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The Changes in Conformation and Complexability of 6,6′-Diamino-2,2′-bipyridine by Protonation

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The reaction of 6,6′-dibromo-2,2′-bipyridine with ammonia in an autoclave gave 6,6′-diamino-2,2′-bipyridine (DABP) in more than 80% yields. DABP behaved as a diacidic base in the pH range of 0 to 10 with the conformational changes. DABP formed complexes with Cu(II), Ni(II), Co(II), and Zn(II). The amino groups at 6 and 6′ positions play a role as strong electron-donationg groups and not as coordination sites. p*K*a values and complex formation constants were estimated.

2,2′-Bipyridine (bpy) is well known as a typical ligand that forms stable complexes[1] with various transition metal ions in a wide pH range. Particularly, in last 15 years, tris(bpy) ruthenium complex has been extensively studied because of its potential applicability to photolysis of water in coupling with an electron acceptor such as methylviologen.[2] Various kinds of bpy derivatives have been synthesized and examined as to the effects of substituents on the complexing properties and on the physical properties of the complexes.[3,4] Among these derivatives, 6,6′-dimethyl-2,2′-bipyridine (Mbpy) exhibits an unique behavior in the complex formation due to the steric hindrance of the substituents at 6- and 6′- positions.[5] Mbpy forms almost exclusively mono or bis complex with various metals, while many other bpy derivatives usually form stable tris-bpy complexes. In a few tris complexes of Mbpy exceptionally known, the methyl substituents were reported to affect on the wavelength and/or life time of luminescence of ruthenium(II) complexes.[6] The recent interest in this field seems to be focussed on the examination of the effect of the substituents on bpy or analougus complexes with various metal ions.[7,8] 6,6′-Diamino-2,2′-bipyridine (DABP) is expected to exhibit interesting properties as a metal ligand. There was, however, no paper reported as to the properties of DABP and its complexing ability with metal ions except only two reports on the synthesis of DABP.[9,10] In this paper, we wish to report an improved synthesis and some physical properties of DABP along with complex formation. The influence of the amino group at 6,6′-positions on the ability of complex formation with some transition metal ions will be discussed.

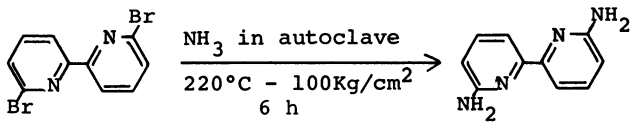
Results

Preparation of 6,6′-Diamino-2,2′-bipyridine. 2,2′-Bipyridine (bpy) is rarely susceptible to either electrophilic or nucleophilic substitution reactions.[11] The usual Chichibabin reaction using sodium amide gave only a trace amount of amino derivatives.[10] Burstall reported that 6,6′-dibromo-2,2′-bipyridine (DBBP) was easily converted to DABP by the reaction with aqueous ammonia in a sealed tube for 14h,[9] but attempted preparation according to the report resulted in unsatisfactory results. An improved amination method was explored.

An unsealed glass ampoule containing DBBP was placed in an autoclave, into which liquid ammonia was added. DBBP was allowed to react with ammonia at 220 °C under a pressure of 100 kgf cm^{-2} (kgf= 9.80665N) for 6 h. After the reaction, the solid in the ampoule was dissolved in dilute aqueous HCl and filtered. Basification of the filtrate with aqueous ammonia gave crude DABP as a precipitate. Purification was effected by sublimation and the total yield was 80%. In these reaction conditions, there was no recovery of DBBP nor char formation and DBBP was considered to be fully converted into DABP. The remainder of DABP might be left unprecipitated in the bacified solution though its limited solubility. The reaction conditions described above were fairly optimized one. Three hours' reaction was not enough fully to convert DBBP into DABP, and longer reaction time more than 10 h also reduced the yield of DABP by noticeable char formation. The presence of metals diminished the yield of DABP, which is the reason why DBBP was placed in a glass ampoule. Imperfect purification of DBBP, especially residual copper, deteriorated the DABP formation and resulted in char formation. This may be due to the catalytic degradation of DBBP or DABP with copper or other metals.

