

Synthesis, solid-state and in-solution structures of a new seven coordinated manganese(II) complex via X-ray diffraction and electrospray ionization mass spectrometry

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Abstract

The structure of the $[\text{Mn}(\text{HPCINOL})(\eta_1\text{-NO}_3)(\eta_2\text{-NO}_3)]$ **1** complex [HPCINOL = 1-(bis-pyridin-2-ylmethyl-amino)-3-chloropropan-2-ol] in the solid-state and in $\text{H}_2\text{O}/\text{MeOH}$ solution was investigated by monocrystal X-ray diffraction and ESI(+)-MS/MS. X-ray reveals that **1** is a seven-coordinated complex with a discrete mononuclear structure in which the manganese(II) ion is coordinated by the tripodal HPCINOL ligand and two nitrate ions, one monodentate and the other bidentate. ESI(+)-MS/MS shows that mononuclear, dinuclear and trinuclear manganese cationic species are present in solution, probably in equilibrium with neutral **1**. This contrasting scenario illustrates for **1** the importance of both solid-state and in-solution characterizations of coordination compounds with potential bioinorganic interest.

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The coordination chemistry of the manganese(II) ion favors formation of four- and six-coordinated metal ions. Five- and seven-coordination are less frequently observed, whereas in discrete molecules coordination numbers higher than seven are rarely encountered [1].

Mn(II) ions play an important role in the action of biological redox enzymes of many microorganisms and plants and animals. This role is exemplified by enzymes such as the oxygen-evolving centers of photosystem II, superoxide dismutases and catalases [2]. Due to this role, efforts have been focused on the preparation and characterization of lighter inorganic analogues that would mimic physico-chemical properties and activities of Mn-dependent

enzymes [3]. Up to date, the majority of the compounds (mainly those prepared with tripodal ligands similar to that presented here) that are mimetic of metalloenzymes turn out to be insoluble in pure water, allowing studies of reactivity only in solvents different from that in which the enzyme activity is evaluated [4].

For the characterization of these metalloenzymes-mimetic compounds, attention has been devoted mainly to their molecular solid-state structures, which have been solved by X-ray diffraction techniques. The assumption is that the structure in the solid-state is preserved in solution, which is likely to hold for most solvents with low polarity and limited coordination abilities. But for polar solvents able to promote ligand exchange (water, DMSO and DMF for instance), significant structural modifications may occur, which would drastically change the structure

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of the solvated complex, while promoting equilibria with other species stabilized by solvation.

As a part of our interest in the development of water soluble synthetic compounds of bioinorganic relevance [5], we report herein the structural behaviour of the mononuclear complex $[\text{Mn}(\text{HPCINOL})(\eta_1\text{-NO}_3)(\eta_2\text{-NO}_3)]$ **1** both in solid-state and in $\text{H}_2\text{O}:\text{MeOH}$ solution.

Fig. 1 shows the Ortep diagram of **1** [6]. The asymmetric cell is formed by two independent molecules with small structural differences. Owing to these differences, only one of these molecules is shown. The Mn(II) ion shows a N_3O_4 coordination environment composed by the tripodal HPCINOL [5b] ligand and by two nitrate ions, one monodentate and the other bidentate. This arrangement results in an infrequent seven-coordinated complex with a distorted pentagonal bipyramid geometry. Note that the ligand coordination mode around the manganese ion is distinct from those previously observed for the copper complexes $[\text{Cu}(\text{HPCINOL})(\text{CH}_3\text{CN})(\text{ClO}_4)_2]$ and $[\text{Cu}(\text{HPCINOL})(\text{Cl})\text{Cl}]$ [5a,5b]. For the copper complexes, the pyridine groups are coordinated *trans* to each other, while in **1** this orientation is *cis*. The alcohol group in **1** is protonated, as indicated by the long Mn–O4 bond length of 2.246(4) Å. The same behaviour was also observed for the alcohol group in the Cu complexes [5a,5b]. All the bond distances in **1** are in agreement with those from similar compounds deposited in CCDC database [7]. Following the analysis of the ADPs one observes a remarkable disorder for the NO_3 group from which only one oxygen atom

