sodium tetraphenylborate, 143-66-8; phenol, 108-95-2; 4-nitrophenol, 100-02-7; platinum, 7440-06-4.

Supplementary Material Available: A listing of atomic thermal parameters for **1** (2 pages). Ordering information is given on any current masthead page. According to policy instituted Jan 1, 1986, the tables of calculated and observed structure factors (12 pages) are being retained in the editorial office for a period of 1 year following the appearance of this work in print. Inquiries for copies of these materials should be directed to the Editor.

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Cadmium-113 NMR of Cadmium(II) Complexes with Ligands Containing N-Donor Atoms. Dependence of the Chemical Shift upon the Ligand Basicity, Chelate Ring Size, Counteranion, and Cadmium Concentration

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^{113}Cd NMR studies were carried out on a variety of Cd(II) complexes with N-containing ligands. The ^{113}Cd chemical shifts of Cd complexes are affected by the counteranions and the concentration. However, when no ligands of the Cd complexes were replaced by counteranions and/or solvents, the ^{113}Cd chemical shifts were independent of the anions and the concentration within experimental error. ^{113}Cd nucleus deshielding of the complexes with 4-substituted pyridines (L) and 4,5,7-substituted 1,10-phenanthrolines (biL) increased with increasing pK_a of the ligands, and the pK_a dependence was enhanced with the formation of higher order complexes: $CdL^{2+} < CdL_2^{2+} < CdL_3^{2+} < CdL_4^{2+} < Cd(biL)_3^{2+}$. In the case of $Cd(biL)_3^{2+}$, the increase of 1 pK_a unit gave a downfield shift of 8.8 ppm. This demonstrates that ^{113}Cd NMR is very sensitive to the Cd–ligand bonding. The ^{113}Cd resonance of tris(diamine)cadmium also remarkably moves downfield as the chelate ring size decreases from seven to five members, i.e., $Cd(NH_2(CH_2)_4NH_2)_3^{2+}$ (227 ppm) < $Cd(NH_2(CH_2)_3NH_2)_3^{2+}$ (259 ppm) < $Cd(en)_3^{2+}$ (347 ppm). The same trend was observed in the series of dicarboxylate and dithiolate Cd complexes, with the pronounced sensitivity arising from chelate ring strain. The chemical exchange rates of labile Cd complexes in ethanol solution were successfully reduced by the use of low temperature (−90 °C), and all ^{113}Cd resonances of $Cd(pyridine)_n^{2+}$ (n = 0–4) and $Cd(imidazole)_n^{2+}$ (n = 0–6) were observed in solution and assigned. The ^{113}Cd chemical shifts of the solution NMR spectra agreed well with those of the solid NMR spectra for the cadmium complexes with imidazole and biL.

Introduction

Several physical techniques, most notably EPR, optical spectroscopy, and magnetic susceptibility, have been extremely useful in providing insight into the structures of metal complexes and the coordination environment in metalloenzymes, such as those containing Fe(II,III), Co(III), and Cu(II). However, these methods are not available for diamagnetic metal ions such as Cd^{2+}, Zn^{2+}, Cu^+, and Ag^+, which have d^{10} electronic configurations. The chemistry of these metal ions has become of interest in recent years because of their important characteristics of possessing properties of both transition and nontransition elements.[1] Organocadmium compounds have been widely used for organic synthesis.[2] Cadmium also plays an important role in the metallothioneins, which are widespread in nature,[3] and is often used to obtain the cadmium derivative of metalloenzymes such as LADH,[4] alkaline phosphatase,[5] carbonic anhydrase,[6] and superoxide dismutase.[7]

The ^{113}Cd chemical shift has been demonstrated to be remarkably sensitive to the coordination environment of the metal ion, including the donor atoms, coordination number, geometry, and solvent. The deshielding of $^{113}Cd^{II}$ increases in the order O < N < S, and the range of the observed shifts exceeds 900 ppm.[8-11] The ^{113}Cd NMR technique has therefore become a valuable tool in cadmium chemistry and bioinorganic chemistry. It has been mainly applied to the study of metallothionein[12,13] and a wide variety of metalloenzymes[4-7,12,13] in which the native Zn^{2+}, Cu^{2+}, Mg^{2+}, or Ca^{2+} ions are replaced by $^{113}Cd^{2+}$.

Attempts at detailed correlation of solution NMR spectra with the coordination environment in cadmium(II) compounds of known structure are hampered by the fast chemical exchange of cadmium(II) complexes with ligands and solvents. Two limiting situations should be considered. If the exchange is rapid on the NMR time scale, then a single averaged chemical shift is obtained.

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On the other hand, resonances for the individual species are observed when the exchange is slow on the NMR time scale. Thus ^{113}Cd solid-state NMR has recently been attempted to obtain isotropic chemical shifts of cadmium(II) complexes in the absence of chemical exchange[14-16] and to provide a powerful tool for structural studies of solid states. However, one of the most important advantages of the ^{113}Cd NMR technique is its applicability to studies on the "solution" structure of cadmium(II) compounds, including the metalloenzymes. An important concern is the development of methods for determining the chemical shift to accurately define distinct chemical species "in solution" and a comparison of the solution ^{113}Cd chemical shift with the solid shift.

Chemical shifts for individual halide complexes have been calculated from the observed shift and the known equilibrium constants.[17-19] The accuracy of this method is, however, limited by the accuracy of the equilibrium constants under investigation. By employing supercooling of aqueous solutions with temperatures down to −55 °C, Ackerman et al.[20] for the first time achieved the slow-exchange limit of the NMR time scale for labile cadmium(II) complexes with glycinate (gly) and observed separate NMR resonances for Cd^{2+}, $Cd(gly)^+$, $Cd(gly)_2$, and $Cd(gly)_3^-$. $^{113}Cd-^{15}N$ spin–spin coupling constants have also been observed for the individual complexes of the cadmium(II)–glycinate system.[21] Also, the use of dimethyl sulfoxide has been found to slow down the chemical exchange of cadmium(II) amine complexes, which is fast in H_2O, and a relationship has been proposed between the ^{113}Cd chemical shift and the ligating amine number.[22]

The relationship between the ^{113}Cd NMR chemical shift of cadmium(II) complexes and the structure/metal–ligand bonding nature is still poorly understood. Thus, this study involved a detailed investigation of the correlation of the ^{113}Cd NMR chemical shift of the cadmium(II) complexes in solution with the basicity of the donor atoms, chelate ring size, counteranion, and cadmium concentration. Furthermore, the solution and solid ^{113}Cd NMR chemical shifts were compared.

