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FULL PAPER

Acid–base and metal ion-binding properties of diaminopropyl D-glucopyranoside and diaminopropyl D-mannopyranoside compounds in aqueous solution

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For three sugar-appended diamine compounds (1,3-diamino-2-propyl β-D-glucopyranoside (2-β-D-Glc-pn), (2*S*)-2,3-diaminopropyl β-D-glucopyranoside (1-β-D-Glc-pn) and 1,3-diamino-2-propyl α-D-mannopyranoside (2-α-D-Man-pn)), acidity constants and stability constants with Ni^{2+}, Cu^{2+} and Zn^{2+} have been measured ($I = 0.16$ M NaCl, 25 °C). The two acidity constants of each of the three sugar-diamines differ by $10^{1.65}$ to $10^{3.09}$, indicating that removal of the proton from HL^+ species is more difficult than deprotonation from the fully protonated dication H_2L^{2+}. Statistical and polar effects, as well as the formation of an intramolecular hydrogen bond, may cause this increased stability of the HL^+ species. The strength of the hydrogen bond and the degree of its formation (percentage) were estimated. The sugar ring has only a small influence on the intramolecular hydrogen bond formation. For the different metal ion–ligand systems, the predominating species in solution are quite different. In the Cu^{2+}–1-β-D-Glc-pn system, the dominant species are always CuL^{2+} and CuL_2^{2+} in the pH range 4 to 10, where the total ligand concentration is larger than total metal ion concentration. For Ni^{2+}, NiL_3^{2+} is also important under these same conditions; however, for Zn^{2+}, the hydrolysis species $ZnL_2(OH)^+$ and $ZnL_2(OH)_2$ predominate in the high pH region. All possible species in the system were included during the calculations, and the corresponding stability constants were determined. The hydrolysis of the metal ions themselves is important in some cases and all possible hydrolysis species were included in the fitting calculation. The stability constant plots log *K versus* p*K* yielded straight reference lines for 1,3-diamine or 1,2-diamine ligands, reflecting the complete absence of sugar oxygen atoms in the metal ion coordination. The linkage between the metal ion and the diamine residue depends solely on the basicity of the ligand.

Introduction

Sugars, especially glucose, are essential feedstocks in biological systems. They are involved in energy metabolism, as well as serving as structural components in plants and animals. The pathway for glucose catabolism in cells is a central highway of energy metabolism, one into which other compounds are channelled when the cell needs them for energy. Because of the great importance of sugar molecules, nature has devised diverse and intricate cycles for their metabolism, both inside and outside the cell.[1] In studying and synthesizing metal complexes of derivatized carbohydrates, we hope to gain access to some of these pathways for possible therapeutic or diagnostic applications.[2]

Although it is known that sugars form (albeit weak) complexes with transition metals, the chemistry of this area remains poorly defined.[2] Some examples of coordinated sugar molecules are metal ion complexes which incorporate *N*-glycoside from an aldose and a diamine, and those in which a sugar amine is modified to form a Schiff-base which can coordinate.[3]

Divalent transition metal ions are central in many biological processes, especially in enzymatic catalysts. Trace amounts of nickel are essential in living systems and form the active sites of many important enzymes; urease, for example, is the enzyme responsible for the breakdown of urea to carbamate and ammonium ion.[4a] Copper is an essential constituent of several redox enzymes as well as hemocyanin, the O_2-carrier in such "blue-blooded" organisms as crabs and lobsters.[4a] Zinc plays a vital role in hundreds[4b] of (mostly hydrolysis) metalloenzymes such as carbonic anhydrase and carboxypeptidase. Another Zn enzyme, arguably the favorite enzyme of chemists, is liver alcohol dehydrogenase, an enzyme which catalyzes the conversion of primary alcohols to aldehydes.[4a]

In this report, acidity constants of three *N*-glycoside compounds, 1,3-diamino-2-propyl β-D-glucopyranoside (2-β-D-Glc-pn), 1,3-diamino-2-propyl α-D-mannopyranoside (2-α-D-Man-pn) and (2*S*)-2,3-diaminopropyl β-D-glucopyranoside (1-β-D-Glc-pn) (Scheme 1), have been examined, as have the stability constants of these ligands with the divalent metal ions Ni^{2+}, Cu^{2+} and Zn^{2+} (by potentiometry) in aqueous solution. The species distribution for each ligand–metal ion system has been analyzed in great detail.

Experimental

Materials

1,3-Diamino-2-propyl β-D-glucopyranoside (2-β-D-Glc-pn),[3d] 1,3-diamino-2-propyl α-D-mannopyranoside (2-α-D-Man-pn),[3d] and (2*S*)-2,3-diaminopropyl β-D-glucopyranoside (1-β-D-Glc-pn)[3c] were synthesized as we have previously described. Atomic

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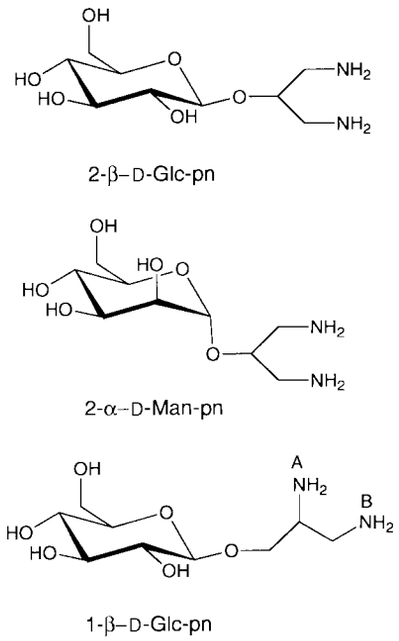


Scheme 1

absorption standard solutions of $Ni(NO_3)_2$, $Cu(NO_3)_2$ and $ZnCl_2$ were purchased from Sigma Chemical Co., St. Louis, MO and used directly. The concentration of titer (1 M NaOH, Fisher Scientific, Nepean, Ontario) was established with potassium biphthalate (Anachemia Canada Inc., Montreal, QC). Sodium chloride (for controlling the ionic strength of the solution) and hydrochloric acid were also purchased from Fisher Scientific, Nepean, Ontario. Water was deionized (Barnstead D8902 and D8904 cartridges) and distilled (Corning MP-1 Megapure still) and CO_2 was removed by boiling under Ar for about 30 minutes.

Measurements

Potentiometric measurements were made with an automatic titration system consisting of a Metrohm 713 pH meter equipped with a Metrohm 6.0233.100 electrode, a model 665 Metrohm Dosimat autoburet and water jacketed titration vessels connected to a Julabo UC circulating bath. Both the pH meter and the autoburet were controlled by an IBN-compatible PC and the titration was controlled with a locally-written QBasic program.

The electrode was calibrated before each titration by titrating a known amount of aqueous HCl with a known amount of NaOH using the same conditions in which the acidity and stability constants were measured ($I = 0.16$ M NaCl, 25 °C). A Gran plot of millivolt (measured) *vs.* pH (calculated) gave a working slope and intercept in order to convert the measured mV data to $-\log[H^+]$ directly. The value of pK_w used was 13.76.[4c]

