The Chemistry of Vitamin B_{12}. Part 30.[1] Co-ordination of Amines, Pyridines and Diazines by Aquacyanocobinamide; Nitrogen-containing Bases as Probes for Basicity and Other Effects in Metal–Ligand Bonding

Mohamed S. A. Hamza and John M. Pratt*
Department of Chemistry, University of Surrey, Guildford GU2 5XH, UK

Equilibrium constants K have been determined by UV/VIS spectrophotometry for the substitution of co-ordinated H_2O in the cobalt(III) corrinoid aquacyanocobinamide by NH_3, four primary alkylamines (pK values 5.3–8.5), NH_2NH_2, NH_2OH, pyridine, four 4-substituted pyridines (pK values 1.9–9.8) and three diazines in aqueous solution with I *ca.* 0.1 mol dm^{-3} at 25 °C. The results demonstrate that both the amines and the six-membered heterocycles obey the linear free energy relationship $\log K = a{\cdot}pK + b$, where $a = 0.58$ and $b = -2.6$ for the amines and $a = 0.47$ and $b = +0.2$ for the azines, and that NH_2NH_2, NH_2OH and the 1,2-diazine pyridazine all show enhanced values of log K which can be ascribed to operation of the α effect. Present and published data have been summarised to show that bases belonging to the three families (amines, six-membered heterocycles and five-membered heterocycles) can routinely be used to probe the role of at least four factors (basicity, the 'group-specific' factors which distinguish the three families, the α effect and steric effects) in metal–ligand bonding.

We have been studying the co-ordination of various nitrogen-containing bases belonging to three families (*viz.* amines with sp^3-hybridised N and five- and six-membered heterocycles with sp^2-hybridised N) by the iron(III) porphyrin microperoxidase-8 (MP-8)[2–5] and by cobalt(III) corrinoids.[1,6] Particular emphasis has been placed on establishing for each family the 'baseline' corresponding to the linear free energy relationship (1),[7] where

$$\log K = a{\cdot}pK + b \qquad (1)$$

K is the stoichiometric equilibrium constant for the substitution of co-ordinated H_2O by the particular base and pK refers to protonation of the free base.

Possible increases in log K (*e.g.* due to operation of the so-called α effect) and decreases in log K (due to steric hindrance) can then be more quantitatively assessed by reference to the values expected from the baseline. Because of their relevance to bioinorganic chemistry we have been particularly interested, first, in establishing whether imidazole (Him) and other five-membered azoles form a family distinct from the six-membered pyridines and diazines in terms of equation (1) and, secondly, in testing if the α effect is operative in metal–ligand bonding. Five-membered azoles provide the main ligands for haemoproteins (His) and for the cobalt corrinoids (*e.g.* 5,6-dimethylbenzimidazole). The α effect is the term given to the excess of reactivity (*e.g.* in organic substitution reactions) above that expected from basicity alone and exhibited by nucleophiles where the donor atom is attached directly to an electronegative atom with one or more lone pairs of electrons.[8] Of the three ligands of interest here, NH_2NH_2 and NH_2OH were both used as exemplars in the original discussion of the α effect in 1962,[8] while the 1,2-diazine pyridazine was shown to exhibit the α effect in 1972.[9] Many potential 'α-effective' ligands such as O_2^-, H_2O_2 and HO_2^-, HN=NH (in N_2 reduction) and NH_2OH (in NO_2^- reduction) are of particular interest to bioinorganic chemists.

