

Equilibrium Studies of 4-Substituted Pyridine 1-Oxide-Iodine Charge-Transfer Complexes

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A homologous series of 4-substituted pyridine 1-oxide-iodine molecular complexes was studied spectrophotometrically in carbon tetrachloride, for the methoxy (I), methyl(II), chloro(III), and nitro(IV) substituents. Due to low solubility, 4-nitropyridine 1-oxide was investigated also in dichloromethane. The values of K (l mole⁻¹), ΔH (kcal mole⁻¹), ΔG (kcal mole⁻¹), and ΔS (cal mole⁻¹ deg⁻¹) for the complexes were determined at 25°C from visible absorption measurements: for (I), 1300, -7.2, -4.2, -9.8; for (II), 200, -6.3, -3.2, -10.6; for (III), 37, -4.6, -2.1, -8.5; for (IV), only K equal to ~ 1 was determined. These data were correlated with the reported results of 4-methylpyridine 1-oxide and pyridine 1-oxide. The log of the equilibrium constant at 25°C for this homologous series plotted versus the pyridine 1-oxide sigma values (σ_{PyNO}) was found to give a linear relationship.

Introduction

In spite of the great interest in the 4-substituted pyridine 1-oxides, few thermodynamic studies of their donor properties have been reported. In a recent study² an ordering of donor strengths of the ligands towards phenol was reported. It was of interest to obtain additional thermodynamic data of the pyridine N-oxides with a reference acid. Another purpose of this work was to investigate a homologous series of aromatic charge-transfer complexes of iodine since few studies have been reported for series which involve minimal changes in the stereochemistry of the complex. In this paper we report studies of iodine complexes with 4-methoxy-, 4-methyl-, 4-chloro-, and 4-nitropyridine 1-oxide. These results are correlated with those reported for 4-methylpyridine 1-oxide³ and pyridine 1-oxide.⁴

Many correlations have been reported for 4-substituted pyridine 1-oxides and various Hammett sigma constants with observable properties of the N-oxides or their complexes. Since most of the correlations involved linear relations with σ and adjusted benzoic

acid sigmas (σ^+ and σ^-), a single set of constants, σ_{PyNO} , was defined for use with pyridine 1-oxide.⁵

Experimental Section

Materials. The 4-methoxy-, 4-methyl-, and 4-nitropyridine 1-oxides were obtained from the Aldrich Chemical Co. and recrystallized from acetone. The 4-chloropyridine 1-oxide was prepared by the method of Ochiai,⁶ from 4-nitropyridine 1-oxide and recrystallized from acetone. All the N-oxides were vacuum-dried for thirty-six hours in an Abderhalden chamber containing phosphorus pentoxide desiccant.

Reagent grade Mallinckrodt iodine was sublimed at reduced pressure and stored in a desiccator in the dark. Analytical reagent grade Mallinckrodt carbon tetrachloride was used as solvent without further purification. Analytical reagent grade Mallinckrodt dichloromethane was purified by a standard technique.⁷

Stability of Solutions. The iodine solutions were observed to give quantitative absorption for weeks after preparation, using a_{λ} (5200 Å) = 924 l mole⁻¹ cm⁻¹. The 4-methylpyridine 1-oxide-iodine complex solutions were observed to deteriorate in eighteen hours when exposed to light but did not change when kept in the sample cell in the Cary 14 for eighteen hours. In a similar manner, the other N-oxides were found to be stable for at least eighteen hours. A 100-ml stock solution of the N-oxide was made up fresh for each run.

Density Corrections. All volumetric solutions were corrected for molar concentration changes due to density change of the solvent when the solutions were made up at one temperature and run at another. The density was determined from $d_t = 1.63255 - 1.99110 \times 10^{-3}t - 0.690 \times 10^{-6}t^2$.⁸

Procedure. All spectroscopic measurements were carried out on the Cary 14 recording spectrophotometer.

(1) Abstracted in part from the M. S. thesis of Robert C. Gardner, University of Utah, Salt Lake City, Utah (1967).

(2) D. W. Herlocker, R. S. Drago, and V. I. Meek, *Inorg. Chem.*, **5**, 2009 (1966).

