Lanthanide(III)-Induced Conversion of 12-Metallacrown-4 to 5-Metallacrown-5 Complexes in Solution

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The conversion of 12-metallacrown-4 complexes with copper(II) in the central cavity to 15-metallacrown-5 complexes with lanthanide(III) ions in the central cavity upon addition of trivalent lanthanide ions was analysed in solution by electrospray ionisation mass spectrometry (ESI-MS), absorption spectrophotometry, circular dichroism and proton NMR spectroscopy. In all cases, copper(II) ions were the ring metals. The lanthanide-induced shifts of the proton resonances in the NMR spectra of different lanthanide(III)-containing 15-metallacrown-5 complexes with tyrosinehydroximate ligands were studied. The dynamics of ligand exchange of α-aminohydroximate-based lanthanide(III)-containing 15-metallacrown-5 complexes were studied in methanol solutions. The ring structure of the 12-metallacrown-4 complex that acts as starting compound for the formation of the 15-metallacrown-5 complexes was optimized by DFT methods using alaninehydroximate as a model ligand.

Introduction

Metallacrowns, a class of macrocyclic compounds discovered by Pecoraro and coworkers in 1989, are inorganic analogues of crown ethers where heteroatoms and metals substitute for the ring carbons.[1,2] Several types of metallacrown complexes with different metals, ligands and ring sizes have been developed.[3] The stoichiometry of the metallacrown complexes depends on the type of ligand used. Aminohydroximate ligands, which are derivatives of hydroxamic acids with an additional amino group as a potential coordinating group, are suitable ligands for metallacrown formation because they can act as bridging ditopic ligands. These ligands form a metallamacrocycle ring with a metal-nitrogen-oxygen backbone in the presence of copper(II) ions. β-Aminohydroximate ligands can form connected six- and five-membered chelate rings giving rise to 12-metallacrown-4 complexes (12-MC-4) with four copper(II) ions in the macrocyclic ring. A fifth copper(II) ion is encapsulated by the four oxygen atoms of the ring leading to a pentanuclear copper(II) complex Cu^{II}[12-MC-4] whose crystal structure has been determined.[4]

On the other hand, α-aminohydroximate ligands form 15-metallacrown-5 (15-MC-5) compounds because these ligands chelate the metals by connected five-membered rings giving rise to a planar metallamacrocycle ring with five copper atoms in the ring. The cavity size of this ring is larger than the cavity size of the 12-metallacrown-4 complexes and affords the incorporation of lanthanide(III)[5–11] or uranyl ions.[11–13] 15-Metallacrown-5 complexes of lanthanide(III) ions with either chiral or nonchiral α-aminohydroximate ligands have been structurally characterized.[5–10] Careri and coworkers showed that α-aminohydroximate ligands form the 12-metallacrown-4 structural motif in aqueous solution in the absence of lanthanide(III) ions.[14] However, those Cu^{II}[12-MC-4] metallacrowns are less stable than those containing β-alaninehydroxamic acid as the ligand. No single crystal structure of 12-metallacrown-4 complexes containing α-aminohydroximate ligands has been determined yet, but solution studies have shown that Cu^{II}[12-MC-4] complexes are converted into (UO_2)[15-MC-5] complexes in aqueous solution upon addition of a uranyl salt.[13]

Although the lanthanide(III)-containing 15-metallacrown-5 complexes with α-aminohydroximate ligands have been thoroughly characterised in the solid state, their formation and self-assembly in solution still remain elusive. The formation of 12-metallacrown-4 complexes with salicylhydroximate ligands has been investigated in solution and data pointed out that some dimeric nickel(II) salicylhydroximate intermediates reorganize in basic solvents to form a 12-metallacrown macrocycle. It was also found that 12-metallacrown-4 copper(II) complexes with salicylhydroximate ligands maintain their structure in solution in the presence of excess ligand or metal ions.[3] In this study, we demonstrate that in the self-assembly of copper(II)-containing 15-metallacrown-5 complexes derived from α-aminohydroximate ligands, the final 15-metallacrown-5 is formed through the lanthanide(III)-templated reassembly of the 12-