Both the α effect and the azole/azine distinction were first noticed in the 1950s in the form of unexpectedly high rate constants in organic substitution reactions. Available rate constants relating to the phenomenon, to be termed the 'α effect' by Edwards and Pearson[8] in 1962, had been collected and reviewed by Jencks and Carriuolo[10] in 1960. Although organic chemists have been well aware of the α effect in rate constants, it was only shown to be associated with enhanced equilibrium constants involving nitrogen-containing bases as the acceptor in hydrogen bonding by Abraham *et al.*[11] as recently as 1989 and as a ligand in co-ordination to MP-8 by us in 1993.[3,4] In spite of the fact that Edwards and Pearson pointed out that they could find no example of the α effect in co-ordination chemistry, this effect appears to have been largely ignored or forgotten by co-ordination chemists apart from a brief suggestion by Taube[12] in 1986 about its possible role in complexes involving O_2^-. The greater reactivity of imidazoles over pyridines was reported by Bruice and Lapinski[13] in 1958 and, although noted by Jencks and Carriuolo,[10] was not included by Edwards and Pearson[8] in their review. The azole/azine distinction at the thermodynamic level was first established in co-ordination to the silver(I) ion by Nakatsuji *et al.*[14] in 1969 and only subsequently in hydrogen bonding[11] and then by us in co-ordination to MP-8[5] and to aquacyanocobinamide.[1] Both organic and co-ordination chemists seem to have been generally unaware of either the 1958 or 1969 work. The development from rate to equilibrium constants involving known ground-state geometries will allow a much more realistic analysis of possible origins of both the α effect and the azole/azine distinction.

In the preceding paper[1] we reported values of K for the co-ordination of imidazole and other members of the azole series by the cobalt(III) corrinoid aquacyanocobinamide [(aq,CN)Cbi]. In this paper we report analogous results on the co-ordination both of sp^3 amines and of the six-membered azine series. The reasons for selecting (aq,CN)Cbi have already been explained.[1] The CN^- ligand is very firmly held and can be considered as inert (at least in the dark), while the H_2O ligand is kinetically very labile. Conversion to the hydroxo complex occurs with pK 11.0,[15a] so that the co-ordination of typical amines with pK values in the range 10–11 can be studied without undue problems arising from competition with OH^- as ligand (contrast MP-8). Aquacyanocobinamide exists as an approximately equal mixture of the two axial isomers which are fairly readily interconverted (*e.g.* in the presence of a trace of free

CN^-),[15b] but their existence is ignored here. Values of log K have previously been published for the co-ordination by (aq,CN)Cbi of NH_3,[16] the three methylamines,[6] pyridine (py),[16] imidazole,[16,17] histamine,[17,18] benzimidazole[16] and the anions derived from imidazole, benzimidazole and adenine.[16] The published values for NH_3, NH_2Me and py have been included in Table 1 and values for NH_3 and py have also been redetermined.

The 'probe' ligands used to test equation (1) for (aq,CN)Cbi (*viz.* ligands 1–6 and 9–15 in Table 1) are the same as those used previously for MP-8.[3,4] The range of pK values available in each series of 'probe' ligands, and hence the accuracy of the test, has increased greatly since the initial work with silver(I) from a span of 1.3[23] to over 5 pK units (pK 5.3–10.6) in the case of the amines (due to inclusion of amines with electronegative substituents such as CN, as first used by Brown *et al.*[24]), from 1.5[23] to over 9 (0.4–9.8) in the azine series (through the inclusion, first, of pyridines with Cl and CN substituents[25] and, then, of the diazines)[4] and from 2.5[14] to 12 (pK 2.3–14.3) in the azole series (through the inclusion of 1,2,4-triazole and the conjugate anions[1,5]). The main shortcoming at present is the lack of suitable amines with a pK below 5. It is curious that Berthon and Enea studied the co-ordination of both pyridines[26] and diazines[27] by silver(I), but in separate papers, and failed to note that they formed a single continuous series, while Toma and Creutz[28] included pyrazine (pyz) and its N-methyl cation in a more general study of nitrogen-containing bases (including imidazole, NH_3 and three pyridine bases) but were not interested in possible differences between the families.

The aims of this paper are (*i*) to confirm that the linear relationship (1) applies to the co-ordination both of amines (using ligands 1–6 in Table 1) and the series of pyridines and diazines (ligands 9–15) by (aq,CN)Cbi and to determine the values of a and b in equation (1) for the two families and (*ii*) to test whether NH_2NH_2, NH_2OH and the 1,2-diazine pyridazine (pydz) (ligands 7, 8, 16) show an enhanced value of log K (above that expected from the baseline) which could be ascribed to the α effect. Since this paper represents completion of the first stage of our present studies on the co-ordination of nitrogen-containing bases, involving parallel studies on the iron(III) porphyrin MP-8 and the cobalt(III) corrinoid (aq,CN)Cbi, we also (*iii*) summarise the patterns observed using nitrogen-containing bases as 'probe' ligands to test for basicity and other effects.

