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Determination of the stability constants of mercury(II) complexes of mixed donor macrobicyclic encapsulating ligands †

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The reactions of mercury(II) with the mixed donor encapsulating ligands 3,6,16-trithia-6,11,19-triazabicyclo[6.6.6]-icosane (AMN_3S_3sar) and 1-amino-8-methyl-6,19-dithia-3,10,13,16-tetraazabicyclo[6.6.6]icosane (AMN_4S_2sar) have been studied. NMR ligand–ligand competition experiments with the ligands 1,4,8,11-tetraazacyclotetradecane ([14]aneN_4), 1-thia-4,7,10-triazacyclododecane ([12]aneN_3S) and ethylenediaminetetraacetic acid (EDTA) with AMN_3S_3sar and Hg(II) indicated that [14]aneN_4 would be an appropriate competing ligand for the determination of the Hg(II) stability constant. Calculations indicated the ratio of concentrations of AMN_3S_3sar, [14]aneN_4 and Hg(II) required for the determination of the stability constant ranged from 1 : 1 : 1 to 1 : 5 : 1. Refinement of the titration curves yielded $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} = 17.7$. A similar competition titration resulted in the determination of the stability constant for the AMN_4S_2sar system as $\log_{10}K[Hg(AMN_4S_2sar)]^{2+} = 19.5$. The observed binding constants for the mixed N/S donor systems and the hexaaza analogues sar (3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane) and diamsar (1,8-diamino-3,6,10,13,16,19-hexazabicyclo[6.6.6]icosane ($\log_{10}K$-[Hg(diamsar)]$^{2+} = 26.4$; $\log_{10}K[Hg(sar)]^{2+} = 28.1$) differ by approximately ten orders of magnitude. The difference is ascribed not to a cryptate effect but to a mismatch in the Hg–N and Hg–S bond lengths in the N/S systems.

Introduction

Competition methods are employed for the determination of very large metal–ligand stability constants in situations where the metal ion binding is so strong that the degree of formation is too large, even at low pH, for the use of the usual potentiometric or spectrophotometric methods.[1] The competition method involves an analysis using various ratios of a ligand of unknown stability (L_A), the metal ion (M) and a reference ligand (L_B) for which the ML_B binding constant is known. The concentrations of L_A, M, L_B, the ML_B binding constant and the protonation constants of L_A and L_B are used to define a pH region in which the metal ion is distributed evenly between L_A and L_B. A potentiometric titration undertaken within this pH region, the crossover region, permits an accurate determination of the unknown stability constant.[1] Examples of this methodology include the determination of the stability constants for Fe(III) complexes with catechol-based ligands (L) where $\log_{10} K$(Fe(III)L) can be of the order of ≈40,[2,3] and for the determination of the stability constants of Ga(III) and In(III) complexes with carboxylic acid based ligands.[1,4]

In a similar manner, for mercury(II) complexes of the macrobicyclic hexaamine cages with which the Hg^{2+} ion forms complexes labile in neutral and basic solutions, the problem of determination of the very large stability constants has been overcome by using ligand–ligand competition methods.[5,6] Thus, the stability constant of $[Hg(sar)]^{2+}$ (sar = 3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane) was determined spectrophotometrically to be ($\log_{10}K[Hg(sar)]^{2+}$) = 28.1, using a competition titration with iodide as the competing ligand.[5] Competition ^{1}H NMR spectroscopy, using sar as the competing ligand, was then used to determine the Hg(II) stability constant of the cage molecule diamsar (diamsar = 1,8-diamino-3,6,10,13,16,19-hexazabicyclo[6.6.6]icosane) with $\log_{10}K[Hg(diamsar)]^{2+} = 26.4$.[5]

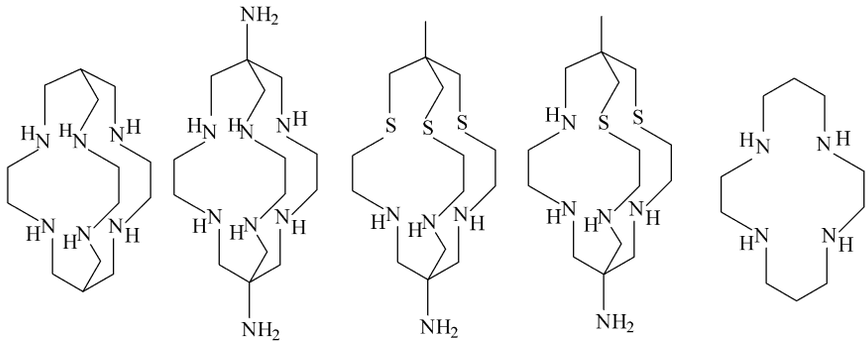
The mixed donor encapsulating ligands 3,6,16-trithia-6,11,19-triazabicyclo[6.6.6]icosane (AMN_3S_3sar) and 1-amino-8-methyl-6,19-dithia-3,10,13,16-tetraazabicyclo[6.6.6]icosane (AMN_4S_2sar), like the hexaaza analogues, form metal complexes in which the metal ion is totally enclosed by the ligand.[7,8] Whilst spectroscopic, electrochemical and structural properties of the mixed donor encapsulating complexes have been studied extensively,[9–12] the thermodynamic properties are less well explored. The interaction of AMN_3S_3sar and AMN_4S_2sar with Hg^{2+} has thus been investigated using ligand–ligand competition NMR experiments and potentiometric methods.