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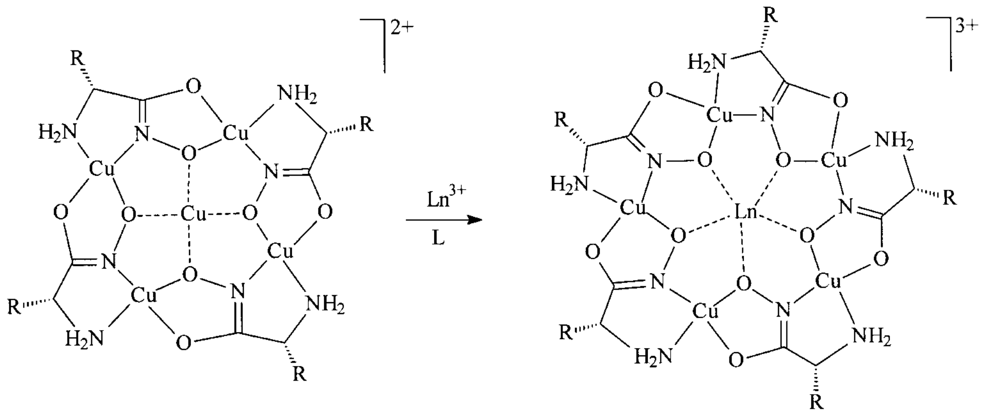
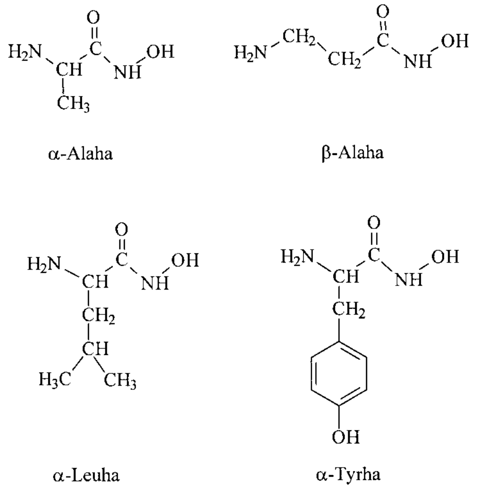


Scheme 1. Schematic representation of lanthanide-induced conversion of 12-metallacrown-4 (left) to 15-metallacrown-5 (right).

metallacrown-4 complex (Scheme 1). Since the structure of the 12-metallacrown-4 complex has not been determined yet, its ring structure with alaninehydroximate as a model ligand was optimized by DFT methods. The solution properties and ligand exchange of 15-metallacrown-5 complexes with α-aminohydroximate ligands and copper(II) ions were studied by a combination of several experimental techniques such as electron spray mass spectrometry (ESI-MS), paramagnetic nuclear magnetic resonance techniques, circular dichroism and UV/Vis spectrophotometry. The evaluation of the properties of metallacrown compounds in solution is important if one envisages solution-based applications of metallacrowns, for example, as sequestering agents for selective recognition of actinide or lanthanide ions and as contrast agents for magnetic resonance imaging applications.



Scheme 2. Schematic representation of α-alaninehydroxamic acid (α-Alaha), β-alaninehydroxamic acid (β-Alaha), α-leucinehydroxamic acid (α-Leuha) and α-tyrosinehydroxamic acid (α-Tyrha).

Results and Discussion

Structure Optimization of Cu^{II}[12-MC-4] by DFT Methods

The structures of the ligands used in this study are presented in Scheme 2. The crystal structures of copper(II)-containing 12-metallacrown-4 complexes, Cu^{II}[12-MC-4], with β-aminohydroximate ligands were determined in the past,[4,8] but to the best of our knowledge no crystal structures of Cu^{II}[12-MC-4] with α-aminohydroximate ligands have been determined. The crystal structure of Cu^{II}[12-MC-4] with β-aminohydroximate ligands shows that the ligands form five- and six-membered chelate rings with the metal ions arranged in an almost planar ring. Dallavalle and coworkers have commented on the structure of Cu^{II}[12-MC-4] with the α-aminohydroximate ligands derived from phenylalanine-, tryptophan- and alaninehydroxamic acid. Because those ligands can form only five-membered chelate rings, this would give rise to a strained structure if planar, so they propose an arrangement of the rings in a cup-conformation with four sp^3-hybridised oxygen atoms bridging the peripheral and central copper(II) ions.[14–15]

In order to gain more insight into the structure of Cu^{II}[12-MC-4] with α-aminohydroximate ligands, we performed density functional theory (DFT) calculations (Figure 1). For comparison, we have also calculated the structure of Cu^{II}[12-MC-4] with β-aminohydroximate ligands by the same method. In both types of complexes (with α-alaninehydroxamic or β-alaninehydroxamic acid as the ligand), the four peripheral copper(II) ions form an almost planar structure. The central copper(II) ion is situated above this quasi-plane. For the complex formed with the α-aminohydroximate ligands, the deviation from planarity is larger than for the complex with β-aminohydroximate ligands. This can clearly be seen by comparing the dihedral angles between the four copper(II) ions: 1.4° in the β-form and 3.0° in the α-form. There is also a difference in the position of the central copper(II) ion above the quasi-plane: in the complex with α-aminohydroximate ligands the distance between the central copper(II) ion and a virtual line connecting two opposite copper(II) ions is 0.98 Å, whereas in the β-form it is only 0.50 Å. Another difference is the coordination of the copper(II) ions in the ring. In the complex with β-aminohydroximate ligands the copper(II) ions have a nearly planar coordination, whereas the deviation from planarity is more pronounced in the complex with α-aminohydroximate ligands. This can be related to the stability of these two structures in solution: the calculated complex-formation constant for Cu^{II}[12-MC-4] with α-Alaha (logβ = 40) is lower than that with β-Alaha (logβ = 49).[14] The difficulties of growing crystals of the α-form could lie in the subtle differences in the proposed structures.

