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Solid-State ^{13}C CP/MAS NMR Investigations of EDTA–Metal Complexes

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Solid-state ^{13}C CP/MAS NMR spectra are reported for different EDTA–metal complexes. The effect of metal binding on the isotropic ^{13}C chemical shift and principal elements of the carboxyl ^{13}C chemical shift anisotropy (CSA) tensor are discussed. © 1997 by John Wiley & Sons, Ltd.

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INTRODUCTION

The chelation of metals by polyaminocarboxylate complexes continues to be important for a variety of research areas. Ethylenediaminetetraacetic acid (EDTA) is a classical model compound for metal complexation and has been the focus in a number of spectroscopic investigations. Solid-state magic angle spinning (MAS) NMR provides a tool to probe the local structure and chemical environment in EDTA–metal complexes. Investigations of the ^{13}C chemical shift anisotropy (CSA) tensor, including molecular orientation of the principal elements, have provided detailed information about the electron distributions for a variety of organic molecules.[1,2] For example, the degree of hydrogen bonding in amino acids and peptides has recently been correlated to variations in the ^{13}C carboxyl tensor elements.[3] The isotropic ^{13}C chemical shifts for select EDTA–metal complexes have been reported,[4] but no CSA tensor information was determined. Changes in the carboxyl carbon ^{13}C CSA tensor resulting from metal binding are of particular interest because complexation directly involves the carboxyl acetate groups.

In this paper, solid-state ^{13}C cross-polarization magic angle spinning (CP/MAS) NMR spectra of EDTA–metal complexes are presented, including the isotropic chemical shifts and evaluation of the carboxyl CSA tensor. The EDTA–metal complexes investigated include uncomplexed ethylenediaminetetraacetic acid (EDTA), ethylenediaminetetraacetic acid diammonium salt hydrate [$(NH_4)_2$-EDTA $\cdot$ xH_2O], ethylenediaminetetraacetic acid disodium salt dihydrate (Na_2-EDTA $\cdot$ $2H_2O$), ethylenediaminetetraacetic acid trisodium salt hydrate (Na_3-EDTA $\cdot$ xH_2O), ethylenediaminetetraacetic acid tetrasodium salt hydrate (Na_4-EDTA $\cdot$ xH_2O), ethylenediaminetetraacetic acid calcium disodium salt hydrate ($CaNa_2$-EDTA $\cdot$ xH_2O), ethylenediaminetetraacetic acid dicalcium salt (Ca_2-EDTA), ethylenediaminetetraacetic acid magnesium disodium salt hydrate ($MgNa_2$-EDTA $\cdot$ xH_2O), ethylenediaminetetraacetic acid dipotassium salt dihydrate (K_2-EDTA $\cdot$ $2H_2O$) and ethylenediaminetetraacetic acid tripotassium salt hydrate (K_3-EDTA $\cdot$ $2H_2O$).

EXPERIMENTAL

EDTA and all metal derivatives were obtained from Aldrich, except for the dicalcium salt, which was obtained from Acros. All chemicals were used without further purification.

Solid-state ^{13}C CP/MAS spectra were obtained using a 4 mm broadband MAS probe on a Bruker AMX400 spectrometer operating at 100.63 MHz. Spectra were obtained using cross-polarization with a 1 ms contact time, a 3.2 μs $\pi/2$ for the ^1H channel and a 60 s recycle delay. Experiments were performed at 298 K and referenced to the carboxyl resonance of external glycine ($\delta = 176.0$ ppm). To address the possibility that the use of cross-polarization may produce distortions in the observed carbonyl CSA tensor, additional tensor analyses were performed on spectra for Na_3-EDTA $\cdot$ xH_2O and EDTA obtained using a standard single pulse Bloch decay with high power decoupling. The values of the principal tensor elements obtained from these single pulse experiment were in good agreement with CP results, with a less than ± 2 ppm experimental error. Isotropic chemical shifts were determined using a 6 kHz spinning speed and 128–1024 scan averages. Spectra for tensor analysis were obtained at a 2 kHz spinning speed with 1024 scan averages. The principal values of the carbonyl chemical shift tensors were

