Crystal structure of the tris 1,2-dimethyl-3-hydroxy-4-pyridinone (DMHP) complex with the Fe(III) ion

Eric T. Clarke, Arthur E. Martell* and Joseph Reibenspies
Department of Chemistry, Texas A&M University, College Station, TX 77843-3255 (USA)

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Abstract

Bidentate 1,2-dimethyl-3-hydroxy-4-pyridinone (DMHP) and its Fe(III) complex have been determined by single crystal X-ray diffraction at low temperature. Free DMHP is orthorhombic, space group *Pbca*, $Z=8$, $a=7.253(2)$, $b=12.989(3)$, $c=13.736(4)$ Å, $V=1293.5(11)$ Å^3. Hydrogen -bonding between the hydroxyl and carbonyl oxygen donor stabilizes DMHP in dimeric units. For the Fe(III) chelate, Fe(III) ion is six-coordinate with a distorted octahedral configuration consisting of six bidentate oxygen donor atoms in FeL$_3$ dodecahydrate; each of the coordinated oxygen atoms of the ligand is bridged by a water molecule to adjacent donors. Chains of water molecules bridge between the Fe(III) complex and hexagonal cylinders of water. The FeL$_3$ chelate is trigonal, space group $P\bar{3}$, $Z=2$, $a=16.614(5)$, $b=16.614(5)$, $c=6.831(3)$ Å, $V=1632.9(10)$ Å^3. The structures were solved by direct methods and refined by least-squares techniques to $R=5.42\%$ (1367 reflections collected) for the free ligand; and $R=5.59\%$ (3999 independent reflections) for the Fe(III) complex.

Introduction

The stabilities and coordination chemistry of Fe(III) with bidentate 1,2-dimethyl-3-hydroxy-4-pyridinone (DMHP) [1, 2] and related hydroxypyridinone ligands [3] have resulted from their efficacy as oral iron chelating agents [3–5] and as agents for the treatment of iron overload conditions [6–8]. Hydroxypyridinones form stable complexes with Fe(III) ion and other trivalent metal ions such as Ga(III), Al(III) and In(III) at acidic and neutral pH [1–3] and are effective as chelating agents for Fe(III) in medicinal applications for the removal of Fe(III) from serum transferrin and storage proteins [9]. The Ga(III), Al(III) and In(III) stabilities of the hydroxypyridinones [1, 3, 10, 11] have also been determined in view of their potential use in medicine as agents for tissue imaging [6, 11, 12] and for treatment of neurological diseases associated with Al(III) ion [13]. X-ray crystal structure determinations of the coordination chemistry of DMHP [14] with Al(III) and Ga(III) ions [13, 15] and In(III) [16] (and related ethyl- and aryl-substituted analogues [12, 17]) have been reported by Orvig and coworkers, and the determination for the Fe(III)–DMHP complex has been incompletely reported in a communication by Charalambous *et al.* [18]. A detailed description of the Fe(III)–DMHP chelate is valuable for the design of Fe(III) sequestering agents [5, 19–21] that involve hydroxypyridinones as bidentate ligands [19] or hexadentate ligands [7].

A determination of the DMHP crystal structure and that of its Fe(III) chelate at 193 K (under nitrogen) is warranted. The results will be compared to the Al(III), Ga(III) and In(III) crystal structures of hydroxypyridinone complexes [12, 13, 15–17] in order to assess the influence of metal ion size and choice of substituent group on metal coordinate bond formation with DMHP.

Experimental

Preparation of Fe(DMHP)$_3$·12H$_2$O

Pure DMHP ligand was kindly supplied by M. M. Jones of Vanderbilt University (*FW*=129). Standard 0.01945 M Fe(NO$_3$)$_3$ was filtered and standardized with Na$_2$H$_2$EDTA in the method of Schwarzenbach *et al.* [22]. A 3:1 ligand:metal complex was prepared by weighing out 93.06 mg of DMHP (0.6695 mmol) and adding 11.4 ml of standard Fe(III) stock solution (0.2218 mmol). The p[H] of the complex solution was adjusted with 10 M KOH to 9.21. The color of the solution was deep maroon. Excess solvent was removed at 70 °C by gentle evaporation under vacuum. Crystals suitable for X-ray structure determination were obtained from water after cooling the complex in the refrigerator for 24 h. Recrystallization from hot water was not necessary. The bulk of the crystals was recovered by filtration,

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*Author to whom correspondence should be addressed.

