FULL PAPER

Dalton
www.rsc.org/dalton

Complexes of divalent transition metal ions with bis(aminomethyl)phosphinic acid in aqueous solution and in the solid state

Vojtěch Kubíček, Pavel Vojtíšek, Jakub Rudovský, Petr Hermann * and Ivan Lukeš
Department of Inorganic Chemistry, Universita Karlova (Charles University), Hlavova 2030, 128 40 Prague 2, Czech Republic. E-mail: petrh@natur.cuni.cz; Fax: +420 22195 1253; Tel: +420 22195 1263

Received 23rd May 2003, Accepted 11th August 2003
First published as an Advance Article on the web 3rd September 2003

Bis(aminomethyl)phosphinic acid, $(NH_2CH_2)_2PO_2H$ (HL), was synthesized using a new procedure. Its coordination ability towards Co(II)/(III), Ni(II), Cu(II) and Zn(II) was studied both in solution and in the solid state. Because of the presence of two nitrogen atoms the ligand exhibits a higher overall basicity than common (aminoalkyl)phosphinic acids. Consequently, the values of the determined stability constants are comparable with those found for (aminoalkyl)phosphonic acids. NMR titrations of Zn(II) point to the interaction of phosphinate with the metal ion in a strong acid solution. The X-ray structures show several coordination modes in the solid state. All-*trans*-$[MCl_2(H_2L\text{-}O)_2(H_2O)_2]Cl_2$, where M(II) are Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Ca(II), and Cd(II), crystallized from acid solutions. The central ion is octahedrally coordinated with two phosphinate oxygen atoms, two molecules of water and two chlorides in all-*trans* arrangement. Amine groups are protonated and non-coordinated. Participation of the donor groups in crystals isolated from neutral solutions depends on the metal ion. All donor atoms are coordinated in monomeric *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-$[Co(L\text{-}N,N,O)_2]^+$. On the other hand, in the zinc(II) complex, two phosphinate oxygen atoms and two amine nitrogen atoms (*trans* to each other) of two different ligand molecules are coordinated in an equatorial plane and two amino groups of the two other ligand molecules are bound in axial positions. Thus, each molecule of the amino acid forms a five-membered *N*,*O*-chelate to one zinc(II) ion and the other amino group is bound to the neighbouring ion creating an infinite chain. Nickel(II) forms a *trans*-*O*,*O*′-$[Ni(H_2O)_2(L\text{-}N,N)_2]$ complex in which the metal ion is chelated by four amine nitrogen atoms forming two six-membered chelates in an equatorial plane and the octahedron is completed with two water molecules at the apical positions. The phosphinate group is not coordinated. The above results point to a relatively low coordination ability of the phosphinate group; however, due to its low pK_A, it is able to bind metal ions at lower pH than other coordinating groups do.

Introduction

(Aminoalkyl)phosphonic or phosphinic acids as phosphorus analogues of naturally occurring aminocarboxylic acids have attracted much interest due to their biological activity.[1,2] Because of the tetrahedral structure of the phosphonic $R\text{–}PO_3H_2$ as well as phosphinic R_2PO_2H (R = alkyl, aryl) acids, they mimic tetrahedral intermediates in hydrolysis of carboxylic esters, amides and peptides. Therefore, aminophosphinic acid derivatives exhibit pronounced biological effects; they strongly inhibit metalloenzymes,[2,3] *e.g.* matrix metalloproteinases and astacins, angiotensin I converting enzyme, thrombin, endothelin converting enzyme, *etc.*, or alter receptor functions, *e.g.* of GABA receptors.[2,4] (Aminoalkyl)phosphinic acid peptides have been also suggested as compounds of interest for a new drug design,[2,5] *e.g.* analgetics, antibiotics or agents against protozoa infections.

The complexing behaviour of (aminoalkyl)phosphonic/phosphinic acids is not so well understood as that of aminocarboxylic acids.[6] Simple (aminoalkyl)phosphonic acids have been extensively studied in solution.[7] In contrast, much less papers have dealt with their complexes in the solid state.[8] The differences in basicity, charge, the electron-releasing effect and the size of relevant donor groups result in the differences in complex-forming properties of aminophosphonic and aminocarboxylic acids in solution. Because of more basic character of the $–PO_3^{2-}$ group compared to $–COO^-$ group, there is a possibility of monodentate co-ordination of the ligands *via* the phosphonate group, thus leaving other donor groups easily accessible to protonation, forming stable protonated complexes. In the case of chelate formation, thermodynamic stability of complexes of (aminoalkyl)phosphonic acids with transition metal ions is usually higher than that of aminocarboxylates, which is caused, at least in the first approximation, by enhanced basicity of the ligands. However, coordination of the second ligand molecule to the same metal ion is disfavoured due to the bulkiness of the phosphonate grouping. For metal ions with higher charges, phosphonates are clearly superior ligands due to a better compensation of Coulombic repulsion by metal ion mainly if more than one phosphonate group is coordinated. Some of their properties are also evident in phosphonodipeptides and their complexes.[9–11] It is possible to compare complexation abilities of distereoisomers. We have shown that the differences are higher than for corresponding carboxylic peptides as a consequence of stronger interactions between side chains in phosphonopeptides. Deprotonation of peptide nitrogen atom and simultaneous coordination to a metal ion was observed only in the case of Cu^{2+} with a higher pK_A corresponding to the reaction. This was explained by electron delocalization in the phosphonate dianion.

On the other hand, little attention has been paid to coordination properties of (aminoalkyl)phosphinic acids in solution[12] and in the solid state.[13–20] The results indicate that, compared to (aminoalkyl)phosphonic and aminocarboxylic acids, the amino groups in (aminoalkyl)phosphinic acids are weakly basic and the phosphinic acid groups are often strongly acidic. Consequently, the complexes exhibit lower stability constants. The influence of the substituent on the phosphorus atom in the phosphinic acid group on coordination properties in phosphinic acid analogues of glycine ($H_2N\text{–}CH_2\text{–}P(R)O_2H$, R = H, Me, Ph, *tert*-Bu) was investigated[21] with the aim to explain the influence of the phosphinic acid pendant groups in

DOI: 10.1039/b305844a

polyazamacrocycles.[22] Phosphinic acid analogues of Gly–Gly with the same substituents on phosphorus atoms exhibit a surprising behaviour.[23] They form with Cu^{2+} very easily a violet $[Cu(phosphinodipeptide)_2]^{2-}$ species where the ligands are coordinated only through amine and deprotonated amide nitrogen atoms. In contrast to Gly–Gly and Gly–Gly(P), the violet complex is formed at a relatively low pH (around 9) even with only a small excess of the ligand and the effect is greatly influenced by the phosphorus atom substituent.

In continuation of our investigations of complexation of transition metal ions with (aminoalkyl)phosphonic/(aminoalkyl)phosphinic acids as well as with their dipeptides,[10,11,21,23] we present here the results obtained with bis(aminomethyl)-phosphinic acid. It is the simplest model for compounds in which the phosphinic acid group is located inside the chain, *e.g.* oligopeptide chain. Such compounds have been investigated as strong inhibitors of a variety of enzymes.[2] Recently, several papers dealing with the complexation ability of polydentate open-chain[24] and macrocyclic[25] ligands containing the $(–NHCH_2)_2PO_2H$ moiety appeared. A preliminary conference report of the work presented has been communicated.[26]

Experimental

General

Reactions with pyrophoric bis[(trimethysilyl)oxy]phosphine ($(Me_3SiO)_2PH$) were performed under an argon atmosphere. $PhtNCH_2Br$[27] (Pht is phtaloyl) and $Na_3[Co(CO_3)_3]\cdot 3H_2O$[28] were prepared using literature procedures. Other chemicals were from commercial sources (Lachema, Aldrich, Fluka or Acros). Dichloromethane was dried over P_2O_5. Water for determination of protonation constants was purified using the Milli-Q (Millipore) purification system. TLC was performed on Silufol silica gel sheets (Kavalier, Votice, Czech Republic) or on Merck 1.05554 F_{254} sheets in a propan-2-ol–25% aq. NH_3–water (7 : 3 : 3) mixture using ninhydrin or UV detection. Elemental analyses were carried out in the Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (Prague). Melting points were determined using a Kofler hot-stage apparatus (Boetius) and are uncorrected. NMR spectra were recorded on a Varian Unity Plus at 400 MHz for ^1H, 169 MHz for ^{31}P and 100 MHz for ^{13}C with internal references TMS for DMSO-d_6 solutions and *t*-BuOH for D_2O solutions and external reference 85% H_3PO_4. Thermogravimetric (TG) analysis was performed at the Institute of Chemical Technology (Prague) on a Stanton Redcroft apparatus at 25–300 °C in air (10 °C min^{-1}). Sulfonate (Dowex 50, Fluka) and carboxylate (Amberlite CG50/N1, Rohm & Haas) cation exchangers were used for ion-exchange column chromatography.

Chemicals and stock solutions for potentiometric titrations

A stock solution of nitric acid (~0.03 M) was prepared by passing a solution of recrystallised potassium nitrate through a Dowex 50W-8 column in the H^+ form because of traces of NO and NO_2 present in the concentrated acid. Carbonate-free KOH solution (~0.2 M) was standardized against potassium hydrogen phthalate and HNO_3 solution against the ~0.2 M KOH solution. Samples of the ligand (HL·HCl) for preparation of stock solutions were dried to constant weight at room temperature in a desiccator over P_2O_5. Analytical concentration of the ligand determined from the weights of the dried ligand was in accordance with its concentration determined together with the refinement of protonation constants using the OPIUM program.

Potentiometric titrations

Titrations were carried out in a vessel thermostatted at 25 ± 0.1 °C, at ionic strength $I(KNO_3)$ = 0.1 mol dm^{-3} and in the presence of extra HNO_3 in the $-\log[H^+]$ range 1.8–11.9 (or till metal hydroxides precipitation) using a PHM 240 pH-meter, a 2 ml ABU 900 automatic piston burette and a GK 2401B combined electrode (Radiometer). The initial volume was 5 cm^3, the concentration of the ligand was 0.004 mol dm^{-3} and ligand-to-metal ratios were 1.1 : 1, 2 : 1 and 4 : 1 (in the case of Cu^{2+} also 0.007 mol dm^{-3} with the same HL : M ratios). Titrations were carried out at least four times, each consisting of about 40 points. An inert atmosphere was ensured by constant passage of argon saturated with the vapor of the solvent used in measurements. The water ion product, $pK_w = 13.78$, and stability constants of M^{2+}–OH^- systems were taken from ref. 29. The protonation constants β_n calculated are concentration constants and are defined by $\beta_n = [H_nL]/([H]^n \times [L])$ ($pK_3 = \log \beta_1$; $pK_2 = \log \beta_2 - \log \beta_1$; $pK_1 = \log \beta_3 - \log \beta_2$); the stability constant are defined by $\beta_{pqr} = [M_pH_qL_r]/[M]^p \times [H]^q \times [L]^r$. The constants (with standard deviations) were calculated with program OPIUM (ref. 30). The program minimises the criterion of the generalised least-squares method using the calibration function

$$E = E_0 + S \times \log[H^+] + j_A \times [H^+] + j_B \times K_w/[H^+]$$

where the additive term E_0 contains the standard potentials of the electrodes used and contributions of inert ions to the liquid-junction potential, S corresponds to the Nernstian slope, the value of which should be close to the theoretical value and $j_A \times [H^+]$ and $j_B \times [OH^-]$ terms are contributions of the H^+ and OH^- ions to the liquid-junction potential. It is clear that j_A and j_B cause deviation from a linear dependence between E and $-\log[H^+]$ only in strong acid and strong alkaline solutions. The calibration parameters were determined from titration of standard HNO_3 with standard KOH solutions before any titration of the ligand to give a pair of calibration titration/titration used for calculations of the constants. The calibration procedure of the glass electrode in the wide pH region described above permitted determination of log β with the statistical standard deviation ±0.01 (even outside the titration pH region; see Supplementary material in ref. 22*b*). However, the real accuracy could be lower and we estimate it to be within ±0.05 log units or even decreased for species with low abundance (5–15%).

