DALTON
FULL PAPER

Al(III)-binding properties of iminodiacetic acid, nitrilotriacetic acid and their mixed carboxylic–phosphonic derivatives†

M. Kilyén,[a] A. Lakatos,[a] R. Latajka,[b] I. Labádi,[c] A. Salifoglou,*[d] C. P. Raptopoulou,[e] H. Kozlowski[f] and T. Kiss*[a,c]

[a] *Biocoordinaton Chemistry Research Group of the Hungarian Academy of Sciences, University of Szeged, PO Box 440, H-6701 Szeged, Hungary. E-mail: tkiss@chem.u-szeged.hu*
[b] *Institute of Organic Chemistry, Biochemistry and Biotechnology, Wroclaw University of Technology, Wybrzeze Wyspiankiego 27, 50-370 Wroclaw, Poland*
[c] *Department of Inorganic and Analytical Chemistry, University of Szeged, PO Box 440, H-6701 Szeged, Hungary*
[d] *Department of Chemistry, University of Crete, Heraklion 71409, Greece*
[e] *Institute of Materials Science, NRCPS "Demokritos", Aghia Paraskevi 15310, Attiki, Greece*
[f] *Faculty of Chemistry, University of Wroclaw, F. Joliot-Curie 14, 50-383 Wroclaw, Poland*

Received 2nd April 2002, Accepted 19th July 2002
First published as an Advance Article on the web 22nd August 2002

Potentiometric, ^1H, ^{31}P NMR spectroscopic and X-ray studies were carried out to investigate the complex formation of Al(III) with iminodiacetic acid (IDA), nitrilotriacetic acid (NTA), their mixed carboxylic–phosphonic and purely phosphonic derivatives. The stability constants of the complexes formed were determined at 25 °C and at 0.2 mol dm^{-3} ionic strength (KCl). It was found that substitution of CO_2^- by PO_3^{2-} increases the overall stability of the complexes, due to the higher basicity of the phosphonic groups. However, the higher spatial requirement of the phosphonic moiety and the greater electrostatic repulsion between the dinegatively charged PO_3^{2-} moieties overcompensate this effect, resulting in a somewhat weaker metal binding capacity for the phosphonic derivatives. According to the ^1H NMR spectra of Al(III) complexes of IDA, complex formation renders the two protons of each CH_2 group inequivalent, while the CH_2 groups of NTA and its derivatives remain chemically and magnetically equivalent in their Al(III) complexes. As no symmetrical arrangements of the donor atoms in their Al(III) complexes can be expected with most of the ligands, the rate of intramolecular rearrangement motions of the binding functional groups seems to be different for the IDA and the NTA derivatives.

Introduction

Aminopolycarboxylates and their mixed carboxylic–phosphonic derivatives are widely used for various purposes, covering fields from analytical chemistry to medicine. Many of the aminophosphonic acids display diverse and useful biological properties. They find applications, for instance, in medicine as antibacterial agents, plant growth regulators, neuromodulators, and NMR imaging agents; their anticancer properties are also known.[1–10] Being structural analogues of amino acids, they can act as their antagonists and compete with their carboxylic counterparts for the metal ions or the active sites of enzymes or other cellular receptors.[1] Containing strong metal binding donor groups, aminophosphonates are able to chelate essential or toxic metal ions. The neurotoxic Al(III), for example, forms strong complexes with aminophosphonates, and thus the latter can be used potentially for the removal of the metal ion Al(III) in the case of overload (chelation therapy). The complex forming properties of aminopolycarboxylates and some of their phosphonic derivatives with divalent and trivalent metal ions have been reported previously.[11–23] Single crystals of mono and bis Al(III) complexes of imino-diacetate[24,25] and nitrilotriacetate[26] have also been isolated and characterized by X-ray diffraction. The studies show that Al(III) and IDA form an octahedral mononuclear anionic complex[24] and a dinuclear complex,[25] the latter representing a relatively rare example of a crystallographically characterized di-(μ-hydroxo) bridging Al(III) dimer. Al(III) and NTA form simple neutral distorted octahedral species and a dihydroxo-bridged dinuclear complex.[26] In both structures, NTA behaves as a tetradentate non-bridging ligand.

In this paper, the Al(III)-binding properties of iminodiacetate (IDA), nitrilotriacetate (NTA) and their phosphonic derivatives, such as *N*-(phosphonomethyl) glycine (IDAP), imino-bis(methylenephosphonic acid) (IDA2P) as well as *N*-(phosphonomethyl) iminodiacetic acid (NTAP), *N*,*N*-bis(phosphonomethyl)glycine (NTA2P) and nitrilo-tris(methylene-phosphonic acid) (NTA3P) have been investigated using potentiometry and multinuclear NMR spectroscopy, in order to (i) describe their speciation with this toxic metal ion and (ii) determine the most probable binding modes in their complexes formed. Solid state isolation and crystallographic characterization of the bis complex Al(III)–IDA are also reported.

Experimental

Reagents

Most of the ligands were Fluka products of puriss quality and were used without further purification. IDA2P was a gift of Prof. J. Soroka (Technical University of Wroclaw, Poland). The aluminium(III) stock solution was prepared from recrystallized $AlCl_3 \cdot 6H_2O$ and its metal concentration was determined gravimetrically *via* its oxinate. The stock solution contained 0.1 mol dm^{-3} HCl to prevent hydrolysis of the aluminium(III)

---

† Electronic supplementary information (ESI) available: tables of crystal data. See http://www.rsc.org/suppdata/dt/b2/b203198c/

DOI: 10.1039/b203198c

ion. IDA, $Al(NO_3)_3{\cdot}9H_2O$ and ethanol used in the synthesis of $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$ were purchased from Fluka. Nanopure water quality was employed for the solution equilibrium studies and for the synthesis of $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$.

Synthesis of $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$ (M_r = 382.31) (1)

The synthetic reaction was carried out in the open air. A quantity of 0.22 g (0.59 mmol) $Al(NO_3)_3{\cdot}9H_2O$ and 0.16 g (1.19 mmol) of IDA were dissolved in 10 cm^3 of water. The reaction mixture was heated up to 40–60 °C. Subsequently, the pH of the reaction mixture was adjusted to ~4 with aqueous KOH, under stirring. The resulting clear solution (both reactants dissolved) was stirred and heated at 50 °C overnight. On the following day, the solution was taken to dryness with a rotary evaporator. The derived residue was re-dissolved in a minimum amount of water. The pH was rechecked (pH ~ 4). Addition of absolute ethanol at 4 °C yielded crystalline material, which was isolated by filtration and dried *in vacuo*. The yield was 0.11 g (50%). Anal: calcd. for **1**, $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$ ($C_8H_{16}O_{11}N_2KAl$, $M_r = 382.31$): C, 25.11; H, 4.19; N, 7.33 Found: C, 24.97; H, 4.08; N, 7.44.

Physical measurements

FT-Infrared measurements were taken on a Perkin Elmer 1760X FT-infrared spectrometer. Elemental analyses were performed by Quantitative Technologies, Inc.

Crystal structure determination

X-Ray quality crystals of compound **1** were grown from water–ethanol mixtures. A single crystal, with dimensions 0.10 × 0.30 × 0.50 mm was mounted on a Crystal Logic dual-goniometer diffractometer, using graphite monochromated MoKα radiation. Unit cell dimensions for **1** were determined and refined by using the angular settings of 25 automatically centered reflections in the range $11 < 2\theta < 23°$. Intensity data were measured by using θ–2θ scans. Three standard reflections were monitored every 97 reflections, throughout data collection, and showed less than 3% variation and no decay. Lorentz, and polarization corrections were applied by using Crystal Logic software. Experimental crystallographic details for **1**: Chemical formula $C_8H_{16}AlKN_2O_{11}$; Formula weight 382.31; T = 298 K; Space group *Pnab* (conventional orientation *Pbcn*); a = 15.352(8) Å; b = 10.392(6) Å; c = 18.54(1) Å; V = 2958(1) $Å^3$; Z = 8; reflections collected/unique/used, 2609/2608 (R_{int} = 0.0323)/2608; 257 parameters refined; R/R_w (2362 reflections with $I > 2\sigma$), 0.0488/0.1290; R/R_w (for all data), 0.0533/0.1319.

