Mixed-ligand Complexes involving Sulfur-containing Ligands. Part 1. Nickel(II) Ternary Complexes of L-Cysteine, D-Penicillamine and L-Cysteic acid with Imidazoles

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Computer-based analysis of the pH-titration data obtained in aqueous perchlorate medium at 37 °C and $I = 0.15$ mol dm^{-3} ($NaClO_4$) for Ni^{II}–A–B ternary systems [A = L-cysteine (Cys), D-penicillamine (pen) or L-cysteic acid (Cya); B = imidazole (Him), histamine (Hist) or L-histidine (His)] showed the presence of the ternary species $NiABH_2$, NiABH, NiAB and $NiAB_2$ in addition to binary species with A or B. Under the same experimental conditions, binary systems of Ni^{II} with Cys, pen, Cya, Him, Hist and His have also been studied. For the NiABH species in the Ni^{II}–Cys–Him, –His and –Hist and Ni^{II}–pen–Him mixed-ligand systems, the site of protonation is on the primary ligand (A), while in the Ni^{II}–A–His and –Hist systems (A = pen or Cya) protonation occurs at the secondary ligand. In the $NiABH_2$ species, one proton is attached to the primary ligand and the other to the secondary ligand. For the NiAB and $NiAB_2$ species the Cys and pen primary ligands bind the metal through the mercapto and amino groups, while Cya binds Ni^{II} in a glycine-like mode. In these species, the Him, Hist and His secondary ligands are respectively mono-, bi- and ter-dentate. The probable reason for the higher stability of $NiAB_2$ species compared to NiAB species in the Ni^{II}–A–Him systems (A = Cys, pen or Cya) is discussed.

Investigations on the complex forming properties and important chemical reactions of the naturally occurring amino acid, L-cysteine and D-penicillamine (3-mercapto-D-valine) have been carried out by several workers.[1–4] The complex chemical equilibria of both L-cysteine and D-penicillamine are determined by the mercapto sulfur donor atom which is soft in character. Through the mercapto group, these compounds participate in both redox and acid–base reactions. The quantitatively important pathway of L-cysteine metabolism is the oxidation to L-cysteic acid. A study of the interaction of Cu^{II} with L-cysteine and D-penicillamine is highly complicated because the complex formation and redox reactions take place simultaneously. A deeper understanding of this type of chemical reaction requires the extension of investigations to complexes of other transition-metal ions such as Ni^{II} which is not susceptible to redox reactions. Moreover, there are few reports[1–4] on systematic investigations of mixed-ligand complexes involving sulfur-containing ligands such as L-cysteine, D-penicillamine and L-cysteic acid. Hence, in this work, equilibrium studies on nine mixed-ligand complex systems of Ni^{II} involving the sulfur-containing ligands L-cysteine (Cys), D-penicillamine (pen) and L-cysteic acid (Cya) as the primary ligands are reported. The interaction of these systems with imidazole (Him), histamine (Hist) and L-histidine (His) is also investigated. The reactivity of the imidazole group of histidyl residues in proteins has assumed great importance in understanding the interaction between proteins and metal ions and is also responsible for most of the buffering power of proteins in the physiological pH range. The studies have been carried out at 37 °C and $I = 0.15$ mol dm^{-3} ($NaClO_4$). Binary systems of Ni^{II} with Cys, pen, Cya, Him, Hist and His have also been studied under the same experimental conditions.

Experimental

Nickel(II) perchlorate was prepared by neutralizing nickel(II) carbonate with perchloric acid and standardized by titration with ethylenediaminetetraacetic acid. All the ligands used in this work were Fluka products of puriss quality. Doubly distilled water was used for the preparation of all solutions. The pH titrations were carried out at 37 °C under nitrogen with a digital pH meter with glass and calomel electrode assembly, to an accuracy of ±0.01 pH unit as described earlier.[5] The electrode system was calibrated by the method of Irving *et al.*[6] The pH titrations involving binary complex systems have been carried out with different metal-to-ligand ratios, varying from 1 : 1 to 1 : 5. A constant ionic strength of 0.15 mol dm^{-3} was maintained by the addition of sodium perchlorate. Similarly, in the ternary systems, titrations were performed using 50 cm^3 portions of solutions containing low concentrations of $Ni(ClO_4)_2$, ligand A (Cys, pen or Cya) and ligand B (Him, Hist or His) in 1 : 1 : 1, 1 : 2 : 1 or 1 : 1 : 2 ratios with known volumes of standard carbonate-free NaOH. The calculations have been restricted to below pH 7.5 in order to avoid complications due to hydrolysis of various complex species at higher pH values. About 125 to 150 experimental points were available for evaluation in each system. All the calculations were made with the aid of the MINIQUAD 75 computer program[7] on a CYBER 180/830A computer. The results obtained for the binary and ternary complex systems are reported in Tables 1 and 2 respectively. The charges of all the complex species reported are omitted for clarity.