Experimental

Materials

1-Amino-8-methyl-6,10,19-trithia-3,13,16-triazabicyclo[6.6.6]-icosane (AMN_3S_3sar), 1-amino-8-methyl-6,19-dithia-3,10,13,16-tetraazabicyclo[6.6.6]icosane (AMN_4S_2sar), 3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane (sar) and $[Hg(sar)](CF_3SO_3)_2$ were available from previous work.[5,7,8] Mercuric perchlorate monohydrate, mercuric acetate and 1,4,8,11-tetraazacyclotetradecane ([14]aneN_4) were purchased from Aldrich and used without further purification. Mercuric nitrate hydrate was purchased from BDH chemicals and used without further purification. Titrant solutions of base (KOH, Et_4NOH) were standardised with 0.100 M Volucon HCl. Titrant solutions of $HClO_4$ were standardized with a previously standardized Et_4NOH solution. Mercury(II) solutions of the appropriate salt were made up to a concentration of 0.1 M and were analyzed by ICP-MS at the CSIRO Tropical Agriculture Analytical Services Facility, St Lucia, QLD.

† Electronic supplementary information (ESI) available: potentiometric competition titration plots and theoretical speciation plots for competition titrations of Hg^{2+}, AMN_3S_3sar and [14]aneN_4. See http://www.rsc.org/suppdata/dt/b1/b103706b/



Physical measurements

NMR spectra were obtained with a Bruker AC200F (200 MHz) NMR spectrometer (^{1}H and ^{13}C) and a Bruker 400 MHz NMR spectrometer (^{1}H). Solutions were made with D_2O, purchased from Aldrich, 0.1 M and 0.001 M NaOD. NaOD solutions were formed by diluting a small volume of a concentrated aqueous solution of NaOH with D_2O.

Competition NMR spectra

^{1}H NMR spectroscopy. ^{1}H NMR spectra were obtained of the ligands both in the presence and absence of mercuric acetate. Milligram quantities of accurately weighed (to 4 decimal places) equimolar amounts (5.3 μmol) of $Hg(CH_3COO)_2$ and a ligand were dissolved in 1.0 mL of solvent. The ligand was dissolved first before adding mercuric acetate. Spectra of the free ligands AMN_3S_3sar, AMN_4S_2sar and [14]aneN_4 were obtained with and without the addition of $NaCH_3COO$ (10.6 μmol). All spectra with sar were obtained in 0.1 M NaOD. A spectrum of $[Hg(sar)](CF_3SO_3)_2$ was obtained in 0.1 M NaOD. Spectra of $Hg(CH_3COO)_2$ and AMN_3S_3sar or AMN_4S_2sar were obtained in D_2O, 0.001 M and 0.1 M NaOD. Competition experiments were performed with $Hg(CH_3COO)_2$ and AMN_3S_3sar or AMN_4S_2sar, competing with [14]aneN_4 in 1.0 mL of 0.001 M NaOD. All competition NMR experiments were performed with equimolar mixtures (5.3 μmol). Both ligands were dissolved first before adding $Hg(CH_3COO)_2$. Spectra were obtained of the mixture of $Hg(CH_3COO)_2$, AMN_3S_3sar or AMN_4S_2sar and [14]aneN_4 in 0.001 M NaOD acidified with glacial acetic acid. The acetate peak at 1.80 ppm was used as a reference.

^{13}C NMR spectroscopy. Equimolar amounts (0.1 mmol) of mercuric perchlorate monohydrate and AMN_3S_3sar or AMN_4S_2sar were mixed in D_2O and the precipitate subsequently formed was removed by gravity filtration. Both ^{13}C and ^{13}C DEPT NMR spectra were obtained of the filtrate, internally referenced with 1,4-dioxane at 0.0 ppm.

Potentiometric titrations

Potentiometric titrations were performed with a Metrohm E665 Dosimat Series 14 automatic titrator which is able to add a minimum titrant volume of 1 μL through a 5 cm^3 burette. The e.m.f. was measured with an Orion 720A Benchtop pH/ISE meter with an Ionode intermediate junction electrode or an Orion Model 8172 Ross Sure-Flow combination glass body electrode. The filling solution of the electrode was an aqueous solution of the same electrolyte (0.1 M) as that of the titrant. All titrations were carried out at constant ionic strength, with an electrolyte solution of 0.1 M KNO_3 or 0.1 M Et_4NClO_4, and performed under a nitrogen atmosphere in a water-jacketed cell maintained at 298.0 K. The solution was allowed to equilibrate for a maximum of five minutes after each addition of titrant. The automatic titrator and the pH meter were connected to an IBM compatible personal computer, which controlled the addition of titrant using a locally written program. For each titration, the pH meter was calibrated using pH 7.0 and pH 4.0 buffer solutions purchased from Labchem and BDH chemicals, respectively. A calibration titration was performed each time using 5–7 × 10^{-3} M $HClO_4$ in 0.1 M Et_4NClO_4 titrated with 0.1 M Et_4NOH, or, 5–7 × 10^{-3} M HNO_3 in 0.1 M KNO_3 titrated with 0.1 M KOH depending on the electrolyte to be used for the following titration. The parameters E_o and pK_w were thereby determined using the program SUPERQUAD.[13]

