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Applications of Cd NMR to Polycadmium Complexes.
II*. $[Cd_x(SPh)_y]^{2x-y}$ Species in Solution in Relation to Metallothionein Aggregates

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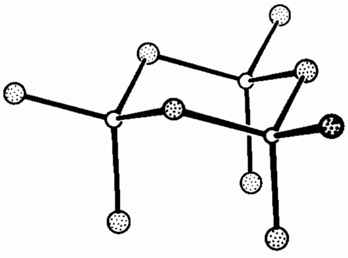
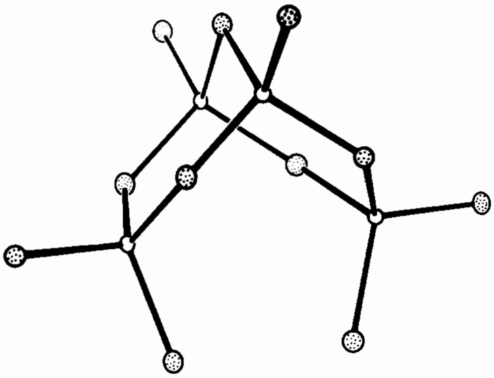
Abstract

^{113}Cd NMR spectra of mixtures of $(Me_4N)_2[Cd(SPh)_4]$ and $(Me_4N)_2[Cd_4(SPh)_{10}]$ in DMF reveal the formation of one major and two very minor new cadmium thiolate species in labile equilibria. Resonance broadening and intensities indicate that the dominant species is monocyclic, probably $[(\mu\text{-}SPh)_3\{Cd(SPh)_2\}_3]^{3-}$, and thus a model for the proposed $Cd_3(S\text{-}cys)_9$ site of metallothioneins.

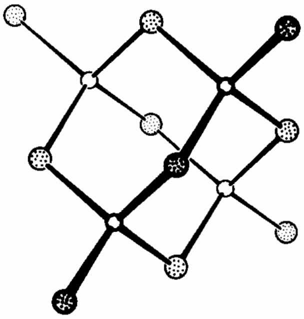
Well-developed Cd NMR measurements of metallothionein proteins from various sources indicate the presence of two metal–cysteine aggregates, formulated as monocyclic $\{M_3(S\text{-}cys)_9\}^{3-}$ (structure I) and bicyclic $\{M_4(S\text{-}cys)_{11}\}^{3-}$ (II) in which the metal atoms M may be Zn and/or Cd, depending on the source and antecedents of the protein sample [1b]. However, no evidence for polymetal thiolate complexes with either of these compositions or structures has yet been published, although the related tricyclic adamantanoid structure $[M_4(SR)_{10}]^{2-}$ (III) is well established for both Zn and Cd [2]. Investigations of the $M^{2+}/^{-}SEt$ systems (M = Fe, Co) using paramagnetically expanded ligand NMR reveal only $[M(SEt)_4]^{2-}$, $[M_2(SEt)_6]^{2-}$ (structure IV) and $[M_4(SEt)_{10}]^{2-}$ as species detectable in solution equilibria and crystallisable from solution [3]. The dimetallic structure IV is intimated for the crystallised complex $[Cd_2(SEt)_6]^{2-}$ [3] and is known in $[Hg_2(SPh)_6]^{2-}$ crystallised with Me_4N^+ [4] but not with Bu_4N^+ [5].



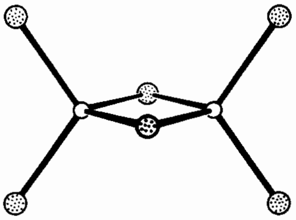
I



II



III



IV

The evidence presently available on metal complexes $[M_p(SR)_{3p}]^{p-}$ with tetrahedrally coordinated

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*Part I is ref. 1(a).

M, particularly the limited but thermodynamically more pertinent evidence from solution, all favours $p = 2$ (**IV**), not the $p = 3$ species **I** proposed for metallothioneins. The closest approach to a synthetic analogue for metallothionein structure **I** is found in planar $[Fe_3(SPh)_3Cl_6]^{3-}$ [6], but the occurrence of this or related complexes in solution has not yet been demonstrated.

