THE TAUTOMERISM OF PYRIMIDINE-2(1H)-ONE, -THIONE AND -N-PHENYLIMINE IN THE ^{1}H- AND ^{13}C-NMR

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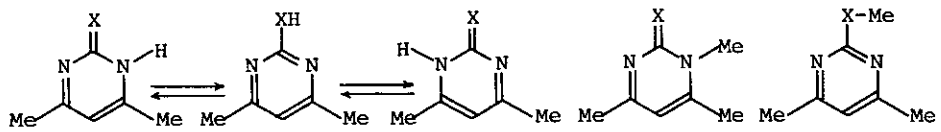
Abstract —— By the ^{1}H- and ^{13}C-NMR spectral measurement, the structures of the predominant tautomers of 4,6-dimethylpyrimidine-2(1H)-one and -thione were regarded to be the lactam form, while the 2-anilino-4,6-dimethylpyrimidine was the main tautomer. Also, the prototropic interconversion between the tautomers was discussed.

The tautomerism between azinones and hydroxy-azines has been extensively investigated in connection with the nucleic bases such as uracil and cytosine. By the UV and IR spectrometric techniques, the predominant tautomer was shown to be the lactam form in pyrimidine-2(1H)-ones.[1-4] Meanwhile, Günther showed by ^{13}C-, ^{1}H- and ^{15}N-NMR spectral studies that pyrazin-2(1H)-one and -thione exist predominantly in the lactam form, while the aminopyrazine form was preferable than pyrazine-2(1H)-imine.[5] However, little attention has been devoted to the NMR spectroscopic studies on the tautomerism of pyrimidine-2(1H)-thiones and -imines. Recently, we have investigated the regioselective preparations[6-9] and the chemical behaviors of pyrimidine-2(1H)-ones, -thiones and -imines.[10-13] In the course of these studies, we measured the ^{1}H- and ^{13}C-NMR spectra of 4,6-dimethylpyrimidine-2(1H)-ones (1), -thiones (4), -N-phenylimines (7), and related compounds (2, 3, 5, 6, 8 and 9), we obtained some remarkable facts in tautomerism of pyrimidine-2(1H)-ones.

The spectral data summarized in the Table. The chemical shifts of methine protons of 1 and 4 were essentially the same with those of the corresponding 1-methyl derivatives (2 and 5), respectively. On the contrary, that of 7 was



	a	b	c		
X= O		1		2	3
X= S		4		5	6
X= N-Ph		7		8	9

approximately the same with that of the 2-methylaminopyrimidine derivative (9). When the ^{13}C-NMR spectrum of 1 was compared with those of 2 and 3, the C-2 carbon signal of 1 at 160.2 ppm also appeared close to that of 2 at 157.5 ppm rather than that of 3 at 169.0 ppm. The resemble tendency was observed in the C-5 carbon signals. From these observations, the preferable tautomers of 1 and 4 were indicated to be the lactam forms 1a and 4a respectively, while 7b was predominant.

When the signals of methyl carbons at the 4- and 6-position and of the C-4 and C-6 carbon were focused, two pairs of signals were observed in compound 2. On the contrary, the C-4 and C-6 carbon appeared at 165.5 ppm as a broad singlet signal with the intensity of two carbon atoms. Also the methyl carbons at the C-4 and C-6 appeared at 22.0 ppm as a quartet signal with a large peak width. When two components are in the equilibrium state with the comparably slow interconversion, the corresponding nuclei of both components are observed as the single broad NMR signal. Therefore, the interconversion of 1a and 1c was slow at room temperature with the comparable ^{13}C-NMR time scale (ca. 5×10^{-8} sec.). Actually, at the elevated temperature, both signals at 165.5 and 22.0 ppm were observed as sharp peaks. This slow interconversion was also observed in the case of 4, but not in the case of 7.

Furthermore, since the position of the NMR signal of the equilibrium mixture depends upon the population of the components, the lactam percent was evaluated to be 76 % from the chemical shift value of C-2 carbon signal of 1 compared with those of 2 and 3. By similar evaluation of the C-2 carbon signals, the the predominant tautomer of 4 was concluded to be 4a with the percentage of

73 %, while the predominant tautomer of 7 was 7b with the lactam percent of 20 %. In conclusion, the ^{1}H- and ^{13}C-NMR measurement supported the previously reported fact that the predominant tautomer of 1 was the lactam form 1a or 1c, and that the lactam percent was changed depending on the substituent group at C-2. Further the slow prototropic interconversion between the tautomers was observed in 1 and 4. These fact seems to be the first observation of the slow prototropic interconversion in the diazine systems.

Table The ^{1}H- and ^{13}C-NMR Data and the Lactam Percent

Compound	X	Chemical Shift (ppm)							Lactam
		H-5	C-2	C-4	C-6	C-5	Me-4	Me-6	%
1	O	6.20	160.2	165.5		105.3	22.0		76
2		6.18	157.5	174.0	157.1	105.8	24.9	20.5	
3		6.68	169.0	165.4		113.7	23.8		
4	S	6.50	180.5	164.8		111.1	21.9		73
5		6.48	183.8	167.9	157.0	111.8	24.6	22.0	
6		6.67	171.5	166.7		115.3	23.8		
7	N-Ph	6.44	159.8	167.4		111.5	23.9		20
8		5.69	151.6	169.7	155.0	102.7	24.8	20.7	
9		6.33	161.8	166.8		110.0	24.1		

EXPERIMENTAL

Materials. Compounds 1, 2, 4 and 5 were prepared by the condensation of acetylacetone with the appropriate ureas catalyzed by hydrochloric acid in ethanol. Compounds 3, 7 and 9 were prepared from 2-chloro-4,6-dimethylpyrimidine according to the method of Abramovitch.[14] Compound 6 was prepared by the direct methylation of 4 with methyl iodide, and 8 was obtained from 4,6-dimethyl-1-phenylpyrimidine-2(1H)-thione by treatment with methylamine.[7]

NMR Measurement. The ^{1}H- and ^{13}C-NMR spectra of the compounds in $CDCl_3$ were obtained at 25°C and 40°C by JEOL-FX100 NMR spectrometer with tetramethylsilane as an internal standard. The lactam percent was evaluated from the C-2 carbon signals of 1, 4 and 7 by the proportions of chemical shift differences with those of the corresponding methyl derivatives.

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