NMR titrations

Measurements of ^1H and $^{31}P\{^1H\}$ NMR spectra in dependence on pH (from 5 M HCl up to precipitation of metal hydroxide) were done at ligand concentration ~0.1 mol dm^{-3} in the presence or absence of $ZnCl_2$ (ratio HL : Zn = 2 : 1, room temperature). pH of the samples was adjusted with dilute aqueous KOH and aqueous HCl. Deuterium oxide (containing 1% *t*-BuOH and 15% H_3PO_4 as an external standards) in an inserted glass capillary was used for frequency lock and the water signal in ^1H NMR was presaturated.

UV-VIS spectra

Metal chloride hydrate (M = Ni(II), Cu(II)) and HL·HCl (two equivalents) were dissolved in water and pH of the sample was carefully adjusted with dilute KOH and aqueous HCl solutions to a value where the maximum of $[M(L)_2]$ species should be present according to distribution diagrams. The Co(III) complex was dissolved in water (without adjusting pH). Spectra were recorded on a UV 300 (Pye Unicam) in the 200–1100 nm range at room temperature.

Crystal structure determinations

The diffraction-quality single crystals of all-*trans*-$[MCl_2(H_2L)_2(H_2O)_2]Cl_2$ complexes were grown from aqueous solution by slow evaporation at room temperature. Single crystals of complexes (*trans*-*O*,*O*-$[Ni(L\text{-}N,N)_2(H_2O)_2]\cdot 2H_2O$, $[Zn(L)_2]\cdot$

$2H_2O$) and ligand (HL·HCl, its solution pH was adjusted with HCl to 2–3) were obtained from aqueous solutions by vapour diffusion of EtOH. Single crystals of *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H_2O were obtained from concentrated aqueous solution on standing in a closed vial. The selected crystals were mounted on glass fibres in random orientation by epoxy glue for measurements at room temperatures and by silicone fat for low-temperature measurements. Diffraction data were collected using a Nonius Kappa CCD diffractometer at 293(2) and at 150(1) K (Cryostream Cooler (Oxford Cryosystem)) and analyzed using the HKL program package (ref. 31). The structures were solved by the direct methods, and refined by full-matrix least-squares techniques (SIR92,[32] SHELXL97[33]). Final geometric calculations were carried out with a recent version of the PLATON program.[34] Scattering factors for neutral atoms used were included in the SHELXL97 program. Hydrogen atoms were localized in all structures (with the exception of two hydrogen atoms of a water molecule in the cadmium(II) complex) on the difference maps and refined isotropically. Tables 1 and 2 give pertinent crystallographic data.

CCDC reference numbers 211306 (Ca), 211312 (Mn), 211308 (Co), 211313 (Ni), 211310 (Cu), 211315 (Zn), and 211307 (Cd) for all-*trans*-[MCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$ (M = Ca, Mn, Co, Ni, Cu, Zn and Cd); 211314 (*trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$]·$2H_2O$); 211316 ([Zn(L)$_2$]·$2H_2O$); 211311 (HL·HCl); and 211309 (*fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H_2O).

See http://www.rsc.org/suppdata/dt/b3/b305844a/ for crystallographic data in CIF or other electronic format.

Bis(phthalimidomethyl)phosphinic acid

In argon atmosphere, the dried $NH_4H_2PO_2$ (2.0 g, 0.024 mol) was suspended in $(Me_3Si)_2NH$ (20 ml) and the mixture was heated at 110 °C (bath temperature) under a small flow of argon for 6 h. The mixture containing pure $(Me_3SiO)_2PH$ was cooled to room temperature and dry dichloromethane (60 ml) was added. After cooling the solution in a water-ice bath, a solution of PhtNCH$_2$Br (12.0 g, 0.05 mol) in dry CH_2Cl_2 (100 ml) was dropped into the solution during 5 min. The reaction mixture was stirred at room temperature for 12 h under argon and then MeOH (20 ml) was added to hydrolyse silyl esters. After 10 min, the reaction mixture was diluted with 50 ml of CH_2Cl_2 and extracted with 6 M HCl (100 ml). After some time, a fine white crystalline solid precipitated in the organic phase. It was filtered off, washed with EtOH (5 ml) and dried in a desiccator over P_2O_5. The aqueous phase was re-extracted with CH_2Cl_2 (2 × 50 ml). The organic layers were collected, dried with anhydrous Na_2SO_4 and the solvent was removed in vacuum to give additional product. Both the fractions were recrystallized together from hot EtOH to give 7.1 g of product (76%).

Mp 280–285 °C (dec.); TLC (ninhydrine): R_f = 0.8; δ_H (DMSO-d$_6$) 4.07, [4 H, d, *J*(PH) 7.6 Hz, 2 CH_2P]; 7.8–8.0, [8 H, m, 2 C$_6H_5$]; δ_P (DMSO-d$_6$): 33.4 [q, *J*(PH) 7.6 Hz]. (Found C, 54.18; H, 3.90; N, 6.67. Calc. for $C_{18}H_{13}N_2O_6P$ (384.24): C, 56.26; H, 3.41; N, 7.29%).

Bis(aminomethyl)phosphinic acid hydrochloride (HL·HCl)

Bis(phthalimidomethyl)phosphinic acid (5.90 g, 0.015 mol) was suspended in a mixture of 6 M HCl (200 ml) and EtOH (50 ml). The mixture was refluxed for 12 h and partly evaporated after cooling. Crystalline phthalic acid was filtered off, washed with cold water and the filtrate was purified on a cation exchange resin column (H^+, Dowex, 3 × 20 cm) by elution with water followed by 5% aqueous ammonia. The fractions containing product were combined, the solvent was evaporated in vacuum and excess of ammonia was removed by repeated evaporation with water. The residue was dissolved in 1 M aqueous HCl (5 ml) and the product was precipitated by slow addition of excess EtOH. Yield 2.20 g HL·HCl (92%).

Mp 290–295 °C (dec.); TLC (ninhydrin): R_f = 0.6; δ_H (D_2O) 3.24 [d, *J*(PH) 9.8 Hz, CH_2P]; δ_P (D_2O) 21.1 (q, *J*(PH) 9.8 Hz). (Found C, 15.33; H, 6.17; N, 16.69; Cl, 22.13. Calc. for $C_2H_{10}ClN_2O_2P$ (160.54): C, 14.96; H, 6.28; N, 17.45; Cl, 22.08%). Thermogravimetry: Decomposition starts at 50 °C with loss of HCl followed by full decomposition of the compound.

Complexes of HL with divalent metal ions from strong acid solutions (general procedure)

Bis(aminomethyl)phosphinic acid hydrochloride (1.2 mmol) and metal(II) chloride hydrate (0.6 mmol) were dissolved in 6 M HCl (10 ml). After dissolution of the solids, the hydrochloric acid was removed in vacuum. The solid residue was dissolved in water (10 ml) and the solution was evaporated again. The dissolution and evaporation was repeated three times. The complex was then dissolved in water (5 ml) and crystallised by free evaporation. Crystals were filtered off, washed with ethanol and dried in a desiccator over P_2O_5. Yields and analytical data are given in Table 3.

Example of thermogravimetric decomposition (all-*trans*-[CoCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$): Loss of two water molecules proceeds at 170–230 °C. Decomposition of the complex starts at 290 °C.

Complexes of HL with Ni(II), Cu(II) and Zn(II) from neutral/alkaline solutions (general procedure)

Chlorides were removed from HL·HCl (0.30 g, 1.88 mmol) on Dowex 50 (H^+-form) with water elution. The free amino acid was eluted with 5% aqueous ammonia. The HL-containing solution was evaporated to dryness in vacuum and this was repeated three times to remove excess ammonia. The residue was dissolved in water (2 ml) and added to the freshly precipitated and washed M(OH)$_2$ (0.94 mmol). After dissolution of the hydroxide, the solution was filtered through a plug of cotton wool. pH of this solution was carefully adjusted (glass electrode) to the required value mentioned below using 10% aqueous solutions of NaOH or $HClO_4$. The complexes crystallized on EtOH vapour diffusion in a large closed vial.

trans-*O*,*O*′-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$]·$2H_2O$: pH of the solution was adjusted to 9.25. Blue needles, losing water of crystallization on long standing. Single crystals were selected from the bulk. Yield 0.27 g (83%). (Found: C, 13.2; H 5.94. Calc. for $C_4H_{16}N_4NiO_4P_2$·$4H_2O$ (376.89): C 12.8, H 6.42%). Thermogravimetry: complete dehydration occurs at 110–120 °C. The anhydrous form is stable up to 350 °C. UV-VIS: $-\log[H^+] = 9.3$: λ_{max} (ε) = 597 (12), 366 nm (18 mol^{-1} dm^3 cm^{-1}).

[Cu(L)$_2$]·$2H_2O$: pH of the solution was adjusted to 8.50. Light blue microcrystalline powder. Yield 0.30 g (93%). (Found: C 13.2; H 5.42. Calc. for $C_4H_{16}CuN_4O_4P_2$·$2H_2O$ (345.72): C 13.9, H 5.83%). Thermogravimetry: dehydration occurs in the range of 150–180 °C. The anhydrous form is stable up to 220 °C. UV-VIS: $-\log[H^+]$ = 8.2: λ_{max} (ε) = 616 (83), 273 nm (4100 mol^{-1} dm^3 cm^{-1}).