Determination of the acidity constants

The acidity constants $K^{H}_{H_2L}$, K^{H}_{HL} for 2-β-D-Glc-pn were determined by titrating ≈0.01 M HCl (30 mL) and NaCl ($I = 0.16$ M, 25 °C) in the presence of 4.0 to 6.0 mM H_2(2-β-D-Glc-pn)$^{2+}$ under Ar with 0.16 M NaOH (≈2.5 mL). The acidity constants $K^{H}_{H_2L}$, K^{H}_{HL} for 2-α-D-Man-pn and 1-β-D-Glc-pn were determined by titrating 1.08 mM HCl (50 ml) and NaCl ($I = 0.16$ M, 25 °C) in the presence of 0.3 mM or 0.6 mM H_2(2-α-D-Man-pn)$^{2+}$ or H_2(1-β-D-Glc-pn)$^{2+}$ under Ar with 0.03 M NaOH (3 mL). The constants for 2-β-D-Glc-pn were calculated using an IBM-compatible computer with a Pentium II processor using the program SUPERQUAD[5] with data taken in the range $5.7 \leq pH \leq 11$, corresponding to about 1% neutralization for the equilibrium H_2(2-β-D-Glc-pn)$^{2+}$/H(2-β-D-Glc-pn)$^+$ and about 98% neutralization for the equilibrium H(2-β-D-Glc-pn)$^+$/2-β-D-Glc-pn. Constants for 2-α-D-Man-pn and 1-β-D-Glc-pn were computed by a curve-fit procedure using a Newton–Gauss nonlinear-least-squares programme similar to that used in other studies.[6–12] Data used were taken in the range $4.2 \leq pH \leq 10.5$ (for 1-β-D-Glc-pn), corresponding to about 1% neutralization for the equilibrium H_2(1-β-D-Glc-pn)$^{2+}$/H(1-β-D-Glc-pn)$^+$ and about 95% neutralization for the equilibrium H(1-β-D-Glc-pn)$^+$/1-β-D-Glc-pn, or $5.8 \leq pH \leq 10.6$ (for 2-α-D-Man-pn), corresponding to about 1% neutralization for the equilibrium H_2(2-α-D-Man-pn)$^{2+}$/H(2-α-D-Man-pn)$^+$ and about 91% neutralization for the equilibrium H(2-α-D-Man-pn)$^+$/2-α-D-Man-pn. More than 50 data points were recorded in each titration. The pH-meter readings (after correction according to the electrode calibration) were used to calculate directly the acidity constants; *i.e.*, these constants are the so-called practical, mixed or Brønsted constants.[13] Their negative logarithms given for aqueous solutions at $I = 0.16$ M (NaCl) and 25 °C may be converted into the corresponding concentration constants by subtracting 0.02 log unit.[13] This conversion term contains both the junction potential of the glass electrode and the hydrogen ion activity.[13,14] The final results for the acidity constants given in Table 1 are from the average of more than 10 independent titrations in each case.

Table 1 Acidity constants of 2-β-D-Glc-pn, 2-α-D-Man-pn and 1-β-D-Glc-pn measured by potentiometric pH titration in aqueous solution and corresponding literature[16,18] values for 1,3-diaminopropane (pn) and 1,2-diaminoethane (en) (25 °C, $I = 0.16$ M NaCl)[a]

Compound	pK_{a1} (H_2L^{2+} = $H^+ + HL^+$)	pK_{a2} (HL^+ = $H^+ + L$)	$pK_{a2} - pK_{a1}$
2-β-D-Glc-pn	7.70 ± 0.02	9.35 ± 0.02	1.65
2-α-D-Man-pn	7.74 ± 0.04	9.46 ± 0.05	1.72
1,3-Diaminopropane (pn)[b]	8.76 ± 0.07	10.54 ± 0.07	1.78
1-β-D-Glc-pn	6.11 ± 0.02	9.20 ± 0.02	3.09
1,2-Diaminoethane (en)	7.19 ± 0.04	9.99 ± 0.05	2.80

[a] Throughout, the error limits are three times the standard error of the mean value (3σ). [b] $I = 0.1$ M.

Determination of the stability constants

The stability constants of Ni^{2+}, Cu^{2+} and Zn^{2+} with the three ligands were determined under the same conditions outlined above, except that Na^+ was partly replaced by M^{2+} ($I = 0.16$ M, 25 °C). The ligand/M^{2+} ratios used in the experiments were $[L]_{tot}/[M^{2+}]_{tot} < 1$ or $[L]_{tot}/[M^{2+}]_{tot} > 2$ (where $[L]_{tot}$ and $[M^{2+}]_{tot}$ are the total ligand and total metal ion concentrations in solution) for calculating the stability constants of the 1 : 1 complexes or 2 : 1 complexes, respectively. The calculations were carried out by a similar curve-fitting procedure using the previously mentioned Newton–Gauss nonlinear-least-square program. All the results for stability constants were from the average of at least three independent titrations.

Results and discussion

Acidity constants

In the range $2 \leq pH \leq 11$, only 2 pK_as were observed for each of the three compounds. From their structures (Scheme 1), it is clear that these correspond to deprotonations of the two diamine nitrogen atoms $RNH_3^+ \longrightarrow RNH_2$. Deprotonation of the OH group of glucose ($pK_a = 12.3$, $I = 0.2$ M NaCl, 25 °C)[15] is unlikely, as is that of the ribose CH_2OH group (nucleoside ribose moieties normally have $pK_a > 12$).[6] We assume similar values for our three compounds; therefore, the carbohydrate moiety should have no effect on the determination of the

Table 2 Micro acidity constants, intramolecular equilibrium constants and percentage of intramolecular hydrogen bond formation in HL^+ for 2-β-D-Glc-pn, 2-α-D-Man-pn, 1,3-diaminopropane (pn), 1-β-D-Glc-pn and 1,2-diaminoethane (en) calculated according to eqn. (1)–(6)

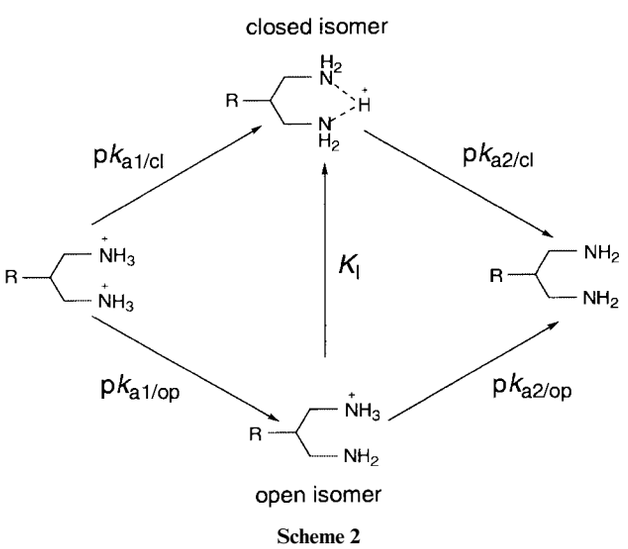
Ligand	$pk_{a1/op/s}$	$pk_{a2/op/s}$	$pk_{a2/op}$	$pk_{a1/op}$	$pk_{a1/cl}$	$pk_{a2/cl}$	K_I	% closed
2-β-D-Glc-pn	8.23	8.83	9.13	7.93	8.09	8.96	0.69	41
2-α-D-Man-pn	8.30	8.90	9.20	8.00	8.09	9.11	0.81	45
pn	9.35	9.95	10.25	9.05	9.07	10.23	0.95	49
1-β-D-Glc-pn	—	—	9.03	6.28	6.60	8.71	0.48	32
en	8.29	8.89	9.78	7.40	7.61	9.57	0.62	38

deprotonation of the protonated amines (the results bear this out). The acidity constants determined for the three carbohydrate-functionalized amines, together with the corresponding values of structurally similar ligands 1,3-diaminopropane (pn) and 1,2-diaminoethane (en), are listed in Table 1.

Comparison of the corresponding pK_a values of 2-β-D-Glc-pn and 2-α-D-Man-pn with those of 1,3-diaminopropane (pn), and of that of 1-β-D-Glc-pn with that of 1,2-diaminoethane (en), shows that the sugar ring makes the amino group about 10 times more acidic (pK_a value about 1 log unit lower). This acidifying effect may not only be caused by the electronegative oxygen atoms on the sugar ring, which decrease the electron density on the amine groups, but also by the solvation effect[7] of the sugar residue. This effect has also been observed in the case of nucleosides and their corresponding nucleobases.[7,8]

Each pair of acidity constants $K^{H}_{H_2L}$ and K^{H}_{HL} for the compounds listed in Table 1 differ by a factor of at least $10^{1.65}$ implying that deprotonation of the second proton (from HL^+) is more difficult than release of the first proton (from H_2L^{2+}). This difference is caused by three factors: statistical and polar effects, as well as the formation of an intramolecular hydrogen bond in the species HL^+. To understand the equilibria completely, it is important to know how strong the intramolecular hydrogen bond is for the different ligands, and whether the sugar residue has any influence on the formation of this hydrogen bond.