Whereas techniques which depend on incomplete d-configurations are denied to $Cd^{2+}/^{-}SR$ systems, Cd NMR can be deployed in the characterisation of complexes $[Cd_x(SR)_y]^{2x-y}$ in solution. The value of such measurements can be reduced by fast metal–thiolate exchange processes which broaden Cd resonance lines, particularly in protic media and with protic reactants: the Cd spectrum of $[Cd_4(SPh)_{10}]^{2-}$ in CH_3CN is broadened by small proportions of Et_3NH^+ [7] and by PhSH. In the experiments described below this problem is minimised by the use of inert quaternary ammonium salts in aprotic DMF solution. The Cd NMR spectra of mixtures of $(Me_4N)_2[Cd(SPh)_4]$ and $(Me_4N)_2[Cd_4(SPh)_{10}]$ species with high and low RS^-/Cd^{2+} ratios, have been examined to assess the occurrence of plausible equilibria such as eqns. (1)–(3) involving the postulated species $[Cd_2(SR)_6]^{2-}$, $[Cd_3(SR)_9]^{3-}$ and $[Cd_4(SR)_{11}]^{3-}$:

$$2[Cd(SR)_4]^{2-} + [Cd_4(SR)_{10}]^{2-} \rightleftharpoons 3[Cd_2(SR)_6]^{2-} \quad (1)$$

$$2[Cd(SR)_4]^{2-} + [Cd_4(SR)_{10}]^{2-} \rightleftharpoons 2[Cd_3(SR)_9]^{3-} \quad (2)$$

$$4[Cd(SR)_4]^{2-} + 5[Cd_4(SR)_{10}]^{2-} \rightleftharpoons 6[Cd_4(SR)_{11}]^{3-} \quad (3)$$

NMR measurements of ^{113}Cd ($I = \frac{1}{2}$) at natural abundance (12.3%) were made with a Bruker CXP300 spectrometer, at 66.6 MHz, locked with d_6-acetone. Chemical shifts are relative to aqueous $Cd(NO_3)_2$, (external, 0.1 M, 300 K).

The significant result from these experiments is the predominance of only one additional resonance line due to one major new species **1**, throughout the range of the reactant ratio Q = moles of $[Cd(SPh)_4]^{2-}$/moles of $[Cd_4(SPh)_{10}]^{2-}$. The chemical shift of **1** is 585 ppm at 230 K where the shifts of $[Cd(SPh)_4]^{2-}$ and $[Cd_4(SPh)_{10}]^{2-}$ are 606 and 592 ppm, respectively. The temperature dependences of these chemical shifts are −0.22 (585), −0.23 (592) and −0.25 (606) ppm K^{-1}. Under certain conditions very weak additional and unrelated resonances can be detected at 573 ppm (230 K), species **2**, and 543 ppm (196 K), species **3**. Representative spectra over the range of Q are shown in Fig. 1.

In these solutions the resonances of **1** and $[Cd(SPh)_4]^{2-}$ are broader than the $[Cd_4(SPh)_{10}]^{2-}$ resonance, at temperatures above 210 K, and the resonance of $[Cd(SPh)_4]^{2-}$ in the mixture is broadened relative to that of the pure compound. Figure 2 shows the temperature dependence of line widths, and reveals that the lowest frequency minor line (**3**, 543 ppm, 196 K) is sharpened sufficiently for observation only below 230 K. At 210 K, $\Delta\nu_{1/2}$ for **1** is reduced to 16 Hz when resolution enhancement is incorporated in the Fourier transformation, but the line displays no evidence of satellite fine structure indicative of $^{113}Cd-^{111,113}Cd$ coupling, such as that easily resolved for the $[Cd_4(SPh)_{10}]^{2-}$ resonance under the same conditions [7, 1a].

