

*J. Synchrotron Rad.* (1999). **6**, 579–581

## XAFS studies of pyranone and pyridinone metal(III) complexes

Walkiria Schlindwein<sup>a</sup>, Maria Rangel<sup>b</sup> and John Burgess<sup>c</sup>

<sup>a</sup>Department of Chemistry & Physics, De Montfort University, Leicester, UK LE1 9BH, <sup>b</sup>Departamento de Química, Instituto de Ciências Biológicas de Abel Salazar, Lg. Prof. Abel Salazar 2, 4000 Porto, Portugal, <sup>c</sup>Department of Chemistry, University of Leicester, Leicester, UK LE1 7RH.

EXAFS studies of solid 3-hydroxy-4-pyranone complexes of iron(III), gadolinium(III) and dysprosium(III) and of aqueous/methanolic solutions of one of the iron(III) complexes, have established metal ligand distances and the locations of solvent molecules associated with the complexes in the solid state and in solution. Similar compounds based on 3-hydroxy-4-pyridinone ligands are particularly attractive for pharmaceutical purposes and EXAFS results of *tris*(1,2-dimethyl-3-hydroxy-4-pyridinonate)iron(III) complex are also reported.

**Keywords:** EXAFS, Pyranone and Pyridinone Metal (III) Complexes.

### 1. Introduction

We have been interested for some time in solvation of 3-hydroxy-4-pyranone and 3-hydroxy-4-pyridinone complexes, with particular relevance to the actual or potential use of these ligands and their complexes for the control of metal levels in, or introduction of isotopes of diagnostic or therapeutic importance into, the body (Hider & Hall, 1991; Burgess, 1993).

The crystal structures of some of these complexes have been established by single crystal X-ray diffraction methods (Nelson, Rettig & Orvig, 1987), but in order to obtain such information in solution or in cases where a satisfactory crystal cannot be grown, the use of EXAFS technique is ideal.

In this paper we first report very close agreement between EXAFS and X-ray diffraction results for *tris*(maltolato)iron(III) – Fe(ma)<sub>3</sub> (ma = maltol = 3-hydroxy-2-methyl-4-pyranone) (Ahmet *et al.*, 1995) and *tris*(1,2-dimethyl-3-hydroxy-4-pyridinonate)iron(III) – Fe(dmpp)<sub>3</sub> (Charalambous, *et al.*, 1988). EXAFS also provides evidence for the presence of coordinated solvent molecules in these compounds and also in *tris*(ethylmaltolato)-gadolinium(III) – Gd(etma)<sub>3</sub> and *tris*(ethylmaltolato)-dysprosium(III) – Dy(etma)<sub>3</sub>, (ethylmaltol = 3-hydroxy-2-ethyl-4-pyranone).

In addition, we demonstrate the presence of three solvent molecules between the ligands for the Fe(ma)<sub>3</sub> complex in solution; these are at a similar distance from the iron as the solvent molecules in the crystalline complex.

### 2. Experimental

EXAFS experiments were performed in the region of the Fe K-edge, Gd L<sub>III</sub>-edge, Dy L<sub>III</sub>-edge using station 7.1 at the Synchrotron Radiation Source, Daresbury Laboratory. The beam energy was 2 GeV and a typical average stored ring current was

120 mA in multibunch mode and high-brilliance configuration. Data were acquired in the EXAFS transmission mode, with argon-filled ion chambers using a Si (111) double crystal monochromator with 50% harmonic rejection.

Powder samples were prepared in the form of homogeneous pellets (~100 μm of thickness) and diluted with boron nitride when necessary.

Solution studies were performed on saturated solutions of the complexes (0.08 mol.dm<sup>-3</sup>) prepared from a mixture of 20:80 % (v:v) water:methanol. The liquid cell used was 2mm thick.

All the experiments were carried out at room temperature and no sample decomposition was observed after irradiation of multiple scans (average of 3 scans per sample).

