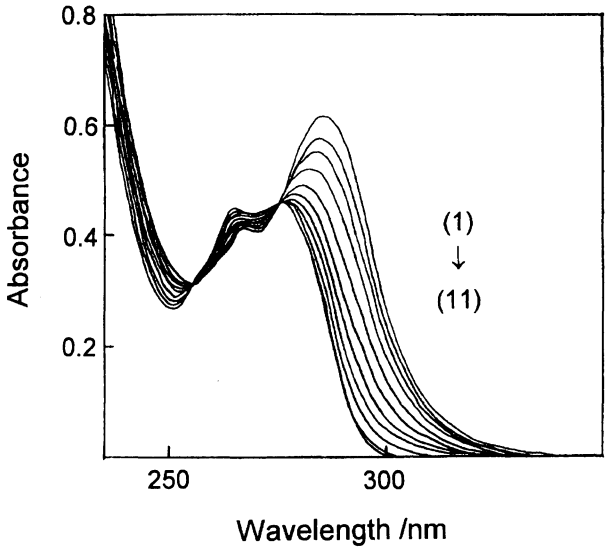

Fig. 2. Spectral change of **2a** with pH change at 25.0 ± 0.2 °C. pH: (1) 0.69, (2) 3.27, (3) 3.63,(4) 3.92, (5) 4.20, (6) 4.46, (7) 4.71, (8) 4.96, (9) 5.34, (10) 6.28, (11) 7.46.

Table 1. Observed pK_a Values of Phenoxypyidines and Methoxypyridines at 25±0.2 °C, and Thermodynamic Data obtained from the Temperature Dependence of pK_a for the Pyridinium Cation Formation

Compounds	pK_a	$\Delta H°$/kcal mol^{-1}	$\Delta S°$/cal K^{-1} mol^{-1}
1a	2.35	−3.2(±0.7)	0.02(±2.4)
1b	3.42	−3.3(±0.5)	4.6(±1.8)
1c	2.26	−2.7(±0.6)	1.3(±2.0)
2a	4.24		
2b	4.86		
3a	6.16		
3b	6.80		

Absorption Spectra of the Phenoxypyridinium Cations and Their Conformations. It is of interest whether **1a** alters the conformation around the C–O bonds from a skew form ($\theta_1=0°$, $\theta_2=90°$) on protonation. The change in the θ_1 and θ_2 angles under the condition that $\theta_1+\theta_2=90°$ has given rise to a ravine on a conformational energy map of the **1a** pyridinium cation calculated by the use of the ab inito STO-3G method. The calculation results also indicate that the change in the nuclear repulsion and electronic energies with a conformational change of the twist ($\theta_1=\theta_2=45°$) to skew forms is quite large, but just the reverse in the energy direction. The total energies are therefore almost constant in the conformation alteration within the rotation angles that $\theta_1+\theta_2=90°$. These results are just the same as the case of diphenyl ether investigated in our previous work.[1] In the twist form ($\theta_1=\theta_2=45°$) of the **1a** pyridinium cation, smaller nuclear repulsion contributes to the conformational stabilization. This suggests that the increasing steric strain with protonation to **1a** of the favorable skew form can be relieved by twisting around the C–O bonds following the so-called one-ring flip mechanism.[2]

Figure 3 shows the absorption spectra of **1a**—**c** and their pyridinium cations. The spectral data observed and calculated by the use of the CNDO/S-CI method are listed in Table 2. The calculation results indicate that the longest wavelength bond of **1a**—**c** is assigned to the ^1L_b band taking its rise in the pyridyl ring. The band is red-shifted and intensified with protonation, which is well known behavior on the formation of the pyridinium cation.[10] However, a shoulder band appears in the longest wavelength band of the **1a** pyridinium cation as is seen from Fig. 3. The CNDO/S-CI calculations yielded clear-cut evidence that the longest wavelength band merged with the weak second band in the twist form of the **1a** pyridinium cation, as is seen from Table 2. These two transitions are contributed from the HOMO→LUMO type charge-transfer configuration and the characteristic ^1L_b configuration of the pyridyl ring. In the case of the **1c** pyridinium cation the longest wavelength band is the ^1L_b character consisting of a single configuration, and the charge transfer configuration has a quite small transition moment because of the preferable skew conformation.[1] Therefore, the skew form of the **1a** pyridinium cation as well as the **1c** cation cannot have an observable weak second band. The observed shoulder band has demonstrated