[Zn(L)$_2$]·$2H_2O$: No pH adjustment. Colorless crystals, losing water of crystallization on long standing. Single crystals were picked up from the bulk. Yield 0.35 g (92%). Thermogravimetry: dehydration starts at 50 °C followed by decomposition. No region of the anhydrous form was observed.

fac-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H_2O

The chloride anion from HL·HCl (0.25 g, 1.56 mmol) was removed on Dowex 50 with water elution. The amino acid was eluted with 5% aqueous ammonia. The HL-containing solution was evaporated to dryness in vacuum and this was repeated three times to remove excess ammonia. The residue was dissolved in water (2 ml). The $Na_3[Co(CO_3)_3]$·$3H_2O$ complex (0.24 g, 0.78 mmol) was suspended in water (5 ml) and the ligand

Table 1 Experimental data for the X-ray difraction studies of all-*trans*-$[MCl_2(H_2L\text{-}O)_2(H_2O)_2]Cl_2$ ($C_4H_{24}Cl_4MN_4O_6P_2$). All complexes are monoclinic, space group $P2_1/n$ (no. 14), $Z = 2$ with M in special position. Data were obtained at room temperature (293(2) K), with the exception of M = Ca and Ni (150(1) K); $\lambda = 0.71070$ Å using CCD rotation scans

Parameter	Ca	Mn	Co	Ni	Cu	Zn	Cd
Formula weight	468.09	482.95	486.94	486.72	491.55	493.38	540.41
Crystal dimension/mm	0.7 × 0.35 × 0.4	0.3 × 0.35 × 0.3	0.5 × 0.5 × 0.4	0.5 × 0.35 × 0.4	0.2 × 0.35 × 0.4	0.6 × 0.3 × 0.16	0.3 × 0.3 × 0.52
Shape	Irregular	Irregular	Prism	Irregular	Irregular	Prism	Plate
Colour	Colorless	Pale pink	Violet	Pale green	Pale blue	Colorless	Colorless
a/Å	8.4190(2)	8.3320(4)	8.2740(2)	8.2110(2)	8.1620(2)	8.2290(2)	8.3050(2)
b/Å	7.9000(2)	7.9230(4)	7.9080(2)	7.8530(2)	8.0250(2)	7.8630(2)	7.9080(2)
c/Å	13.6270(3)	13.3980(8)	13.2520(4)	13.2350(5)	13.3400(3)	13.3150(3)	13.5910(3)
α/°	90	90	90	90	90	90	90
β/°	102.423(1)	103.325(4)	103.028(2)	103.042(2)	104.285(1)	103.033(2)	102.386(1)
γ/°	90	90	90	90	90	90	90
V/Å^3	885.11(4)	860.65(4)	844.77(4)	831.39(5)	846.75(4)	839.35(4)	871.83(4)
D_c/g cm^{-3}	1.756	1.864	1.914	1.944	1.928	1.952	2.059
μ/mm^{-1}	1.17	1.60	1.86	2.03	2.14	2.32	2.08
F(000)	484.0	494.0	498.0	500.0	502.0	504.0	540.0
θ range of data collection/°	3.58–27.50	3.01–28.33	3.16–27.54	3.16–27.53	3.15–27.48	3.14–27.50	3.07–27.54
Index ranges $h/k/l$	0 ⟶ 10/0 ⟶ 10/−17 ⟶ 17	0 ⟶ 11/–10 ⟶ 10/−17 ⟶ 16	0 ⟶ 10/0 ⟶ 10/−17 ⟶ 16	0 ⟶ 10/0 ⟶ 10/−17 ⟶ 16	0 ⟶ 10/0 ⟶ 10/−17 ⟶ 17	0 ⟶ 10/0 ⟶ 10/−17 ⟶ 16	0 ⟶ 10/−10 ⟶ 10/−17 ⟶ 17
Reflections collected	3942	5048	3838	3803	3872	3841	14605
R_σ	0.0250	0.0362	0.0291	0.0439	0.0259	0.0247	0.0278
Reflections observed [$I > 2\sigma(I)$]	1887	1852	1841	1640	1814	1803	1886
Independent reflections	1991	2038	1922	1910	1933	1922	1997
R_{int}	0.0102	0.0245	0.0258	0.0321	0.0172	0.0165	0.0514
Coeffs. in weighting scheme[a]	0.0194	0.0400	0.0339	0.0659	0.0351	0.0189	0.0309
	0.3798	0.1402	0.4540	0.0922	0.3536	0.5553	11.2365
Data/restrains/parameters	1991/0/146	2038/0/146	1922/0/146	1910/0/146	1933/0/146	1922/0/146	1997/0/138
Goodness-of-fit on F^2	1.148	1.217	1.113	1.069	1.055	1.060	1.303
Final R, R' indices [$I \geq 2\sigma(I)$][b]	0.0197	0.0291	0.0268	0.0367	0.0208	0.0190	0.0467
	0.0545	0.0833	0.0761	0.1040	0.0636	0.052	0.1370
Maximum shift/esd	0.000	0.000	0.001	0.003	0.001	0.000	0.001
Largest diff. peak and hole/e Å^3	0.372/−0.262	0.596/−0.461	0.401/−0.487	0.750/−1.182	0.479/−0.604	0.401/−0.357	3.48/−0.87

[a] $w = 1/[\sigma^2(F_0^2) + (A \times P)^2 + B \times P]$, where $P = (F_0^2 + 2F_c^2)/3$ (SHELXL97, ref. 33). [b] $R = \Sigma|F_0 - F_c|/\Sigma|F_c|$, $R' = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2}$ (SHELXL97, ref. 33).

Table 2 Experimental data for the X-ray difraction studies of HL·HCl, *trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$]·2H$_2$O, [Zn(L)$_2$]·2H$_2$O and *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H$_2$O

Parameter	HL·HCl	[Ni(L)$_2$(H$_2$O)$_2$]·2H$_2$O	[Zn(L)$_2$]·2H$_2$O	[Co(L)$_2$](ClO$_4$)·H$_2$O
Empirical formula	$C_2H_{10}ClN_2O_2P$	$C_4H_{24}N_4NiO_8P_2$	$C_4H_{20}N_4O_6P_2Zn$	$C_4H_{18}ClCoN_4O_9P_2$
Formula weight	160.54	376.92	347.55	422.54
T/K	150(1)	293(2)	293(2)	293(2)
Crystal dimension/mm	0.3 × 0.2 × 0.2	0.1 × 0.4 × 0.07	0.1 × 0.2 × 0.4	0.2 × 0.3 × 0.3
Shape	Prism	Needle	Plate	Irregular
Colour	Colorless	Blue	Colorless	Brown orange
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1$ (no.4)	$P2_1/c$ (no.14)	$P2_1/c$ (no.14)	$P2_1/n$ (no.14)
a/Å	4.9780(2)	8.030(1)	5.6990(1)	10.2410(3)
b/Å	7.6100(3)	6.397(1)	17.2390(3)	9.4680(2)
c/Å	8.3910(3)	14.353(2)	6.2940(2)	15.1850(5)
α/°	90	90	90	90
β/°	94.750(3)	104.814(9)	90.351(2)	104.466(2)
γ/°	90	90	90	90
V/Å^3	316.78(2)	712.8(2)	618.34(2)	1425.68(7)
Z	2	2	2	4
D_c/g cm^{-3}	1.683	1.756	1.867	1.969
λ/Å	0.71070	0.71070	0.71070	0.71070
μ/mm^{-1}	0.77	1.62	2.27	1.67
F(000)	168.0	396.0	360.0	864.0
θ range of data collection/°	3.62–27.47	3.40–25.12	3.45–34.99	3.49–27.54
Index ranges *h*/*k*/*l*	0 ⟶ 6/−9 ⟶ 9/−10 ⟶ 10	0 ⟶ 9/0 ⟶ 7/−16 ⟶ 16	−9 ⟶ 9/−25 ⟶ 25/−9 ⟶ 10	0 ⟶ 13/0 ⟶ 12/−19 ⟶ 19
Reflections collected	1443	1261	13538	6554
R_σ	0.0356	0.0719	0.0339	0.0310
Reflections obsd. [$I > 2\sigma(I)$]	1354	1014	2414	2898
Independent reflections	1442	1256	2670	3278
R_{int}	—	0.0168	0.0406	0.0245
Coeffs. in weighting scheme[a]	0.0211; 0.1474	0.0926; 0.5343	0.0327; 0.2042	0.0455; 0.5651
Data, restrains, parameters	1442/0/113	1256/0/136	2670/0/120	3278/0/291
Goodness-of-fit on F^2	1.055	1.084	1.055	1.051
Final *R*, *R*′ indices [$I \geq 2\sigma(I)$][b]	0.0242 0.0602	0.0604 0.1576	0.0284 0.0742	0.0311 0.0827
Maximum shift/esd	0.001	0.001	0.001	0.000
Diff. peak and hole/e Å^3	0.286; −0.349	0.986; −0.859	0.722; −0.744	0.606; −0.518

[a] $w = 1/[\sigma^2(F_0^2) + (A \times P)^2 + B \times P]$, where $P = (F_0^2 + 2F_c^2)/3$ (SHELXL97, ref. 33). [b] $R = \Sigma|F_0 - F_c|/\Sigma|F_c|$, $R' = [\Sigma w(F_0^2 - F_c^2)^2/\Sigma w(F_0^2)^2]^{1/2}$ (SHELXL97, ref. 33).

Table 3 Yields and analytical[a] data for all-*trans*-[MCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$ complexes

Complex	Analysis (%)				Yield[b] (%)
	C	H	N	Cl	
[CaCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	13.5 (10.3)	5.33 (5.17)	14.9 (12.0)	26.3 (30.3)	45
[MnCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	10.3 (10.0)	4.46 (5.01)	11.3 (11.6)	29.0 (29.4)	60
[CoCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	10.4 (9.9)	4.58 (4.97)	11.4 (11.5)	28.7 (29.1)	72
[NiCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	10.5 (9.9)	4.81 (4.97)	11.5 (11.5)	28.8 (29.1)	28
[CuCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	10.2 (9.8)	4.57 (4.92)	11.1 (11.4)	28.7 (28.9)	65
[ZnCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	10.3 (9.7)	4.46 (4.90)	11.2 (11.4)	28.3 (28.7)	52
[CdCl$_2$(H$_2$L)$_2$(H$_2$O)$_2$]Cl$_2$	9.3 (8.9)	4.10 (4.48)	10.0 (10.4)	26.2 (26.2)	81

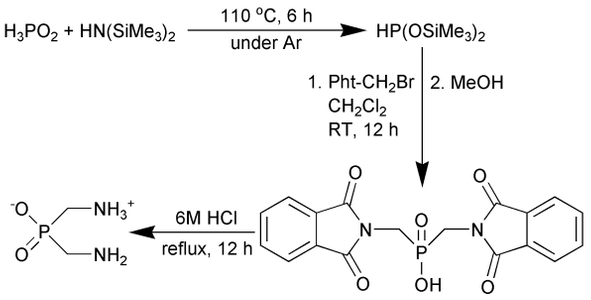
[a] Required values are given in parentheses. [b] Yields strongly depend on the volume of mother solution left over the crystals due to a high solubility of the complexes.

solution was added. The mixture was left for a week in the refrigerator (5 °C). After that 70% aqueous HClO$_4$ (0.07 g) was added and the mixture was left in the refrigerator for another few weeks. The deep-red solution was purified on an Amberlite CG50 column (2 × 20 cm). Cobalt(III) complex and HClO$_4$ were eluted with water and the free ligand and cobalt(II) species were trapped on the column. The cobalt(III)-containing fraction was evaporated to a small volume (*ca.* 2 ml) and the solution was left to crystallize in a closed flask. After two weeks, red-violet crystals were filtered and dried in air, yield 0.03 g (12% based on the starting cobalt complex). Found: C, 11.9; H 4.46. Calc. for $C_4H_{16}ClCoN_4O_8P_2$·H$_2$O (421.54): C 11.4, H 4.29%. Thermogravimetry: dehydration starts at 50 °C and is complete at 140 °C. The anhydrous form is stable up to 280 °C. UV-VIS: −log[H$^+$] = 6.5: λ_{max} (ε) = 510 (70), 368 (154), 207 nm (14600 mol^{-1} dm^3 cm^{-1}).

