

# Structural studies on an iron(III) complex containing (*Z*)-2-(2-aminothiazol-4-yl)-*N*-(2-hydroxyethyl)-2-(hydroxyimino)acetamide, a model compound for a cephalosporin antibiotic Cefdinir

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(*Z*)-2-(2-Aminothiazol-4-yl)-*N*-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) has been employed as a model compound for a cephalosporin antibiotic, Cefdinir. A trinuclear iron(III) complex  $[\text{Fe}_3\text{L}_6]\text{Cl}[\text{OH}]_2$  **1** has been obtained from a methanol solution containing HL and  $\text{FeCl}_3$  and its structure determined by X-ray crystallography: monoclinic, space group  $P2_1/n$ ,  $a = 15.559(1)$ ,  $b = 19.295(2)$ ,  $c = 10.963(1)$  Å,  $\beta = 101.29(1)^\circ$ ,  $Z = 2$ . The molecular structure contains a linear Fe(1)–Fe(2)–Fe(1') arrangement, the central atom Fe(2) being an inversion centre. Atom Fe(1) is co-ordinated to three molecules of L through the thiazole and oximate nitrogen atoms to form Fe(1)L<sub>3</sub>, and Fe(2) to six oximate oxygen atoms of the two Fe(1)L<sub>3</sub> units. The two Fe(1)L<sub>3</sub> units are bridged by the central iron atom Fe(2). The Mössbauer spectrum of **1** gave an apparent doublet signal consisting of two doublets, A and B, assigned to Fe(1) and Fe(2), respectively. The isomer shifts  $\delta$  of these doublets are the same (0.26 mm s<sup>-1</sup>), and are typical for high-spin iron(III). In addition, the reflectance spectrum did not show any intervalence bands. These spectral data indicate that the three iron atoms are high-spin iron(III). The compound co-ordinates to iron(III) *via* the thiazole ring nitrogen atom and the oximate nitrogen atom (2N mode) in methanol which is different from that in water, where L prefers to co-ordinate to an iron(III) through the oximate oxygen atom and the amide oxygen atom (2O mode).

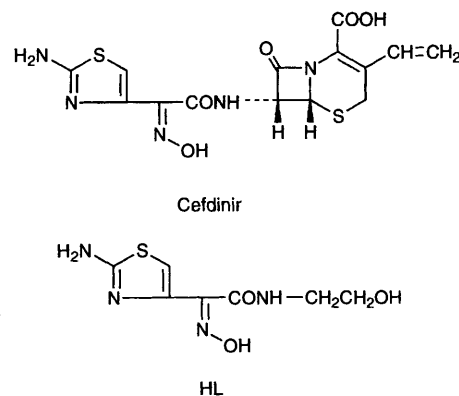
Interactions between metals and medicines are becoming important subjects for study, since the activities of some drugs are influenced by such interactions. A number of studies have been carried out on the relationship between the effectiveness of some medicines and their co-ordination properties to metal ions.<sup>1–8</sup>

(–)-(6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-(hydroxyimino)acetamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (Cefdinir) is an orally active semisynthetic cephalosporin antibiotic which has a structure characterized by oxime, amide and thiazole groups, which can co-ordinate to metal ions. We have reported that its bioavailability was reduced when co-administered with iron supplements,<sup>9</sup> and this was presumed to be due to complex formation with iron in the digestive tract.<sup>10</sup> Our potentiometric and spectrophotometric studies indicated that the thiazole, oxime and amide groups were involved in complexation with iron(II) and -(III) in aqueous solution.<sup>10</sup> In the present study we employed (*Z*)-2-(2-aminothiazol-4-yl)-*N*-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) as a model of Cefdinir for an X-ray crystallographic study to clarify the co-ordination properties of Cefdinir, since the co-ordination sites have been found to be on the side chain at the 7 position of the cephalosporin ring. A iron(III) complex of HL was prepared and its molecular structure determined by means of X-ray crystallography.