Acid-base Properties of DABP. 2,2′-Bipyridine (bpy) and 1,10-phenanthrorine (phen) have been thought to be monoacidic base though they have two sites for potonation.[12] The second protonation occurs, however, only in a strong acid such as concentrated sulfuric acide.[13,14] The acid-base properties of DABP, which has four potentially basic nitrogen atoms in the molecule, were examined and it was found to act as a diacidic base in the pH range from 0 to 10.

The absorption spectra of DABP changed with pH (Fig. 1). Stepwise protonation is suggested. Figure 1-A shows the spectral change of DABP with isosbestic points due to the first protonation step, where DABP changed from free form to monoprotonated form with isosbestic points. Figure 1-B shows the spectral change of DABP with different isosbestic points from monoprotonated form to diprotonated form. The pattern of the spectral change in the first step is very similar to that of bpy, suggesting that this is due to monoprotonation step. This was confirmed by acid-base titration. The second step is diprotonation process. This



Scheme 1.

is not experimentally confirmed but plausibly considered to be so by the exsistence of isosbestic points in the spectral change. As shown in Fig. 1, DABP showed two stages of equilibrium substantially separated from each other, suggesting that the proton dissociation constants for mono and diprotonated forms of DABP were greatly different from each other. The pKa_4 for the first protonation stage and pKa_3 for the second protonation stage of DABP were determined to be 6.72 and 2.2 respectively by plotting the absorbances at 360 nm for the first stage protonation, and at 350 and 250 nm for the second stage protonation against pH (Fig. 2). The values are larger than those of bpy (4.5 and −0.5).[15,13] The pKa_4 was very close to 6.86 of 2-aminopyridine (Ampy),[16] where the amino group effects to strengthen the basicity of pyridine ring by its strong electron donating property.

The chemical shifts of ^{1}H-NMR spectra of DABP and related compounds in various media are listed in Table 1. The assignment was according to the literature.[17,18] The chemical shifts of DABP in DMSO were nearly close to those of Ampy except 3-H, and were shifted to upper field comparing with those of bpy. This indicates that the electron distribution on pyridine ring of DABP is similar to that of Ampy and their electron density are higher than that of bpy, being consistent with the pKa data described above.

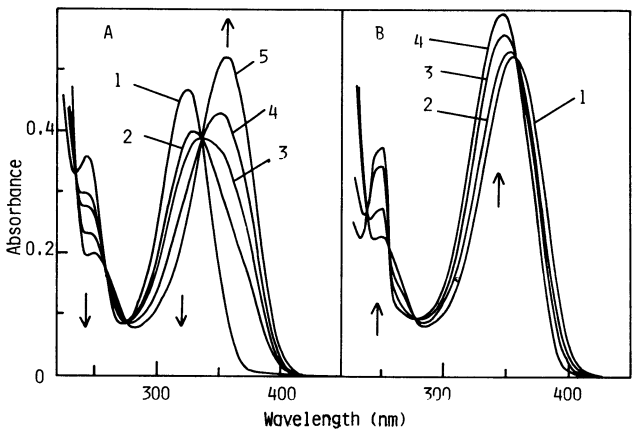


Fig. 1. The spectral Change of DABP (3.33×10^{-5} mol dm^{-3}).
A:Change from free to monoprotonated form 1) pH 10.00, 2) pH 7.00, 3) pH 6.57, 4) pH 6.00, 5) pH 4.90.
B: Change from mono to diprotonated form 1) pH 3.63, 2) pH 2.35, 3) pH 1.46, 5) pH 0.60.

Complex Formation. DABP showed the spectral change by complexation with metal ions. Figure 3 shows the spectral change of DABP as a function of Cu(II) concentration.