Ligand titrations. Ligand solutions (0.9–1.1 × 10^{-3} M) containing a strong electrolyte (0.1 M Et_4NClO_4 or 0.1 M KNO_3) were acidified with the corresponding acid to 5–7 × 10^{-3} M. Potentiometric titrations of the free ligands AMN_3S_3sar, AMN_4S_2sar and [14]aneN_4 were performed. Titrations of [14]aneN_4 were performed with Et_4NClO_4 as the supporting electrolyte. Data were obtained by titrating 10 mL aliquots of acidified ligand solutions with successive additions of base controlled so as to cause a decrease of 4 mV per potential reading. At least three titrations were performed with each ligand. The stepwise protonation constants and concentrations of the ligand solutions were determined with SUPERQUAD.[13]

Hg(II) and AMN_3S_3sar (or AMN_4S_2sar) titrations. Data were obtained by mixing a 0.1 cm^3 aliquot of a Hg(II) solution with a 10 cm^3 aliquot of AMN_3S_3sar solution in the reaction vessel. Titrations were performed with both KNO_3 and Et_4NClO_4 as the supporting electrolyte. Titrant was added to the mixture so as to cause a decrease of 4 mV per potential reading.

Hg(II), AMN_3S_3sar (or AMN_4S_2sar) and [14]aneN_4 competition titrations. Data were obtained by mixing stoichiometric amounts of Hg(II) and [14]aneN_4 solutions with varying aliquots of AMN_3S_3sar solution to achieve a molar ratio of Hg : AMN_3S_3sar : [14]aneN_4 ranging from 1 : 1 : 1 to 1 : 5 : 1. Titrations were performed with Et_4NClO_4 as the supporting electrolyte. Back titrations were performed at the completion of a titration with base. Alkaline solutions of Hg(II), AMN_3S_3sar and [14]aneN_4 were retained and titrated with $HClO_4$ (0.1 M) under the same conditions. Titrant volumes were added so as to cause a decrease of 4 mV per potential reading outside the pH range of 3.5–9. Titrant volumes were fixed at 1 μL for the pH range of 3.5–9.

Results and discussion

Protonation constants

Typical titration curves for AMN_3S_3sar and AMN_4S_2sar are shown in Fig. 1 and protonation constants are listed in Table 1 along with those reported for the hexaamine encapsulating ligands.[14] In the titrations with AMN_3S_3sar there were no notable differences between using KNO_3 and Et_4NClO_4 as the electrolyte suggesting that there was no significant interaction

Table 1 Protonation and Hg(II) stability constants for various ligands (L)

Species	AMN_3S_3sar [a,b]	AMN_4S_2sar [a,b]	sar [5,14,c]	diamsar [5,14,c]	[14]aneN$_4$ [15,17,b]	EDTA [15,b]	[12]aneN$_3$S [15,b]
HL	9.70	10.16	11.95	11.44	11.4	10.37	9.53
H_2L	5.74	7.50	10.33	9.64	10.27	6.13	8.15
H_3L	2.5	4.78	7.17	6.49	1.6	2.69	3.09
H_4L	<2.0	<2.0	≈0	5.48	0.9	2.00	—
H_5L	—	<2.0			—	1.5	—
H_6L	—	—			—	0.0	—
[HgL]	17.7	19.5	28.1	26.4	23.0 [d]	21.5	24.32
[Hg(HL)]	5.3	5.9	—		—	3.2	—

[a] This work. [b] I = 0.1 mol L^{-1}; 298 K. [c] I = 1.0 mol L^{-1}; 298 K. [d] I = 0.2 mol L^{-1}; 298 K.

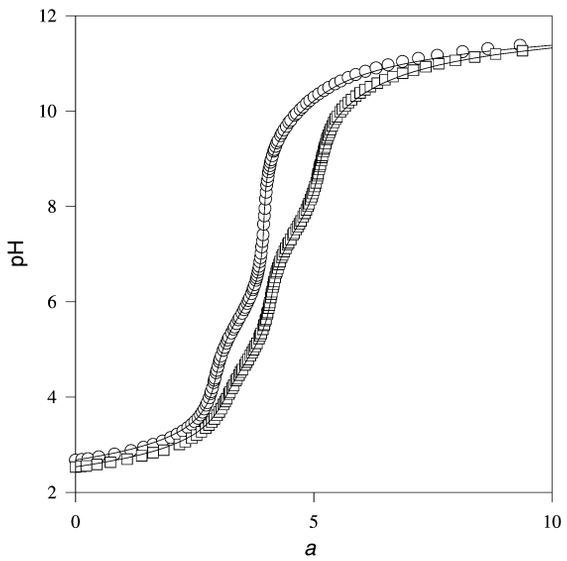


Fig. 1 Titration curves of AMN_3S_3sar and AMN_4S_2sar (0.1 M Et_4NClO_4, 298 K); AMN_3S_3sar (○ exp; — calc); AMN_4S_2sar (□ exp; — calc) ("a" is the number of mmol of base added per mmol of ligand present in solution).

between AMN_3S_3sar and K^+, assuming that the cation, Et_4N^+ is too large to interact with the AMN_3S_3sar cage. For this ligand there are four possible protonatable groups, the primary amine and three secondary amines. Two of the sites were too acidic to be observed within the working pH range of the titration and were therefore unable to be refined with SUPERQUAD.[13] Thus, the magnitudes of K_3 and K_4 were determined by fixing values for $\log_{10}K_3$ and $\log_{10}K_4$ within the model and finding, by trial and error, which values gave the best fit of the experimental data (Fig. 1). In the titrations with AMN_4S_2sar three of the five possible protonatable groups could be refined with SUPERQUAD, and the two corresponding to the very acidic sites were determined in the same manner as above.