## Experimental

### Materials

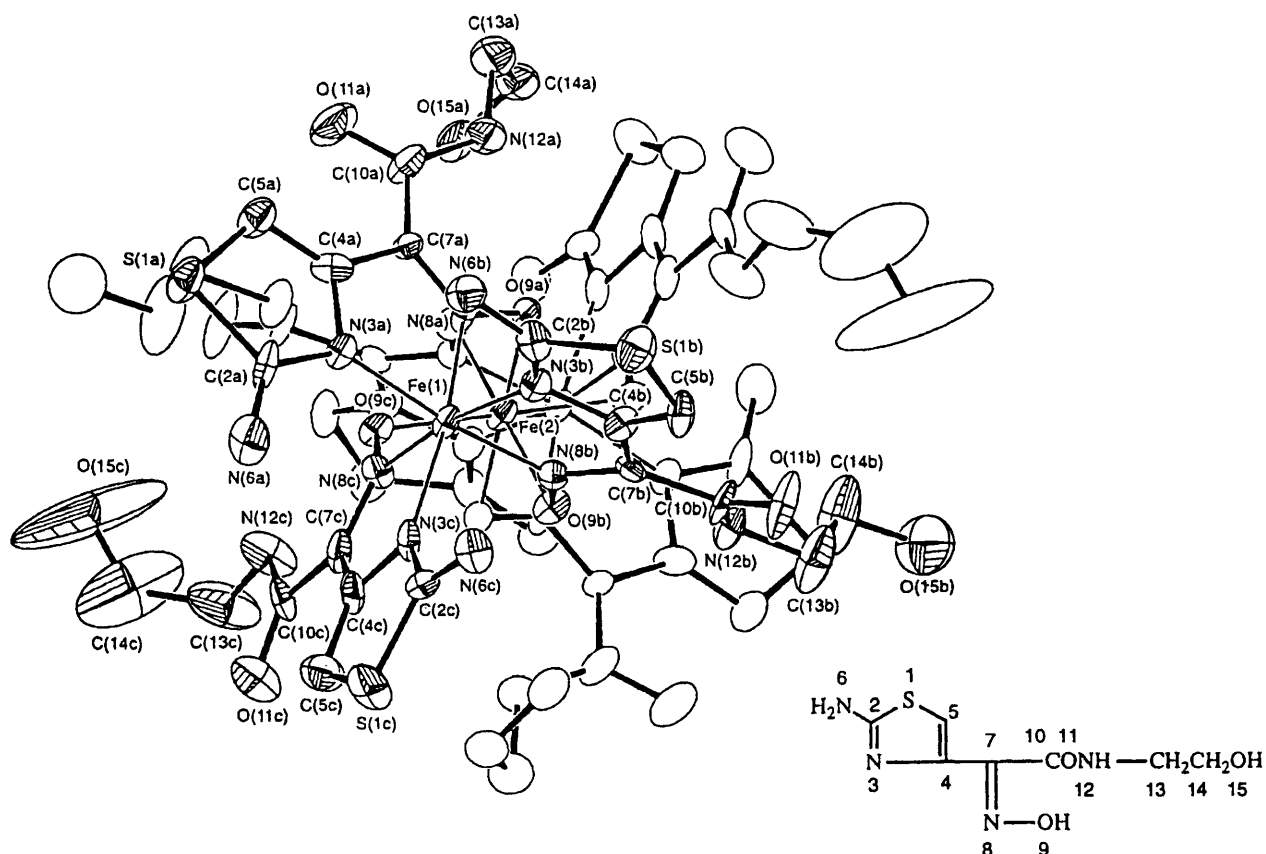
The compound  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  (reagent grade) was obtained from Wako Pure Chemicals Ltd. (Osaka, Japan). The compound HL was obtained in a total yield of 40% by acetylating (*Z*)-2-(2-aminothiazol-4-yl)-2-hydroxyiminocarboxylic acid with acetic anhydride, subsequently converting the acetylated compound



into a carbonyl chloride form with phosphorus pentachloride, then in the presence of *N,N'*-bis(tetramethylsilyl)urea coupling the carbonyl chloride and 2-aminoethanol, and finally hydrolysing with ammonium chloride (Found: C, 36.40; H, 4.45; N, 24.50. Calc. for  $\text{C}_7\text{H}_{10}\text{N}_4\text{O}_3\text{S}$ : C, 36.50; H, 4.40; N, 24.35%).  $\delta_{\text{H}}[(\text{CD}_3)_2\text{SO}]$  3.36 (4 H, m,  $\text{CH}_2\text{CH}_2$ ), 4.67 (1 H, t, OH), 6.69 (1 H, s,  $\text{C}_3\text{HNS}$ ), 7.10 (2 H, s,  $\text{NH}_2$ ), 8.22 (1 H, t, CONH) and 11.18 (1 H, s, NOH).

### Preparation of complex 1

Compound HL (70 mg, 300  $\mu\text{mol}$ ) was dissolved in methanol (ca. 20 cm<sup>3</sup>) and  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  (27 mg, 100  $\mu\text{mol}$ ) added. The solution was warmed at ca. 40 °C for about 30 min. After cooling to room temperature, a small amount of diethyl ether was added and the resulting blackish red solution was allowed to stand at room temperature. After a few weeks, shiny black prisms of complex **1** were obtained and dried *in vacuo* overnight (Found: C, 30.95; H, 3.35; N, 20.30. Calc. for  $\text{C}_42\text{H}_{56}\text{ClFe}_3\text{N}_{24}\text{O}_{20}\text{S}_6$ : C, 31.30; H, 3.50; N, 20.85%).