Experimental Section

Materials. Reagent grade cadmium salts, $Cd(ClO_4)_2·6H_2O$, $CdCl_2·H_2O$, $CdBr_2·4H_2O$, CdI_2, $CdSO_4·^3/_8H_2O$, $Cd(CH_3COO)_2·2H_2O$, $Cd(HCOO)_2·2H_2O$, and $Cd(NO_3)_2·4H_2O$ were obtained from Wako Pure Chemical Inc. and were used without further purification. $Cd(ClO_4)_2·6H_2O$ was dried over P_2O_5 at 60 °C for 3 h under reduced pressure, giving $Cd(ClO_4)_2·2H_2O$. $Cd(ClO_4)_2·2H_2O$ was dissolved in ethanol solutions containing a ligand or the solution of the ligand only. Ethylenediamine (en), 1,3-propanediamine (tn), 1,4-butanediamine (tmd), imidazole (im), and 2- and 4-substituted pyridines (py) were obtained from Wako Pure Chemical Inc. and purified by distillation under reduced pressure (except for 4-CNpy). Reagent grade 2,2′-bipyridine (bpy) and 1,10-phenanthroline (phen) and their derivatives (Tokyo Kasei Co. Ltd.) were used without further purification. Ethanol was dried by heating under reflux over magnesium turnings and then distilled. The other chemicals were reagent grade material.

Syntheses of Cadmium Complexes. Tris(diamine)cadmium (diamine = en, tn, tmd) was prepared by a modified method of Bergerhoff[23] and dissolved in aqueous and ethanolic solutions. Cadmium/imidazole and cadmium/2- and 4-substituted pyridine solutions were prepared by adding $Cd(ClO_4)_2·2H_2O$ to the ethanol solution of the ligand. $[Cd(biL)_3](ClO_4)_2$ (biL = bpy, phen, and their derivatives) were prepared with use of a modified method of Inskeep[24] and dissolved in acetonitrile to form a 0.1 M solution. The samples of (dicarboxylato)cadmium(II) were prepared by adding $Cd(ClO_4)_2·2H_2O$ to sodium dicarboxylate in aqueous solution.

^{113}Cd NMR Spectra. Solution ^{113}Cd NMR experiments were performed at 44.27 MHz on a JEOL FX200 NMR spectrometer equipped with a multinuclear broad-band probe. Tubes of 10- and 15-mm diameter were used throughout. Standard acquisition parameters were as follows: (1) spectral width, 40 kHz; (2) pulse delay, 0.1 ms; (3) acquisition time, 0.02 s; (4) data points, 16 384; (5) pulse width, 14 μs (45° pulse); (6) collected number of scans, 1000–5000. ^{113}Cd chemical shifts are referenced to an aqueous (D_2O) solution of 0.1 M $Cd(ClO_4)_2$ at 23 °C. Shifts to increasing frequency are more positive. Solid $^{113}Cd-^1H$ cross-polarization NMR experiments, with magic-angle spinning, were performed on a JEOL GX270 spectrometer equipped with a GSH-27MU accessory at a frequency of 59.9 MHz for ^{113}Cd. Rotor speeds of 3.8–4.7 kHz were employed. Experimental conditions were as follows: cross-polarization time, 6 ms; spectral width, 50 kHz; acquisition time, 0.03 s; recycle time of the experiments, 5 s; collected number of scans, 100–1000.

Table I. ^{113}Cd NMR Chemical Shifts for $[Cd(en)_3]^{2+}$ at 23 °C

$[Cd(en)_3]X_2$	solvent	concn, M	chem shift, ppm[a]
$[Cd(en)_3](ClO_4)_2$	en	1.0	347
	en	0.5	348
	en	0.25	349
	en	0.1	348
	en	0.05	347
	30% en	0.34	350[b]
$[Cd(en)_3](ClO_4)_2$	H_2O	0.5	347
	H_2O	0.25	346
$[Cd(en)_3](NO_3)_2$	H_2O	0.5	346
$[Cd(en)_3]SO_4$	H_2O	0.5	347
$[Cd(en)_3]Cl_2$	H_2O	0.5	347
$[Cd(en)_3]Br_2$	H_2O	0.5	346
$[Cd(en)_3]I_2$	H_2O	0.5	346
$[Cd(en)_3](NO_3)_2$	Me_2SO	1.0	353[c]
$[Cd(en)_3]Cl_2·H_2O$	solid		361[d]

[a] With respect to 0.1 M $Cd(ClO_4)_2$ aqueous solution at 23 °C. [b] With respect to 0.5 M $Cd(ClO_4)_2$ aqueous solution (Bain, A. D.; Eaton, D. R.; Hux, R. A.; Tong, J. P. K. *Carbohydr. Res.* **1980**, *84*, 1). [c] Reference 22. [d] Solid ^{113}Cd NMR chemical shift.

Results and Discussion

Effect of Cadmium Concentration and Counteranion. The ^{113}Cd chemical shifts of cadmium(II) complexes in solution are sensitive to the concentration and the counteranion. This makes it difficult to correctly determine the chemical shift in solution and has reduced the utility of the ^{113}Cd NMR technique in the solution chemistry of Cd compounds. Elucidation of the origin of the concentration effect is therefore an important problem in solution ^{113}Cd NMR. Maciel and Borzo[25] have shown that the ^{113}Cd chemical shift for the aqueous solution of $Cd(ClO_4)_2$ exhibits a concentration dependence (8.1 ppm) that extends over the concentration range of 0.1–4.2 M. ^{113}Cd spectra of aqueous solutions of $Cd(NO_3)_2$ shift significantly upfield with increasing concentration.[26,27] Addition of KNO_3 to the $Cd(NO_3)_2$ solution also caused significant upfield shift of the ^{113}Cd resonance even without a change in the Cd concentration (Table S-I, supplementary material). For example, a 14 M HNO_3 solution of 1.0 M $Cd(NO_3)_2$ gave −102 ppm, which is close to the solid ^{113}Cd resonance (−100 ppm) of $Cd(NO_3)_2·4H_2O$[28] and indicates the predominant formation of $Cd(NO_3)_2·4H_2O$ in such a high concentration of NO_3^-. Similarly, addition of $NaClO_4$ to the $Cd(ClO_4)_2$ solution led to an upfield shift. The increase in the concentration of the

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Table II. ^{113}Cd Chemical Shifts for Cd(4-Me-py)$_n$ (n = 0–4) in Ethanol Solution

		chem shift at −90 °C, ppm[a]					
[Cd(ClO$_4$)$_2$], M	[4-Me-py], M	A	B	C	D	E	chem shift at 23 °C, ppm[a]
0.5	0.0	−21					−39
0.5	0.5	−21	11	42			−15
0.5	1.0		11	42	72		12
0.5	1.5		11	42	72		33
0.5	2.0				72	101	48

[a] With respect to 0.1 M Cd(ClO$_4$)$_2$ aqueous solution at 23 °C.