The speciation plot for AMN_3S_3sar (Fig. 2) shows that very little of the tetraprotonated form of the ligand is formed even at pH 2. At this pH approximately 70% of the ligand exists as the triprotonated form but its abundance rapidly declines with increasing pH. The relatively low composition of the tri- and tetra-protonated forms of the ligand, due to the high acidity of the corresponding protonations, is the reason why the values for K_3 and K_4 were unable to be refined for the data obtained. At pH 4.5 the predominant ligand species is the diprotonated form, at pH 8 the majority of the ligand is monoprotonated while at pH 12 AMN_3S_3sar becomes fully deprotonated. The speciation plot for AMN_4S_2sar (Fig. 2) shows that the ligand is fully deprotonated at pH 12, it exists predominantly as its monoprotonated form at pH 9, the diprotonated form at pH 6 and at pH 2.5 most of the ligand is triprotonated. Very little of the tetraprotonated species is formed at pH 2.

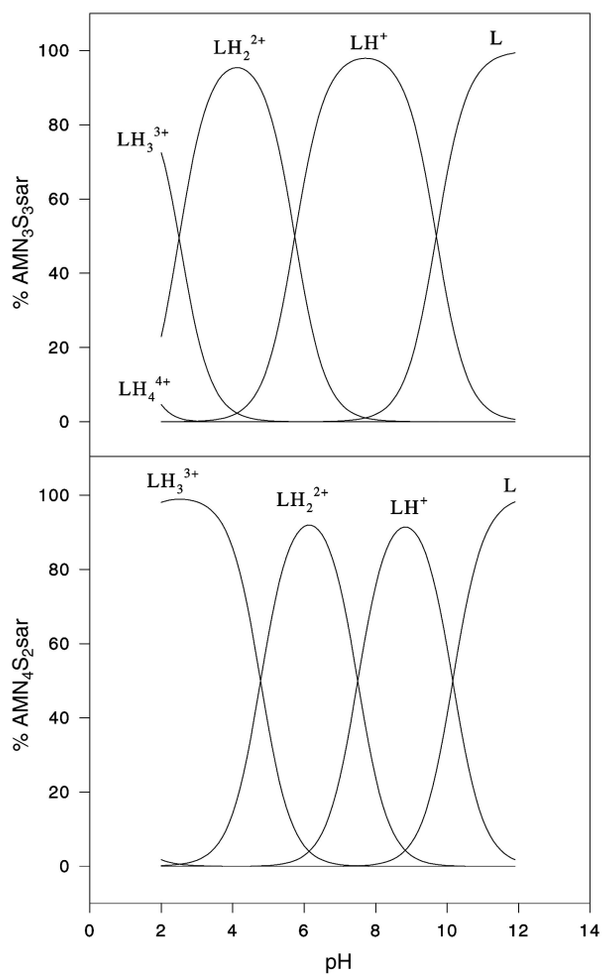


Fig. 2 Experimental speciation plots for AMN_3S_3sar and AMN_4S_2sar.

NMR characterization of the Hg(II) complexes

^{13}C NMR indicates that the Hg(II) centre is symmetrically bound within the cavity along the C_3 axis of the AMN_3S_3sar molecule, as only seven resonances are observed (δ −9.9 (CH_2); −12.2 (C_q); −20.7, −21.9, −30.0 (CH_2); −31.2 (C_q); −32.6 (CH_3)) suggesting that the Hg(II) centre is coordinated to each of the three secondary amines within the cavity of the macrobicyclic ligand. The ^{13}C NMR spectrum of a stoichiometric mixture of $Hg(ClO_4)_2$ and AMN_4S_2sar in D_2O solution exhibited fifteen resonances (δ −6.8, −8.7, −9.3, −9.6 (CH_2); −13.5 (C_q); −18.2, −18.5, −20.4, −20.7, −22.3, −23.2 (CH_2); −29.4, −29.9, (CH_2); −30.0 (C_q); −35.0 (CH_3)) whereas the free ligand displays an eleven line spectrum (δ −9.1, −10.4, −10.7, (CH_2); −13.3 (C_q); −18.0, −18.3, −18.8, −26.0 (CH_2); − 27.1 (C_q); −33.8 (CH_2); −41.4 (CH_3)) indicating formation of an unsymmetric complex where all the methylene moieties are unique due to Hg(II) coordination. It can be assumed, therefore, that the Hg(II) centre is coordinated to each of the four

secondary amines within the cavity of the AMN_4S_2sar ligand.

