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Studies of the Magnetic Circular Dichroism and Tautomerism of Pyridinols (Pyridinones) and Pyrimidinols (Pyrimidinones)

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The magnetic circular dichroism(MCD) spectra of pyridinols (pyridinones) and pyrimidinols (pyrimidinones) were measured in the wavenumber region of 27000—50000 cm^{-1}. The transition energies, the oscillator strengths, and the Faraday *B* terms were calculated within the framework of the INDO/S-CI approximation. The calculated results for the $\pi^* \leftarrow \pi$ transitions were in good agreement with the experimental results. The lactim-lactam tautomerism of 3-pyridinol(3(1*H*)-pyridinone) and 2-pyrimidinol (2-pyrimidinone) was discussed.

The electronic structures of the derivatives of pyridine and pyrimidine have been extensively studied by many investigators.[1–11] In particular, some of these compounds, such as uracil, cytosine, thymine, and vitamin B_6, have attracted special interest because of their biological importance. The ultraviolet spectra of the pyridine and pyrimidine derivatives have been interpreted[2–5, 7–10] by means of SCF-MO calculations of the Pariser-Parr-Pople(PPP) procedure[12] and the complete neglect of the differential overlap (CNDO) method.[13,14]

Considerable attention has also been paid to the problem of tautomerism between lactam and lactim forms, which can be expected in these heterocyclic compounds because of the presence of labile hydrogen atoms. Mason and his co-workers have investigated pyridinol-pyridinone and pyrimidinol-pyrimidinone tautomerism in aqueous solutions by the measurements of the UV-absorption spectra.[1] The measurements of the UV and IR spectra have suggested that some of the hydroxy derivatives of pyrimidine favor the lactam-pyrimidinone forms.[15] The tautomerism of 4-pyrimidinol(4-pyrimidinone) and 4,6-pyrimidinediol(6-hydroxy-4-pyrimidinone, *etc.*) has been investigated by NMR spectroscopy.[16,17] The tautomeric stability of substituted pyridines and pyrimidines has been discussed on the basis of the SCF-MO calculation in the CNDO/2 approximation.[11]

On the other hand, magnetic circular dichroism (MCD) spectroscopy has made remarkable progress in providing valuable information on the electronic structures of ions and molecules.[18,19] The MCD spectra of derivatives of pyrimidine and purine and other heterocyclic compounds have been reported, and the electronic and molecular structures of these compounds studied.[20–26] In addition, the signs and magnitudes of the MCD spectra of azines,[22] azanaphthalenes,[23] aza-replaced alternant hydrocarbons,[24] indole,[25] and purine derivatives[26,27] have been calculated by the quantum mechanical SCF-MO procedures.

More recently, Jonas and Michl have reported the MCD spectra of pyridinones and pyrimidinones and interpreted them in terms of the π-electron theory.[28] Although the present work partially overlaps with their work, they have investigated mainly the keto forms of these compounds in acetonitrile solutions.

In this work we measured the MCD spectra of 2- and 4-pyridinols(2- and 4-pyridones), 3-pyridinol(3-(1*H*)-pyridinone), 2- and 4-pyrimidinols(2- and 4-pyrimidinones), and uracil, both in aqueous and in relatively nonpolar solvents. We also calculated the signs and the magnitudes of the MCD of the tautomers of these pyridine and pyrimidine derivatives within the framework of the intermediate neglect of the differential overlap (INDO) procedure.[29,30] The lactam-lactim tautomerism of these heterocyclic compounds is also discussed.

Experimental

The 2-pyridinol(2-pyridone), 3-pyridinol(3(1*H*)-pyridinone), and 4-pyrimidinol(4-pyrimidinone) were purified by recrystallization from benzene. The 4-pyridinol(4-pyridone) and uracil were also recrystallized from water. The 2-pyrimidinol(2-pyridone) was liberated with sodium hydroxide from its hydrochloride and was purified by vacuum sublimation and recrystallization from ethanol. Spectro-grade dioxane, heptane–dioxane (7:3 in volume), ethanol, and a phosphate buffer solution (pH 6—7) were used as solvents.