Continuous variation method was applied to the DABP-metal systems in a buffer solution of pH 9.3. The total concentration of metal and ligand employed was 2.00×10^{-5} mol dm^{-3}. The result confirmed the 1:1 stoichiometry of the DABP-metal systems except with Zn(II) (Fig. 4). There was nothing observed to indicate the formation of DABP tris complexes. In this respect, DABP resembles Mbpy in the pattern of the complex formation,[5] suggesting that the amino groups at 6 or 6′-positions act like methyl groups of Mbpy. The formation constants of 1:1 complexes ($\log K_1$) were obtained at pH 4.0 and 9.3 by the Rose-Drago method (Table 2). Typical examples are shown in Fig. 5. The constant for Zn(II) at pH 9.3 was not obtained, because Zn(II) forms only 2:1 complex (DABP:Metal) at the

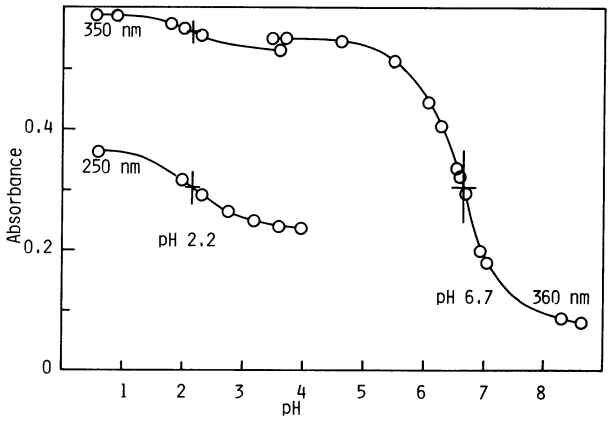


Fig. 2. The Absorbance of DABP (3.33×10^{-5} mol dm^{-3}) as a Function of pH.

TABLE 2. THE COMPLEX FORMATION CONSTANTS ($\log K_1$)

Metal ion	$\log K_1$		$\log K_{ex}$ calcd	
	pH 4.0	pH 9.3	pH 4.0	pH 9.3
Cu(II)	4.82	6.67	0.82	−0.05
Ni(II)	3.30	5.82	−0.70	−0.90
Co(II)	1.82	4.96	−2.18	−1.76
Zn(II)	2.17	—*	−1.83	—
Cu(I)	4.07	6.00	−0.10	−0.70

*) $\log K_2=11.7$

TABLE 1. CHEMICAL SHIFTS OF DABP AND RELATED COMPOUNDS

	Solvent	Position				$\delta_3-\delta_5$
		3	4	5	6	
Ampy	: DMSO	6.35	7.18	6.27	7.74	0.08
+1/2 eq. mol D_2SO_4	: D_2O	6.87	7.70	6.77	7.61	0.10
	: D_2SO_4	8.04	8.63	7.99	8.54	0.05
bpy	: DMSO	8.15	7.72	7.24	8.43	0.91
+1/2 eq. mol D_2SO_4	: D_2O	8.07	8.07	7.65	8.48	0.42
	: D_2SO_4	8.26	8.66	8.14	8.72	0.12
DABP	: DMSO	7.36	7.36	6.38		0.98
+1/2 eq. mol D_2SO_4	: D_2O	6.78	7.33	6.48		0.30
+ eq. mol D_2SO_4	: D_2O	7.05	7.64	6.80		0.25
	: D_2SO_4	7.49	8.21	7.41		0.08

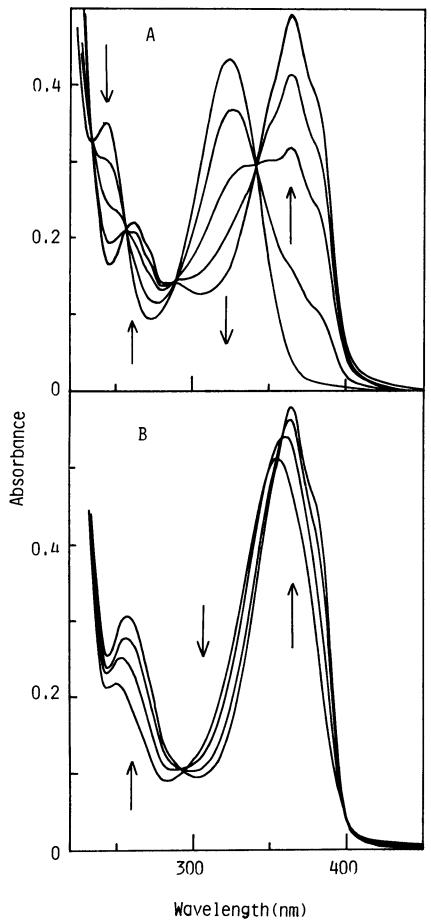


Fig. 3. The Spectral Change of DABP (3.33×10^{-5} mol dm^{-3}) as a Function of Cu(II) Concentration.
A: In pH 9.3 buffer solution
B: In pH 4.0 buffer solution.