Results and discussion

Synthesis of the ligand and its crystal structure

The HL ligand was synthesised by Maier in a multi-step synthesis some time ago.[35] Here we used a different, simpler and scalable approach based on the Arbuzov reaction of intermediate (Me$_3$SiO)$_2$PH which is now widely used in the synthesis of phosphinic acids.[36] (Scheme 1). The pyrophoric phosphine is synthesised *in situ* by reaction of ammonium hypophosphite and (Me$_3$Si)$_2$NH.[37] Alkylation of the phosphine with alkyl halogenides leads to mono- and disubstituted phosphinic acids. However, the reaction is not usually used for the synthesis of monoalkylphosphinic acids. Even if the phosphine : RX ratio is 1 : 1, mixture of the starting phosphine, monoalkylphosphinic and dialkylphosphinic acid is obtained.[38] Here, the use of an excess of the halogenide gave a high yield of the protected



Scheme 1

ligand. Deprotection led to the desired ligand isolated as a stable monohydrochloride salt. The ligand can be prepared as free base but this form decomposes during several days in the solid state as well as in aqueous solution.

In the solid state, HL·HCl is protonated on both nitrogen atoms (Fig. 1a). Deprotonated phosphinate shows almost the same P–O(1) and P–O(2) bond lengths (Table 4), which are intermediate between P=O and P–O bond lengths. Structure parameters around the phosphorus atom are almost the same as those found in the structure of (aminomethyl)-methylphosphinic acid ($^{+}NH_3CH_2P(Me)O_2^{-}$)[39a] and recently published bis(*N*-morpholinomethyl)phosphinic acid ([$(OC_4H_8NHCH_2)_2PO_2$]Cl·H_2O[39b] where only O–P–O (115.9°) and C–P–C (101.7°) angles (aminomethylphosphinic acid) and C–P–C (101.5°) angle (morpholinophosphinic acid) are slightly different. The structure is stabilized by strong intermolecular hydrogen bonds N–H ··· O (2.96–2.98 Å). The presence of N–H ··· Cl hydrogen bonds can be also proposed as the Cl^- are close to the nitrogen atoms (3.17–3.24 Å). The hydrogen bond-stabilized structure is formed by layers of ligand molecules intercalated in layers of chloride anions (Fig. 1b).

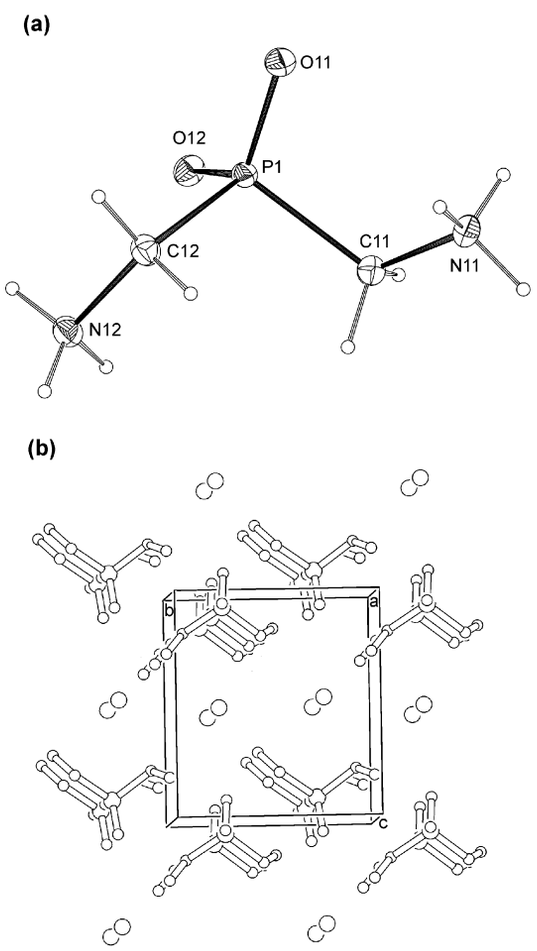


Fig. 1 Molecular structure of the $(H_2L)^+$ cation with the atom numbering scheme (a) and crystal packing of HL·HCl as seen along the *a* axis (b).

Table 4 Bond lengths (Å) and angles (°) in the crystal structure of HL·HCl

Bond or angle	Length or angle
P(1)–O(11)	1.505(1)
P(1)–O(12)	1.498(1)
P(1)–C(11)	1.832(2)
P(1)–C(12)	1.831(2)
O(11)–P(1)–O(12)	118.29(7)
O(11)–P(1)–C(11)	108.6(1)
O(2)–P(1)–C(1)	108.1(1)
O(12)–P(1)–C(11)	108.6(1)
O(12)–P(1)–C(12)	108.6(1)
C(11)–P(1)–C(12)	103.7(1)

Table 5 Protonation constants of HL (β_n) and its stability constants (β_{pqr}) with Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} [a]

Ion	Species	log β
H^+	HL	8.509(6)
	$(H_2L)^+$	15.580(7)
	$(H_3L)^{2+}$	16.35(2)
Co^{2+}	$[Co(HL)]^{2+}$	10.37(6)
	$[Co(L)]^+$	4.074(5)
	$[Co(L)_2]$	6.79(7)
	[Co(OH)(L)]	−5.1(1)
	$[Co(OH)_2(L)]^-$	−14.84(2)
Ni^{2+}	$[Ni(HL)]^{2+}$	11.0(1)
	$[Ni(L)]^+$	5.580(7)
	$[Ni(L)_2]$	9.41(2)
	$[Ni(OH)(L)_2]^-$	−1.46(4)
Cu^{2+}	$[Cu(HL)]^{2+}$	12.71(5)
	$[Cu(L)]^+$	7.64(1)
	$[Cu(HL)(L)]^+$	19.79(3)
	$[Cu(L)_2]$	13.05(2)
	$[Cu(OH)(L)_2]^-$	3.07(4)
	$[Cu(OH)_2(L)_2]^{2-}$	−8.66(3)
Zn^{2+}	$[Zn(HL)]^{2+}$	10.6(1)
	$[Zn(L)]^+$	4.12(2)
	$[Zn(L)_2]$	7.53(6)
	$[Zn(OH)(L)_2]^-$	−1.07(9)
	$[Zn(OH)_2(L)_2]^{2-}$	−10.6(1)

[a] Values in parenthesis are standard deviations given by OPIUM.

Solution studies

The ligand possesses three protonation sites and we were able to determine all the corresponding protonation (dissociation) constants (Table 5). Basicities of amino groups (pK_A 8.51 and 7.07) show that the one value is higher and the other is lower than those determined for simple (aminomethyl)phosphinic acids (8.07–8.43).[21] Nevertheless, the found basicity is much lower than that of glycine (9.56)[40] or of (aminomethyl)phosphonic acid (10.05).[40] The values indicate that the electron-withdrawing effect of phosphinate efficiently decreases the amine basicity even in the case of two amino groups in a molecule. In comparison with propane-1,3-diamine (10.52 and 8.74),[40] the constants observed for HL are more close to each other. This can be explained by the presence of the negatively charged phosphinate group between the positively charged amino groups, releasing electrostatic repulsion. The phosphinate group is protonated only at low $-\log[H^+]$ and the value is comparable with those determined for the phosphinic acid analogues of glycine[21] and Gly–Gly.[23] The diprotonated form of the ligand is stable in a wide region of $-\log[H^+]$ up to physiological pH.

In all the systems studied the expected species $[M(L)]^+$, $[M(L)_2]$ and protonated $[M(HL)]^{2+}$ were found. In addition, hydroxo species [Co(OH)(L)] and $[Co(OH)_2(L)]^-$ were observed

Table 6 Derived stability constants and constants of similar ligands[a]

Ion	Equilibrium	pK_A or log K			
		HL	Gly(P)[b]	Gly($P^{t\text{-Bu}}$)[c]	Gly[d]
H^+	$HL \rightleftharpoons H + L$	8.51	10.05	8.427	9.56
	$H_2L \rightleftharpoons H + HL$	7.07	5.39	1.204	2.36
	$H_3L \rightleftharpoons H + H_2L$	0.77	0.4		
Co^{2+}	$[Co(HL)] \rightleftharpoons H + [Co(L)]$	6.30	7.34		
	$Co + L \rightleftharpoons [Co(L)]$	4.07	4.45	3.17	4.67
	$[Co(L)] + L \rightleftharpoons [Co(L)_2]$	2.72	3.64		3.79
Ni^{2+}	$[Ni(HL)] \rightleftharpoons H + [Ni(L)]$	5.4	6.44		
	$Ni + L \rightleftharpoons [Ni(L)]$	5.58	5.25	3.62	5.78
	$[Ni(L)] + L \rightleftharpoons [Ni(L)_2]$	3.83	3.73	2.65	4.80
Cu^{2+}	$[Cu(HL)] \rightleftharpoons H + [Cu(L)]$	5.07	4.44		
	$[Cu(HL)(L)] \rightleftharpoons H + [Cu(L)_2]$	6.74			
	$Cu + L \rightleftharpoons [Cu(L)]$	7.64	8.12	5.37	8.12
	$[Cu(L)] + L \rightleftharpoons [Cu(L)_2]$	5.41	6.50	0.90	6.88
Zn^{2+}	$[Zn(HL)] \rightleftharpoons H + [Zn(L)]$	6.5	6.72		
	$Zn + L \rightleftharpoons [Zn(L)]$	4.12	5.00		4.96
	$[Zn(L)] + L \rightleftharpoons [Zn(L)_2]$	3.41			4.23

[a] Charges are omitted for simplicity. [b] Gly(P) (aminomethyl)phosphonic acid (ref. 40). [c] Gly($P^{t\text{-Bu}}$) = aminomethyl(*t*-butyl)phosphinic acid (the most basic of the simple alkyl(aminomethyl)phosphinic acids, ref. 21). [d] Gly glycine (ref. 40).