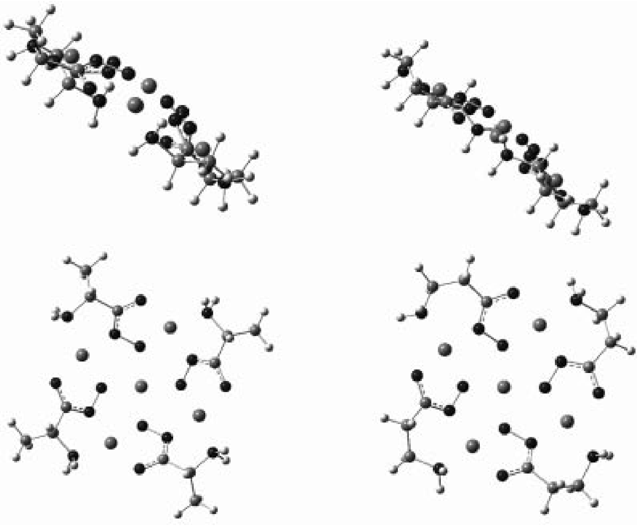


Figure 1. Structure of Cu^{II}[12-MC-4] with α-alaninehydroxamic acid (left) and β-alaninehydroxamic acid (right) resulting from the DFT calculation.

Titration of $[Cu_5L_4]^{2+}$ with Lanthanide(III) Ions Monitored by Optical Spectroscopy

Complex formation between α-aminohydroxamic acid and copper(II) ions can lead to several species depending on the pH of the solution. When copper(II) ions and α-Alaha are mixed in a 1:3 ratio, the distribution diagram shows that, in the pH range 4.5–5.5, the pentanuclear $[Cu_5(\alpha\text{-Alaha})_4]^{2+}$ complex is the most abundant species in solution.[14] When copper(II) ions and α-Leuha are mixed in a 1:1 ratio and the pH of the final solution is around 4.5, the only detectable complex in solution is also a pentanuclear $[Cu_5(\alpha\text{-Leuha})_4]^{2+}$ complex.[13] In the present study, the starting solutions for the titrations were also prepared by mixing the ligand and copper(II) acetate in a 1:1 ratio, so we can assume that under these conditions the pentanuclear complex is the most abundant species in solution. This was confirmed by ESI-MS results and will be discussed later.

The UV/Vis absorption spectrum of $[Cu_5(\alpha\text{-Leuha})_4]^{2+}$ at pH 4.5 is characterised by two prominent absorption bands with maxima at 650 nm and 343 nm. Similarly, the maximum absorbance for $[Cu_5(\alpha\text{-Tyrha})_4]^{2+}$ has been observed at 660 and 346 nm. The λ_{max} values in the visible region are in agreement with those calculated for $[Cu_5(\alpha\text{-Pheha})_4]^{2+}$ and $[Cu_5(\alpha\text{-Trpha})_4]^{2+}$ metallacrowns.[15] Bands at 352 and 336 nm have also been observed in these complexes and could be assigned to $N^-\text{–}O^-_{(nitrogen)}\rightarrow Cu^{II}$ and $N^-\text{–}O^-_{(oxygen)}\rightarrow Cu^{II}$ charge-transfer transitions.

Since the α-aminohydroxamic acids used in this study are chiral, their copper(II) complexes are expected to be optically active as well. The CD spectrum of $[Cu_5(\text{D-}\alpha\text{-Leuha})_4]^{2+}$ shows a positive Cotton effect at 350 nm and two negative peaks at 558 and 646 nm. The two latter peaks

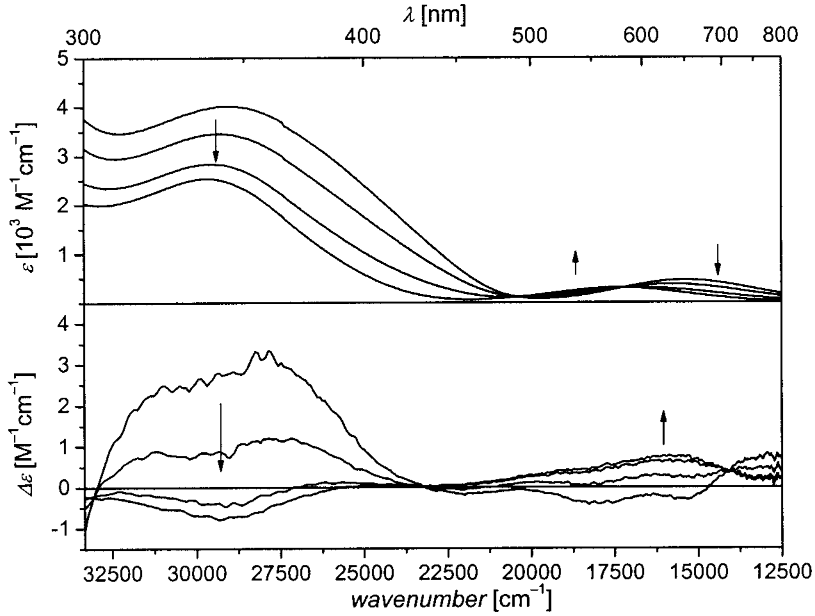


Figure 2. Changes in UV/Vis and CD absorption spectra of Cu^{2+}/D-α-Leuha solutions in water upon addition of Gd^{3+}. The Gd^{3+} ion was added in 0.33-equivalent increments relative to the 12-metallacrown-4 concentration.

