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^{1}H- and ^{13}C-NMR as tools to study aluminium coordination chemistry—aqueous Al(III)–citrate complexes

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Contents

Abstract

Based on the use thermodynamic and solid state structure data, ^{1}H- and ^{13}C-NMR is a very useful tool to understand the conformational and dynamic behavior of complexes containing organic ligands in solution. In this paper we describe shortly the possibilities of the assignation of the spectra by means of modern NMR techniques. From the assigned spectra the scalar and dipolar couplings make it possible to determine the orientation of the ligand around the metal ion and the distances between hydrogen atoms in space. Aluminium–citrate complexes are reviewed as examples. It is shown that with the armory of correlation NMR spectroscopy unique insight can be obtained in the behavior of Al–citrate species even if oligomers are present in the solution.

Keywords: Al(III)–citrate complexes; Aluminium coordination; NMR spectroscopy; Solution structure

1. Introduction

NMR spectroscopy is increasingly used in solution coordination chemistry [1] in order to study thermodynamics and the dynamics of solution equilibria. For this purpose, beyond ^{1}H, ^{13}C and ^{31}P nuclei, mainly the

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^{19}F and the NMR active metal nuclei can be used successfully [2,3]. Usually NMR spectra are interpreted in the same way as any other type of spectra, namely: peak observation as an indicator of existent species, determination of speciation if other—more sensitive—methods are not available, or verification of the speciation determined by other methods. Impressive examples can be found in the literature supporting this enumeration, e.g. the application of combined NMR and pH-potentiometric method for equilibrium analysis, measuring nuclei from both the ligand and metal sides [4–6]. There is also a unique example from aluminium coordination chemistry where quantitative ^{27}Al-NMR was used as complementary source of information, like an ion selective electrode, to determine the stability constants of oligo-carboxylic acids by means of potentiometry [7–9].

The NMR spectra contain more, mainly structural and conformational information. This feature is elaborated for ^{1}H and ^{13}C nuclei in details, and is widely used in organic and metal-organic chemistry [10], but from time to time appears in the classical coordination chemistry [11–13]. The limited application may be due to the facts that: (i) the techniques and the interpretations, worked out for non-complexed organic molecules, often cannot be directly applied to the coordinated organic ligands; (ii) usually the organic ligands studied are small molecules, therefore clarifying conformational problems is less challenging; (iii) the metal ions are close to the observed proton and carbon nuclei of the ligands causing line broadening which reduces the possibility of resolving the valuable scalar couplings; even though the metals are not paramagnetic; (iv) the nuclear Overhauser enhancement (nOe) being a key for structure determination of large organic molecules is much weaker for small molecules and is often covered by exchange effects for the complexed ligands [14]. On the other hand, the frequent appearance of chemical exchange made coordination chemistry play an important pioneering role in the development of dynamic NMR [15–17].

For aluminium complexes the spectroscopic tools are not as readily available as in the case of transition metal complexes [18]. The lack of the unpaired electrons and the ligand field sensitive d electrons limits the possibility of the ESR and UV–vis spectroscopy. ^{27}Al-NMR was expected to bring valuable results, as it did indeed in many cases mainly for large ligands like proteins [2,18–20]. However, because of the unfavorable NMR properties of Al, being a quadrupolar nucleus and causing few 100 Hz line width values, the small and important differences in chemical shifts often escape from detection [18]. The application of nuclei other than proton, carbon and aluminium led to important information about the equilibrium, dynamic and even structural properties of aluminium complexes with inorganic ligands [21–23]. As a matter of fact NMR is the most important source of information for aluminium complexes in solution, moreover solid state NMR also found its territory beside X-ray diffraction [19,24,25].

In the case of small organic ligands the application of ^{1}H- and ^{13}C-NMR goes without saying, but it is not as trivial as for larger organic ligands. The assignment of the spectra is sometimes not very straightforward, and the situation becomes even more desperate when oligomers, like poly-nuclear aluminium complexes are investigated. For example, in the previous Aluminium Chemistry Issue of Coordination Chemistry Reviews it was explicitly stated that the '^{1}H spectra (of Al citrates) are not particularly informative' they consist "... many lines overlapping and forming second-order coupling patterns, (...) gives little information on the number of species formed other than there are multiple species". However, it was pointed out, that '^{13}C-NMR spectrum is far more useful' although "... resonance assignment remains a problem and thus a full analysis of this system has not been possible" [20]. The difficulties in assignment can be overcome by application of two-dimensional NMR techniques [26]. The assignment, of course, is not an end in itself but it is useful, because once the assignment is successful, information from the identified scalar (J_{HH} and J_{HC}) and dipolar couplings (nOe) can be used for structural and conformational analysis. In this paper we present our efforts, which have recently been done in this direction, using just the Al–citrate system as target [27]. The Al–citrates have been chosen as an intellectual challenge, although the importance of these complexes in bio-inorganic chemistry cannot be overestimated [7–9] [28–36]. The use of NMR capacity for solution structure analysis is important because the solid structure, determined by X-ray diffraction is sometimes not valid in solution. This was demonstrated recently by a combined use of NMR spectroscopy and X-ray crystallography. Kiss, Salifoglou and their coworkers, in order to compare the solid state and solution species, prepared single crystals of the different Al–citrate complexes and determined their structure. The crystals so obtained were dissolved and the kinetics of equilibration was followed by ^{1}H-, ^{13}C-NMR [37–39]. Summarizing the results of these and some earlier studies [27,40] three types of behavior can appear. (i) The dissolved complex decomposes and the thermodynamically stable species are formed. (ii) The dissolved complex remains partly the same as in solid state, but the structure is slightly different, e.g. fluxional motions equalize the differences between citrates around the aluminium. (iii) The dissolved complex remains the same as in solid state, what has been suspected in the case of $Al_3(OH)_3(H_{-1}Cit)_3^{4-}$ complex and we prove here in this paper [40].