Experimental

Materials.—Aquacyanocobinamide was prepared from cyanocobalamin (vitamin B_{12}) (BDH) as previously described.[29] The nitrogen-containing bases were obtained as follows: 2,2,2-trifluoroethylamine and 4-(dimethylamino)pyridine from Fluka; $NH_2CH_2CN{\cdot}HCl$ and β-aminopropionitrile (monofumarate salt) from Sigma; $N_2H_4{\cdot}H_2O$ from BDH; $NH_2OH{\cdot}HCl$ and all the remaining amines and heterocycles from Aldrich. To remove impurities which interfered with the spectrophotometric titration 4-cyanopyridine was purified by recrystallisation from a CH_2Cl_2–Et_2O mixture[30] and pydz by distillation; all other reagents were used as received.

Methods.—UV/VIS spectra were recorded and spectrophotometric titrations carried out on a Philips PU 8740 or 8720 spectrophotometer in a 1 cm pathlength cell (except where otherwise stated), thermostatted at 25 °C and containing a *ca.* 10^{-5} mol dm^{-3} aqueous solution of (aq,CN)Cbi. For quantitative work the ionic strength was fixed at *ca.* 0.1 mol dm^{-3} using $NaHCO_3$–Na_2CO_3 buffers for reagents 14 and 15 (with high pK values), phosphate buffer pH 6.5 for reagents 7 and 8 (which act as reducing agents at higher pH) and phosphate buffer pH 9.0 for all the other bases. Solutions of the reagents were prepared by titrating the free base with $HClO_4$ or the acid salt with NaOH to the appropriate pH before adding the buffer. Where necessary (*e.g.* to check the buffers, to confirm no change in pH at high concentrations of added base), pH measurements were made with a Hanna HI B417 pH meter and appropriate glass electrode standardised at pH 4.00 and 7.00.

Table 1 Equilibrium constants K for the substitution of co-ordinated H_2O in (aq,CN)Cbi by amines and azines at 25 °C with I *ca.* 0.1 mol dm^{-3}

Ligand		pK of free base[a]	log K[b]/ dm^3 mol^{-1}	λ_γ[c]/nm
1	NH_2CH_2CN	5.3	0.55	357.5
2	$NH_2CH_2CF_3$	5.7	0.78	357
3	$NH_2CH_2CH_2CN$	7.7	1.6	357.5
4	$NH_2CH_2CH_2Br$	8.5	2.5	358
5	NH_3	9.25	3.15[d]	360
6	NH_2Me	10.62	3.4[e]	362
7	NH_2NH_2[f]	8.12	3.1	359
8	NH_2OH[f]	5.96	2.46[g]	359
9	Pyrazine	0.37 (0.65)	0.6	360
10	Pyrimidine	1.10	0.7	361
11	4-Cyanopyridine	1.9	0.9	358
12	Pyridine	5.17	2.3[h]	361
13	4-Methylpyridine	6.02	3.1	362.5
14	4-Aminopyridine	9.11	4.6	362.5
15	4-(Dimethylamino)-pyridine	9.76	4.75	363
16	Pyridazine[f]	2.33	2.6	*i*

[a] Values of pK from ref. 19 except for 4-(dimethylamino)pyridine from ref. 20 and the value for pyrazine in parentheses from ref. 21. [b] All values of log K ± 0.1 or better but ± 0.2 for ligands 1 and 9–11, where the end-point could not be observed directly. [c] Values ± 0.5 nm or, for ligands 1 and 9–11, ± 1 nm. [d] *cf.* 3.35 in ref. 16. [e] From ref. 6. [f] Ligands used to probe the α effect. [g] *cf.* 2.4 in ref. 22. [h] *cf.* 2.6 in ref. 16. [i] Impossible to locate maximum accurately because of the rising background absorption.