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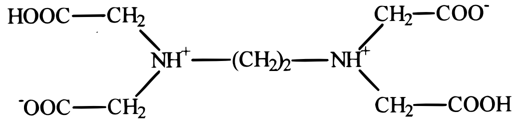
obtained by computer simulations using the methods of Herzfeld and Berger.[5]

RESULTS AND DISCUSSION

The ^{13}C CP/MAS spectra for EDTA and the EDTA–metal complexes at a 6 kHz spinning speed are presented in Fig. 1. At this speed very few spinning sidebands are observed, allowing the isotropic chemical shifts (δ_{iso}) to be easily identified. These results are presented in Table 1. The carboxyl resonances are observed between $\delta = 169$ and 180 ppm, the acetate methylene resonances occur between $\delta = 54$ and 65 ppm and the ethylenic methylenes are between $\delta = 45$ and 54 ppm.[4,6] For the various EDTA–metal complexes there are clear differences in both the chemical shift and the number of observed resonances. The spectra for the uncomplexed EDTA Fig. 1(a) shows two distinct resonances of approximately equal intensity for the carboxyl carbons and three different methylene resonances. The absolute value of the chemical shifts are slightly different than reported earlier,[4] most likely resulting from differences in referencing. The widely separated carboxyl resonances (*ca.* 6 ppm) in uncomplexed EDTA have been attributed to the zwitterion form, in which the nitrogens are protonated, leaving protonated and unprotonated carboxyl groups as shown in Scheme 1.[4]



Scheme 1

For the zwitterion molecular species three distinct methylene resonances are predicted. The proposed crystalline zwitterion agrees with the reported x-ray structure of EDTA[7] in which both nitrogens are protonated and are involved in trifurcated hydrogen bonds. The ^{13}C NMR spectra of the ammonium ion complex $(NH_4)_2$-EDTA $\cdot x H_2O$ [Fig. 1(b)] reveals two closely spaced carboxyl resonances (*ca.* 0.6 ppm separation), suggesting very similar chemical environments. The presence of three distinct methylene resonances still indicates an inequivalence between adjacent carboxyl groups. The spectra for Na_2-EDTA $\cdot 2H_2O$ [Fig. 1(c)] and