2. Experimental

2.1. Chemicals

$AlCl_3$ solution was prepared from 99.9999% purity Al wire (Ajka, Hungary) as described elsewhere [21]. $Na_3Cit \cdot 5H_2O$, where $Cit = C_6H_5O_7^{3-}$ and H_3Cit, (Reanal p.a.) were used without further purification. $(Na)_4[Al_3(H_{-1}Cit)_3(OH)(H_2O)]NO_3 \cdot 5H_2O$ was prepared as described elsewhere [40,27]. For NMR study a weighted amount of this complex was used prepared at least 1 day before measurements. Hydrochloric acid solutions were made by diluting 37% HCl (Merck p.a.) solution and standardized against potassium hydrogen phthalate. Concentrated NaOH solutions were prepared by weight in D_2O and were used to adjust pH in Al–citrate samples. pH measurements were done following literature [41,27]. The other Al–citrate species were not prepared in solid state but rather the pH and total concentrations of the metal and the ligand, calculated from Öhman's data, were set up in the NMR tube and kept until the equilibrium reached [8,35]. Examples of the circumstances applied can be seen in the text of tables and figures. The speciation was checked on the basis of known NMR data shown in Tables 1–3. Because of the slow equlibration the samples were checked time to time for at least 1 month.

2.2. NMR techniques

^1H- and ^{13}C-NMR spectra were recorded on a Bruker AM 360 and a Bruker DRX 500 spectrometers using D_2O as solvent and internal deuterium lock at 22 °C. Chemical shifts were calibrated using the signal of DSS in D_2O. For H–H correlations the standard 2D COSY (COrrelation SpectroscopY) and phase sensitive NOESY Bruker programs were used. Typical repetition times were set as follows: 3 s for ^1H spectra, as long as 50 s for ^{13}C spectra, in order to let the carbon atoms having no attached protons relax. Proton carbon correlations were measured in direct (HETCOR, HETeronuclear CORrelation spectroscopy), or inverse detection mode (HMQC, HSQC HMBC), using gradient pulses. $^1J_{CH}$ correlations were detected by HETCOR, long-range $^2J_{CH}$, $^3J_{CH}$ correlations by gradient selected HMQC sequence [42]. The measurements were performed by the standard Bruker programs, provided with the spectrometers. Spectral analysis was done by the WinNMR© program of Bruker Co.

In the following section we give a short explanation of the NMR methods above mentioned:

COSY is the most frequently used two-dimensional NMR experiment, which shows correlations (cross peaks see Fig. 2) between scalar coupled protons. Usually the geminal ($^2J_{HH}$) and vicinal ($^3J_{HH}$) couplings are observed, but under special conditions $^4J_{HH}$ and $^5J_{HH}$ may be detected (vide infra) [43].

HETCOR is a two dimensional H–X method resulting in cross peaks between the detected X nuclei (usually ^{13}C, see Fig. 3) and protons which are at one bond distance from the X nuclei.

HSQC (Heteronuclear Single Quantum Coherence) is used for the same purpose as HETCOR but it is an inverse (proton) detection method. It is completed usually with gradient pulses in the z direction, which dramatically decreases the measuring time. The typical length of an experiment can be less then 1 h, depending of course on the concentration. By varying the delay times long-range $^2J_{CH}$, $^3J_{CH}$ couplings are detected (see Figs. 4 and 5) [42].

HMQC (Heteronuclear Multiple Quantum Coherence) is the simplest technique designed to correlate proton and carbon nuclei. HSQC is superior to HMQC in the case of crowded ^{13}C spectrum otherwise with regard to sensitivity these two sequences should be identical [42].

HMBC (Heteronuclear Multiple Bond Coherence) is a special pulse sequence for measuring long-range proton–carbon couplings, which suppresses correlations via $^1J_{CH}$ [42].

NOESY (Nuclear Overhauser Enhancement SpectroscopY) gives cross peaks caused by dipolar cross-

Table 1
NMR data for free citrate and $AlCit_2^{3-}$ at different pH values

Species	pH	^1H-NMR		^{13}C-NMR			
		δ (ppm)	$^2J_{HH}$ (Hz)	CH_2	C(q)	COO(t)	COO(c)
H_iCit (0.5 M)	4.2	2.83 2.70	15.7	42.8	77.1	179.4	182.8
Cit^{3-} (0.5 M)	10.4	2.62 2.46	15.4	48.6	78.0	182.2	184.8
$Al(Cit)_2^{3-}$; $c_{cit} = 1$ M, $c_{Al} = 0.25$ M	4.2	– [a]	–	ca. 45.6, (broad)	77.1	179.4	185.3

At pH 4.2 free citrate is present as $HCit^{2-}$ and H_2Cit^- in ratio 1:1, at pH 10.4 the deprotonated Cit^{3-} is present.
[a] Under these circumstances no acceptable spectrum was detected.

Table 2
NMR data for $Al_3(H_{-1}Cit)_3(OH)_4^{7-}$ (*Sy*) at pH 10.6

^{1}H-NMR		^{13}C-NMR							
δ (ppm)	$^2J_{HH}$ (Hz)	CH_2 (ppm)	$^1J_{CH}$ (Hz)	C(q) (ppm)	$^2J_{C,C,H}$ (Hz)	CO(t) (ppm)	$^2J_{COO,C,H}$ (Hz)	CO(c) (ppm)	$^3J_{COO,C,H}$ (Hz)
2.6	16.9	48.4	126.4	76.9	6.2	182.4	4.6	190.1	4.6 [a]
2.5					4.6		6.2		

$c_{cit} = 0.46$ M, $c_{Al} = 0.46$ M.
[a] Quintet.

relaxation between protons being in close spatial relationship. Measuring the rate of growth of the nuclear Overhauser effect (nOe) or the intensity of steady state nOe inter nuclear distances can be determined [14].

EXSY (EXchange SpectroscopY) gives cross peaks between signals belonging to nuclei, which are in chemical exchange by using the same pulse sequence as NOESY [44].