**Fig. 1** Molecular structure of  $[\text{Fe}_3\text{L}_6]\text{Cl}[\text{OH}]_2$  **1** showing 50% probability thermal ellipsoids and the atom-labelling scheme. Chloride and hydroxide ions are omitted

## Crystallography

Diffraction data were collected using a Rigaku AFC-5R automated four-circle diffractometer with Ni-filtered Cu-K $\alpha$  radiation ( $\lambda = 1.54178 \text{ \AA}$ ). The unit-cell constants were refined from 20 centred reflections ( $39.0 < 2\theta < 40.7^\circ$ ). Intensity data in the range  $2\theta < 125^\circ$  were collected by the  $\omega$ -2 $\theta$  scan technique;  $\omega$ -scan width  $(1.8 + 0.15 \tan \theta)^\circ$ , scan speed  $8.0^\circ \text{ min}^{-1}$ . The intensities of 5149 unique reflections were measured in the range  $0 \leq 2\theta \leq 125^\circ$  ( $h -18$  to  $18$ ;  $k 0-22$ ;  $l 0-13$ ), of which 2108 having  $F_o > 3\sigma(F_o)$  were used in subsequent refinement. The intensities of three reflections, chosen as standards and measured every 100, showed no significant variations ( $< 2\%$ ). Data were corrected for Lorentz and polarization effects. An empirical absorption correction based on a series of  $\psi$  scans was applied;<sup>11,12</sup> maximum and minimum correction factors were 0.9964 and 0.8141, respectively. The crystallographic data are summarized in Table 1.

The structure was solved by direct methods (MULTAN 78)<sup>13</sup> and refined on  $F$  by a block-diagonal least-squares method using the program HBL5-V.<sup>14</sup> Anisotropic thermal parameters were used for non-hydrogen atoms. The positions of the hydrogen atoms of the thiazole and ethylene groups of L in the complex were calculated based on an idealized molecular geometry. These hydrogen atoms with isotropic thermal parameters were included in further refinement. The weighting scheme used was  $w = 1/\sigma^2(F_o)$ . The final  $R$  and  $R'$  values were 0.077 and 0.089 for 2108 reflections. Atomic scattering factors are from ref. 15. All computations were carried out on an ACOS 2020 computer at the Computation Center, Osaka University, and on an ACOS S-850 computer at the Crystallographic Research Center, Institute for Protein Research, Osaka University. The atomic positional parameters for the non-hydrogen atoms are listed in Table 2.

Complete atomic coordinates, thermal parameters, and bond

lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.* 1996, Issue 1.

## Spectroscopy

For Mössbauer measurements about 10 mg of the crystals of complex **1** were placed in a cryostat at  $25^\circ\text{C}$ . Spectra of **1** containing *ca.* 10%  $^{57}\text{Fe}$  were measured with a standard constant-acceleration spectrometer using a 512-channel analyser on an Austin Science S-600 system. The velocity resolutions for a wide velocity range ( $-11$  to  $+11 \text{ mm s}^{-1}$ ) and a narrow velocity range ( $-4$  to  $+4 \text{ mm s}^{-1}$ ) were 0.08477 and  $0.03438 \text{ mm s}^{-1}$  per channel, respectively. A  $0.925 \text{ GBq } ^{57}\text{Co/Rh}$  matrix was used as a  $\gamma$ -radiation source at room temperature. The spectrum at narrow velocity was fitted by a least-squares method using a Lorentzian line shape.<sup>16</sup>

A diffuse-reflectance spectrum of complex **1** was recorded in the wavelength range 250–1500 nm on a Hitachi U-3400 spectrophotometer. An absorption spectrum was recorded for an iron(III) ( $0.2 \text{ mmol dm}^{-3}$ )–HL ( $0.4 \text{ mmol dm}^{-3}$ ) solution in methanol on a Shimadzu UV 2000 spectrophotometer.

## Results and Discussion

### Crystal structure of complex 1

Views showing the structural features of complex **1** are given in Figs. 1 and 2. Bond lengths and angles around the iron atoms and average bond lengths and angles for the ligands are presented in Table 3.