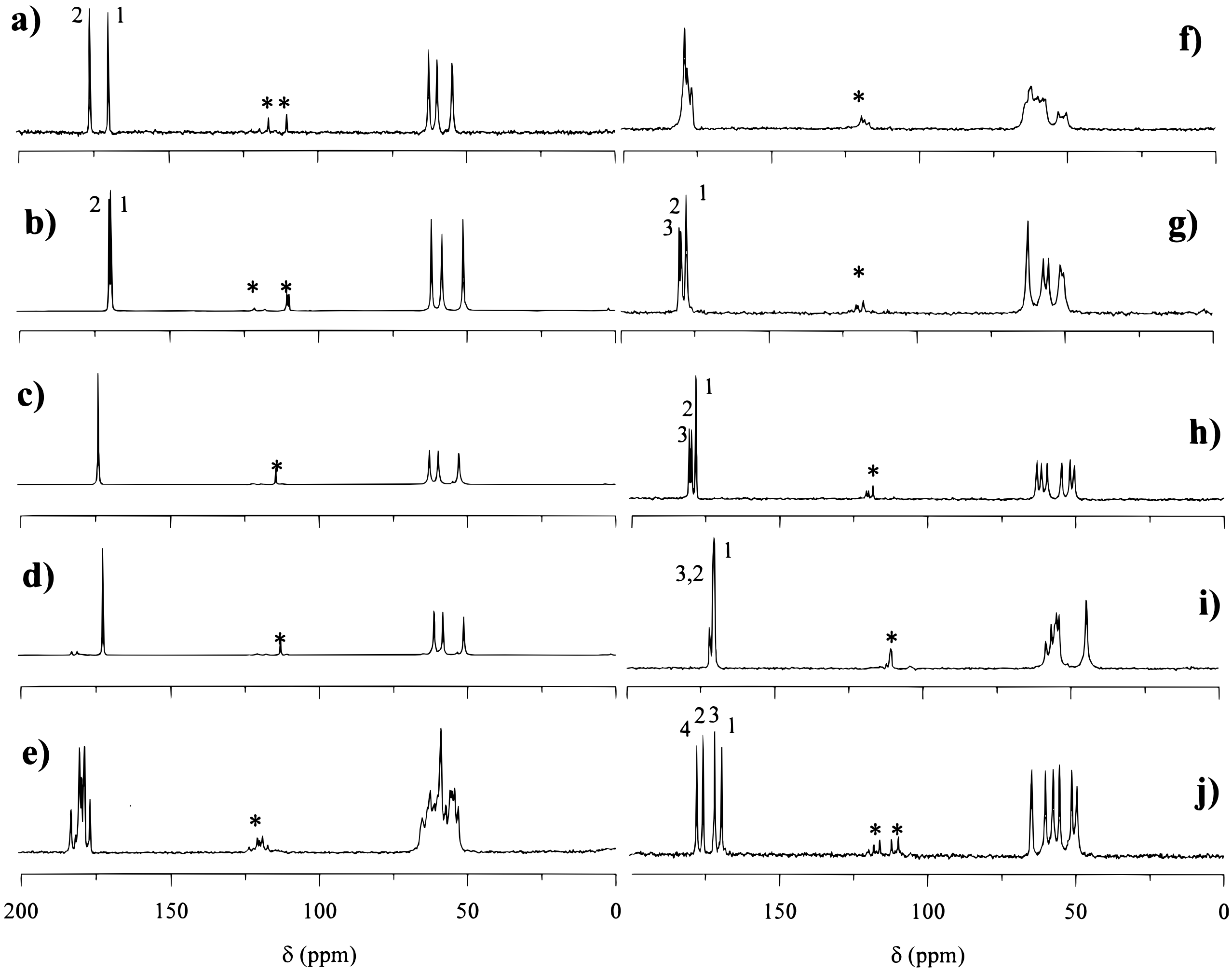


Figure 1. ^{13}C CP/MAS NMR spectra of (a) EDTA, (b) $[NH_4]_2$-EDTA$\cdot x H_2O$, (c) Na_2-EDTA$\cdot 2H_2O$, (d) Na_3-EDTA$\cdot x H_2O$, (e) Na_4-EDTA$\cdot x H_2O$, (f) $CaNa_2$-EDTA$\cdot x H_2O$, (g) Ca_2-EDTA, (h) $MgNa_2$-EDTA$\cdot x H_2O$, (i) K_2-EDTA$\cdot 2H_2O$ and (j) K_3-EDTA$\cdot 2H_2O$. Spectra were obtained using a spinning speed of 6 kHz, contact time 1 ms, recycle delay 60 s and 128 to 1024 scan averages. Spinning sidebands are denoted by asterisks. Resolvable carboxyl resonances are numbered, with the isotropic chemical shift and tensor elements given in Table 1.

Table 1. ^{13}C chemical shifts and carboxyl CSA tensor elements in EDTA–metal complexes

Molecule	δ_{iso} (ppm)[a]	δ_{11} (ppm)[b]	δ_{22} (ppm)[b]	δ_{33} (ppm)[b]	δ_{iso} (ppm)[c]	δ_{iso} (ppm)[d]
EDTA (1)	168.6	244	159	104	61.3, 58.5	53.4
EDTA (2)	174.7	242	173	109		
$[NH_4^+]_2$-EDTA·xH$_2$O (1)	169.4	243	160	105	61.7, 58.2	51.1
$[NH_4^+]_2$-EDTA·xH$_2$O (2)	170.0	248	154	108		
Na$_2$-EDTA·2H$_2$O	172.4	246	167	104	61.2, 58.1	51.1
Na$_3$-EDTA·xH$_2$O	172.6	248	165	105	61.1, 58.2	51.2
Na$_4$-EDTA·xH$_2$O	179	—	—	—	58	—
CaNa$_2$-EDTA·xH$_2$O	179.2	240	188	110	60	52
Ca$_2$-EDTA (1)	177.7	237	186	110	62.3, 57.12	51.3, 50.2
Ca$_2$-EDTA (2)	179.4	—	—	—	55.28	
Ca$_2$-EDTA (3)	180.1	—	—	—		
MgNa$_2$-EDTA·xH$_2$O (1)	178.1	235	190	108	63.0, 61.5	51.9, 50.4
MgNa$_2$-EDTA·xH$_2$O (2)	179.6	239	190	110	59.6, 54.6	
MgNa$_2$-EDTA·xH$_2$O (3)	180.4	237	197	107		
K$_2$-EDTA·2H$_2$O (1)	170.3	244	159	108	57.6	46.4
K$_2$-EDTA·2H$_2$O (2)	171.6	—	—	—		
K$_2$-EDTA·2H$_2$O (3)	172.0	—	—	—		
K$_3$-EDTA·2H$_2$O (1)	169.3	249	153	106	64.5	51.0
K$_3$-EDTA·2H$_2$O (2)	171.5	241	161	112	59.9	49.3
K$_3$-EDTA·2H$_2$O (3)	175.5	241	176	110	57.3	
K$_3$-EDTA·2H$_2$O (4)	177.6	241	178	114	55.1	