2.3. Interpretation of NMR data

Once the correct assignment is done, the most common NMR parameter is the chemical shift. Even though coordination does not occur through proton and carbon atoms, they bear important information about the coordination sites. Thus, in the spectrum of a complex the coordination site can be easily located, compared to the spectrum of the ligand, as due to deshielding effects a higher chemical shift (lower field) value is observed. This simple approximation is mainly valid for larger molecules, as in the case of small ligands all proton and carbon nuclei are close enough to the donor atoms. We shall see examples later that in the case of small molecules, when more donor atoms are present and they affect each other, the chemical shift may even have an opposite change. Also there are indications that the direction in the variation of chemical shift for ^{13}C nuclei is not as straightforward as in the case of the protons.

The other important parameter is the scalar coupling. The geminal ($^2J_{HH}$) proton–proton couplings have a value between −12 and −17 Hz. For the $R–C^{\alpha}H_2–COO^-$ fragment this value depends on the torsion angle between the projection of the C^{α}–R bond (fixed) and the projection in the plane of the C–O bond (rotating). A schematic view of two limiting conformations is shown in Scheme 1, together with the sense of rotation.

If the conformation is close to (a) then the coupling constant is about −17––19 Hz, if it is close to (b) then $^2J_{HH}$ is about −11––13 Hz. For the free citrate the value is −15.2––15.9 Hz depending on the pH, thus indicating an average of 30° between the C–R and the COO^- plane [45–47]. In the later considerations we use the absolute value of the coupling constants, since generally we do not confirm the sign. The $^2J_{CH}$ couplings are usually small, about 2–6 Hz, except in the case when they act through the lone pair electron of the CO group [48].

The most important structural information is obtained from the $^3J_{HH}$ and $^3J_{CH}$ scalar couplings by using the semi-empirical Karplus-type equations [49]:

$$^3J = A\cos^2\phi + B\cos\phi + C$$

where the constants A, B, C can be determined both experimentally and theoretically for a group of similar compounds [43,48]. The definition of the ϕ angle and the verbal statements used are illustrated in Scheme 2.

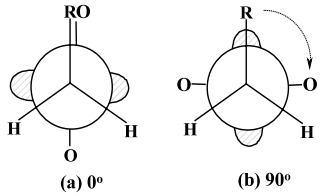
Aydin and Günther, taking into account the effects of different substituent, derived a Karplus-type equation of the form: $^3J_{CH} = 4.50 - 0.87\cos\phi + 4.03\cos 2\phi$. However, in most cases only approximate positions can be predicted, i.e. close to *gauche* when the torsion angle is about 60°, close to *trans* when it is about 180° or close to *eclipsed* when it is about 0°. It is shown as (a, b and c) in Scheme 2, respectively.

Higher order coupling is usually observed in the case of conjugate systems. The values of $^4J_{HH}$ can be as large as 2.5 Hz observed when the protons occupy the so called W position at the two ends of three sp^3 carbons: H–C–C–C–H [43,50]. Even for small deviations from the plane of the five nuclei, the coupling constant decreases to about 1 Hz. This is a hardly detectable value in the 1D ^{1}H-NMR spectrum, particularly if a quadrupolar ion is present causing some line broadening. Still, this coupling may come to light in the finely tuned 2D COSY experiments.

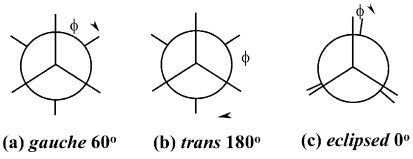
The third important element for structural elucidation is the nOe. This is the dipolar coupling between two nuclei, which relax each other by opening double or zero quantum transitions for spin-lattice relaxation [14]. The efficiency of this 'cross-relaxation' depends on the internuclear distance and on the rotational correlation time (τ_c) of the molecular motion. The nOe is not too large for small molecules and sometimes is covered by chemical exchange in the NOESY spectrum. Fortunately, the cross peaks origin from nOe usually have opposite sign for small molecules than those which arise due to exchange, therefore the origin can be distinguished when they do not appear parallel [44]. Another

Table 3
NMR data for $Al_3(H_{-1}Cit)_3OH^-(H_2O)^{4-}$, 0.5 M (dissolved sodium salt), pH 7.2

CH_2/citrate	^{1}H-NMR			^{13}C-NMR								
	δ (ppm)	$^2J_{HH}$ (Hz)	$^4J_{HH}$ (Hz)	δ_{CH2} (ppm)	$^1J_{C,H}$ (Hz)	$^3J_{C,C,H}$ (Hz)	δ(q) (ppm)	$^2J_{C,C,H}$ (Hz)	δ(t) (ppm)	$^2J_{COO,C,H}$ (Hz)	δ(c) (ppm)	$^3J_{COO,C,H}$ (Hz)
1/**I**	2.84 2.60	17.03	ca. 2	46.2	124.9	6.2 7.7	75.9	4.6	180.4	6.2	180.7	6.2
2/**I**	2.82 2.64	17.64	ca. 2	44.3	131.0	6.2 7.7	75.9	4.6	185.2	3.1	180.7	6.2
3/**II**	2.72 2.57	17.85	–	47.5	127.9	–	78.2	6.2	180.4	6.2	185.4	7.7 6.2–7.7
4/**II**	2.70 2.62	16.41	–	45.4	131.0	–	78.2	6.2	183.3	6.2	185.4	7.7 6.2–7.7
5/**III**	2.66 2.58	14.56	–	48.8	131.5	–	78.0	ca. 4.6	179.7	6.2	180.9	ca. 3.1
6/**III**	2.76	–	–	48.4	131.0	–	78.0	ca. 4.6	180.1	6.2	180.9	ca. 3.1



Scheme 1.



Scheme 2.

disturbing factor can be the molecular weight, as it affects the τ_c parameter. At molecular weight about 1000 g mol^{-1} cross peak intensity passes through zero, and makes this method hardly useful [14].