are either due to d-d transitions of the copper(II) ion or due to the presence of nonequivalent chromophores in the metallacrown. If L-α-Leuha was used as the ligand, the CD spectrum of the resulting $[Cu_5(\text{L-}\alpha\text{-Leuha})_4]^{2+}$ looked as a mirror image of the $[Cu_5(\text{D-}\alpha\text{-Leuha})_4]^{2+}$ spectrum, with two bands at 558 and 646 nm having positive Cotton effects and a band at a 350 nm having a negative Cotton effect. The CD spectrum of $[Cu_5(\text{L-}\alpha\text{-Tyrha})_4]^{2+}$ showed a weak positive Cotton effect at 350 nm and a weak negative Cotton effect at 672 nm. The stepwise addition of Gd^{3+} to the aqueous solution of $[Cu_5(\text{D-}\alpha\text{-Leuha})_4]^{2+}$ and $[Cu_5(\text{L-}\alpha\text{-Tyrha})_4]^{2+}$ caused significant changes both in the UV/Vis and in the CD spectra. As seen in Figure 2, the UV/Vis and CD spectra are characterised by isosbestic points, suggesting the presence of only two interconverting species in the solutions. At the end point of the titration of $[Cu_5(\text{L-}\alpha\text{-Tyrha})_4]^{2+}$ with Gd^{3+}, one band having a negative Cotton effect is observed at 557 nm. The ligand field analysis of lanthanide(III)-containing 15-metallacrown-5 copper(II) species was in accordance with this finding and suggested that three d-d transitions should be expected in the ligand field region, and the transition around ca. 556 nm should be the most intense.[5] After titration of $[Cu_5(\text{L-}\alpha\text{-Tyrha})_4]^{2+}$ with Gd^{3+}, the UV/Vis spectra are characterised by two prominent absorption bands with maxima at 581 nm and 340 nm. Similar absorption spectra have also been observed for the other lanthanide(III)-containing 15-metallacrown-5 complexes with L-α-Tyrha as ligand ($Ln^{3+} = Y^{3+}$, La^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, Er^{3+}, Tm^{3+}). The absorption spectra of the different lanthanide-containing metallacrown complexes are virtually independent of the lanthanide(III) ions. The peak maxima in the spectra differ less than 2 nm from those of the gadolinium(III)-containing metallacrowns.

$[Cu_5L_4]^{2+}$ Titration with Lanthanide(III) Monitored by ESI-MS

Electrospray ionisation mass spectrometry (ESI-MS) is an effective method for studying the speciation of metal complexes in solution and was applied in studies of different metallacrown systems.[16] The method has been proven to be very useful in providing solution molecular weights of the formally neutral metallacrown complexes after the loss of bound anions. ESI-MS results indicate that solutions containing a copper(II) salt and α-Leuha in a 1:1 ratio form exclusively 12-MC-4 species in the solution, with peaks at 447 and 930 *m/e*, which could be assigned to the pentanuclear species $[Cu_5(\alpha\text{-Leuha})_5]^{2+}$ (447.2 calcd.) and $[Cu_5(\alpha\text{-Leuha})_5](Cl)^+$ (929.8 calcd.), respectively.

As seen in Figure 3, the addition of gadolinium(III) to the $[Cu_5(\alpha\text{-Leuha})_4]^{2+}$ solution caused disappearance of the peaks which were assigned to the 12-MC-4 species and the appearance of new peaks at 627 and 1319 *m/e*, which could be assigned to the 15-MC-5 species $[Gd(NO_3)Cu_5(\alpha\text{-Leuha})_5]^{2+}$ (628.9 calcd.) and $[Gd(NO_3)_2Cu_5(\alpha\text{-Leuha})_5]^+$ (1319.8 calcd.), respectively.

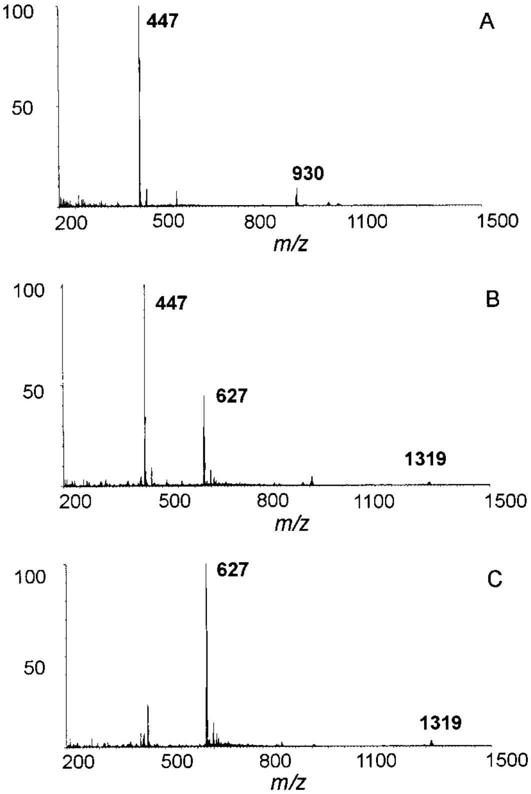


Figure 3. Positive-ion mode ESI-MS spectra of Cu^{2+}/Leuha solutions containing different amounts of Gd^{3+} relative to the 12-metallacrown-4 concentration: (a) 0.0 equiv., (b) 0.5 equiv., (c) 1.0 equiv.