(3) T. Kubota, *Nippon Kagaku Zasshi*, **78**, 196 (1957); *CA.*, **53**, 2777 (1959).

(4) T. Kubota, *J. Am. Chem. Soc.*, **87**, 458 (1965).

(5) J. H. Nelson, R. G. Garvey, and R. O. Ragsdale, *J. Heterocyclic Chem.*, **4**, 591 (1967).

(6) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

(7) L. F. Fieser, "Experiments in Organic Chemistry", D. C. Heath and Co., Boston, Mass. (1964).

(8) "International Critical Tables of Numerical Data, Physics, Chemistry, and Technology", McGraw-Hill Book Co., Inc., New York, Vol. III, p. 28 (1928).

meter equipped with a thermostatted sample and reference chamber and a thermostatted sample cell holder. The sample cells were matched 10 cm Beckman quartz cells. The thermocouple, fitted in a tapered glass joint, was placed in the sample cell during each run and the millivolt reading recorded by a Sargent model SR potentiometric recorder. The temperature in the cell was capable of being read and maintained to $\pm 0.2^\circ\text{C}$. That thermal and chemical equilibrium were attained was noted by the fact that no temperature change was recorded by the thermocouple placed in the cell and no absorption change was seen on the Cary 14 after about fifteen minutes. Generally, the reference solution and the three or four sample solutions were scanned from 6000 to 4000 Å on the same section of chart paper so that all the curves together would show evidence of an isobestic point, which indicates a simple acid-base equilibrium.

Calculations. The equilibrium constants were calculated from the Drago-Rose equation:⁹

$$K_{\text{eq}}^{-1} = \frac{A - A_A}{(a_{\text{DA}} - a_A)b} - (C_D + C_A) + \frac{C_D C_A (a_{\text{DA}} - a_A)b}{A - A_A} \quad (1)$$

The terms are defined as follows: A , absorbance of system at a given wavelength; A_A , absorbance due to initial iodine concentration; a_{DA} , molar absorptivity of complex; a_A , molar absorptivity of iodine; C_A , initial concentration of iodine; C_D , initial concentration of the N-oxide; b , cell path length in cm. The quantity $(A - A_A)$ was obtained directly from the Cary 14 as the net absorption (difference between the baseline and the complex absorption) when an iodine solution of the same concentration as the initial iodine concentration in the sample cell, C_A , was used in the reference cell. A wavelength was chosen at which the molar absorptivity of the N-oxide was zero or negligible.

Results

In the Figures 1 and 2 are shown respectively the spectra of the 4-methoxy pyridine 1-oxide and 4-chloro pyridine 1-oxide at various concentrations, complexed with iodine and run with iodine in the reference cell. The visible region was scanned from 6000 to 4000 Å. In this region the free donor generally did not absorb.

Upon addition of N-oxides, charge transfer complexes show a shift in frequency from the visible iodine band which has an absorption maximum at 5200 Å in carbon tetrachloride. These shifts from the free iodine absorption band to shorter wavelengths are listed in Table I. The approximate values result from a strong overlap of the donor absorption peak. A large number of determinations of a_A for free iodine were made at several wavelengths: (5200 Å) 924; (4400 Å) 88.1; (4300 Å) 40.2; and (4200 Å) 28.2 l mole⁻¹ cm⁻¹.