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washed with water, and dried in a vacuum oven at 60 °C for 12 h in preparation of elemental analysis. The crystals used for X-ray structure determination were kept in the mother liquor just prior to mounting. *Anal.* (Galbraith, Knoxville, TN): Calc. for $FeC_{21}N_3H_{24}O_6 \cdot 3H_2O$, $FW = 524$: C, 48.09; N, 8.02; H, 5.73. Found: C, 48.60; N, 7.95; H, 5.68%. The analysis indicates that 9 waters of crystallization had been removed in the drying procedure compared to the 12 waters found in the crystal structure.

Methods

For the determination of the structure of free DMHP, a colorless needle (0.16 mm × 0.16 mm × 0.48 mm) was mounted on a glass fiber with epoxy cement at room temperature and cooled to 193 K in a nitrogen cold stream (Nicolet LT-2). A single crystal of $Fe(DMHP) \cdot 12H_2O$ was obtained as a red plate (0.08 mm × 0.20 mm × 0.44 mm) from the mother liquor and was mounted and examined in the same manner as the free DMHP crystal. (Cell parameters and other crystal data for DMHP and its Fe(III) complex are summarized in Table 1). Examination was performed on a Nicolet R3m/V X-ray diffractometer (oriented graphite monochromator; Mo Kα $\lambda = 0.71073$ Å radiation). The cell parameters (Table 1) were calculated from the least-squares fitting of the setting angles for 25 reflections (2θ av. = 23.2°). Omega scans for several intense reflections indicated acceptable crystal quality, albeit, the quality of the crystal of the Fe(III) complex was relatively poor.

Data were collected for DMHP and $Fe(DMHP)_3 \cdot 12H_2O$ with θ–2θ scans (Table 1), with variable scan rates (1.50 to 15.00°/min). The intensity (I) and its standard deviation ($\sigma(I)$) were calculated from $I = (\text{total counts} - \text{background counts})/\text{time}$; $\sigma(I) = ((\text{total counts} + \text{background counts})/\text{time}^2)^{1/2}$. Three control reflections, collected every 97 reflections, showed no significant trends. Background measurements were determined by stationary crystal and stationary counter techniques at the beginning and end of each scan for 50% of the total scan time.

Lorentz and polarization corrections (L_p) were applied as described in Table 1.

$$L_p = [\{1 + \cos^2(12.2°)(\cos^2\theta)/(1 + \cos^2(12.2°)\} \\ + \{(1 + |\cos(12.2°)|(\cos^2 2\theta)/(1 + \cos(12.2°))\}] \\ \times [1/2 \sin 2\theta]$$

The unscaled structure factor (F_o) and its standard deviation, $\sigma(F_o)$, were calculated from $(F_o) = (I/L_p)^{1/2}$; $\sigma(F_o) = (I)/2L_pF_o$. For the determination of the free ligand, no absorption correction was applied, whereas a semi-empirical absorption correction (SHELXTL-Plus reference manual [23]) was used for the Fe(III) chelate. Reflections measured at their azimuthal angle, ψ, cor-

TABLE 1. Crystal data and analysis parameters (193 K)[a]

Empirical formula	$C_7H_9NO_2$	$FeC_{21}H_{48}N_3O_{18}$
Formula weight	139.2	686.5
Morphology	needle	plate
Crystal dimensions (mm)	0.16 × 0.16 × 0.48	0.08 × 0.20 × 0.44
Space group	orthorhombic, *Pbca*	trigonal, $P\bar{3}$
Lattice parameters		
a (Å)	7.253(2)	16.614(5)
b (Å)	12.989(4)	16.614(5)
c (Å)	13.736(4)	6.831(3)
Volume (Å^3)	1293.5(11)	1632.9(10)
Z	8	3
D_{calc} (g/cm^3)	1.429	1.396
$F(000)$ (e^-)	592	730
μ(Mo Kα) (mm^{-1})	0.099	0.534
Transmission factors	(none)	0.6710–0.9440
2θ range (°)	4.0–50.0	4.0–50.0
Reflections collected	1367	3999
Unique observed reflections	1151($I > 2\sigma(I)$)	1905 ($I > 2\sigma(I)$)
Residuals: R; R_w (%)	5.42; 5.50	5.59; 5.19
Goodness of fit	3.28	1.45
Largest Δ/σ	0.0125	0.0012
Largest difference peak	0.55	0.58
Index ranges, h, k, l	$0 \leqslant h \leqslant 8$	$-19 \leqslant h \leqslant 0$
	$0 \leqslant k \leqslant 15$	$0 \leqslant k \leqslant 19$
	$0 \leqslant l \leqslant 16$	$-8 \leqslant l \leqslant 8$
Extinction coefficient[b], χ	0.0011(2)	(none)
Scan width (w) + Kα separation	1.2°	1.2°