The MCD spectra were recorded with a JASCO J-20A recording circular dichrometer equipped with a 1.25 T electromagnet. The absorption spectra were measured on a Hitachi EPS-3T recording spectrophotometer.

The experimental values of the Faraday *B* terms were obtained from the MCD spectra by the use of the method of moments,[18] after the overlapping bands had been resolved by the Gaussian curve-fitting procedure.

Theoretical

The wavefunctions obtained from the INDO/S-CI approximation were used for calculating the Faraday *B* terms. The bonding parameter for the oxygen atom was determined so that the transition energies of some ketones are well reproduced ($\beta_0 = -31$ eV). The other parameters of the INDO/S calculation are the same as those of the previous work.[27] The configuration interaction among singly excited configurations below 12 eV was taken into consideration.

The molecular structures of uracil and 2-pyrimidinone were taken from the experimental data[31,32] obtained by the X-ray crystal analysis. However, no experimental data have been reported for the remaining compounds. The bond lengths and bond angles of pyridinones and 4-pyrimidinone were taken from those of 2-pyrimidinone.[32] The molecular structures of 3-pyridinol and 2-pyrimidinol were estimated from those of pyridine, pyrimidine, and phenol.

The Faraday *B* terms were calculated according to the expression derived by Buckingham and Stephens.[18]

TABLE 1. OBSERVED AND CALCULALED TRANSITION ENERGIES, OSCILLATOR STRENGTHS, AND FARADAY B TERMS

Compd	$\tilde{\nu}_{obsd} \times 10^{-3}$ / cm^{-1}	$\tilde{\nu}_{calcd} \times 10^{-2}$ / cm^{-1}	f_{obsd}	f_{calcd}	$B_{obsd} \times 10^4$ / βD^2 cm	$B_{calcd} \times 10^4$ / βD^2 cm	Symmetry
2-Pyridone		26.0		0.001		−0.4	A″
	34.5[a]	32.7	0.123	0.204	8.6	12.7	A′
		40.0		0.000		−0.1	A″
		41.2		0.004		2.8	A″
	45.2[a]	43.0	0.137	0.319	−5.2	−15.4	A′
3(1*H*)-Pyridinone		22.0		0.002		−4.0	A″
	32.0[a] 27.4[e]	23.6	0.083	0.152	6.7	16.7	A′
		26.3		0.001		0.8	A″
		33.0		0.002		2.0	A″
	41.1[a]	34.8	0.080	0.241	−9.8	−13.6	A′
4-Pyridone		21.0		0.000		0.0	A″
	38.6[a]	35.9	0.133	0.032	14.3	14.0	A′
		36.3		0.003		7.0	A″
	40.6[a]	38.6	0.148	0.438	−13.5	−24.2	A′
		41.7		0.000		0.1	A″
2-Pyrimidinone		27.3		0.000		0.0	A″
		31.4		0.004		−5.0	A″
	34.3[a]	32.6	0.100	0.146	7.5	13.2	A′
		41.5		0.003		0.3	A″
		43.9		0.000		0.6	A″
	47.4[a]	45.8	0.223	0.378	−2.2	−8.9	A′
4(3*H*)-Pyrimidinone		26.1		0.001		−0.2	A″
		34.0		0.007	6.8	9.4	A″
	36.4[d]	34.4	0.082	0.166		0.5	A′
		39.5		0.000		−0.2	A″
	45.3[d]	42.4	0.122	0.009	−2.1	−6.6	A″
		43.7		0.301		−1.4	A′
		44.1		0.011		−2.4	A″
Uracil		25.4		0.001		−0.1	A″
		31.4		0.000		0.0	A″
	39.0[a]	39.8	0.165	0.298	7.4	7.6	A′
		45.0		0.000		0.1	A″
		46.1		0.094		6.3	A′
	49.1[a]	47.6	0.255	0.162	−2.2	−16.4	A′
3-Pyridinol		34.4		0.008		−1.7	A″
	36.4[b]	37.5	0.065	0.083	4.8	6.8	A′
		41.9		0.000		0.0	A″
		45.6		0.000		0.7	A″
	45.8[b]	46.3	0.129	0.262	−4.5	−19.5	A′
2-Pyrimidinol		32.8		0.013		−3.2	A″
		37.6		0.000		0.0	A″
	37.4[c]	39.2	0.081	0.085	6.8	6.8	A′
		44.2		0.000		0.0	A″
		48.9		0.001		−20.0	A″
		49.0		0.342		4.3	A′