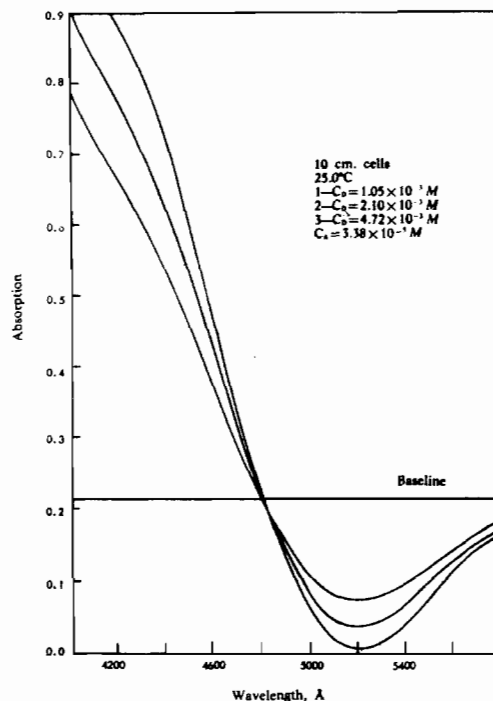


Figure 1. The visible absorption spectra for the 4-methoxy pyridine 1-oxide at various concentrations complexed with iodine and run with iodine of the same initial concentration in the sample cell as in the reference solution, with CCl_4 as the solvent.

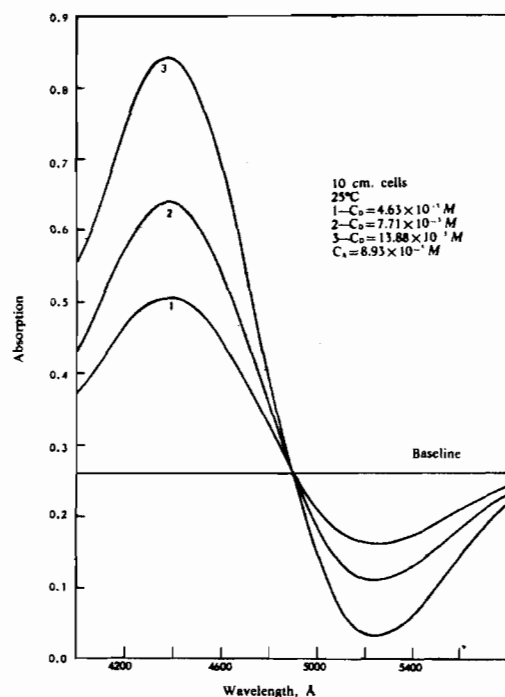


Figure 2. The visible absorption spectra for the 4-chloro pyridine 1-oxide at various concentrations complexed with iodine and run with iodine of the same initial concentration in the sample cell as in the reference solution, with CCl_4 as the solvent.

The values of K_{eq} and $(a_{\text{DA}} - a_A)b$ were determined from the experimental values of absorption and concentration using equation (1) in a computer routine.

(9) R. S. Drago, R. L. Carlson, N. J. Rose, and D. A. Wenz, *J. Am. Chem. Soc.*, 83, 3572 (1961).

Table I. Shifted I₂ bands for 4-substituted pyridine 1-oxide-iodine complexes in carbon tetrachloride

Donor substituent	Wavelength, Å
Methoxy	~4100
Methyl	4250
Hydrogen ^a	4410
Chloro	4390
Nitro, in CH ₂ Cl ₂	~4500

^a See reference (4).

The absorptivity of the complex can be determined from the values of $(a_{DA}-a_A)b$ and a_A , making sure to take note of the proper sign of the absorption value at the wavelength used. The values of K_{eq} and a_{DA} at the various wavelengths along with the confidence limits are presented in Table II. The confidence limits were determined on the basis of $a^* = a \pm c_n R$, (a^* is the population mean of the value, a is the average of the value, c_n is a constant corresponding to the desired confidence level, and R is the range).¹⁰

Table II. Equilibrium constants and absorptivity values for the 4-substituted pyridine 1-oxide-iodine complexes

Wavelength (Å)	Keq (l mole ⁻¹)			a_{DA} (l mole ⁻¹ cm ⁻¹)			
4-Methoxypyridine 1-Oxide							
	32°	25°	18°	32°	25°	18°	
4200	1058 ± 131	1313 ± 228	1862 ± 213	2311 ± 157	2355 ± 105	2428 ± 78	
5200	1197 ± 120	1492 ± 269	3830 ± 1218	246 ± 28	209 ± 21	449 ± 51	
4-Methylpyridine 1-Oxide							
	32°	25°		32°	25°		
5200	171 ± 12	205 ± 9		189 ± 8	177 ± 13		
Pyridine 1-Oxide ^a							
	33°	23°	15°	7°	33°	23°	15°
4400	56.5	77.9	106	134	1840	1860	1850
							1880
4-Chloropyridine 1-Oxide							
	32°	25°	18°	32°	25°	18°	
4400	30.9 ± 1.1	36.7 ± 1.9	48.7 ± 1.4	1987 ± 64	2028 ± 52	1989 ± 41	
5200	30.2 ± 6.1	36.3 ± 7.1	43.6 ± 4.1	173 ± 11	163 ± 11	149 ± 3	
4-Nitropyridine 1-Oxide							
		25°	18°				
4200			~1				
5200		~.4					
				Solvent: CCl ₄			
				Solvent: CH ₂ Cl ₂			