The molecular structure contains a trinuclear complex  $\text{Fe}_3\text{L}_6$  with a linear  $\text{Fe}(1)\text{--Fe}(2)\text{--Fe}(1')$  arrangement, the central  $\text{Fe}(2)$  atom being an inversion centre. The distance between  $\text{Fe}(1)$  and  $\text{Fe}(2)$  is  $3.404(2) \text{ \AA}$ . Atom  $\text{Fe}(1)$  is co-ordinated to three

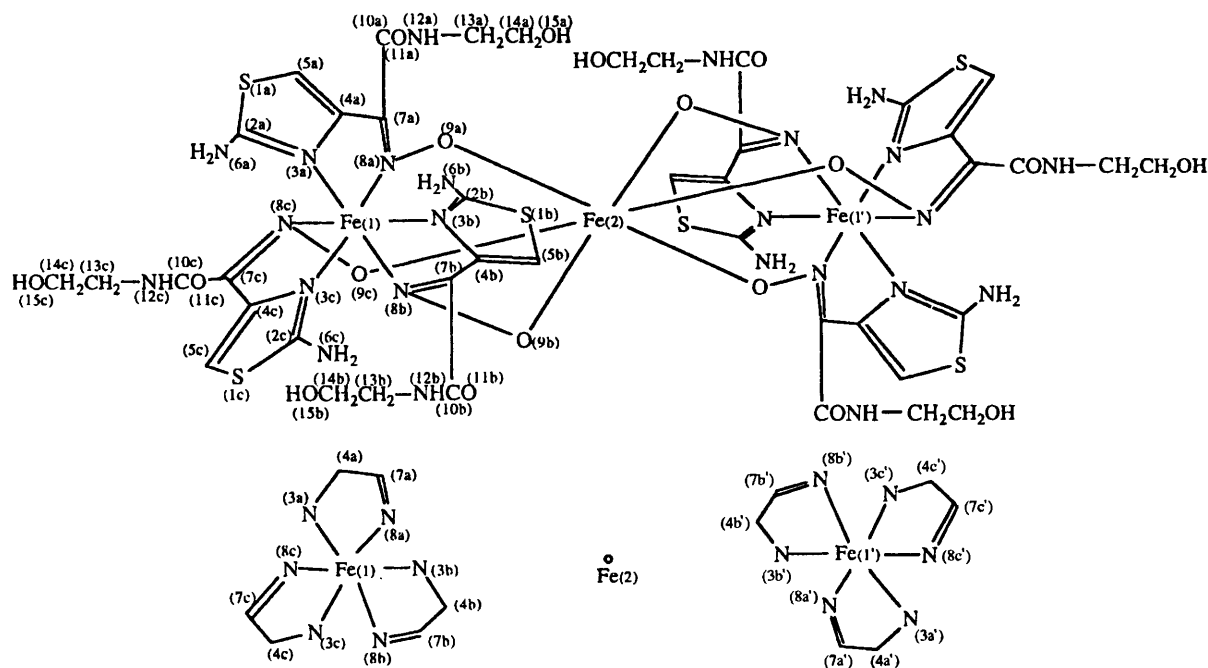


Fig. 2 The two Fe(1)L<sub>3</sub> units bridged by the inversion centre Fe(2); Fe(1') is symmetry-related to Fe(1). Chloride and hydroxide ions are omitted

Table 1 Crystallographic data for [Fe<sub>3</sub>L<sub>6</sub>]Cl[OH]<sub>2</sub> 1

|   |  |
|---|--|
| Formula   | C <sub>42</sub> H <sub>56</sub> ClFe <sub>3</sub> N <sub>24</sub> O <sub>20</sub> S <sub>6</sub> |
| <i>M</i>  | 1612.45  |
| Colour and habit  | Shiny black prisms   |
| Crystal system  | Monoclinic   |
| Space group   | <i>P</i> 2 <sub>1</sub> / <i>n</i>   |
| <i>a</i> /Å   | 15.559(1)  |
| <i>b</i> /Å   | 19.295(2)  |
| <i>c</i> /Å   | 10.963(1)  |
| $\beta$ /°  | 101.29(1)  |
| <i>U</i> /Å <sup>3</sup>  | 3227.6(4)  |
| <i>Z</i>  | 2  |
| Crystal dimensions/mm   | 0.10 × 0.08 × 0.05   |
| <i>D<sub>m</sub></i> = <i>D<sub>c</sub></i> /g cm <sup>-3</sup> | 1.659  |
| $\mu$ (Cu-K $\alpha$ )/cm <sup>-1</sup>                         | 83.10  |
| <i>F</i> (000)  | 1654   |
| No. of unique data  | 5149   |
| No. of data used in refinement                                  | 2108 ( $ F_o  > 3\sigma(F_o)$ )  |
| <i>R</i> <sup>a</sup>   | 0.077  |
| <i>R</i> <sup>b</sup>   | 0.089  |

$$^a \Sigma ||F_o| - |F_c|| / \Sigma |F_o|, \quad ^b [\Sigma w(|F_o| - |F_c|)^2 / \Sigma w(F_o)^2]^{1/2}.$$

molecules of L through the thiazole and oximate nitrogen atoms (2N co-ordination mode) to form FeL<sub>3</sub>. The two Fe(1)L<sub>3</sub> units are related and bridged by the inversion centre, Fe(2), which is co-ordinated to six oximate oxygen atoms of the two Fe(1)L<sub>3</sub> units. Thus, the three molecules of L in each Fe(1)L<sub>3</sub> unit form three oximate N–O bridges between Fe(1) and Fe(2).