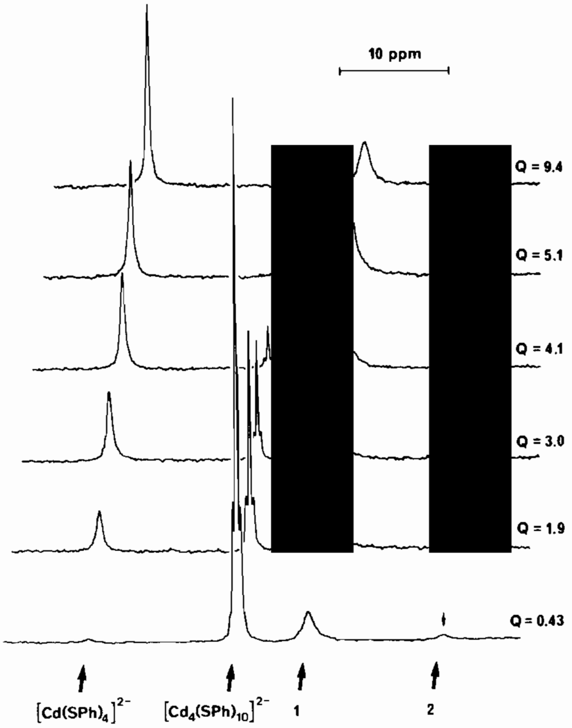

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Fig. 1. Representative ^{113}Cd NMR spectra (66.6 MHz) of mixtures of $(Me_4N)_2[Cd(SPh)_4]$ and $(Me_4N)_2[Cd_4(SPh)_{10}]$, in DMF at 230 K, relaxed with $Cr(acac)_3$. Q is the molar ratio $[Cd(SPh)_4]^{2-}/[Cd_4(SPh)_{10}]^{2-}$, at total Cd concentrations of 0.3–0.8 M. Arrows identify the resonances of the product species **1** (585 ppm) and **2** (573 ppm): the very weak resonance of product **3** at 543 ppm is off scale. Each spectrum resulted from 3000 28 μs pulses.

Determination of the composition of the new species **1** is in principle possible by quantitative characterisation of the equilibrium in which it is formed, using Cd resonance intensities. Knowledge of nuclear relaxation rates is essential in order to avoid saturation in such experiments. Preliminary estimates of the longitudinal relaxation times (T_1) for $(Me_4N)_2[Cd(SPh)_4]$ and $(Me_4N)_2[Cd_4(SPh)_{10}]$ in DMF at 260 K are 1.2 s and 0.4 s, respectively. These T_1 values decrease with temperature reduction, and are decreased further in equilibrium mixtures: in an equilibrium mixture of $[Cd(SPh)_4]^{2-}$, $[Cd_4$-

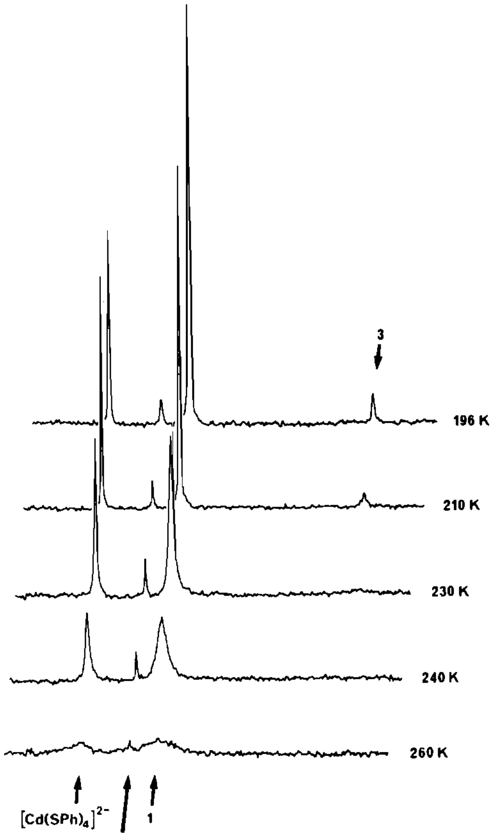

Fig. 2. The temperature dependence of ^{113}Cd resonance line-widths in a mixture of $[Cd(SPh)_4]^{2-}$ plus $[Cd_4(SPh)_{10}]^{2-}$ (Q = 3.9) in DMF, showing the different broadening characteristics of 3, 1 and $[Cd(SPh)_4]^{2-}$, and $[Cd_4(SPh)_{10}]^{2-}$. Product 2 is not detectable in this mixture.