Results and Discussion

Binary Complex Equilibria.—Ni^{II}–A *binary systems*, A = L-

Table 1 Stability constants for the proton and nickel(II) complexes of Cys, pen, Cya, Him, Hist and His binary systems [T = 37 °C, I = 0.15 mol dm^{-3} (NaClO$_4$)]*

	Ligand (B)					
Parameter	Cys	pen	Cya	Him	Hist	His
log β_{HB}	10.31(2)	10.89(1)	8.41(1)	6.55(2)	9.39(8)	8.96(3)
log β_{H_2B}	18.53(7)	18.89(5)	10.56(4)	—	15.34(1)	14.96(5)
log β_{H_3B}	19.93(8)	20.80(9)	—	—	—	17.37(9)
log β_{NiBH}	—	—	—	—	11.85(3)	13.08(5)
log β_{NiB}	9.14(9)	11.50(3)	5.93(4)	3.37(5)	6.36(2)	8.84(2)
log β_{NiB_2H}	25.86(9)	—	—	—	17.86(4)	21.04(7)
log β_{NiB_2}	20.21(5)	23.41(2)	10.53(6)	5.70(9)	11.22(2)	15.94(4)
log β_{NiB_3}	—	—	—	7.90(9)	—	—
log β_{NiB_4}	—	—	—	9.57(11)	—	—
pK^{H}_{NiBH}	—	—	—	—	5.49	4.24
p$K^{H}_{NiB_2H}$	5.68	—	—	—	6.64	5.10
log $K^{NiB}_{NiB_2}$	11.07	11.91	4.60	2.33	4.86	7.10
log $K^{NiBH}_{NiB_2H}$	—	—	—	—	6.01	7.96
log $K^{NiB_2}_{NiB_3}$	—	—	—	2.20	—	—
log $K^{NiB_3}_{NiB_4}$	—	—	—	1.67	—	—
log P	—	—	—	—	2.46	4.12

* Cys, pen and Cya act as primary ligands (A) in the ternary systems.

Table 2 Stability constants of the ternary mixed-ligand systems Ni^{II}–A–B. A = Cys, pen or Cya; B = Him, Hist or His [T = 37 °C, I = 0.15 mol dm^{-3} (NaClO$_4$)]

	Ni^{II}–Cys–B			Ni^{II}–pen–B			Ni^{II}–Cya–B		
	B = Him	Hist	His	B = Him	Hist	His	B = Him	Hist	His
log β_{NiABH_2}	—	27.56(9)	29.18(9)	—	29.13(9)	—	—	23.83(9)	23.93(9)
log β_{NiABH}	19.84(6)	23.09(7)	23.77(9)	21.46(4)	23.76(8)	24.50(9)	—	18.15(9)	19.72(9)
log β_{NiAB}	13.80(6)	16.94(8)	18.36(7)	15.29(7)	18.14(8)	19.93(7)	10.60(9)	12.49(7)	14.11(6)
log β_{NiAB_2}	16.43(9)	—	—	17.87(9)	—	—	13.56(9)	—	—
p$K^{H}_{NiABH_2}$	—	4.47	5.41	—	5.37	—	—	5.68	4.21
pK^{H}_{NiABH}	6.04	6.15	5.41	6.17	5.62	4.57	—	5.66	5.61
log K^{NiA}_{NiAB}	4.66	7.80	9.22	3.79	6.64	8.43	4.67	6.56	8.18
log K^{NiB}_{NiAB}	10.43	10.58	9.52	11.92	11.78	11.09	7.23	6.13	5.27
log $K^{NiAB}_{NiAB_2}$	2.63	—	—	2.58	—	—	2.96	—	—
Δ log K_{NiABH}	—	—	—	—	0.41	−0.08	—	0.37	0.71
Δ log K_{NiAB}	1.29	1.44	0.38	0.42	0.28	−0.41	1.30	0.20	−0.66
Δ log K_{NiAB_2}	1.59	—	—	0.67	—	—	1.94	—	—
log X_{NiAB}	1.69	2.45	0.57	1.47	1.65	0.51	4.97	3.23	1.75
log X_{NiAB_2}	3.08	—	—	2.76	—	—	7.02	—	—