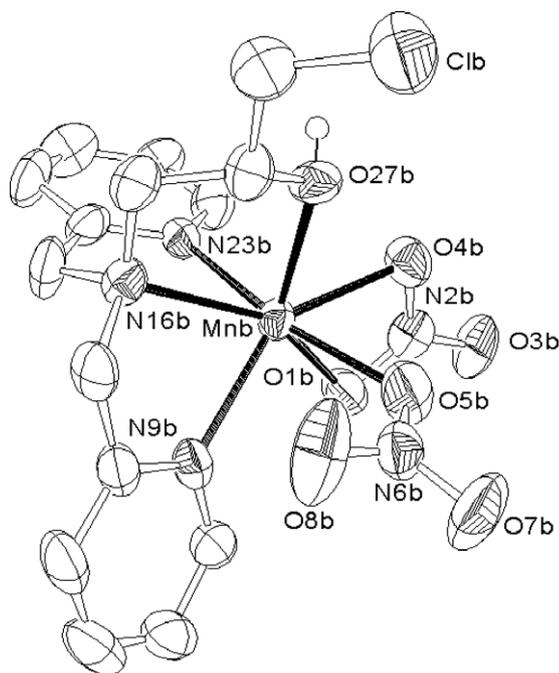


Fig. 1. $[\text{Mn}(\text{HPCINOL})(\eta_1\text{-NO}_3)(\eta_2\text{-NO}_3)]$ **1** complex structure showing the atom labeling scheme. Selected bond distances (Å) for the $\text{Mn}-\text{N}_3\text{O}_4$ coordination: MnB–O27B 2.246(4), MnB–O5B 2.265(5), MnB–N9B 2.278(5), MnB–N23B 2.294(5), MnB–O1B 2.327(4), MnB–O4B 2.332(4), and MnB–N16B 2.362(5).

(O5) is coordinating the Mn ion. This NO_3 disorder can be observed in both molecules in the asymmetric unit of **1** and seems to be a consequence of packing. This conclusion arises from the observation that: (i) the Mn–O (NO_3) distances in **1** are about 2.30(5) Å long and the Mn–O5 is the shortest/strongest one and (ii) O7 and O8, the other two oxygen atoms of the disordered nitrate group, establish competitive hydrogen bonds with the atoms arising from different **1** complexes. Thus, modeling the NO_3 disorder with split oxygen atoms would not bring any additional information about the chemical properties of **1**, since the Mn coordination would not be affected by this model correction.

At room temperature, **1** is highly soluble only in polar solvents such as DMSO, DMF and H_2O . Its water solubility is therefore a welcome property owing to the interest in developing coordination compounds with biological activities. To evaluate whether the solid state structure of **1** would be stable in solution, the ESI(+) mass spectrum (Fig. 2) of a $\text{H}_2\text{O}:\text{MeOH}$ (1:1) solution of **1** was acquired, since ESI–MS has been shown to be a useful tool to characterize coordination compounds in solution [5c,8]. Methanol was added to facilitate spraying.

Fig. 2 also shows proposals for the major detected species. Owing to the gentle ionization process and based on ESI–MS/MS experiments (see supporting material), the assigned ions are unambiguously detected from solution and have been directly transferred (no gas-phase dissociation) to the gas-phase by ESI. This assumption is supported by the observation for these gaseous ions of no direct precursor–product relationships when their collision-induced dissociation was performed via ESI(+)-MS/MS experiments. The MS data indicates therefore that structure of **1** is not fully preserved in aqueous solution, hence its possible biological activity (studies of catalase activity are being carried out) should not be limited to the structure of the solid-state. Thus, in water solution, **1** is in equilibrium at least with four cationic species, those proposed in Fig. 2. Note that, being a neutral species, **1** is not detected in the ESI(+)-MS.