The structure of **1** was solved by direct methods using SHELXS-86[27] and refined by full-matrix least-squares techniques on F^2 with SHELXL-93.[28] All non-H atoms in the structure of **1** were refined anisotropically. All the H-atoms of the anions in **1** were located by difference maps and were refined isotropically.

CCDC reference number 186435.

See http://www.rsc.org/suppdata/dt/b2/b203198c/ for crystallographic data in CIF or other electronic format.

Potentiometric measurements

The stability constants of the proton and Al(III) complexes of the ligands were determined by pH–potentiometric titrations of 10.0 cm^3 samples. The ligand concentrations used were 0.002 mol dm^{-3} and 0.004 mol dm^{-3}. Metal ion to ligand ratios of 0 : 1, 0 : 4, 1 : 1, 1 : 2 and 1 : 4 were employed. The ionic strength was adjusted to 0.2 mol dm^{-3} with KCl. The temperature was maintained at 25 ± 0.1 °C during the measurements. The titrations were performed with a carbonate-free KOH solution of known concentration (*ca.* 0.2 mol dm^{-3}), under a purified argon atmosphere, until precipitation had occurred. For the pH-metric titration of IDA2P and NTA3P ligands, the back titration method was used, due to precipitation in the weakly acidic pH range, in the beginning of the titrations, presumably due to the low solubility of the neutral protonated 1 : 1 complexes Al(IDA2P)H and $Al(NTA3P)H_3$. In these cases, titration of basic samples (pH ~ 10) was carried out with 0.2 mol dm^{-3} HCl solution; at pH < 3, a pH equilibrium could not be reached within 10 min due to slow precipitation. These titration points were omitted from further evaluation. The reproducibility of the titration points included in the evaluation was within 0.005 pH unit throughout the pH range.

Potentiometric measurements of the ligands in the absence and presence of aluminium(III) were performed with an Orion 710A precision digital pH meter or Molspin Automatic Titrator, equipped with a Metrohm 6.0234.100 type combined glass electrode, which was calibrated for hydrogen ion concentration according to Irving *at al.*[29] The stability constants $\beta_{pqr} = [M_pL_qH_r]/[M]^p[L]^q[H]^r$ were calculated with the aid of the PSEQUAD computer program.[30] The stability constants used for the hydroxo species of Al(III) were taken from ref. 31 and corrected to I = 0.2 M, using the Davies equation: −5.49 for $[AlH_{-1}]^{2+}$, −13.54 for $[Al_3H_{-4}]^{5+}$, −108.62 for $[Al_{13}H_{-32}]^{7+}$ and −23.40 for $[AlH_{-4}]^-$. Because of the different charges of the fully deprotonated ligands, the charge of the formulae of the complexes formed is omitted in most cases, and it is indicated only when a formula pertains unambiguously to a single species.

NMR measurements

The ^1H,^{31}P NMR spectra were recorded at 25 °C on a Bruker AMX300 spectrometer. In the ^1H NMR spectra, chemical shifts were referenced to the TMS signal, as an external standard, while in the ^{31}P NMR spectra 85% orthophosphoric acid was used as an external standard. The samples were prepared in D_2O. The concentrations of the ligand solutions were 0.05–0.02 mol dm^{-3}, and the samples with Al(III)–ligand ratio of 1 : 2 at various pH values were examined. All NMR measurements were run on samples at adjusted pH values, after pH equilibrium had been reached.

Results and discussion

In order to provide a more complete characterisation of the complexation features of the herein reported ligand groups with the Al(III) ion, aside from the solution speciation and structural description of the complexes formed in the respective Al(III)-ligand systems, attempts were also made to isolate some of the complexes in the solid state.

Crystallographic studies

Synthesis. The complex $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$ (**1**) was synthesized in aqueous solutions. Aluminium nitrate reacted expediently with iminodiacetic acid in water at pH ~ 4. KOH was instrumental in two aspects: (i) it helped to adjust the pH of the reaction mixture for optimal isolation of the product, and (ii) it provided the counterion for balancing the anionic charge of the reaction product. Isolation of the resulting product was achieved by addition of ethanol at 4 °C.

The overall stoichiometric reaction leading to complex **1** is shown schematically in eqn. (1).

Elemental analysis on the K^+ salt of the isolated crystalline material suggested the formulation $K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O$. The crystalline product was further characterized by FT-IR spectroscopy. The three-dimensional structure of **1** was

$$Al(NO_3)_3{\cdot}9H_2O + 2HN(CH_2COOH)_2 + 4KOH \xrightarrow{pH\sim4} K[Al(C_4H_5O_4N)_2]{\cdot}3H_2O + 3KNO_3 + 10H_2O \qquad (1)$$

determined by X-ray crystallography for one of the isolated single crystals.

Complex **1** is stable, in the crystalline form, in the air indefinitely. It is insoluble in alcohols (CH_3OH, i-PrOH), acetonitrile, and dimethyl sulfoxide (DMSO). It readily dissolves in water.

X-Ray crystallography of $K[Al(C_4H_5O_4N)_2]\cdot 3H_2O$ (1). The X-ray crystal structure of **1** consists of discrete anions and cations. Complex **1** crystallizes in the orthorhombic space group *Pnab* (conventional orientation *Pbcn*) with eight molecules in the unit cell. The ORTEP diagram of the anion in **1** is shown in Fig. 1.

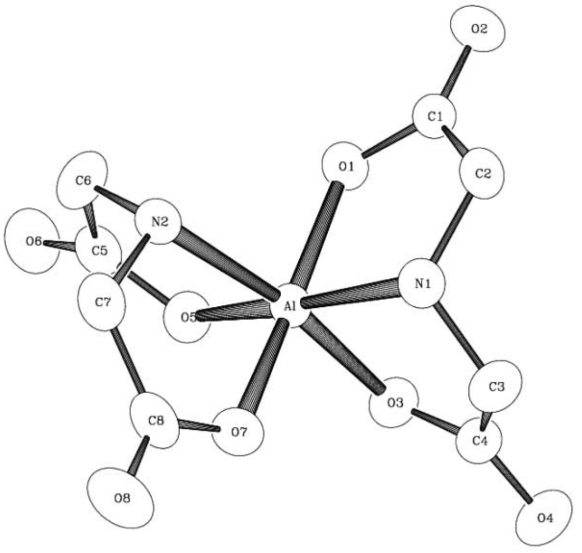

Fig. 1 ORTEP diagram of the anion $[Al(C_4H_5O_4N)_2]^-$ in **1** with thermal ellipsoids representing 50% probability surfaces.

The anion in **1** is a mononuclear species with the Al(III) ion being octahedrally coordinated by two iminodiacetate ligands in a tridentate fashion. The same anionic complex had been previously reported.[24] Both IDA ligands employ the imino nitrogens and the two carboxylates to coordinate to Al(III). Each iminodiacetate ligand, upon coordination to Al(III) forms two five membered chelate rings, contributing to the overall high stability of the complex anion.

Beyond the conventional coordination of the two iminodiacetate ligands to Al(III), it appears that the two ligands adopt a variable conformational mode upon binding to the metal ion with respect to each other. Specifically, the arrangement of the two dicarboxylate ligands in the coordination sphere of Al(III) is such that the two imino nitrogens are not *trans* to each other. In fact, they are placed *cis* to each other in the assembled octahedron.