3. ^{1}H- and ^{13}C-NMR of Al(III)–citrate system

3.1. Speciation of Al^{3+}–citrate system from the NMR point of view

The known speciation in the Al–citrate system is a result of long term efforts [8,32,34,35,37]. Equilibration is time dependent, such that earlier studies derived less precise stability constants for certain species. The ongoing slow processes, which make the difficulties, are the hydrolysis and the oligomerization. Throughout this study we used the stability constants determined by Öhman et al. [8,35]. We found that the systems could be described satisfactorily with these values, even at high concentrations which were very important for NMR studies at high concentrations.

The résumé of equilibrium studies showed that several different species are formed, but, depending on the pH and concentrations, three complexes are dominant. Of course, in dilute solutions other species show up or even become dominant but we kept the condition so that only these three complexes were present in measurable amount in our samples. Applying ligand excess (at ca. pH 4) a mononuclear bis-coordinated species is formed: $Al(Cit)_2^{3-}$. The correct formula may be written as $AlH_2(H_{-1}Cit)_2^{3-}$ at ca. pH 4, indicating the deprotonation of OH donor group but protonation of two carboxylates. The deprotonated forms of this bis-ligand complex are the first mononuclear aluminium–citrate complexes, characterized by X-ray in solid state [38]. Also the ^{1}H- and ^{13}C-NMR spectra of $H_xAl(H_{-1}Cit)_2^{(5-x)-}$ in aqueous solution have already been described [27,38]. Dissolving this solid a slow decomposition takes place and the equilibrium solution finally formed is the same as that the Öhman model predicts. The intermediate species, appeared during the dissolution and equilibration, have recently been clarified by combined ^{1}H- and ^{13}C-NMR and X-ray diffraction methods [39].

At lower ligand excess very stable trinuclear complexes are formed. One of them, $Al_3(H_{-1}Cit)_3(OH)(H_2O)^{4-}$, was prepared in solid form, shows a highly non-symmetric structure by X-ray crystallography [40]. A similar situation is suspected in solution looking at the number of peaks and the observed chemical shifts of the ^{13}C-NMR spectrum. However, deeper analysis of this NMR observation has not appeared yet in the written literature, only some indications have been reported [20,40].

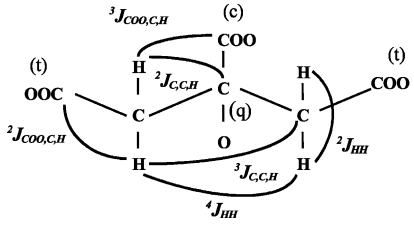
By increasing the pH, another trinuclear species, $Al_3(H_{-1}Cit)_3(OH)_4^{7-}$, becomes stable with a highly symmetric tentative structure, C_{3v} [8,35]. Precise potentiometric studies showed the degree of oligomerization and the composition of this complex. The structure was predicted on the basis chemical evidences, but so far no single crystal could be prepared for X-ray analysis.

3.2. ^{1}H- and ^{13}C-NMR of $Al(Cit)_2^{3-}$

It was already found that the central and one terminal carboxylate (see Scheme 3 for names and notations used throughout this paper) group coordinate in the solid state, while the other terminal carboxylate remains non-coordinated probably due to sterical reasons [38].

However, in solution the situation is different. The ^{1}H- and ^{13}C-NMR data collected for the free citrate and $Al(Cit)_2^{3-}$ species are shown in Table 1.

It can be seen clearly from Table 1, that both the coordinated species and free citrate show very simple spectra, i.e. one ^{13}C-NMR signal for each of the methylene, quaterner and central carboxyl groups and for the two terminal carboxyl carbons. The assignment was made on the basis of the chemical shifts and using the integration of ^{13}C-NMR spectra recorded in inverse gated decoupling (quantitative) mode. This spectral result of $Al(Cit)_2^{3-}$ indicates the same chemical environment *on average* for all $-CH_2-$ groups in the complex. Another feature of both ^{1}H and ^{13}C spectra is that the peaks of the free ligand show their natural line width,



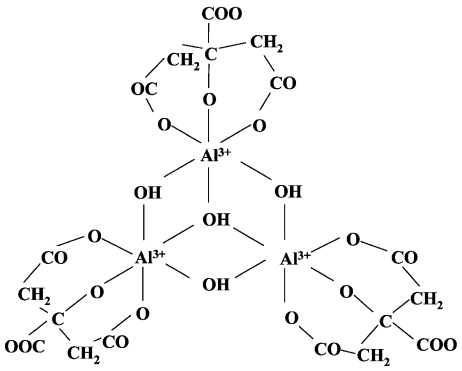
Scheme 3.

while those of $Al(Cit)_2^{3-}$ have remarkable line broadening when both species are present, indicating an exchange process without involving the free ligand. These spectra contain very little information about structure. We can state that if the X-ray structure of the solid is valid in solution, then this complex is a fluxional molecule, as the solid structure shows non-equivalence for the $-CH_2-$ and terminal carboxylic groups, while the NMR spectra show the opposite [38]. In accordance with earlier observation an *intra molecular* dynamic process may occur permuting the positions of $-CH_2-COO^-$ arms of the citrate ligand [27]. This is a typical example of the case when NMR spectra contain no structural information other than that, the coordination happened, as line broadening makes even the observation of the ^{1}H-NMR spectrum for $Al(Cit)_2^{3-}$ impossible at this pH and at room temperature. According to the expected deshielding the ^{1}H chemical shift of the ligand decreases by deprotonation. The ^{13}C chemical shift of the carboxyl groups in free citrate decreases with increasing degree of protonation (high field shift). However, the effect of the coordination is not so clear, because the coordinated central carboxyl (X-ray) has shifted downfield while the other carbons have shifted to high field (Table 1). Another explanation is possible, namely coordination through the two terminal carboxylate in solution but this is not probable, because there is no good reason for the change of coordination mode by dissolution.

3.3. ^{1}H- and ^{13}C-NMR of $Al_3(H_{-1}Cit)_3(OH)_4^{7-}$ (*Sy*)

According to the equilibrium studies this complex is exclusively formed at pH > 8 and at low ligand excess, very close to the 1:1 citrate to Al ratio. However, at higher citrate excess it is still dominant in a wide pH range co-existing with the free ligand. Observed NMR data are collected in Table 2.

