DALTON

Co-ordination ability of amino acid oximes. Potentiometric, spectroscopic and structural studies of complexes of 2-cyano-2-(hydroxyimino)acetamide

Tatiana Yu. Sliva,[*,a] **Anna M. Duda,**[b] **Tadeusz Głowiak,**[b] **Igor O. Fritsky,**[a]
Vladimir M. Amirkhanov,[a] **Andrei A. Mokhir**[a] **and Henryk Kozłowski**[*,b]

[a] *Department of Chemistry, Shevchenko University, 252017 Kiev, Ukraine*
[b] *Faculty of Chemistry, University of Wrocław, F. Joliot-Curie 14, 50383 Wrocław, Poland*

X-Ray crystallographic and solution studies have revealed the first examples of complexes of Cu^{2+} and Ni^{2+} with an oxime derivative in which completely deprotonated ligand molecules bind in *trans* position because of the lack of a hydrogen bond between the hydroxyl oxygens which usually stabilises the *cis* positioning.

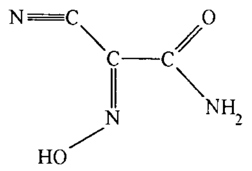
Oximes of amino acids and peptides were shown to be specific and efficient ligands for Cu^{2+} and Ni^{2+} ions.[1,2] The complexes formed are stable and soluble and extensive dimer formation for Cu^{2+}-containing systems is observed at pH >5. The binuclear complex formation results from the two alternative donor centres at the oxime (=N−OH) group (N and O) in the ligands which both have a high affinity for M^{2+} and cannot both co-ordinate to the same metal ion. The co-ordination properties of oxime analogues of amides or peptides are, to a large extent, governed by the presence of a planar RC(=NOH)CONH framework which may allow the formation of different chelate rings with virtually no change in conformation. The formation of bis complexes of the $MH_{-1}L_2$ type having *cis* ligand co-ordination stabilised by hydrogen bonding between the oxime oxygens is the most characteristic feature of complexes with amino acid or amide analogues. The deprotonation of the first proton of the bis complex of Ni^{2+} has a critical impact on binding ability of the neighbouring nitrogen. In the case of 2-(hydroxyimino)propanamide complexes the NiL_2 species having both oxime hydroxyl groups protonated is octahedral, while its deprotonated product $NiH_{-1}L_2$ is square-planar. There is no change of binding groups during this deprotonation process. The only change possible is the distinct shift of electron density from the deprotonated hydroxyl group of the oxime moiety towards the neighbouring oxime nitrogen. The exceptional stability of the $NiH_{-1}L_2$ complex with the amide ligand is also seen in the log *K* value (7.64) of the deprotonation reaction $NiL_2 \longrightarrow NiH_{-1}L_2$ when compared to that for deprotonation of free amide (9.87) or removal of the proton from the $NiH_{-1}L_2$ species (10.54). The same behaviour is observed for the acidic form of the oxime ligand.

In this work the binding ability of a compound having a strongly electron-withdrawing cyano group at the α-carbon of an amide oxime is studied. This modification may have a critical impact on the role of hydrogen bonding in co-ordination of oxime by affecting the basicity of the oxime hydroxyl group.

Experimental

Synthesis of 2-cyano-2-(hydroxyimino)acetamide (H_2chia)

The oxime was synthesized by treating cyanocetamide (Fluka) with sodium nitrite in aqueous solution in the presence of acetic acid; the sodium salt formed was then treated with hydrochloric acid in order to obtain the free oxime as described elsewhere,[3] the purity being checked by elemental analysis and NMR spectroscopy, [Found (Calc. for $C_3H_3N_3O_2$): C, 31.55: (31.85); H, 2.9 (2.65); N, 37.1 (37.15)%]. Potentiometry also showed the oxime to be near 100% pure and a very good fit was obtained between calculated and experimental titration curves with alkali over the whole pH range.