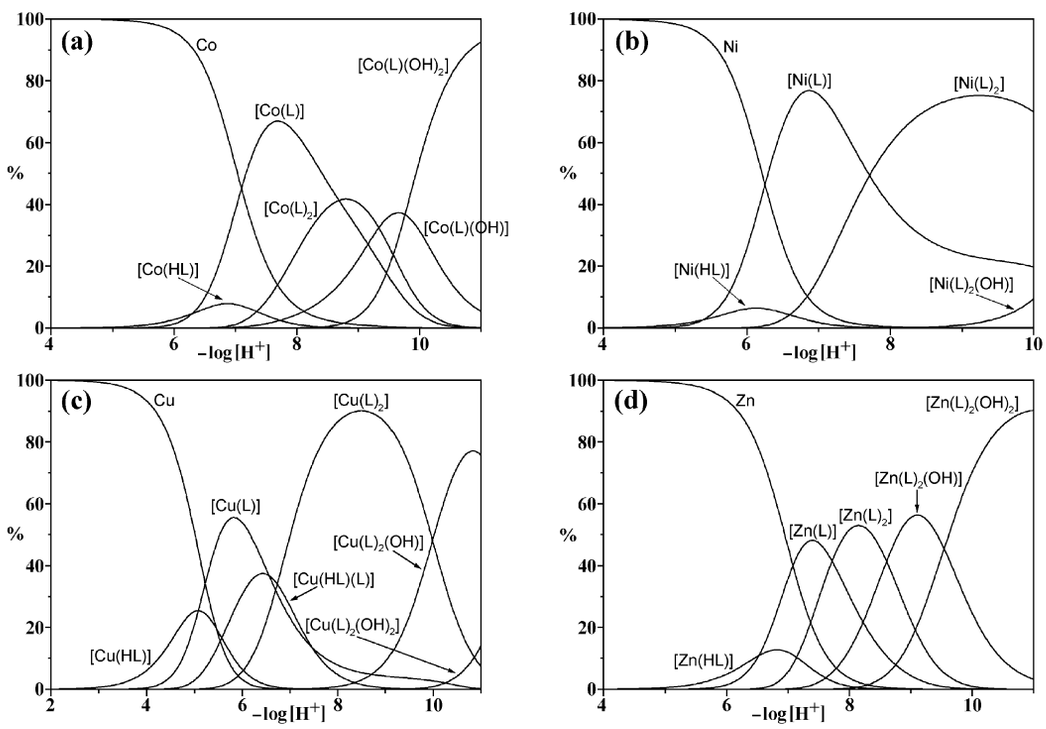


Fig. 2 Distribution diagrams of (a) Co^{2+}–HL (c_L = 0.004 mol dm^{-3}, c_{Co} = 0.001 mol dm^{-3}); (b) Ni^{2+}–HL (c_L = 0.004 mol dm^{-3}, c_{Ni} = 0.002 mol dm^{-3}); (c) Cu^{2+}–HL (c_L = 0.004 mol dm^{-3}, c_{Cu} = 0.002 mol dm^{-3}) and (d) Zn^{2+}–HL (c_L = 0.004 mol dm^{-3}, c_{Zn} = 0.001 mol dm^{-3}).

in the system with Co(II), while, in the Zn(II) and Cu(II) systems, the $[M(OH)(L)_2]^-$ and $[M(OH)_2(L)_2]^{2-}$ were identified and in Ni(II) the $[Ni(OH)(L)_2]^-$ was only confirmed. As expected, the formation of the hydroxo complexes is the easiest for zinc(II) and disadvantageous for nickel(II).

Complexation starts in dependence on a metal ion from $-\log[H^+] = 4$ (Cu(II)) to 6 (Co(II)) with formation of both the protonated $[M(HL)]^{2+}$ and non-protonated $[M(L)]^+$ species (Fig. 2). The $[M(HL)]^{2+}$ is present only in a very low concentration, except for the Cu^{2+} system where its abundance is about 20% (M : L ratio 1 : 1). On the basis of comparison of pK_A of the ligand and the protonated complexes, it is evident that in the $[M(HL)]^{2+}$ species one amino group is coordinated and the other is protonated (Tables 5 and 6). In $[M(L)]^+$, coordination of both the amino groups is assumed. Their stability constants decrease in the expected order Cu(II) > Ni(II) > Zn(II) > Co(II) and are lower than that found for propylene-1,3-diamine,[40] because of lower basicity of the amino groups. In systems with the molar ratios metal : ligand = 1 : 2 and higher, species $[M(L)_2]$ were found with high abundances. Their stability constants also increase in the expected order. In these species, coordination of four amino groups from two ligand molecules is also assumed. Positions of the absorption bands in the visible region for $[Ni(L)_2]$ (366 and 597 nm) and $[Cu(L)_2]$ (616 nm) correspond to those observed for the complexes with common amino acids. This points to the mixed amine and (phosphinate-*O*)/H_2O coordination spheres in both the species with four nitrogen atoms presumably in the equatorial plane (see below for the structure of Ni(II) complex). The phosphinate groups could be also coordinated. On the other hand, easy formation of the

hydroxo-species $[M(OH)(L)_2]^-$ and $[M(OH)_2(L)_2]^{2-}$ at pH ~8 would indicate coordination of water molecules instead of the phosphinate group in the neutral region.

To confirm or to exclude the phosphinate coordination to the central ion, ^{31}P and ^1H NMR titrations of the ligand solution in the absence or presence of Zn(II) in molar ratio M : L = 1 : 2 were carried out; the results are shown in Fig. 3. A comparison of ^{31}P NMR titration curves of both the solutions shows no differences in the chemical shifts in the range from strong acid to pH about 4. The small differences in the pH range 4–8 correspond to the deprotonation and coordination of amino groups. In contrast to the ^{31}P, the ^1H NMR spectra are more sensitive. The changes in ^1H NMR spectra in dependence on pH of the free ligand (Fig. 3) correspond at pH < 1 to the deprotonation of phosphinic acid group and at pH > 6 to deprotonation of amino groups. In the presence of Zn(II), we can see analogous changes due to deprotonations; however, the deprotonations are slightly shifted to the acid region. The chemical shifts also moved to lower values in comparison with the free acid. There is no difference in the chemical shifts between the solution of the free ligand and its solution in the presence of zinc(II) in 2 M and 6 M HCl and, thus, only in this region the phosphinic acid group is fully protonated and non-coordinated. The large differences between the values observed for the free ligand and its solution with Zn(II) pH = 0–5 indicate coordination of the phosphinate group. The changes above pH 5 correspond to the coordination of amino groups.

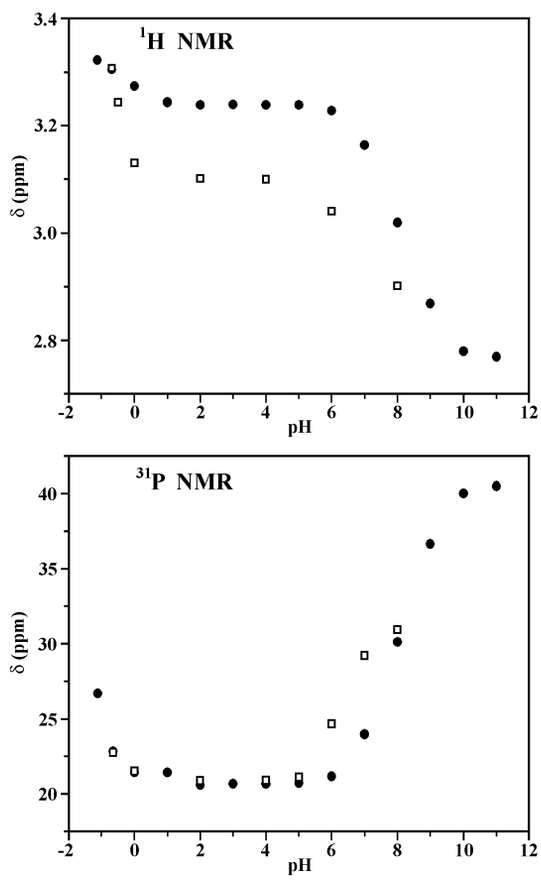
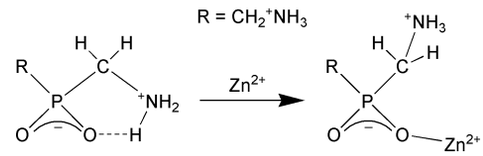


Fig. 3 NMR titration of HL in the absence (full circles ●) or presence of Zn(II) (0.5 equiv., open squares □).

Explanation of the mentioned low sensitivity of phosphorus nuclei and high sensitivity of methylene hydrogen atoms to coordination results from the following considerations. It is known that a deprotonated phosphinate or phosphonate group interacts with a protonated amino group inside of a molecule of both the acids and the largest changes in ^{31}P NMR shifts are caused by deprotonation of amino groups.[41] Thus, the



Scheme 2

interaction of the negatively charged phosphinate with positive charge of metal ion, instead of the protonated amine, does not result in any significant changes in shielding of phosphorus nuclei. On the other hand, as shown in Scheme 2 the methylene hydrogen atoms in non-coordinated species are directed outside the phosphinate group interacting with amino group(s). If the phosphinate group is bound to a positively charged metal ion, the protonated amino group turns due to the charge repulsion. Then, the methylene hydrogen atoms are close to the metal ion and thus are influenced with its charge. The orientation of methylene group in the structure of all-*trans*-$[CoCl_2(H_2L\text{-}O)_2(H_2O)_2]Cl_2$ is also shown in Fig. 4. The X-ray structure investigation of all-*trans*-$[MCl_2(H_2L\text{-}O)_2(H_2O)_2]Cl_2$ (see below) shows the ionic interaction of metal ions with the phosphinate group leaving both amino groups protonated and thus supports the suggested coordination in acid region for all the divalent metal ions studied. This fact is relevant for biological studies as similar phosphinate inhibitors were found to bind to a metal ion in the active centre of enzymes.[42] The HL is a tridentate ligand and, thus, both the amino and phosphinate groups are available to form two five-membered rings in the coordination sphere of $[M(L)]^+$ and $[M(L)_2]$ species with divalent ions. However, the X-ray structures (see below) indicate that this coordination arrangement seems to be disadvantageous due to the phosphinate size and its rigidity and, therefore, HL can be coordinated only through amino groups which form a six-membered ring or through a single amino and phosphinate groups, which form only one five-membered ring.