A list of interatomic distances and bond angles for **1** are provided in Table 1 of the Electronic Supplementary Information.† The Al–O distances in **1** (1.856(2)–1.874(3) Å) are similar to corresponding distances in other mononuclear aluminium carboxylate complexes such as $(NH_4)_5[Al(C_6H_4O_7)_2]\cdot 2H_2O$ (**2**) (1.844(3)–1.961(3) Å), $(NH_4)_4[Al(C_6H_5O_7)(C_6H_4O_7)]\cdot 3H_2O$ (**3**) (1.836(1)–1.959(1) Å), $K_4[Al(C_6H_5O_7)(C_6H_4O_7)]\cdot 4H_2O$ (**4**) (1.821(1)–1.954(1) Å)[32] and $[Al(OH)(C_4H_5O_4N)(H_2O)]_2\cdot 2H_2O$ (1.847(2)–1.889(3) Å).[25] Moreover, it appears that the O–Al–O angles (88.93(12)– 97.54(12)°) are also similar to those observed in the mononuclear species $K[Cr\{HN(CH_2COO)_2\}_2]\cdot 3H_2O$ (88.9(2)–95.6(2)°)[33] $K[Co\{NH(CH_2COO)_2\}_2]\cdot 2.5H_2O$ (87.5(2)–93.0(2)°)[34] and $Li_2Ni[NH(CH_2COO)_2]_2\cdot 4H_2O$ (88.8(1)°)[35] exhibiting octahedral coordination geometries. The Al–N distances in **1** (2.045(3)–2.056(3) Å) are consistent with those encountered in the aforementioned complexes.

One potassium counter ion is present in **1**. It counterbalances the 1– charge generated on the complex anion. The cation is in contact with the carboxylate oxygens of the iminodiacetate anion and the lattice water oxygens at distances in the range 2.672(3)–2.908(5) Å (8 contacts). Two intermolecular hydrogen bonds between the imino nitrogens and the carboxylate oxygens of the iminodiacetate ligand are responsible for the formation of chains (HN1 ··· O5′ (x, $-0.5 + y$, $1.5 - z$) = 2.144 Å, N1 ··· O5′ = 3.025 Å, N1–HN1 ··· O5′ = 161.8°; HN2 ··· O3′ (x, $-0.5 + y$, $1.5 - z$) = 2.304 Å, N2 ··· O3′ = 3.096 Å, N2-HN2 ··· O3′ = 170.2°). The presence of water molecules of crystallization in **1** is also responsible for the formation of an extensive hydrogen-bonding network.

FT-IR spectroscopy. The FT-infrared spectrum of **1** in KBr confirmed the presence of vibrationally active carboxylate groups. Specifically, antisymmetric and asymmetric vibrations for the carboxylate groups of the coordinated citrate ligands were present in the spectrum. The antisymmetric stretching vibrations $\nu_{as}(COO^-)$ were present for the carboxylate carbonyls in the range 1685–1648 cm^{-1}. Symmetric vibrations $\nu_s(COO^-)$ for the same groups were present in the range 1385–1338 cm^{-1}. The observed carbonyl vibrations appeared to be shifted to lower frequency values in comparison to the corresponding vibrations in free iminodiacetic acid, thus indicating changes in the vibrational status of the citrate ligand coordinated to the aluminum.[36] The difference between the symmetric and antisymmetric stretches, $\Delta(\nu_{as}(COO^-) - \nu_s(COO^-))$, was greater than 200 cm^{-1}, indicating that the citrate carboxylate groups were either free or coordinated to Al(III) in a monodentate fashion.[36] Confirmation of the latter assessment was provided by the X-ray crystal structures of complex **1**. The above described tentative assignments were in agreement with previous assignments in mononuclear Al(III) complexes[37] and consistent with infrared frequencies attributed to carboxylate containing ligands bound to different metal ions.[38–40]

Discussion of the synthetic and structural data. The synthesis and isolation of **1** in a reproducible fashion constitutes a major advancement in the relevant chemistry of Al(III) with dicarboxylates. The same anionic complex had been previously isolated from a reaction mixture not specifically designed for the synthesis of complex **1**.[24] To this end, the present synthetic effort offers (i) a targeted rational synthetic procedure for the complex and (ii) a detailed account of its structural features. The iminodiacetate ligand possesses three potential binding sites, two carboxylates and one imino nitrogen. By virtue of the latter type of site, the iminodiacetate ligand acts as a tridentate Al(III) ion binder creating an octahedral coordination sphere around it. The crystallographic geometric data support the octahedral arrangement of the two iminodiacetate ligands around Al(III) with the two carboxylate terminals coordinated to the metal ion in a monodentate fashion. The latter assertion was amply confirmed by the FT-IR data on complex **1**.

In view of the dianionic nature of each iminodiacetate ligand coordinated to Al(III) the total charge of the derived complex is 1–. This anionic charge is counterbalanced by a monocation of K^+. The latter is involved in coordination with iminodiacetate oxygens as well as molecules of water in the lattice. Thus, the cation acts a mediator between the waters of crystallization and the anionic complex. The anions are hydrogen bonded through the imino nitrogens and the carboxylate oxygens. Moreover, the water molecules of crystallization provide an excellent scaffold for hydrogen bond formation throughout the lattice, thus offering their contribution to the stability in the lattice of **1**.

The complex anion as a mononuclear entity is similar to other mononuclear complexes reported in the past with all-oxygen or mixed oxygen-nitrogen terminal ligands. In this case, it should further be noted that the coordination environment created by the two ligands is such that the two imino nitrogens are *cis* to each other. Examples of a similar *cis* arrangement of

Table 1 Proton and Al(III) complex formation constants of IDA and its phosphonic derivatives at 25 °C and at $I = 0.20$ mol dm^{-3} (KCl)

	IDA	IDAP	IDA2P
log K(NH$_2$)	9.30(4)	10.03(4)	10.85(11)
log K(PO$_3^{2-}$)	—	5.38(3)	6.11(9)
log K(PO$_3^{2-}$)	—	—	4.88(4)
log K(COO$^-$)	2.56(4)	2.18(5)	—
log K(COO$^-$)	1.72(7)	—	—
log β(AlAH)	11.83(7)	15.55(4)	19.41(8)
log β(AlA)	8.18(8)	12.08(4)	14.24(9)
log β(AlAH$_{-1}$)	4.07(5)	6.18(6)	7.78(8)
log β(AlAH$_{-2}$)	−2.41(5)	−1.86(8)	−1.10(19)
log β(AlA$_2$H)	—	24.56(12)	28.42(16)
log β(AlA$_2$)	15.33(6)	—	—
Fitting[a]	0.0168	0.0073	0.0159
No. of points	437	368	188
logK_{AlA} − ΣlogK_H	−5.40	−5.51	−7.40

[a] Average difference between experimental and calculated titration curves expressed in cm^3 of titrant.

Table 2 Proton and Al(III) complex formation constants of NTA and its phosphonic derivatives at 25 °C and at $I = 0.20$ mol dm^{-3} (KCl)

	NTA	NTAP	NTA2P	NTA3P
log K(NH$_2$)	9.59(7)	10.54(2)	11.51(8)	12.29(12)
log K(PO$_3^{2-}$)	—	5.49(3)	6.31(6)	7.04(8)
log K(PO$_3^{2-}$)	—	—	4.90(6)	5.71(3)
log K(PO$_3^{2-}$)	—	—	—	4.47(5)
log K(COO$^-$)	2.45(6)	2.30(3)	1.96(18)	—
log K(COO$^-$)	1.7 (2)	1.37(15)	—	—
log K(COO$^-$)	1.23(21)	—	—	—
log β(AlAH$_3$)	—	—	—	32.13(9)
log β(AlAH$_2$)	—	20.02(9)	25.25(7)	29.44(6)
log β(AlAH)	13.05(9)	18.54(4)	22.44(6)	24.84(6)
log β(AlA)	11.98(4)	15.76(5)	18.11(5)	18.76(7)
log β(AlAH$_{-1}$)	6.75(5)	9.04(6)	10.05(8)	12.19(7)
log β(AlAH$_{-2}$)	−1.64(5)	−0.36(6)	−0.42(7)	—
Fitting[a]	0.0057	0.0070	0.0053	0.00103
No. of points	507	517	620	552
logK_{AlA} − ΣlogK_H	−2.96	−3.94	−6.57	−10.75

[a] Average difference between experimental and calculated titration curves expressed in cm^3 of titrant.

the nitrogens in the coordinated iminodiacetate ligands include the complexes K[Cr{HN(CH$_2$COO)$_2$}$_2$]·3H$_2$O[33] and K[Co{NH(CH$_2$COO)$_2$}$_2$]·2.5H$_2$O.[34] An exception in this structural chemistry appears to be the case of the analogous Ni(II) complex, Li$_2$Ni[NH(CH$_2$COO)$_2$]$_2$·4H$_2$O,[35] which contains the nitrogens on the two coordinated ligands in a *trans* arrangement.