The equilibria involved in the deprotonation of H_2L^{2+} are illustrated in Scheme 2, in which R is a sugar ring (for 2-β-D-Glc-pn or 2-α-D-Man-pn) or a hydrogen atom (for pn). After the first step of the deprotonation, either an open isomer or a closed isomer may form. The measured values of pK_{a1} and pK_{a2} are the average values of the two pathways (according to the state function property of ΔG, eqn. (1)).



Scheme 2

$$pk_{a1/op} + pk_{a2/op} = pk_{a1/cl} + pk_{a2/cl} = pK_{a1} + pK_{a2} \quad (1)$$

In order to calculate the equilibrium constant K_I, one of the micro acidity constants must be known. We can estimate $pk_{a1/op}$ or $pk_{a2/op}$ by taking into account the statistical and polar effects.

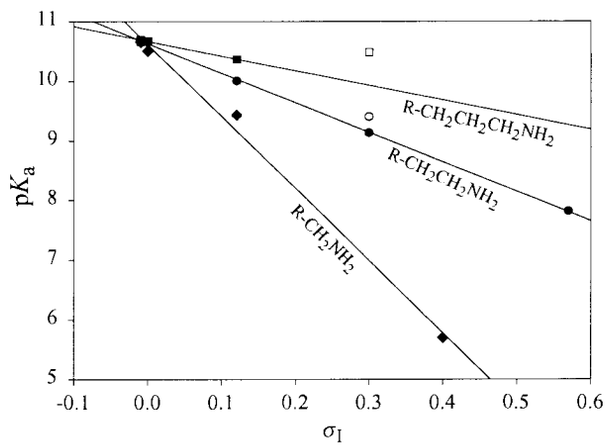


Fig. 1 Linear relationships between the acidity constants (pK_a)[18,19] and the polar substituent constants (σ_I)[17] for R–CH_2NH_2 (◆, from left to right, R = CH_3, H, C_6H_5, CF_3), R–$CH_2CH_2NH_2$ (●, from left to right, R = CH_3, H, C_6H_5, H_5C_2OOC, CN), and R–$CH_2CH_2CH_2NH_2$ (■, from left to right, R = CH_3, H, C_6H_5) (25 °C, I = 0–0.1 M). The corresponding points for CH_3O–$CH_2CH_2NH_2$ (○) and CH_3O–$CH_2CH_2CH_2NH_2$ (□) are given for comparison, but were not used for the linear regression.

With the exception of 1-β-D-Glc-pn, for all the other ligands (including pn and en) the two amine groups have the same chemical environment, ammonium deprotonation from the two groups should have similar acidity constants. For the first deprotonation step, however, there are two positions which can be deprotonated, but only one position which can be protonated. This requires the measured acidity constant to be 2 times more acidic. For the second deprotonation step, the reverse situation obtains. Considering this statistical effect, the two acidity constants should differ by a factor of 4, or $10^{0.6}$,[7] hence the micro acidity constants can be calculated according to eqns. (2) and (3).

$$pk_{a1/op/s} = (pK_{a1} + pK_{a2})/2 - 0.3 \quad (2)$$

$$pk_{a2/op/s} = (pK_{a1} + pK_{a2})/2 + 0.3 \quad (3)$$

The results of these calculations are listed in the second and the third columns of Table 2.

In the H_2L^{2+} species, however, each NH_3^+ group encounters repulsion from the other NH_3^+ group and, in the HL^+ species, the NH_3^+ group experiences a polar effect from the NH_2 group. This effect can be estimated by the polar substituent constants σ_I[17] (I = inductive). For a series of substituted amine ligands R–$CH_2NH_3^+$, R–$CH_2CH_2NH_3^+$ and R–$CH_2CH_2CH_2NH_3^+$ (where R is a non-hydrogen-bonding substituent),[18,19] when the pK_a values of the ligands are plotted against σ_I, linear relationships were obtained (Fig. 1). When R is a hydrogen-bonding substituent such as –OCH_3, the corresponding data points fall above the straight lines. This difference simply reflects intramolecular hydrogen bond formation such as is seen with our systems. Because the polar substituent constant for an –NH_2 group is 0.17,[17] one can obtain the micro acidity constants

($pk_{a2/op}$) from the straight lines in Fig. 1 for the open isomers of $H(en)^+$ and $H(pn)^+$. These values are listed in the fourth column of Table 2. As soon as $pk_{a2/op}$ is obtained, $pk_{a1/op}$ can be calculated according to eqn. (1) and these results are listed in the fifth column of Table 2. The differences between $pk_{a2/op}$ and $pk_{a2/op/s}$ (0.89 for en and 0.30 for pn) express the polar effect of the amino group. The corresponding values of $pk_{a2/op}$ for 2-β-D-Glc-pn and 2-α-D-Man-pn can be obtained by adding 0.30 to the corresponding values of $pk_{a2/op/s}$, and $pk_{a1/op}$ was subsequently calculated by employing eqn. (1) and $pk_{a2/op}$.

As soon as $k_{a1/op}$ is obtained, $k_{a1/cl}$ can be calculated from eqn. (4).[7]

$$K_{a1} = k_{a1/op} + k_{a1/cl} \quad (4)$$

When $k_{a1/cl}$ is known, according to Scheme 2, the intramolecular equilibrium constant K_I can now be calculated according to eqn. (5).

$$K_I = 10^{(pk_{a1/op} - pk_{a1/cl})} \quad (5)$$

The degree of formation of the closed species with the intramolecular hydrogen bond can be calculated from K_I according to eqn. (6).

$$\% \text{ closed} = K_I/(1 + K_I) \times 100 \quad (6)$$

The calculated K_I values and the percentage of the closed species for all five ligands are summarized in Table 2.

For 1-β-D-Glc-pn, because the two amino groups are no longer in the same chemical environment, values of $pk_{a1/op/s}$ and $pk_{a2/op/s}$ cannot be estimated in the same way as for the other ligands. Comparing the structure of 1-β-D-Glc-pn with that of 2-β-D-Glc-pn, one can see that the distance of the amine group A to the sugar ring in 1-β-D-Glc-pn (Scheme 1) is identical to the distance of the amine group to the sugar ring in 2-β-D-Glc-pn. Comparing the $pk_{a1/op}$ value of 2-β-D-Glc-pn with that of pn (listed in the second column of Table 2), we know that the sugar ring makes the $pk_{a1/op}$ value decrease by 1.12 log unit. Therefore, we can estimate that the $pk_{a1/op}$ value of 1-β-D-Glc-pn is also 1.12 lower than $pk_{a1/op}$ value of en. This can be expressed additively as $pk_{a1/op}$ (1-β-D-Glc-pn) = 7.40 − 1.12 = 6.28. Starting from this value, the other constants for this ligand can be calculated. By comparison of the values listed in the last two columns of Table 2, it is clear that the estimation is reasonable.

These results show that, indeed, the sugar ring has only a small influence on the formation of intramolecular hydrogen bonds, although it does have a significant effect on the deprotonation of the ligands. This analysis proves that the main factor making the two acidity constants different from each other is the polar effect (especially for 1,2-diamine ligands), while the intramolecular hydrogen bond is weak for this kind of system. This result agrees with the observation in biological systems that the aliphatic $–NH_2$ group very rarely acts as a hydrogen bond acceptor, although it often acts as a hydrogen bond donor.[20] The $–NH_3^+$ group is a poorer donor than the $–NH_2$ group and the length of the hydrogen bond between two nitrogen atoms is longer than when N–H is a donor and H_2O is an acceptor.[20]

As is seen in Fig. 1, if the substituent is $–OCH_3$, the corresponding data point is above the straight line and this pK_a increase can be attributed to the formation of an intramolecular hydrogen bond. Here K_I and "%closed" also can be estimated with a similar method and the results for $CH_3O–CH_2CH_2NH_3^+$ and $CH_3O–CH_2CH_2CH_2NH_3^+$ are $K_I = 0.87$, %closed = 47% and $K_I = 2.71$, %closed = 73%, respectively.