In D_2O, spectra of AMN_3S_3sar, and a mixture of $Hg(CH_3COO)_2$ and AMN_3S_3sar, are significantly different implying complexation in D_2O. The presence of satellite peaks from the coupling of protons from AMN_3S_3sar with ^{199}Hg (nuclear spin ½, natural abundance 16.8%) as well as the presence of AB coupling from the protons of the encapsulated complex, indicate the presence of $[Hg(AMN_3S_3sar)]^{2+}$. Similar spectral characteristics are observed for the spectra of $[Hg(sar)]^{2+}$ and $[Hg(diamsar)]^{2+}$ in 0.1 M NaOD.[5] NMR experiments confirmed that $[Hg(sar)]^{2+}$ decomplexation does not occur in a solution of 0.1 M NaOD. However, spectra obtained in 0.1 M NaOD of free AMN_3S_3sar and an equimolar mixture of $Hg(CH_3COO)_2$ and AMN_3S_3sar show very little difference, indicating that the Hg(II) complex does not form under these conditions. These results suggest the Hg(II) stability constant of AMN_3S_3sar is significantly lower than those of sar and diamsar (Table 1).[5] This is because the hydroxide ion has a greater affinity for Hg(II) than AMN_3S_3sar at very high pH. The stability constants reported for mercury(II) hydroxide species are $\log_{10}K[Hg(OH)]^+ = 10.04$ and $\log_{10}K[Hg(OH)_2] = 11.16$ (298 K; $I = 0.5$ mol L^{-1}) .[15] Conversely, the N_6 cages, sar and diamsar, have a greater affinity for Hg(II) than the hydroxide ion even at high pH.

Metal–ligand stability constants, direct potentiometric titration

A metal–ligand stability constant was unable to be refined by SUPERQUAD[13] from the data obtained from the titration curve for Hg(II) and AMN_3S_3sar or AMN_4S_2sar. Theoretical speciation plots were calculated using SUPERQUAD,[13] assuming equimolar Hg^{2+} and AMN_3S_3sar and using the previously determined protonation constants of the ligand. By varying the estimate of the unknown stability constant for the $[Hg(AMN_3S_3sar)]^{2+}$ complex, a series of theoretical speciation plots were obtained. The plots suggested that for $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} < 16$, H^+ would be an effective competitor with Hg^{2+} for AMN_3S_3sar, particularly around pH 2. Consequently, at low pH there would be a substantial amount of protonated AMN_3S_3sar and free Hg^{2+} which would convert to the complex $[Hg(AMN_3S_3sar)]^{2+}$ as the pH was increased. However, the theoretical plots suggested that if the stability constant was greater than 16, the Hg^{2+} ion has such a strong affinity for AMN_3S_3sar that protons, even at low pH, are no longer an effective competitor for the ligand. Hence, almost 100% of AMN_3S_3sar exists as its Hg^{2+} complex for the complete pH range studied and a metal–ligand stability constant could not be obtained by a metal–ligand potentiometric titration. Similarly, speciation plots indicate that a Hg(II) stability constant can only be refined from a Hg(II) and AMN_4S_2sar titration if $\log_{10}K[Hg(AMN_4S_2sar)]^{2+}$ is less than ≈19. Thus, since direct potentiometric titration data cannot be refined by SUPERQUAD we can conclude that $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} > 16$ and $\log_{10}K[Hg(AMN_4S_2sar)]^{2+} > 19$.

Although polarographic methods have been reported for the determination of large stability constants of mercury complexes[17] we chose instead to employ potentiometric methods. To do this successfully requires the application of a competing ligand with a set of characteristics such that it will compete successfully with the encapsulating ligands over a precise range of pH and concentration conditions. In order to find an appropriate competing ligand it is necessary to carefully examine the reaction between the competing ligand, the target ligand (the encapsulating ligand) and the metal ion in question in order to be sure that the appropriate complexes are being formed. Whilst, in theory, many competitors could be chosen, in fact the conditions for the competition experiment have to be chosen precisely such that the refinement produces results which are chemically meaningful. We have chosen to explore the competition experiments with three potential competition partners using NMR spectroscopy to fully understand the species present in solution under defined conditions of concentration and pH.

A mixture of equimolar amounts of metal (M) and two ligands (L_A and L_B) can be used to obtain the relative stability of the ML_A and ML_B complexes when the conditions are such that L_A and L_B are fully deprotonated (*i.e.* no other competing equilibria have a substantial influence). If resonances were only observed for $[ML_A]$ and free L_B then $\log_{10}K[ML_A] > (\log_{10}K[ML_B] + 2)$. If resonances in the NMR spectrum for both complexes, $[ML_A]$ and $[ML_B]$, are observed it is assumed that the metal–ligand stability constants are within two orders of magnitude. When all four general species $[ML_A]$, $[ML_B]$, L_A and L_B, are present, integration of the appropriate resonances in the ^1H NMR spectrum can accurately determine the relative stability.

Metal–ligand stability constants, ^1H NMR competition experiments

In order to gauge the magnitude of the stability constant of the $[Hg(AMN_3S_3sar)]^{2+}$ complex competition NMR experiments were undertaken. Ligands such as [12]aneN$_3$S[16] and EDTA and [14]aneN$_4$[15,17] were examined as possible competitors.

A competition ^1H NMR spectrum of a mixture of $Hg(CH_3COO)_2$, AMN_3S_3sar and [14]aneN$_4$ in 0.001 M NaOD revealed only free AMN_3S_3sar and the formation of $[Hg([14]aneN_4)]^{2+}$. It can therefore be concluded that the Hg(II) stability constant for AMN_3S_3sar falls below 21.0 since $\log_{10}K[Hg([14]aneN_4)]^{2+} = 23.0$.[15,17] Similar experiments with EDTA suggested that the stability constant for the Hg(II) encapsulated complex should be <19.5.