#### Oxidation states of the iron atoms

It was reported that, in water, L co-ordinates to iron(II) through the thiazole and oximate nitrogen atoms (2N co-ordination mode) and to iron(III) through the oximate and amide oxygen atoms (2O co-ordination mode).<sup>10</sup> These co-ordination modes are consistent with the fact that, in general, iron-(II) and -(III) prefer to co-ordinate to nitrogen and oxygen atoms, respectively. However, the mode of co-ordination of L to Fe(1) in complex 1 is the same as that of the iron(II) complexes formed in water. This suggests the possibility that Fe(1) is divalent in

spite of the employment of the iron(III) salt FeCl<sub>3</sub>·6H<sub>2</sub>O in the preparation of 1. Complex 1 contains, besides the trinuclear unit Fe<sub>3</sub>L<sub>6</sub>, one chloride ion as a counter ion and two oxygen atoms. The latter, which are related by the inversion centre at Fe(2), are not co-ordinated to any iron atoms. They are considered to be water molecules or hydroxide ions, however it was impossible to distinguish them from the X-ray analysis due to poor crystal quality.\* Considering that each L in 1 has one negative charge, the deprotonated oxime O<sup>-</sup>, and that the whole molecule should be neutral, there are two possible cases, Fe<sup>III</sup>Fe<sup>III</sup>Fe<sup>III</sup> or Fe<sup>II</sup>Fe<sup>III</sup>Fe<sup>II</sup>, where the oxygen atoms are from hydroxide ions or water molecules, respectively. Thus, it is impossible to determine whether Fe(1) is di- or tri-valent by the X-ray analysis, although Fe(2) is obviously trivalent.

The Mössbauer spectra of complex 1 gave an apparent doublet. By means of least-squares curve-fitting techniques,<sup>16</sup> this has been found to consist of two components, doublets A and B (Fig. 3). Since the relative areas of A and B are 65 ± 15 and 35 ± 10%, respectively, the doublets can be assigned to Fe(1) and Fe(2), respectively. The isomer shifts  $\delta$  of these doublets are the same (0.26 mm s<sup>-1</sup>). This value is typical for high-spin iron(III) atoms, although some low-spin iron(II) atoms which are co-ordinated to ligands forming strong ligand fields show isomer shifts at about 0.26 mm s<sup>-1</sup>. In addition, the reflectance spectrum of 1 did not give any intervalence bands showing the existence of iron-(II) and -(III) (Fig. 4). Thus, since Fe(2) is trivalent, Fe(1) is also presumably high-spin iron(III).

#### Co-ordination modes of HL

The absorption spectrum of an iron(III) (0.2 mmol dm<sup>-3</sup>)–HL (0.4 mmol dm<sup>-3</sup>) solution in methanol gave charge-transfer (c.t.) bands at 480 and 530 nm corresponding to those observed in the reflectance spectrum of 1 (Figs. 4 and 5), but no other strong c.t. bands showing the existence of other complex species. This result shows that 1 is probably formed as the major

\* The crystal described in the text was used for data collection in spite of its poor quality because single crystals were extremely difficult to obtain, and repeated attempts by many methods over a year failed to produce better crystals.