cysteine (Cys), D*-penicillamine (pen) or* L*-cysteic acid (Cya).* Though the bridging nature of the mercapto sulfur in both Cys and pen in their nickel(II) complexes has been highlighted previously,[8,9] under the present experimental conditions such polynuclear complex species have been found to be absent. In the Ni^{II}–Cys system NiA, NiA$_2$H and NiA$_2$ types of species have been detected, while only NiA and NiA$_2$ have been found in the Ni^{II}–pen and –Cya systems.

The log β_{NiA} values obtained in both the Ni^{II}–Cys and –pen systems (Table 1) suggest that the ligands bind the metal through the mercapto and primary amino groups in their NiA complexes. The log $K^{NiA}_{NiA_2}$ values are slightly higher than the respective log K^{Ni}_{NiA} values. This may probably be accounted for by considering the ability of sulfur to accept electrons from the metal ion by π bonding, thereby facilitating the addition of the second sulfur atom to the metal ion, *i.e.* in the NiA$_2$ complexes involving Cys and pen the ligands bind the metal in a bidentate manner through the mercapto sulfur and amino nitrogen atoms. The NiA$_2$H species in the Ni^{II}–Cys system has been found to be favoured at low pH indicating the possibility that the extra proton is attached to the primary amino group of the ligand. Thus, in this species, the protonated Cys will bind the metal through the mercapto and carboxylato groups while the other Cys binds through the mercapto and primary amino groups. This ambidentate binding of Cys has also been well demonstrated by others.[1,8–10]

The respective log K^{Ni}_{NiA} and log $K^{NiA}_{NiA_2}$ values of 5.93 and 4.60 obtained in the Ni^{II}–Cya system bear favourable comparison with the values of 5.70 and 4.70 reported[4] in the nickel(II)–glycine system. This indicates that Cya binds Ni^{II} in a glycine-like mode in both the 1:1 and 1:2 complexes in the Ni^{II}–Cya system.

Ni^{II}–B *binary systems,* B = *imidazole (Him), histamine (Hist) or* L*-histidine (His).* In the Ni^{II}–Him system the computer analysis of the pH-titration data showed the presence of NiB, NiB$_2$, NiB$_3$ and NiB$_4$ species. Both the Ni^{II}–Hist and –His systems showed the presence of NiBH, NiB, NiB$_2$H and NiB$_2$ types of species.

The results obtained for the Ni^{II}–Him system (Table 1) show that the stepwise formation constants for the NiB, NiB$_2$, NiB$_3$ and NiB$_4$ complexes decrease from NiB to NiB$_4$. This indicates that, as in the case of the Cu^{II}–Him system,[11] the binding of the first imidazole by Ni^{II} is much stronger and thus decreases the affinity for binding of Him at the other three available ligand sites around the metal.

Nickel(II) forms a six-membered chelate ring in the NiB Hist complex through the imidazole and primary amino nitrogen atoms. The higher log β_{NiB} value of 8.84 for the NiB His complex compared to that of 6.36 for the NiB Hist complex indicates that His is tridentate in its NiB complex. In the NiBH Hist complex the extra proton can be attached either to the imidazole nitrogen or to the primary amino group of histamine. As in the case of ZnBH and CuBH Hist complexes,[11,12] where the extra proton is attached to the primary amino group of the ligand, in the NiBH Hist complex also, it may be predicted that it is attached to the primary amino group of the ligand. The parameter log P (log P = log β_{NiBH}–log β_{HB}) has been calculated to characterize the nature of the metal–ligand binding. The value obtained in the Hist system of 2.46 is *ca.* 0.9 log units less than that obtained for the NiB complex species in the $\mathrm{Ni^{II}}$–Him system. This difference may be attributed to the decrease in the basicity of the primary amino group of the Hist ligand during formation of the NiBH complex. If this is taken into consideration, it may be concluded that in the NiBH Hist complex $\mathrm{Ni^{II}}$ binds Hist through the imidazole nitrogen and the proton resides with the primary amino group of the ligand. Similarly, the log P value obtained for the NiBH species in the $\mathrm{Ni^{II}}$–His system is 4.12, which is *ca.* 0.8 log units higher than the value expected for the nickel(II) binding with Him. In addition to this, the decrease in the basicity of the primary amino group during complexation should also be taken into consideration. If so, it may be concluded that in the NiBH His complex species the metal ion should bind the protonated ligand through both the imidazole nitrogen and the carboxylato oxygen atoms resulting in a seven-membered chelate ring which will be stabilized due to the π-acceptor property of the imidazole group.