Potentiometric studies

Titrations involved an ionic background of 0.1 mol dm^{-3} KNO_3, a pro-ligand concentration of 3×10^{-3} mol dm^{-3} and metal-to-pro-ligand ratios of 1 : 1, 1 : 2, 1 : 3 and 1 : 5. Stability constants for the complexes of H^+, Cu^{2+} and Ni^{2+} were calculated from titrations carried out using total volumes of 2 cm^3. Alkali was added from a 0.100 cm^3 micrometer syringe which had been calibrated by weight titrations and the titration of standard materials. The pH-metric titrations were performed at 25 °C using a MOLSPIN automatic titration system with a microcombined glass–calomel electrode calibrated in hydrogen-ion concentration using HNO_3.[4] Titrations were performed in triplicate and the SUPERQUAD computer program was used for stability constant calculations ($\beta_{pqr} = [M_pH_rL_q]/[M]^p[H]^r[L]^q$).[5] Standard deviations quoted refer to random errors only. They are, however, a good indication of the importance of a particular species in the equilibrium.

Spectroscopic studies

Absorption spectra were recorded on a Beckman DU 650 spectrophotometer. The metal-ion concentrations were 2.5×10^{-3} mol dm^{-3} and the metal-to-pro-ligand molar ratios were 1 : 1, 1 : 2 and 1 : 5. The EPR spectra were recorded on a Brüker ESP 300E spectrometer at X-band (9.3 GHz) at 120 K, in ethane-1,2-diol–water (1 : 2) as a solvent. Concentrations used in the spectroscopic measurements were similar to those given for potentiometric titrations.

Syntheses of complexes

Nickel(II). The compound $NiCl_2 \cdot 6H_2O$ (0.238 g, 1 mmol) was dissolved in acetonitrile (20 cm^3) and added to a solution of the acetamide (0.226 g, 2 mmol) in acetonitrile (10 cm^3). A 25% aqueous solution (1.44 cm^3) of tetramethylammonium hydroxide was added dropwise. The dark brown solution was set aside

Table 1 Protonation constants and complex-formation constants of 2-cyano-2-(hydroxyimino)acetamide at 25 °C and I = 0.1 mol dm^{-3} KNO_3

Species	log β	log β*
HL	5.12(1)	9.87
Nickel(II) complexes		
NiL	3.38(1)	4.82
$NiH_{-1}L_2$	−1.88(1)	—
$NiH_{-2}L_2$	−7.72(3)	−8.97
Copper(II) complexes		
CuL	3.74(1)	7.87
$Cu_2H_{-2}L_2$	−1.06(2)	5.66
$CuH_{-2}L_2$	−6.64(2)	−4.74

* Data for 2-(hydroxyimino)propanamide.[1]

Table 2 Spectral parameters (visible and EPR) for metal(II)–2-cyano-2-(hydroxyimino)acetamide systems at 25 °C and I = 0.1 mol dm^{-3} (KNO_3). Pro-ligand concentration 2.5 × 10^{-3} mol dm^{-3} and metal-to-pro-ligand molar ratio 1:5 (for Ni^{2+}) and 1:2 (for Cu^{2+})

Species (binding mode)	UV/VIS λ/nm	ε/dm^3 mol^{-1} cm^{-1}
NiL (N, N$^-$)	395.0^a 517.0^b 645.0^b 974.0^b	79 2 0.8 1.2
$NiH_{-1}L$ (N, N$^-$)	395.0^a 535.0^{b,c} 986.0^b	355 17 3
$NiH_{-2}L_2$ (2 × N, N$^-$)	398.0^a 539.0^c	708 100
CuL (N, N$^-$)	710.0	47^d
$Cu_2H_{-2}L_2$ (N, N$^-$, O$^-$)	662.0	64
$CuH_{-2}L_2$ (2 × N, N$^-$)	607.0	155^e

[a] Intraligand transition. [b] d–d Transition of O_h nickel(II) complex. [c] d–d Transition of square-planar nickel(II) complex. [d] $A_{\parallel}$ 156 G, $g_{\parallel}$ 2.260. [e] $A_{\parallel}$ 188, $g_{\parallel}$ 2.222.

for 48 h at room temperature. The crystalline precipitate of the anionic complex was filtered off, washed with acetonitrile and dried in a vacuum desiccator over $CaCl_2$. Red-brown needle-shaped single crystals suitable for X-ray analysis were obtained by recrystallisation from acetonitrile–water (3:1) upon slow evaporation in the air at room temperature. Yield 65% [Found (Calc. for $C_{14}H_{30}N_8O_6$): C, 36.2 (36.15); H, 6.45 (6.5); N, 24.1 (24.1); Ni, 12.8 (12.6)%].