Theoretical speciation plots were calculated using realistic values for species concentrations, known stability constants for the $[Hg([14]aneN_4)]^{2+}$ complex and protonation constants of both ligands in question. Variation of the estimate of the unknown stability constant for the $[Hg(AMN_3S_3sar)]^{2+}$ complex resulted in a series of theoretical speciation plots. These speciation plots showed a crossover region for $\log_{10}K$ values for $[Hg(AMN_3S_3sar)]^{2+}$ of 17 and above (Fig. 3). The pH at which the crossover region occurs increased with increasing $[Hg(AMN_3S_3sar)]^{2+}$ stability. Yet, for $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} = 16.0$ no crossover region is observed and for $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} = 19$ a crossover at pH 8.5 is predicted. From the direct potentiometric titration and the related theoretical speciation plots it was established that no formation of $[Hg(AMN_3S_3sar)]^{2+}$ would be observed for the acidified mixture when the stability constant is below 16.0. ^1H NMR spectra under acidic conditions showed peaks characteristic of $[Hg(AMN_3S_3sar)]^{2+}$ and free [14]aneN$_4$, confirming the speciation plots and that $\log_{10}K[Hg(AMN_3S_3sar)]^{2+}$ is above 16.0 and below 19.5. The fact that no resonances were observed for $[Hg([14]aneN_4)]^{2+}$ or free AMN_3S_3sar indicate that the $[Hg(AMN_3S_3sar)]^{2+}$ stability constant lies in the upper portion of this range. In summary, for equimolar mixtures of Hg(II), AMN_3S_3sar and [14]aneN$_4$, theoretical speciation plots and ^1H NMR show that the major composition of the solution changes from $[Hg(AMN_3S_3sar)]^{2+}$ and free protonated [14]aneN$_4$ at low pH to $[Hg([14]aneN_4)]^{2+}$ and free protonated AMN_3S_3sar at high pH when the stability constant of $[Hg(AMN_3S_3sar)]^{2+}$ is between 17.0 and 19.5, which is ideal for a potentiometric competition titration.

Direct potentiometric titration of Hg(II) and AMN_4S_2sar combined with theoretical speciation plots showed that $\log_{10}K[Hg(AMN_4S_2sar)]^{2+}$ is greater than 19. Competition experiments were performed with the ligand [14]aneN$_4$ in 0.001 M NaOD. The ^1H NMR spectrum of an equimolar mixture of $Hg(CH_3COO)_2$, AMN_4S_2sar and [14]aneN$_4$ shows complete formation of $[Hg([14]aneN_4)]^{2+}$ and free AMN_4S_2sar

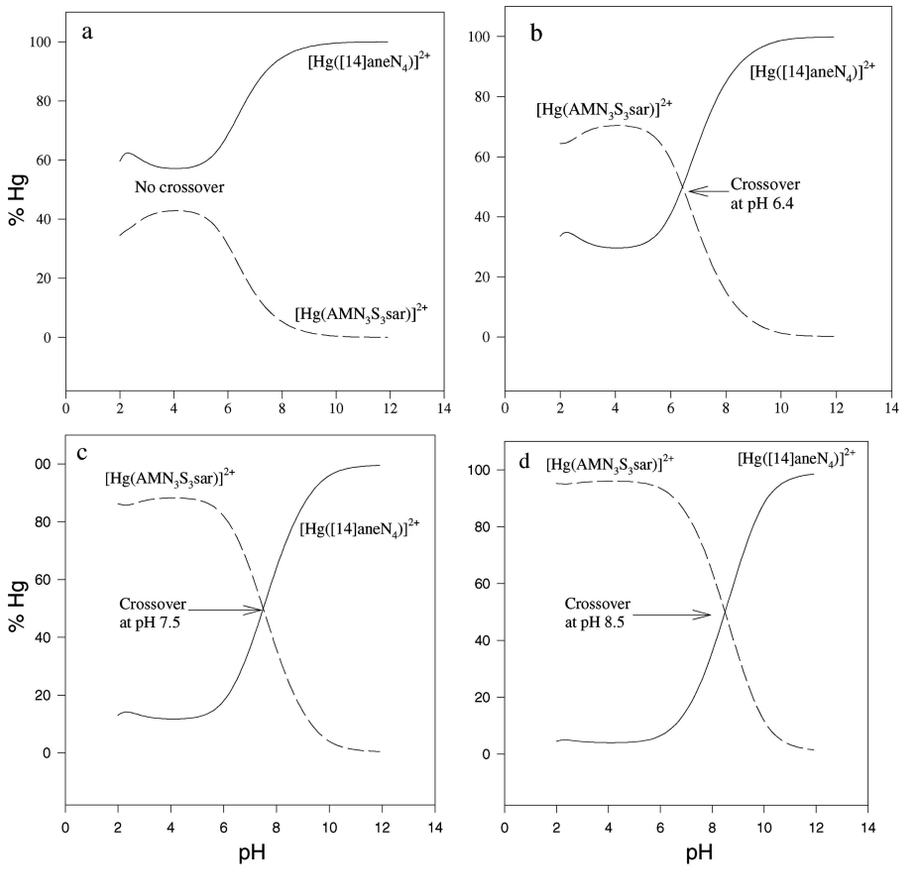


Fig. 3 Theoretical speciation plots for competition titrations (relative ratios Hg^{2+} : AMN_3S_3sar : [14]aneN$_4$, 1 : 1 : 1) $\log_{10}K[Hg(AMN_3S_3sar)]^{2+}$ = 16.0 (a), 17.0 (b), 18.0 (c), 19.0 (d).