Table III. ^{113}Cd NMR Chemical Shifts for Cadmium(II) Complexes with Pyridine Derivatives in Ethanol at −90 °C

		chem shift, ppm[a]				
ligand	pK_a	Cd^{2+}	CdL^{2+}	CdL_2^{2+}	CdL_3^{2+}	CdL_4^{2+}
4-Me-py	6.04	−21	11	42	72	101
4-CH$_2$=CH-py	5.40	−21	11	42	71	98
4-Ac-py	3.51	−21	10	40	67	93
4-CN-py	1.90	−21	9	39		
2-Me-py	5.09	−21	−2	17		

[a] With respect to 0.1 M Cd(ClO$_4$)$_2$ aqueous solution at 23 °C.

cadmium salt itself, needless to say, causes an increase of counteranions and thus promotes the coordination of the anions to cadmium. This led to the conclusion that the concentration dependence of the ^{113}Cd resonance of the cadmium salt solutions is attributable to the coordination of the counteranions to cadmium ions. The chemical shifts of metal nuclei NMR are often obtained at zero anion concentration[29] or an infinite dilution.[26,27] Extrapolations of both of the plots of ^{113}Cd NMR resonances vs. the concentrations of cadmium(II) perchlorate and the anion gave 0.5 ± 0.5 ppm (Figure S-1, supplementary material). What we are interested in on the basis of these observations is the chemical shift of the cadmium(II) complex in which the six coordination sites of cadmium are occupied by the ligands. In ethylenediamine solvent (15 M), the dissociation of $[Cd(en)_3]^{2+}$ scarcely occurs, judging from the stepwise stability constant, log K_3 = 1.76.[30] It should be noted that the ^{113}Cd chemical shift, 348 ± 1 ppm, of $Cd(en)_3^{2+}$ does not exhibit the concentration dependence within experimental error and is almost equal to the solid ^{113}Cd chemical shift (361 ppm) of $Cd(en)_3Cl_2 \cdot H_2O$ (Table I). This finding clearly demonstrates that the ^{113}C chemical shift of the cadmium(II) complex, in which none of the coordinating ligands are substituted for the solvents and the anion, is independent of the concentration.

It is well-known that the counteranions of cadmium salts significantly affect the ^{113}Cd chemical shift.[27] ^{113}Cd chemical shifts were obtained for 0.1 M aqueous solutions of eight popular cadmium(II) salts (Table S-I). For example, $Cd(CH_3COO)_2$ and $CdCl_2$ gave values of −37 and 132 ppm, respectively. The deshielding trend with regard to the ^{113}Cd chemical shifts of the cadmium(II) salts is $CdCl_2 > CdBr_2 > CdI_2 > Cd(ClO_4)_2 > CdSO_4 > Cd(HCOO)_2 > Cd(NO_3)_2 > Cd(CH_3COO)_2$.[31] The ^{113}Cd resonances of these salts shift significantly as the anion concentration increases because of the progression of anion complex formation. For example, 1 M $Cd(HCOO)_2$ in HCOOH and 1 M $Cd(CH_3COO)_2$ in CH_3COOH give −27 and −75 ppm, respectively.

On the other hand, the ^{113}Cd resonances of $Cd(en)_3^{2+}$ were not influenced substantially by the counteranions NO_3^- (346 ppm), SO_4^{2-} (347 ppm), ClO_4^- (347 ppm), I^- (346 ppm), Br^- (346 ppm), and Cl^- (347 ppm) (Table II).

^{113}Cd NMR Spectra of Cd(II) Complexes in the Equilibrium State. The complexes with monodentates such as pyridine do not have a large stability constant. In solution, some species coexist at equilibrium. Reduction of the chemical exchange in cadmium(II) complexes with 4-methylpyridine (4-Me-py) by cooling is illustrated in Figure 1, for which an ethanol solution of 0.5 M

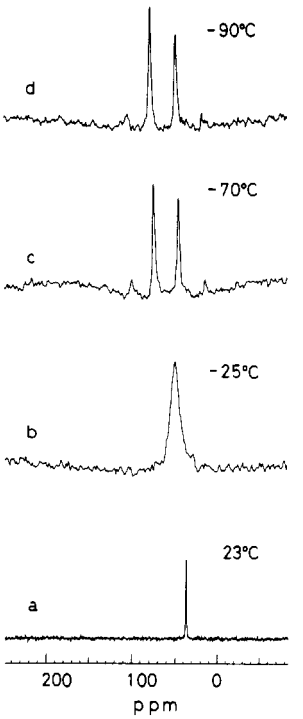

Figure 1. ^{113}Cd NMR spectra of an ethanol solution of 0.5 M Cd(ClO$_4$)$_2$ and 1.5 M 4-methylpyridine. The reference was 0.1 M Cd(ClO$_4$)$_2$ in D_2O at 23 °C; a line broadening of 4.7 Hz was used.

