Notes

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Studies on 1-Alkyl-2(1*H*)-pyridone Derivatives. XX.[1] Nuclear Magnetic Resonance Spectra of 1-Methyl-2(1*H*)-thiopyridone, 1-Methyl-2(1*H*)-thioquinolone, and 2-Methyl-1(2*H*)-thioisoquinolone

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Tomisawa and his collaborators[1] examined the reactivity of 1-Methyl-2(1*H*)-thiopyridone (I) and its benzene-fused homologs in comparison with that of their oxygen derivatives. As a part of their studies, nuclear magnetic resonance (NMR) spectra of these thiones were analysed in relation to their reactivity. Stewart and Siddall[3] already reported the NMR spectrum of I, but no studies seem to have been made on the NMR spectra of benzene-fused homologs of I and their protonated derivatives.

Material and Method

Chemical Compounds——1-Methyl-2(1*H*)-thiopyridone[4] (I), 1-methyl-2(1*H*)-thioquinolone[4] (II), 2-methyl-1(2*H*)-thioisoquinolone[1] (III), 1-methyl-2(1*H*)-pyridone[5] (IV), 1-methyl-2(1*H*)-quinolone[6] (V), and 2-methyl-1(2*H*)-isoquinolone[6] (VI) were all synthesized by the authentic preparative method. The solvents used for the measurement of NMR spectra were all commercial products of special grade reagent.

NMR Measurements——The NMR spectra were measured with a Hitachi 60 MHz R20 spectrometer, operating at 60 MHz, and measured at 23°. Chemical shift was calibrated from the signal of tetramethylsilane used as the internal standard and expressed in δ ppm unit. Concentration of the chemicals measured was 5% (w/v).

Chemical shift is dependent on the concentration to a certain extent and the value extrapolated to infinite dilution should be used[3] but, for the qualitative discussions in the present study, chemical shift data obtained in the present work are considered to be fully sufficient for its purpose. Assignment of the signals was confirmed by the use of deuterated compounds reported in the preceding paper.[1] The resonance position of the chemical shift was read directly from the spectrum chart by the first-order analysis.

Result and Discussion

Table I gives the chemical shift data of I, II, and III, and their corresponding oxygen derivatives in $CDCl_3$, CH_3COOD, 10% D_2SO_4–CH_3COOD, and 50% D_2SO_4–CH_3COOD. Also shown in this table are the chemical shifts of the related protons in the parent bases of these derivatives, pyridine (VII), quinoline (VIII), and isoquinoline (IX).

The chemical shift of the protons in all the compounds tended to shift to a lower magnetic field with increasing acidity of the solvent. Qualitatively, pyridine, quinoline, and isoquinoline seemed to take the protonated form already in acetic acid, while their 2-thio and 2-oxo derivatives are not protonated in acetic acid but considered to take the protonated form in 50% D_2SO_4–CH_3COOD. Measurement of NMR spectra by gradually changing the concen-

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[1] Part XIX: H. Tomisawa and C. H. Wang, *Chem. Pharm. Bull.* (Tokyo), **21**, 2607 (1973).

[2] Location: *Komatsushima, Sendai 983, Japan.*

[3] W.E. Stewart and T.H. Siddall III, *J. Phys. Chem.*, **74**, 2027 (1970).

[4] A. Gutbiel, *Ber.*, **33**, 3359 (1900).

[5] E.A. Prill and S.M. McElvain "Organic Syntheses", Collected Vol. II, 1943, p. 419.

[6] H. Decker, *J. Prakt. Chem.*, **47**, 31 (1893).

Table I. Chemical Shifts (ppm) of Thiopyridones, Pyridones, Pyridines, and Their Benzene-fused Homologues in Various Solvents

Compds	Position	Solvent			
		$CDCl_3$	AcOH	10% D_2SO_4 in AcOH	50% D_2SO_4 in AcOH
Pyridine series I	3	7.74	7.68	8.18—8.36	8.41—8.56
	4	7.22	7.28	8.12—8.36	8.41—8.56
	5	6.66	6.72	7.74	8.00
	6	7.72	7.92	8.72	8.85
	N-Me	4.00	3.92	4.30	4.54
IV	3	6.52	6.72	7.50	7.47
	4	7.34	7.51	8.22	8.30
	5	6.12	6.41	7.38	7.40
	6	7.26	7.61	8.32	8.22
	N-Me	3.50	3.60	4.04	4.08
VII	3	7.24	7.91	8.18	8.12
	4	7.66	8.41	8.72	8.68
Quinoline series II	3	7.38	7.42	8.22	8.00
	4	7.66	7.62	8.72	8.65
	N-Me	4.30	4.20	4.52	4.48
V	3	6.68	6.81	7.58	7.52
	4	7.64	7.82	8.70	8.68
	N-Me	3.70	3.70	4.20	4.22
VIII	3	7.32	7.82	7.89	$\sim$8.1
	4	8.10	8.76	9.23	9.20
Isoquinoline series III	3	7.41	7.56	8.56	8.82
	4	6.83	6.89	8.12	8.48
	8	9.10	9.15	$<$8.0	$<$8.0
	N-Me	4.04	4.01	4.64	4.90
VI	3	7.02	7.25	7.75	7.88
	4	6.44	6.64	7.45	7.81
	8	8.41	8.39	8.55	8.58
	N-Me	3.55	3.60	4.00	4.18
IX	3	8.51	8.66	8.65	8.58
	4	7.52	8.14	8.25	8.20

tration of D_2SO_4 indicated that protonation of the thiones was completed in a much more acidic medium than that of the corresponding oxo derivatives. This fact agrees with the p*K*a data already reported by Katritzky, *et al.*[7] and Barlin.[8]