Results

The amines and heterocycles studied here, together with their published pK values, are listed in Table 1. Preliminary experiments, scanning the spectrum over the range 300–600 nm, showed that all the bases gave products showing very similar spectra with the main γ band situated in the range 357–362 nm for the amines and 358–363 nm for the heterocycles (see Table 1) compared to 354 nm in the starting (aq,CN)Cbi; *cf.* the spectrum of (aq,CN)Cbi and its imidazole complex shown in Fig. 2 of ref. 1. Equilibrium was established rapidly in each case, good to excellent isosbestic points were observed (at *ca.* 315, 357, 380, 508 and 530 nm) and, where studied, co-ordination of the base could be reversed by acidification. The only complication observed was the appearance of the 470 nm band of cobalt(II) due to some reduction by NH_2NH_2 and NH_2OH at pH ⩾ 8, hence the quantitative work was carried out at pH 6.5.

Quantitative determinations of the equilibrium constants K were carried out in duplicate titrations under the conditions given above, following the rise in absorbance in the region of either the α or the γ band (*i.e. ca.* 550 or 360 nm). Analysis of the data confirmed a stoichiometry of 1.0 ± 0.1 base per Co in each case and gave the values of log K listed in Table 1. Qualitative tests were carried out to exclude the possible formation of bridged dimers with both NH_2NH_2 and pyz; varying the Co concentration over a 10-fold range (from low concentration in 4 cm cells to high concentration in 1 cm cells) under conditions of pH and ligand concentration chosen to give *ca.* 50% formation of the complex showed no significant difference in spectrum, *i.e.* provided no evidence for a cobalt-dependent monomer–dimer equilibrium.

Discussion

Table 1 lists the values of log K determined here for both series of nitrogen-containing bases, together with published values for NH_3, py (both redetermined here) and NH_2Me (not redetermined), the pK for protonation of the free base and the wavelength of the main (γ) band of the product. No corrections have been made for statistical factors (see ref. 5). All the equilibria correspond to one base per Co and no evidence for the formation of any dimer was found with the potentially bridging ligands NH_2NH_2 and pyrazine. All the complexes with bases show very similar spectra (*cf.* Fig. 2 of ref. 1) with a slight but generally systematic shift in the γ band to longer wavelength as the basicity increases: from 357 to 362 nm in the amines and from 358 to 363 nm in the azine series (see Table 1) compared to a shift from 359.5 to 361 nm in the neutral azoles and further to 363 nm with imidazolate.[1] With MP-8 there is a parallel but smaller shift with basicity, *viz.* 403–404 nm for the amines,[3] 403–405 nm for the azines[4] and 404–405 nm for the neutral azoles but out to 407 nm for imidazolate.[5]

The values of log K for co-ordination are plotted against the pK for protonation of the free ligand (all values from Table 1) for the amines in Fig. 1 and the azines in Fig. 2; open circles denote the three ligands used to test for the α effect. The filled square corresponds to use of the higher pK given in parentheses for pyz; the higher pK clearly gives a better fit both here and with MP-8[4] and will be used in future. Ignoring the three open circles, both families show a reasonably good linear dependence of log K on pK in agreement with equation (1) for over 5 pK units with $a = 0.58$ and $b = -2.6$ in the case of the amines and for over 9 pK units with $a = 0.47$ and $b = 0.18$ (*i.e.* 0.2) in the case of the azines including two diazines; *cf.* the azole series with $a = 0.4$ and $b = 1.3$ for over 12 pK units.[1] As in the case of MP-8,[4,5] the six-membered azine and five-membered azole series are distinct. Preliminary experiments suggest that pyrazole and 1,2,3-triazole, which are known to behave somewhat differently from imidazole and 1,2,4-triazole towards the proton in solution and in the gas phase (see references given elsewhere),[5] behave more like azines than azoles.[31] Comparison of the values of log K observed for NH_2NH_2 (3.1), NH_2OH (2.5) and the 1,2,diazine pydz (2.6) with those expected from the relevant baseline (*viz.* 2.1, 0.9 and 1.3) show that the values of log K have been significantly increased in all three cases (by *ca.* 1.0, 1.6 and 1.3); as in the case of MP-8,[3,4] this increase can be ascribed to operation of the α effect.