**Table 2** Atomic coordinates for non-hydrogen atoms in  $[\text{Fe}_3\text{L}_6]\text{Cl}[\text{OH}]_2 \mathbf{1}$ 

| Atom   | X/a        | Y/b        | Z/c       | Atom   | X/a        | Y/b        | Z/c        |
|--------|------------|------------|-----------|--------|------------|------------|------------|
| Fe(2)  | 0          | 0          | 0         | N(8b)  | -0.0595(7) | 0.1344(5)  | 0.021(1)   |
| Cl(a)  | 0          | 0.5        | 0         | O(9b)  | -0.0636(6) | 0.0859(4)  | -0.0671(8) |
| Fe(1)  | 0.0519(2)  | 0.1605(1)  | 0.1213(2) | C(10b) | -0.2251(8) | 0.1403(7)  | -0.012(2)  |
| S(1a)  | 0.3240(3)  | 0.1910(3)  | 0.3597(5) | O(11b) | -0.2844(6) | 0.1757(6)  | 0.015(2)   |
| C(2a)  | 0.2332(8)  | 0.2169(7)  | 0.251(2)  | N(12b) | -0.2357(7) | 0.0882(6)  | -0.091(2)  |
| N(3a)  | 0.1657(6)  | 0.1743(5)  | 0.238(1)  | C(13b) | -0.324(2)  | 0.0682(9)  | -0.156(3)  |
| C(4a)  | 0.189(1)   | 0.1186(7)  | 0.319(2)  | C(14b) | -0.339(2)  | -0.006(1)  | -0.152(3)  |
| C(5a)  | 0.269(1)   | 0.1209(8)  | 0.396(2)  | O(15b) | -0.425(1)  | -0.0211(8) | -0.209(2)  |
| N(6a)  | 0.2354(9)  | 0.2749(6)  | 0.186(2)  | S(1c)  | 0.0777(3)  | 0.3494(2)  | -0.1254(5) |
| C(7a)  | 0.1211(8)  | 0.0626(7)  | 0.307(2)  | C(2c)  | 0.0450(9)  | 0.3079(8)  | -0.003(2)  |
| N(8a)  | 0.0549(6)  | 0.0769(5)  | 0.217(2)  | N(3c)  | 0.0670(7)  | 0.2398(5)  | 0.008(2)   |
| O(9a)  | -0.0049(6) | 0.0260(4)  | 0.1781(8) | C(4c)  | 0.1113(9)  | 0.2218(7)  | -0.089(2)  |
| C(10a) | 0.137(1)   | -0.0042(8) | 0.377(2)  | C(5c)  | 0.125(2)   | 0.2723(9)  | -0.170(2)  |
| O(11a) | 0.2143(8)  | -0.0186(6) | 0.423(2)  | N(6c)  | 0.0016(8)  | 0.3411(6)  | 0.078(2)   |
| N(12a) | 0.0658(8)  | -0.0392(6) | 0.392(2)  | C(7c)  | 0.1315(8)  | 0.1477(7)  | -0.088(2)  |
| C(13a) | 0.073(2)   | -0.1073(9) | 0.455(2)  | N(8c)  | 0.1094(7)  | 0.1140(5)  | 0.006(2)   |
| C(14a) | 0.046(2)   | -0.1632(8) | 0.371(2)  | O(9c)  | 0.1186(6)  | 0.0444(4)  | 0.0106(9)  |
| O(15a) | 0.0940(7)  | -0.1698(5) | 0.274(2)  | C(10c) | 0.1758(9)  | 0.1182(8)  | -0.187(2)  |
| S(1b)  | -0.1166(3) | 0.2859(3)  | 0.3404(5) | O(11c) | 0.1868(8)  | 0.1538(6)  | -0.278(2)  |
| C(2b)  | -0.0182(9) | 0.2495(7)  | 0.322(2)  | N(12c) | 0.198(1)   | 0.0495(6)  | -0.176(2)  |
| N(3b)  | -0.0274(7) | 0.2104(5)  | 0.222(2)  | C(13c) | 0.231(2)   | 0.017(2)   | -0.281(3)  |
| C(4b)  | -0.1155(9) | 0.2055(7)  | 0.159(2)  | C(14c) | 0.322(3)   | 0.012(3)   | -0.261(3)  |
| C(5b)  | -0.1704(9) | 0.2436(7)  | 0.207(2)  | O(15c) | 0.374(3)   | -0.006(3)  | -0.164(2)  |
| N(6b)  | 0.0554(8)  | 0.2606(6)  | 0.402(2)  | OH     | 0.011(2)   | 0.3795(9)  | 0.552(2)   |
| C(7b)  | -0.1327(8) | 0.1596(7)  | 0.052(2)  |        |            |            |            |

**Table 3** Bond lengths (Å) and angles (°) around the iron atoms, and average bond lengths and angles for the ligands, in  $[\text{Fe}_3\text{L}_6]\text{Cl}[\text{OH}]_2 \mathbf{1}$ 

## Around Fe atoms

|               |          |             |          |
|---------------|----------|-------------|----------|
| Fe(2)···Fe(1) | 3.404(2) | Fe(2)-O(9a) | 2.032(9) |
| Fe(2)-O(9b)   | 1.996(9) | Fe(2)-O(9c) | 2.017(9) |
| Fe(1)-N(3a)   | 1.99(1)  | Fe(1)-N(8a) | 1.92(1)  |
| Fe(1)-N(3b)   | 2.05(1)  | Fe(1)-N(8b) | 1.93(1)  |
| Fe(1)-N(3c)   | 2.02(1)  | Fe(1)-N(8c) | 1.91(1)  |