Speciation studies

Iminodiacetate derivatives. Potentiometric titrations of IDA, and its mixed carboxylic–phosphonic and purely phosphonic derivatives indicate stepwise dissociation of the protons from the COOH, PO$_3$H$_2$ and $^+$NH functions in the measurable pH range. The protonation constants (log K values) are listed in Table 1.

The first proton of each PO$_3$H$_2$ group is rather acidic and dissociates at pH < 1. Hence, it is in the monoprotonated form, PO$_3$H$^-$ in the beginig of pH-metric titration. The protonation constants of the ligands (listed in Table 1) are the mean values of the data determined by us in the past[41–42] and in the herein-reported work. The data are in good agreement and are within the indicated experimental error with those reported previously.[41–43] The Al(III)–ligand titration curves were jointly evaluated on the assumption of the formation of various 1 : 1 and 1 : 2 complexes with different protonation states. The best fit with the experimental data was obtained with the speciation model listed in Table 2. Speciation curves for the complexes formed in the Al(III)–ligand systems as a function of pH are depicted in Fig. 2.

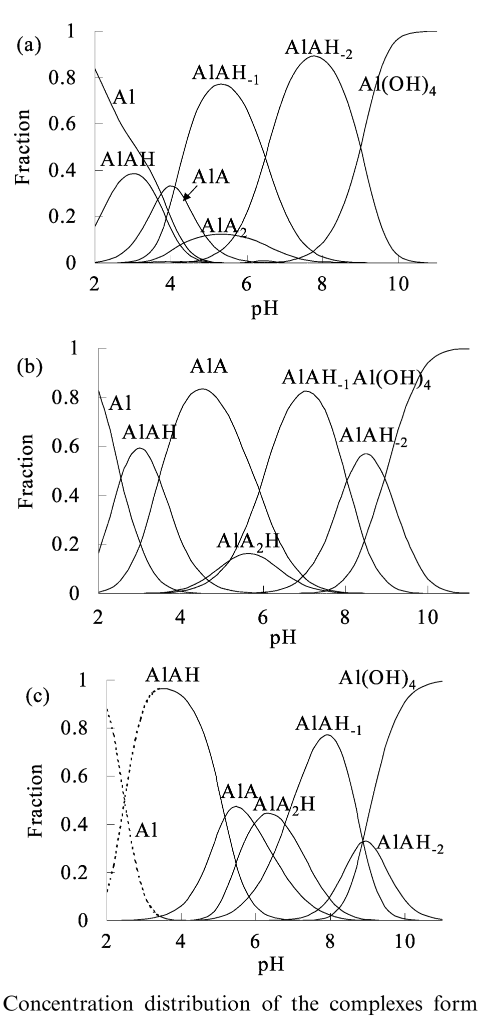

Fig. 2 Concentration distribution of the complexes formed in the Al(III)–IDA (a), Al(III)–IDAP (b), Al(III)–IDA2P (c) systems as a function of pH; $c_{Al} = 0.002$ mol dm^{-3}, $c_{ligand} = 0.004$ mol dm^{-3}.

As seen in Fig. 2, protonated species are formed in all three systems. In the [Al(IDA)H]$^{2+}$ species, either a monodentate carboxylate coordination or a weak (COO$^-$, COO$^-$) chelation with formation of an 8-membered chelate ring may be assumed. The imino group remains protonated. In the case of the phosphonic derivatives, the presence of an extra dissociable proton on each phosphonic group, as compared with the carboxylic group, makes the formation of the protonated complex AlAH more favourable. Thus, the latter complex becomes the predominant species in the pH range 2–4 (see Fig. 2). In the mixed carboxylic–phosphonic derivatives, the phosphonate moiety can compete with the carboxylate group for Al(III) binding, resulting in the formation of various binding isomers: monodentate (COO$^-$) or (PO$_3^{2-}$) coordination or (COO$^-$, PO$_3^{2-}$) chelation, again through formation of an 8-membered chelate ring. Due to the relatively low affinity of Al(III) for amino donors,[44,45] the imino group probably remains protonated in these complexes too. Upon increasing the pH, the protonated species AlAH undergoes deprotonation with pK values of 3.65 for IDA, and 3.47, 5.17 for its phosphonic derivatives IDAP and IDA2P, respectively, to form AlA complexes. This deprotonation very likely occurs on the $^+$NH group, and rearrangement to a stable (5 + 5)-membered joint chelate ring system through the tridentate coordination of the ligands takes place.

The overall stability of the AlA complexes increases with the number of phosphonate moieties, due to the increase in the basicity of the donor groups (see Table 1). Despite this fact,

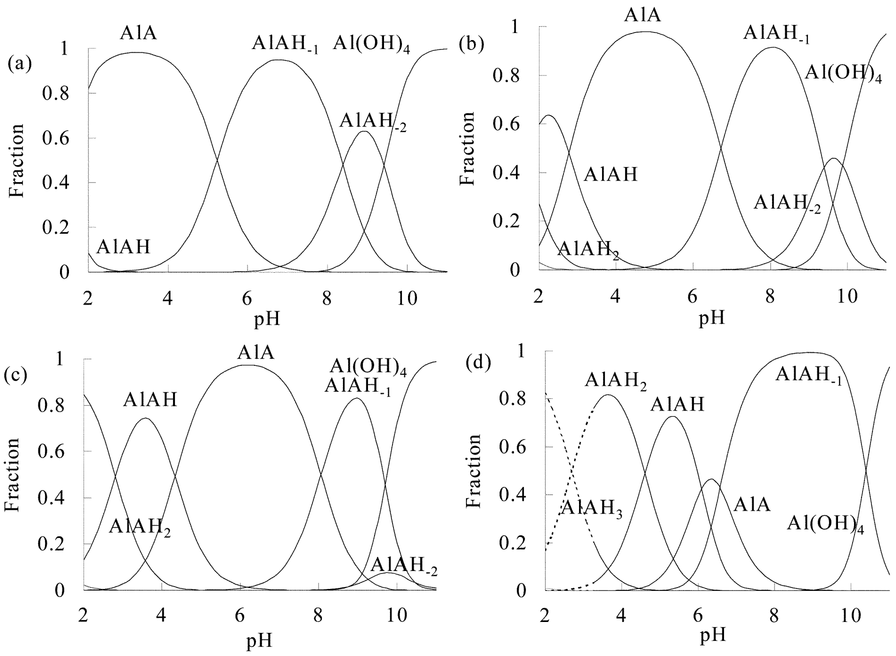

Fig. 3 Concentration distribution of the complexes formed in the Al(III)–NTA (a), Al(III)–NTAP (b), Al(III)–NTA2P (c) systems as a function of pH; $c_{\mathrm{Al}} = 0.002$ mol dm^{-3}, $c_{\mathrm{ligand}} = 0.004$ mol dm^{-3}.

the basicity-adjusted stability constants (log $K_{\mathrm{AlA}} - \Sigma$ log K_{H}), which take into account the differences in the basicities of the coordinating donor groups, decrease in the order IDA ≅ IDAP > IDA2P (see last row of Table 1). These constants also indicate that aminopolycarboxylates are more effective binders than the phosphonic derivatives, due to the stability decreasing effects of the larger spatial requirement and the higher charge of the phosphonate groups. This is also reflected in the shift of the pH of the formation maximum of the corresponding AlA species to higher pH values upon PO_3^{2-}/CO_2^{-} substitution (see Fig. 2). Upon increasing the pH, AlA species undergoes further deprotonation. Protons may be liberated from the water molecules in the coordination sphere of Al(III), resulting in the formation of mixed hydroxo species of the type AlAH$_{-1}$ and AlAH$_{-2}$, or more precisely, AlA(OH) and AlA(OH)$_2$. For iminodiacetic acid, these species predominate in a wide pH range. The species AlAH$_{-1}$ is formed over the pH range 4–7, while AlAH$_{-2}$ is stable over the pH range 6–9. The binding mode in these mixed hydroxo species is similar to that in AlA. The geometry of the complex, however, may change from octahedral to tetrahedral, and this might be the reason for the significant increase in the acidity of the water molecule in complex AlA (p$K_{\mathrm{AlA}} = -4.11$) compared to that of the aqua ion (pK (Al(H$_2$O)$_6$) = -5.52). Even though, for the phosphonic derivatives, the pK(AlA) values are higher than that of the aqua ion (pK = 5.90 and 6.46, respectively), a similar change in geometry may be assumed. As seen in Fig. 2, in the higher pH range, the OH$^-$ starts to displace the ligand molecule from the coordination sphere of the metal ion, resulting finally in the formation of the tetrahedral hydroxo complex [Al(OH)$_4$]$^-$.