[a] Carboxyl ^{13}C isotropic chemical shift. Externally referenced to the carboxyl peak in glycine ($\delta = 176.0$ ppm).

[b] Principal value chemical shifts are labeled δ_{11}, δ_{22}, δ_{33} using the convention that δ_{11} is the greatest high-frequency and δ_{33} the greatest low-frequency chemical shifts.[13] The standard deviation of the carboxyl CSA tensor elements is ±2 ppm.

[c] Acetate methylene ^{13}C isotropic chemical shift.

[d] Ethylenic methylene ^{13}C isotropic chemical shift.

Na$_3$-EDTA·xH$_2$O [Fig. 1(d)] are very similar with three distinct methylene resonances, but only one carboxyl resonance observed for these two compounds. The crystal structure for Na$_2$-EDTA·2H$_2$O has been reported,[8] showing that the H atoms are associated with the amine group and that the Na atoms are coordinated to five nearly equivalent carboxyl acetate groups bridging different EDTA molecules, along with hydrogen bonding to a coordinated water molecule. For the H$_2$EDTA$^-$ ion species, such as Na$_2$-EDTA·2H$_2$O[8] and K$_2$-EDTA·2H$_2$O,[9,10] the crystal structure shows that the metal possesses a weak EDTA–nitrogen bond strength and is not strongly coordinated to the nitrogen. These are commonly referred to as *uncoordinated* EDTA–metal complexes.[11] The spectra for the Na$_4$EDTA·xH$_2$O complex [Fig. 1(e)] has multiple resonances for both the carboxyl and methylene resonances, with the carbonyl resonances being distinctly to high frequency, ranging from 177 to 184 ppm. The observed ^{13}C spectrum in Fig. 1(e) is different from that reported previously for Na$_4$-EDTA·xH$_2$O.[4] Unfortunately, it is unclear what additional characterization was performed in that study to assure that the Na$_4$-EDTA salt was indeed isolated during their synthetic preparation. The syntheses of the disodium and tetrasodium salts have been shown to controlled by pH.[8] The observation of multiple resonances in Fig. 1(e) is in good agreement with the reported crystal structure[8] in which four different Na environments are present. These include a seven-coordinated Na structure in which two amine N and four acetate O of the same EDTA are complexed, while the remaining coordination site is to an acetate O of an adjacent EDTA molecule. The second sodium environment involves three acetate O coordinations involving different EDTA ligands plus two waters of hydration. The third sodium environment involves five acetate O from three different EDTA molecules and a single water of hydration. Finally, the fourth sodium environment is coordinated to four acetate groups from different EDTA molecules and two waters of hydration. The variety of metal binding environments would be expected to produce multiple resonances as observed in Fig. 1(e). It is interesting that unlike previous investigations that found commercial preparations of Na$_3$-EDTA·xH$_2$O to be an equimolar mixture of the Na$_2$-EDTA·2H$_2$O and Na$_4$-EDTA·xH$_2$O complexes, the NMR spectra of Na$_3$-EDTA·xH$_2$O Fig. 1(d) clearly shows a single compound.