Analyzing these data one can observe that the NMR spectra of *Sy* show the same pattern as those of the free ligand, therefore, we can state that all three citrates are equivalent and have the same coordination mode. This means that this oligomer is very symmetric. The detailed dynamic analysis [27] showed that, similarly to $Al(Cit)_2^{3-}$, the *Sy* complex is also fluxional. At lower temperature the fluxional motion can be slowed down resulting in two AB doublets in the ^{1}H-NMR spectrum indicating that two chemical environments exist for CH_2 groups. Unfortunately, no solid state structure is available, therefore, there is no possibility to find similarities or differences with that, or to have at least some kind of starting point for the interpretation of this simple solution spectrum. Öhman-based on the hydrolytic behavior of the Al^{3+} aqua ion-proposed a structure having C_{3v} symmetry [8]. The skeleton of this cluster is an OH bridged Al trimer, and each Al coordinates one

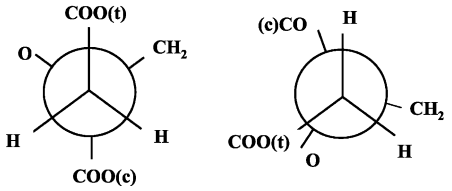


Scheme 4.

citrate but the ligands do not have bridging positions, as seen in Scheme 4.

This tentative structure at least is not in contradiction with the NMR data so far. The ^{13}C-NMR peak of the central carboxylic group has a remarkable downfield shift indicating deshielding compared to the non-protonated free ligand. This may be attributed to coordination with the Al^{3+}. This seems to be in clear contradiction with the structure in Scheme 4. However, the chemical shift is not always the best indication of the coordination in the case of small ligands. We have briefly discussed above that the chemical shift of central COO^- somehow behaves in an opposite way, i.e. the chemical shift *increases* with deprotonation (low field shift) [51,52]. In this special case probably the whole $-O-C(q)-COO^-$ unit determines the extent of deshielding. The $^3J_{COO,C,H} = 4.6$ Hz indicates an averaged position between the *gauche* (ca. 60°) and *trans* (ca. 180°) or *eclipsed* (ca. 0°) state of the C–H and C(q)–C(c) bonds. Building the model of Scheme 4 it turns out that the two CH_2 groups of one citrate ligand have different conformations. One shows an almost perfect *gauche* position while the other points about 20 and 140 from the C(q)–C(c) bond illustrated on Scheme 5.

Since these two positions exchange rapidly at room temperature [27] an average coupling constant of 4.6 Hz from the four protons to C(c)O is not against the Karplus formula. Another valuable $^3J_{C,C,H}$ could not be determined because of the exchange broadening of the peaks of CH_2 carbons, however this contains information about the type of fluxional motion [27].



Scheme 5.

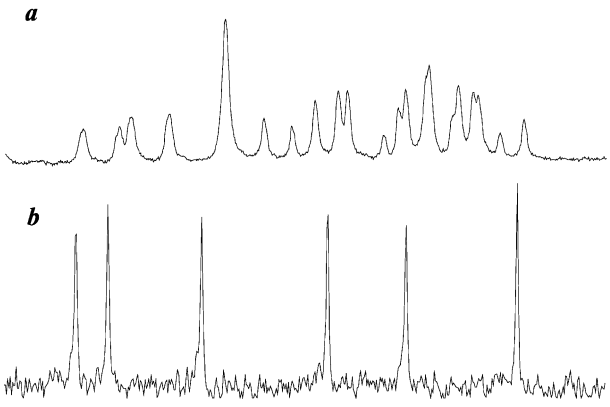
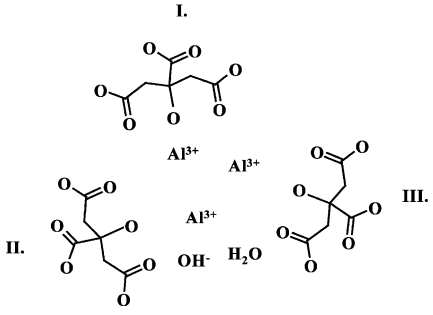


Fig. 1. (a) ^{1}H-NMR (500 MHz) spectrum of the *As* complex with $c_{Al} = c_{cit} = 0.5$ M at pH 7.2; and (b) $-CH_2-$ region of the ^{13}C-NMR (125 MHz) inverse gated spectrum of the same sample measured at 295 K.

3.4. ^{1}H- and ^{13}C-NMR of $Al_3(H_{-1}cit)_3OH(H_2O)^{4-}$ (*As*)

This trinuclear species is present in the $4 < pH < 9$ range under our experimental conditions. Preparing a sample containing only the $Al_3(H_{-1}Cit)_3(OH)^{4-}$ complex, its ^{1}H- and ^{13}C-NMR spectra were recorded (Fig. 1). (The spectra were recorded on a sample described in the title of Table 3. However, in order to check the identity and the reproducibility other samples were also made with different concentrations but the same pH.) The proton spectrum appears as a rather complicated pattern with several overlapping signals, in this way integration gives no help for assignment. The ^{13}C-NMR spectrum gives as many signals as the number of carbon atoms are in the cluster [40]. Remembering the previous sections we cannot state that the simpler NMR spectrum we have the better the situation we are in. On the contrary, if the NMR spectrum is rich in detail there will be more chance to extract structural information from that. In order to extract this information the assignment of peaks has to be done. It is followed by the determination of scalar and dipolar couplings.

Before starting the assignment a schematic picture is drawn to refer easily to the respective protons and



Scheme 6.