Metal ion complex formation with 2-β-D-Glc-pn, 2-α-D-Man-pn and 1-β-D-Glc-pn

Before discussing the stability constants determined for the ligands studied, all possible reactions (equilibria) in the metal ion–ligand systems must be defined. Because the coordination ability of carbohydrate OH substituents is very weak (*e.g.* for Cu^{2+}–D-glucose, log $K = -0.82$ and for Cu^{2+}–D-mannose log $K = -0.27$)[21] only coordination of the amine nitrogen atoms is considered; the results bear this out (*vide infra*). For a bidentate N-donor ligand with a divalent transition metal ion in aqueous solution, the ligand deprotonation equilibria are described by eqns. (7) and (8), the metal/ligand complexation/hydrolysis

$$H_2L^{2+} \rightleftharpoons L + 2H^+ \quad \beta_2 = [H^+][L]^2/[H_2L^{2+}] \quad (7)$$

$$HL^+ \rightleftharpoons L + H^+ \quad \beta_1 = [H^+][L]/[HL^+] \quad (8)$$

equilibria by eqns. (9) to (16), and the simple mononuclear metal ion hydrolysis equilibria by eqns. (17) to (20).

$$M^{2+} + HL^+ \rightleftharpoons M(HL)^{3+} \quad \beta_{M(HL)} = [M(HL)^{3+}]/[M^{2+}][HL^+] \quad (9)$$

$$M^{2+} + L \rightleftharpoons M(L)^{2+} \quad \beta_{M(L)} = [M(L)^{2+}]/[M^{2+}][L] \quad (10)$$

$$M(L)^{2+} + OH^- \rightleftharpoons M(L)(OH)^+ \quad \beta_{M(L)(OH)} = [M(L)(OH)^+]/[M(L)^{2+}][OH^-] \quad (11)$$

$$M^{2+} + HL^+ + L \rightleftharpoons M(HL)(L)^{3+} \quad \beta_{M(HL)(L)} = [M(HL)(L)^{3+}]/[M^{2+}][HL^+][L] \quad (12)$$

$$M^{2+} + 2L \rightleftharpoons M(L)_2^{2+} \quad \beta_{M(L)_2} = [M(L)_2^{2+}]/[M^{2+}][L]^2 \quad (13)$$

$$M(L)_2^{2+} + OH^- \rightleftharpoons M(L)_2(OH)^+ \quad \beta_{M(L)_2(OH)} = [M(L)_2(OH)^+]/[M(L)_2^{2+}][OH^-] \quad (14)$$

$$M(L)_2^{2+} + 2OH^- \rightleftharpoons M(L)_2(OH)_2 \quad \beta_{M(L)_2(OH)_2} = [M(L)_2(OH)_2]/[M(L)_2^{2+}][OH^-]^2 \quad (15)$$

$$M^{2+} + 3L \rightleftharpoons M(L)_3^{2+} \quad \beta_{M(L)_3} = [M(L)_3^{2+}]/[M^{2+}][L]^3 \quad (16)$$

$$M^{2+} + H_2O \rightleftharpoons M(OH)^+ + H^+ \quad Q_{11} = [M(OH)][H^+]/[M^{2+}] \quad (17)$$

$$M^{2+} + 2H_2O \rightleftharpoons M(OH)_2 + 2H^+ \quad Q_{12} = [M(OH)_2][H^+]^2/[M^{2+}] \quad (18)$$

$$M^{2+} + 3H_2O \rightleftharpoons M(OH)_3^- + 3H^+ \quad Q_{13} = [M(OH)_3^-][H^+]^3/[M^{2+}] \quad (19)$$

$$M^{2+} + 4H_2O \rightleftharpoons M(OH)_4^{2-} + 4H^+ \quad Q_{14} = [M(OH)_4^{2-}][H^+]^4/[M^{2+}] \quad (20)$$

Cu^{2+} and Zn^{2+} can also form polynuclear binary hydrolysis species (*e.g.* $M_2(OH)_2^{2+}$, $M_2(OH)_6^{2-}$); the equilibria in eqns. (21) and (22) were also included in the calculations.[22]

$$2M^{2+} + 2H_2O \rightleftharpoons M_2(OH)_2^{2+} + 2H^+ \quad Q_{22} = [M_2(OH)_2^{2+}][H^+]^2/[M^{2+}]^2 \quad (21)$$

$$2M^{2+} + 6H_2O \rightleftharpoons M_2(OH)_6^{2-} + 6H^+ \quad Q_{26} = [M_2(OH)_6^{2-}][H^+]^6/[M^{2+}]^2 \quad (22)$$

For specific metal ion–ligand combinations, not all these equilibria must be included in the calculations; in some systems, because the complexes formed between a metal ion and a ligand are very stable, hydrolysis of the metal ion and of the metal ion complexes is negligible.

Stability constants of 1-β-D-Glc-pn

The en analog 1-β-D-Glc-pn formed the most stable complexes with all three metal ions studied; the system was relatively simple (Table 3).

Table 3 Logarithms of the stability constants of 1-β-D-Glc-pn with Ni^{2+}, Cu^{2+} and Zn^{2+} (25 °C, $I = 0.16$ M NaCl)

Reaction	log β		
	Ni^{2+}	Cu^{2+}	Zn^{2+}
$M^{2+} + HL^{+} \rightleftharpoons M(HL)^{3+}$	2.61 ± 0.04	4.3 ± 0.35	2.3 ± 0.3
$M^{2+} + L \rightleftharpoons M(L)^{2+}$	6.97 ± 0.07	10.05 ± 0.04	5.49 ± 0.08
$M(HL)^{3+} \rightleftharpoons M(L)^{2+} + H^{+}$	−4.84 ± 0.08 [a]	−3.5 ± 0.35 [a]	−6.0 ± 0.3 [a]
$M^{2+} + HL^{+} + L \rightleftharpoons M(HL)(L)^{3+}$	9.2 [b]	13.98 ± 0.10	—
$M(L)^{2+} + OH^{-} \rightleftharpoons M(L)(OH)^{+}$	—	—	4.2 ± 0.20
$M^{2+} + 2L \rightleftharpoons M(L)_2^{2+}$	12.94 ± 0.15	18.85 ± 0.10	9.80 ± 0.08
$M(L)(HL)^{3+} \rightleftharpoons M(L)_2^{2+} + H^{+}$	—	−4.33 ± 0.14 [a]	—
$M(L)_2^{2+} + OH^{-} \rightleftharpoons M(L)_2(OH)^{+}$	—	—	4.20 ± 0.10
$M(L)_2^{2+} + 2OH^{-} \rightleftharpoons M(L)_2(OH)_2$	—	—	8.0 ± 0.2
$M^{2+} + 3L \rightleftharpoons M(L)_3^{2+}$	17.25 ± 0.10	—	—

[a] Calculated according to eqn. (23). [b] Estimated value.

Table 4 Negative logarithms of hydrolysis equilibrium constants for Ni^{2+}, Cu^{2+} and Zn^{2+} in aqueous solution ($I = 0.16$, 25 °C) [a]

Reaction	pQ		
	Ni^{2+}	Cu^{2+}	Zn^{2+}
$M^{2+} + H_2O \rightleftharpoons M(OH)^{+} + H^{+}$	10.15	8.29	9.25
$M^{2+} + 2H_2O \rightleftharpoons M(OH)_2 + 2H^{+}$	19	17.6	17.2
$M^{2+} + 3H_2O \rightleftharpoons M(OH)_3^{-} + 3H^{+}$	30	27.8	28.4
$M^{2+} + 4H_2O \rightleftharpoons M(OH)_4^{2-} + 4H^{+}$	43	39.0	40.6
$2M^{2+} + H_2O \rightleftharpoons M_2(OH)^{3+} + H^{+}$	10.4	—	8.71
$2M^{2+} + 2H_2O \rightleftharpoons M_2(OH)_2^{2+} + 2H^{+}$	—	10.65	—
$2M^{2+} + 6H_2O \rightleftharpoons M_2(OH)_6^{2-} + 6H^{+}$	—	—	57.5

[a] The values listed in the table are calculated according to the following equation with $I = 0.16$ M: $pQ = pK + a\,I^{1/2}/(1 + I^{1/2}) + b[M]$ where [M] is the concentration of the metal ion, and the pK and a values are given in ref. 22. When the metal ion concentration is very low (in the present studies $[M] < 10^{-3}$ M), the term b[M] can be ignored.