Cd(ClO$_4$)$_2$ and 1.5 M 4-Me-py was examined by ^{113}Cd NMR from +23 to −90 °C. At room temperature (23 °C), a single resonance (Figure 1a) was observed, indicating rapid chemical exchange. As the temperature was lowered, the resonance broadened (Figure 1b) and then resolved into two distinct resonances (Figure 1c,d). The stepwise stability constants, K_n, of $Cd(py)^{2+}$, $Cd(py)_2^{2+}$, and $Cd(py)_3^{2+}$ have been reported to be 19.1, 5.1, and 1.91, respectively.[30] This obviously shows that the stepwise formation of the 4-Me-py complexes progresses from solvated cadmium(II) with an increase in the 4-Me-py concentration. This progression is illustrated in Figure 2. The measured ^{113}Cd chemical shifts are listed in Table II. On the basis of the stability constants and Scheme I, ^{113}Cd chemical shifts can be assigned as follows: A, Cd^{2+}; B, CdL^{2+}; C, CdL_2^{2+}; D, CdL_3^{2+}; E, CdL_4^{2+}. No resonances of the higher order complexes, CdL_5^{2+} and CdL_6^{2+}, were observed even at 10-fold concentration of 4-Me-py to Cd^{2+} ([4-Me-py]/[Cd^{2+}] = 10), indicating that the formation of CdL_5^{2+} and CdL_6^{2+} is very difficult even at low temperature. In fact, only $[Cd(4\text{-Me-py})_4](ClO_4)_2$ was isolated even from 4-Me-py solvent.[32]

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(31) These salts partially dissociate under the conditions.

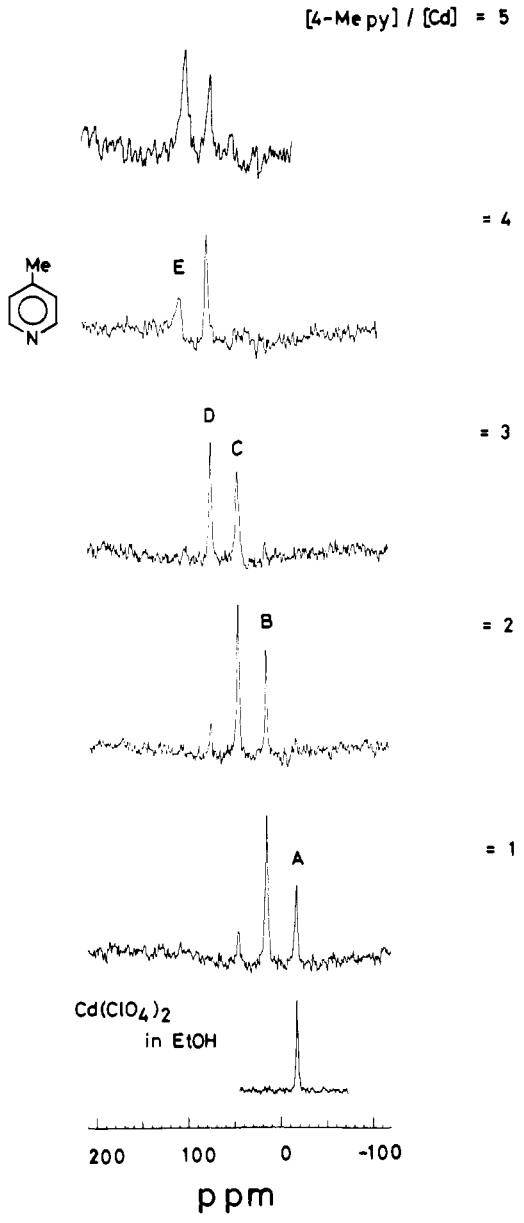

Figure 2. ^{113}Cd NMR spectra of ethanol solutions at −90 °C. All solutions contain 0.5 M $Cd(ClO_4)_2$. The mole ratio of 4-methylpyridine to $Cd(ClO_4)_2$ was varied from 0 to 5. The reference was 0.1 M $Cd(ClO_4)_2$ in D_2O at 23 °C; a line broadening of 4.7 Hz was used.

Similarly, the ^{113}Cd chemical shifts of cadmium(II) complexes with 4-Me-py, 4-cyanopyridine (4-CN-py), 4-vinylpyridine (4-CH_2=CH-py), and 4-acetylpyridine (4-Ac-py) were observed in ethanol solution at −90 °C (Table III). The resonances of Cd-(4-Me-py)$_4^{2+}$ solutions ranging from 0.1 to 0.5 M were independent of the concentration: all of the chemical shifts for 0.1, 0.2, 0.3, and 0.5 M Cd(4-Me-py)$_4^{2+}$ are 101 ppm. Pronounced downfield shifts of ^{113}Cd NMR spectra for the dihalide complexes, CdX_2, in Me_2SO and the trihalide complexes, CdX_3, in water, which result from the change of the octahedral to the tetrahedral complex, have been reported by Drakenberg et al.[18] In the case of cadmium(II) 4-substituted pyridine complexes, the difference in the ^{113}Cd chemical shifts between CdL_{n-1}^{2+} and CdL_n^{2+} is 32–30 ppm for n = 1, 31–30 ppm for n = 2, 30–27 ppm for n = 3, and 27–26 ppm for n = 4: with values slightly decreasing with an increase of numbers of binding L (Table III). In contrast to the halide complexes, no drastic gaps in the shifts were observed for the cadmium(II) 4-substituted pyridine complexes, indicating that

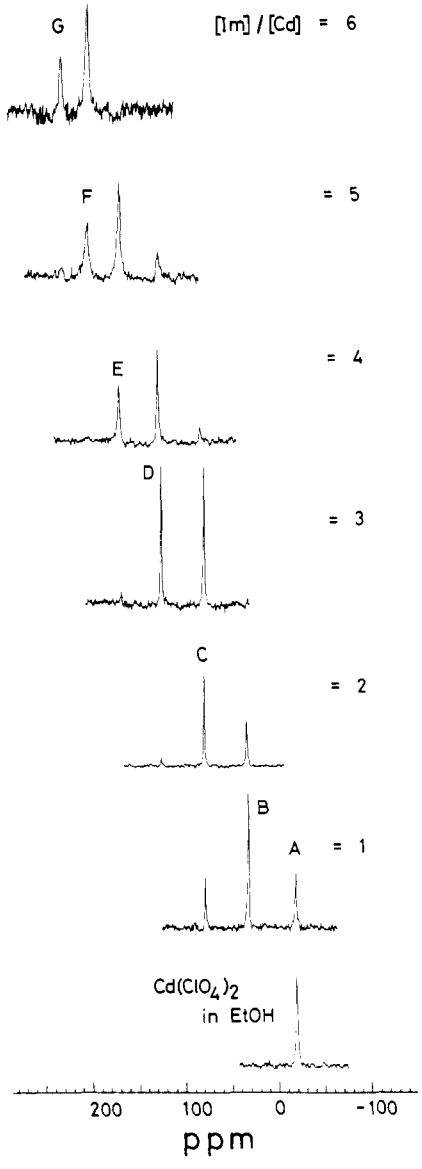

Figure 3. ^{113}Cd NMR spectra of ethanol solutions at −90 °C. All solutions contain 0.5 M $Cd(ClO_4)_2$. The mole ratio of imidazole to $Cd(ClO_4)_2$ was varied from 0 to 6. The reference was 0.1 M $Cd(ClO_4)_2$ in D_2O at 23 °C; a line broadening of 4.7 Hz was used.

no pronounced shifts occur on the geometry change of octahedral to tetrahedral.

