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Cadmium-113 nuclear magnetic resonance studies of cadmium(II)–carboxylate complexes in aqueous solution

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A variety of complexes of cadmium with mono- and di-carboxylic acids in aqueous solution were investigated using ^{113}Cd NMR spectroscopy. A single averaged chemical shift was obtained even at reduced temperature, showing that the cadmium–monocarboxylate complexes are undergoing rapid exchange in solution. Using the known stability constants, the individual chemical shifts were calculated to be in the range δ −22 to −24 and −39 to −40 for $[CdL]^+$ and $[CdL_2]$ (L = carboxylate) species respectively: carboxylates with higher basicity tend to increase the shielding of the cadmium in the complexes. In case of dicarboxylic acids $HO_2C(CH_2)_nCO_2H$ (n = 0–3) the ^{113}Cd nucleus showed greater shielding with increasing n. The upfield chemical shift observed for the dialkyl-substituted malonate complexes of Cd^{II} compared to the malonate complex is caused by the steric effect hindering ring formation.

Cadmium-113 NMR spectroscopy has been widely used as a probe of the metal-ion binding sites in many biological systems, such as metallothionein[1,2] and metalloenzymes,[3–7] as ^{113}Cd chemical shifts are highly sensitive to the donor atoms, co-ordination number and geometry. However, the nature of the binding sites of these biological systems is usually very complex. Accumulation of chemical shift data on well defined model systems in both the solid and solution state may be useful in the interpretation of the ^{113}Cd NMR probe data.

In complexes of known crystal structures a consistent correlation was found between the ^{113}Cd NMR chemical shift and the identity of the ligands attached to Cd^{2+}.[8–14] The solution state is more dynamic and different cadmium complexes may be formed. Where the cadmium complexes formed are dynamically stable, the chemical shift data on individual species are readily obtainable.[15] In other cases where the complexes undergo rapid exchange in solution it is possible to observe the individual species by decreasing the temperature to slow the exchange sufficiently on the NMR time-scale.[16–18] Munakata *et al.*[16] studied cadmium complexes of several model ligands containing N-donor atoms in solution using this approach. In complexes where the exchange cannot be slowed sufficiently the chemical shifts of the individual species may be calculated from a single averaged chemical shift and the known stability constants. This method has been used to obtain the chemical shifts for individual cadmium halide complexes in solution.[19,20]

In this paper the results of studies of the complexation between cadmium(II) ion and carboxylates in aqueous solution using ^{113}Cd NMR spectroscopy are presented. Carboxylate functional groups are found in abundance in many biological and naturally occurring materials.[21,22] The relationship between structure and chemical shift has been investigated for some oxo-cadmium compounds in the solid state,[8–14] but little is reported on ^{113}Cd NMR studies of such compounds in solution. The cadmium monocarboxylate complexes rapidly exchange even at low temperature (−90 °C) in ethanol medium. Therefore the chemical shifts of the individual complexes were calculated from the observed chemical shift in aqueous solution and known stability constants. The focus has been placed on a better understanding of the effects that basicity of the donor ligands, chelate ring size, steric effect of neighbouring groups, and counter ions have on the ^{113}Cd chemical shifts of cadmium carboxylate complexes in aqueous solution.

Experimental

Materials and preparation

The carboxylic acids were reagent grade (Aldrich Co.) used without further purification. The stock cadmium(II) solution was prepared by dissolving $Cd(ClO_4)_2 \cdot 6H_2O$ (Alfa), $CdSO_4$ (Aldrich Co.) and $Cd(NO_3)_2 \cdot 6H_2O$ (Aldrich Co.) in doubly deionized water in a dinitrogen atmosphere free from interfering CO_2. Its concentration was measured by atomic absorption spectroscopy (Instrumental laboratory Video 12). A stock solution of isotopically enriched cadmium was prepared by dissolving 95.8% ^{113}Cd-enriched metal (Isotec Inc., product number 77-066-01-7; 0.5 g) in an aliquot of hot concentrated $HClO_4$ and was subsequently diluted with doubly deionized water to 0.102 mol dm^{-3}.

For NMR study, series of sample solutions (10 cm^3) were prepared for each carboxylic acid, where the $Cd(ClO_4)_2$ was kept constant at 5.56×10^{-2} mol dm^{-3} and the carboxylic acid concentration was varied from 0.025 to 0.6 mol dm^{-3}. The cadmium oxalate complexes readily formed precipitates at this high cadmium concentration. In this case the total cadmium concentration was kept constant at 1.02×10^{-3} mol dm^{-3} (enriched ^{113}Cd isotope) and the oxalic acid concentration was varied from 0.05 to 0.15 mol dm^{-3}. The ionic strength was adjusted by adding an appropriate quantity of 1.0 mol dm^{-3} $NaClO_4$ to each sample solution, thus keeping the sum of the salts and ligand concentration constant at 1.0 ± 0.1 mol dm^{-3}. The sample solutions were adjusted to pH 6.0 using $HClO_4$ and NaOH (carbonate free, Baker Co.), and the pH was measured using a glass electrode coupled to a digital pH meter (Metrohm type 632).