As in the NiBH Hist and His complexes, in which the extra proton resides with the primary amino group of the respective ligands, it may also be inferred that in the Ni(BH)B Hist and His complexes the extra proton is attached to the primary amino nitrogen atoms. Thus, in the Ni(BH)B Hist complex, the unprotonated ligand will bind the metal in a bidentate manner through the imidazole and primary amino nitrogen atoms leading to a six-membered chelate ring while the protonated ligand with the protonated primary amino group binds the metal through the imidazole nitrogen atom. In the Ni(BH)B His complex, one His will bind the metal in a tridentate manner and the other His with its protonated amino group binds the metal through the imidazole nitrogen and carboxylato oxygen atoms. The log β values of 17.86 and 21.04 obtained respectively for the $\mathrm{NiB_2H}$ Hist and His complexes can be accounted for by considering these structural aspects.

The log $\beta_{\mathrm{NiB_2}}$ values obtained in the $\mathrm{Ni^{II}}$–Hist and –His systems are 11.22 and 15.94 respectively. In the $\mathrm{NiB_2}$ Hist complexes both the Hist ligands bind the metal through the imidazole and primary amino nitrogen atoms resulting in two six-membered chelate rings giving a co-ordination number of four for the metal ion. The higher log $\beta_{\mathrm{NiB_2}}$ value obtained in the $\mathrm{Ni^{II}}$–His system compared to the $\mathrm{Ni^{II}}$–Hist system suggests that both His ligands bind the metal in a tridentate manner giving a co-ordination number of six to $\mathrm{Ni^{II}}$.

Ternary Complex Equilibria.—$\mathrm{Ni^{II}}$–A–B *ternary systems.* A = L-*cysteine* (*Cys*), D-*penicillamine* (*pen*) *or* L-*cysteic acid* (*Cya*); B = *imidazole* (*Him*), *histamine* (*Hist*) *or* L-*histidine* (*His*). The $\mathrm{Ni^{II}}$–A–Him systems (A = Cys or pen) showed the presence of three ternary species of stoichiometry NiABH, NiAB and $\mathrm{NiAB_2}$. The $\mathrm{Ni^{II}}$–Cya–Him system gave rise to the formation of NiAB and $\mathrm{NiAB_2}$ ternary species. In the $\mathrm{Ni^{II}}$–A–Hist (A = Cys, pen or Cya) and $\mathrm{Ni^{II}}$–A–His (A = Cys or Cya) systems the $\mathrm{NiABH_2}$, NiABH and NiAB types of ternary species have been found to be present. The $\mathrm{Ni^{II}}$–pen–His system showed the presence of NiABH and NiAB ternary species. The various binary species due to ligands A and B found in addition to the above ternary species for the ternary systems are given in Table 1. Sovago *et al.*[1] in their studies on the $\mathrm{Ni^{II}}$–pen–Hist and –His systems have reported the formation of only NiAB species.