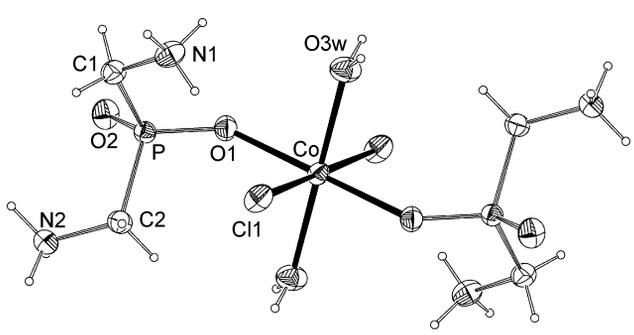


Fig. 4 Molecular structure of all-*trans*-$[CoCl_2(H_2L\text{-}O)_2(H_2O)_2]^{2+}$ cation with atom numbering scheme.

Considering the hard/soft character of the ions and ligand, it is well known that the phosphonate/phosphinate group is a hard donor. This follows from correlation of the stability constants found for carboxylic and phosphonic amino acids because the relative stabilization (ratio of stability constants of these amino acids) decreased in the order Cu(II) > Zn(II) ≈ Co(II) > Ni(II).[6] The highest relative stabilization of copper(II) is due mainly to a high basicity of the amino group(s) and a similar affinity to the phosphonate group to that of zinc(II) and cobalt(II).[6] The nickel(II) ion is relatively soft and shows a much lower affinity to hard phosphinate as follows from a comparison of the other ions studied. Stability constants determined for $[Cu(L)]^+$, $[Cu(L)_2]$, $[Ni(L)]^+$ and $[Ni(L)_2]$ are relatively high and well compared with those for other phosphorus-containing amino acids (Table 4). Therefore, we assume a dominant coordination only through both the nitrogen atoms and formation of six-membered chelates (see also UV-VIS

Table 7 Geometry of the centrosymmetric coordination shell of M(II) (inversion center in atom M) and of the phosphinate group in all-*trans*-$[MCl_2(H_2L\text{-}O)_2(H_2O)_2]^{2+}$ cations (interatomic distances in Å, bond angles in °)

Parameter	Ca	Mn	Co	Ni	Cu	Zn	Cd
M–Cl(1)	2.6818(3)	2.5173(5)	2.4536(4)	2.3968(6)	2.3402(4)	2.4096(3)	2.536(4)
M–O(3w)	2.355(1)	2.222(1)	2.125(2)	2.090(2)	2.382(1)	2.151(1)	2.336(4)
M–O(1)	2.3020(9)	2.165(1)	2.101(1)	2.081(1)	1.9724(9)	2.1150(9)	2.282(4)
O(1)–M–Cl(1)	88.38(2)	87.78(3)	87.76(3)	87.26(4)	87.58(3)	87.23(3)	87.0(1)
O(1)–M–O(3w)	91.85(3)	92.99(5)	92.59(5)	92.94(6)	94.60(4)	93.27(4)	93.9(2)
Cl(1)–M–O(3w)	93.00(3)	90.25(4)	89.68(4)	90.47(4)	89.69(2)	89.96(3)	91.3(1)
M–O(1)–P	140.90(5)	142.04(7)	142.58(7)	141.54(9)	141.56(6)	141.26(6)	138.7(2)
P–O(1)	1.5111(9)	1.509(1)	1.512(1)	1.512(2)	1.5169(9)	1.513(1)	1.517(4)
P–O(2)	1.4988(9)	1.498(1)	1.497(1)	1.501(2)	1.499(1)	1.498(1)	1.486(4)
P–C(1)	1.828(1)	1.829(2)	1.823(2)	1.824(2)	1.826(1)	1.827(1)	1.823(6)
P–C(2)	1.825(1)	1.829(2)	1.824(2)	1.828(2)	1.828(1)	1.827(1)	1.824(2)
O(1)–P–O(2)	117.53(5)	117.19(7)	117.14(7)	116.81(9)	115.80(6)	117.06(6)	116.7(2)
O(1)–P–C(1)	107.52(5)	107.77(7)	108.15(7)	108.42(8)	109.33(6)	108.07(6)	107.9(2)
O(1)–P–C(2)	107.68(5)	107.95(7)	108.17(7)	108.25(9)	107.44(6)	108.18(6)	108.0(3)
O(2)–P–C(1)	108.88(5)	108.39(7)	107.98(8)	109.22(9)	108.52(6)	107.91(6)	108.8(3)
O(2)–P–C(2)	108.77(5)	109.09(7)	109.05(7)	107.68(7)	108.54(6)	109.05(6)	108.8(2)
C(1)–P–C(2)	105.85(6)	105.88(8)	105.78(8)	105.9(1)	106.86(7)	106.04(7)	106.1(3)

spectra). This coordination mode was found in the structure of *trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$] (see below). In [Zn(L)]$^+$ and [Co(L)]$^+$, the same considerations lead to the suggestion that the ligand is coordinated mainly by a single amino group and the phosphinate group. Such an explanation is supported by isolation of a zinc(II) complex where the ligand bridges the metal ions through the other amino group (see below).

Synthesis of complexes and their crystal structures

From acid solutions obtained by dissolution of HL·HCl and MCl_2, where M are the metals studied above (Co, Ni, Cu and Zn), complexes of the general formula all-*trans*-$[MCl_2(H_2O)_2(H_2L\text{-}O)_2]Cl_2$ easily crystallize. The same complexes were obtained with other divalent ions such as Ca(II), Mn(II) and Cd(II). The X-ray structural investigation has shown that all the complexes are isostructural. The octahedral coordination sphere of the metal ions is formed by two oxygen atoms (mutually *trans*) of two phosphinate groups, two molecules of water (mutually *trans*) and two chloride anions. The nitrogen atoms were found protonated and non-coordinated. A representative molecular structure is shown in Fig. 4 and selected bond lengths and angles are listed in Table 7. From the table, it is clear that the bond lengths M–O_P, M–O_w and M–Cl increase with the increasing ionic radius of the metal ions, except for M–O_w in the Cu(II) complex due to the Jahn–Teler distortion. This structural motif with protonated amines and coordinated phosphinates was also observed in the manganese(II) complex of (aminomethyl)methylphosphinic acid (HL′) all-*trans*-[MnCl$_2$(HL′-*O*)$_2$(H$_2$O)$_2$] (ref. 14) and in the tetraaqua complex of Co(II) with piperazine-1,4-diylbis-(methylphosphinic) acid.[19] In an analogous complex of HL′, the Mn–O(1) distance is slightly shorter (2.141 Å) and the O(1)–P–O(2) angle is less open (113.8°).[14] Surprisingly, the bromide analog of the above complex of HL′ is polymeric with –Mn–(O–P–O)$_2$–Mn– eight-membered rings and non-coordinated bromide anions.[13]

Crystals suitable for X-ray structure determination of the Ni(II) and Zn(II) complexes with coordinated amines were prepared in a reproducible way only after carefully adjusting the pH to a value that was estimated from the distribution diagrams. It was necessary to remove foreign anions and, therefore, the complexes were prepared from the zwitterionic form of the ligand and freshly precipitated metal hydroxides. We tested this and modified procedures also for the preparation of Co(II) and Cu(II) complexes. For Co(II), we were unable to get any defined solids and the copper(II) complex was obtained only as a microcrystalline powder.

Molecular structures of the nickel(II) and zinc(II) complexes are shown in Figs. 5 and 6, respectively. Selected bond lengths and angles are listed in Table 8. In the centrosymmetric *trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$], the metal ion is chelated by four amino nitrogen atoms of two ligand molecules forming two six-membered *N*,*N*-chelate rings in the equatorial plane and the octahedron is completed with two water molecules in apical positions (Fig. 5). The phosphinate group is not coordinated, P–O(11) and P–O(12) lengths are virtually the same and both oxygen atoms form hydrogen bonds to the coordinated molecule of water in the neighbouring molecule, O(12) ··· O(13w) = 2.65 Å, and to the solvate water, O(11) ··· O99 = 2.75 Å.

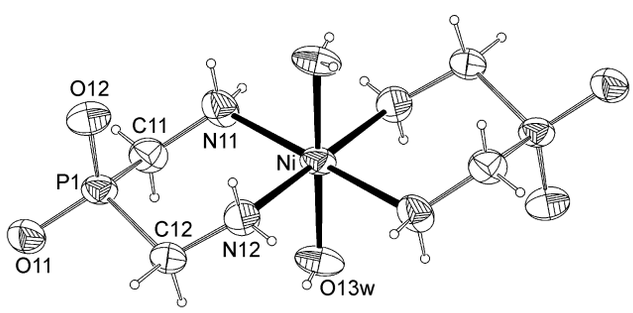


Fig. 5 Molecular structure of *trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$] with atom numbering scheme.

Zinc(II) in polymeric [Zn(L)$_2$] forms the octahedral coordination sphere with the centre of symmetry on the central ion (Fig. 6). The coordination sphere consists of two phosphinate oxygen atoms O(11) and two amino nitrogen atoms N(11) (*trans* to each other) of two different ligand molecules in the equatorial plane forming a five-membered *N*,*O*-chelate. The octahedron is completed with two additional amino nitrogen atoms N(12) of the two other ligand molecules which are bound to two neighbouring zinc(II) ions forming an indefinite chain. The bond lengths in the expected range are listed in Table 8. The P–O(11) (to the coordinated oxygen) and P–O(12) (to the non-coordinated oxygen) bond lengths are practically the same. This indicates only ionic interaction of phosphinate with the central ion. The Zn–O(11) length (2.157 Å) in this complex is slightly longer than the length of the corresponding bond present in "acidic" complex (2.115 Å, Table 7). The O(12) shows three weak hydrogen bonds (2.77–2.93 Å) to the molecule of

Table 8 Bond lengths (Å) and angles (°) in *trans*-*O*,*O*-[Ni(L-*N*,*N*)$_2$(H$_2$O)$_2$]·2H$_2$O, [Zn(L)$_2$]·2H$_2$O and *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H$_2$O