Scheme I

$$Cd^{2+} + 6L \rightleftharpoons CdL^{2+} + 5L \rightleftharpoons CdL_2^{2+} + 4L \rightleftharpoons CdL_3^{2+} + 3L \rightleftharpoons CdL_4^{2+} + 2L \rightleftharpoons CdL_5^{2+} + L \rightleftharpoons CdL_6^{2+}$$

In the case of 2-Me-py, only 1:1 and 1:2 complexes, Cd(2-Me-py)$^{2+}$ and Cd(2-Me-py)$_2^{2+}$, were observed and no formation of Cd(2-Me-py)$_3^{2+}$ was observed even at the mole ratio of 2-Me-py to Cd of 20.

The imidazole group occurs in a number of biologically important molecules and plays an important role in the chemistry of several biological systems by providing binding sites in metalloproteins.[33] No slow-exchange ^{113}Cd NMR spectra of cadmium(II) imidazole complexes have yet been studied in solution. Cadmium(II) imidazole complexes show larger stability constants than the corresponding pyridine complexes: K_1 = 631, K_2 = 126, K_3 = 33.5, K_4 = 13.5.[30] Seven ^{113}Cd NMR signals for Cd–imidazole systems were clearly observed separately in ethanol at −90 °C, as illustrated in Figure 3. On the basis of the stability

(32) Anal. Calcd for tetrakis(4-methylpyridine)cadmium(II) perchlorate, $C_{24}H_{28}Cl_2CdN_4O_8$: C, 42.14; H, 4.10; N, 8.19. Found: C, 44.04; H, 4.24; N, 8.51.

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Table IV. NMR Chemical Shifts of Solution and Solid ^{113}Cd NMR for Tris Complexes of Cd with 1,10-Phenanthroline, 2,2-Bipyridine, and Their Derivatives, $Cd(biL)_3^{2+}$, at 23 °C

biL	pK_a	soln[a] chem shift, ppm[b]	solid chem shift, ppm[b]
5-NO_2-phen	3.22	243	229
5-Cl-phen	4.07	247	239
phen	4.93	254	244
5-Me-phen	5.27	259	270
2,9-Me_2-phen	5.85	143	129
4,7-Me_2-phen	5.95	267	
bpy	4.18	243	247
4,4′-Me_2-bpy	5.39	254	265

[a] Acetonitrile solution of 0.05 M $[Cd(biL)_3](ClO_4)_2$. [b] With respect to 0.1 M $Cd(ClO_4)_2$ aqueous solution at 23 °C.

constants and Scheme I, the ^{113}Cd chemical shifts can be assigned as follows: A, Cd^{2+}, −20 ppm; B, $Cd(im)^{2+}$, 32 ppm; C, $Cd(im)_2^{2+}$, 79 ppm; D, $Cd(im)_3^{2+}$, 125 ppm; E, $Cd(im)_4^{2+}$, 167 ppm; F, $Cd(im)_5^{2+}$, 201 ppm; G, $Cd(im)_6^{2+}$, 231 ppm. The chemical shift of $Cd(im)_6^{2+}$ is in good agreement with the solid ^{113}Cd NMR chemical shift.[34] This is the first case in which the seven species in the equilibrium state were successfully observed. The technique used of cooling the nonaqueous solution is very effective for reducing the chemical exchange of a labile cadmium(II) complex. The appeal of this approach derives from the ability to measure the chemical shift directly without the intervention of assumptions regarding the species undergoing exchange. As the stepwise formations of the complexes progress from the solvated Cd(II), ^{113}Cd nucleus deshielding increases, and the differences in the chemical shift between $Cd(im)_{n-1}^{2+}$ and $Cd(im)_n^{2+}$ are 52 ppm for $n = 1$, 47 ppm for $n = 2$, 46 ppm for $n = 3$, 42 ppm for $n = 4$, 34 ppm for $n = 5$, and 30 ppm for $n = 6$. The deshielding efficiency by imidazole slightly decreases with increasing binding numbers of imidazole. The trend is the same as observed for 4-Me-py. Summers and Marzilli[22] reported that ^{113}Cd chemical shifts can be calculated, usually within 5%, by using the following relationship: shift = $75A + 51B + 31C$, where A, B, and C are the numbers of primary, secondary, and tertiary amine donors, respectively. The deshielding constant per tertiary amine, 30 ppm, is reasonable for 4-substituted pyridines but is fairly smaller than the 50–40 ppm for imidazole. The ^{113}Cd chemical shift of cadmium(II) complexes with chelate ligand containing primary amines is also extensively affected by the chelate ring size, as described above. Therefore, the relationship must be carefully used.

Effect of Ligand Basicity. One of the most successful correlations of the stability constant of the metal complex has been with the basicity (pK_a) of the ligand.[35] Indeed there is frequently a linear correlation between pK_a and the logarithm of the stability constant for complex formation.[36] However, no correlations of this fundamental factor, the basicity of the ligand, with the chemical shifts of other metal nuclei as well as ^{113}Cd have been reported.