Therefore, it is thought that the chemical shift in $CDCl_3$ reflects the electronic structure of the thione- and one-types of compounds (I, II, III, IV, V, and VI) shown in Chart 1, while the chemical shift in 50% D_2SO_4–CH_3COOD reflects those of the protonated form of thiol- and ol-type structure (Ia, IIa, IIIa, IVa, Va, and VIa). On the basis of such considerations, effects of substituents on the chemical shifts in $CDCl_3$ and in 50% D_2SO_4–CH_3COOD was estimated and, the shifts induced by introducing of substituent were considered to be the substituent effects of =S, =O, –SH, and –OH in the pyridine and pyridinium ring respectively. The results are summarized in Tables II and III.

As will be clear from these tables, all the protons in 2-oxo compound shifts 0.5 to more than 1 ppm to a higher magnetic field, compared to those of unsubstituted bases. Introduction of 2-OH group into the pyridinium ion also results in a higher magnetic field compared to the protons in the parent ion, and this fact endorses the electron-donating effect of =O and –OH groups against the pyridine ring, although a part of this diamagnetic shift may be attributed to reduction of the ring current effect[3] of the π-electrons. On the other hand, 2-thione and 2-thiol groups also show tendency to shift the protons of pyridine and pyridinium

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7) M.J. Cook, A.R. Katritzky, P. Linda, and R.D. Tack, *J. Chem. Soc.*, **1972**, 1295.
8) G.B. Barlin, *J. Chem. Soc.*, **1972**, 1459.

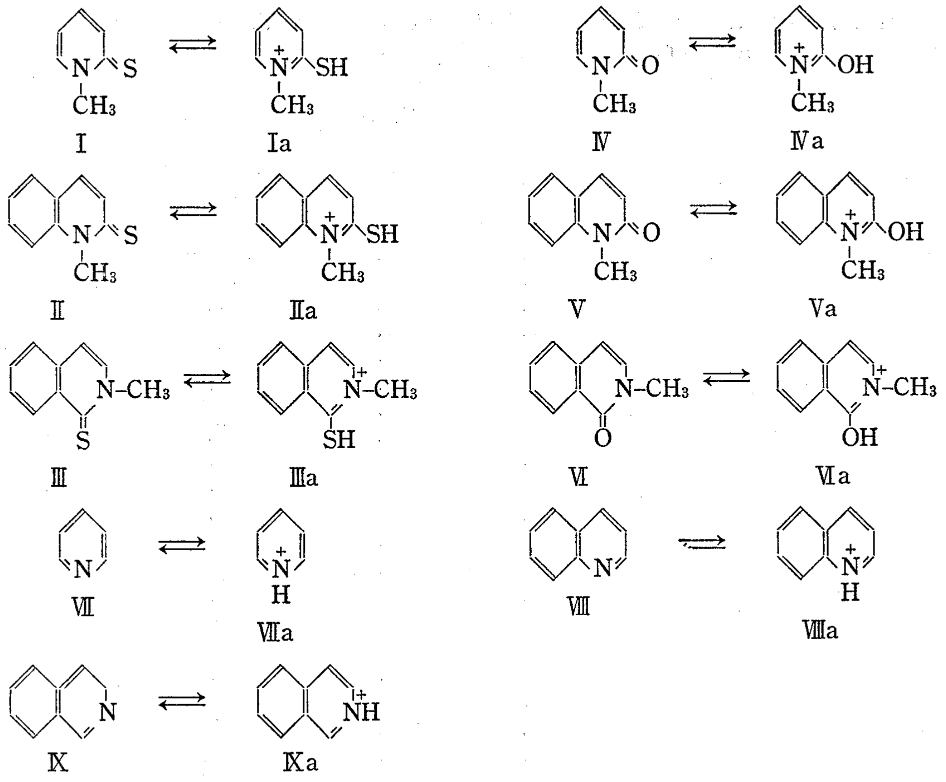


Chart 1

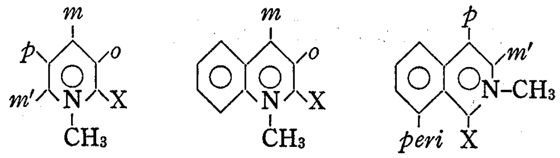
TABLE II. Chemical Shift Differences (ppm) Induced by Replacement of the Substituents at Position Two