A similar trend was observed upon addition of Gd^{3+} to the solution of $[Cu_5(\alpha\text{-Tyrha})_4]^{2+}$: the peaks corresponding to $[Cu_5(\alpha\text{-Tyrha})_4]^{2+}$ disappeared, and new positive-mode ESI-MS peaks appeared at *m/e* = 753 and 1570 corresponding to $[(Gd)Cu_5(\alpha\text{-Tyrha})_5](NO_3)^{2+}$ (753.9 calcd.) and $[(Gd)Cu_5(\alpha\text{-Tyrha})_5](NO_3)_2{}^+$ (1569.9 calcd.), respectively. In the ESI-MS spectra taken in the negative mode, only one peak at 1693 *m/e* appeared corresponding to $[(Gd)Cu_5(\alpha\text{-Tyrha})_5](NO_3)_4{}^-$ (1692.8 calcd.). These results indicate that after addition of 1 equiv. gadolinium relative to the 12-metallacrown-4, complete conversion of 12-metallacrown-4 to 15-metallacrown-5 occurs, and that the gadolinium(III)-containing 15-metallacrown-5 is the only species formed in solution.

$[Cu_5L_4]^{2+}$ Titration with Lanthanide(III) Monitored by NMR

In paramagnetic molecules, the NMR signals of protons close to the paramagnetic centres are broadened. Metallacrowns containing paramagnetic copper(II) ions and a paramagnetic lanthanide(III) ion in the cavity are therefore expected to give very broad signals with bad resolution. The extent of paramagnetic-induced line broadening depends on the electronic relaxation time of the paramagnetic metal centres. Broad lines are expected for complexes with copper(II) ions because of the relatively long electronic relaxation time of this ion ($\tau_s = 1–5 \times 10^{-9}$ s).[17] However, a shortening of the electronic relaxation times of the metal ions involved can occur as a consequence of magnetic coupling.[18] The copper(II) ions in the 15-MC-5 ring are antiferromagnetically coupled so that the τ_s value is lower than it would be in the absence of magnetic coupling.[6,16] As a consequence, one could in principle observe signals in high resolution NMR experiments.

We studied the conversion of a 12-metallacrown-4 to a 15-metallacrown-5 in [D$_4$]MeOH by solution proton NMR spectroscopy. Spectra of solutions containing equimolar amounts of the copper(II)/aminohydroximate ligand (L-Leuha) and different amounts of lanthanide(III) ions were recorded after one day (Figure 4). The four different samples prepared contained 0.00, 0.33, 0.66 and 1.00 equiv. $Nd(NO_3)_3$ (relative to the amount of 12-metallacrown-4). The first spectrum, without any neodymium(III), shows only one broad peak at ca. 1 ppm. In the sample with 0.33 equiv. of neodymium(III), the signal at 1 ppm disappears and two new signals appear at approximately. 31 ppm and 16 ppm in addition to four other signals that appear between $\delta = 0$ and 4 ppm (Figure 4). 2D-COSY experiments revealed that the peaks experiencing the largest paramagnetic shift, at 31 ppm and 16 ppm, belong to the α and γ protons of L-Leuha, respectively. The peaks of the methyl groups appear at $\delta = 0.5$ and 1.5 ppm, indicating that these two groups are magnetically nonequivalent. The other two weak signals that appear between $\delta = 0$ and 4 ppm are from the magnetically nonequivalent β-protons of the ligand. Addition of more neodymium(III) ions increased the intensity of all peaks, and only a slight shift to lower field was observed. We attempted a similar NMR titration experiment for the metallacrown system with L-Tyrha ligands. Unfortunately, solutions containing equimolar amounts of copper(II) and L-Tyrha *without* lanthanide(III) were turbid at those high concentrations and no NMR spectra of the starting solutions could be obtained. On the other hand, copper(II)/L-Tyrha solutions *with* lanthanide(III) ions were clear, and their NMR spectra are discussed later.

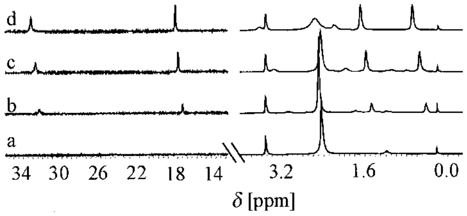


Figure 4. Proton NMR spectra of Cu^{2+}/Leuha solutions in [D$_4$]MeOH containing different amounts of Nd^{3+} relative to the 12-metallacrown-4 concentration: (a) 0.00 equiv., (b) 0.33 equiv., (c) 0.66 equiv., (d) 1.00 equiv.