while no resonances were observed for free [14]aneN$_4$ and a Hg(II) complex of AMN_4S_2sar. Since $\log_{10}K[Hg([14]aneN_4)]^{2+}$ is 23.0, the stability constant of $[Hg(AMN_4S_2sar)]^{2+}$ is probably below 21.0. Hence, the stability constant of AMN_4S_2sar is predicted to be within the range of 19.0 and 21.0. Theoretical speciation plots of the competition titrations (ESI)† showed that only a narrow range of conditions ($[Hg(AMN_4S_2sar)]^{2+}$ stability, relative concentrations) will produce competition potentiometric titrations with [14]aneN$_4$ that can refine the Hg(II) stability constant of AMN_4S_2sar. The more basic protonations of AMN_4S_2sar, compared to AMN_3S_3sar, give a lower differential between the acidities of AMN_4S_2sar and [14]aneN$_4$ compared with AMN_3S_3sar and [14]aneN$_4$. The smaller difference between protonations of AMN_4S_2sar and [14]aneN$_4$ can be observed in the theoretical speciation plots of Hg(II), AMN_4S_2sar and [14]aneN$_4$ under certain conditions where seemingly two crossover regions occur. The second crossover region arises because the third protonation of [14]aneN$_4$ is significantly more acidic than the corresponding protonation of AMN_4S_2sar. When five times more AMN_4S_2sar is present relative to Hg^{2+} and [14]aneN$_4$, and $\log_{10}K[Hg(AMN_4S_2sar)]^{2+} \leq 20.0$, the second crossover region at high pH would be well defined. The solution before this crossover region would be composed of ≈100% of the Hg(II), present as $[Hg(AMN_4S_2sar)]^{2+}$, with no $[Hg([14]aneN_4)]^{2+}$ present, while after the crossover region the solution would consist of no $[Hg(AMN_3S_3sar)]^{2+}$ and mainly $[Hg([14]aneN_4)]^{2+}$. Thus, suitable conditions for the potentiometric competition titrations have been established.

Metal–ligand stability constants, potentiometric competition titrations

A series of titrations were performed, varying the AMN_3S_3sar concentration relative to the Hg(II) and [14]aneN$_4$ concentrations. The titrations were performed obtaining as many points as possible between pH 3.5 and 9. Titration curves

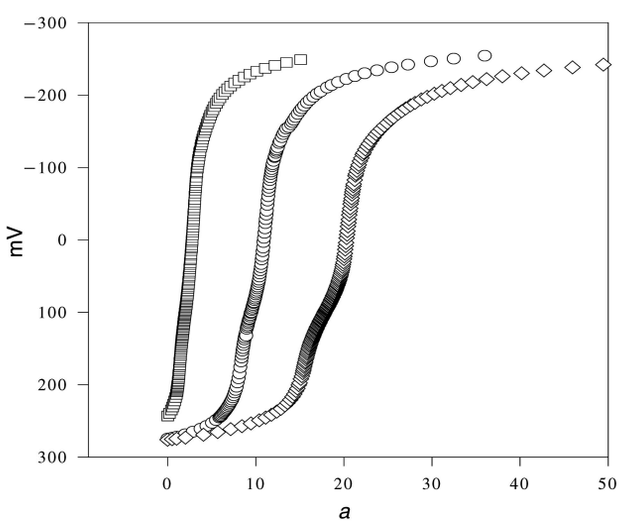


Fig. 4 Potentiometric competition titrations (Hg(II), AMN_3S_3sar, [14]aneN$_4$; 0.1 M Et_4NClO_4, 298 K) ("*a*", the number of mmol of base added per mmol of [14]aneN$_4$ present in solution) (relative ratios Hg^{2+} : AMN_3S_3sar : [14]aneN$_4$, □ 1 : 1.04 : 1.12; ○ 1 : 2.59 : 1.10; ◇ 1 : 5.19 : 1.12).

(Fig. 4) were plotted using the parameter "*a*", defined as the number of mmol of base added per mmol of [14]aneN$_4$ present in solution. The titration curves produced show an inflection point which becomes more pronounced as the relative concentration of AMN_3S_3sar increases. Data were analyzed in the pH range encompassing the inflection point (pH 4–8). It was necessary to include a protonated mercury complex species, $[Hg(AMN_3S_3sarH)]^{3+}$, for the data to be refined successfully. Back titrations (ESI)† were performed by titrating basic solutions of Hg(II), AMN_3S_3sar and [14]aneN$_4$ with $HClO_4$. Once again as many points as possible were collected from around

the crossover region and data were analysed from pH 8 to pH 4. The stability constants obtained from the forward and reverse titrations were $\log_{10}K[Hg(AMN_3S_3sar)]^{2+} = 17.7(0.2)$ and $\log_{10}K_H[Hg(AMN_3S_3sarH)]^{3+} = 5.3(0.1)$, the reactions defined as:

$$AMN_3S_3sar + Hg(II) \rightleftharpoons [Hg(AMN_3S_3sar)]^{2+}, \text{ and}$$

$$[Hg(AMN_3S_3sar)]^{2+} + H^+ \rightleftharpoons [Hg(AMN_3S_3sarH)]^{3+}$$

with $K = [HgL]/([Hg][L])$ and $K_H = [HgLH]/([HgL][H^+])$ (L = AMN_3S_3sar) (Table 1). It is most likely that the extra proton of $[Hg(AMN_3S_3sarH)]^{3+}$ is located at the primary amine site.