In the presence of excess ligand, the bis complexes of type AlA$_2$H and AlA$_2$ are also formed in the systems studied. Even though bis complex formation is not favoured in solution in any of these systems, because of steric and electrostatic reasons, a bis complex K[Al(IDA)$_2$]·3H$_2$O could be isolated from the Al(III)–IDA system at pH ~ 4, where otherwise the mono complex [AlA]$^+$ is the predominant species and [AlA$_2$]$^-$ is formed only at ~ 15 %. In the bis complexes [AlA$_2$], the N atom stands adjacent to O donors (COO$^-$, PO_3^{2-}), which have a high affinity for the hard Al(III). This favours deprotonation of NH_2^+ group of the ligand, followed by its coordination to Al(III) through formation of a tridentate (5 + 5)-membered joint chelate system. The coordination of two ligand molecules in a tridentate fashion saturates the octahedral coordination sphere of Al(III), as that was demonstrated by the X-ray structure of the complex K[Al(IDA)$_2$]·3H$_2$O.

Nitrilotriacetate derivatives. Four protons are titratable in NTA and its phosphonic derivatives in the measurable pH range (see Table 2). The log K values of the PO$_3$H$_2$ groups are ~ 1, and these values, if at all, can be determined pH-metrically only with rather high uncertainties. The carboxylic functions are deprotonated in the usual pH range 2–3.5. The next deprotonation occurs in the pH range 4–7 and corresponds to the PO$_3$H$^-$ groups. The most basic donor for all these ligands is the tertiary amino group, with pK values 9.59, 10.54, 11.51 and 12.29 (see Table 2). The basicity increases with increasing number of phosphonic groups, due to their negative charge and electron repelling effect.

The NTA-like ligands are potentially tetradentate metal ion binders. It is worth noting that only 1 : 1 complexes are formed with most of the metal ions,[41,42] because the tetradentate coordination of the first ligand molecule allows only the unfavoured bidentate coordination of the second ligand. The stability constants calculated by the joint evaluation of the titration curves, obtained at various Al(III) to ligand ratios, are listed in Table 2.

The substitution of COO$^-$ donors by PO_3^{2-} hinders further the coordination of a second ligand molecule, due to the larger space requirement and the higher charge of the phosphonate group. Hence, NTA derivatives do not form bis complexes in comparison with the corresponding iminodiacetic derivatives (*cf.* Tables 1 and 2). The species distribution curves for the complexes formed in the Al(III)–NTA-type and aminophosphonate derivative ligand systems are depicted in Fig. 3.

The more COO$^-$ groups are replaced by PO_3^{2-} groups the higher the tendency is for the ligands to form protonated complexes. While for NTA, only the AlAH species occurs in a small amount (less than 10%), for its mixed carboxylic–phosphonic derivatives the AlAH$_2$ species appears in a high amount (70–80%), while for NTA3P even the AlAH$_3$ species forms at a significant concentration at pH < 3. Owing to the high affinity of the NTA-like ligands for Al(III), complex formation reactions between the metal ion and the protonated forms of the ligands are almost complete at acidic pH, and the free Al(III) ion is present at rather low concentrations at the starting pH values.

In spite of this, pH-metry can be applied for the determination of stability constants as the equilibrium system is better "fixed" to the uncomplexed Al(III)–hydroxo species in the high pH range. In these systems, actually, proton displacement reactions between $[Al(OH)_4]^-$ and the protonated forms of the ligands were monitored. Accordingly, the stability constants listed in Table 2 can be considered as reliable values.[31,46] There can be diverse binding modes for the ligands in the protonated complexes. The ligands can coordinate in a monodentate, bidentate or tridentate fashion to Al(III) *via* the carboxylates in the NTA, and through the carboxylates and phosphonate groups in the complexes of mixed carboxylic–phosphonic derivatives. The coordination of all phosphonate groups to Al(III) in the NTA3P complexes is not likely, because of the high electrostatic repulsions between the phosphonate arms. In all of these protonated species, formed in the weakly acidic pH range, the amino group remains presumably in an uncoordinated protonated form. As the pH increases, the protonated forms undergo further deprotonation, resulting finally in the formation of AlA complexes. Similar to the IDA derivatives, the formation maximum for the AlA species shifts to higher pH values with increasing number of phosphonate groups in the molecule (see Fig. 3). NTA-type ligands are potentially tetradentate, however, participation of all donors in Al(III) binding is not always obvious. Namely, the basicity-adjusted stability constant, which is about two orders of magnitude larger for NTA than for IDA indicates binding of an additional donor in the NTA complex. The difference is only 1.2 log units for NTAP and IDAP and only 0.4 log units for NTA2P and IDA2P. This continuously decreasing differential stability rise between the corresponding NTA and IDA derivatives may suggest a parallel existence of binding isomers with tridentate and tetradentate coordination of the NTA derivatives. Accordingly, NTA can coordinate to Al(III) either in a tridentate (COO^-, N, COO^-) $(COO^-)_{free}$ or in a tetradentate fashion, as that was found in the solid state.[26] Tetradentate coordination of NTA predominates in solution too. However, this type of coordination for the NTA-type ligands seems to be less and less favoured as the number of the phosphonate moieties increases in the molecules. In the Al(III)–NTA system, deprotonation of AlA species starts at pH ~ 4 and results in the formation of the mixed hydroxo species $AlAH_{-1}$ and $AlAH_{-2}$. For its phosphonic derivatives, these species occur only at pH > 6. The binding mode in the Al(III)-hydroxo complexes is similar to that presented previously for the IDA complexes. These four ligands form stable complexes with Al(III) over the physiological pH range, and $[Al(OH)_4]^-$ appears only at pH > 8. It is interesting to note that in the Al(III)–NTA3P system the $AlAH_{-1}$ species is the predominant species in solution at pH ~ 8.

NMR studies

IDA derivatives. In order to get more accurate information on the complex formation processes involving Al(III) with these aminophosphonates, ^1H and ^{31}P NMR measurements were also carried out. In general, we found that the NMR spectra of the Al(III)–ligand (sometimes even the H^+–ligand) systems were rather complicated, especially for the mixed carboxylate–phosphonate derivatives. This suggests formation of rather asymmetric complexes, or formation of various binding isomers, which may be a general trend in Al(III)–organophosph(on)ate systems.[47] The complete elucidation of the NMR features of the Al(III)–ligand systems would need extensive multinuclear NMR measurements, including ^{13}C and ^{27}Al NMR. However, as the value of information these results may provide, concerning the Al(III) binding behaviour of the ligands, is not always very high, we did not attempt to explore this field in depth, but used NMR just to obtain several basic characteristics for the binding ability of the ligands and their binding modes in the complexes.

The ^1H NMR spectra of IDA consist of one singlet, since the two CH_2 groups are magnetically equivalent. The signal at $\delta = 3.88$ ppm, pH ~ 2, is shifted upfield to $\delta = 3.66$ ppm, upon increasing the pH to ~ 5, when IDA is in the HA^- form, and $\delta = 3.60$ ppm at pH ~ 9, when it exists partly in the A^{2-} form.