It is interesting to note that in the case of 12-metallacrown-4, which is formed in the absence of any lanthanide(III) in solution, most of the NMR signals could not be detected. However, in the case of 15-metallacrown-5 complexes, which are formed upon addition of neodymium(III), the NMR signals of the ligand become observable. This difference points to the different electronic relaxation of the copper(II) ions in the 12-metallacrown-4 and 15-metallacrown-5. This difference is not surprising if one considers that the coordination around copper(II) ions is nearly square planar in 15-metallacrown-5,[12] but square pyramidal in 12-metallacrown-4, as shown by our DFT calculations.

NMR Analysis of $Ln(NO_3)_3[15\text{-}MC_{Cu^{II}N(L\text{–}Tyrha)}\text{-}5]$

Paramagnetic shift reagents, which are used to induce large NMR shifts in organic molecules to which they are coordinated, are available for most classes of compounds. One factor that has led to the widespread application of lanthanide-containing shift reagents (LSR) is that the shifts observed in the NMR spectrum are highly predictable.[19–22] This is a result of the magnetic properties of the lanthanide ions. In this study we do not focus on the effect that paramagnetic metallacrown compounds have on nuclei of a substrate molecule, but on the lanthanide induced shift (LIS) of the ligand protons of the metallacrown compounds. ^{1}H NMR spectra of $Ln(NO_3)_3[15\text{-}MC_{Cu^{II}N(L\text{–}Tyrha)}\text{-}5]$ containing different lanthanide(III) ions in the central cavity were recorded in [D$_4$]MeOH solutions to examine the influence of lanthanide(III) ions on the chemical shift. The values of ^{1}H NMR resonances of the metallacrowns formed with Ln^{3+} (Ln = La, Ce, Pr, Nd, Sm, Eu, Tb, Dy, Ho, Er, Tm) and Y^{3+} are shown in Figure 5.

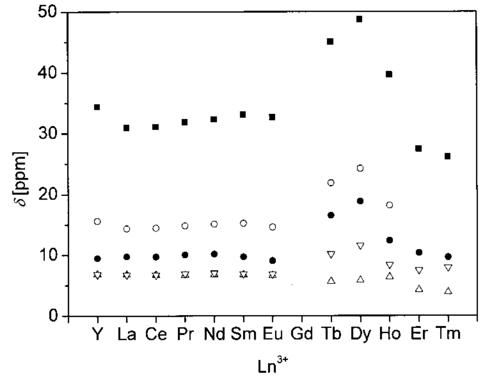


Figure 5. Proton NMR resonances for $Ln(NO_3)_3[15\text{-}MC_{Cu^{II}N(L\text{–}Tyrha)}\text{-}5]$ with different Ln^{3+} ions and Y^{3+} [α-protons (squares), β-protons (empty and filled circles), aromatic protons (triangles pointing upwards and downwards)].

The assignment of the peaks was made with the help of 2D-COSY experiments with $Nd(NO_3)_3[15\text{-}MC_{Cu^{II}N(L\text{–}Tyrha)}\text{-}5]$ (see below). The magnitude of the shift for the aromatic protons is less than that for the signals of the two β-protons and the α-proton. This is consistent with the fact that the proton in closest proximity to a paramagnetic centre is shifted farthest. $La(NO_3)_3[15\text{-}MC_{Cu^{II}N(L\text{–}Tyrha)}\text{-}5]$ has four distinct proton resonances [at ≈ 31 ppm (1H), ≈ 14 ppm (1H), ≈ 10 ppm (1H) and at 6.7 ppm (4H)] that are paramagnetically shifted due to the copper(II) ions in the metallacrown ring. The spectra of the 15-metallacrown-5 complexes with Y^{3+}and Ce^{3+} are similar to the spectrum of the complex with La^{3+}. For the Ln(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] complexes with Ln^{3+} = Pr^{3+}, Nd^{3+}, Sm^{3+} and Eu^{3+} the signals of the aromatic protons appear as two separate resonances. 2D-COSY experiments with Nd(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] showed a coupling between the resonances at ca. 15 ppm and ca. 10 ppm belonging to the two β-protons of the CH$_2$ group of the ligand. Interestingly, only one of these signals (the one at ca. 10 ppm) couples with the signal belonging to the α-proton (at ca. 32 ppm). From this, we infer that the β-protons of the CH$_2$ group are magnetically nonequivalent. The spectrum of Gd(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] exhibits excessive line broadening of the signals due to the paramagnetic gadolinium(III) ion and is not discussed here. For the Ln(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] complexes with Ln^{3+} = Tb^{3+}, Dy^{3+} and Ho^{3+} the paramagnetic shift is even larger. The signals belonging to the α- and the β-protons of the complex with Dy^{3+} experience the largest upfield shifts of the lanthanide series. One resonance signal of the aromatic protons of those three metallacrowns has shifted upfield, the other has shifted slightly downfield. 2D-COSY experiments with Dy(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] showed only one coupling signal between the resonances belonging to the aromatic protons. The integration values of the peak belonging to the α-proton (1H), the two peaks belonging to the β-protons (1H each) and the two signals belonging to the aromatic protons (2H each) are consistent with this assignment. However if we consider the spectra of the Ln(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] complexes with Ln = Er^{3+} and Tm^{3+} one proton resonance is missing. Again, 2D-COSY experiments with Er(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] showed only one coupling signal between the resonances belonging to the aromatic protons. Presumably, the missing resonance must belong to one β-proton.