The CaNa$_2$-EDTA·xH$_2$O complex [Fig. 1(f)] also shows multiple broadened resonances for both the carboxyl and methylene carbons, differing slightly from the previously reported ^{13}C MAS spectra.[4] The spectrum for the Ca$_2$-EDTA complex [Fig. 1(g)] reveals three distinct carbonyl resonances, with five resolvable methylene peaks. This spectrum is very similar to that observed for the MgNa$_2$-EDTA·xH$_2$O complex [Fig. 1(h)], which shows three clearly resolved carboxyl resonances along with six methylene carbon resonances. The appearance of multiple sharp and well resolved carbonyl and methylene resonances suggests significant departure from C_2 symmetry or the presence of two inequivalent molecules in the unit cell. The narrow and well resolved resonances observed in Fig. 1(h) contrast with the broadened and unresolved spectra for the MgNa$_2$-EDTA·xH$_2$O complex previously reported.[4] The crystal structure for the

$Na_2[H_2OMgEDTA] \cdot 5H_2O$ complex[12] reveals a seven-coordinated $[H_2OMgEDTA]^{-2}$ anion with C_2 symmetry in which the Mg lies below the average coordination plane of the four acetate oxygens. For this crystal structure the Na ions have an irregular octahedral coordination with three acetate ligands from two adjacent EDTA molecules along with three water molecules forming the coordination polyhedron.

For the K_2-EDTA$\cdot 2H_2O$ complex [Fig. 1(i)] three carboxyl resonances with very small separation are observed and the spectrum is very similar in appearance to those of Ca_2-EDTA [Fig. 1(g)] and $MgNa_2$-EDTA$\cdot xH_2O$ [Fig. 1(h)], except that the carbonyl resonances in the potassium complex are distinctly to low frequency. The crystal structure for K_2-EDTA$\cdot 2H_2O$[9,10] shows a zwitterionic EDTA with uncoordinated nitrogens in which the K cations are bridging between EDTA acetate groups. The K_3-EDTA$\cdot 2H_2O$ complex [Fig. 1(j)] shows four approximately equal intensity carboxyl resonances and six methylene resonances. No crystal structure has been reported for this complex, but the multiple resonances reveal either total inequivalence in the structure or two types of molecules in the unit cell.

Although large variations in the carboxyl isotropic chemical shift are not observed, EDTA with coordinated and uncoordinated nitrogens are distinguishable (see Table 1). For example, the average isotropic ^{13}C chemical shifts for the metal–EDTA complexes investigated are shown in Fig. 2. For compounds that involve nitrogen coordination of a metal ion by EDTA (i.e. Na_4-EDTA$\cdot xH_2O$, $CaNa_2$-EDTA$\cdot xH_2O$ and $MgNa_2$-EDTA$\cdot xH_2O$), the average value of the carbonyl isotropic chemical shift is $\delta \sim 179$–180 ppm, 5 ppm to high frequency from the average chemical shifts observed for EDTA complexes without nitrogen coordination. This observed trend would suggest that the Ca_2-EDTA complex, with an average chemical shift of $\delta \approx 180$ ppm, involves nitrogen coordination. Complexes in which the reported crystal structure reveal the metal is uncoordinated to the EDTA except by hydrogen bonding through the carboxyl acetate groups (e.g. Na_2-EDTA$\cdot 2H_2O$ and K_2-EDTA$\cdot 2H_2O$) show an average chemical shift that is the same as observed for uncomplexed free EDTA. Even with this similarity, metal–EDTA complexes with uncoordinated nitrogens can be easily distinguished from the uncomplexed EDTA by the lack of the low-frequency carbonyl resonance at $\delta = 168.6$ (see Table 1). The ^{13}C chemical shifts of the low-frequency ethylenic CH_2 resonances also show a large *ca.* 3–8 ppm low-frequency shift between free EDTA and those complexes containing metal. There is no apparent correlation between the observed methylene chemical shift and nitrogen-coordinated *vs.* uncoordinated structures for the EDTA–metal complexes investigated.

The principal values of the carboxyl ^{13}C CSA tensor for the investigated metal–EDTA complexes were determined from simulation of the spinning sideband manifold for spectra acquired using a spinning speed of 2 kHz. As an example, the experimental and simulated spectra for uncomplexed EDTA are presented in Fig. 3, and show excellent agreement. The chemical shifts of the principal tensor elements are given in Table 1, where variations due to metal binding can be easily evaluated. It has recently been reported that the least shielded CSA tensor element, δ_{11}, could be used to distinguish between protonated (>250 ppm) and deprotonated (<250 ppm) carboxy groups in amino acids and peptides, and lies in the O—C—O plane.[3] In EDTA, a similar trend in the δ_{11} tensor chemical shifts was not observed, with all of the observed principal δ_{11} values ranging between 235 and 249 ppm. The δ_{22}