Stability and structure of NiAB *and* $\mathrm{NiAB_2}$ *species.* As indicated previously for the NiA binary species in the $\mathrm{Ni^{II}}$–Cys and –pen binary systems, the ligands bind the metal through the mercapto and amino groups. The same type of binding may be expected in the NiAB and $\mathrm{NiAB_2}$ ternary species in ternary systems involving Cys or pen primary ligands. Thus, for the $\mathrm{NiAB_2}$ species in the Ni–A–Him (A = Cys or pen) systems, the metal ion would be four-co-ordinate due to the bidentate binding of Cys or pen primary ligands and monodentate binding of two Him ligands. In the NiAB species of these systems the fourth co-ordination site would be occupied by a solvent water molecule. The metal ion in the NiAB species for the $\mathrm{Ni^{II}}$–A–Hist (A = Cys or pen) systems would also be four-co-ordinate due to bidentate binding of both the Cys or pen primary and Hist secondary ligands. The log β_{NiAB} values of 16.94 and 18.14 obtained in the Cys and pen ternary systems with histamine are slightly higher than the respective log $\beta_{\mathrm{NiAB_2}}$ value of 16.43 and 17.87 obtained in the corresponding systems with imidazole, though in both the complex species the metal ion has a co-ordination number of four. This may be due to the fact that the co-ordination of the Hist secondary ligand in the NiAB species in the $\mathrm{Ni^{II}}$–A–Hist (A = Cys or pen) systems results in the formation of a six-membered chelate ring, while the binding of two Him secondary ligands in a monodentate manner in the $\mathrm{NiAB_2}$ species in the $\mathrm{Ni^{II}}$–A–Him (A = Cys or pen) systems does not result in the formation of a chelate ring. Hence, the chelate effect will be responsible for the higher stability of the Hist relative to the Him species. Surprisingly, the log β_{NiAB} value of 12.49 obtained in the $\mathrm{Ni^{II}}$–Cya–Hist system is less than the log $\beta_{\mathrm{NiAB_2}}$ value of 13.56 obtained in $\mathrm{Ni^{II}}$–Cya–Him system. In these systems, the respective log $K^{\mathrm{NiB}}_{\mathrm{NiAB}}$ and log $K^{\mathrm{NiB_2}}_{\mathrm{NiAB_2}}$ values obtained are comparable to the log $K^{\mathrm{Ni}}_{\mathrm{NiA}}$ value obtained in the $\mathrm{Ni^{II}}$–Cya binary system indicating that the Cya primary ligand binds the metal in a glycine-like mode in both the NiAB and $\mathrm{NiAB_2}$ ternary species making the metal ion four-co-ordinate. The chelate effect in the former species due to the bidentate binding of Hist secondary ligand is expected to give a higher log β_{NiAB} value compared to the log $\beta_{\mathrm{NiAB_2}}$ value. The observed reverse trend suggests that the π-acceptor properties of two imidazole groups make $\mathrm{NiAB_2}$ species in the $\mathrm{Ni^{II}}$–Cya–Him system more stable than the NiAB species in the $\mathrm{Ni^{II}}$–Cya–Hist system. Thus, the results obtained in the $\mathrm{Ni^{II}}$–Cya–Him and –Hist systems show different trends from those obtained in the $\mathrm{Ni^{II}}$–A–Him and –His systems (A = Cys or pen).

The log β_{NiAB} values obtained in the $\mathrm{Ni^{II}}$–A–His (A = Cys, pen or Cya) systems are higher than those obtained in the corresponding Hist systems. This indicates that for the NiAB species in the His secondary-ligand systems, His binds the metal in a terdentate manner. The $\Delta\log K_{\mathrm{NiAB}}$ values obtained in all the ternary systems are higher than the statistically expected values[13,14] indicating that the NiAB mixed species are markedly stabilized compared to the NiA or NiB binary species. In most cases (Table 2) this parameter is positive showing that the secondary ligands add on to the NiA primary ligand binary complex species rather than to the aquated metal ion. The disproportionation constant, log X_{NiAB} ($X = [\mathrm{NiAB}]^2/[\mathrm{NiA_2}][\mathrm{NiB_2}]$) values[13] obtained in the above systems are also greater than the statistically expected value of 0.6 indicating that the formation of NiAB type of species in all the systems is more favoured compared to the formation of $\mathrm{NiA_2}$ or $\mathrm{NiB_2}$ types of binary complexes.