a) In an aqueous solution. b) In an ethanol solution. c) In a heptane-dioxane (7:3 in volume) solution. d) In a dioxane solution. e) The absorption maximum in a cyclohexane-saturated solution. Taken from Ref. 8.

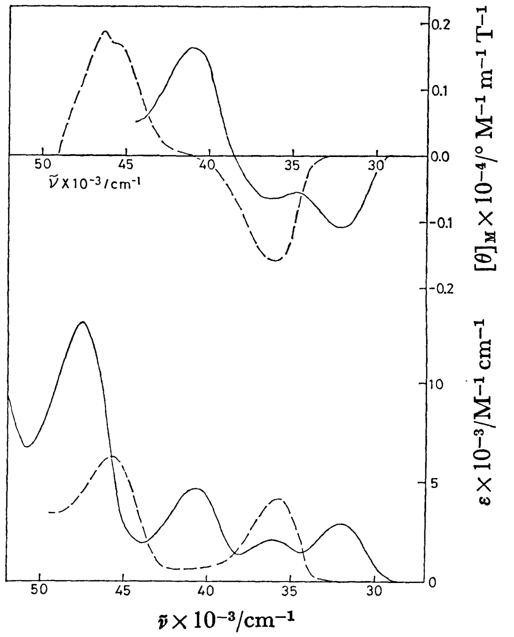

Fig. 1. MCD (upper) and absorption (lower) spectra of 3-pyridinol (3(1*H*)-pyridinone) in aqueous (——) and ethanol (----) solutions.

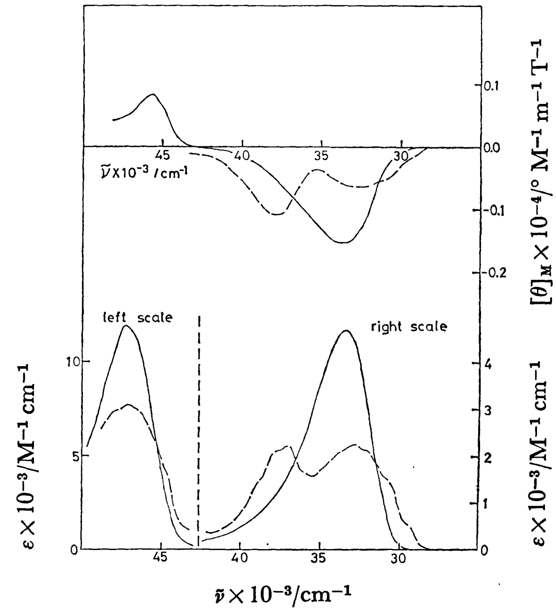

Fig. 2. MCD (upper) and absorption (lower) spectra of 2-pyrimidinol (2-pyrimidinone) in aqueous (——) and heptane-dioxane (7:3 in volume) (----) solutions.

The details of the calculation of the *B*-terms were reported in a previous paper.[27]

Results and Discussion

The experimental MCD and absorption spectra of 3-pyridinol(3(1*H*)-pyridinone) are presented in Fig. 1. The molar ellipticity $[\theta]_M$ per unit of magnetic field is shown in ° $M^{-1}\,m^{-1}\,T^{-1}$, and the molar extinction coefficient, ε, in $M^{-1}\,cm^{-1}$ (1 M = 1 mol dm^{-3}).