The data analysis was performed using the Daresbury EXAFS suite programs, EXCALIB and EXCURV92 - 'Curved Wave Theory' using multiple scattering restrained ( $w_{\text{distance}} = 0.5$ ) refinement (Binstead, *et al.*, 1995) and SPLINE for the background subtraction (Ellis, 1993). In EXCURV92 the phaseshifts were calculated using the Hedin-Lundquist exchange potentials. The amplitude factor, AFAC was fixed to 0.9. The coordination number,  $N_n$ , was not refined but set constant as 3 atoms for each shell, which is equivalent to 3 similar units or 3 ligand rings.

### 3. Results and Discussion

In systems that contain ring structures, e.g. the pyranone and pyridinone ligands, multiple scattering is an important factor (Strange, *et al.*, 1987) because of the focusing effect caused by the strong forward scattering from the nearest neighbour atom, and this normally increases the EXAFS contribution from shells of atoms further away from the target atom; this is the case for the shell at ~ 4.10 Å. Restrained refinement with  $w_{\text{distances}} = 0.5$  gives the best fit to the experimental data and a detailed description of the methodology used comparing single scattering with multiple scattering, constrained and restrained refinements will be published elsewhere (Schlindwein, *et al.*, to be published).

Analysis of the EXAFS results for the solid non crystalline *tris*(maltolato)iron(III) indicates an average of 3 oxygen atoms at 1.98 Å, 3 oxygen atoms at 2.04 Å, 3 carbon atoms at 2.77 Å, 3 carbon atoms at 2.76 Å, 3 carbon atoms at 4.06 Å, 3 carbon atoms at 4.19 Å and 3 oxygen atoms at 3.95 Å from solvent of crystallisation (Table 1a). These distances to the atoms in the chelate rings may be compared with the average values of 3 oxygen atoms at 2.00 Å, 3 oxygen atoms at 2.07 Å, 6 carbon atoms at 2.77 Å, 3 carbon atoms at 4.12 Å, 3 carbon atoms at 4.20 Å reported for anhydrous *tris*(maltolato)iron(III) (anhydrous because recrystallised from chlorobenzene) from single crystal X-ray diffraction (Ahmet, *et al.*, 1995) (Table 1b).

Analysis of the EXAFS results for saturated aqueous methanolic solutions of *tris*(maltolato)iron(III) revealed average peaks at 1.97 Å and 2.03 Å for oxygen atoms, 2.76 Å, 2.77 Å, 4.07 Å and 4.12 Å for carbon atoms and 3.96 Å for oxygen atoms (Table 1c). The first six distances correspond to the chelate ring atoms, the seventh suggesting the presence of solvent molecules in a position very similar to that of the solvent of crystallisation in the solid state at 3.96 Å. It thus appears that it is possible to locate, and count, solvating molecules associated with complexes of this type in solution. The quality of the fit, expressed in terms of the R-factor (Binsted, *et al.*, 1992), is  $R_{\text{EXAFS}} = 16.8\%$ ,  $R_{\text{distances}} = 0.8\%$  and  $R_{\text{total}} = 17.6\%$  for the solid state (table 1a) and  $R_{\text{EXAFS}} = 24.0\%$ ,  $R_{\text{distances}} = 1.4\%$  and  $R_{\text{total}} = 25.4\%$  for the solution (Table 1c). The 3 oxygen atoms from

solvent are statistically significant at the 1% level (Joyner, *et al.*, 1987).

The Fe K-edge EXAFS and Fourier transform spectra of the *tris*(maltolato)iron(III), solid and solution, are presented in Figure 1.