It is interesting to compare the stabilities of NiAB and $\mathrm{NiAB_2}$ species in the $\mathrm{Ni^{II}}$-A-Him (A = Cys, pen or Cya) systems. For the Cys system the $\Delta\log K_{\mathrm{NiAB_2}}$ value of 1.59 is higher than the $\Delta\log K_{\mathrm{NiAB}}$ value of 1.29 as is the log $X_{\mathrm{NiAB_2}}$ value (3.08) which is higher than log X_{NiAB} (1.69). Similarly, $\Delta\log K$ and log X values for the $\mathrm{NiAB_2}$ species in the pen and Cya imidazole systems are more positive than those for the NiAB species. This trend demonstrates that the $\mathrm{NiAB_2}$ species are more stable than the NiAB species. As in the case of $\mathrm{Cu^{II}}$– and $\mathrm{Zn^{II}}$–A–Him mixed-ligand systems,[15,16] it appears that the relative stabilities of

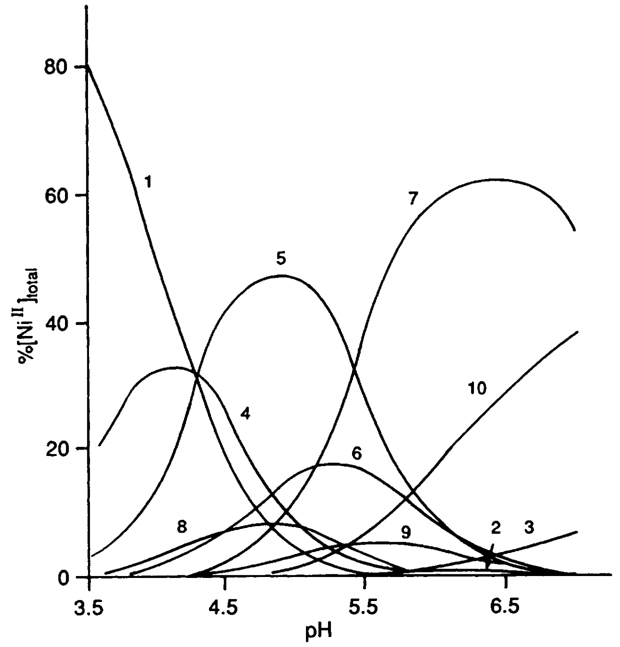

Fig. 1 Species distribution diagram for the $\mathrm{Ni^{II}}$–Cys(A)–His(B) system ($c_{\mathrm{Ni}} = 3.021 \times 10^{-3}, c_{\mathrm{A}} = 3.022 \times 10^{-3}, c_{\mathrm{B}} = 6.074 \times 10^{-3}$ mol dm^{-3}). Unbound $\mathrm{Ni^{II}}$ (1), $\mathrm{NiA_2H}$ (2), $\mathrm{NiA_2}$ (3), NiBH (4), NiB (5), $\mathrm{NiB_2H}$ (6), $\mathrm{NiB_2}$ (7), $\mathrm{NiABH_2}$ (8), NiABH (9) and NiAB (10). The species NiA was found at too low a concentration to be depicted

NiAB and $\mathrm{NiAB_2}$ species in the $\mathrm{Ni^{II}}$–A–Him systems also depend on the size of the chelate ring formed by the primary ligand, A. In the case of copper(II) and zinc(II) mixed-ligand systems it has been shown[15,16] that where the primary ligand forms a five-membered chelate ring the $\mathrm{MAB_2}$ species will be more stable than the MAB species. Conversely, if the primary ligand forms a six-membered chelate ring, or more than one chelate ring, the stability of MAB species is now higher than that of $\mathrm{MAB_2}$ species. In all the above nickel(II) mixed-ligand systems, co-ordination of the primary ligands results in the formation of a five-membered chelate ring and hence as in the case of copper(II) and zinc(II) mixed systems[15,16] the stability of $\mathrm{NiAB_2}$ species is higher than that of NiAB species.

