Influence of transition metal electron configuration on the structure of metal-EDTA complexes

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ABSTRACT. The vibrational spectra of cold complexes of ethylenediaminetetraacetic acid (EDTA) with transition metal dications in vacuo show how the electronic structure of the metal provides a geometric template for interaction with the functional groups of the binding pocket. The OCO stretching modes of the carboxylate groups of EDTA serve as structural probes, informing on the spin state of the ion as well as the coordination number in the complex. The results highlight the flexibility of EDTA in accepting a large range of metal cations in its binding site.

TOC GRAPHICS

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Supramolecular structures that can bind metal cations are important in a broad range of chemical scenarios, including binding sites in metalloenzymes, sensing of metal ions, the effective removal of metal cations (to decrease their toxicity), and ionophores for flow batteries. Ethylenediaminetetraacetic acid (EDTA) is a widely used chelator for metal cations, forming a binding pocket generated by its two N atoms and four COO- groups (see Figure 1). It has a remarkably high affinity for nearly all metal cations in the periodic system, and it is frequently used as an enzyme inhibitor for metalloenzymes.

The near-universal ability of EDTA to accommodate metal cations comes from its molecular flexibility, which allows it to respond to the chemical nature of the metal ion it binds. As a consequence, one expects the geometry of the binding pocket around a given ion to be a function of ion size, but also dependent on the electronic structure of the metal ion itself. For example, while alkaline earth dications present to their chemical environment as simple, spherically symmetric charge distributions, transition metal ions structure their environment through the occupation of their \( d \)-orbitals. In many transition metal complexes, the structural template of the electronic structure of the metal ion even dominates the structure of the ligand frame around the metal ion.

In the condensed phase, the environment (e.g., protein or solvent) influences the interactions of ions with ion receptors and chelators such as EDTA. In addition, the presence of solvent molecules can mask the spectroscopic response of the complex under study, and the spectroscopic signatures can be rather broad. Experiments on mass selected ions circumvent many of these problems, allowing one to gauge the intrinsic interactions between ion and chelator. Cryogenic preparation of the target ions serves to further simplify their spectroscopic response. In pioneering work, Wang and coworkers concluded on the basis of photoelectron spectra and density
functional theory (DFT) calculations of divalent first-row transition metal complexes with EDTA that all complexes adopt a hexa-coordinated structure. However, they attributed penta-coordinated conformations to Cu(II)-EDTA complexes as well, and they recognized that the coordination number of the bound metal ion could, in principle, vary from four to six.

Figure 1. Structure of EDTA complexes with metal dications. (a) [M(II)\textperiodcentered EDTA]\textsuperscript{2−} line drawing; equatorial and axial ligands are labeled “eq” and “ax”, respectively. (b-d) Calculated ball-and-bond type structures of [M(II)\textperiodcentered EDTA]\textsuperscript{2−} complexes in hexa- (b), penta- (c), and tetra-coordinated (d) geometries, using M = Zn as an example. Carbon atoms are shown in grey, nitrogen in blue, oxygen in red, and the central metal atom in blue-grey. Dotted lines show the coordination of the metal atom.

In the present work, we use cryogenic ion vibrational spectroscopy (CIVS) and DFT calculations to characterize the ion-chelator interactions for complexes of selected divalent transition metal ions M\textsuperscript{2+} (M = Mn, Co, Ni, Cu, Zn). Our experimental and computational methods are described in ref. 12 and Supporting Information. All calculations were carried out with the Q-Chem electronic structure package.\textsuperscript{13}

Figure 2 shows the experimental infrared (IR) signatures of [M(II)-EDTA]\textsuperscript{2−}\cdot N\textsubscript{2} complexes in the fingerprint region of the spectrum. There are two regions of interest, a lower frequency range
(1300 – 1400 cm\(^{-1}\)) and a higher frequency range (1600 – 1700 cm\(^{-1}\)), containing IR signatures belonging predominantly to the OCO stretching modes of the carboxylate groups of EDTA. The lower frequency range mainly contains the signatures of linear combinations of the symmetric OCO stretching vibrations, while linear combinations of the antisymmetric stretching motions are found in the higher frequency range.