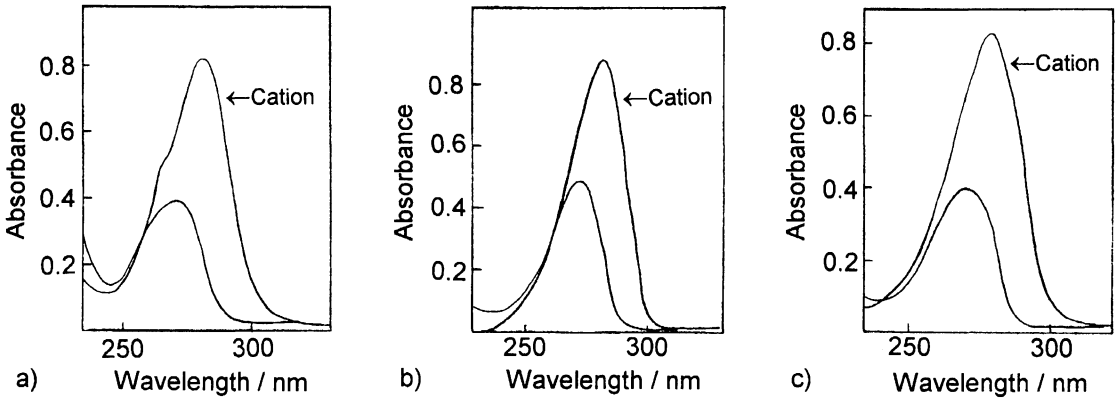

Fig. 3. Absorption spectra of 8.20×10^{-5} mol dm^{-3} **1a** and the **1a** pyridinium cation (a), 1.10×10^{-4} mol dm^{-3} **1b** and the **1b** pyridinium cation (b), and 8.52×10^{-5} mol dm^{-3} **1c** and the **1c** pyridinium cation (c) observed in 0.5 mol dm^{-3} HCl solution.

Table 2. Spectral Data of Longest Wavelength Bands for **1a**—**c** and Their Pyridinium Cations, and the CNDO/S-CI Calculation Results

Compounds	Neutral		Pyridinium cation		
	Observed[a]	Calculated[b,c]	Observed[a]	Calculated[b] λ/nm	
	λ/nm	λ/nm	λ/nm	Skew[d]	Twist[e]
1a	270.5(4600)	260.1(0.078)	281.0(10200)	283.7(0.35)	287.4(0.41)
			266.0(sh)[f]		254.3(0.04)
1b	271.0(4400)	260.1(0.077)	281.1(7890)	287.1(0.30)	
1c	270.1(4610)	260.0(0.078)	279.2(9540)	283.2(0.35)	

a) Values at the maximum intensity. Values in parentheses are the molar extinction coefficient at the maximum intensity in dm^3 mol^{-1} cm^{-1} unit. b) Values in parentheses are the oscillator strength. c) Calculated for a skew form ($\theta_1=0°$, $\theta_2=90°$) of **1a** and **1c**. d) Calculated for a skew form ($\theta_1=0°$, $\theta_2=90°$) of **1a** and **1c**. e) Calculated for a twist form ($\theta_1=\theta_2=45°$) of **1a**. f) Shoulder band.

that the twist form ($\theta_1=\theta_2=45°$) is preferred for the **1a** pyridinium cation. It seems that the protonation to the nitrogen atom of **1a** causes a conformational alteration from the skew form ($\theta_1=0°$, $\theta_2=90°$) to the twist ($\theta_1=\theta_2=45°$).

Temperature Dependence on the Acid Dissociation Constants. If **1a** alters the conformation from the skew form with proton addition, a difference in the $\Delta H°$ values between **1a** and **1c** is expected. The temperature dependence of pK_a was therefore investigated for the proton addition systems of **1a**—**c**. Good linear relations were obtained between the $R\ln K_a$ and $1/T$ values, the changes in enthalpy ($\Delta H°$) and entropy ($\Delta S°$) pertinent to the proton addition being assessed from the slope and intercept as listed in Table 1. The small difference in the $\Delta H°$ values between **1a** and **1b**, **c** is mainly contributed from the steric repulsion difference with regard to protonation, because both **1c** and the **1c** pyridinium cation predominantly occupy a symmetric skew conformation ($\theta_1=0°$, $\theta_2=90°$), but **1a** is able to preferentially alter the conformation into the twist form with proton-addition as described above. As a result of twisting around the C–O bonds of **1a** with protonation, the $\Delta H°$ value of **1a** is smaller than that of **1c**.

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