Parameter	[Ni(L)$_2$(H$_2$O)$_2$]·2H$_2$O	[Zn(L)$_2$]·2H$_2$O	[Co(L)$_2$](ClO$_4$)·H$_2$O
M–N(11)	2.136(5)	2.132(1)	1.982(2)
M–N(12)	2.124(5)	2.264(1)[c]	1.978(2)
M–O(11)	2.110(4)[a]	2.1566(9)	1.898(1)
M–N(21)	[b]	[b]	1.968(2)
M–N(22)	[b]	[b]	1.982(2)
M–O(21)	[b]	[b]	1.914(1)
N(11)–M–N(12)	92.9(2)	89.63(4)	87.13(8)
N(11)–M–O(11)	91.9(2)[a]	84.98(4)	88.37(8)
N(11)–M–N(21)	[b]	[b]	177.80(7)
N(11)–M–N(22)	[b]	[b]	93.63(8)
N(11)–M–O(21)	[b]	[b]	92.50(7)
N(12)–M–O(11)	93.2(2)[a]	91.43(4)[c]	89.64(7)
N(12)–M–N(21)	[b]	[b]	92.41(8)
N(12)–M–N(22)	[b]	[b]	177.93(7)
N(12)–M–O(21)	[b]	[b]	89.72(7)
O(11)–M–N(21)	[b]	[b]	88.74(7)
O(11)–M–N(22)	[b]	[b]	92.30(7)
O(11)–M–O(21)	[b]	[b]	178.89(6)
N(21)–M–N(22)	[b]	[b]	86.92(8)
N(21)–M–O(21)	[b]	[b]	90.38(6)
N(22)–M–O(21)	[b]	[b]	88.33(6)
M–O(11)–P(1)			104.52(7)
M–O(21)–P(2)			103.53(7)
P(1)–O(11)	1.506(4)	1.531(1)	1.546(1)
P(1)–O(12)	1.501(4)	1.5123(9)	1.482(2)
P(1)–C(11)	1.801(6)	1.821(1)	1.815(2)
P(1)–C(12)	1.810(6)	1.823(1)	1.818(2)
O(11)–P(1)–O(12)	118.1(2)	116.81(5)	116.70(8)
O(11)–P(1)–C(11)	108.6(3)	106.50(5)	101.98(9)
O(11)–P(1)–C(12)	107.8(2)	108.59(5)	101.82(9)
O(12)–P(1)–C(11)	107.6(3)	109.47(6)	116.2(1)
O(12)–P(1)–C(12)	108.2(2)	108.64(5)	114.8(1)
C(11)–P(1)–C(12)	105.9(3)	106.34(6)	103.3(1)
P(2)–O(21)	[b]	[b]	1.541(1)
P(2)–O(22)	[b]	[b]	1.492(1)
P(2)–C(21)	[b]	[b]	1.809(2)
P(2)–C(22)	[b]	[b]	1.815(2)
O(21)–P(2)–O(22)	[b]	[b]	116.82(8)
O(21)–P(2)–C(21)	[b]	[b]	101.9(1)
O(21)–P(2)–C(22)	[b]	[b]	102.87(9)
O(22)–P(2)–C(21)	[b]	[b]	115.2(1)
O(22)–P(2)–C(22)	[b]	[b]	115.1(1)
C(21)–P(2)–C(22)	[b]	[b]	103.0(1)

[a] Coordinated H$_2$O molecule. [b] Centrosymmetric coordination shell. [c] Nitrogen atom from further ligand molecule in the endless polymeric chain.

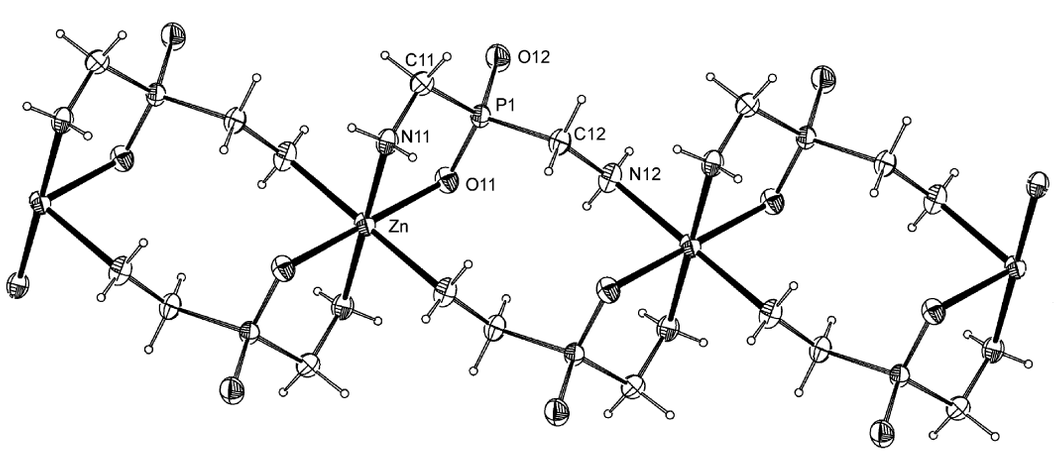


Fig. 6 Molecular structure of [Zn(L)$_2$] with atom numbering scheme.

water and to the amino group of a neighbouring molecule. For comparison, the solid-state structure of zinc(II) complex with (aminomethyl)methylphosphinic acid (HL′), [Zn(HL′-*O*)$_2$Cl$_2$] consists of indefinite chains formed by zinc atoms and bridging ligands coordinated through oxygen atoms only (to different zinc atom).[15] The amine group is protonated and a tetrahedral

arrangement of Zn(II) is completed by two chloride anions. The Zn–O bond distances in the complex of HL′ are significantly shorter (1.970 and 1.928 Å).[15]

The expected coordination sphere formed by two molecules of the ligand coordinated to the same ion through phosphinate and also through both amino groups were observed only for Co(III). The *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$](ClO$_4$)·H$_2$O was prepared by the reaction of the cobalt(III) carbonate complex with ligand in the presence of HClO$_4$. Unfortunately, a large proportion of trivalent cobalt was reduced to the divalent one during the reaction. The complex was purified on a carboxylic cation exchanger. Its water eluate was concentrated and the desired complex was obtained on slow evaporation in air. In the *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$]$^+$, the ligand is facially coordinated with all nitrogen atoms in an equatorial plane (Fig. 7). The octahedron is axially flattened due to shorter Co–O bond lengths (1.898 and 1.913 Å) than Co–N ones (1.968–1.982 Å) (Table 8). Bond angles around the central ion are deformed because the ligand is too small to reach vertexes of a regular octahedron (up to 7°). As expected, the P–O length of non-coordinated oxygen is significantly shorter than the other. Perchlorate anions are highly disordered and, like water molecules, participate in the network of intermolecular hydrogen bonds stabilizing the crystal structure. In the UV-VIS spectrum of the *fac*-*N*,*N*,*O*-*trans*-*O*,*O*′-[Co(L-*N*,*N*,*O*)$_2$]$^+$, two bands at 368 nm ($^1T_{2g}$) and 510 nm ($^1T_{1g}$) only were found. Surprisingly, no splitting or significant broadening of the $^1T_{1g}$ level, typical for *trans* isomers, was observed.[45] It corresponds with the short Co–O bond lengths mentioned above and, therefore, the geometry is more similar to N_6 or *cis*-N_4O_2 species. The parameters 10 *Dq* and *B*, 21 500 and 475 cm^{-1}, are in the range observed for similar Co(III) complexes of macrocyclic ligands derived from cyclam with two methylphosphonate pendant arms.[46]

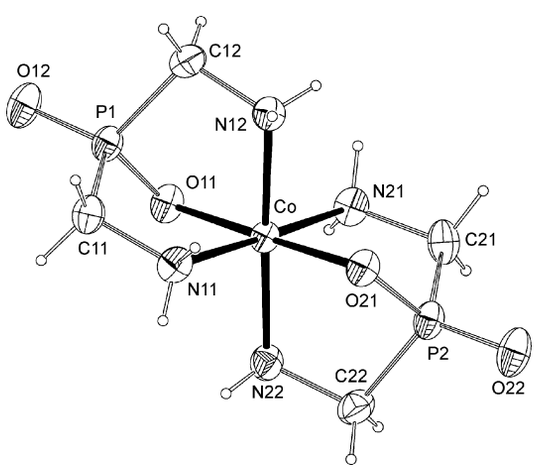


Fig. 7 Molecular structure of *fac*-*N*,*N*,*O*-*trans*-*O*,*O*'-[Co(L-*N*,*N*,*O*)$_2$]$^+$ with atom numbering scheme.

Conclusions

Comparing molecular structures of [Zn(L)$_2$], [Ni(L)$_2$], and [Co(L)$_2$]$^+$ species, we found three different coordination modes in dependence on the properties of the central ions. We assume that the ligand HL is too small and rigid to possess the octahedral apexes and to easily form two chelate rings. The rigidity is only overcome in [Co(L)$_2$]$^+$ due to the covalent contribution of small Co(III) and short Co–O and Co–N bonds. In the Zn(II) and Ni(II) complexes, the M–O and M–N bond lengths are larger (see Table 8) and, therefore, an analogous coordination sphere is not advantegous. Both the ions differ in their soft/hard character and this results in different coordination ability towards phosphinate. Zinc(II) forms polymeric structure and the phosphinate group is non-coordinated in the nickel(II) complex. From this point of view, the –N–CH$_2$–P(O)(OH)–CH$_2$–N– should be selective for complexation of small ions. A typical feature of complexation for most phosphinic and aminophosphinic acids is the formation of the eight-membered [M–(O–P–O)$_2$–M] ring, in which two phosphinate groups link two metal ions forming dimeric[16,21,43] or polymeric motifs.[21,44] This eight-membered ring is also formed in complexes with coordinated amines.[17,21,43] The absence of the ring in the structures presented is surprising, probably corresponding with suppression of the coordination ability of the phosphinate group between two aminomethyl groups capable of forming a six-membered chelate ring. From acidic solutions, complexes with another coordinating mode were prepared. Coordination through phosphinate oxygen atoms confirms the ability of the phoshinic acid group to bind metal ions even at strongly acidic pH. The results presented in this paper help in understanding the behaviour of phosphorus acid enzyme inhibitors as well as of more complex ligands such as macrocycles containing phosphorus acid pendant arms.

Acknowledgements

We thank Dr J. Ederová (Institute of Chemical Technology, Prague) for TG measurements. This work was supported by the Ministry of Education of the Czech Republic (grant CEZJ 07/98:143100011), the Grant Agency of the Czech Republic (grant 203/02/0493 and 203/03/0168) and EU COST D18.