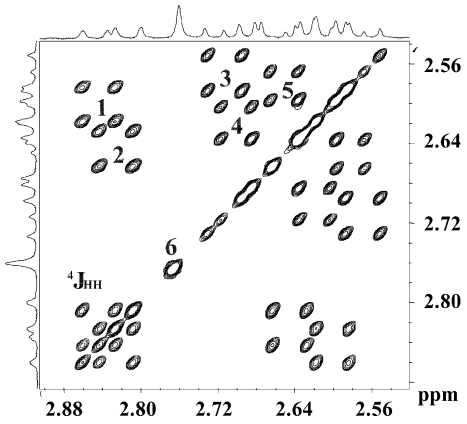


Fig. 2. 500 MHz COSY 45 spectrum of the *As* complex. The numbers identify the AB doublet pairs.

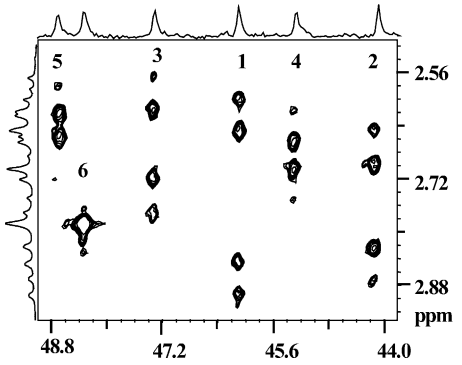


Fig. 3. ^{13}C detected HETCOR (360 MHz) spectrum of the *As* complex. The numbers originate from the COSY spectrum in Fig. 2.

carbons of the three ligands around the metals, see Scheme 6.

Since the ^{1}H-NMR spectrum of the free ligand is a pair of AB doublets with the geminal $^{2}J_{HH}$ coupling constant value varying between 14 and 15.5 Hz depending on pH, we could expect the same pattern for each of the coordinated ligands in the *As* complex. Thus, in the most complicated case six pairs of AB type doublets, i.e. 24 signals, can be observed.

The measured COSY45, see Fig. 2, shows five pairs of doublets and one singlet signal. They are numbered 1, 2, 3, 4, 5, 6. To correlate these proton signals with the carbon atoms to which they are attached, a HETCOR experiment was run in the CH_2 region (Fig. 3).

From the COSY45 spectrum one can suppose that each proton of the five CH_2, marked with 1, 2, 3, 4, 5, have different chemical environments. While the sixth CH_2, 6, does not show any coupling pattern, probably as a consequence of local symmetry or of some dynamic process. Another important feature of this spectrum is the appearance of extra cross peaks between 2.80 and 2.88 ppm marking connectivities between protons 1 and 2 being situated on different $-CH_2-$ groups. As this is possible only if they are on the same citrate, doublets

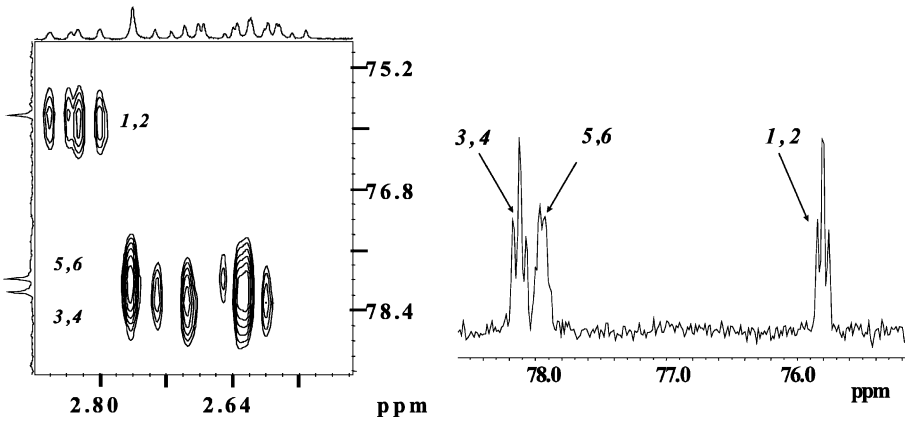


Fig. 4. Gradient pulse, inverse (^{1}H) detected, long range HMBC spectra (500 MHz), with regulated delay D6 = 50 ms, corresponding to $^nJ_{CH} = 10$ Hz of the *As* complex, zoomed for quaternary carbon region (left). The proton coupled ^{13}C-NMR of the same region.

denoted with 1 and 2 can be assigned to ligand **I**. In order to continue the tracing of the complete framework of the *As* complex we recorded long range heteronuclear correlation spectra. The quaternary carbon region is shown in Fig. 4.

As there are three C(q) carbons in the molecule, each of them has to point out the protons found at two-bond distance on both neighboring CH_2 groups. Using this reasoning, in accordance with our previous statement protons 1 and 2 are on the same citrate, **I**. It turns out that protons 3 and 4 belong to the same citrate which we denoted **II**, and finally, protons 5 and 6 are on citrate marked with **III**. At this point of the work we already know which protons belong to which citrate. Note, that not all protons give cross peaks to the quaternary carbons, but only one on each CH_2 group indicating that $^2J_{CH}$(q) must be geometry dependent.

In this complex vicinal proton–proton coupling unfortunately does not exist (these are very valuable for conformational analysis [43]) therefore, the multiple bond coupling constants $^4J_{HH}$ and $^3J_{HC}$ can help to find the conformation of the coordinated ligands [43,48]. To be able to determine these coupling constants, the assignment of the carbonyl region of the ^{13}C-NMR spectrum has to be done. This is solved by investigation

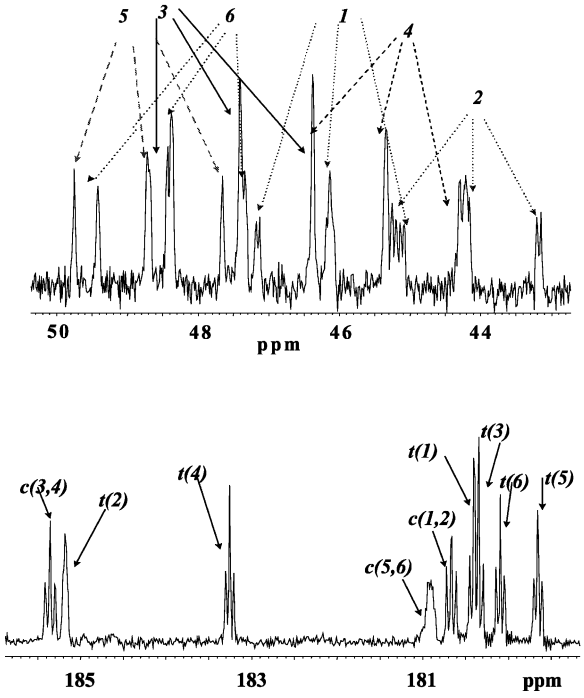


Fig. 6. Proton coupled ^{13}C-NMR (125 MHz) spectrum of a 0.8 M *As* solution at pH 7.3; $-CH_2-$ region (above), and –COO region (below) indicating the assignment.