[a] Errors of last significant figures appear in parentheses. [b] $F^* = F_c/[1 + 0.002_\chi F_c^2/\sin 2\theta]^{1/4}$.

responding to 360° rotation of the crystal about its diffraction vector, were utilized to apply a correction to the reflections (Table 1).

The structures were solved by direct methods (SHELXS, SHELXTL-Plus program package, Sheldrick [23]). Full matrix least-squares anisotropic refinement for all non-hydrogen atoms, quantity minimized $\Sigma w(|F_o| - |F_o|)^2$; $w^{-1} = \sigma^2 F + gF^2$, $g = 0.00010$, yielded the residuals at convergence * as summarized in Table 1. $R = 0.056$, $R_w = 0.052$ for the Fe(III) chelate; $R = 0.054$ and $R_w = 0.055$ for the free ligand. Free DMHP was refined in space group *Pbca* (61) [24], whereas $Fe(DMHP)_3 \cdot 12H_2O$ was assigned to space group $P\bar{3}$, by inspection of systematic absences.

Hydrogen atom positions were located in the difference Fourier map for free DMHP. For the Fe(III) complex they were placed in idealized positions with isotropic thermal parameters fixed at 0.08 Å. (Owing to the poor quality of the tris Fe(III) DMHP crystal, the hydrogen atom positions were not calculated.) Neutral atom scattering factors and anomalous scattering correction terms were taken from Ibers and Hamilton [25]. The extinction correction used for refinement of DMHP was 0.0011(2) at convergence in the method of Larson [26]. In the Fe(III) chelate, the site occupancy of Fe metal ion was fixed at 1/3 occupancy by symmetry.

TABLE 2. Final atom coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for DMHP and $Fe(DMHP)_3 \cdot 12H_2O$

Atom	x	y	z	U_{eq}[a]
DMHP				
O_1	1286(3)	4032(2)	4751(1)	31(1)
O_2	177(3)	5562(1)	3511(1)	28(1)
N	1425(3)	3560(2)	1809(2)	23(1)
C_1	1307(4)	3859(2)	3835(2)	22(1)
C_2	1896(4)	2914(2)	3405(2)	24(1)
C_3	1925(4)	2793(2)	2425(2)	25(1)
C_4	834(4)	4503(2)	2173(2)	21(1)
C_5	772(4)	4639(2)	3157(2)	22(1)
C_6	336(4)	5325(2)	1459(2)	27(1)
C_7	1473(5)	3370(2)	755(2)	34(1)
$Fe(DMHP)_3 \cdot 12H_2O$				
Fe	3333	6667	888(2)	23(1)
O_1	2533(2)	5536(2)	2611(4)	32(1)
O_2	2181(2)	6062(2)	−742(4)	32(1)
N	118(2)	3798(2)	−220(5)	28(2)
C_1	1758(3)	4964(3)	1783(6)	27(2)
C_2	1098(3)	4076(3)	2540(7)	34(2)
C_3	306(3)	3532(3)	1537(7)	36(2)
C_4	728(3)	4633(3)	−1033(6)	31(2)
C_5	1552(3)	5223(3)	−33(7)	25(2)
C_6	515(3)	4878(3)	−2954(6)	39(2)
C_7	−755(3)	3134(3)	−1208(7)	43(2)
O_{1w}	1837(2)	975(2)	5601(4)	46(2)
O_{2w}	3155(2)	1794(2)	2653(4)	42(2)
O_{3w}	2781(2)	4869(2)	6238(4)	44(2)
O_{4w}	821(2)	1881(2)	10301(4)	34(1)

[a] e.s.d.s. are given in parentheses.