**Table 1**

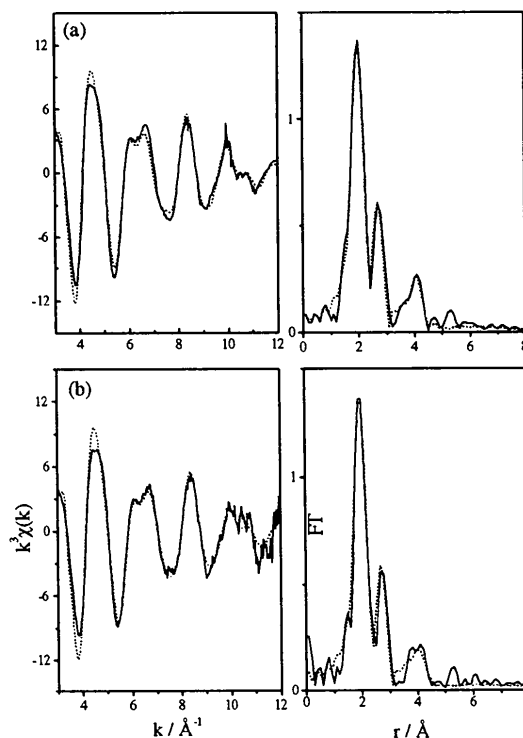
XAFS Best-fit parameters for Metal(III) 3-hydroxy-4-pyranone and 3-hydroxy-4-pyridinone complexes using multiple scattering restrained refinement ( $w_{\text{distances}} = 0.5$ ). The refined parameters are shown in bold.

Parameters	(a) Fe (ma) <sub>3</sub> solid	(b) Fe (ma) <sub>3</sub> solid XRD	(c) Fe (ma) <sub>3</sub> solution	(d) Gd (etma) <sub>3</sub> solid	(e) Dy (etma) <sub>3</sub> solid	(f) Fe (dmpp) <sub>3</sub> solid	(g) Fe (dmpp) <sub>3</sub> solid XRD
$E_f$	<b>-1.88</b>	<b>-3.50</b>	<b>-0.9</b>	<b>-0.12</b>	<b>-1.32</b>	<b>-2.87</b>	<b>-3.01</b>
$r_1$ O	<b>1.98</b>	2.00	<b>1.97</b>	<b>2.67</b>	<b>2.65</b>	<b>1.99</b>	1.99
$r_2$ O	<b>2.04</b>	2.07	<b>2.03</b>	<b>2.82</b>	<b>2.79</b>	<b>2.04</b>	2.04
$r_3$ C	<b>2.77</b>	2.77	<b>2.76</b>	<b>3.17</b>	<b>3.38</b>	<b>2.78</b>	2.79
$r_4$ C	<b>2.76</b>	2.77	<b>2.77</b>	<b>3.23</b>	<b>3.43</b>	<b>2.78</b>	2.80
$r_5$ C	<b>4.06</b>	4.12	<b>4.07</b>	<b>4.04</b>	<b>4.74</b>	<b>4.13</b>	4.15
$r_6$ C	<b>4.19</b>	4.20	<b>4.12</b>	<b>4.13</b>	<b>4.83</b>	<b>4.16</b>	4.19
$r_7$ O	<b>3.95</b>	-	<b>3.96</b>	<b>2.63</b>	<b>2.57</b>	<b>3.94</b>	-
$\alpha_{1,2}$	<b>0.012</b>	<b>0.012</b>	<b>0.013</b>	<b>0.001</b>	<b>0.011</b>	<b>0.006</b>	<b>0.007</b>
$\alpha_{3,4}$	<b>0.010</b>	<b>0.010</b>	<b>0.011</b>	<b>0.009</b>	<b>0.012</b>	<b>0.007</b>	<b>0.008</b>
$\alpha_{5,6}$	<b>0.009</b>	<b>0.032</b>	<b>0.013</b>	<b>0.025</b>	<b>0.007</b>	<b>0.019</b>	<b>0.022</b>
$\alpha_7$	<b>0.008</b>	-	<b>0.007</b>	<b>0.008</b>	<b>0.009</b>	<b>0.005</b>	-
$\phi_2$	<b>11.1</b>	12.1	<b>13.3</b>	12.13	15.8	<b>102.2</b>	103.1
$\phi_3$	<b>57.8</b>	57.5	<b>58.9</b>	57.5	58.4	<b>115.3</b>	115.8
$\phi_4$	<b>27.3</b>	28.0	<b>27.4</b>	28.0	28.3	<b>129.5</b>	130.2
$\phi_5$	<b>65.3</b>	63.9	<b>66.0</b>	63.9	64.2	<b>131.3</b>	132.0
$\phi_6$	<b>23.8</b>	23.6	<b>22.5</b>	23.6	24.5	<b>111.8</b>	112.8
$R_{\text{EXAFS}}$	16.8	23.2	24.0	28.6	25.8	17.7	19.4
$R_{\text{distance}}$	0.8	0.0	1.4	0.5	0.9	0.4	0.0
$R_{\text{total}}$	17.6	23.2	25.4	29.1	26.7	18.1	19.4
p	17	4	17	17	17	17	4
$N_i$	34.8	21.2	34.4	27.3	31.2	34.5	21.2
$N_i/p$	2.0	5.3	2.0	1.6	1.8	2.0	5.8
$\Phi \times 10^4$	0.5	3.5	1.1	1.5	1.3	0.7	3.4
$\text{Fl} \times 10^6$	0.2	1.3	0.4	0.7	0.6	0.3	1.6