The ^{113}Cd chemical shifts of $Cd(biL)_3(ClO_4)_2$ in acetonitrile were measured and are summarized in Table IV, where biL is phen, 5-chloro-1,10-phenanthroline (5-Cl-phen), 5-methyl-1,10-phenanthroline (5-Me-phen), 5-nitro-1,10-phenanthroline (5-NO_2-phen), 4,7-dimethyl-1,10-phenanthroline (4,7-Me_2-phen), 2,9-dimethyl-1,10-phenanthroline (2,9-Me_2-phen), and 2,2′-bipyridine (bpy). Similarly to $Cd(en)_3^{2+}$, $Cd(biL)_3^{2+}$ complexes scarcely dissociate in acetonitrile, judging from the stability constant. For example, log K_1, log K_2, and log K_3 for $Cd(phen)_3^{2+}$ are 5.93, 4.59, and 3.78, respectively. In fact, the single resonance of $Cd(phen)_3^{2+}$ did not shift by addition of a large excess of phen and was not split by cooling the solution to −40 °C, indicating

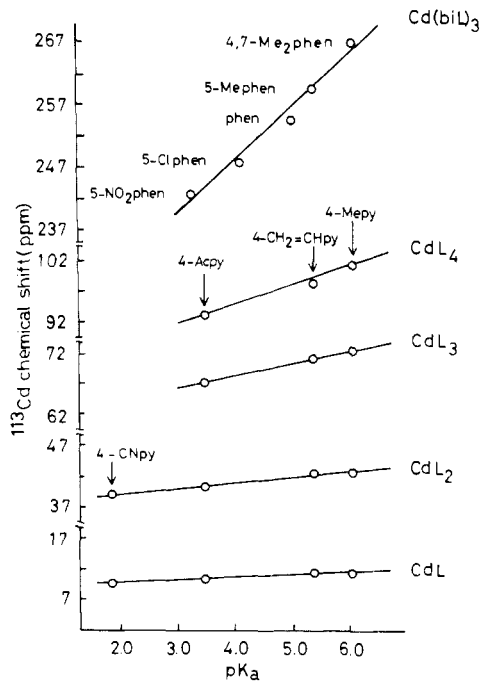

Figure 4. Plot of ^{113}Cd chemical shifts of cadmium complexes with 4-substituted pyridines (L) and 1,10-phenanthroline and its derivatives (biL) against pK_a values of the ligands. The reference was 0.1 M $Cd(ClO_4)_2$ in D_2O at 23 °C.

that the resonance obtained at 23 °C can be assigned to $Cd(phen)_3^{2+}$ but is not an averaged signal. The agreement between the solid and solution ^{113}Cd chemical shifts is within experimental error. Figure 4 illustrates that the ^{113}Cd chemical shift correlates well with the pK_a value of the ligands and the pK_a dependence of ^{113}Cd chemical shifts increases with the progression of complex formation, $CdL^{2+} < CdL_2^{2+} < CdL_3^{2+} < CdL_4^{2+} < Cd(biL)_3^{2+}$, where L and biL represent 4-substituted pyridine and 1,10-phenanthroline derivatives, respectively. It should be noted that the ^{113}Cd nucleus deshielding increases with increasing ligand basicity, i.e., metal–ligand σ bonding. The covalently bonded cadmium(II) complex has been found to yield resonances that are deshielded with respect to those of the corresponding ionic complex.[8,11] Recently, it has been predicted by an ab initio theoretical study on the ^{113}Cd NMR chemical shifts of Cd complexes that the chemical shifts are dominated by the paramagnetic contribution to the shielding constant and increase with increasing electron-donor ability of the ligand.[37] Thus, the above findings demonstrates that ^{113}Cd NMR is extremely useful for providing insight into the cadmium–ligand bonding nature in the cadmium(II) complex.

In contrast with ^{113}Cd, the ^{63}Cu nucleus of the copper(I) complex is deshielded by the π-bonding ligand and the increasing order of deshielding of ^{63}Cu corresponds well to that of the increasing π-acceptor capability of the ligands, RCN < 4-Me-py < 3-Me-py < py < RNC < ArNC, rather than the basicity.[38] The deshielding order of ^{113}Cd nuclei of halide complexes, $CdCl_4^{2-} > CdBr_4^{2-} > CdI_4^{2-}$,[17-19] also differs from that of ^{63}Cu nuclei, CuI > CuCl > CuBr.[39] Although both Cd(II) and Cu(I) are closed-shell (d^{10}) cations, Cu(I) is a softer acid than Cd(II).[40] Soft metal ions prefer to coordinate soft ligands and hard metal ions prefer to coordinate hard ligands.[41] The ab initio theoretical study has shown that the ^{63}Cu NMR chemical shift increases with increasing electron acceptability of the ligand.[37] Therefore, it is not surprising that ^{113}Cd chemical shifts correlate well with the

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Table V. ^{113}Cd Chemical Shifts of Cd(diamine)$_3^{2+}$, Stability Constants, β_n, of Cd(diamine)$_n^{2+}$ (n = 1–3), and pK_a Values of Diamines

diamines	log β_1[a]	log β_2[a]	log β_3[a]	pK_a[a]		chem shift ppm[b]
$H_2N(CH_2)_2NH_2$ (en)	5.45	9.98	11.74	7.08	9.89	347
$H_2N(CH_2)_3NH_2$ (tn)	4.50	7.20	8.0	8.74	10.52	259
$H_2N(CH_2)_4NH_2$ (tmd)	3.60			9.44	10.72	227
$CH_3NH(CH_2)_2NHCH_3$	5.20	8.74	10.59	7.01	9.98	229

[a] Reference 30. [b] ^{113}Cd chemical shifts of 0.5 M Cd(diamine)$_3$(ClO$_4$)$_2$ aqueous solution, with respect to 0.1 M Cd(ClO$_4$)$_2$ aqueous solution at 23 °C.

basicity of the ligand, whereas ^{63}Cu chemical shifts are sensitive to the π-acceptor capability of ligands.

Steric factors in the formation and structure of a metal complex are as important as the basicity of the ligand. The cadmium(II) complexes with 2-methylpyridine (2-Me-py) and 2,9-Me$_2$-phen Cd(2-Me-py)$^{2+}$, Cd(2-Me-py)$_2^{2+}$, and Cd(2,9-Me$_2$-phen)$_3^{2+}$[42] yielded resonances that were remarkably shielded with respect to the corresponding mono(4-substituted pyridine), bis(4-substituted pyridine), and tris(4,5,7-substituted 1,10-phenanthroline) complexes, respectively (Tables IV and V). It is well-known that substitution at the 2- and 6-positions of pyridine, the 6- and 6′-positions of bpy, and the 2- and 9-positions of phen lowers the stability of the complex formed because the substituents crowd the metal ion.[30,43] The upfield shift of the ^{113}Cd NMR resonance of the Cd complexes with 2-Me-py and 2,9-Me$_2$-phen reflects well the steric hindrance of the methyl groups.