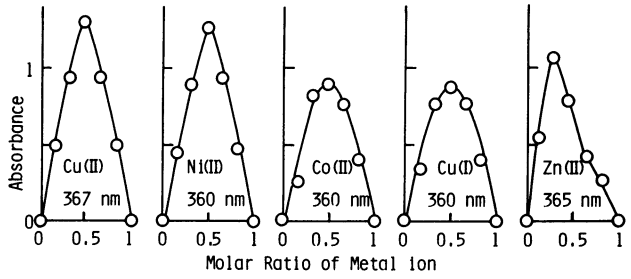


Fig. 4. Continuous Variation Method in pH 9.3 Buffer Solution at 20°C.
[M]+[DABP]=2.0×10^{-4} mol dm^{-3}.

pH. At pH 1.0, the spectral changes of DABP was too small to estimate the complex formation constants. Cu(II) had the highest complexability at pH 9.0 among the metal ions employed and the order of abilities of complexation were Cu(II)>Cu(I)>Ni(II)>Co(II). This order was the same as for bpy.[19] The log K_1 values of DABP were smaller than those of bpy but larger than those of Mbpy.[20] The complex formation constants observed at pH 4.0 were smaller than those at pH 9.3. The order of the ability of complexation of metals with DABP at pH 4.0 was the same as that at pH 9.3 and also the same as that of bpy except Zn(II).

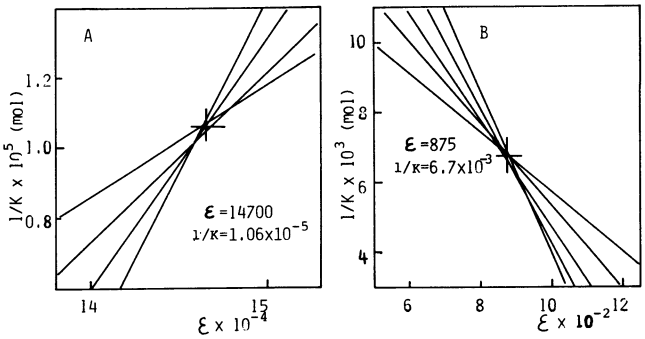


Fig. 5. Rose-Dorago Plots of Metal-DABP Systems at 20°C.
A: Co(II)-DABP system in pH 9.3 buffer solution
B: Zn(II)-DABP system in pH 4.0 buffer solution.

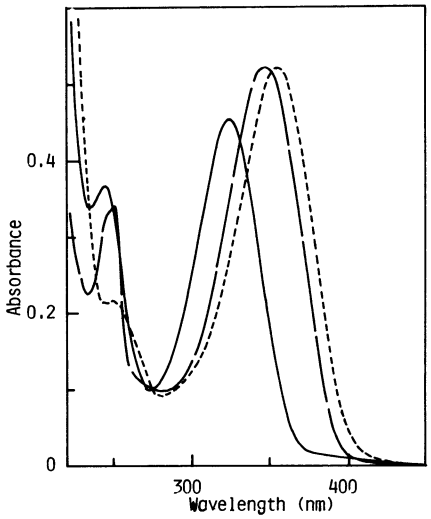


Fig. 6. Comparison of the Spectra of DABP (3.33×10^{-5} mol dm^{-3}) in Buffer Solutions of Different pH.
—— pH 9.3, ------ pH 4.0, ——pH 1.0.