^a See reference (4).

The 95% confidence level was used. From graphs of log K_{eq} versus $1/T$, the ΔH values have been determined as the best fit of the points using a least squares computer routine except for the 4-methylpyridine 1-oxide where K_{eq} was determined at two temperatures. These values are shown in Table III. Results were only obtained at two temperatures for the methylpyridine 1-oxide-iodine complex since the thermodynamic properties had previously been reported.³

(10) H. A. Laitinen, "Chemical Analysis", McGraw-Hill Book Co., Inc., New York, pp. 547-548 (1960).

Table III. The thermodynamic properties of the 4-substituted pyridine 1-oxide-iodine complexes, at 25°C

Donor substituent	$-\Delta H$ (Kcal/mole)	$-\Delta G$ (Kcal/mole)	$-\Delta S$ (cal/deg mole)
Methoxy	7.2	4.2	9.8
Methyl	6.3 (6.15) ^a	3.2	10.6 (10.8) ^a
Hydrogen ^b	5.75	2.57	10.67
Chloro	4.65	2.1	8.5
Nitro ^c		-0.3	

^a See reference (3). ^b See reference (4). ^c Determined from Figure 5 by using $\sigma_{PYNO} = 1.19$ for 4-nitropyridine 1-oxide.

Discussion

The data reported in Table III indicate increasing donor strength of the 4-substituted pyridine 1-oxide with increasing electron donating ability of the 4-substituent. The relative basicity of the N-oxides according to the substituent from strongest donor to least is as follows: CH₃O > CH₃ > H > Cl > NO₂.

The correlation of log K_{eq} versus σ_{PYNO} ⁵ is illustrated in Figure 3. Since σ_{PYNO} is defined on the basis of pK_a of the protonated N-oxides, there is a parallel relation between pK_a and iodine-complexing ability of electron donors. This relation has been noted before on other systems.¹¹ In the past, linear correlations with substituted pyridine N-oxides⁵ were made with adjusted benzoic acid sigmas (in some cases σ^+ , σ^- , and σ were used for one plot), whereas this work indicates that only a single set of constants is needed

(11) V. G. Krishna and M. Chowdhury, *J. Phys. Chem.*, 67, 1067 (1963); H. Tsubomura, *J. Am. Chem. Soc.*, 82, 40 (1960), as examples.

when the constants are defined on the basis of the pK_a values.

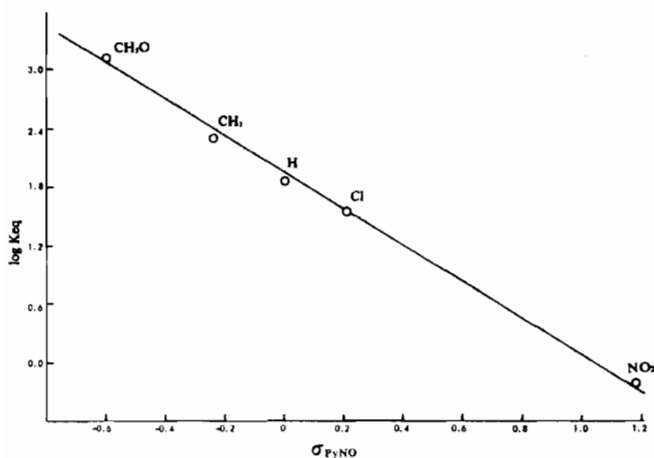
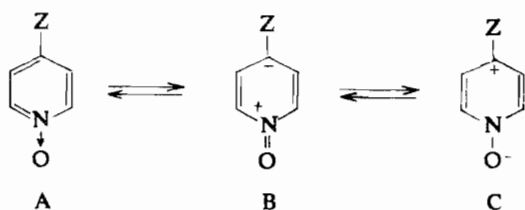


Figure 3. Log Keq versus σ_{PyNO} values for various 4-substituted pyridine 1-oxides.