Under the experimental condition $[L]_{tot}/[Cu^{2+}]_{tot} < 1$, the titration data could be fitted with the equilibria in eqns. (7) to (10) in the pH range 3.0 to 5.5; only two complexes were important with excess Cu^{2+}:$Cu(HL)^{3+}$ and $Cu(L)^{2+}$. Although it is possible to form hydrolysis species (*e.g.* $Cu(L)(OH)^{+}$), the concentration of this species was very low even at pH = 6. During the evaluation, the hydrolysis of Cu^{2+} itself was also included by employing eqns. (17)–(21) (Table 4),[22] but the fitting showed that hydrolysis did not influence the stability constants in the range studied, $3.0 \leq pH \leq 5.5$. This fact can be clearly seen in the species distribution diagram (Fig. 2, upper, $[L]_{tot}/[Cu^{2+}]_{tot} = 0.5$). At pH < 6.0, all the hydrolysis species contained very low fractions of the total copper concentration; therefore, the stability constants of log $K_{Cu(HL)}$ and log K_{CuL} could be determined. For the former, however, because of the low fraction of this species over the whole pH range (Fig. 2), only a value with a large error limit could be obtained (Table 3). It should be noted that in the species distribution diagram the polynuclear species $Cu_2(OH)_2^{2+}$ was the main hydrolysis product in the solution, in agreement with the literature,[22] even though the concentration of Cu^{2+} in our experimental solution was quite low ($<10^{-3}$ M).

Under the experimental conditions $[L]_{tot}/[Cu^{2+}]_{tot} > 2$, eqns. (12) and (13) were included in the fit of the experimental data. Fig. 2 (lower) shows the species distribution diagram for this system when $[L]_{tot}/[Cu^{2+}]_{tot} = 2.5$. It is clear that the hydrolysis of Cu^{2+} could also be ignored in this case because, only at pH ≈ 12, was formation of hydrolysis species observed (Fig. 2, lower).

Equilibrium constants corresponding to the deprotonation of the monoprotonated complexes ($Cu(HL)^{3+}$ and $Cu(L)(HL)^{3+}$) given in Table 3 (rows 3 and 7) could be calculated from the measured constants according to eqn. (23).

$$pK^{H}_{M(HL)} = pK^{H}_{HL} + \log K^{M}_{M(HL)} - \log K^{M}_{M(L)} \qquad (23)$$

In eqn. (23), pK^{H}_{HL} is the acidity constant listed in the third column of Table 1, while $K^{M}_{M(HL)}$, $K^{M}_{M(L)}$ and $K^{H}_{M(HL)}$ correspond to the reactions in rows 1, 2 and 3 in Table 3, respectively. $K^{H}_{M(HL)}$ reflects the acidifying effect of the metal ion coordinated at one amino nitrogen toward the proton on the other amine nitrogen. Comparing the values of $pK^{H}_{Cu(HL)}$ (Table 3, column 3, row 3) with pK^{H}_{HL} (Table 1, column 3, row 4), one can see that the Cu^{2+} had a quite strong acidifying effect (9.20 − 3.5 = 5.7).

Under the experimental condition $[L]_{tot}/[Ni^{2+}]_{tot} < 1$, the titration data could be fitted well by including only eqns. (7) to (10) for the two species $Ni(HL)^{3+}$ and $Ni(L)^{2+}$. The hydrolysis of Ni^{2+} did not play a role at pH < 7 although it was included in the calculation. At $[L]_{tot}/[Ni^{2+}]_{tot} > 2$, eqns. (12), (13) and (16) had to be included in the fit; three stability constants, log $K^{Ni}_{Ni(L)}$, log $K^{Ni}_{Ni(L)_2}$ and log $K^{Ni}_{Ni(L)_3}$ were determined under this condition (Table 3) and no hydrolysis was detected in the entire range $3.4 \leq pH \leq 10$. The species distribution diagram at $[L]_{tot}/[Ni^{2+}]_{tot} = 3.2$ is shown in Fig. 3; hydrolysis started only at pH > 11 and had no influence on the determined stability constants.

Although the tendency towards hydrolysis of Zn^{2+} is similar to that of Cu^{2+} (Table 4), hydrolysis played a greater role in the stability constants of Zn^{2+} with 1-β-D-Glc-pn, because of the comparably weak coordination of Zn^{2+} with 1-β-D-Glc-pn (Table 3). In many cases, the complexes of Zn^{2+} had a stronger tendency to form hydrolysis species than did Zn^{2+} itself in aqueous solution.[9] When $[L]_{tot}/[Zn^{2+}]_{tot} < 1$, the hydrolysis species $Zn(L)(OH)^{+}$ was significant and the corresponding stability constant could be determined; eqns. (7) to (11) were included in the calculation. The stability constant of the protonated species $Zn(HL)^{3+}$ could only be determined with a large error limit because the fraction of this species in solution was always low (Table 3, Fig. 4 upper). Formation of the hydrolysis species $Zn(OH)^{+}$, $Zn(OH)_2$, $Zn(OH)_3^{-}$, $Zn(OH)_4^{2-}$, $Zn_2(OH)^{3+}$ and $Zn_2(OH)_6^{2-}$ (eqns. (16) to (22)) were included in the calculation with the appropriate constants (Table 4) during the evaluation.

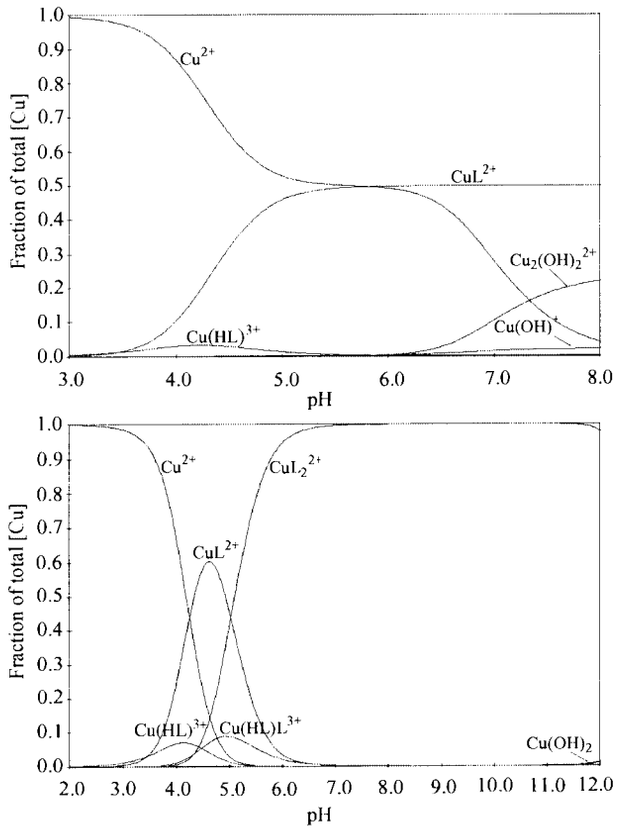


Fig. 2 Species distribution diagrams for the Cu^{2+}–1-β-D-Glc-pn system; upper: $[L]_{tot}/[Cu^{2+}]_{tot} = 0.5$ ($[L]_{tot} = 0.3$ mM, $[Cu^{2+}]_{tot} = 0.6$ mM), lower: $[L]_{tot}/[Cu^{2+}]_{tot} = 2.5$ ($[L]_{tot} = 0.75$ mM, $[Cu^{2+}]_{tot} = 0.3$ mM), $I = 0.16$ M NaCl, 25 °C.