Discussion

The Protonation Site and the Conformation of Protonated DABP. ^{1}H NMR spectrum of DABP in DMSO showed nearly the same chemical shifts as that of Ampy except the signal due to the ring proton at 3 position. The proton at 3 position of bpy in either protic or aprotic solvent is known to show an anomalous chemical shift comparing to the proton at 5 position due to the effect of diamagnetic anisotropy of neighbouring pyridine ring, and the conformation of bpy in solution is predicted by the relative chemical shift of the proton at 3 position to that at 5 postion $\delta_{H\text{-}3}-\delta_{H\text{-}5}$).[18] The relative chemical shifts of DABP in DMSO were 0.98, which is almost the same as that (0.91) of bpy. Bpy in solution is known to have transoidal conformation,[15,18] suggesting that the free form of DABP has transoidal conformation in the solution.

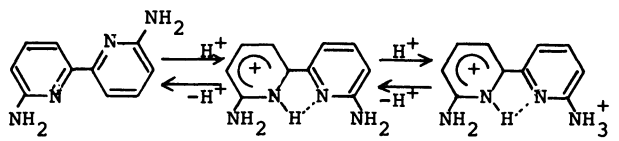
The UV absorption spectrum also supports transoidal conformation of free DABP. Figure 6 shows the absorption spectra of DABP in buffer solutions of pH 9.3, pH 4.0, and pH 1.0 corresponding to free, monoprotonated, and diprotonated form of DABP. Bpy has two bands at 232 nm and 279 nm in basic

solution.[15] Free form of DABP also has two bands at 244 and 325 nm. The spectral shapes of bpy and DABP resembles each other except that the two peaks of DABP are at longer wave lengths than those of bpy.

Monoprotonated DABP seems to have a cisoidal conformation, and the site for protonation seems to be on the ring nitrogen and not on the amino groups. Two bands of monoprotonated DABP appeared at 251 nm and 357 nm, being red-shifted in comparison with those of the free form. The monoprotonation of bpy is known to cause the red-shift comparing with free form.[15] The relative chemical shift ($\delta_{H\text{-}3}-\delta_{H\text{-}5}$) of monoprotonated DABP is 0.30 ppm and is near to 0.40 ppm of monoprotonated bpy. This also suggests that the monoprotonated DABP has the same conformation as that of monoprotonated bpy, which is known to have cisoidal conformation.[15] Thus monoprotonated DABP is concluded to have the cisoidal conformation to form chelation ring and the bacisity of the pyridine ring is increased as 100 times large as that of bpy by introduction of amino groups at 6- and 6'- positions.

The second protonation seems to be different from that of bpy. Two bands still appeared at 252 nm and 348 nm in the absorption spectrum of diprotonated DABP, whereas the second protonation on bpy leads to loss of one of the two peaks to exhibit only one absorption at 290 nm.[13] The second protonation on bpy at the other pyridine ring causes repulsive interaction between the two protonated sites and makes two pyridine rings twisted.[15] The disappearance of one of the two peaks observed in bpy seems to be due to the destruction of the coplanarity of the linked aromatic rings and is not observed in the case of 1,10-phenanthrorine,[13] nor in the dication of bpy formed by *N*-alkylation with 1,2-dichloroethane.[18] The second protonation on DABP is suggested not to destroy the conjugation so much as in the case of bpy. ^{1}H-NMR spectra also suport the consideration. The relative chemical shift of proton at 3 position to that at 5 position was 0.25 ppm, and being close to 0.3 ppm of monoprotonated DABP. Thus the secondly protonated DABP has still cisoidal conformation, and therefore, the second protonation is plausively considered to occur at amino group.

In a strong acid, however, the destruction of cisoidal conformation seems to be caused by the third and fourth protonation.[21] The relative chemical shifts of 3 position to that of 5 position in D_2SO_4 were 0.12, 0.08, and 0.05 ppm respectively for bpy, DABP, and Ampy. The value of DABP is intermediate between those of bpy and Ampy. In these conditions, bpy has twisted conformation and the proton at 3 position is not affected so much by the neighbouring aromatic rings. Thus the first and second stage protonation of DABP were suggested to occur as shown in scheme 2. It may be plausible from the electrostatic point of view too.



Scheme 2.

This may be the reason that the *K*a for the second protonation of DABP became larger about 1000 times than that of bpy.