$r_n$  = distance, in Å, from the central atom for shell n;  $\alpha_n$  = Debye-Waller factor  $2\sigma^2$ , in Å<sup>2</sup>, for shell n;  $R_{\text{total}} = R_{\text{EXAFS}} + R_{\text{distances}}$  = R-factor in %;  $\phi_n$  = polar coordinates for shell n, in angle; p = number of parameters;  $N_i$  = number of independent parameters;  $\Phi$  = fit index; F.I. = fit index that takes into account the degree of overdeterminacy of the system.

Analysis of the EXAFS results obtained for solid samples of hydrated *tris*-(ethylmaltolato)-dysprosium(III) and gadolinium(III) showed three oxygen atoms at 2.63Å (Gd) (Table 1d) and two oxygen atoms at 2.57Å (Dy) (Table 1e), and six further oxygen atoms (Gd - three at 2.67Å and three at 2.82Å; Dy - three at 2.65Å and three at 2.79Å). The latter may be assigned to the donor oxygen atoms of the ethylmaltol ligands, the former to coordinated solvent molecules. The solvent molecules are also rather more distant from the cation than in the aqua-ions of Gd<sup>3+</sup> and Dy<sup>3+</sup>, where average bond distances are Gd-OH<sub>2</sub> = 2.37Å to 2.41Å and Dy-OH<sub>2</sub> = 2.37Å to 2.40Å from X-ray and neutron diffraction (Habenschuss & Spedding, 1979; Nielson, & Tromp, 1991) and EXAFS (Yamaguchi, *et al.*, 1992; Benazeth, *et al.*, 1998) studies of appropriate aqueous solutions. It is difficult to be completely confident in the number of oxygens in the 2.63/2.57Å peaks but

the best fit is obtained when assuming two or three oxygens for the Gd compound, two for the Dy compound.



**Figure 1**

Best  $k^2$ -weighted EXAFS theoretical fit (left) and Fourier transform (right) of the Fe(ma)<sub>3</sub> (a) solid and (b) solution samples. The solid line is the experimental and the dotted line is the theory.

A higher coordination number for Gd (9) than for Dy (8) is, like the differences in cation-oxygen distances, consistent with their relative positions in the lanthanide series (Shannon & Prewitt, 1969), but it should be mentioned that thermogravimetric analysis of hydrated *tris*-ethylmaltolato-gadolinium(III) strongly suggested two waters coordinated to the gadolinium (Ahmed, *et al.*, 1994).

In all cases, the appropriate number of carbon atoms was seen at the expected distances for the respective ligand carbons. A recent structure determination of hydrated dysprosium *tris*-picolinate by X-ray diffraction showed two waters coordinated to the dysprosium as well as the three picolinate ligands (Fang, *et al.*, 1996). However, in this case the two solvent molecules are at distances, 2.33Å and 2.38Å, very similar to those in the aqua-ions.

Analysis of the EXAFS results for the non crystalline Fe(dmpp)<sub>3</sub> indicates an average of 3 oxygen atoms at 1.98Å, 3 oxygen atoms at 2.04Å, 6 carbon atoms at 2.78Å, 3 carbon atoms at 4.13Å, 3 carbon atoms at 4.16Å and 3 oxygen atoms at 3.94Å from solvent of crystallisation (Table 1f). These distances to the atoms in the chelate rings may be compared with the average values of 3 oxygen atoms at 1.99Å, 3 oxygen atoms at 2.04Å, 3 carbon atoms at 2.79Å, 3 carbon atoms at 2.80Å, 3 carbon atoms at 4.15Å, 3 carbon atoms at 4.19Å reported for the crystalline *tris*(1,2-dimethyl-3-hydroxy-4-pyridinonate) iron(III) complex (Charalambous, *et al.*, 1988) (Table 1g).