Equipment

The ^{113}Cd NMR investigations were performed on a Bruker AM 300 spectrometer operating at 66.57 MHz. All measurements were made with an outer 10 mm NMR tube containing the sample solutions and a sealed 5 mm inner tube with 0.1 mol dm^{-3} $Cd(ClO_4)_2$ (reference) aqueous (D_2O, field lock) solution. The temperature of the samples was kept constant at 24 °C by flowing heated air around the tube mounted coaxially in the probe head. Positive chemical shifts are downfield from the reference and indicate decreased shielding. The spectra were obtained using a 30° pulse width

Table 1 Cadmium-113 chemical shifts of the cadmium(II)-carboxylate complexes in aqueous solution

Ligand	pK_a[a]	$\log \beta_1$[a]	$\log \beta_2$[a]	δ_f[b]	$\delta_{1:1}$[b]	$\delta_{1:2}$[b]
Formic acid	3.53	1.04	1.74	−0.6	−9.6	−16.7
Benzoic acid	4.00	1.01	1.65	−0.4	−21.7	−39.0
Acetic acid	4.58	1.24	1.86	−0.3	−22.1	−40.0
Propanoic acid	4.68	1.19	1.86	−0.4	−24.1	−40.3

[a] From ref. 24. [b] Given in ppm relative to 0.1 mol dm $^{-3}$ $Cd(ClO_4)_2$ aqueous (D_2O) solution.

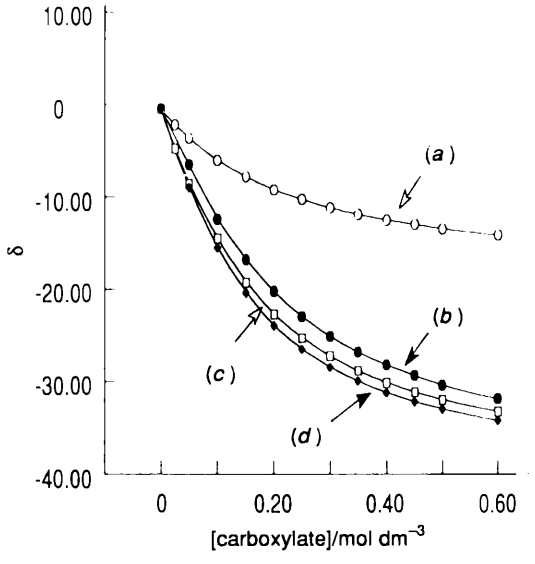

Fig. 1 Plots showing the ^{113}Cd chemical shift change of cadmium complexes of (*a*) formate, (*b*) benzoate, (*c*) acetate and (*d*) propanoate

(6 μs), acquisition time of 0.885 s, and a relaxation delay of 2.2 s.

Results and Discussion

Effects of basicity of monocarboxylate ligands

A plot of the ^{113}Cd chemical shift change caused by the increase in the monocarboxylate-to-cadmium ratio is shown in Fig. 1. An X-ray diffraction study of aqueous cadmium perchlorate solution has shown that the solvated cation is six-co-ordinated $[Cd(H_2O)_6]^{2+}$.[23] When monocarboxylates are added to the solution to form cadmium–carboxylate complexes there is an upfield chemical shift compared to that of the 0.1 mol dm $^{-3}$ $Cd(ClO_4)_2$ standard (see Fig. 1). This suggests that the cadmium ion becomes more shielded when co-ordinated water molecules are substituted by monocarboxylates. The reason may be that lone-pair electrons of a water molecule are more effectively directed toward cadmium ion than are those of carboxylate. Such a phenomenon was also observed in a solid-state ^{113}Cd NMR study of cadmium–carboxylate complexes.[13] The plot in Fig. 1 shows that the cadmium in monocarboxylate complexes tends to become more shielded in the order of increasing basicity as seen in Table 1: propanoic > acetic > benzoic > formic acid. This trend is opposite to that observed by Munakata *et al.*[16] in their ^{113}Cd NMR study on compounds containing N-donor atoms. In compounds such as 4-substituted pyridines and 4,5,7-substituted 1,10-phenanthrolines, lone pair electrons from the N-donor can easily be directed toward the central cadmium ion: an increase in the basicity of the ligands would strengthen the metal–ligand bonding causing the cadmium ion to become more deshielded.[16]