## For L ligands

|             |         |             |         |
|-------------|---------|-------------|---------|
| S(1)-C(2)   | 1.74(2) | S(1)-C(5)   | 1.73(2) |
| C(2)-N(3)   | 1.33(2) | C(2)-N(6)   | 1.34(2) |
| N(3)-C(4)   | 1.40(2) | C(4)-C(5)   | 1.34(2) |
| C(4)-C(7)   | 1.47(2) | C(7)-N(8)   | 1.32(2) |
| C(7)-C(10)  | 1.51(2) | N(8)-O(9)   | 1.35(1) |
| C(10)-O(11) | 1.24(2) | C(10)-N(12) | 1.34(2) |
| N(12)-C(13) | 1.48(2) | C(13)-C(14) | 1.43(4) |
| C(14)-O(15) | 1.36(4) |             |         |

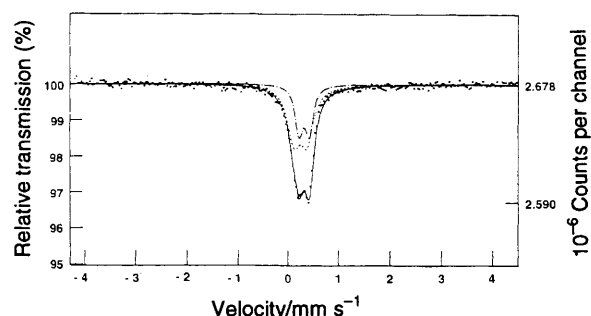
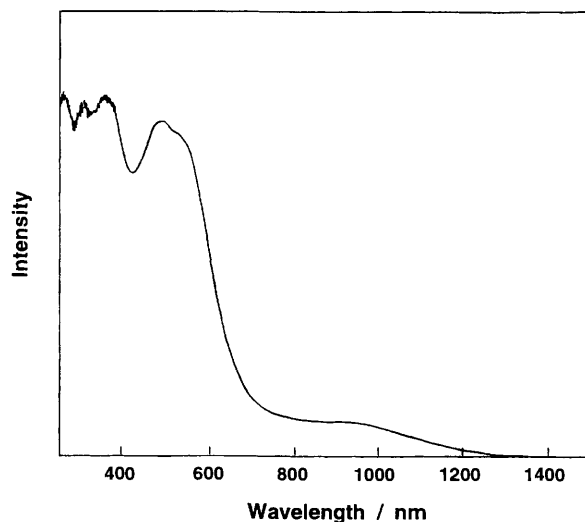
## Around Fe atoms

|                   |          |                   |          |
|-------------------|----------|-------------------|----------|
| O(9a)-Fe(2)-O(9b) | 92.3(4)  | O(9a)-Fe(2)-O(9c) | 92.6(4)  |
| O(9b)-Fe(2)-O(9c) | 92.9(4)  | N(3a)-Fe(1)-N(8a) | 80.6(5)  |
| N(3a)-Fe(1)-N(3b) | 98.2(5)  | N(3a)-Fe(1)-N(8b) | 171.5(5) |
| N(3a)-Fe(1)-N(3c) | 95.7(5)  | N(3a)-Fe(1)-N(8c) | 91.0(5)  |
| N(8a)-Fe(1)-N(3b) | 93.0(5)  | N(8a)-Fe(1)-N(8b) | 90.9(5)  |
| N(8a)-Fe(1)-N(3c) | 169.3(5) | N(8a)-Fe(1)-N(8c) | 90.3(5)  |
| N(3b)-Fe(1)-N(8b) | 82.0(5)  | N(3b)-Fe(1)-N(3c) | 97.5(5)  |
| N(3b)-Fe(1)-N(8c) | 170.6(5) | N(8b)-Fe(1)-N(3c) | 92.7(5)  |
| N(8b)-Fe(1)-N(8c) | 89.2(5)  | N(3c)-Fe(1)-N(8c) | 79.6(5)  |