ESI(+)-MS/MS studies showed that the ion of m/z 1349.6 dissociates by the loss of neutral molecules of HNO_3 and $[\text{Mn}(\text{HPCINOL})(\text{NO}_3)_2]$ to form the fragments of m/z 1285 and m/z 815, respectively. The ESI(+)-MS detection of the ion of m/z 931 reveals the presence, in solution, of a cationic species containing three manganese ions and only two ligand molecules. This cation indicates therefore that, to some extension, an interesting dissociative Mn–ligand process occurs in the $\text{H}_2\text{O}:\text{MeOH}$ solution. This observation rationalizes also the presence in solution and hence the ESI(+)-MS detection of the ion of m/z 699 containing only one manganese and two ligand molecules. The ESI(+)-MS/MS of the ion of m/z 931 shows that it fragments to a dinuclear manganese ion of m/z 696 (signal of very low intensity in ESI(+)-MS) probably by the loss of $\text{Mn}(\text{NO}_3)_2$ and 2-methylene-oxirane. The ion of m/z 878 loses a HNO_3 molecules to form $[\text{Mn}_2(\text{HPCINOL})(\text{PCl}-$

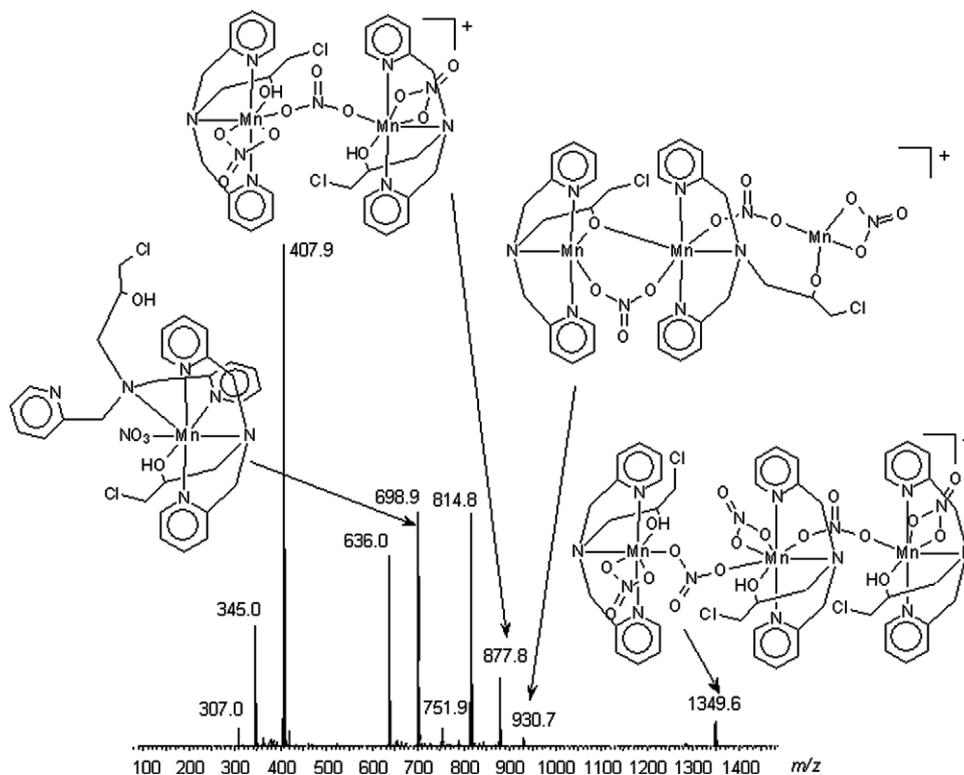


Fig. 2. ESI(+)-MS for a H₂O:MeOH (1:1) solution of [Mn(HPCINOL)(η₁-NO₃)(η₂-NO₃)] **1** and proposals for main ions present in solution.

NOL)(NO₃)₂]⁺ of *m/z* 815, which in turn loses a HNO₃ molecule to form [Mn₂(PCINOL)₂(NO₃)]⁺ of *m/z* 752. The ESI(+)-MS/MS of the latter reveals that its dissociation is associated with the detection in the ESI(+)-MS of the fragment ions of *m/z* 345 and 309 (other fragments of low intensity are also formed, see [supporting material](#)).