In an initial attempt, the temperature was gradually decreased to reduce the exchange rate sufficiently to identify the individual chemical shift values of each species present in solution. However, the single NMR signal observed at −90 °C in ethanol medium was broad and unresolved, showing that the exchange rate is rapid even at this low temperature. Therefore the individual chemical shifts of the cadmium carboxylate complexes in aqueous solution were calculated using equation (1), in an approach similar to that applied in the earlier

$$\delta_{obs} = P_f\delta_f + P_{1:1}\delta_{1:1} + P_{1:2}\delta_{1:2} \quad (1)$$

cadmium halide studies.[19] Here δ_{obs} is the single value of the exchange-averaged chemical shift of the cadmium–carboxylate complex formed in aqueous solution obtained from the ^{113}Cd NMR spectra, P_f and δ_f are the mole fraction and chemical shift of the free cadmium ion, $P_{1:1}$ and $\delta_{1:1}$ those of $[CdL]^+$ (L = carboxylate; 1:1 complex) and $P_{1:2}$ $\delta_{1:2}$ those of $[CdL_2]$ (1:2 complex). A constant ionic strength of 4.5 mol dm $^{-3}$ was used in the cadmium halide complexation study[19] to obtain the individual chemical shifts. In cadmium–carboxylate systems, however, extensive precipitation occurred at such high ionic strength. Therefore the total ionic strength was kept nearly constant at 1.0 ± 0.1 mol dm $^{-3}$. The test showed that the cadmium chemical shift is least affected when perchlorate anion is added to keep the ionic strength nearly constant (see Fig. 2). Applying the literature values of the stability constants of $[CdL]^+$ and $[CdL_2]$,[24] the mole fractions of these complexes and free cadmium ion were calculated at given cadmium and carboxylate concentrations with the use of a modified COMIC computer program.[25] A least-squares treatment was subsequently applied to determine the individual chemical shifts of each carboxylate complex as expressed in equation (1). The accuracy of this method may be affected by (*i*) the experimental uncertainties in the measured values of the stability constants, and (*ii*) additional complexes such as $[CdL_3]^-$ may be formed. However, cadmium is not known to form strong complexes with carboxylates and the experimental data obtained under these experimental conditions were adequately interpreted by the formation of just $[CdL]^+$ and $[CdL_2]$. Even for Eu^{3+} ion with a strong preference for carboxylates a luminescence study showed that $Eu(O_2CMe)_3$, is only formed when the acetate-to-europium ratio exceeds 100:1.[26] Lead–carboxylate complexation was interpreted similarly with just two species, namely $[PbL]^+$ and $[PbL_2]$.[27]

The individual chemical shift values obtained for the formate, acetate, benzoate and propanoate complexes of cadmium are summarized in Table 1. The results show that there is increasing shielding of ^{113}Cd in $[CdL]^+$ or $[CdL_2]$ as the ligand becomes more basic. Excluding formate, the individual chemical shifts for $[CdL]^+$ and $[CdL_2]$ are found in the ranges δ −22 to −24 and −39 to −40, respectively. The chemical shifts of the cadmium–formate complexes appeared downfield ($[CdL]^+$, δ −9.6; $[CdL_2]$, δ −16.7). It is as yet unclear why these values differ from those of the other monocarboxylates even when the difference in basicity is taken into consideration.

The solid $Cd(O_2CH)_2{\cdot}2H_2O$ investigated by cross-polarization magic angle spinning (CP MAS) gave two chemical shifts δ 26 and 21 [referenced to 0.1 mol dm $^{-3}$ $Cd(ClO_4)_2$ and I = 4.5 mol dm $^{-3}$] for the two distinct six-co-ordinate sites.[14] Similarly, the chemical shift for $Cd(O_2CMe)_2$ in aqueous solution was

δ −40. Two chemical shifts (δ −46[14] and −58[12]) have been given for the seven-co-ordinated solid $Cd(O_2CMe)_2 \cdot 2H_2O$, depending on the selection of the standard reference. Since different conditions were used it is difficult to make direct comparison of the values obtained from the solution and solid: when the chemical shift of 0.1 mol dm^{-3} $Cd(ClO_4)_2$ aqueous (D_2O) solution is δ 0 then that of 0.1 mol dm^{-3} $Cd(ClO_4)_2$ at I = 4.5 mol dm^{-3} is δ −15. The chemical shift values of $[CdL_2]$ species formed in aqueous solution seemed different from those of solids, even when the use of different reference materials is taken into consideration. This suggests that the $[CdL_2]$ species formed in aqueous solution under rapid-exchange conditions may not be the same as those in the solids. Cadmium-113 chemical shifts are said to be highly sensitive to co-ordination number and geometry.[13]