## For ligands

|                   |          |                   |          |
|-------------------|----------|-------------------|----------|
| C(2)-S(1)-C(5)    | 91.7(8)  | S(1)-C(2)-N(3)    | 114(1)   |
| S(1)-C(2)-N(6)    | 122(1)   | N(3)-C(2)-N(6)    | 125(1)   |
| Fe(1)-N(3)-C(2)   | 138(1)   | Fe(1)-N(3)-C(4)   | 112.2(9) |
| C(2)-N(3)-C(4)    | 110(1)   | N(3)-C(4)-C(5)    | 117(1)   |
| N(3)-C(4)-C(7)    | 114(1)   | C(5)-C(4)-C(7)    | 129(1)   |
| S(1)-C(5)-C(4)    | 109(1)   | C(4)-C(7)-N(8)    | 112(1)   |
| C(4)-C(7)-C(10)   | 121(1)   | N(8)-C(7)-C(10)   | 126(1)   |
| Fe(1)-N(8)-C(7)   | 120.3(9) | Fe(1)-N(8)-O(9)   | 119.8(8) |
| C(7)-N(8)-O(9)    | 119(1)   | Fe(2)-O(9)-N(8)   | 110.0(7) |
| C(7)-C(10)-O(11)  | 118(1)   | C(7)-C(10)-N(12)  | 117(1)   |
| O(11)-C(10)-N(12) | 125(2)   | C(10)-N(12)-C(13) | 119(2)   |
| N(12)-C(13)-C(14) | 113(2)   | C(13)-C(14)-O(15) | 117(2)   |

species in methanol. The co-ordination mode is different from that in water, where L co-ordinates to an iron(III) through the

**Fig. 3** Mössbauer spectrum of complex **1** at 25 °C. The signal consists of two components, doublet A (---) and doublet B (-.-.-). The spectral parameters, quadrupole splitting  $\Delta E_Q$  and isomer shift  $\delta$ , of these doublets are almost the same:  $\Delta E_Q = +0.28$ ,  $\delta = 0.26$  for A,  $\Delta E_Q = +0.32$ ,  $\delta = 0.26$  mm s<sup>-1</sup> for B**Fig. 4** Diffuse-reflectance spectrum of  $[\text{Fe}_3\text{L}_6]\text{Cl}[\text{OH}]_2 \mathbf{1}$ , showing two charge-transfer (c.t.) bands and a broad d-d band at about 480, 540 (shoulder) and 1000 nm, respectively

oximate oxygen atom and the amide oxygen atom (2O co-ordination mode).<sup>10</sup> In water this mode is stable since the oxime group can be deprotonated easily. The co-ordination mode of

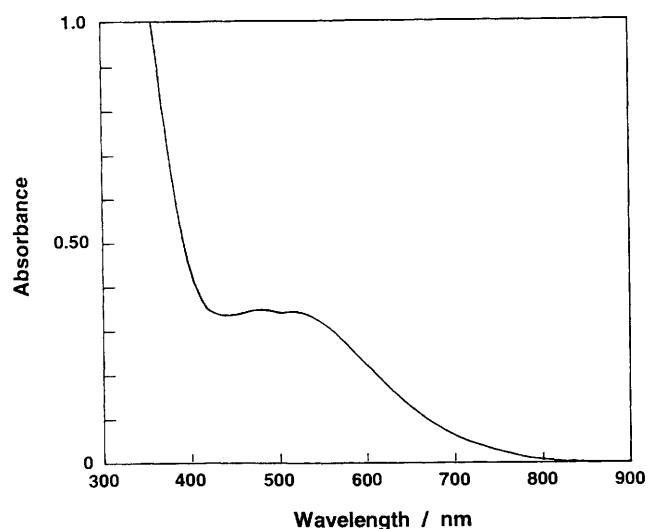


Fig. 5 Absorption spectrum of an iron(III) ( $0.2 \text{ mmol dm}^{-3}$ )-HL ( $0.4 \text{ mmol dm}^{-3}$ ) solution in methanol

HL depends on the solvent, as does that of 3-(3,4-dihydroxyphenyl)-L-alanine (L-dopa).<sup>17</sup>

On the other hand, the deprotonation at the oxime moiety is depressed in hydrophobic media,<sup>18</sup> and therefore, the 2O coordination cannot occur easily in methanol. Consequently the 2N mode is probably more stable in methanol. The oxime group can be deprotonated easily even in methanol after the 2N coordination is formed, since the electron density of the hydrogen atom of the oxime is decreased. Thus, the oximate oxygen atom of L co-ordinated to iron(III) in the 2N mode should have a high affinity for another iron(III) atom and oximate bridges between two iron(III) atoms are formed to give the trinuclear complex.

## Conclusion

The molecular structure of complex 1, which was obtained from a methanol solution containing HL and  $\text{FeCl}_3$ , has been determined by X-ray crystallography. It consists of three iron(III) ions and six L anions. The structure is characterized by

the iron bridge between two  $\text{FeL}_3$  units. The present studies indicate that the co-ordination mode of HL depends on the solvent, and suggest that Cefdinir may co-ordinate to iron(III) through the thiazole and oximate nitrogen atoms (2N mode) under hydrophobic conditions in biological systems.

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