Copper(II). A 25% aqueous solution (0.72 cm^3, 2 mmol) of tetramethylammonium hydroxide was added to a suspension of [Cu(Hchia)]·0.5H_2O[6] (0.297 g, 1 mmol) in water (5 cm^3). In 30 min red crystals were filtered off, washed with water and acetone and dried in vacuum. Single crystals suitable for X-ray analysis were grown by slow diffusion of methanol vapour into a 15% solution of the complex in acetonitrile. Yield 70% [Found (Calc. for $C_{14}H_{30}CuN_8O_6$): C, 35.55 (35.8); H, 6.55 (6.45); Cu, 13.75 (13.5); N, 23.7 (23.85)%].

Crystallography

Crystal data and parameters for data collection and structure refinement are presented in Table 3, while selected distances and angles are collected in Tables 4 and 5, respectively. For X-ray analysis a needle-shaped single crystal was chosen and sealed in a glass capillary to avoid crystal powdering.

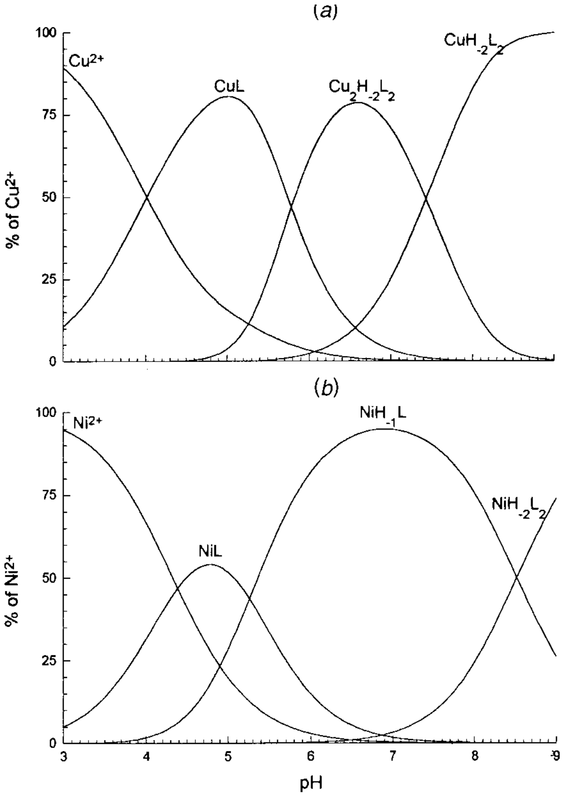


Fig. 1 Species distribution curves for the complexes formed in the Cu^{2+}–H_2chia (*a*) and Ni^{2+}–H_2chia (*b*) systems as a function of pH. Pro-ligand concentration 0.003 mol dm^{-3}, and metal-to-ligand molar ratios 1:5 (for nickel) and 1:3 (for copper)

Data collection and processing. Intensity data were collected at 293(2) K with a KM4 computer-controlled four-circle diffractometer.[7] The structure was solved by direct methods and refined by full-matrix least squares, using SHELXL 93[8] with anisotropic thermal parameters for non-hydrogen atoms. All H atoms were located from the successive Fourier-difference maps and only their displacement parameters included in the refinement. Correction for extinction was taken into account in the course of refinement.

Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1997, Issue 1. Any request to CCDC for this material should quote the full literature citation and the reference number 186/279.

Results and Discussion

Solution studies

2-Cyano-2-(hydroxyimino)acetamide (H_2chia) exhibits one measurable protonation constant corresponding to protonation of the hydroxyimino group C=NO$^-$. Its value, log K = 5.12, is more than six orders of magnitude lower than that of 2-(hydroxyimino)propanoic acid (log K = 11.6[1]) and more than four and half orders of magnitude lower than that of 2-(hydroxyimino)propanamide (log K = 9.87[1]). This very acidic behaviour of the oxime hydroxyl group derives from the strong electron-withdrawing effect of the 2-cyano substituent.