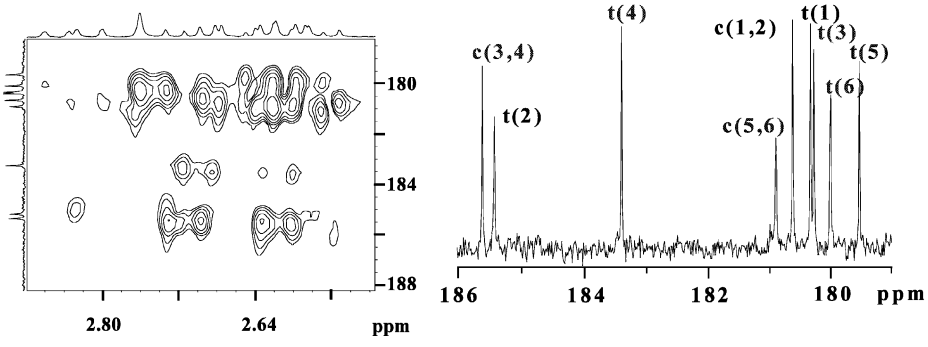


Fig. 5. Gradient pulse, inverse (^{1}H) detected long range HMBC spectra (500 MHz) with regulated delay D6 = 200 ms, corresponding to $^nJ_{CH} = 2.5$ Hz of the *As* complex, zoomed for carboxyl region (left), ^{13}C (125 MHz) power gated spectrum of the same sample (right).

of the carbonyl range of recorded long range HMBC spectrum, as illustrated in Fig. 5. The carbonyls are denoted with t if they are terminal and with c if they are central. The numbers indicate the closest CH_2 groups (e.g. c(3, 4) means central carbonyl between the $C(2)H_2$ and $C(3)H_2$, while t(3) refers to terminal carbonyl in the immediate neighborhood of $C(3)H_2$) and chemical shift data are collected in Table 3.

At this point the remaining experiment is the proton coupled ^{13}C-NMR spectrum, in order to find $^{n}J_{HC}$ coupling constants, which hopefully carry the necessary structural information. The fragments of these spectra are shown in Figs. 4 and 6, while the measured coupling constants appear in Table 3.

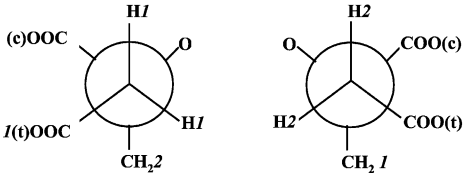
Trying to obtain dipolar coupling data 2D NOESY spectra were recorded with different mixing times. Weak anti-phase cross peaks were found between the geminal protons, which are indeed close to each other, but no other dipolar connections could be established. Beyond these cross peaks only the so called auto-peaks showed up, i.e. cross peaks between the side bands of AB doublet pairs. The $Al_3(H_{-1}Cit)_3(OH)^{4-}$ complex is not an ideal subject for NOESY study because it is probably nOe silent, as the rotation correlation time falls into the range where the nOe intensities cross zero. We have made efforts to escape from this range by heating the sample in order to accelerate the tumbling motion of the molecule but without success.

The amount of information collected from Table 3 is enough to describe the possible conformation of each citrate ligand in solution and to make a comparison with the solid X-ray structure.

4. Characterization of $Al_3(H_{-1}Cit)_3(OH)(H_2O)^{4-}$ in solution

4.1. Citrate *I*

The appearance of the $^{4}J_{HH}$ coupling indicates that one H–C–C–C–H unit is in plane being W shaped. Both geminal coupling constants (ca. 17 and ca. 18 Hz) suggest that the $C(H_2)$–C(q) bond lies in an angle of about ±20–40 and ±30–50° from the COO^- plane (refer to Scheme 1). Both C(1) and C(2) carbons are doublets from $^{3}J_{C,C,H}$ coupling of one of the protons sitting on the opposite CH_2 group, e.g. in this way: H–C(2)–C–C(1). The values are 6.2 and 7.2 Hz which



Scheme 7.

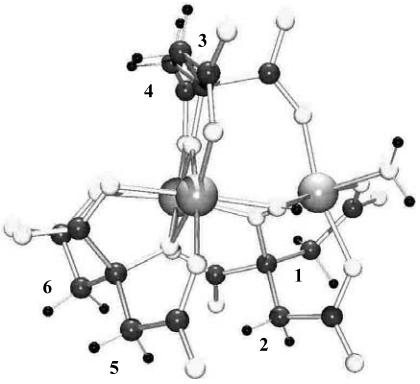


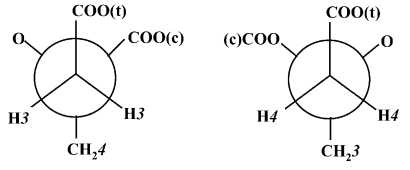
Fig. 7. A view of the solid state structure of $Al_3(H_{-1}Cit)_3(OH)(H_2O)^{4-}$ using X-ray data from the literature [40].

correspond to approximate *trans* position (about 180°) of one hydrogen for each carbon drawn on Scheme 7 (this shows the Newman projection of the ligand from both ends). The other protons are in a *gauche* position, this is probably the reason why the coupling constants could not be observed.