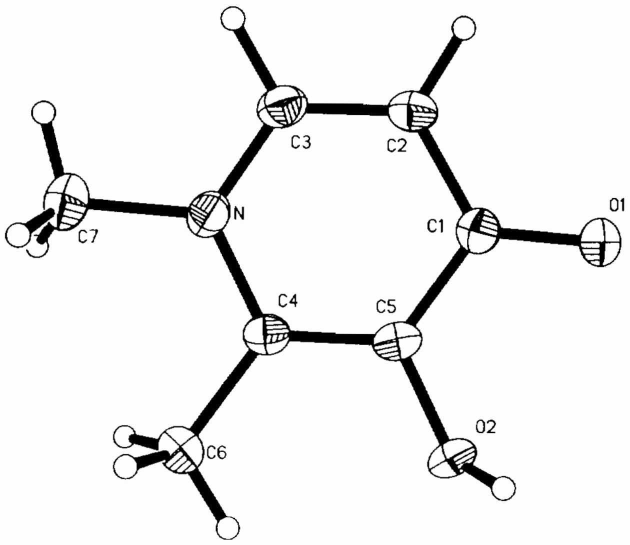

Fig. 1. Structure of DMHP and atom numbering scheme.

Results

Crystal structures of DMHP and its tris Fe(III) chelate, $Fe(DMHP)_3$ dodecahydrate, were determined from samples that were recovered from water (Tables 1 and 2). DMHP is planar (Figs. 1 and 2) with delocalization of C–C, C=C and N=C bonds in the ring structure (Table 3). The bond lengths of the hydroxyl and keto oxygen donors are 1.363(3) and 1.278(3) Å, respectively. Delocalization of the ring is enhanced upon loss of the hydroxyl proton and coordination of the oxygen donor atoms to Fe(III) in a facial or distorted octahedral coordination geometry (Figs. 3 and 4). Changes in bond length are most noticeable at C(1)–C(5) where the C–C bond of the free ligand is shortened by 0.021 Å (from 1.431(4)) to 1.410(5) Å in the Fe(III) chelate, and when the C=C bond at C(4)–C(5) is correspondingly lengthened from 1.363(4) to 1.400(4) Å upon coordination. The N=C bonds are alternately lengthened and shortened compared to the free ligand by as much as 0.029 Å. Ketonic character of the C=O donor is partially maintained in the Fe(III) complex where the C=O bond is lengthened by 0.009 Å to become 1.287(4) Å, while the C–O(H) bond is shortened by 0.017 Å by delocalization to 1.346(4) Å (compared to 1.363(3) Å in the free ligand). Corresponding changes in the ring bond angles are small: the largest shift is in the C(2)–C(1)–C(5) angle with an increase of 2.3°

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*Residuals, $R_{int} = [\Sigma F^2 - (F_{mean})^2]/\Sigma F^2$; $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $R_w = \{[\Sigma w(|F_o| - |F_c|)^2]/[\Sigma w(|F_o|)^2]\}^{1/2}$; $S = \{[\Sigma w(|F_o| - |F_c|)^2]/[|N_{data}| - |N_{parameters}|]\}^{1/2}$.

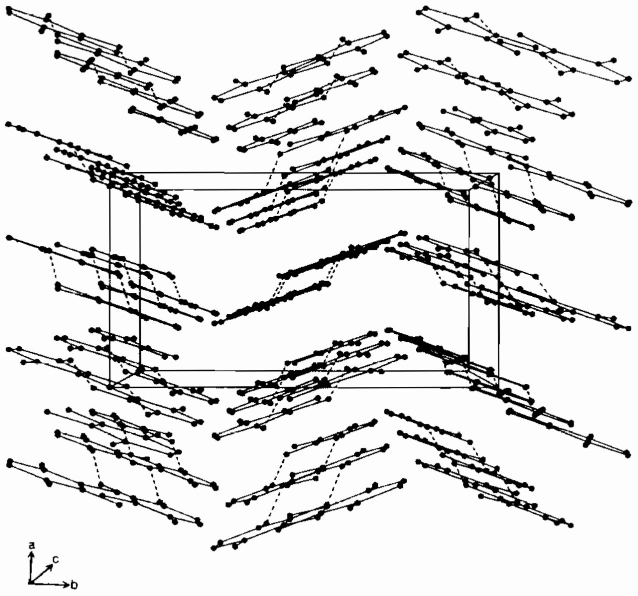

Fig. 2. Packing diagram of DMHP in dimeric units which are viewed down the c axis. Hydrogen bonds between hydroxyl oxygen atoms O(2) and carbonyl oxygens O(1) are depicted by dashed lines.