In the ^1H NMR spectrum of the metal containing sample, recorded at pH ~ 3, in addition to the signal of the free ligand (3.71 ppm), three doublets of the complexed IDA are observed (Fig. 4). The splitting of the resonances indicates that complex formation results in the inequivalence of the two protons in each CH_2 group. Accordingly, we should have had two pairs of asymmetric doublets. Actually, we only observe three asymmetric doublets at $\delta = 3.92$, 3.90 and 3.28 ppm ($^2J_{HH} = 17.85$ Hz). The intensity of the doublet at $\delta = 3.28$ is exactly double that of the other two doublets. It is very likely that, while the signals of the H_a protons of the two methylene groups appear at different chemical shift values, the H_b protons give rise to one doublet (3.28 ppm). Just by chance, they appear at the same chemical shift value. This is also supported by its approximately two fold relative intensity compared to that of the other two signals occurring at $\delta = 3.90$ and 3.92 ppm. These doublets can be ascribed to the AlAH and AlA species, which are in fast proton exchange, indicated by the slight upfield shifts of the signals in the pH range 2–4.

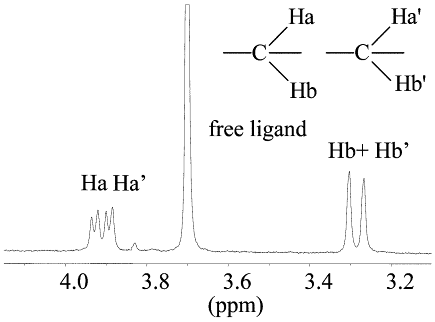

Fig. 4 ^1H NMR parameters of Al(III)–IDA system at pH 3; $c_{Al} = 0.025$ mol dm^{-3}, $c_{IDA} = 0.05$ mol dm^{-3}.

The ^1H NMR spectra at pH ~ 5 were rather complex and the relative intensity of the signals depended on the ligand concentration (Fig. 5). Because of the overlapping processes occurring in the system, the signals could not be clearly identified. The decrease of the relative intensity for some of the signals, with a concurrent increase for others at different ligand concentrations, is very likely the result of changes in the ratio of the mono and bis complexes with ligand concentration. This observation is in good agreement with the speciation results (Fig. 2).

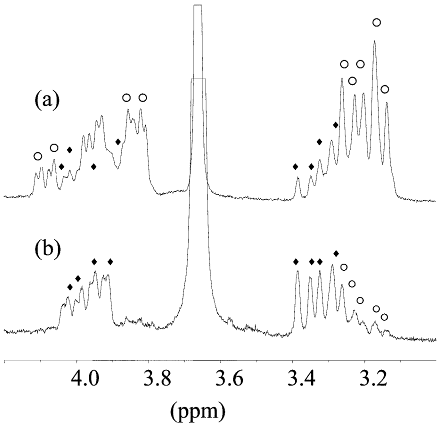

Fig. 5 ^1H NMR parameters of Al(III)–IDA system at pH 5 at 1 : 2 metal ion to ligand ratio (a) $c_{IDA} = 0.02$ mol dm^{-3}, (b) $c_{IDA} = 0.05$ mol dm^{-3}, (o) indicates 1 : 1 and (◆) 1 : 2 complexes.

Table 3 ^1H NMR parameters of Al(III)-NTA system at different pH values

pH	δ (ppm)	Assignment
2.0	4.0389	free ligand
	3.7923	AlA
3.5	3.8168	free ligand
	3.7923	AlA
5.0	3.8055	free ligand
	3.7810	AlA + AlA(OH)
7.0	3.8111	free ligand
	3.7075	AlA(OH)
8.0	3.7979	free ligand
	3.6887	AlA(OH) + AlA(OH)$_2$
9.0	3.7075	free ligand
	3.6454	AlA(OH)$_2$

In solutions of 0.004 mol dm^{-3} ligand concentration, the predominant species are the 1 : 1 AlA and AlAH$_{-1}$ complexes. The bis complex can be detected only in a small quantity (< 10% at pH ~ 5) at 0.004 mol dm^{-3} ligand concentration. As the ligand concentration increases, formation of the bis complex becomes progressively favored, and at 0.05 mol dm^{-3} ligand concentration it reaches > 50%.

At pH > 8 the ^1H NMR spectra simplify again. Four doublets, at 3.86, 3.16 ($^2J_{HH}$ = 17.85 Hz) and 3.85, 3.14 ppm ($^2J_{HH}$ = 17.40 Hz) could be detected, corresponding to the magnetically inequivalent protons of the two CH$_2$ groups. These doublets should belong to the species AlAH$_{-2}$. The ligand coordinates to Al(III) through the two carboxylates and the amino group, and there are also two OH$^-$ groups in the coordination sphere of Al(III) resulting in a rather unsymmetrical geometry.

The ^1H NMR spectra of the IDA2P ligand exhibit a doublet (J = 4.52 Hz) due to coupling with the ^{31}P nucleus, indicating that the two CH$_2$ groups, in a similar fashion to IDA, are chemically and magnetically equivalent. These resonances display a slight shift in the range δ = 3.117–3.351 ppm, in the pH range 3.5–9.0, due to the deprotonation of the phosphonic functions (see Table 2). In the presence of Al(III), the ^1H NMR spectra are complicated and the signals are rather broad (not shown). The two singlets of the same intensity, appearing at δ = 2.291 and 2.793 ppm, can be assigned to the magnetically inequivalent protons of the two CH$_2$ groups of the 1 : 1 species. The more complex signals of lower intensity at δ = 3.42 and 3.69 ppm most likely belong to the bis complex AlA$_2$H (see Figure 2c). At pH > 9, the OH$^-$ displaces the coordinated ligands and the signal for the free ligand is observed again.

NTA derivatives. Consistent with the observations for IDA, the CH$_2$ groups of NTA are magnetically equivalent, since the ^1H NMR spectra show only one singlet, which is shifted upfield with increasing pH due to the stepwise deprotonation processes. A significant broadening of the peak is observed at pH > 9. This may be explained by the partial deprotonation of the NH$^+$ group of NTA, which cannot then participate in the formation of H-bonding or other ionic interactions.

The ^1H NMR spectra of Al(III)–NTA show only one signal for the bound ligand in the pH range 2–9. The chemical shift data obtained at different pH values are listed in Table 3.

The chemical and magnetic equivalence of the three CH$_2$ groups suggest a symmetrical structure for the AlA complex, with three carboxylates and the amino group bound to the metal ion. This is similar to the rather asymmetric crystal structure reported previously.[26] Thus, the complete equivalence of the CH$_2$ groups, can only be explained if fast intramolecular motions of the coordinated methylenecarboxylate arms are assumed in solution. Further deprotonation of the coordinated water molecules takes place at pH > 5, which results in a slight upfield shift of the resonance. Complexes AlAH$_{-1}$ and AlAH$_{-2}$ are formed in these processes. The species at different protonation states are in fast proton exchange.

The ^1H NMR spectra of the mixed carboxylate–phosphonate derivatives are rather complicated, both in the absence and especially in the presence of Al(III), due to the inequivalence of the CH$_2$ groups, which is the result of their different chemical environment and the asymmetry of the complexes formed. However, the ^{31}P NMR spectrum of NTA3P consists of a single resonance, which can be attributed to the three magnetically equivalent phosphonate groups of the ligand (see Fig. 6). With increasing pH, the signal is shifted upfield and becomes sharper, due to the stepwise deprotonation process and the fast internal rearrangement motions of the various structures formed through hydrogen bonding between the phosphonate groups and the protonated imino function.

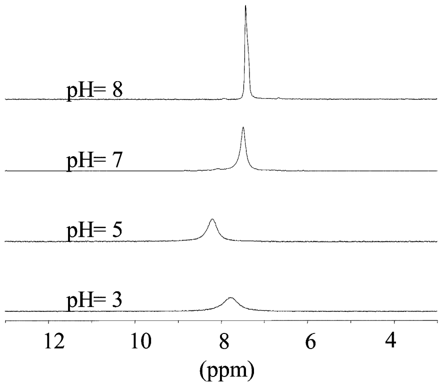

Fig. 6 ^{31}P NMR spectra of the NTA3P ligand at different pH values; c_{Al} = 0.025 mol dm^{-3}, c_{NTA3P} = 0.05 mol dm^{-3}.