Lanthanide-induced shifts (LIS) for nuclei of a ligand upon coordination arise by two possible mechanisms. These two mechanisms are the pseudocontact and contact shift.[23] The contact shift of a nucleus directly bound to a lanthanide(III) ion is usually very large, but decreases rapidly as the number of bonds between the lanthanide(III) ion and the nucleus under study increases. Because there are at least four bonds between the central lanthanide(III) ion of the metallacrown and the ligand protons, the contribution of the contact shift is negligible, and the pseudocontact shift contribution can be considered as the most important one. In addition, shifts resulting from the pseudocontact mechanism are highly predictable.[19] If we look at the shifts belonging to the α-proton of the different Ln(NO$_3$)$_3$[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] complexes, it can be seen that complexes with Ln = Pr, Nd, Sm, Eu, Tb, Dy and Ho have a similar effect as upfield shift reagents with a relative ordering of the shifts Dy > Tb > Ho > Sm > Eu > Nd > Pr, whereas complexes with erbium(III) and thulium(III) have a similar effect as downfield shift reagents. It is not surprising that the direction of the shifts and the relative ordering is nearly the same as the shifts of a substrate recorded in the presence of the shift reagent [Ln(dpm)$_3$], where the shifts also result mainly from the pseudocontact mechanism.[24]

Ligand Exchange in Ln$^{\mathrm{III}}$[15-MC-5] Complexes

Previous ligand exchange studies for the copper(II) based metallacrowns Cu[12-MC$_{\mathrm{Cu^{II}N(shi)}}$-4] and Cu[12-MC$_{\mathrm{Cu^{II}N(anha)}}$-4] showed the kinetic inertness towards ligand exchange in methanol.[16] On the other hand, vanadyl-containing metallacrown complexes [9-MC$_{\mathrm{(VO)N(shi)}}$-3] and [9-MC$_{\mathrm{(VO)N(nha)}}$-3], unable to sequester metal ions in their cavities, were found to be kinetically labile in methanol.[25]

We tested the dynamics of ligand exchange of α-aminohydroximate-based 15-metallacrown-5 complexes with central lanthanide(III) cavity ions in methanol. ^{1}H NMR was used to monitor the ligand exchange for 15-metallacrown-5 complexes containing L-Tyrha and L-Pheha aminohydroximate ligands. The equimolar solutions of Nd[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] (**1**) and Nd[15-MC$_{\mathrm{Cu^{II}N(L-Pheha)}}$-5] (**2**) were mixed and after 1 h the ^{1}H NMR spectrum of the mixture shows two sets of peaks appearing at the same ppm values as for the separate solutions of **1** and **2** (Figure 6). After 1 d at room temperature, new peaks appeared in the spectra. When this mixture was kept for 2 d at 37 °C, some of those new peaks were resolved into multiplets. A similar spectrum was obtained in an experiment where the ligands L-Tyrha and L-Pheha were mixed in the presence of copper(II) and neodymium(III). We were wondering whether some metallacrowns containing both L-Tyrha and L-Pheha ligands (mixed-ligand metallacrowns) were forming in solution after a long period of time or initially at the time of their synthesis with both L-Tyrha and L-Pheha in the reaction mixture. If this takes place, the environment of the protons of one ligand will depend on the adjacent ligand in the metallacrown ring and they will not be magnetically equivalent anymore. This can be an explanation why the peaks are resolved into multiplets.

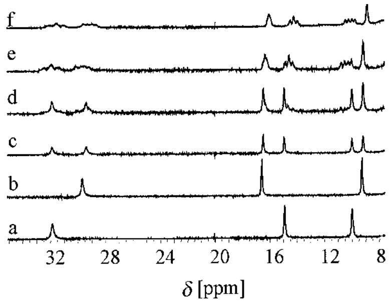


Figure 6. Proton NMR spectra of (a) Nd[15-MC$_{\mathrm{Cu^{II}N(L-Tyrha)}}$-5] (**1**), (b) Nd[15-MC$_{\mathrm{Cu^{II}N(L-Pheha)}}$-5] (**2**), (c) a 1:1 mixture of **1** and **2** after 1 h, (d) 1 d, (e) 2 d at 37 °C, (f) control experiment in which the metallacrown is synthesised from a [D$_4$]MeOH solution containing both L-Tyrha and L-Pheha, copper(II) and neodymium(III) in the reaction mixture.

In order to further understand the exchange process we used ESI-MS to probe the mass distribution of the complexes in solution. When initially both L-Tyrha and L-Pheha ligands (1:1) were allowed to react with the copper(II) and lanthanide(III) ions, a uniform distribution of ESI-MS peaks with values corresponding to different $\mathrm{Ln^{III}}$[15-$\mathrm{MC_{Cu^{II}N(L\text{–}Pheha)_{\mathit{x}}(L\text{–}Tyrha)_{\mathit{y}}}}$-5] complexes with the x/y ratios 5:0, 4:1, 3:2, 2:3, 1:4 and 0:5 was observed. This distribution points to the formation of mixed-ligand metallacrowns and means that there is no preference for one of the two ligands.