TABLE 3. Selected interatomic distances (Å) and angles (°) for DMHP and $Fe(DMHP)_3 \cdot 12H_2O$[a, b]

	DMHP	$Fe(DMHP)_3 \cdot 12H_2O$
Bond distances		
O(1)–C(1)	1.278(3)	1.287(4)
O(2)–C(5)	1.363(3)	1.346(4)
O(2)–H(1)	0.850	
$O(1)–Fe_{av}$		2.046(3)
$O(2)–Fe_{av}$		1.998(3)
C(1)–C(2)	1.427(4)	1.424(5)
C(2)–C(3)	1.356(4)	1.352(6)
N–C(3)	1.356(4)	1.368(7)
N–C(4)	1.391(4)	1.362(5)
C(4)–C(5)	1.363(4)	1.400(5)
C(1)–C(5)	1.431(4)	1.410(5)
N–C(7)	1.469(4)	1.469(7)
C(4)–C(6)	1.494(4)	1.475(5)
C(2)–H(2)	1.003	[c]
C(3)–H(3)	1.029	[c]
$C(6)–H(6)_{av}$	0.960	[c]
$C(7)–H(7)_{av}$	0.960	[c]
Bond angles		
O(1)–Fe–O(2)		80.8(1)
O(1)–Fe–O(2A)		98.4(1)
O(1)–Fe–O(1B)		90.2(1)
O(2)–Fe–O(2A)		91.9(1)
O(2)–Fe–O(1B)		98.5(1)
O(1)–Fe–O(1A)		90.2(1)
O(2)–Fe–O(1A)		167.4(1)
Fe–O(1)–C(1)		112.1(3)
Fe–O(2)–C(5)		111.9(3)
O(1)–C(1)–C(5)	120.9(3)	117.8(3)
O(2)–C(5)–C(1)	118.4(3)	116.9(3)
O(1)–C(1)–C(2)	124.2(3)	125.0(4)
O(2)–C(5)–C(4)	118.6(3)	122.0(4)
C(1)–C(5)–C(4)	123.0(3)	121.1(3)
N–C(4)–C(5)	118.7(3)	119.0(4)
C(3)–N–C(4)	120.3(2)	120.8(3)
N–C(3)–C(2)	122.1(3)	122.1(4)
C(1)–C(2)–C(3)	120.9(3)	119.7(4)
C(2)–C(1)–C(5)	114.9(3)	117.2(3)
C(5)–C(4)–C(6)	123.4(3)	121.9(4)
N–C(4)–C(6)	117.9(2)	119.1(3)
C(4)–N–C(7)	120.6(2)	121.9(4)
C(3)–N–C(7)	119.0(2)	117.3(3)

[a] Refer to Figs. 1 and 3 for atom numbering scheme. [b] e.s.d.s. are given in parentheses. [c] Hydrogen positions were not found by refinement.

over 114.9(3)°. The C(2)–C(1)–C(5) bond angle becomes more acute by 1.9°.

The ligand crystallized in dimeric units (Fig. 2) in a herring-bone pattern. The contents of several unit cells are shown translated along the a axis and viewed down the c axis in the packing diagram. The dimers are held together by H-bonding interactions between the hydroxyl groups O(2) and the carbonyl oxygen O(1) atoms of adjacent ligands which are oriented in head-to-tail fashion. For the dimers, the intermolecular non-bonded O(2)...O(1) distance is 2.666(2) Å. The ligand planes are oriented about 168° relative to each other as calculated from the observed angles of C(1)–O(1)...O(2) = 140° and C(5)–O(2)...O(1) = 128°. The ligand bond distances and angles are consistent with those reported by Nelson *et al.* [14], except that the O...O non-bonded interaction was previously reported as 2.692(3) Å at higher temperature.