Complexes with 2-cyano-2-(hydroxyimino)acetamide

The complex species evaluated from the potentiometric calculations for Cu^{2+} and Ni^{2+} are collected in Table 1. Results

Table 3 Crystal data and structure refinement for the 2-cyano-2-(hydroxyimino)acetamide complexes*

Empirical formula	$C_{14}H_{30}N_8NiO_6$	$C_{14}H_{30}CuN_8O_6$
M	465.18	470.00
(Cu-Kα)/Å	1.541 80	1.541 78
a/Å	7.905(2)	7.683(2)
b/Å	8.589(2)	8.754(2)
c/Å	9.017(2)	9.059(2)
α/°	107.11(3)	108.42(3)
β/°	97.69(3)	97.46(3)
γ/°	101.36(3)	98.44(3)
U/Å^3	561.5(2)	561.6(2)
D_c/Mg m^{-3}	1.376	1.390
μ/cm^{-1}	16.47	1.773
F(000)	246	247
Crystal size/mm	0.15 × 0.18 × 0.18	0.4 × 0.4 × 0.2
θ Range for data collection/°	5.24–80.35	5.24–58.05
hhl Ranges	0–10, −10 to 10, −11 to 11	−1 to 8, −9 to 9, −9 to 9
Reflections collected	2302	1704
Independent reflections	2302	1553 [R_{int} = 0.0137]
Data, parameters	2143, 146	1553, 137
Goodness of fit on F^2	1.073	0.892
$R1$, $wR2$ Final indices [$I > 3\sigma(I)$]	0.0356, 0.1092	0.0330, 0.0860
Weighting scheme, w	$1/[\sigma^2(F_o^2) + (0.0722P)^2 + 0.1537P]$	
	where $P = (F_o^2 + 2F_c^2)/3$	0.0126(13)
Extinction coefficient	0.0058(14)	0.269, −0.263
Largest difference peak and hole/e Å^{-3}	0.269, −0.263	

* Details in common: triclinic, space group $P\bar{1}$; Z = 1; full-matrix least-squares refinement on F^2.

Table 4 Selected bond lengths (Å) and angles (°) for the nickel(II)–2-cyano-2-(hydroxyimino)acetamide complex

Ni–N(2^i)	1.858(2)	Ni–N(1)	1.899(2)
Ni–N(2)	1.858(2)	Ni–N(1^i)	1.899(2)
N(2^i)–Ni–N(2)	180.0	N(2^i)–Ni–N(1^i)	83.62(7)
N(2^i)–Ni–N(1)	96.38(7)	N(2)–Ni–N(1^i)	96.38(7)
N(2)–Ni–N(1)	83.62(7)	N(1)–Ni–N(1^i)	180.0

Symmetry transformation used to generate equivalent atoms: i $-x$, $-y$, $-z$.

Table 5 Selected bond lengths (Å) and angles (°) for the copper(II)–2-cyano-2-(hydroxyimino)acetamide complex

Cu–N(2)	1.895(2)	Cu–N(1)	2.056(2)
N(2)–Cu–N(2^i)	180.0	N(2^i)–Cu–N(1)	98.40(8)
N(2)–Cu–N(1)	81.60(8)	N(1)–Cu–N(1^i)	180.0

Symmetry transformation as in Table 4.

obtained earlier for 2-(hydroxyimino)propanamide[1] are also shown for comparison. Copper(II) forms three major complexes: two monomeric, CuL and $CuH_{-2}L_2$, and the dinuclear species $Cu_2H_{-2}L_2$ (Fig. 1). The latter is EPR silent in the region pH 5.5–6.5. The same three species were also observed, among others, in the case of 2-(hydroxyimino)propanamide. The strongly acidic character of the present oxime donor results in much less stable complexes when compared to those of 2-(hydroxyimino)propanamide. The stability constant for the dimeric species differs by more than six orders of magnitude (Table 1). The EPR and absorption spectral data collected in Table 2 indicate the involvement of two or four nitrogen atoms.[1,2] In the dinuclear species the involvement of deprotonated hydroxyimino oxygen is most likely, as was found earlier in similar oxime systems in the analogous pH regions.[1] Unfortunately, the strong intraligand transitions observed in the range 400–200 nm do not allow one to observe $O^-_{oxime}\rightarrow Cu^{2+}$ charge-transfer band to support this binding mode (see ref. 1).