In a similar manner analysis of the data from a titration with AMN_4S_2sar, Hg(II) and [14]aneN$_4$ (ESI),† using SUPERQUAD[13] indicated that $\log_{10}K[Hg(AMN_4S_2sar)]^{2+} = 19.5(0.1)$, with $\log_{10}K_H[Hg(AMN_4S_2sarH)]^{3+} = 5.9(0.1)$.

Conclusions

For the $[Hg(AMN_3S_3sar)]^{2+}$ complex the complexation process is reversible and it was possible to fit the data to the proposed model for each titration. For $[Hg(AMN_4S_2sar)]^{2+}$ the titration was not reversible on the time scale of the potentiometric analysis, suggesting that the rate of Hg(II) removal from the cage was slow in the pH range 9–3. For the N_6 encapsulated complex $[Hg(diamsar)]^{2+}$ the extrusion of the metal ion from the cavity is slow in the pH ranges employed.[5] The difference in behavior between the N_3S_3sar and N_4S_2sar ligands suggests that the addition of the extra secondary amine donor in the latter is sufficient to alter the kinetics of H^+ assisted metal ion removal in these systems.

For the mixed aza–thia encapsulating ligands, the stability constants ($\log_{10}K[Hg(AMN_3S_3sar)]^{2+} = 17.7$; $\log_{10}K[Hg(AMN_4S_2sar)]^{2+} = 19.5$) are approximately ten orders of magnitude less than those of the analogous hexaaza cage molecules (Table 1).[5] The difference does not, however, accord with the differences seen in the case of macrocyclic systems where replacement of a secondary amine donor with a thiaether has little affect on the magnitude of the binding constant ($\log_{10}K[Hg(II)\text{-}[12]aneN_4)]^{2+} = 25.5$; $\log_{10}K[Hg([12]aneN_3S)]^{2+} = 24.32$ and $\log_{10}K[Hg([16]aneN_5)]^{2+} = 27.4$; $\log_{10}K[Hg([16]aneN_4S)]^{2+} = 25.15$).[16] Kimura has suggested that the macrocyclic effect is limited for large metal ions such as Hg(II) and that the magnitude of the binding constant is a reflection of the number of secondary amines bound to the metal ion.[17] The enhanced stability of $[Hg(sar)]^{2+}$ and $[Hg(diamsar)]^{2+}$ compared with $[Hg([14]aneN_4)]^{2+}$ (Table 1) has thus been attributed to the two extra amine donors in the extra strand of the sar ligand, not to a cryptate effect.[5] Similar conclusions may be drawn from a comparison between the Hg(II) binding constants reported for the branched ligand *N*,*N*,*N*′,*N*′-tetrakis(2-aminoethyl)ethane-1,2-diamine ($\log_{10}K = 29.6$),[18] the macrocyclic ligand [18]aneN$_6$ ($\log_{10}K = 29.1$),[19] and the macrobicyclic ligands sar and diamsar.[5]

The observed decrease in Hg(II) stability for increasing thiaether coordination for cage molecules may be due to a number of factors. The Hg(II) ion may be present in an *exo*-conformation and within the cavity of the AMN_3S_3sar ligand. However, the ^{13}C NMR spectrum of the complex formed in solution suggests that the species present is highly symmetrical and although this does not preclude an *exo*-configuration it suggests that it is less likely. Hg(II), although exhibiting a propensity for low coordination numbers, does form hexadentate complexes with ligands with mixed amine/thiaether donors, for example $[Hg([18]aneN_2S_4)]^{2+}$ ([18]aneN$_2$S$_4$ = 1,4,10,13-tetrathia-7,16-diazacyclooctadecane),[20] thus the octahedral environment would not be expected to be problematic. It may be that the preorganised nature of the macrobicyclic ligand cannot accommodate the mismatch between Hg–N and Hg–S bond lengths. It would be expected that the size of the AMN_3S_3sar cage cavity would be larger than for the hexaza cages, which have been estimated to have a radius of ≈2.3 Å.[14] For the $[Hg(diamsar)]^{2+}$ complex the average Hg–N bond lengths are 2.35 Å[21] and this appears to be typical of a range of Hg–N bond lengths reported previously (*e.g.* for $[Hg([12]aneN_3S)(NO_3)](NO_3)$, $[Hg([12]aneN_2OS)(NO_3)_2]$ ([12]aneN$_2$OS = 1-oxa-7-thia-4,10-diazacyclododecane), $[Hg([9]aneN_2S)_2](HgBr_4)$ ([9]aneN$_2$S = 1-thia-4,7-diazacyclononane), $[Hg([12]aneNO_2S)(NO_3)_2]$ ([12]aneNO$_2$S = 1,7-dioxa-4-thia-10-azacyclododecane) and $[Hg([18]aneN_2S_4)]^{2+}$ ([18]aneN$_2$S$_4$ = 1,4,10,13-tetrathia-7,16-diazacyclooctadecane) the Hg–N bond distances range from 2.277(12) to 2.473(11) Å).[20–24] Typically the Hg–S(thiaether) distances in the same macrocyclic ligands range from 2.5146(6) to 2.735(4) Å.[20,22–24] The ionic radius of Hg^{2+} is 1.10 Å.[25] The mismatch between cage cavity size and Hg(II) ion size would increase as the number of thiaether donors increased in the two ligands AMN_4S_2sar and AMN_3S_3sar. The expectation would be that the stability constants would follow the sequence $N_6 > N_4S_2 > N_3S_3$ as observed for the encapsulating ligands employed in this study.

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