Stability and Structure of NiABH *and* $\mathrm{NiABH_2}$ *Species*.—The formation of NiABH species has been found to be most favoured above pH 4 in all the systems. The $\mathrm{p}K^{\mathrm{H}}_{\mathrm{NiABH}}$ values obtained in the $\mathrm{Ni^{II}}$–Cys–Him, –His and –Hist systems are comparable indicating the possibility of the attachment of the extra proton to the Cys primary ligand, possibly onto the amino group as in $\mathrm{NiA_2H}$ Cys binary species. Thus, the Cys primary ligand in all these systems would bind the metal through the mercapto and carboxylato groups. The detection of NiABH species in the $\mathrm{Ni^{II}}$–pen–Him system is rather surprising since in the $\mathrm{Ni^{II}}$–pen and $\mathrm{Ni^{II}}$–Him binary systems no protonated binary species of the types NiAH, $\mathrm{NiA_2H_2}$ or $\mathrm{NiA_2H}$ have been detected. So, whether the proton is attached with the pen primary ligand or with the Him secondary ligand is to be ascertained. The possibility of attachment to the Him secondary ligand can be ruled out since imidazole nitrogen is the only co-ordinating group available in this ligand at low pH ranges. Therefore, the site of protonation in this NiABH species should be with the pen primary ligand, possibly to its amino group. In the NiABH species in the $\mathrm{Ni^{II}}$–pen–Hist and –His systems the proton can be attached either to the primary or to the secondary ligand. The more likely possibility is attachment to the secondary ligand since in the $\mathrm{Ni^{II}}$–pen binary system no protonated binary species have been detected and such species have been detected only in the $\mathrm{Ni^{II}}$–Hist and His binary systems.

The possibility for the site of protonation in the NiABH species in the $\mathrm{Ni^{II}}$–pen–Him system to be the pen primary ligand, and that in the $\mathrm{Ni^{II}}$–pen–Hist and –His systems to be at the Hist and His secondary ligands is reflected in the $\mathrm{p}K^{\mathrm{H}}_{\mathrm{NiABH}}$ values obtained in these three systems (Table 2). They follow the trends of the $\mathrm{p}K_{\mathrm{a}}$ values of the amino group of pen, Hist and His ligands. Similarly for the NiABH species in the $\mathrm{Ni^{II}}$–Cya–Hist and –His systems, the proton should reside with the Hist or His secondary ligands, possibly with their primary amino groups since in the $\mathrm{Ni^{II}}$–Cya binary system no protonated binary species have been detected. Since the log β_{NiABH} value obtained in the His secondary ligand systems is higher than that of the corresponding Hist secondary ligand systems (Table 2), it can be concluded that in the NiABH species of the His secondary ligand systems the protonated His binds the metal through the imidazole nitrogen and carboxylato oxygen atoms. In all the above cases the $\Delta\log K_{\mathrm{NiABH}}$ values obtained are higher than the statistical values[13,14] indicating the preference for the formation of NiABH species.

In the $\mathrm{NiABH_2}$ species in the $\mathrm{Ni^{II}}$–Cys–Hist and –His, $\mathrm{Ni^{II}}$–pen–Hist and $\mathrm{Ni^{II}}$–Cya–Hist and –His systems, it may be inferred that one proton resides with the primary ligand and the other with the secondary ligand. It is rather surprising that $\mathrm{NiABH_2}$ species are detected in the pen and Cya primary ligand systems since no protonated binary species were detected in the $\mathrm{Ni^{II}}$–pen or $\mathrm{Ni^{II}}$–Cya binary systems. However, the $\mathrm{p}K^{\mathrm{H}}_{\mathrm{NiABH_2}}$ values obtained in these systems follow the trends of the $\mathrm{p}K_{\mathrm{a}}$ values of the amino group of both the primary and secondary ligands.

Species Distribution Plots.—Estimation of equilibrium concentrations of free metal ion, complexing agent and metal complexes as a function of pH provides a useful picture of metal-ion binding towards the primary and secondary ligands. In all the species distributions the concentration of the ternary complexes increases with increasing pH, thus making $\mathrm{Ni^{II}}$ biologically available in the physiological pH range. In all the systems reported NiAB ternary species occur in greater concentration than either NiA or NiB binary species. This is in accordance with the conclusion arrived from the statistical parameter $\Delta \log K$ that ternary complex formation is preferred over that of the binary analogues. The concentration of the $\mathrm{NiAB_2}$ type of species in the $\mathrm{Ni^{II}}$–A–Him (A = Cys, pen or Him) systems has been found to be more favoured at a ratio Ni:A:B of 1:1:2 rather than at 1:1:1 or 1:2:1 ratios. The monoprotonated NiABH and diprotonated $\mathrm{NiABH_2}$ species have been found to be most favoured at lower pH values. In order to indicate the qualitative features observed in the species distribution plots in these systems, the speciation diagram obtained for $\mathrm{Ni^{II}}$–Cys–His system at a $\mathrm{Ni^{II}}$:Cys:His ratio of 1:1:2 is shown in Fig. 1.

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