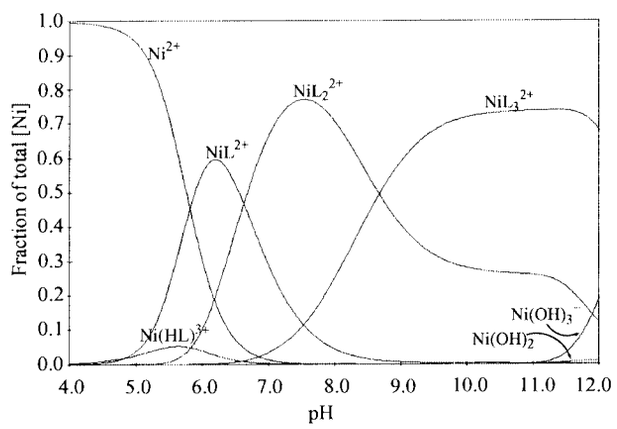


Fig. 3 Species distribution diagram for the Ni^{2+}–1-β-D-Glc-pn system; $[L]_{tot}/[Ni^{2+}]_{tot} = 3.2$ ($[L]_{tot} = 0.96$ mM, $[Ni^{2+}]_{tot} = 0.3$ mM), $I = 0.16$ M NaCl, 25 °C.

Under the experimental condition $[L]_{tot}/[Zn^{2+}]_{tot} > 2$, all possible reactions mentioned above except eqn. (12) were included in the fit. The fit was very good and the species distribution diagram (Fig. 4, lower) showed that the hydrolysis species were predominant at pH > 9. By comparison of the species distribution diagram with the results in Table 3, it can be seen that the error limits given in Table 3 correspond to the highest fraction of the species in the species distribution diagram. With the highest fraction more than 10% in the pH range of the calculation, the corresponding stability constants of the species could be well determined (small error limit), otherwise a large error limit was found. For example, formation constants for $Zn(HL)^{3+}$ and $ZnL(OH)^{+}$ were determined only with large errors, as were those for $Zn(L)_2(OH)^{+}$ and $Zn(L)_2(OH)_2$. The species distribution diagrams (Fig. 4) show that the hydrolysis of Zn^{2+} can never be neglected.

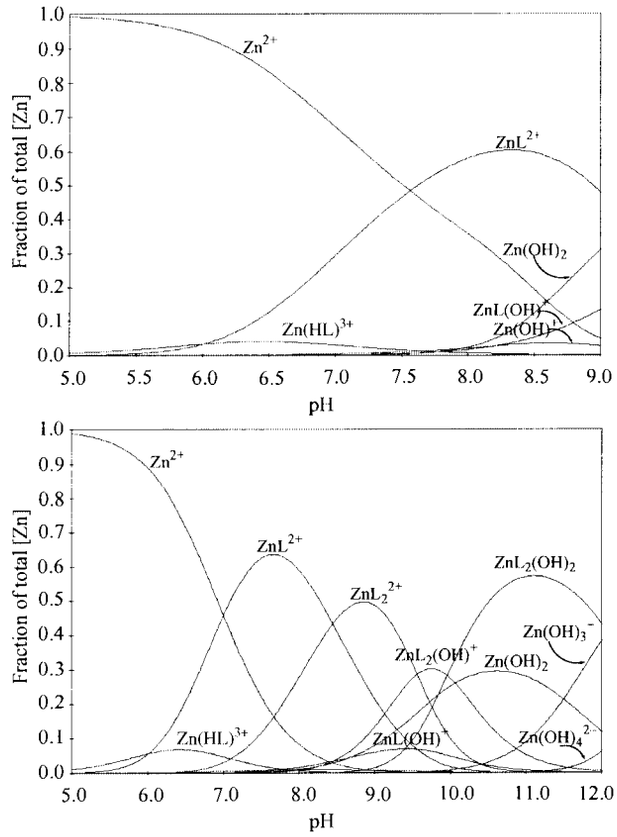


Fig. 4 Species distribution diagrams for the Zn^{2+}–1-β-D-Glc-pn system; upper: $[L]_{tot}/[Zn^{2+}]_{tot} = 0.75$ ($[L]_{tot} = 0.45$ mM, $[Zn^{2+}]_{tot} = 0.6$ mM), lower: $[L]_{tot}/[Zn^{2+}]_{tot} = 2.5$ ($[L]_{tot} = 0.75$ mM, $[Zn^{2+}]_{tot} = 0.3$ mM), $I = 0.16$ M NaCl, 25 °C.

Stability constants of 2-α-D-Man-pn and 2-β-D-Glc-pn

These two compounds form six-membered rings with a metal ion, whereas 1-β-D-Glc-pn forms a five-membered ring. Many years ago, Irving *et al.* showed that an increase in chelate ring size from 5 to 6 causes a decrease in complex stability.[23] Thus, the stabilities of the complexes formed by 2-α-D-Man-pn and by 2-β-D-Glc-pn with Ni^{2+}, Cu^{2+} and Zn^{2+} are lower than the corresponding stabilities of 1-β-D-Glc-pn complexes. This, together with the hydrolysis of the metal ions and their complexes, makes the determination of the stability constants more difficult for these two ligands, and the values determined have larger error limits. The results obtained are summarized in Tables 5 and 6.

For the Cu^{2+}–1-β-D-Glc-pn system no complex hydrolysis species were observed (*vide supra*); however, the hydrolysis species $Cu(L)(OH)^{+}$, $Cu(L)_2(OH)^{+}$ and $Cu(L)_2(OH)_2$ were found in the evaluation of the Cu^{2+}–2-α-D-Man-pn and Cu^{2+}–2-β-D-Glc-pn systems. Because there is a comparatively weak interaction between Cu^{2+} and these two ligands, only some of the constants mentioned above can be determined, especially for 2-β-D-Glc-pn. Although most of the stability constants listed in Tables 5 and 6 have large error limits, it is reassuring to see that the most important stability constants, the formation constants for $Cu(L)^{2+}$ and $Cu(L)_2^{2+}$, are obtained with acceptable error limits.

In Fig. 5, the species distribution diagram is shown for the 2-α-D-Man-pn system at $[L]_{tot}/[Cu^{2+}]_{tot} = 2.5$ (similar results, not shown, were obtained for 2-β-D-Glc-pn system). It is clear that with excess ligand the hydrolysis of Cu^{2+} is suppressed and does not play a prominent role, even at pH 11. With 2-β-D-Glc-pn, we attempted to fit the data by including the dimer $[Cu_2L_2(OH)_2]^{2+}$ instead of $CuL(OH)^{+}$ because this type of mixed hydroxo complex with bridging OH^{-} groups between the metal centers is well-known in the literature;[24] however, the fit with

Table 5 Logarithms of the stability constants of 2-α-D-Man-pn with Ni^{2+}, Cu^{2+} and Zn^{2+} (25 °C, I = 0.16 M NaCl)

Reaction	log β		
	Ni^{2+}	Cu^{2+}	Zn^{2+}
$M^{2+} + HL^{+} \rightleftharpoons M(HL)^{3+}$	2.9 ± 0.2	4.67 ± 0.15	—
$M^{2+} + L \rightleftharpoons M(L)^{2+}$	5.53 ± 0.09	8.63 ± 0.04	4.3 ± 0.2
$M(HL)^{3+} \rightleftharpoons M(L)^{2+} + H^{+}$	−6.8 ± 0.2[a]	−5.50 ± 0.14[a]	—
$M(L)^{2+} + OH^{-} \rightleftharpoons M(L)(OH)^{+}$	—	6.2 ± 0.3	4.5 ± 0.5
$M^{2+} + 2L \rightleftharpoons M(L)_2^{2+}$	9.3 ± 0.2	14.84 ± 0.05	8.3 ± 0.2
$M(L)_2^{2+} + OH^{-} \rightleftharpoons M(L)_2(OH)^{+}$	—	4.1 ± 0.2	5.2 ± 0.2
$M(L)_2^{2+} + 2OH^{-} \rightleftharpoons M(L)_2(OH)_2$	—	7.2 ± 0.3	9.3 ± 0.3
$M^{2+} + 3L \rightleftharpoons M(L)_3^{2+}$	12.3 ± 0.3	—	—

[a] Calculated according to eqn. (23).