Also the correlation in Figure 3 helps to substantiate that the active donor center is the oxygen atom. The relations between log Keq and pK_a suggest a similarity of the bonding mechanism between hydrogen bonding and iodine complexing where the charge-transfer force is probably important. In the pyridine ring conjugation occurs directly with the reactive site, and resonance structures (shown below) such as B are important for deactivating groups and structures such as C for activating substituents.



The effect of different types of substituents is transmitted through the ring to the oxygen atom, thus changing its ability to act as an electron pair donor. This can be seen by a comparison of Keq at 25° for the 4-methoxypyridine 1-oxide-iodine complex (1300) with that for the 4-chloropyridine 1-oxide complex (37), the neutral case being the pyridine 1-oxide complex (76.9).⁴

Due to solubility difficulties, the 4-nitropyridine 1-oxide was run in dichloromethane at 25°C (in addition to carbon tetrachloride) in order to establish the

relative equilibrium constant for this weakly-basic donor. Since the determination of Keq and other thermodynamic properties of the N-oxide-iodine charge-transfer complexes requires very careful measurements and much effort (also solubility difficulties with some complexes such as 4-nitro-, and 4-carbomethoxypyridine 1-oxides limit the complexes which can be studied), one can obtain a good estimate of these properties for other substituted pyridine 1-oxides by use of Figure 3 and the appropriate σ_{PyNO} .⁵ The experimental studies on 4-nitropyridine 1-oxide indicated that the equilibrium constant is less than one and on the basis of Figure 3 the equilibrium constant is estimated as 0.6.

The homologous series of compounds studied also indicates that steric effects have not been a factor, as evidenced by the fairly constant entropy values. Changing the substituent in the 4 position has little steric effect upon the complex. Since the entropy value is relatively constant, a linear correlation is also found by plotting the enthalpy term versus the σ_{PyNO} or pK_a values.

It is of interest to compare the thermodynamic properties of the pyridine-iodine complex,^{12,13} ($\Delta H = -7.8$ kcal/mole, $\Delta G = -3.3$ kcal/mole, and $\Delta S = -15.5$ cal/deg-mole) with the N-oxide complexes. It is surprising that the free energy is such a small negative number (smaller than the value for the 4-methoxypyridine 1-oxide) whereas for pyridine the pK_a is 5.19 and for 4-methoxypyridine 1-oxide the pK_a is 2.05. Pyridine is a much stronger base towards the hydrogen ion than the aromatic N-oxides, but part of the difference in its inability to be a stronger base towards iodine is reflected in the large negative entropy term for the pyridine complex. In pyridine, iodine approaches the 2 and 6 hydrogens close enough so that there is steric repulsion, but with the N-oxides iodine is further removed from the pyridine ring so that this repulsion is greatly diminished. If ΔS for the pyridine-iodine complex were similar to that for the N-oxide complexes an equilibrium constant of approximately 5000 would be expected.

Acknowledgment. Work was supported by a grant from the University of Utah Research Fund.

(12) C. Reid and R. S. Mulliken, *J. Am. Chem. Soc.*, **76**, 3869 (1954).

(13) Later work^{14,15,16} indicates a slightly different equilibrium constant at room temperature, but a temperature study was not made. This difference in equilibrium constant would probably not effect Reid and Mulliken's thermodynamic values very much.

(14) A. I. Popov and R. H. Rygg, *J. Am. Chem. Soc.*, **79**, 4622 (1957).

(15) A. G. Maki and E. K. Plyler, *J. Phys. Chem.*, **66**, 766 (1962).

(16) G. Aloisi, G. Cauzzo, G. Giacometti, and U. Mazzucato, *Trans. Faraday Soc.*, **61**, 1406 (1965).