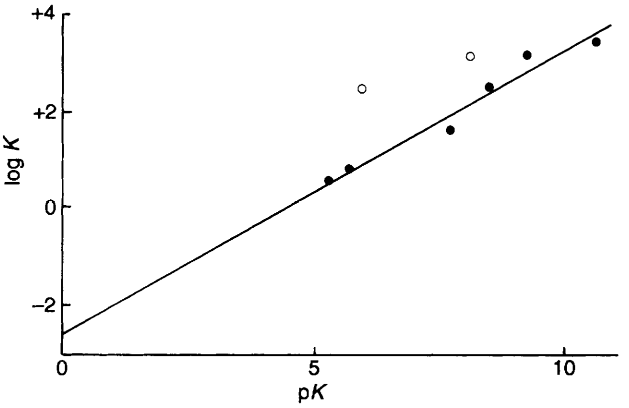

Fig. 1 Plot of log K (for co-ordination) *vs.* pK (for protonation of the free base) for the amines. Data from Table 1 (ligands 1–8). The two open circles indicate the ligands NH_2NH_2 and NH_2OH used to test for the α effect. The solid line corresponds to the equation log K = 0.58 pK − 2.6

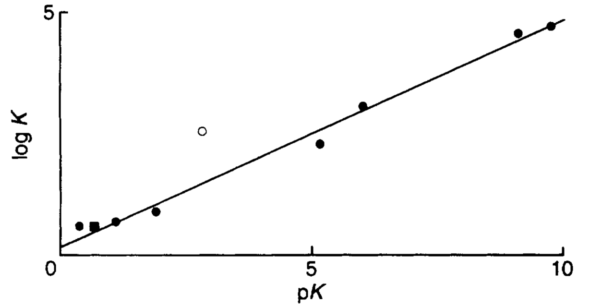

Fig. 2 Plot of log K (for co-ordination) *vs.* pK (for protonation of the free base) for the six-membered pyridines and diazines. Data from Table 1 (ligands 9–16); the filled square corresponds to use of the higher pK 0.65 for pyz (given in parentheses in Table 1). The open circle denotes the ligand pydz used to test for the α effect. The solid line corresponds to the equation log K = 0.47 pK + 0.18

The results on (aq,CN)Cbi in this and the previous paper,[1] together with our results on MP-8[3–5] and related data in the literature, are discussed in terms of (*a*) basicity effects, the values of *a* and *b* in equation (1) and the differences between azoles and azines in particular, and (*b*) the α effect. We have shown earlier[6] that α branching in the amines reduces the value of log K towards (aq,CN)Cbi ($NH_3 \approx NH_2Me > NHMe_2 > NMe_3$); steric effects will be discussed again in a later publication.

Basicity Effects and 'Group-specific' Factors.—The values of *a* and *b* which we have determined for the three families of nitrogen-containing bases with the two metal ions [in MP-8 and (aq,CN)Cbi] are listed in Table 2, together with published values of *a* and *b* for the analogous equilibria where the base acts as the acceptor in hydrogen-bond formation in an organic solvent and rough values for the nitriles which we have calculated from the line given in Fig. 8 of ref. 11. The three baselines observed with (aq,CN)Cbi are compared in Fig. 3; for the analogous comparison in the case of MP-8 see Fig. 3 of ref. 5. The data in Table 2 show that there are basic similarities between co-ordination and hydrogen bonding in spite of the very different equilibria and solvents: for each Lewis acid the values of *a* fall slightly in the order amines > azines > azoles, while the values of *b* increase significantly in the same order. The two types of equilibria are complementary: hydrogen-bond formation in an organic solvent allows one to study some nitrogen-containing bases (*e.g.* RCN) and many oxygen-containing bases which could not compete with H_2O, while co-ordination in aqueous solution allows one to study charged species which could not easily be formed in an organic solvent.