Effect of chelate-ring size of dicarboxylate

Two neighbouring carboxylates attached to a macromolecule may participate in metal-ion co-ordination as a chelation unit thus creating a strong binding site.[21,22] Therefore, the co-ordination behaviour of compounds with two carboxylates linked by carbon–carbon bonds was investigated by ^{113}Cd NMR spectroscopy. A single averaged chemical shift was also obtained for these cadmium(II)–dicarboxylate complexes. A low-temperature NMR study in ethanol medium could not be carried out due to the poor solubility of the dicarboxylic acids. Plots of the ^{113}Cd chemical shift change resulting from the increase in dicarboxylate-to-cadmium concentration ratio, for oxalate and higher members of the dicarboxylate series, are shown in Fig. 3. The chemical shift changes seem to depend on the chain size of the dicarboxylate ligands oxalate (ox), malonate (mal), succinate (succ) and glutarate (glu). The results show an increased shielding order of five- < six- < seven- ≈ eight-membered chelate rings, *i.e.* Cd(ox) (δ + 11.0) < Cd(mal) (−19.1) < Cd(succ) (−35.3) ≈ Cd(glu) (−35.9). Similar trends were observed in diamine[16] and in dithiolate series.[28] The cadmium nucleus of the Cd(ox) complex is the most deshielded: oxalate may be capable of forming a strong five-membered chelate ring with Cd^{II}. The Cd(mal) complex seems somewhat less deshielded compared to Cd(ox): malonate may form a six-membered chelate ring with Cd^{II} which is more strained. An upfield change in the chemical shift is observed for the cadmium–succinate and –glutarate systems (Fig. 3): the changes appear to follow a similar pattern as those of some of the cadmium–monocarboxylate systems in Fig. 1. Thus the ^{113}Cd nucleus becomes more shielded as the chelate ring becomes larger and hence more strained. It has been suggested that the stability of dicarboxylates decreases when the chelate-ring size increases from five to eight owing to the increased ring strain.[29,30]

The cadmium complexation study was extended to alkyl-substituted malonates. The presence of bulky alkyl groups on the central tetrahedral carbon (methylene carbon) may add to the ring strain of the six-membered chelate-ring system. The chemical shift changes observed for the cadmium(II) complexes of malonate, methyl-, dimethyl- and diethyl-malonate are given in Fig. 4. The magnitude of the upfield chemical shift is in the order dimethylmalonate > diethylmalonate > methylmalonate > malonate which is the same as the order of bulkiness of the alkyl groups. The steric strain induced by the presence of neighbouring bulky alkyl groups seems to be important for malonate which is capable of forming a six-membered ring complex with Cd^{II}. The data in Fig. 4 suggest that when both methylene hydrogens are substituted by either

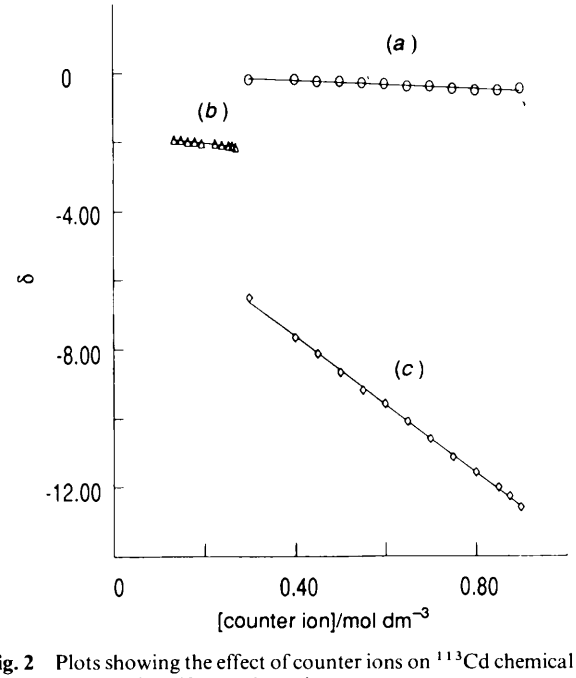

Fig. 2 Plots showing the effect of counter ions on ^{113}Cd chemical shift: (*a*) perchlorate, (*b*) sulfate and (*c*) nitrate