	Position	Substitution at position 2					
		Pyridine series			Pyridinium ion series		
		-H→=S $\delta_{\mathrm{I}}-\delta_{\mathrm{VII}}$	-H→=O $\delta_{\mathrm{IV}}-\delta_{\mathrm{VII}}$	=O→=S $\delta_{\mathrm{I}}-\delta_{\mathrm{IV}}$	-H→-SH $\delta_{\mathrm{Ia}}-\delta_{\mathrm{VIIa}}$	-H→-OH $\delta_{\mathrm{IVa}}-\delta_{\mathrm{VIIa}}$	-OH→-SH $\delta_{\mathrm{Ia}}-\delta_{\mathrm{IVa}}$
Pyridine series	3	−0.50	+0.72	−1.22	−0.29—−0.44	+0.65	−0.94—−1.09
	4	+0.44	+0.32	+0.12	+0.27—+0.12	+0.38	−0.11—−0.26
	5	+0.58	+1.12	−0.54	+0.12	+0.72	−0.60
	6			−0.46			−0.63
	N-Me			−0.50			−0.46
		$\delta_{\mathrm{II}}-\delta_{\mathrm{VIII}}$	$\delta_{\mathrm{V}}-\delta_{\mathrm{VIII}}$	$\delta_{\mathrm{II}}-\delta_{\mathrm{V}}$	$\delta_{\mathrm{IIa}}-\delta_{\mathrm{VIIIa}}$	$\delta_{\mathrm{Va}}-\delta_{\mathrm{VIIIa}}$	$\delta_{\mathrm{IIa}}-\delta_{\mathrm{Va}}$
Quinoline series	3	−0.06	+0.64	−0.70	∼+0.10	+0.58	−0.48
	4	+0.44	+0.46	−0.02	+0.55	+0.52	+0.03
	N-Me			−0.06			−0.26
		$\delta_{\mathrm{III}}-\delta_{\mathrm{IX}}$	$\delta_{\mathrm{VI}}-\delta_{\mathrm{IX}}$	$\delta_{\mathrm{III}}-\delta_{\mathrm{VI}}$	$\delta_{\mathrm{IIIa}}-\delta_{\mathrm{IXa}}$	$\delta_{\mathrm{VIa}}-\delta_{\mathrm{IXa}}$	$\delta_{\mathrm{IIIa}}-\delta_{\mathrm{VIa}}$
Isoquinoline series	3	+1.10	+1.49	−0.39	−0.24	+0.70	−0.94
	4	+0.69	+1.08	−0.39	−0.28	+0.39	−0.67
	8			−0.69			>+0.6
	N-Me			−0.49			−0.72

δ_N: The chemical shift of protons in compounds *N* (I→IX, Ia→IXa).
N: The compounds numbers shown on Chart 1.

ion to a higher magnetic field but the magnitude of this shift is considerably smaller than that by the oxo compounds. The most characteristic of the effect of thione and thiol groups is that, while they give a large higher shift to protons in the *meta* position, they inversely give a considerably large lower shift to protons in the *ortho* position.

TABLE III. Substituent Effect of Oxo and Thioxo Groups on *ortho*, *meta*, and *para* Protons



X: -H, =O, =S, -OH, or -SH

	ortho	*meta*	*meta'*	*para*	*peri*	N-CH_3
-H→=O						
Pyridine series	+0.72	+0.32		+1.12		
Quinoline series	+0.64	+0.46				
Isoquinoline series			+1.49	+1.08		
-H→=S						
Pyridine series	−0.50	+0.44		+0.58		
Quinoline series	−0.06	+0.44				
Isoquinoline series			+1.10	+0.69		
-H→-OH						
Pyridine series	+0.65	+0.38		+0.72		
Quinoline series	+0.58	+0.52				
Isoquinoline series			+0.70	+0.39		
-H→-SH						
Pyridine series	−0.37	+0.20		+0.12		
Quinoline series	+0.10	+0.55				
Isoquinoline series			−0.24	−0.28		
=O→=S						
Pyridine series	−1.22	+0.12	−0.46	−0.54		−0.50
Quinoline series	−0.70	−0.02				
Isoquinoline series			−0.39	−0.39	−0.69	−0.49
-OH→-SH						
Pyridine series	−1.02	−0.18	−0.63	−0.60		−0.46
Quinoline series	−0.48	+0.03				−0.26
Isoquinoline series			−0.96	−0.67	>+0.6	−0.72

unit: ppm

Summarizing these results, it may be considered that both =S and -SH groups are giving electron-donating effect on the pyridones to considerably lesser extent compared to the oxy derivatives. It was further suggested that thio substituents give a magnetically large anisotropic effect on the neighboring protons. This assumption is endorsed by the fact that the SH group substituted in the isoquinoline gives an abnormally large higher shift to the *peri*-proton at position 8 and that the =S group inversely gives a large lower field shift to the *peri*-proton, which cannot be anticipated from its electronic effect.

The diamagnetic effect on the proton in *meta* position is quite large, irrespective of =S or -SH group, and reason for it should be examined in future.

It is hoped that changes in the NMR spectra of these derivatives due to changes in concentration will be examined so as to make a more detailed analysis of their NMR data in relation to their electronic structure in ground state.

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