The distorted octahedral geometry of the Fe(III) chelate with three DMHP ligands (Fig. 3) has three-fold symmetry directed along the c axis and is isostructural with the tris DMHP complexes of Al(III), Ga(III) and In(III) reported by the Orvig research group [13, 15, 16]. The Fe(III) ion is displaced relative to the ligand planes at an average of 0.188(1) Å. Each of these metal complexes is crystallized with 12 water molecules that are held in a network and are stabilized by hydrogen-bonding interactions between the waters of crystallization (formed in bridges and cylinders) and the ligand oxygen atoms that are coordinated to the Fe(III) ion. The cylinders appear at the corners of the unit cell (Fig. 4) and are connected to the Fe(III) complex via water molecules O(2W) and O(3W). O(3W) also forms a bridge between coordinated O(1) and O(2) atoms and their counterparts in adjacent ligands which are oriented at 120° and translated one unit cell along the c axis. The hexagonal geometry of the cylinders is imposed by an S_6 symmetry operation on water molecules O(1W) and O(4W). The O(W)...O(W) intermolecular distances for water molecules contained in the bridges and hexagonal cylinders range from 2.73(4) to 2.80(4) Å, while the hydrogen bonds between the

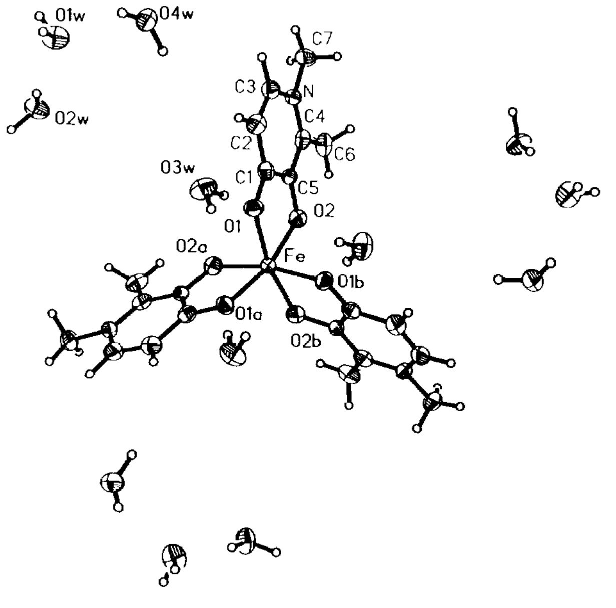

Fig. 3. Distorted octahedral complex of Fe(DMHP)$_3$·12H$_2$O and atom numbering scheme. Positions of the four water molecules O(W) involved in water chains and cylinders are labelled. See Fig. 4.

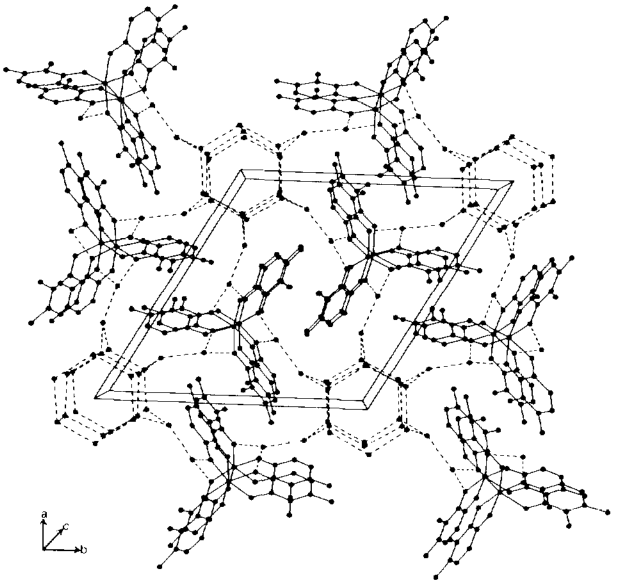

Fig. 4. Packing diagram of Fe(DMHP)$_3$·12H$_2$O. Hydrogen bonding interactions within chains and cylinders of water are illustrated together with the water bridging between coordinated oxygen donors. The contents of two unit cells are shown translated along the *c* axis.

water molecules are about 1.74 to 1.90 Å. The interplanar stacking distance between the Fe(III) centers is ~6.83 Å. The quality of the crystal data set would not allow for an exact description of the hydrogen atom positions; information about hydrogen bonds were inferred from the O–O distances. More detailed descriptions of the hydrogen-bonding interactions in the water cylinders for the dodecahydrates of tris hydroxypyridinone complexes with other trivalent metal ions are found in the references of Orvig and co-workers [13, 15–17]. The present work serves to confirm the previous structure of the free ligand reported by Nelson *et al.* [14] and to provide more information about its Fe(III) chelate than that which has already been reported [18].