**Figure 2.** Experimental IR spectra of [M(II)-EDTA\(^{2-}\)\cdot N\(_2\)] complexes in the fingerprint region (from top to bottom: M = Ca, Mn, Co, Ni, Cu, Zn, metal identity given in each trace). Data for M = Ca taken from ref. 7. Note the break of the wavenumber axis (1420 – 1570 cm\(^{-1}\), no significant IR signal was found in this range). See Figure S1 for spectra without axis break.
The spectrum of \([\text{Ca(II)-EDTA}]^{2-}\) provides the starting point for our discussion. As described previously,\(^7,9\) this is a complex with \(C_2\) symmetry, where the metal ion is hexa-coordinated by the EDTA binding pocket. The antisymmetric OCO stretching motions of the EDTA moiety form four linear combinations, which give rise to partially resolved features in the higher frequency range. The feature at 1656 cm\(^{-1}\) represents the radial all-in-phase linear combination of the local OCO antisymmetric stretching motions, while the strong peak at 1632 cm\(^{-1}\) contains two unresolved modes, each pairing the motions of one equatorial and one axial ligand. The shoulder at 1615 cm\(^{-1}\) is the signature of a mode which combines the motions of equatorial ligands radially in phase, with the axial ligands opposite in phase (see Figure S2 in ref. \(^7\)). The peak at 1365 cm\(^{-1}\) contains the four unresolved analogous vibrational modes consisting of linear combinations of the symmetric OCO stretching vibrations.

For transition-metal complexes with EDTA, the patterns in the regions of the symmetric and antisymmetric stretching vibrations vary with the identity of the ion. For example, although the patterns for Ca and Mn complexes appear very similar in their simplicity, the spectrum of \([\text{Mn(II)-EDTA}]^{2-}\) does not show significant intensity for the highest frequency component of the antisymmetric OCO stretching modes, which is clearly observed in the Ca complex. Most strikingly, the symmetric stretching patterns for \(M = \text{Co, Ni, Cu, and Zn}\), and the antisymmetric stretching modes for \(M = \text{Co, Cu, and Zn}\) show considerably different substructure than the alkaline earth metal complexes.\(^7\)

Since these patterns depend on the interaction of the metal ion with the carboxylate groups of the EDTA pocket, the electronic structure of the metal ions will play a key role in the spectroscopic properties. For \(M = \text{Mn, Co, and Ni}\), different spin states of the metal ion are possible. Corroborating earlier results by Wang and coworkers,\(^11\) our DFT calculations predict that the high
spin states are lowest in energy in each case (see Table S1), and judging from the natural orbital analysis, the unpaired electrons are localized on the metal center (Figure S2). The match of the computed high-spin and experimental IR spectra is generally quite good (Figure 3). For M = Mn, the symmetric stretching region is recaptured better by the predicted spectrum of the sextet state. Similarly, for M = Ni, the predicted pattern of antisymmetric stretching modes clearly allows identification of the triplet state as a better fit to the experimental spectrum. Both of these cases independently corroborate photoelectron spectroscopy and computational results assigning the high spin states to [M(II)\·EDTA]^- complexes. For M = Co, the IR spectrum does not serve to uniquely identify the spin state, but based on the relative energies of the different states, we assume that the experimental IR spectrum belongs to the quartet state. The peculiar substructure of the antisymmetric stretching bands therefore cannot be explained by the presence of different spin states, but has structural reasons, as will be explained further below.
Figure 3. Experimental IR spectra of [M(II)-EDTA]$^{2-}$-N$_2$ complexes (from top to bottom: M = Mn, Co, Ni, metal identity given in each panel, spin, $S$, shown for each calculated trace) in comparison with DFT ($\omega$B97X-D/Def2-TZVPP) calculations for hexa-coordinated structures with different spin states. The calculated frequencies were scaled by 0.950 to match the signature of the main antisymmetric OCO stretching feature for [Ca(II)-EDTA]$^{2-}$. The dashed lines represent experimental and computed intensities multiplied by 3.

The influence of the electronic structure on the IR patterns can be rationalized by the population of $d$-orbitals in the metal ion and the resulting structural differences between the different complexes. In particular, the different $d$-orbital occupations result in differences in the calculated
distances of the metal ion to the closest O atoms for equatorial and axial ligands in the EDTA binding pocket (see Table S2). This difference in interaction strength is reflected in the ratio of the equatorial and axial metal-oxygen distances, $d_{eq}$, and $d_{ax}$ (see Figure 4). For the alkaline-earth metals with their spherical charge distribution, this ratio is in a narrow band around 1.01, with deviations from this value by 0.01, despite the large disparity in ion radius. For the transition metal ions studied in the present work, the range of values of this ratio is much larger, showing the significant difference in interactions between equatorial and axial ligands, even though the ion radii are rather similar for the ions studied here. As a result, the kinematic coupling between the local OCO stretching oscillators with similar frequencies changes, and the participation of the individual carboxylate groups in each mode as well as the frequencies of each mode change as well (Table S3).