In the case of Ni^{2+}-containing solutions the three major complexes formed are monomeric NiL, $NiH_{-1}L$ and $NiH_{-2}L_2$ species (Fig. 1). According to the absorption spectra (Table 2) the latter bis complex is square planar, while the first two are both octahedral. The binding mode is likely to be the same as that observed for Cu^{2+}, *i.e.* involving the nitrogen donors of the ligand (see below). The interesting feature of the nickel system is the much lower difference in stabilities between the complexes of the present derivative and that of 2-(hydroxyimino)propanamide (Table 1).

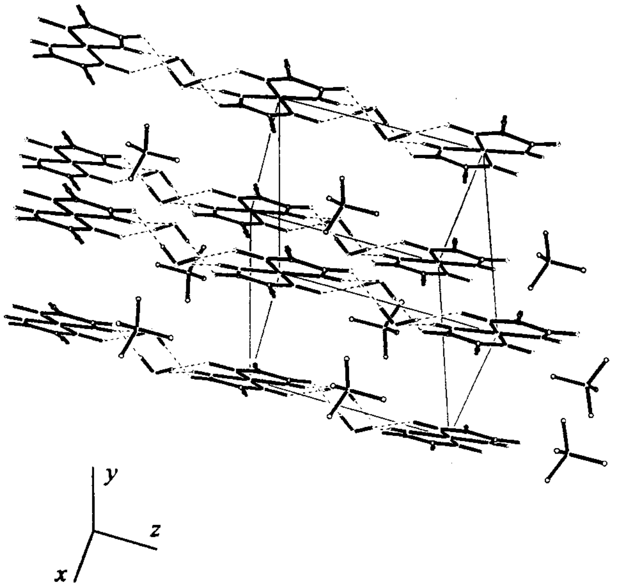


Fig. 2 Packing of molecules of the copper(II)–2-cyano-2-(hydroxyimino)acetamide complex

Crystal structures of the complexes $[NMe_4]_2[M\{N(O)C(CN)C(O)N\}_2]\cdot 2H_2O$ (M = Ni or Cu)

Both copper and nickel ions give the same molecular structure for the $MH_{-2}L_2$ complex, consisting of tetramethylammonium cations, complex anions $MH_{-2}L_2$, and water molecules. In the crystal packing (Fig. 2) the complex anions are linked by hydrogen bonds into chains spread along the z direction. The

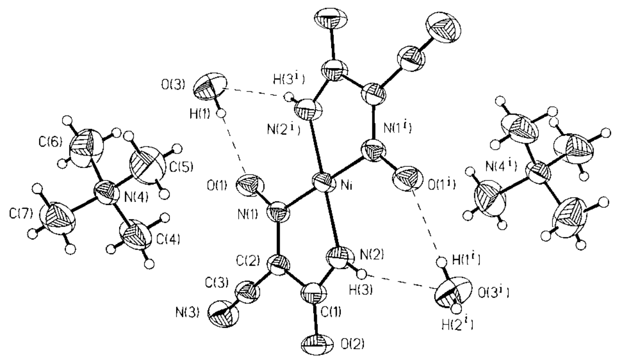


Fig. 3 Crystal structure of the nickel(II)–2-cyano-2-(hydroxyimino)-acetamide complex

hydrogen bonds are formed between the amide and oxime oxygen atoms and the proton of the amide group and water. The NMe_4^+ cations form columns along the *z* axis of the crystal, occupying empty spaces between the translational chains of the complex anions. In complex anion (Fig. 3, for Ni^{2+}) the metal atom occupies a partial position at the centre of symmetry. The distorted square-planar co-ordination sphere consists of four nitrogen atoms belonging to the deprotonated hydroxyimino and amide groups. The two dianions of 2-cyano-2-(hydroxyimino)acetamide are situated in *trans* position with respect to each other. The $Cu-N_{oxime}$ and $Cu-N_{amide}$ distances are 2.056 and 1.895 Å respectively, noticeably different, while *e.g.* in the complex of Cu^{2+} with 2-(hydroxyimino)-propanamide[9] these distances are in the ranges 1.91–1.94 and 1.92–1.95 Å, respectively, *i.e.* close to each other. The elongation of the $Cu-N_{oxime}$ bond in the present complex clearly indicates the strong electron-withdrawing effect of the 2-cyano substituent (see above).