The ^1H NMR spectrum of the Al(III)–NTA3P system consists of a doublet for the free ligand at 3.70 ppm, which in the presence of Al(III) is shifted upfield to 3.46 ppm with increasing pH. In more acidic solutions (pH ~ 3), complex formation could not be monitored because precipitation occurred in the system. The ^1H NMR spectrum in the pH range 5–6.6 is very complicated (Fig. 7), as the various isomeric forms of AlA give separate resonances. These isomers, due to the broad signals observed, could not be identified, but the tridentate and partial tetradentate coordination of the ligand can be assumed. The complete coordination of all three phosphonate groups to the same Al(III) is not likely, since the phosphonate group has a high charge and a large space requirement. Surprisingly, at pH > 8 the ^1H NMR spectrum simplifies and only a sharp doublet is observed at 2.92 ppm for the Al(III) bound in the complex. This symmetric doublet reflects the formation of the species AlAH$_{-1}$, which should be fully symmetrical as all three CH$_2$ are chemically and magnetically equivalent. This can be achieved by assuming a trigonal bipyramidal complex arising from the

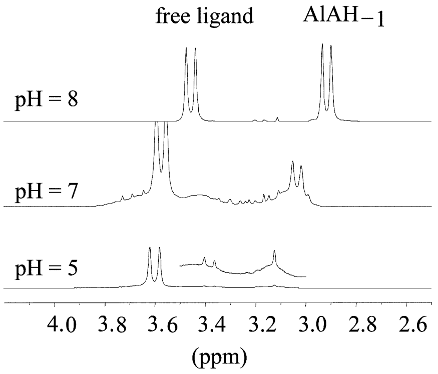

Fig. 7 ^1H NMR parameters of Al(III)–NTA3P system at different pH values; c_{Al} = 0.025 moldm^{-3}, c_{NTA3P} = 0.05 mol dm^{-3}.

tripodal coordination of the ligand, with three phosphonate groups in the equatorial plane and one N in the axial position. The other apical position is occupied by the OH$^-$ ion. This kind of a symmetrical five coordinate trigonal-bipyramidal structure is not very frequent for Al(III) complexes. We found only two examples in the literature: AlCl$_3$(PMe$_3$)$_2$[48] and AlCl$_3$(morpholine)$_2$[49] characterized in the solid state. The single-crystal Raman spectrum and the X-ray study showed, for example, that the trimethylphosphine groups are in axial positions in the AlCl$_3$(PMe$_3$)$_2$ compound. In solution, such a kind of geometry has not been demonstrated yet. The other alternative, which could explain the NMR feature of the complex, is that AlAH$_{-1}$ forms an asymmetric complex, but due to the fast intramolecular rearrangement motions of the various isomeric forms on the NMR time scale, the signals of the individual non-equivalent CH$_2$ groups cannot be seen. Only an average signal is observed, *i.e.* the complex molecule is fluxional. This latter binding feature seems to be more likely in solution.

Conclusion

The phosphonic derivatives of IDA and NTA are very effective binders of Al(III). As with the parent ligands IDA and NTA, due to the oligodentate coordination of the ligands through formation of joint chelate systems, the aforementioned phosphonic derivatives can prevent hydrolysis of the metal ion and precipitation of the Al(OH)$_3$ even in equimolar solutions up to pH ~ 8. (The solids precipitating with IDA2P and NTA3P at weakly acidic pH, are the poorly soluble neutral phosphonato complexes of the ligands). It was found that bis complexes, which would saturate the coordination sites of the Al(III) ion, are hardly formed due to the large spatial requirement of the ligands and the electrostatic repulsion between the 1 : 1 complex and the second charged ligand moiety. Accordingly, at higher pH, the water molecules in the free coordination sites of the 1 : 1 complex will lose protons and thus mixed hydroxo complexes (AlAH$_{-1}$ and AlAH$_{-2}$) form. At pH > 9, OH$^-$ displaces the ligand molecule from the coordination sphere, a process which is accompanied by a change in geometry, from octahedral to tetrahedral, and the very stable species [Al(OH)$_4$]$^-$ is formed.

The stability constants of the AlA complexes, as a function of the number of the substituted carboxylate groups by phosphonates, are depicted in Fig. 8. For comparison, the stability constants of the respective complexes of Cu(II)[41] and VO(IV)[42] are also shown in Fig. 8. It is seen that the stability of the complexes increases with increasing number of the more basic phosphonate groups. However, the opposite trend in the basicity adjusted stability constants ($\log K_{\mathrm{AlA}} - \Sigma \log K_{\mathrm{H}}$) shows that this stability increase is overcompensated by the higher spatial requirement and electrostatic repulsion between the PO$_3^{2-}$ groups. This means that the carboxylic derivatives are more effective metal ions binders than the phosphonic ones. A comparison of the log *β*(MA) values, depicted in Fig. 8 for Al(III), Cu(II) and VO(IV) complexes reveals several differences in the coordination behaviour of these metal ions with the ligands studied. Interestingly enough, Al(III) forms the least stable complexes with the aminopolycarboxylates (IDA and NTA), while with the phosphonic derivatives (IDA2P and NTA3P) the respective Al(III) complexes have the highest stability. This is connected with the considerably higher 'slope' of the log *K*(ML) *vs.* $n_{\mathrm{PO_3H_2}}$ relationship, which can be explained by the higher charge of the Al^{3+} ion, as compared with that of the dipositively charged Cu^{2+} and VO^{2+} ions, which results in a significantly higher electrostatic contribution to the overall stability of the Al(III) complexes. The opposite trend in the corresponding Cu(II) and VO(IV) complexes of IDA and NTA derivatives, namely, that complexes of VO(IV)–IDA derivatives are somewhat weaker than the corresponding Cu(II) complexes, while the stability sequence is just the opposite for the NTA derivatives, has been explained earlier[41] by invoking differences in the binding mode of the complexes.

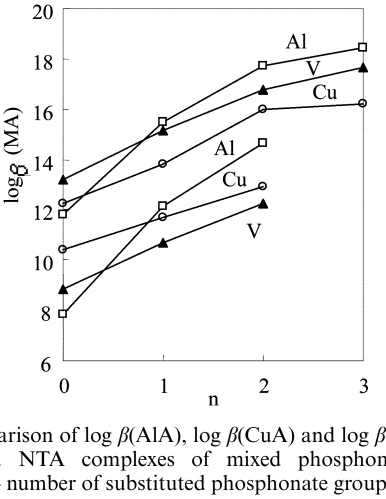

Fig. 8 Comparison of log *β*(AlA), log *β*(CuA) and log *β*(VOA) values for IDA and NTA complexes of mixed phosphonic–carboxylic derivatives; *n* – number of substituted phosphonate groups.

The NMR spectra of the Al(III) complexes of the aminophosphonate derivatives are rather complicated. Even the corresponding nuclei of the CH$_2$, PO$_3^{2-}$, or CO$_2^-$ groups of the symmetrical ligands are not always equivalent chemically and/or magnetically, due to the formation of complexes with low symmetry and, also, the parallel formation of various binding isomers.[47] According to the ^{1}H NMR spectra of Al(III) complexes with IDA, complex formation results in the inequivalence of the two protons in each CH$_2$ group, while the CH$_2$ groups of NTA and its derivatives are chemically and magnetically equivalent. Since usually no symmetrical arrangements of the donor atoms can ordinarily be expected with any of the ligands, the rate of the intramolecular rearrangement motions within the complex molecules seems to be different for the IDA and the NTA derivatives.

Acknowledgements

The work has been carried out in the frame of COST D8 research project, and was supported by Hungarian Science Research Fund (OTKA 23776/97), the Hungarian Ministry of Education (FKFP 0013/97) and the Department of Chemistry, University of Crete, Greece. The General Secretariat for Research and Technology (GSRT), Greece, is gratefully acknowledged for providing research funds on aluminium related research (Grant No. 97EL-106).