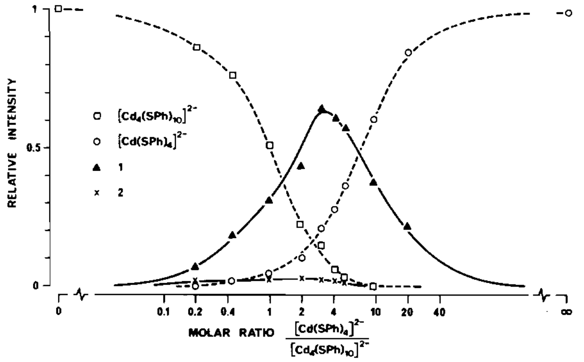

Fig. 3 Variation of integrated ^{113}Cd resonance intensity (per mole Cd, relaxed with $Cr(acac)_3$) for the reactants and two products 1 and 2 in mixtures of $[Cd(SPh)_4]^{2-}$ and $[Cd_4(SPh)_{10}]^{2-}$ in DMF at 230 K, as dependent on their molar ratio Q.

$(SPh)_{10}]^{2-}$ and **1** at 230 K the T_1 values of all three resonances are *ca.* 0.25 s. Intensities of the lines have been measured at 230 K, using $Cr(acac)_3$ as a paramagnetic relaxant as necessary to confirm the absence of intensity reduction by saturation. Paramagnetic chemical shifts were *ca.* +2 ppm. Normalised intensities for the species involved are shown in Fig. 3. The concentration of **1** is maximised as *ca.* 65% of total cadmium at $Q \approx 3$, and the concentration of **2** is maximised at only 4% of total cadmium at $Q \approx 2$. Disregarding the minor species **2**, the intensity data for solutions with appreciable concentrations of $[Cd(SPh)_4]^{2-}$, $[Cd_4(SPh)_{10}]^{2-}$ and **1** adhere more closely to the equilibrium constant expression for eqn. (2) than to the expression for equilibrium eqn. (1), but the quality and quantity of the data are insufficient at this stage to confirm unambiguously that species **1** is $[Cd_3(SPh)_9]^{3-}$, and not $[Cd_2(SPh)_6]^{2-}$. Current experiments are directed at the removal of instrumental uncertainties and the acquisition of more numerous and reliable intensity data, in order to confirm the formulae of the new $[Cd_x(SPh)_y]^{2x-y}$ species.

These observations and their interpretations can be summarised as follows: (i) One dominant (**1**) and two minor (**2**, **3**) new cadmium thiolate species have been detected. (ii) The formation stoichiometry shows that **1** must be a polycadmium thiolate complex, despite the non-detection of confirmatory Cd–Cd coupling which is probably reduced by fast Cd exchange processes. (iii) The faster Cd exchange of **1** with $[Cd(SPh)_4]^{2-}$ than with $[Cd_4(SPh)_{10}]^{2-}$ indicates that species **1** is more likely to be monocyclic, $[(\mu\text{-}SPh)_p\{Cd(SPh)_2\}_p]^{p-}$, than polycyclic. (iv) The single resonances and the chemical shifts of **1** (and of **2**) are consistent with $(\mu\text{-}SPh)_2Cd(SPh)_2$ coordination and with the monocyclic structure type, but cannot differentiate monocycles according to the value of p. (v) It is probable that **1** is $[Cd_3(SPh)_9]^{3-}$, in contradistinction to the dimetallic monocycle **IV** observed in other thiolate systems. (vi) There is no evidence of appreciable concentrations of a bicyclic species $[Cd_4(SPh)_{11}]^{3-}$ (**II**) with two distinct Cd sites $(\mu\text{-}SPh)_3Cd(SPh)$ and $(\mu\text{-}SPh)_2Cd(SPh)_2$. The 20 ppm range of the chemical shift scale for cadmium with benzenethiolate coordination is sufficient for it to be very unlikely that the two sites have chemical shifts coincident by less than 0.1 ppm, but mechanisms for rapid intramolecular interchange of the two sites are conceivable.

Although lability reduces some of the power of Cd NMR applied to these systems, further studies with other thiolates should elucidate the existence and structures of $[Cd_x(SR)_y]^{2x-y}$ species in solution. Attempts to isolate **1** are in progress.

Acknowledgements

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