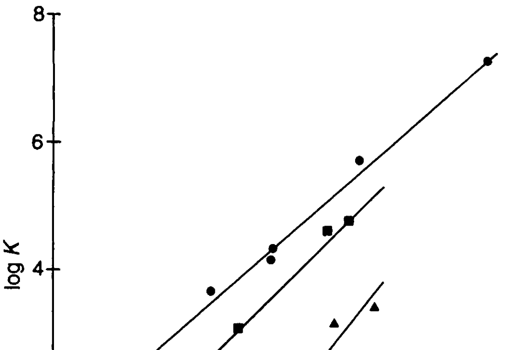

Fig. 3 Comparison of the plots of log K [for co-ordination to (aq,CN)Cbi] *vs.* pK (for protonation of the free base) for ligands used to probe basicity (but not the α or steric) effects belonging to the three series of the five-membered azoles and azolate anions (●, data from ref. 1), the six-membered pyridines and diazines (■, data from Table 1, using the higher pK for pyz) and amines (▲, data from Table 1). The solid lines correspond to the equation log K = a·pK + b with the values of a and b listed in Table 2. Note that different scales have been used for the x- and y-axes in order to separate the three groups more clearly

Table 2 Comparison of values of *a* and *b* in equation (1) for nitrogen-containing bases acting as ligands to cobalt(III) in (aq,CN)Cbi and iron(III) in MP-8 and as hydrogen-bond acceptors towards 4-nitrophenol in 1,1,1-trichloroethane

Hybridisation of donor N	Family of bases	Ligand to Co^{III}[a]		Ligand to Fe^{III}[b]		Hydrogen-bond acceptor[c]	
		a	*b*	*a*	*b*	*a*	*b*
sp^3	Amines RNH_2	0.58	−2.6	0.43	−0.5	0.37	−1.1
sp^2	Six-membered azines	0.47	+0.2	0.36	+0.8	0.27	+1.1
	Five-membered azoles	0.42	+1.3	0.34	+2.1	0.29	+1.6
sp	Nitriles RCN					*ca.* 0.2	*ca.* +3

[a] Values from this paper (amines, azines) and ref. 1 (azoles). [b] Values from refs. 3 (amines), 4 (azines) and 5 (azoles). [c] All values from ref. 11 (those for nitriles calculated from the line given in Fig. 8, ref. 11).

Two conclusions may be drawn from the observed parallels between co-ordination and hydrogen bonding. First, the fact that hydrogen bonding cannot involve π bonding means, as we have already pointed out,[5] that the differences in *b* between the families cannot be related to differences in π bonding as has sometimes been proposed. Secondly, the fact that similar differences between the families of nitrogen-containing bases are shown both by co-ordination in water and by hydrogen bonding in an aprotic solvent, when referred to the p*K* in water as the standard, suggests that these differences may be related to differences in the water structure around the protonated base.

Are the patterns of Table 2 observed with other metal ions or Lewis acids? Although substituted pyridines (by far the easiest series to study until now) have often been used to test equation (1), there are surprisingly few direct comparisons of several pyridines with several imidazoles or amines, let alone nitriles. Relevant data can be summarised as follows. As mentioned above, a systematic difference between the azoles and azines has already been noted. (*i*) Rate constants for catalysis of the hydrolysis of *p*-nitrophenylacetate by various nucleophiles in 28.5% aqueous EtOH, where values of $a = 0.82$ and $b = -4.3$ over four p*K* units for the imidazoles and a lower but apparently parallel line with fewer experimental points for the pyridines with *a ca.* 0.8 and (if one assumes $a = 0.82$) *b ca.* −5.0 can be calculated from the straight lines in Fig. 3 of ref. 13. (*ii*) Equilibrium constants (both K_1 and K_2) for the co-ordination of various pyridines and imidazoles by silver(I) in aqueous solution, where values of $a = 0.28$ and $b = +1.2$ over 2.5 p*K* units for the imidazoles and $a = 0.28$ and $b = +0.5$ over 1.5 p*K* units for the pyridines can be calculated from the straight lines relating to log K_1 in Fig. 1 of ref. 14. (*iii*) Values of log β_2 for equilibrium (2) in $CHCl_3$, where P is a synthetic porphyrin

$$[Fe^{III}PCl] + 2B \rightleftharpoons [Fe^{III}PB_2]^+Cl^- \qquad (2)$$

and B a substituted imidazole or pyridine, which suggested comparable values of *a ca.* 0.8 for both series with *b ca.* −3.2 for two imidazoles with N-Me (complications due to ion-pairing occurred with N–H bonds) and *b ca.* −4.5 for three pyridines.[32] There are many other examples (*e.g.* the $HgMe^+$ ion)[33] where the single point for Him lies significantly above the line for several pyridines.