#### 4. Conclusion

These systems illustrate the value of the EXAFS technique in establishing the geometry of solid hydrates and of hydrated complexes in solution, and provide examples of the usefulness of EXAFS in structure determination for solids which are not obtainable in forms suitable for X-ray diffraction. The results reveal the location of solvent molecules associated with the complexes in the solid and solution states. The local structure around the metal centre is maintained in solution. We plan to use EXAFS in the near future to investigate solvation of inorganic complexes in mixed aqueous solvents, including an examination of pharmaceutically relevant complexes in water-saturated 1-octanol and to establish structures of metal complexes of pyridinones containing long hydrocarbon chain substituents.

#### Acknowledgements

Dr S.Gurman, Dr. L. Murphy and Dr. R. Strange are gratefully thanked for their help with the EXAFS multiple scattering analysis. We also thank the JNICT, British Council and EPSRC for their support.

#### References

- Ahmed, S., Burgess, J., Hurman, B. & Parsons, S.A. (1994). *Polyhedron*, **13**, 23-25.
- Ahmet, M. T., Frampton, C. S. & Silver, J. (1988). *J. Chem. Soc., Dalton Trans.*, 1159-1163.
- Benazeth, S., Purans, J., Chalbot, M-C., Nguyen-van-Duong, M.K., Nicolas, L., Keller, F. & Gaudemer, A. (1998). *Inorg. Chem.*, **37**, 3667-3674.
- Binsted, N., Strange, R.W. & Hasnain, S.S. (1992). *Biochemistry*, **31**, 12117-12125.
- Burgess, J. (1993). *Transition Met. Chem.* **18**, 439-448.
- Charalambous, J., Dodd, A., McPartlin, M., Matondo, S.O.C., Pathirana, N.D. & Powell, H.R. (1988). *Polyhedron*, **7(21)**, 2235-2237.
- Ellis, P. (1993), PhD Thesis, University of Sydney, Australia. The version of the SPLINE used in this paper has been modified by Ian Harvey, Daresbury Laboratory (1996).
- Fang, Ma Jian-, Hai, Hu Ning- & Zuan, Ni Jia- (1996). *Polyhedron*, **15**, 1797-1799.
- Habenschuss, A. & Spedding, F.H. (1979). *J.Chem. Phys.*, **70**, 2797-2806.
- Hider, C.R. & Hall, A.D., (1991). *Progr. Med. Chem.*, **28**, 41-173.
- Joyner, R.W., Martin, K.J. & Meehan, P. (1987). *J.Phys. C*, **20**, 4005-4012.
- Nelson, W.O., Rettig, S.J. & Orvig, C. (1987). *J. Am. Chem. Soc.*, **109**, 4121-4123.
- Nielson, G.W. & Tromp, R.H. (1991). *Annu. Rep. Chem., Section C, Royal Society of Chemistry*, **88**, 45-75.
- Patel, M.S. (1992). PhD Thesis, Leicester University, UK.
- Shannon, R. D. & Prewitt, C.T. (1969). *Acta Crystallogr.*, **25B**, 925-946, assign ionic radii of 1.20 and 1.17 Å for  $Gd^{3+}$  and  $Dy^{3+}$  respectively, in eight-coordination.
- Strange, R.W., Blackburn, N.J., Knowles, P.F. & Hasnain, S.S. (1987). *J. Am. Chem. Soc.*, **109**, 7157-7162.
- Yamaguchi, T., Tanaka, S. & Wakita, H. (1992). In *Rare Earths and Materials of the 21st Century*, ed. G. Adachi and H. Nagai, The Rare Earth Society of Japan, 330-335.

(Received 10 August 1998; accepted 3 December 1998)