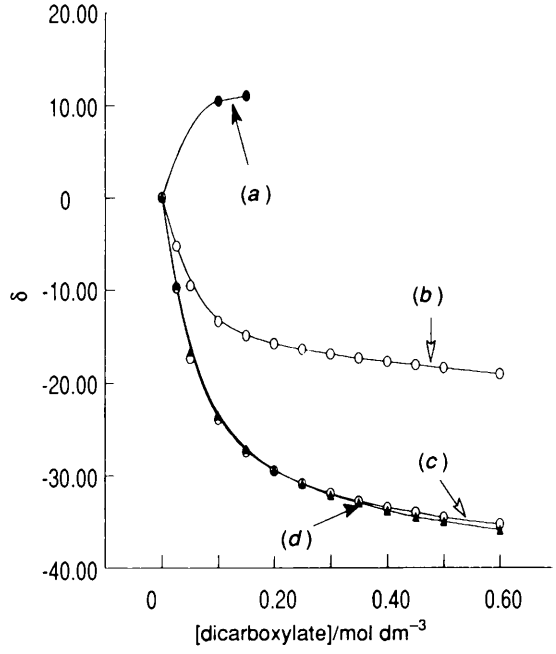

Fig. 3 Plots showing the chelate ring-size effect on the ^{113}Cd chemical shift: (*a*) oxalate, (*b*) malonate, (*c*) succinate and (*d*) glutarate

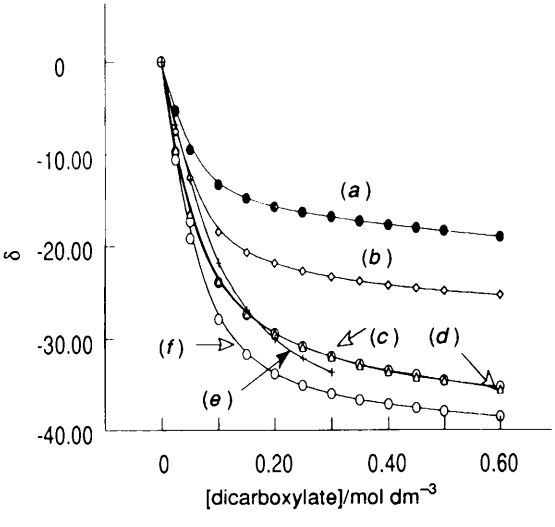

Fig. 4 Plots showing the steric effect on the ^{113}Cd chemical shift: (*a*) malonate, (*b*) methylmalonate, (*c*) succinate, (*d*) methylsuccinate, (*e*) diethylmalonate and (*f*) dimethylmalonate

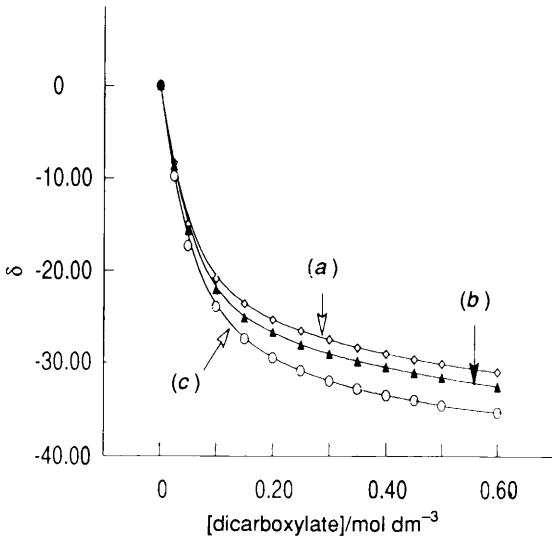

Fig. 5 Plots showing the ^{113}Cd chemical shift change of cadmium complexes of (*a*) maleate, (*b*) phthalate and (*c*) succinate

methyl or ethyl groups the six-membered ring may be interrupted by the added steric strain. In contrast, the chemical shift changes observed for succinate and methylsuccinate are nearly identical, showing that the presence of the methyl group has no effect on the complexation properties of succinate.

Phthalate-like sites are regarded as strong metal-binding sites in natural macromolecules.[21,22] The chemical shift changes with the dicarboxylates phthalate and maleate are given in Fig. 5. Similar upfield chemical shift changes as for the cadmium–succinate complexes are observed even though the two carboxylate groups are now bonded to unsaturated carbons in a planar arrangement.

Conclusion

Cadmium-113 NMR spectroscopy has been applied to the study of cadmium–carboxylate complexes formed in aqueous solution under rapid-exchange conditions. The chemical shifts of the complexes seem to be affected by the ligand basicity, ring size and steric strain caused by neighbouring groups.

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