Effect of Chelate Ring Size. The ^{113}Cd chemical shifts of 0.5 M tris(diamine)cadmium(II) complexes in the corresponding diamine were observed at 23 °C and summarized in Table V. The dissociation of Cd(en)$_3^{2+}$ is negligible because of the large stability constant. In fact, the ^{113}Cd chemical shifts of 0.5 M Cd(en)$_3^{2+}$ in aqueous (347 ppm) and ethylenediamine (348 ppm) solutions are substantially the same as that, 353 ppm, for Cd(en)$_3^{2+}$ in Me$_2$SO and were not affected by the counteranions and the complex concentration, as described above. This demonstrates that the resonance observed for a tris(diamine)cadmium solution at 23 °C is due to Cd(diamine)$_3^{2+}$ but is not an averaged signal. Similarly, the dissociation of another tris(diamine)cadmium(II) complex can be considered to be negligible from its stability constant.

The shifts are extensively affected by the chelate ring size of ethylenediamine (en), 1,3-propanediamine (tn), and 1,4-butanediamine (tmd). It should be noted that the deshielding order is five- > six- > seven-membered chelate ring; i.e., Cd(en)$_3^{2+}$ > Cd(tn)$_3^{2+}$ > Cd(tmd)$_3^{2+}$. The same trend was found in the series of the dicarboxylate, oxalate (ox), malonate (mal), succinate (suc), and glutarate (glu) complexes and in the series of dithiolate,[11] 1,2-ethanedithiolate (edt), 1,3-propanedithiolate (pdt), 1,4-butanedithiolate (bdt), and 1,5-pentanedithiolate (pedt) complexes: Cd(ox) (−1 ppm) > Cd(mal) (−2.6 ppm) > Cd(suc) (−9 ppm) > Cd(glu) (−25 ppm); Cd(edt) (829 ppm) > Cd(pdt) (663 ppm) > Cd(bdt) (648 ppm) > Cd(pedt) (646 ppm).[11]

In general, the stability of a chelate complex decreases as the chelate ring size increases from five to eight members,[44] because the size and preferred bond angles for carbon atoms usually make the five-membered ring the most stable, unlike organic ring systems, and then the chelate ring strain increases with the number of members.[45] For example, in tris(diamine)cobalt(III) the Co–N bond distance increases as the chelate ring size increases from five to seven members; [Co(en)$_3$]$^{3+}$ (1.978 Å[46]) < [Co(tn)$_3$]$^{3+}$ (1.979 Å[47]) < [Co(tmd)$_3$]$^{3+}$ (1.991 Å[48,49]). This demonstrates

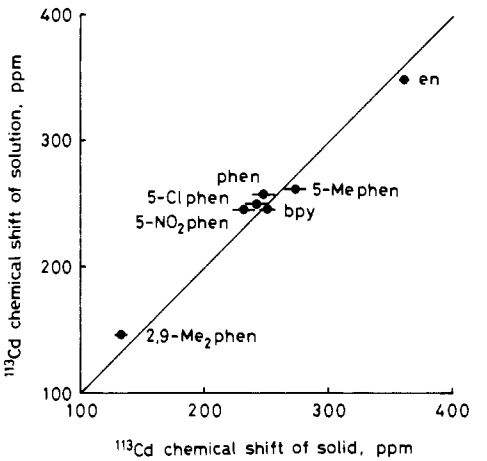

Figure 5. Comparison of the ^{113}Cd chemical shifts of Cd(biL)$_3^{2+}$ complexes between solution and solid. The rod length represents line width of the solid NMR spectra. The reference was 0.1 M Cd(ClO$_4$)$_2$ in D$_2$O at 23 °C.

that a five-membered chelate ring can form with the least strain and the strain increases as the number of members increase. It should be kept in mind that the chelate ring strain overcomes the basicity because the pK_a values of the diamines increase in the order of en (7.08 and 8.89) < tn (8.74 and 10.52) < tmd (9.44 and 10.72). The decreasing order of the stability constants of Cd–diamine complexes, Cd(en)$_n^{2+}$ > Cd(tn)$_n^{2+}$ > Cd(tmd)$_n^{2+}$, shows that the chelate ring strain also increases in the order of Cd(en)$_3^{2+}$ < Cd(tn)$_3^{2+}$ < Cd(tmd)$_3^{2+}$, which corresponds well to the decreasing order of deshielding of the ^{113}Cd nucleus (Table V). It is concluded that the larger the chelate ring strain of the Cd complex is, the more the ^{113}Cd nucleus is deshielded. Cd(bpy)$_3^{2+}$ and Cd(phen)$_3^{2+}$ lead to a further upfield shift than Cd(en)$_3^{2+}$ in spite of the five-membered chelate ring. This may be mainly attributable to the low basicity of bpy (pK_a = 4.18) and phen (pK_a = 4.93). The replacement of en in Cd(en)$_3^{2+}$ with N,N'-Me$_2$-en produces a upfield shift of nearly 118 ppm. The pronounced upfield shifts suggest steric hindrance of the methyl groups, which weakens the Cd–N bond because both pK_a values are almost the same.

Comparison of Solution ^{113}Cd NMR Spectra with the Solid NMR Spectra. One of the most important advantages of the ^{113}Cd NMR technique is its applicability to both solutions and solids. Comparison of ^{113}Cd chemical shifts between the solution and the solid NMR is especially noteworthy in connection with the effects of solvent, packing, and counteranion upon the structure of the cadmium complexes. The ^{113}Cd NMR spectra of solid [Cd(biL)$_3$](ClO$_4$)$_2$ complexes were measured (Table IV). The line width, 700–1900 Hz, are very large compared with those in solution (10–40 Hz). A plot of the solution ^{113}Cd chemical shifts of Cd(II) complexes with en and biL vs. those of the solid give a good linear correlation with the slope equal to 1 as shown in Figure 5. This is the first systematic comparison of both chemical shifts. The good linear correlation clearly demonstrates that the structures of these cadmium complexes in solution are substantially

(42) Anal. Calcd for tris(2,9-dimethyl-1,10-phenanthroline)cadmium(II) perchlorate, $C_{42}H_{36}Cl_2CdN_6O_8$: C, 53.89; H, 3.88; N, 8.98. Found: C, 52.26; H, 3.48; N, 8.47.