Discussion

The description of the intramolecular bond distances and angles for Fe(DMHP)$_3$·12H$_2$O and in interaction with the waters of crystallization is consistent with the literature descriptions for the structures of the Al(III), Ga(III) and In(III) tris complexes of 2-methyl-3-hydroxy-4-pyridinone ligands with different N-substituents: N-methyl [13, 16]; N-ethyl [17]; and N-tolyl [12]. The metal complexes are dodecahydrates, except for the cases of the tolyl-substituted complexes with Al(III) and Ga(III) ions which are reported as 5.5 hydrates, owing to the greater steric demands of the tolyl groups with the exclusion of some of the water molecules [12]. The change of N-substituent group does not effect significant changes in M–O bond lengths and angles, as evidenced by the keto oxygen bond lengths to Ga(III) ion for N-methyl, N-ethyl and N-tolyl substituents, which are 1.967(3), 2.000(1) and 1.996(2) Å, respectively [12, 13, 17], while the O–Ga–O bond angles were 83.22(12), 83.03(6) and 83.15(7)°. Similar observations were made for the hydroxyl oxygen bonds to Ga(III) and also for both types of oxygen bonds to Al(III).

Trends among bond lengths and angles for the oxygen donor atoms to the trivalent metal ions are apparent in Table 4. The hydroxyl oxygen O(2) bond to the metal ion is shorter than the carbonyl oxygen O(1) bond to metal ions in each case, and the M–O bond lengths show a regular trend of In(III) ≫ Fe(III) > Ga(III) ≫ Al(III) [13, 16, 18]. This comparison indicates qualitatively the differences in the stabilities of the

TABLE 4. Average chelated bond distances (Å) and angles (°) in tris DMHP complexes of trivalent metal ions[a]

	In(III)[b]	Fe(III)[c, d]	Ga(III)[e]	Al(III)[e]
M–O (C–OH)	2.134(2)	1.998(3)	1.967(3)	1.893(2)
M–O (C=O)	2.165(2)	2.046(3)	1.990(3)	1.923(2)
C–O (C–OH)	1.343(3)	1.346(4)	1.342(5)	1.327(3)
C–O (C=O)	1.289(3)	1.287(4)	1.304(5)	1.299(3)
O–M–O (*cis*)	77.87(6)	80.8(1)	83.22(12)	84.23(6)

[a] e.s.d.s. are given in parentheses. [b] Ref. 16. [c] Present work. [d] Ref. 18: Fe–O (C–OH) = 1.998(4), Fe–O (C=O) = 2.038(4), C–O (C–OH) = 1.342(7), C–O (C=O) = 1.299(8) Å. [e] Ref. 13.

TABLE 5. Calculated M–O (C–OH) bond distances (Å) for the trivalent metal ion chelates of DMHP

	In(III)	Fe(III)	Ga(III)	Al(III)
O–M observed	2.134	1.998	1.967	1.893
Metal crystal radii[a]	0.940	0.785	0.760	0.675
Apparent O radii	1.194	1.213	1.207	1.218
Calculated O radii[b, c]	1.21(2)	1.21(2)	1.21(2)	1.21(2)
O–M calculated[d]	2.15(2)	2.00(2)	1.97(2)	1.89(2)

[a] Ref. 27. [b] Range: 1.20(2)–1.22(2) Å. Oxygen ionic radii (as RO–) were calculated as the difference between Na–O bond distances in sodium *o*-nitrophenolate, from ref. 28 (bidentate oxygen gives 2.296 and 2.320 Å bond lengths), and the Na^+ ion radius = 1.10(2) Å for $CN = 2$, which was estimated from bond data in ref. 27 and discussion in ref. 29. [c] e.s.d.s. are given in parentheses. [d] Calculated from the sum of metal crystal radii and estimated (calculated) oxygen crystal radii.