In the nickel(II) complex with 2-cyano-2-(hydroxyimino)-acetamide the $Ni-N_{oxime}$ and $Ni-N_{amide}$ distances are 1.899 and 1.858 Å, respectively, relatively close to each other, although the bond distance with oxime nitrogen is also the longer as also found in the copper complex. Both distances are very close to those observed for the nickel complex with 2-(hydroxyimino)-propanamide in which the $Ni-N_{oxime}$ and $Ni-N_{amide}$ bond lengths are 1.872 and 1.853 Å, respectively.[2]

The geometrical parameters of the present ligand are similar to those observed for other ligands having deprotonated oxime and amide groups. The distances N(1)-O(1) of 1.289 and 1.281 Å and N(1)-C(1) of 1.302 and 1.314 Å for copper and nickel respectively, are close to those reported for the N-co-ordinated deprotonated oxime group.[10] This indicates that the CNO^- moiety exists in the nitroso-form.[11]

Conclusion

The high acidity of the oxime hydroxyl group in 2-cyano-2-(hydroxyimino)acetamide changes considerably the co-ordination mode of the oxime ligand with Cu^{2+} and Ni^{2+} ions. Although the donor atoms bound to the metal ions are the same as with 2-(hydroxyimino)propanamide, two molecules of the propanamide ligand are bound in *cis* position, while in the case of the 2-cyano derivative the ligands are *trans* to each other. The major factor deciding the *cis* positions of the ligand molecules in the major complex, $MH_{-1}L_2$, formed with oxime analogues of amino acids is the hydrogen bond between the two hydroxyl oxygens. This hydrogen bond is not present in the corresponding complex of the 2-cyano derivative, $MH_{-2}L_2$, due to the very acidic oxime hydroxyl group. The $MH_{-1}L_2$ species is not observed in the present case.

Acknowledgements

This work was supported by the Polish State Committee for Scientific Research (KBN 3T09A06908). T. Yu. Sliva thanks Kasa J. Mianowskiego for financial support.

References

1 Ch. O. Onindo, T. Yu. Sliva, T. Kowalik-Jankowska, I. O. Fritsky, P. Buglyo, L. D. Pettit, H. Kozlowski and T. Kiss, *J. Chem. Soc., Dalton Trans.*, 1995, 3911.
2 T. Yu. Sliva, T. Kowalik-Jankowska, V. M. Amirkhanov, T. Glowiak, L. D. Pettit, I. O. Fristky and H. Kozlowski, *J. Inorg. Biochem.*, in the press.
3 C. A. Schultze, *Berichte*, 1909, **42**, 735.
4 H. M. Irving, M. H. Miles and L. D. Pettit, *Anal. Chim. Acta*, 1967, **68**, 475.
5 P. Gans, A. Sabatini and A. Vacca, *J. Chem. Soc., Dalton Trans.*, 1985, 1195.
6 V. V. Skopenko, R. D. Lampeka and Yu. L. Zub, *Zh. Neorg. Khim.*, 1981, **26**, 142.
7 *KUMA M4 Software User Guide, Version 3.1*, Kuma Diffraction, Wrocław, 1986.
8 G. M. Sheldrick, SHELXL 93, Program for refinement of crystal structures, University of Göttingen, 1993.
9 Yu. A. Simonov, V. Kh. Kravtsov, I. O. Fritsky, E. E. Gubina, R. D. Lampeka, T. S. Iskenderov and A. Zh. Zhumabaev, *Koord. Khim.*, 1995, **21**, 407.
10 I. O. Fritsky, R. D. Lampeka, V. V. Skopenko, Yu. A. Simonov, A. A. Dvorkin and T. I. Malinovsky, *Z. Naturforsch., Teil B.*, 1993, **48**, 270.
11 K. V. Domasevich, A. N. Chernega, S. V. Lindeman and Yu. T. Struchkov, *Zh. Neorg. Khim.*, 1995, **40**, 426.

Received 23*rd July* 1996*; Paper* 6/05125A