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(44) The stability constants of Cd(ox), Cd(mal), Cd(suc), and Cd(glu) are > $10^{2.33}$, $10^{2.3}$, $10^{2.1}$, and $10^{2.0}$, respectively.[30] For Cd(diamine)$_3$, see Table V.

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(49) The Co–N bond distances in parentheses are average values.

the same as those in the solid state when ligand dynamics are unimportant in the solution.

Conclusions

The present work yielded the following results. (1) ^{113}Cd chemical shifts of cadmium salts are very sensitive to the counteranions and the concentration. However, no effect is observed on $Cd(en)_3^{2+}$, in which no en is replaced by the anions. Thus, the effects of the counteranion and the concentration are attributable to the coordination of the counteranion to the cadmium. (2) ^{113}Cd nucleus deshielding of Cd complexes increases with increasing pK_a of the ligand, i.e., Cd-ligard σ bonding and the progression of ligand substitution. For example, $Cd(4\text{-Me-py})_4^{2+}$ exhibits a downfield shift of 8.8 ppm/pK_a unit. (3) As the chelate ring size of cadmium chelate compounds decreases from eight to five members, the ^{113}C nucleus of the compounds becomes more deshielded due to the decrease of chelate ring strain. (4) The exchange rates of the cadmium complexes with imidazole and pyridine and its derivatives were sufficiently reduced by cooling of the nonaqueous solution, such as ethanol, and all ^{113}Cd resonances of several species at equilibrium state can be clearly observed separately. (5) The chemical shifts of the solution NMR spectra of cadmium complexes with im, en, bpy, phen, and the derivatives agree well with those of the solid NMR spectra, indicating that both structures are substantially the same.

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Registry No. $[Cd(en)_3](ClO_4)_2$, 100515-34-2; $[Cd(en)_3](NO_3)_2$, 56123-55-8; $[Cd(en)_3]SO_4$, 41305-53-7; $[Cd(en)_3]Cl_2$, 15613-78-2; $[Cd(en)_3]Br_2$, 56123-54-7; $[Cd(en)_3]I_2$, 92798-55-5; $Cd(en)_3^{2+}$, 18153-92-9; $Cd(tn)_3^{2+}$, 66862-16-6; $Cd(tmd)_3^{2+}$, 100515-37-5; $Cd(CH_3NH(CH_2)_2NHCH_3)_3^{2+}$, 88425-83-6; $Cd(5\text{-}NO_2\text{-phen})_3^{2+}$, 100570-89-6; $Cd(5\text{-Cl-phen})_3^{2+}$, 100515-35-3; $Cd(phen)_3^{2+}$, 30261-46-2; $Cd(5\text{-Me-phen})_3^{2+}$, 37662-38-7; $Cd(2,9\text{-}Me_2\text{-phen})_3^{2+}$, 100570-90-9; $Cd(4,7\text{-}Me_2\text{-phen})_3^{2+}$, 38614-63-0; $Cd(bpy)_3^{2+}$, 18475-59-7; $Cd(4,4'\text{-}Me_2\text{-bpy})_3^{2+}$, 100515-36-4; ^{113}Cd, 14336-66-4.

Supplementary Material Available: Table S-I, showing NMR chemical shifts of cadmium salts at 23 °C, and Figure S-1, showing the effects of concentrations of $Cd(ClO_4)_2$ and ClO_4^- on the ^{113}Cd chemical shifts (2 pages). Ordering information is given on any current masthead page.

Contribution from the Departments of Chemistry, University of St. Andrews, St. Andrews, Fife KY16 9ST, U.K., and University of Edinburgh, Edinburgh EH9 3JJ, U.K.

Carbon-13 NMR Study of the Binding of Nitroprusside and Hexacyanoferrate(II) to Aquocobalamin, Vitamin B_{12a}

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High-frequency ^{13}C NMR spectroscopy using nitroprusside 90% enriched in ^{13}C shows that nitroprusside forms discrete 1:1 and 1:2 complexes in solution with aquocobalamin (vitamin B_{12a}). No binding occurs with cyanocobalamin (vitamin B_{12}), and it is concluded that the complexes contain Fe-C-N-Co fragments, involving in the 1:1 complex the axial cyano ligand and in the 1:2 complex a trans pair of equatorial cyano ligands. Similar complexes are formed between hexacyanoferrate(II) and aquocobalamin (but not cyanocobalamin), showing that the nitrosyl ligand is not crucial for complex formation. Similar, but much weaker, complexes are formed between nitroprusside or hexacyanoferrate(II) and the simpler complex aquomethylcobaloxime.

Introduction

Sodium nitroprusside, $Na_2[Fe(CN)_5NO]\cdot 2H_2O$, is a powerful hypotensive agent that is widely used in the treatment of severe hypertension, in the management of myocardial infarction, and in the induction of surgical hypotension.[1] Although nitroprusside is a valuable drug, there have been many reports[2,3] that the nitroprusside ion is metabolized in red blood cells with rapid release of cyanide into the bloodstream. However our own work[4-6] has cast considerable doubt on a number of earlier reports: we have found no decomposition of nitroprusside in whole blood[6] but find on the other hand that, under the analytical conditions normally employed for the determination of cyanide,[7] ready liberation of cyanide occurs from the primary photoproduct[8] of nitroprusside, the labile d^5 aqua ion $[Fe(CN)_5H_2O]^{2-}$. Furthermore, the photolysis of nitroprusside is rapid under normal lighting conditions.

As a possible antidote to potential cyanide poisoning induced by the administration of nitroprusside, independent of whether the cyanide is derived from a metabolic or a photochemical process, the use of aquocobalamin has been suggested[9] (this material is often referred to as hydroxocobalamin; but its pK_a is 8.1, and hence at physiological pH, it is primarily in the aquo form[10]). While some reports indicate that the administration of aquocobalamin alongside nitroprusside reduces levels of free cyanide in both red cells and plasma,[3,9,11] others suggest that aquocobalamin raises free cyanide.[12]

Preliminary experiments[13] have shown that aquocobalamin significantly influences the pharmacokinetics of the hypotensive action of nitroprusside, suggesting the possibility that aquocobalamin, far from merely being an antidote[9] to potential cyanide liberation from nitroprusside, actually interacts with the nitro-

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