The copper(II) and lanthanide(III) metal ions can be viewed as templates around which the macrocyclic ring in 15-metallacrown-5 complexes is formed. However the reactants, the α-aminohydroximate ligands, are forming a ring only through coordination with the copper(II) ions and not through inter- or intramolecular reaction of the ligands between themselves. This could allow easy rearrangement and mixing of the different ligands since they are only coupled together through coordination bonds to the copper(II) ions. This is not surprising, as it is known that copper(II) complexes are among the most labile complexes of the d-block metal(II) ions.[26]

Conclusions

The easy conversion of $\mathrm{Cu^{II}}$[12-MC-4] to a $\mathrm{Ln^{III}}$[15-MC-5] is accomplished by addition of $\mathrm{Ln^{III}}$ ions in solution. Evidence for the presence of only two metallacrown species in the conversion process was obtained by UV/Vis and CD spectrophotometry. Complete disappearance of $\mathrm{Cu^{II}}$[12-MC-4] and formation of $\mathrm{Ln^{III}}$[15-MC-5] was proved by ESI-MS spectrometry and NMR spectroscopy. Due to the labile copper(II)–ligand bond, easy mixing of the different α-aminohydroxamate ligands can take place in solution, leading to a mixture of different metallacrown complexes.

Experimental Section

Reagents: L-Leucine methyl ester hydrochloride, D-leucine methyl ester hydrochloride, L-tyrosine methyl ester hydrochoride and L-phenylalanine methyl ester hydrochoride were obtained as pure products from Acros Organics. All other chemicals and solvents were reagent grade. L-Leucine hydroxamic acid, D-leucine hydroxamic acid, L-tyrosine hydroxamic acid and L-phenylalanine hydroxamic acid were prepared via their respective methyl esters as reported in ref.[27].

Equipment and Techniques: Positive- and negative-mode electrospray mass spectra (ESI-MS) were obtained with a Q-tof 2 (Micromass, Manchester UK) instrument. The samples were injected into the apparatus after dissolution in acetonitrile or in methanol.

UV/Vis absorption spectra were recorded with a Shimadzu UV-1601PC spectrophotometer using quartz cells of 1 cm path length. Circular dichroism spectra were measured with a JASCO J-810 spectropolarimeter using quartz cells of 2 cm path length. The spectra were collected in the 200–900 nm range. The solutions for the measurements were always freshly prepared before measurement. The concentration of the copper(II) and α-aminohydroxamic acid solutions was 2 mM. The pH of the solution was determined before and after each measurement.

^{1}H NMR spectra were recorded in deuterated water (D_2O) or methanol ([D_4]MeOH) solutions with a Bruker Avance 300 spectrometer operating at 300 MHz. In the titration experiment, to four 500-μL solutions in [D_4]MeOH containing equimolar amounts of $Cu(OAc)_2$ and L-leucine hydroxamic acid (0.1 M) were added 0.00, 0.33, 0.66 and 1.00 equiv. $Nd(NO_3)_3$. This was achieved by adding respectively 0, 20, 40 and 60 μL of a neodymium(III) nitrate solution in [D_4]MeOH (0.166 M) and adjusting the total volume of the NMR samples to 600 μL. Solutions of $Ln(NO_3)_3$[15-$\mathrm{MC_{Cu^{II}N(L\text{–}Tyrha)}}$-5] complexes with different lanthanide(III) ions and yttrium(III) were prepared by dissolving some crystals in [D_4]-MeOH. In the ligand-exchange experiments, two solutions containing metallacrown complexes (0.02 M in [D_4]MeOH) with different α-aminohydroxamic acids were mixed together. This NMR sample was also heated for 2 d at 37 °C in a water bath. In the control experiment, metallacrown was formed by adding neodymium(III) nitrate solution (240 μL, 0.166 M) in [D_4]MeOH to a solution of $Cu(OAc)_2$ (0.2 mmol) and both α-aminohydroxamic acids (0.1 mmol of each). Chemical shifts were referenced to sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) or to the solvent peak. Two-dimensional proton–proton correlation spectroscopy (2D COSY) was performed by applying the standard Bruker pulse sequence, and confirmed the assignment of the proton resonances.

Computational Details: The optimisation of the geometrical structures was accomplished by density-functional theory (DFT) as implemented in the Amsterdam Density Functional program package[28,29] ADF2002.03.[30] A triple zeta (TZP) basis set of Slater type orbitals was used. The frozen core approximation was employed, including all orbitals up to 2p for the copper atoms and 1s for the carbon, nitrogen and oxygen atoms. The local density functional of Vosko, Wilk and Nusair[31] was used, with the exchange and correlation corrections from Becke[32] and Perdew[33], respectively (BP86). The complexes were fully optimized without symmetry constraints.

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