Four electronic transitions are identified in the MCD and absorption spectra of 3-pyridinol (3(1*H*)-pyridinone) in an aqueous solution, while only two bands are observed in an ethanol solution. The lactim 3-pyridinol and lactam 3(1*H*)-pyridinone forms have been shown to exist in equilibrium in an aqueous solution.[1] The two MCD bands observed at 36400 cm^{-1} and 45800 cm^{-1} in an ethanol solution are assigned to the $\pi^*\leftarrow\pi$ transitions of the lactim 3-pyridinol form. On the other hand, the two MCD bands at 32000 cm^{-1} and 41100 cm^{-1} which appear in an aqueous solution are attributable to the $\pi^*\leftarrow\pi$ transitions of the lactam 3(1*H*)-pyridinone form.

The MCD and absorption spectra of 2-pyrimidinol (2-pyrimidinone) are presented in Fig. 2. 2-Pyrimidinol (2-pyrimidinone) exhibits positive and negative MCD bands at 34300 cm^{-1} and 47400 cm^{-1} respectively in an aqueous solution. It has been shown by a UV spectrographic comparison with 1-methyl-2-pyrimidinone that 2-pyrimidinol (2-pyrimidinone) predominantly exists in the lactam 2-pyrimidinone form in an aqueous solution.[1] On the other hand, in a heptane-dioxane (7:3 in volume) solution the lowest MCD bands decrease in intensity, and a new negative MCD band appears at 37400 cm^{-1} (Fig. 2), This band can reasonably be assigned to the lowest $\pi^*\leftarrow\pi$ transitions of the lactim 2-pyrimidinol form, which is in equilibrium with the lactam 2-pyrimidinone form in heptane–dioxane (7:3 in volume).

The MCD spectra of the remaining compounds were in agreement with those reported by Jonas and Michl.[28]

The experimental and calculated results are summarized in Table 1. The calculated transition energies of 3(1*H*)-pyridinone are much smaller than the experimental ones. A similar difficulty has been met with in the CNDO/S-CI calculation reported by Cignitti and Paoloni.[8] They have also reported that the lowest absorption band of 3(1*H*)-pyridinone, observed at 32000 cm^{-1} in an aqueous solution, shows a large hypsochromic shift in a saturated cyclohexane solution.[8] The solvent shift can be explained by the fact that ground state has a larger dipole moment than the low-lying excited states and is stabilized by the dipole-dipole interaction with the polar solvent. However, the calculated results for the $\pi^*\leftarrow\pi$ transitions of the remaining compounds are in satisfactory agreement with the experimental data. In particular, the calculated signs of the Faraday *B* terms agree perfectly with the experimental results. The signs of the Faraday *B* terms of the first and second $\pi^*\leftarrow\pi$ transitions are positive and negative respectively, both for the lactam form and for the lactim form.

On the other hand, several $\pi^*\leftarrow$n transitions are predicted in the ultraviolet region. The lowest $\pi^*\leftarrow$n transition of pyridinones and pyrimidinones is characterized by the transition from the nonbonding 2p orbital of oxygen to the unoccupied π orbitals. The second $\pi^*\leftarrow$n transition of pyrimidinones and the low-lying $\pi^*\leftarrow$n transitions of 3-pyridinol and 2-pyrimidinol correspond to the transition from the nonbonding orbital of the aza nitrogen atom to unoccupied π orbitals.

Although the first $\pi^*\leftarrow$n transition of pyridinone and pyrimidinone is predicted in the wavenumber region of 21000—27000 cm^{-1}, no distinct MCD or absorption band is found in this spectral region. The first $\pi^*\leftarrow n$ transition is probably hidden behind the tail of the lowest absorption band; otherwise, it has too small an intensity to be observed. It should be noted that the calculated transition energy of the lowest $\pi^*\leftarrow n$ transition of these compounds is not very reliable, because it has been shown to be sensitive to the choice of the two-center electron repulsion integrals.[8]

We have calculated the magnetic mixing among excited electronic states caused by the external magnetic field. The Faraday B terms of the two lowest $\pi^*\leftarrow\pi$ transitions proved to be mainly induced by the magnetic mixing between the two lowest $\pi^*\leftarrow\pi$ states, leading to the opposite sign of the B terms of these transitions. The magnetic mixing between the $\pi^*\leftarrow\pi$ state and the $\pi^*\leftarrow n$ state is small except when the energy separation of the two states is very small, and it does not make a large contribution to the MCD spectrum.

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