Table 6 Logarithms of the stability constants of 2-β-D-Glc-pn with Ni^{2+}, Cu^{2+} and Zn^{2+} (25 °C, I = 0.16 M NaCl)

Reaction	log β		
	Ni^{2+}	Cu^{2+}	Zn^{2+}
$M^{2+} + L \rightleftharpoons M(L)^{2+}$	5.44 ± 0.06	8.37 ± 0.06	3.95 ± 0.08
$M(L)^{2+} + OH^{-} \rightleftharpoons M(L)(OH)^{+}$	—	4.5 ± 0.2	3.8 ± 0.2
$M^{2+} + 2L \rightleftharpoons M(L)_2^{2+}$	9.06 ± 0.10	14.41 ± 0.08	—
$M(L)_2^{2+} + OH^{-} \rightleftharpoons M(L)_2(OH)^{+}$	—	4.3 ± 0.2	—
$M^{2+} + 3L \rightleftharpoons M(L)_3^{2+}$	11.69 ± 0.15	—	—

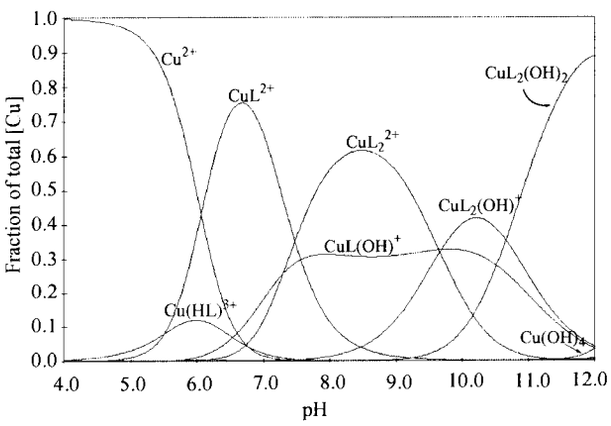


Fig. 5 Species distribution diagram for the Cu^{2+}–2-α-D-Man-pn system; $[L]_{tot}/[Cu^{2+}]_{tot}$ = 2.5 ($[L]_{tot}$ = 0.75 mM, $[Cu^{2+}]_{tot}$ = 0.3 mM), I = 0.16 M NaCl, 25 °C.

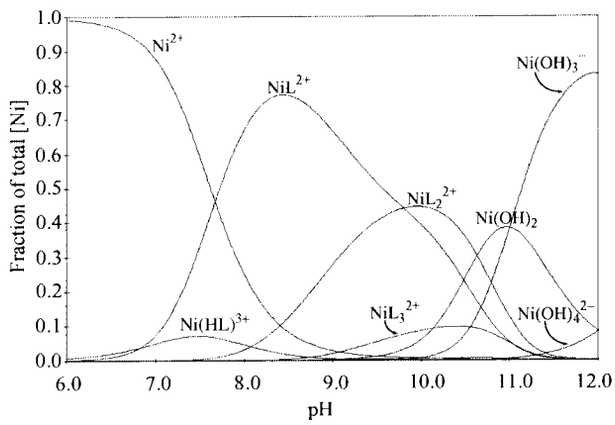


Fig. 6 Species distribution diagram for the Ni^{2+}–2-α-D-Man-pn system; $[L]_{tot}/[Ni^{2+}]_{tot}$ = 3.2 ($[L]_{tot}$ = 0.96 mM, $[Ni^{2+}]_{tot}$ = 0.3 mM), I = 0.16 M NaCl, 25 °C.

$[Cu_2L_2(OH)_2]^{2+}$ was poorer than that including $CuL(OH)^{+}$. The result is understandable since the concentrations of the metal ion and ligand were quite low (<10^{-3} M) under the experimental conditions.

2-α-D-Man-pn and 2-β-D-Glc-pn both form $Ni(L)^{2+}$, $Ni(L)_2^{2+}$ and $Ni(L)_3^{2+}$ complexes under the experimental conditions. The three corresponding stability constants, log $K^{Ni}_{Ni(L)}$, log $K^{Ni}_{Ni(L)_2}$ and log $K^{Ni}_{Ni(L)_3}$ can be determined but because of the hydrolysis of Ni^{2+}, the last two values were obtained with relatively large error limits (Tables 5 and 6). The species distribution diagram for the Ni^{2+}–2-α-D-Man-pn system ($[L]_{tot}/[Ni^{2+}]_{tot}$ = 3.2) is shown in Fig. 6. That the fraction of $Ni(L)_3^{2+}$ is so low, even in the range 9 ≤ pH ≤ 10, explains why its stability constant was obtained with large error terms. At pH > 10, hydrolysis of Ni^{2+} predominated; therefore, calculations were limited to pH ≤ 10. In the Ni^{2+}–2-β-D-Glc-pn system, the distribution diagram (not shown) was almost identical with the distribution diagram for the Ni^{2+}–2-α-D-Man-pn system.

The weak coordination and the strong tendency toward hydrolysis of Zn^{2+} makes the stability constant measurement of the Zn^{2+}–2-α-D-Man-pn and Zn^{2+}–2-β-D-Glc-pn systems very difficult. Although all the possible reactions mentioned above exist in the systems, only a few stability constants could be determined and most of them had large errors. For 2-β-D-Glc-pn, even the stability constant of $Zn(L)_2^{2+}$ could not be determined with a reasonable error. The species distribution diagram for 2-α-D-Man-pn in Fig. 7 indicates the complexity of these systems. Hydrolysis of Zn^{2+} always predominated over the whole pH range used for evaluation of the stability constants.

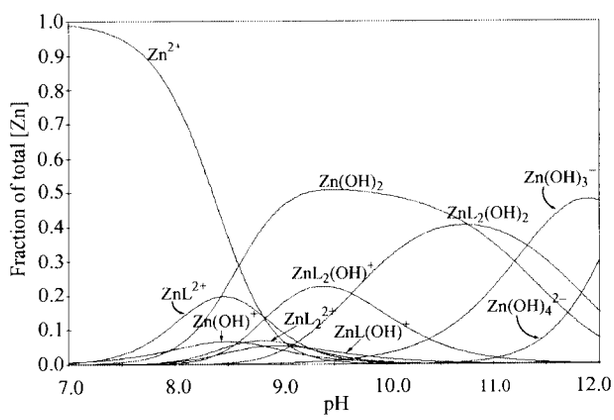


Fig. 7 Species distribution diagram for the Zn^{2+}–2-α-D-Man-pn system; $[L]_{tot}/[Zn^{2+}]_{tot}$ = 2.5 ($[L]_{tot}$ = 0.75 mM, $[Zn^{2+}]_{tot}$ = 0.3 mM), I = 0.16 M NaCl, 25 °C.

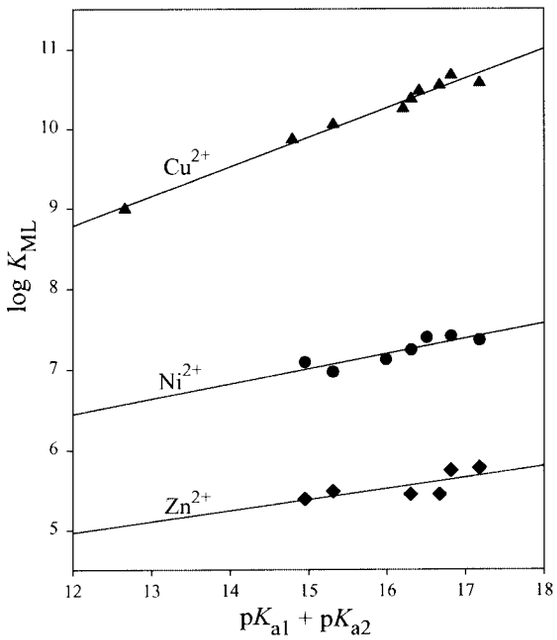


Fig. 8 Plot of log K_{ML} *vs.* $pK_{a1} + pK_{a2}$ for 1,2-diamine ligand systems (from left to right: 2,3-diaminopropanoic acid methyl ester, *cis*-2,3-diaminotetralin (1,2,3,4-tetraanhydronaphthalene), *trans*-2,3-diaminotetralin (1,2,3,4-tetraanhydronaphthalene), 1-β-D-Glc-pn, *cis*-1,2-diaminocyclohexane, 1,1-dimethylenediamine, 2,3-butylenediamine, 1,2-butylenediamine, 2-methyl-1,2-diaminopropane, DL-2,3-butylenediamine, *meso*-2,3-diaminobutane, 1,2-diaminopropane, 1,2-diaminoethane).