Exchange of Proton with Metal Ion and the Effects of the Amino Group. Absorption spectra of Ni(II) complex with DABP in buffer solutions of pH 9.3 and 4.0 are shown in Fig. 7 along with that of monoprotonated DABP. Spectra of Ni(II) complex at pH 9.3 and pH 4.0 were almost the same as each other and very close to that of monoprotonated DABP, suggesting that complexing site for metal ions is the site where protonation occurs, and that proton and metal ion compete with each other in coordination. Supposing an equilibrium of ternary system among L, LH, and LM (Scheme 3), the equilibrium constants of the exchange between proton and metal ions (K_{ex}) can be estimated either by using the values of log K_1 at pH 9.3 and p*K*a or by using log K_1 at pH 4.0 for any of the metal ions forming 1 : 1 complex with DABP. The two independently obtained values of K_{ex} were nearly the same for Ni(II) and Co(II). Therefore, there is considered to exsit the ternary equilibrium among L, LH, and LM in moderate pH region and the metal decomplexation at lower pH region is also considered to be

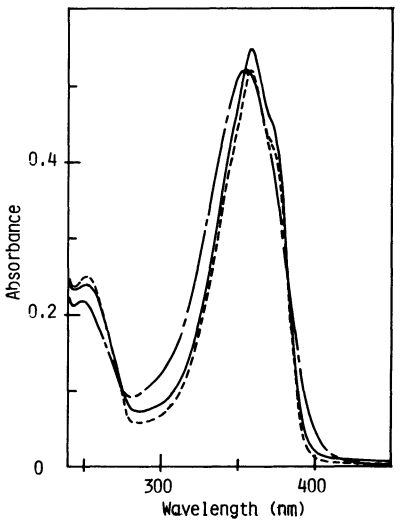
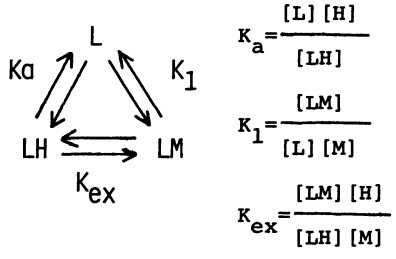


Fig. 7. Comparison of the Spectra of DABP (3.33×10^{-5} mol dm^{-3}) and DABP–Ni Systems in Different Buffer Solutions.
------ with excess amounts of Ni(II) in pH 9.3, —— with excess amounts of Ni(II) in pH 4.0, —·— in pH 4.0 without metal ion.



Scheme 3.

due to the exchange of metal ion with proton.

As discussed above, the sites for protonation and metal complexation of DABP are the ring nitrogen atoms. Electron donation by amino groups increases the basicity of ring nitrogen atoms of DABP and influences the complex formation properties. However, basicity is not directly related to complex formation ability. The ability of complex formation of DABP was less than that of bpy, although DABP has higher basicity than bpy. Mbpy which has higher bacicity than bpy is known to have less complexability than bpy. The substituents at 6- and 6′- positions decrease the complexability. For the compounds having similar steric effects, however, the basicity of the complexing site determines the complexability. The complex formation constants of DABP (log K_1=6.7 for Cu(II)) is larger than that of Mbpy (4.23) according to the higher basicity of DABP (pKa=6.7) than that of Mbpy (4.88). The differences in log K_1 and pKa are found to be almost parallel.

DABP forms only 1:1 complex with metal ions such as Cu(II), Ni(II), and Co(II) and no bis nor tris complexes due to the steric hindrance of the amino groups. Therefore, the complexes of DABP are more pH-sensitive than tris complexes of other bipyridine derivatives. Although pKa of 2,2′-bipyrazine is 0.5, tris-(bipyrazine)ruthenium is stable in concentrated sulfuric acid.[7] And tris(bipyridine) complex with Fe(II) is stable in the pH region of 1.0—9.0, though pKa of bipyridine is 4.5.[22] Whereas, the stability constant of DABP drastically changes between pH 4.0 and pH 9.3 about 100 times. This pH-sensitive properties of DABP for complex formation can be used as a pH- swich for selective uptake and release of metal ions.[24]