The pattern of five-membered azoles and six-membered azines behaving as two distinct families of ligands (or nucleophiles) with similar slope *a* but higher (by 0.5–1.5) intercept *b* for the azole ligands appears to be fairly general; it is observed with the d^{10} Ag^+ and $HgMe^+$ ions as well as the d^5 iron(III) and d^6 cobalt(III) ions. By contrast, the difference between the azines and the amines is not so universal; pyridines, diazines and primary amines all share the same line with Ag^+ (*cf.* the data in refs. 23, 26 and 27) and probably also with the $HgMe^+$ ion.[33] Rather surprisingly, it appears that the distinction between sp^3- and sp^2-hybridised nitrogen atoms is less fundamental than that between N in a five- or six-membered heterocycle.

There appear to be no other comparable data for the sp-hybridised nitriles. The only first-row transition metal ion which appears able to co-ordinate MeCN in competition with water is the d^{10} copper(I) ion, where log K_1 3.3 has been determined by indirect methods;[34] *cf.* also gold(I) with log K_1 1.3,[35] though co-ordination appears not to have been reported with silver(I). Some indication of likely values of *a* and *b* for the nitriles may, however, be obtained from studies on hydrogen bonding, where the approximate values of *a ca.* 0.2 and *b ca.* +3 (included in Table 2) suggest a continuation of the pattern in which changing the hybridisation from sp^3 through sp^2 to sp causes a gradual decrease in *a* (*ca.* 0.4, 0.3, 0.2) and a marked increase in *b* (*ca.* −1, +1, +3). By analogy, one might expect reasonably 'normal' values of *a* and *b* for the co-ordination of nitriles, but their abnormally negative p*K* values (*e.g.* MeCN, *ca.* −10)[11] effectively prevents co-ordination to most first-row metal ions in competition with H_2O.

Our present results and the above analysis demonstrate more emphatically than before (*i*) that the linear relationship (1) holds for a wide range of metal ions, families of bases and p*K* values, and (*ii*) that the azoles and azines, as well as the amines and nitriles, form distinct families which share similar values of the slope *a* but differ in the intercept *b*. We have provisionally termed these factors which determine the magnitude of *b* and the separation between the lines for the different families 'group-specific' factors;[5] their origin remains to be established, but differences in the structure of water around the protonated base will probably form at least part of the explanation.

The α Effect.—Our demonstration of enhanced values of log *K* for NH_2NH_2, NH_2OH and the 1,2-diazine pydz towards both MP-8[3,4] and (aq,CN)Cbi appear to represent the first clear-cut examples of a typical α effect in metal–ligand bonding. The α effect has also been observed in enhanced equilibrium constants for hydrogen bonding with pydz and azoles (*e.g.* 4-butyl-1,2,4-triazole)[11] but apparently not yet with any amines or their derivatives such as oximes or hydrazones. There has been little interest in pydz as a ligand; we would, however, recommend it as a standard 'probe' for the α effect. In contrast to NH_2NH_2 and NH_2OH it is not a potential reducing agent and its fixed geometry makes it easier to interpret experimental results. Because of its low p*K* value (2.3) it can readily be studied as the neutral base even when the pH needs to be lowered in order to prevent competition from OH^- as ligand and it can easily be assessed against the baseline of substituted pyridines, extended with pyrimidine if necessary.