In(III), Fe(III), Ga(III) and Al(III) complexes and shows an inverse relationship between the stabilities of complexes and the average bond distance between the metal ion and the donor oxygen atoms. As indicated in Table 4 the bond distances between M and O(H) for the Fe(III) and Ga(III) complexes are nearly the same, with those of Ga(III) being ~0.03 Å shorter than those of Fe(III). This correlates with the slightly higher stability of the Ga(III) complexes. The In(III) complex is much less stable corresponding to a longer M–O bond distance of almost 0.14 Å. The Al(III) complex which is also much less stable has ~0.07 Å shorter bond distance corresponding to a lower effective radius of the metal ion. Presumably the Al(III) ion is too small to meet the optimum requirements demanded by the bite size of the ligand and this correlates with the fact that the O–M–O angle indicted in Table 4 is the largest for the Al(III) complex.

Table 5 shows a very good correlation between the M–O observed bond distances and the calculated distances for the In(III), Fe(III), Ga(III) and Al(III) complexes. The calculated values were obtained from the crystal radii of the octahedral metal and the bidentate oxygen from the table published by Shannon [27]. In all cases the calculated values were within the estimated standard deviations which are due mostly to the uncertainty of the crystal radius of bidentate oxygen, 1.21 ± 0.02 Å. A similar correlation could be obtained by using the effective radii of the octahedral metal ions and bidentate oxygen listed in the same Table.

The average bond distances given in Table 6 of the tris Fe(III) chelate of catecholate and hydroxamate ligands together with the bond distances of DMHP are compared with their Fe(III) complex stability constants. One would expect that the average metal oxygen distance should be smaller if the complexes are more stable. However, the comparison of trends in M–O distances does not reflect the trends in stabilities that are generally accepted. The average catechol distance is a little lower than that of DMHP (a hydroxypyridinone ligand) indicating a more stable complex with the former. For the hydroxamate ligands listed, however, and DMHP, there is very little difference in the average M–O bond distances, although because of the ring resonance in DMHP it is thought that its complexes are somewhat more stable than those of the simple hydroxamic acids. Delocalization between the negative oxygen of DMHP and the carbonyl group could tend to equalize the negative charge on DMHP more than that which occurs in the hydroxamic acid. This is reflected somewhat in the greater binding of hydrogen ion since the pK_a of DMHP (9.8) is somewhat higher than the pK_as of the hydroxamic acids (~8–9). With acetylacetone, containing two equivalent oxygen donors and a total charge of −1 the M–O distance is not distinguishably different from the average of the hydroxamates.

The wide variation of the Fe(III) stability constants in Table 6 is in sharp contrast to the almost invariance in the M–O distances. These effects reflect internal constitutional properties of the ligands and are at least partially reflected by their affinities for hydrogen ions (their p*K* values). Other factors, which are steric in nature, depend on the structure of the ligand, and the degree of preorganization; these factors are more complex and are not related in any simple manner to either the p*K* or the M–O bond distance.

TABLE 6. Average bond distances (Å), angles (°) and stabilities of six-coordinate Fe(III) chelates[a]

Ligand	M–O (C–OH or N–OH)	M–O (C=O)	O–M–O	Log stability constants
DMHP (3:1)	1.998(3)	2.046(3)	80.8(1)	35.9[b]
Catechol[c]	2.015(6)		81.3(1)	(44.9)[d]
Bicapped TRENCAM[e]	2.012(2)		77.75(11)	43.1
Ferrichrome A[f]	1.980(4)[g]	2.033(3)	78.1(2)	
Ferrioxamine E[h]	1.953(3)[g]	2.055(4)	78.9(1)	32.49[i]
Acetylacetone (3:1)[j]		1.992(6)	87.1(3)	25.3[d]

[a] e.s.d.s. are given in parentheses. [b] Refs. 1 and 2. [c] Ref. 28. [d] Ref. 30 (value is uncertain). [e] Ref. 20. [f] Ref. 31. [g] Hydroxamate N–O(H). [h] Ref. 32. [i] Ref. 33. [j] Ref. 34.

Supplementary material

Tables listing structure factors, anisotropic thermal parameters, hydrogen atom coordinates, torsion angles, intermolecular non-bonding distances, and least-squares planes, are available from the authors.

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