Experimental

6,6′-Dibromo-2,2′-bipyridine (DBBP). To a suspension of 2,6-dibromopyridine(50 g, 0.21 mol) in diethyl ether (350 cm^3), which was cooled under −60 °C in liquid nitrogen-hexane bath, butyllithium (2.2 mol dm^{-3} in hexane, 130 cm^3, 0.29 mol) was added slowly. Then the reaction mixture was cooled to −90 °C and a fine powder of anhydrous copper(II) (14.2 g, 1.04 mol) was added. The mixture was allowed to warm to −70 °C with efficient stirring. After 30 min, oxygen was bubbled slowly through the solution at −50 °C for 30 min. The reaction mixture was poured into aqueous HCl (6N, 500 cm^3) with stirring. The solid part was collected by filtration, washed with water and dried under vacuum. The dried solid was extracted with hot benzene. The benzene extract was evaporated. The residue was recrystallized from benzene to give colorless needles of DBBP in pure form, 20.2 g (61%). Mp 225—226 °C (lit.[23] 226—227 °C).

6,6′-Diamino-2,2′-bipyridine (DABP). DBBP (3.0 g, 9.6 mmol) was placed in a glass ampoule. Liquid ammonia (30 g) was also placed in another ampoule. The unsealed ampoules were placed in an 500 cm^3 autoclave, and heated up to 220 °C. The inner pressure rised up to 100 kgf cm^{-2}. Heating was continued for 6 h. After the reaction, the solid in the glass ampoule was dissolved in dilute aqueous HCl (50 cm^3) and filtered in order to remove insoluble matters, and unreacted starting material. Aqueous ammonia was added into the filtrate to precipitate a solid , which was collected by filtration, washed with aqueous ammonia and water, and dried under vacuum. The crude products were sublimated under vacuum (2 mmHg (270 Pa)-150—200 °C) to give 1.42 g (80%) of purified DABP, mp 185—186 °C (lit,[9] 186 °C). Found C, 64.67; H, 5.19; N, 30.21%. Calcd for $C_{10}H_{10}N_4$ C, 64.50; H, 5.41; N, 30.09%. The reaction for 3 h gave unreacted starting material (0.81 g, 27%) and DABP (0.93 g, 52%).

Spectral Measurements. The absorption spectra were recorded with a JASCO UVIDEC-505 spectrophotometer at 20 °C. The buffer solutions used were as follows: pH 1.0, HCl-KCl buffer; pH 4.0, 0.2 mol dm^{-3} acetic acid-sodium acetate buffer; pH 9.3, 0.2 mol dm^{-3} potassium borate buffer. The ionic strength was not adjusted. ^{1}H-NMR spectra were recorded with JEOL JMN-MH 100 spectrometer. The chemical shifts were determined by 10 mmol of substance in 0.4 cm^3 DMSO-d_6 with tetramethylsilane (TMS) as internal standard or in 0.4 cm^3 D_2O with TMS as external standard, and reported in ppm from TMS.

Determination of Complex Formation Constants. Metal salts used were, Cu(II)$Cl_2\cdot 2H_2O$, Ni(II)$Cl_2\cdot 6H_2O$, Co(II)$Cl_2\cdot 6H_2O$, Zn(II)$(CH_3COO)_2\cdot 2H_2O$, and Cu(I)Cl of Special grade quality (Wako Pure Chemical Co). Typical procedure is as follows: 0.01 cm^3 of metal solution (0.01—1.0 mol dm^{-3}) was added to 3 cm^3 of buffer solution containing 1.00×10^{-7} mol of DABP. The changes of absorbance and composition of the solution were plotted according to Rose-Dorago Method. Wavelengths used for the determination were as follows. Cu(II), 367 nm; Ni(II), 360 nm; Co(II), 360 nm; Zn(II), 365 nm; Cu(I), 360 nm.

Continuous variation method. The total concentration of metal ions and DABP was 2.00×10^{-5} mol dm^{-3}. The differences in absorbance were plotted against the composition of the solutions (metal ion/DABP). The wavelengths used for the measurement were the same ones used in the experiment described above.

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