It is generally assumed that non-bridging NH_2NH_2 and NH_2OH co-ordinate to Fe^{III} and Co^{III} through a single N atom, although there appear to be no structural data to confirm this. By contrast, η^2 co-ordination of derivatives of NH_2NH_2 and NH_2OH is well established for metal ions with few d electrons such as molybdenum[36,37] and might be considered as a structural manifestation of the α effect; unfortunately, no associated equilibrium or rate constants for co-ordination have been reported. Stabilisation of HN=NH as the reaction intermediate in nitrogen fixation through η^2 co-ordination has been suggested as the likely role for molybdenum or vanadium in the nitrogenase enzymes.[38] It might appear that the typical α effect does not operate in silver(I) complexes, since pyridazine does not give an enhanced value of log K; it was, however, noted that the apparently normal value of ΔG_1 for co-ordination of the first pyridazine masked compensation between abnormally negative values of ΔH_1 and ΔS_1, which they ascribed to the symmetrical η^2 co-ordination of both N atoms.[27] Our understanding of 'α-effective' ligands is clearly at an early stage.

We have suggested[4] an explanation for the origin of the α effect in the specific case of pydz because of its fixed geometry (but applicable, by extension, to other such molecules and ions) and based on the analysis by Taft and co-workers[39] of the differences between gas-phase and aqueous-phase basicities of two azines (pydz and pyridine) and two azoles (imidazole and pyrazole). They explained the observed differences in terms of two main effects, *viz.* electrostatic repulsion (between vicinal lone pairs or vicinal N–H bonds sharing a positive charge) and the inductive effect of an aza substituent in the ring, which are directly opposed in the case of the protonation of the neutral pydz. Because of the likely different dependence of these two main effects on the degree of charge removed (greater with H^+ than with the other Lewis acids), on the charge on the heterocycle (co-ordination of the 1,2,4-triazolate anion appears to show no α effect) and probably on interaction with the *cis* ligands in the metal complex, there are clearly many factors to be sorted out. The α effect will be discussed again in a later publication.

Conclusion

The emerging pattern can be summarised as follows. The linear free energy relationships (1) between log K and pK can be considered as the structural members in constructing the grid of log K values resulting from the interplay between the basicity of the nitrogen-containing base on the one hand (together with the 'group-specific' factors) and the Lewis acidity of the metal ion on the other (together with any other more metal-specific effects); similar linear relationships have been found between pK values in aqueous solution and proton affinities in the gas phase for substituted pyridines.[40] The α effect and steric effects, which serve to increase and decrease the value of log K respectively above and below that expected from basicity alone, are observed irrespective of the family of base used and can be considered as ancillary factors superimposed on the more fundamental basicity and 'group-specific' factors. Both the similarities in the slope a between the three families and the difference in the intercept b between the five-membered azoles and six-membered azines were somewhat unexpected. Nitrogen-containing bases can, therefore, be routinely used to probe the role of at least four factors in metal–ligand bonding: basicity and 'group specific' factors (using the series of amines 1–6 and azine ligands 9–15 in Table 1 and the azole ligands in ref. 1); steric effects (using α and β branching in the amines, 2-substitution in the azoles and azines); and the α effect (using NH_2NH_2 and NH_2OH for the amines, pydz for the azines and, in principle, 4-substituted 1,2,4-triazoles for the five-membered azoles). The most obvious gap at present is the lack of data and lack of suitable probes for the nitriles and other ligands with sp-hybridised N.

In addition to developing the co-ordination chemistry of iron porphyrins and cobalt corrinoids which is of particular interest to bioinorganic chemistry, our more general contributions to co-ordination chemistry have been (*i*) to extend the range of pK values available for the probe ligands, especially to establish a convenient series of probe ligands for the routine testing of azoles, hence (*ii*) to demonstrate more emphatically than before that azoles and azines form two distinct families of bases, (*iii*) to establish the occurrence of the α effect in metal–ligand bonding and suggest pydz as a convenient probe for the α effect and (*iv*) to demonstrate[1] how values of a may in principle be obtained for kinetically inert complexes by determining the value of pK_c for ionisation of a co-ordinated nitrogen-containing base.

In the next stage of this work we wish to exploit the opportunity offered by the cobalt(III) corrinoids for studying the interplay between varying the basicity (and family) of the base and the Lewis acidity of the metal ion through varying the *trans*-ligand X (in the established order of increasing σ-donor power from $X = H_2O$ through CN^- to CH_3^-)[41] as a means of providing further insight into the factors which determine the magnitude of a and b.

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