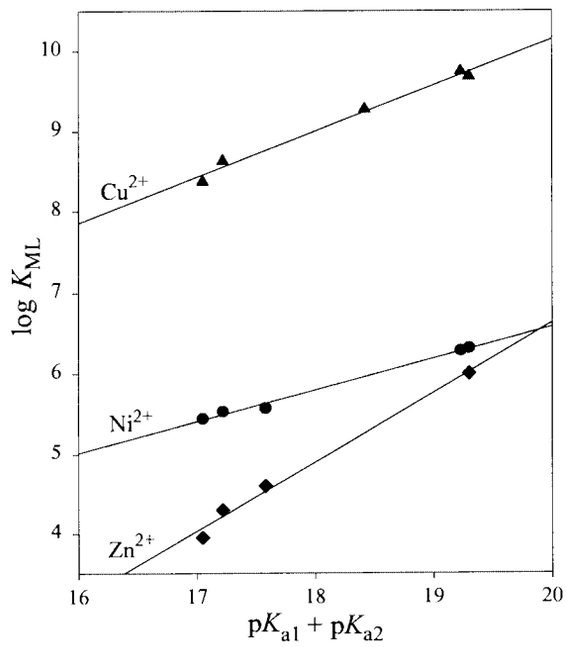


Fig. 9 Plot of log K_{ML} *vs.* $pK_{a1} + pK_{a2}$ for 1,3-diamine ligand systems (from left to right: 2-β-D-Glc-pn, 2-α-D-Man-pn, 2-hydrotrimethylethylenediamine, 2-dimethylene-1,3-propylenediamine, 1,3-butylenediamine, 1,3-diaminopropane).

Although appropriate hydrolysis constants were included, it was still impossible to obtain good values simply because complexation with the ligand was not the main reaction in the solution. Any error introduced by the hydrolysis would have a big influence on the results.

Stability constants of 1,2-diamine and 1,3-diamine systems

It is well known that, for a given metal ion, there is a linear relationship between stability constants log *K* and acidity constants p*K* for a series of structurally similar ligands.[25] For example, Sigel and co-workers have very recently established a linear relationship between the stability constants of transition metal ions with benzimidazole-type compounds and the acidity constants of those ligands.[10] This correlation is very useful for understanding the coordination situation of the ligand and can be used to check if the stability constant as measured is reasonable.[11] It is also known that, for a series of bidentate ligands, a similar correlation exists between the stability constants and the sum of the two acidity constants.[26,27]

In order to test the results reported herein for 1-β-D-Glc-pn, log *K* was plotted *vs.* p*K* ($pK_{a1} + pK_{a2}$) using known stability constants[16,18] for several 1:1 complexes of 1,2-diamine analogs with Ni^{2+}, Cu^{2+} and Zn^{2+} (Fig. 8). For Cu^{2+}, nine pair values in the range $12.7 \leq pK_{a1} + pK_{a2} \leq 17.2$ yielded a remarkably straight line. Cu^{2+}–1-β-D-Glc-pn fell right on the line; therefore, log $K^{Cu}_{Cu(L)}$ measured in this work agrees well with the reported values for other 1,2-diamine ligands.[16,18] This correlation also verifies conclusively that no carbohydrate oxygen atom participates in the coordination because any further interaction would increase the corresponding stability constant.[12] Although the corresponding Ni^{2+} and Zn^{2+} plots have fewer values and narrower pK_a ranges (Fig. 8), it is evident that the straight lines obtained and the values of log $K^{Ni}_{Ni(L)}$ and log $K^{Zn}_{Zn(L)}$ all correlate well. That the correlations between log $K^{M}_{M(L)}$ and $pK_{a1} + pK_{a2}$ for 1:1 complexes of 1,3-diamine ligands (Fig. 9) lie on different reference lines agrees with previous observations,[25] and reflects the difference between 5-membered chelate and 6-membered chelate rings (*vide infra*). Because of the aforementioned difficulties with hydrolysis, the correlation is less close for Zn^{2+}. The correlations between log $\beta^{M}_{M(L)_2}$ and $pK_{a1} + pK_{a2}$ for a series of 1,2-diamine ligands are also possible and the linear relationship is especially good for Cu^{2+} (not shown). Taken together these results suggest that the stabilities of the metal ion complexes of the three ligands presented herein depend solely on the basicity of the ligands and have no contribution from the carbohydrate moiety, in agreement with the weak coordination ability of sugars.[21] This bodes well for our beginning studies of these ligands as bioconjugates, using the diamine to chelate a metal ion and a carbohydrate as a bio-directing unit.

Comparing the coordination properties of Ni^{2+}, Cu^{2+} and Zn^{2+}

Another significant result obtained in this work is that for different metal ions, the species predominating in solution are quite different. This fact reflects the native properties of the metal ions themselves. It is well known that Cu(II), as a result of the Jahn–Teller distortion,[28] forms squares planar or distorted octahedral complexes. With 1-β-D-Glc-pn as the ligand, because of the strong coordination ability of the ligand, the geometry of $Cu(L)_2^{2+}$ is almost certainly square-planar (perhaps with a loosely bound water as a fifth ligand). Consequently, further coordination to form $Cu(L)_3^{2+}$ or $Cu(L)_2(OH)^+$ is quite unfavorable and hence the species $Cu(L)_2^{2+}$ predominates over a large pH range. When 2-α-D-Man-pn or 2-β-D-Glc-pn coordinate, however, the geometry of the complex $Cu(L)_2^{2+}$ is most likely distorted octahedral, and, by hydrolysis, $Cu(L)_2(OH)^+$ and $Cu(L)_2(OH)_2$ formed. Ni(II) complexes take on a variety of geometries, such as octahedral, square pyramidal, tetrahedral, and square planar.[28] With the ligands studied herein, Ni(II) appears to prefer an octahedral geometry, especially with 1-β-D-Glc-pn. Aqueous Zn(II) ions, such as $[Zn(H_2O)_6]^{2+}$, are strong acids and their salts hydrolyze readily in water,[28] a property of Zn(II) which governs its complexes in aqueous solution. For all three ligands studied, the hydrolysis products were predominant in neutral and basic solutions.

The results of Tables 3 and 5 afford another interesting conclusion regarding Zn^{2+}. In the 5-membered chelates of 1-β-D-Glc-pn (Table 3), this metal ion behaves normally, *i.e.*, it does not change its coordination number/geometry, whereas in the

6-membered chelates of 2-α-D-Man-pn (Table 5) it does, as is borne out from the following comparisons:

(a) Ni^{2+}: $\log K_1 - \log K_2 = 6.97 - 5.97 = 1.00 \pm 0.17$

Cu^{2+}: $= 10.05 - 8.80 = 1.25 \pm 0.11$

Zn^{2+}: $= 5.49 - 4.31 = 1.18 \pm 0.11$

(b) Ni^{2+}: $\log K_1 - \log K_2 = 5.53 - 3.77 = 1.76 \pm 0.2$

Cu^{2+}: $= 8.63 - 6.21 = 2.42 \pm 0.06$

Zn^{2+}: $= 4.3 - 4.0 = 0.3 \pm 0.3$

It is evident, in (a) that Zn^{2+} behaves like Ni^{2+} and Cu^{2+}, whereas in (b) the log K_2 for Zn^{2+} is "too high"; the latter observation indicates that Zn^{2+} changes its coordination number from 6 to 4.[29]

The well-known Irving–Williams series of stability indicates that the stability of complexes of the divalent metal ions investigated in this study should fall in the following order: Ni(II) < Cu(II) > Zn(II).[23,30] Comparing the analogous values of log $K^{M}_{M(L)}$ and log $\beta^{M}_{M(L)_2}$ in Tables 3, 5 and 6, it can be seen that each of the three ligands follow the Irving–Williams series; however, for hydrolysis species (*e.g.* log $\beta^{M}_{M(L)_2(OH)}$ or log $\beta^{M}_{M(L)_2(OH)_2}$), the values for Zn(II) are often larger than for Cu(II).

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