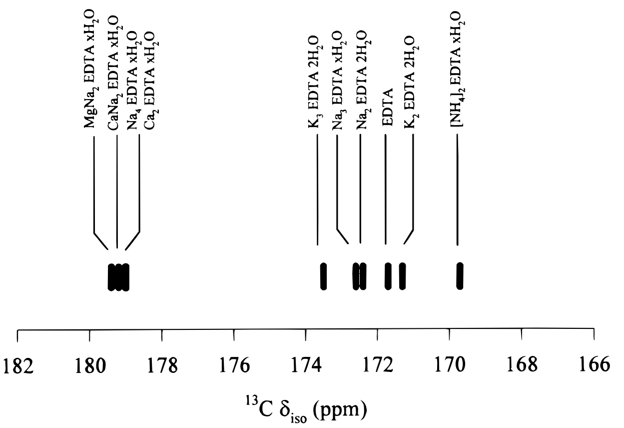


Figure 2. The average ^{13}C isotropic chemical shift for the carboxyl resonances in the EDTA and EDTA–metal complexes investigated. Complexes which show strong nitrogen coordination to the metal are clearly shifted to high frequency from EDTA complexes where nitrogens are uncoordinated.

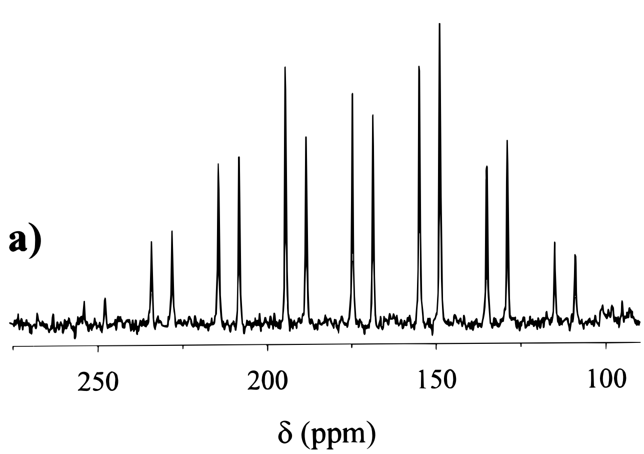


Figure 3. (a) Experimental spectra and (b) theoretical simulation of the carboxyl ^{13}C CSA tensor sideband manifold in uncomplexed EDTA obtained using a spinning speed of 2 kHz. The principal components of the CSA tensor were obtained from an iterative Herzfeld and Berger type analysis. Chemical shifts of the CSA tensor elements are shown in Table 1.

tensor chemical shifts in amino acids are also known to be highly variable and dependent on hydrogen bonding strength, while the orientation of the δ_{22} in organic compounds is dependent on the protonation state of the carboxyl group.[1] For the EDTA–metal complexes investigated here, those systems in which the metal is known to be coordinated strongly to nitrogen in the EDTA anion, (i.e. Na_4-EDTA $\cdot$ xH_2O, $CaNa_2$-EDTA $\cdot$ xH_2O and $MgNa_2$-EDTA $\cdot$ xH_2O) the δ_{22} tensor elements are significantly shifted to high frequency, ranging from 188 and 197 ppm. Unfortunately, the tensor elements for the Na_4-EDTA $\cdot$ xH_2O salt were not obtainable, giving only two EDTA–metal complexes with known nitrogen coordination to support this trend. For the Ca_2-EDTA complex the deshielded δ_{22} tensor component (186 ppm) indicates that metal–nitrogen coordination occurs for this complex, agreeing with the average isotropic chemical shift value discussed earlier. The δ_{33} tensor element of the carboxyl group shows some small variations, and is typically oriented perpendicular to the COO^- plane.[1] No clear correlation with metal binding or nitrogen coordination is observed.

These results show that solid-state ^{13}C CP/MAS NMR, in particular evaluation of the carbonyl isotropic chemical shift and CSA tensor, can be used to investigate the structure and coordination environments of EDTA–metal complexes. The complexation of EDTA and EDTA derivatives to metal-containing surfaces is currently being pursued.

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