With respect to the ion of *m/z* 699, two different fragmentation pathways are observed. It loses a neutral HPCINOL molecule to form [Mn(HPCINOL)NO₃]⁺ of *m/z* 408 or a HNO₃ molecule to form [Mn(HPCINOL)(PCINOL)]⁺ of *m/z* 636. The ESI(+)-MS/MS of the ion of *m/z* 408 reveals that this fragment ion is also the source of the ions of *m/z* 345 (loss of HNO₃) and 309 (loss of both HNO₃ and HCl). In turn, the ion of *m/z* 345 dissociates to the fragment ion of *m/z* 309 by HCl loss.

Thus, based on the results presented above, it is clear that the HPCINOL ligand is able to stabilize Mn(II) ion, forming in the solid-state the mononuclear seven-coordinated manganese complex [Mn(HPCINOL)(η₁-NO₃)(η₂-NO₃)] **1**. This complex is water soluble, being an interesting candidate for biological/medicinal studies. The characterization of **1** in H₂O:MeOH solution by ESI(+)-MS reveals that the single mononuclear solid-state structure **1** is not fully preserved in aqueous solutions, since trinuclear, dinuclear and mononuclear manganese ions with compositions [Mn₃(HPCINOL)₃(NO₃)₅]⁺, [Mn₃(HPCINOL)₂(NO₃)₂]⁺, [Mn₂(HPCINOL)₂(NO₃)₂]⁺ and [Mn(HPCINOL)₂(NO₃)]⁺ of *m/z* 1348, 931, 878 and 699, respectively, were detected, and their solution precedence confirmed by ESI(+)-MS/MS experiments. This work illustrates for **1** the importance

of both solid-state and in-solution characterizations of coordination compounds with potential biological relevance.

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Appendix A. Supplementary material

CCDC 633329 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.inoche.2007.04.001](https://doi.org/10.1016/j.inoche.2007.04.001).

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- [6] *Crystallographic data for 1*: $M_r = 470.73$, monoclinic, space group Pc , $a = 10.039(2) \text{ \AA}$, $b = 10.336(2) \text{ \AA}$, $c = 19.720(4) \text{ \AA}$, $\beta = 104.39(3)^\circ$, $V = 1982.1(7) \text{ \AA}^3$, $Z = 4$, $T = 293 \text{ K}$, $\rho_c = 1.574 \text{ Mg/m}^3$, $\mu = 0.849 \text{ mm}^{-1}$, sample size = $0.30 \times 0.10 \times 0.13 \text{ mm}^3$. $F(000) = 964$. X-ray diffraction data collection was performed on an Enraf–Nonius Kappa-CCD using graphite-monochromated $\text{MoK}\alpha$ radiation (COLLECT) [9]. Final unit cell parameters were based on all reflections (DIRAX9) [10]. Data integration and scaling of the reflections were performed with the EVALCCD suite [11]. An empirical absorption correction using equivalent reflections was performed with the program SADABS [12]. 16633 reflections were collected with completeness to $\theta = 27.55$ equal to 98.8%. $R_1 = 0.1114$, $wR_2 = 0.1420$ (for all 7193 unique reflections), $R_{\text{int}} = 0.0636$. $R_1 = 0.0560$, $wR_2 = 0.1226$, $\text{GOF} = 1.011$ (for the 4527 unique reflections with $I > 2\sigma(I)$). The structure was solved by direct methods using the SHELXS program [13]. The positions of all atoms could be unambiguously assigned on consecutive difference Fourier maps. Refinements were performed using SHELXL [13] based on F^2 through full-matrix least square routine. Hydrogen atoms were added in the structure according to the riding model [14]. Hydrogen atoms of the CH and CH_2 groups were set isotropic with the atomic displacement parameter 20% larger than the equivalent isotropic displacement parameter of the nearby riding atom. The asymmetric unit of **1** is composed by two $[\text{Mn}(\text{HPCl-NOL})(\eta_1\text{-NO}_3)(\eta_2\text{-NO}_3)]$ molecules with minor structural differences among them.
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