Figure 4. Calculated aspect ratio of equatorial to axial metal-oxygen bond distances (see Table S3) as a function of ion radius for different divalent metal cations. Open squares show the data for alkaline earth metals, while filled circles show data for the transition metals under study in the present work.
Within the hexacoordinated structures of \([\text{M(II)}\cdot\text{EDTA}]^{2-}\) complexes, the predicted overall pattern in the antisymmetric stretching region remains simple, with little structure that would be resolvable in our experiment. However, the antisymmetric stretching region for \(M = \text{Cu}\) and \(\text{Zn}\) shows complex substructure. Wang and coworkers\(^{11}\) proposed that the complexes for these metal ions could be penta- or even tetra-coordinate, rather than hexa-coordinate (see Figure 1). Figure 5 shows the experimental IR spectra for \(M = \text{Co}, \text{Cu}\) and \(\text{Zn}\) compared to simulated IR spectra for different coordination isomers. The predicted IR patterns in the antisymmetric stretching region shift significantly to the blue for decreasing coordination numbers of the metal ion. Different from the results of Wang and coworkers, who calculated the hexa-coordinated structures to be lowest in energy,\(^{11}\) we find the lowest energy isomers to be penta-coordinated in all three cases (see Table 1).

**Table 1. Relative Energies (in cm\(^{-1}\)) of \([\text{M(II)}\cdot\text{EDTA}]^{2-}\) Isomers (M = Co, Cu, Zn) With Different Coordination Numbers using \(\omega\text{B97X-D/Def2-TZVPP.}\)**

<table>
<thead>
<tr>
<th>Coordination</th>
<th>Co(^{a})</th>
<th>Cu</th>
<th>Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>126</td>
<td>505</td>
<td>108</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>5977</td>
<td>1048</td>
<td>4667</td>
</tr>
</tbody>
</table>

\(^{a}\) spin state with \(S = 3/2\)

Wang and coworkers\(^{11}\) calculated the barriers between hexa- and penta-coordinated isomers to be around 1 eV, except for \(M = \text{Cu}\) (0.29 eV), so the thermal occupation probability of different isomers at cryogenic temperatures can be neglected. However, these complexes are formed from solutions at room temperature, where the thermal energy content of \([\text{M(II)}\cdot\text{EDTA}]^{2-}\) complexes
can be estimated at ca. 0.5 eV, and they may suffer energetic collisions during the first stages of the electrospray source. They may also adopt a penta-coordinated structure in solution, which could persist in the gas phase. Rapid cooling in the cryogenic ion trap can kinetically freeze ionic species in structures at higher energies. In view of these arguments, we explain the rich substructure in the spectra of \([\text{Co(II-EDTA)}]^2-, [\text{Cu(II-EDTA)}]^2-,\) and \([\text{Zn(II-EDTA)}]^2-\) with coexisting hexa- and penta-coordinated isomers. For \(M = \text{Zn}\), this is consistent with work by Williams, Armentrout, and coworkers\(^{14-15}\) who showed that the \(\text{Zn}^{2+}\) ion prefers 5-fold coordination in hydrated cluster ions.

In summary, we present IR spectra and quantum-chemical calculations on complexes of transition metal dications (Mn, Co, Ni, Cu, Zn) with EDTA. The IR signatures of the OCO stretching modes of these complexes encode the interactions of the chelated ion with the functional groups of the binding pocket. The complexes are generally found to be in their highest possible spin states, which is an interesting observation, since EDTA has been variously characterized as a strong- or weak-field ligand.\(^{16-18}\) In addition, all are likely to show hexa-coordinated metal ions. However, EDTA complexes with Co, Cu, and Zn dications exhibit substructure in the region of the antisymmetric OCO stretching modes that indicate the presence of several coordination isomers. The electronic structure of the chelated ions affects the contribution of each carboxylate group to the OCO stretching motions in each mode, and thereby influences the corresponding IR signatures. The results highlight the variability of EDTA in accommodating ions of different sizes and show how the electronic structure of the guest atom imposes a shape template in the interaction with the EDTA binding pocket.
Figure 5. Experimental IR spectra of [M(II)-EDTA]^{2-}·N₂ complexes (from top to bottom: M = Co, Cu, Zn, metal identity given in each panel, coordination number, C, shown for each calculated trace) in comparison with DFT (ωB97X-D/Def2-TZVPP) calculations for different coordination numbers of the EDTA binding pocket.
ASSOCIATED CONTENT

Supporting Information. Experimental methods; Experimental IR spectra of [M(II)-EDTA]^{2-} \cdot N_2 complexes in the fingerprint region; Computational methods; Adiabatic energy gaps; Wave function properties of the five lowest eigenstates of [Mn(II) \cdot EDTA]^{2-}; Frontier natural orbitals of the lowest sextet state of [Mn(II) \cdot EDTA]^{2-}; Calculated metal-oxygen distances; Qualitative amplitude of equatorial and axial OCO oscillators.

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Notes
The authors declare no competing financial interests.

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