The central carbonyl of this citrate **I** seems to be a triplet, with coupling constant 6.2 Hz. Modeling these observations, it is easy to find that the only possible conformation satisfying these requirements is the one drawn on Scheme 7. According to Scheme 7, the ^{13}C-NMR–COO(c) signal has to split into a doublet due to the *trans* H1 proton, and into another doublet because of the *trans* H2 proton. As the coupling constant values ($^{3}J_{COO,C,H}$) are almost the same a pseudo triplet has to be formed, as is indeed observed. Turning to the solid structure in Fig. 7 careful investigation results in finding *one and only one* coordinated citrate with this steric arrangement.

4.2. Citrate *II*

In the absence of observable $^{3}J_{H,C,C}$ coupling on the $C(3)H_2$ and $C(4)H_2$ carbon atoms an arrangement of approximate *gauche* conformation of 3,4 methylene H atoms is supposed, as this orientation yields a hardly detectable vicinal coupling constant <2 Hz. In this case with respect to the –COO(c) group H3 atoms will possess a *gauche* and H4 atoms a *trans* position. This will end up in $^{3}J_{COO,C,H}$ values ca. 7, and <2 Hz for H3; and in <2 and ca. 7 Hz for H4. Following the argument presented for citrate **I** a pseudo-triplet is expected for –COO(c) (3,4). This pattern appears indeed at 185.39



Scheme 8.

ppm (see Fig. 6). The orientation of the C(3)–C(q) bond to the plane of $C(t3)OO^-$ is almost *eclipsed* while that of C(4)–C(q) is about 30° off the plane of $C(t4)OO^-$ on the basis of the geminal coupling constants. Scheme 8 (this shows the Newman projection of the ligand from both ends) represents the detected conformations, and we can find this arrangement for another citrate in the solid structure as shown in Fig. 7.

4.3. Citrate *III*

The situation is analogous with the one met at citrate **II**, as no $^3J_{H,C,C}$ constants are detected. The difference is the appearance of two almost equivalent H atoms CH_2 6. This causes a multiple splitting of –COO(c), first a triplet, than because of one of the H5 protons each resonance will split into a doublet. This pattern appears at 180.95 ppm. (see Fig. 6, right). The geminal $^2J_{HH}$ coupling for H5 is smaller than those values found for 1, 2, 3, 4. Therefore, the orientation of the C(5)–C(q) bond to the plane of $C(t5)OO^-$ is closer to the perpendicular on the basis of the geminal coupling constants. By now it is not surprising to identify the third citrate form in the solid having this conformation.

Studying the model built on the basis of X-ray data, shown in Fig. 7, we concluded that our statements concerning the orientation the C(n)–C(q) bonds to the neighborhood carboxylates are very approximate. Therefore, detailed investigations on the effect of coordination on the geminal HH coupling may result in more precise data and this will serve coordination chemistry well, as the $-CH_2COO^-$ molecular unit very often appears in small, important ligands.

Comparative investigation of the ^{13}C chemical shifts of the central carbonyls in the three complexes studied confirms that one has to be very careful to use these data. In our early thinking we were convinced, that the three separated COO^- signals between 183 and 186 ppm (Fig. 6) belong to the central carboxylates just on the basis of the difference in chemical shifts but it turned out that this is not the case (see above). After the identification of the COO^-(c) peaks of *As* we can see from Table 3 that there are two types of central carboxylates, one has a peak at 185.7 ppm while the other two have peaks at around 181 ppm. In the $Al(Cit)_2^{3-}$ we find the central carboxylates at 185.3 ppm. It might be straightforward that the coordination mode is the same for COO^-(c) donor groups with similar chemical shifts. However, as seen in Fig. 7 the coordination mode of citrate **III** is similiar to the citrates in $Al(Cit)_2^{3-}$ but their COO^-(c) chemical shifts are different (Fig. 7, Tables 1 and 3). These observations support our statement above that the deshielding effects for small ligands upon coordination are complicated processes and should be assigned with extreme cautions. On the other hand, it would be a great mistake to disregard the information from the chemical shifts. In our system, for example, when the $Al_3(H_1Cit)_3OH(H_2O)^{4-}$ transforms to $Al_3(H_{-1}Cit)_3(OH)_4^{7-}$ the COO^-(c) chemical shift increases the as high as 190 ppm. This indicates that in this reaction the central carboxylate group experience the largest change, which is in accordance with the structures discussed above.

5. Conclusion and prospects

The objective of this work was to show the application of ^1H- and ^{13}C-NMR to characterize metal complexes containing small organic ligands. The Al–citrate system is a typical example in many senses. On one hand it shows almost all effects that the coordination chemist suffers from when using this spectroscopy: i.e. broad lines, overlapping complicated spectra or indeed too simple spectra etc. On the other hand there is at least one species, which could be characterized in detail and used as a prototype for further conformational analysis of other systems.

Summarizing our results, the $Al_3(H_{-1}Cit)_3OH(H_2O)^{4-}$ complex has a similar structure as in the solid form. This is not surprising because dynamic studies proves it to be a very rigid non-fluxional species with resistance to ligand exchange [27]. Examining all the possibilities offered by ^1H- and ^{13}C-NMR a certain solution structure has been suggested. However, we could not perform precise calculations for the conformations because of the lack of valid parameters in the Karplus-type equations describing the scalar couplings in coordinated small ligands. There can be mass relationships between scalar coupling and conformational parameters, taking into account diverse substituent and ring effects, but for quantitative reasons they are operative only for the organic molecules, which have been subject to a huge amount of investigation of this kind. Therefore, in applying Karplus-type equations to obtain dihedral angle values for coordinated ligands, one has to be exceptionally careful because a large amount of test data is needed to support the relationship. In this sense, the existence of complexes which are expected to show the same solution and solid state structure provide the possibility to elaborate application of the power of NMR correlation spectroscopy for equilibrium coordination chemistry in general.

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