References

1 P. Kafarski and B. Lejczak, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1991, **63**, 193.
2 *Aminophosphonic and Aminophosphinic Acids. Chemistry and Biological Activity*, ed. V. P. Kukhar and H. R. Hudson, Wiley, Chichester, 2000 and references cited therein.
3 J. Buchardt, M. Ferreras, C. Krog-Jensen, J.-M. Delaissé, N. T. Foged and M. Meldal, *Chem. Eur. J.*, 1999, **5**, 2877; V. Dive, J. Cotton, A. Yiotakis, A. Michaud, S. Vassiliou, J. Jiráček, G. Vazeux, M.-T. Chauvet, P. Cuniasse and P. Corvol, *Proc. Natl. Acad. Sci. USA*, 1999, **96**, 4330.
4 J. Ong, D. I. B. Kerr, H. Bittiger, P. C. Waldmeier, P. A. Baumann, N. G. Cooke, S. J. Mickel and W. Froestel, *Eur. J. Pharmacol.*, 1998, **362**, 27.
5 H. Chen, F. Noble, B. P. Roques and M.-C. Fournié-Zaluski, *J. Med. Chem.*, 2001, **44**, 3523.
6 T. Kiss and I. Lázár, in *Aminophosphonic and Aminophosphinic Acids. Chemistry and Biological Activity*, ed. V. P. Kukhar and H. R. Hudson, Wiley, 2000, ch. IX, pp. 285–326; I. Lukeš, J. Kotek, P. Vojtíšek and P. Hermann, *Coord. Chem. Rev.*, 2001, **216–217**, 287.
7 T. Kiss, J. Balla, G. Nagy, H. Kozlowski and J. Kowalik, *Inorg. Chim. Acta*, 1987, **138**, 25; T. Kiss, E. Farkas and H. Kozlowski, *Inorg. Chim. Acta*, 1989, **155**, 281; E. Matczak-Jon and W. Wojciechowski, *Inorg. Chim. Acta*, 1990, **173**, 85; E. Matczak-Jon, B. Kurzak, W. Sawka-Dobrowolska, P. Kafarski and B. Lejczak, *J. Chem. Soc., Dalton Trans.*, 1996, 3455; E. Matczak-Jon, B. Kurzak, W. Sawka-Dobrowolska, B. Lejczak and P. Kafarski, *J. Chem. Soc., Dalton Trans.*, 1998, 161; B. Kurzak, E. Matczak-Jon and M. Hoffmann, *J. Coord. Chem.*, 1998, **43**, 243; E. Matczak-Jon, W. Sawka-Dobrowolska, D. Dobrzynska and M. Hoffmann, *Polyhedron*, 1999, **18**, 2169.
8 G. I. Sinyavskaya, *Koord. Khim.*, 1991, **17**, 1599; G. I. Sinyavskaya, *Koord. Khim.*, 1992, **18**, 899; P. Fenot, J. Darriet, C. Garrigou-Lagrange and A. Cassaigne, *J. Mol. Struct.*, 1978, **43**, 49; T. Glowiak, W. Sawka-Dobrowolska, B. Jezowska-Trzebiatowska and A. Antonow, *Inorg. Chim. Acta*, 1980, **45**, L105; T. Glowiak, W. Sawka-Dobrowolska, B. Jezowska-Trzebiatowska and A. Antonow, *J. Crystallogr. Mol. Struct.*, 1980, **10**, 1; S. Drumel, P. Janvier, D. Deniaud and B. Bujoli, *J. Chem. Soc., Chem. Commun.*, 1995, 1051; S. J. Hartmann, E. Todorov, C. Cruz and S. C. Sevov, *Chem. Commun.*, 2000, 1213.
9 M. Hariharan, R. J. Motekaitis and A. E. Martell, *J. Org. Chem.*, 1975, **40**, 470; T. Kiss, E. Farkas, H. Kozlowski, Z. Siatecki, P. Kafarski and B. Lejczak, *J. Chem. Soc., Dalton Trans.*, 1989, 1053.
10 P. Hermann and I. Lukeš, *J. Chem. Soc., Dalton Trans.*, 1995, 2605; P. Hermann, I. Lukeš, P. Vojtíšek and I. Císařová, *J. Chem. Soc., Dalton Trans.*, 1995, 2611.

11 L. Bláha, I. Lukeš, J. Rohovec and P. Hermann, *J. Chem. Soc., Dalton Trans.*, 1997, 2621; I. Lukeš, L. Bláha, F. Kesner, J. Rohovec and P. Hermann, *J. Chem. Soc., Dalton Trans.*, 1997, 2629.
12 I. Lukeš, P. Hermann and P. Pech, *Collect. Czech. Chem. Commun.*, 1989, **54**, 653; T. Kiss, E. Farkas, M. Jezowska-Bojczuk, H. Kozlowski and E. Kowalik, *J. Chem. Soc., Dalton Trans.*, 1990, 377; K. B. Yatsimirski, L. B. Tsymbal and E. I. Sinyavskaya, *Zh. Neorg. Khim.*, 1990, **35**, 117; T. Kiss, M. Jezowska-Bojczuk, H. Kozlowski, P. Kafarski and K. Antczak, *J. Chem. Soc., Dalton Trans.*, 1991, 2275; I. Lukeš, K. Bazakas, P. Hermann and P. Vojtíšek, *J. Chem. Soc., Dalton Trans.*, 1992, 939.
13 T. Glowiak and W. Sawka-Dobrowolska, *Acta Crystallogr., Sect. B*, 1977, **33**, 2698.
14 T. Glowiak and W. Sawka-Dobrowolska, *Acta Crystallogr., Sect. B*, 1977, **33**, 2763.
15 Z. Žák, J. Kožíšek and T. Glowiak, *Z. Anorg. Allg. Chem.*, 1981, **477**, 221.
16 W. Sawka-Dobrowolska and T. Glowiak, *Acta Crystallogr., Sect. C*, 1983, **39**, 345.
17 T. Glowiak, *Acta Crystallogr., Sect. C*, 1986, **42**, 62.
18 J. F. Britten, C. J. L. Lock and Z. Y. Wang, *Acta Crystallogr., Sect. C*, 1993, **49**, 881.
19 I. Lukeš, I. Císařová, P. Vojtíšek and K. Bazakas, *Polyhedron*, 1995, **14**, 3163.
20 M. P. Lowe, S. J. Rettig and C. Orvig, *J. Am. Chem. Soc.*, 1996, **118**, 10446.
21 J. Rohovec, I. Lukeš, P. Vojtíšek, I. Císařová and P. Hermann, *J. Chem. Soc., Dalton Trans.*, 1996, 2685.
22 (*a*) K. Bazakas and I. Lukeš, *J. Chem. Soc., Dalton Trans.*, 1995, 1133; (*b*) J. Rohovec, M. Kývala, P. Vojtíšek, P. Hermann and I. Lukeš, *Eur. J. Inorg. Chem.*, 2000, 195.
23 M. Lukáš, M. Kývala, P. Hermann, I. Lukeš, D. Sanna and G. Micera, *J. Chem. Soc., Dalton Trans.*, 2001, 2850.
24 T. R. Varga, R. Király and E. Brücher, *ACH–Models Chem.*, 1999, **136**, 431; L. Xu, S. J. Rettig and C. Orvig, *Inorg. Chem.*, 2001, **40**, 3734.
25 B. Song, T. Storr, S. Liu and C. Orvig, *Inorg. Chem.*, 2002, **41**, 685; S. Aime, C. Cavallotti, E. Gianolio, G. B. Giovenzana, G. Palmisano and M. Sisti, *Tetrahedron Lett.*, 2002, **43**, 8387.
26 V. Kubíček, P. Hermann, I. Lukeš, J. Kotek, P. Vojtíšek and I. Císařová, *J. Inorg. Biochem.*, 2001, **86**, 301.
27 G. W. Pucher and T. B. Johnson, *J. Am. Chem. Soc.*, 1922, **44**, 817.
28 H. F. Bauer and W. C. Drinkard, *Inorg. Synth.*, 1966, **8**, 202.
29 C. F. Baes Jr. and R. E. Mesmer, *The Hydrolysis of Cations*, Wiley, New York, 1976.
30 M. Kývala and I. Lukeš, *International Conference, Chemometrics '95*, p. 63, Pardubice, Czech Republic, 1995; full version of "OPIUM" is available (free of charge) on http://www.natur.cuni.cz/~kyvala/opium.html.
31 Z. Otwinovski and W. Minor, *HKL Denzo and Scalepack Program Package*, Nonius BV, Delft 1997;; for a reference see: Z. Otwinovski and W. Minor, *Methods Enzymol.*, 1997, **276**, 307.
32 A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi and G. Polidori, *J. Appl. Crystallogr.*, 1994, **27**, 435.
33 G. M. Sheldrick, *SHELXL-97, Program for refinement of crystal structures*, University of Göttingen, Germany, 1997.
34 A. L. Spek, *PLATON—A Multipurpose Crystallographic Tool*; see: http://www.cryst.chem.uu.nl/platon/.
35 L. Maier, *J. Organomet. Chem.*, 1979, **178**, 157.
36 M. Bujard, V. Gouverneur and C. Mioskowski, *J. Org. Chem.*, 1999, **64**, 2119.
37 K. Issleib, M. Mögelin and A. Balszuweit, *Z. Anorg. Allg. Chem.*, 1985, **530**, 16; E. A. Boyd, M. Corless, K. James and A. C. Regan, *Tetrahedron Lett.*, 1990, **31**, 2933.
38 S. Chen and J. K. Coward, *J. Org. Chem.*, 1998, **63**, 502.
39 (*a*) T. Glowiak and W. Sawka-Dobrowolska, *Acta Crystallogr., Sect. B*, 1977, **33**, 1522; (*b*) F. Kašpárek, Z. Trávnícek, V. Bekárek and J. Marek, *Pol. J. Chem.*, 2002, **76**, 1389.
40 A. E. Martell and R. M. Smith, *Critical Stability Constants*, Plenum Press, New York, 1974–1989, vol. 1–6; *NIST Standard Reference Database 46 (Critically Selected Stability Constants of Metal Complexes)*, version 5.0, 1994.
41 T. G. Appleton, J. R. Hall, A. D. Harris, M. A. Kimlin and I. J. McMahon, *Aust. J. Chem.*, 1984, **37**, 1833; K. Popov, E. Niskanen, H. Rönkkömäki and H. J. Lajunen, *New J. Chem.*, 1999, **23**, 1209; J. Kotek, P. Vojtíšek, I. Císařová, P. Hermann, P. Jurečka, J. Rohovec and I. Lukeš, *Collect. Czech. Chem. Commun.*, 2000, **65**, 1289.
42 F. Grams, V. Dive, A. Yiotakis, I. Yiallouros, S. Vassiliou, R. Zwilling, W. Bode and W. Stöcker, *Nat. Struct. Biol.*, 1996, **3**, 671.
43 F. Cecconi, C. A. Ghilardi, P. Gili, S. Midollini, P. A. L. Luis, A. D. Lozano-Gorrin and A. Orlandini, *Inorg. Chim. Acta*, 2001, **319**, 67; J. Rohovec, P. Vojtíšek, I. Lukeš, P. Hermann and J. Ludvík, *J. Chem. Soc., Dalton Trans.*, 2000, 141.
44 J. S. Haynes, K. W. Oliver, S. J. Rettig, R. C. Thompson and J. Trotter, *Can. J. Chem.*, 1984, **62**, 891; W. V. Cicha, J. S. Haynes, K. W. Oliver, S. J. Rettig, R. C. Thompson and J. Trotter, *Can. J. Chem.*, 1985, **63**, 1055.
45 A. B. P. Lever, *Inorganic Electronic Spectroscopy*, Elsevier, Amsterdam, 1984, pp. 473–505.
46 J. Kotek, I. Císařová, P. Hermann, I. Lukeš and J. Rohovec, *Inorg. Chim. Acta*, 2001, **317**, 324.