References

1 T. Kiss, M. Jezowska-Bojczuk, H. Kozlowski, P. Kafarski and K. Antczak, *J. Chem. Soc., Dalton Trans.*, 1991, 2275.
2 J. P. Solvin and E. M. Tobin, *Biochim. Biophys. Acta*, 1981, **177**, 637.
3 R. J. Johnson, T. Inouye, A. Goldin and G. P. Stark, *Cancer Res.*, 1976, **36**, 2720.
4 J. G. Allen, F. R. Athyerton, M. J. Hall, C. H. Hassal, S. W. Holmes, R. W. Lambert, L. J. Norbert and P. S. Ringrose, *Nature (London)*, 1978, **272**, 56.
5 M. J. O'Connel, J. Rubin, A. J. Schutt, C. G. Hoertel and L. K. Kools, *Cancer Treat. Rep.*, 1983, **67**, 1141.
6 F. R. Atherton, C. H. Hassal and R. W. Lambert, *J. Med. Chem.*, 1986, **29**, 29.
7 J. C. Bousquet, S. Saini, D. D. Strak, P. F. Hahn, M. Nigam, J. Wittenberg and J. T. Ferrucci, *Radiology*, 1988, **166**, 693.
8 V. M. Runge, D. Y. Gelblum, M. L. Pacetti, F. Carolan and G. Heard, *Radiology*, 1990, **177**, 393.
9 S. V. Deshpande, S. J. Denardo, D. L. Kukis, M. K. Moi, M. J. McCall, G. L. Denard and C. L. Meares, *J. Nucl. Med.*, 1990, **31**, 473.
10 K. Sawada, T. Ichikawa and K. Uehara, *J. Chem. Soc., Dalton Trans.*, 1996, 3077.
11 R. P. Carter, R. L. Carrol and R. R. Irani, *Inorg. Chem.*, 1967, **6**, 939.

12 H. E. L. Madsen, H. H. Christensen and C. Gottlieb-Peterson, *Acta Chem. Scand. Ser. A*, 1978, **32**, 79.

13 M. Wozniak and G. Nowogrocki, *Talanta*, 1979, **26**, 1135.

14 M. A. Martell and R. M. Smith, *Critical Stability Constants*, vol. V, Plenum, New York, 1982, p. 183.

15 R. J. Motekaitis and A. E. Martell, *J. Coord. Chem.*, 1985, **14**, 138.

16 T. G. Appleton, J. R. Hall and I. J. McMahon, *Inorg. Chem.*, 1986, **25**, 726.

17 B. Radomska, E. Matczak-John and W. Wojciechowski, *Inorg. Chim. Acta*, 1986, **124**, 83.

18 T. Kiss, J. Balla, G. Nagy, H. Kozlowski and J. Kowalik, *Inorg. Chim. Acta*, 1987, **138**, 25.

19 P. H. Smith and K. N. Raymond, *Inorg. Chem.*, 1988, **27**, 1056.

20 T. Kiss and E. Farkas, *J. Chem. Soc., Dalton Trans.*, 1989, 1053.

21 L. O. Öhman, *Polyhedron*, 1990, **9**, 199.

22 M. A. Dhansay and P. W. Linder, *J. Coord. Chem.*, 1993, **28**, 133.

23 M. Jezowska-Bojczuk, T. Kiss, H. Kozlowski, P. Decock and J. Bariycki, *J. Chem. Soc., Dalton Trans.*, 1994, 811.

24 S. P. Petrosyants, M. A. Malyarik and A. B. Ilyukhin, *Russ. J. Inorg. Chem.*, 1996, **41**, 1521 (*Zh. Neorg. Khim.*, 1996, **41**, 1595).

25 S. P. Petrosyants and M. A. Malyarik and A. B. Ilyukhin, *Russ. J. Inorg. Chem.*, 1995, **40**, 744 (*Zh. Neorg. Khim.*, 1995, **40**, 769).

26 G. C. Valle, G. G. Bombi, B. Corain, M. Favarato and P. Zatta, *J. Chem. Soc., Dalton Trans.*, 1989, 1513.

27 G. M. Sheldrick, SHELXS-86, Structure Solving Program, University of Göttingen, Germany, 1986.

28 G. M. Sheldrick, SHELXL-93, Structure Refinement Program, University of Göttingen, Germany, 1993.

29 H. M. Irving, M. G. Miles and L. D. Petit, *Anal. Chim. Acta*, 1967, **38**, 475.

30 L. Zékány, I. Nagypál and G. Peintler, PSEQUAD for Chemical Equilibria, Technical Software Distributions, Baltimore, MD, 1991.

31 L. O. Öhman and S. Sjöberg, *Acta Chem. Scand.*, 1982, **A36**, 47.

32 M. Matzapetakis, M. Kourgiantakis, M. Dakanali, C. P. Raptopoulou, A. Terzis, A. Lakatos, T. Kiss, I. Banyai, L. Iordanidis, T. Mavromoustakos and A. Salifoglou, *Inorg. Chem.*, 2001, **40**, 1734.

33 D. Mootz and H. Wunderlich, *Acta Crystallogr.*, 1980, **B36**, 445.

34 A. B. Corradi, C. G. Palmieri, M. Nardelli, M. A. Pellingelli and M. E. V. Tani, *J. Chem. Soc., Dalton Trans.*, 1973, 655.

35 N. J. Mammano, D. H. Templeton and A. Zalkin, *Acta Crystallogr.*, 1977, **B33**, 1251.

36 G. B. Deacon and R. Philips, *J. Coord. Chem. Rev.*, 1980, **33**, 227.

37 T. L. Feng, P. L. Gurian, M. D. Healy and A. R. Barron, *Inorg. Chem.*, 1990, **29**, 408.

38 (*a*) M. Matzapetakis, C. R. Raptopoulou, A. Terzis, A. Lakatos, T. Kiss and A. Salifoglou, *Inorg. Chem.*, 1999, **38**, 618; (*b*) M. Matzapetakis, C. R. Raptopoulou, A. Tsochos, B. Papefthymiou, N. Moon and A. Salifoglou, *J. Am. Chem. Soc.*, 1998, **50**, 13266; (*c*) M. Matzapetakis, M. Dakanali, C. R. Raptopoulou, V. Tangoulis, A. Terzis, N. Moon, J. Giapintzakis and A. Salifoglou, *J. Biol. Inorg. Chem.*, 2000, **5**, 469; (*d*) M. Matzapetakis, N. Karligiano, A. Bino, M. Dakanali, C. R. Raptopoulou, V. Tangoulis, A. Terzis, J. Giapintzakis and A. Salifoglou, *Inorg. Chem.*, 2000, **39**, 4044.

39 W. P. Griffith and T. D. Wickins, *J. Chem. Soc. A*, 1968, 397.

40 N. Vuletic and C. Djordjevic, *J. Chem. Soc., Dalton Trans.*, 1973, 1137.

41 P. Buglyó, T. Kiss, M. Dyba, M. Jezowska-Bojczuk, H. Kozlowski and S. Boushina, *Polyhedron*, 1997, **16**, 3447.

42 D. Sanna, I. Bódi, S. Bbouhsina, G. Micera and T. Kiss, *J. Chem. Soc., Dalton Trans.*, 1999, 3275.

43 K. Sawada, W. Duan, M. Ono and K. Satoh, *J. Chem. Soc., Dalton Trans.*, 2000, 919.

44 R. B. Martin, *Acc. Chem. Res.*, 1994, **27**, 204.

45 T. Kiss, I. Sóvágó, I. Tóth, A. Lakatos, R. Bertani, A. Tapparo, G. Bombi and R. B. Martin, *J. Chem. Soc., Dalton Trans.*, 1997, 1967.

46 R. J. Motekaitis and A. E. Martell, *Inorg. Chem.*, 1980, **19**, 1646.

47 D. Champmartin, P. Rubini, A. Lakatos and T. Kiss, *J. Inorg. Biochem.*, 2001, **84**, 13.

48 I. R. Beattie, G. A. Ozin and H. E. Blayden, *J. Chem. Soc. A*, 1969, 2535.

49 G. Müller and C. Krüger, *Acta Crystallogr.*, 1984, **C40**, 628.