Two Polymeric Complexes of Norfloxacin with Iron(II) and Their Magnetic Properties

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The reaction of H-Norf with (NH₄)₂Fe(SO₄)₂·6H₂O and Fe(OH)₃ (or Fe₂O₃) affords Fe(H-Norf)₂(SO₄)·2H₂O (1) and Fe(Norf)₂·4H₂O (2), respectively, both of which have 2D polymeric structures. Their interesting magnetic properties are also reported. Crystal data for 1: monoclinic, P2₁/c, a = 23.166(1), b = 10.0492(4), c = 7.7264(3) Å, β = 98.379(1)°, V = 1779.50(13) Å³, Z = 2; for 2: monoclinic, P2₁/c, a = 5.8411(12), b = 21.685(4), c = 13.265(3) Å, β = 99.20(3)°, V = 1658.6(6) Å³, Z = 2.

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Introduction

Norfloxacin (H-Norf, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid), an extremely potent antibacterial agent with a wide spectrum of activity, is increasingly used for the treatment of many infections.[1] The suggested modes of action of H-Norf are either an inhibition of metalloenzyme DNA-gyrase or an interaction with the DNA molecule via a metal complex intermediate, and it has been proposed that a copper or iron complex could be involved in these interactions with DNA.[2] Some quinolones inhibit the cytochrome P450 system, which also involves an iron(II) ion, and it has been reported that iron(II) sulfate impairs the absorption of quinolones due to the formation of chelates.[3] To date, no solid-state structure of an Fe-quinolone complex has been available to support this theory.

Iron deficiency anaemia is rather common but can be treated easily. By comparison, iron overload disease (IOLD) is relatively rare but can result in serious medical complications, including cirrhosis, primary liver cancer, diabetes, cardiomyopathy and arthritis. Since humans are unable to actively excrete iron, excess iron, once taken up, deposits in tissue in the form of solid FeOOH which then can lead to organ damage and ultimately death. More than 500000 patients worldwide who suffer IOLD (haematological defects such as β-thalassaemia major) can be treated by an iron chelator such as Desferal (siderophore desferrioxamine-B).[4] To date, no reaction product of a metal ion with quinolone derivatives is known to be a polymeric structure both in weakly acidic and basic solutions, although a number of metal ion complexes have been reported.[5] To our surprise, the reaction of H-Norf with (NH₄)₂Fe(SO₄)₂·6H₂O and Fe(OH)₃ (or Fe₂O₃) affords Fe(H-Norf)(SO₄)·2H₂O (1) and Fe(Norf)₂·4H₂O (2) (Scheme 1), respectively, both of which have a 2D polymeric structure. Herein we report the synthesis of 1 and 2, their solid-state structures, and magnetic properties.

Results and Discussion

Crystals of dark brown 1 and brown-red 2 were harvested from the reaction of H-Norf with (NH₄)₂Fe(SO₄)₂·6H₂O and Fe(OH)₃, respectively (Scheme 1). The IR spectra of both 1 and 2 show two very strong peaks at 1621 and 1571 cm⁻¹ for 1, and 1621 and 1462 cm⁻¹ for 2, indicating that the carboxylic acid groups of H-Norf are deprotonated (in comparison, those of free H-Norf are at 1710 and 1621 cm⁻¹). A strong peak at 1023 cm⁻¹ in the IR spectrum of 1 indicates that there is an uncoordinated SO₄²⁻. It is
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interesting to note that in weakly basic solution the N atom of the piperidyl ring can take part in the coordination to the metal ion, while in weakly acidic solution, this N atom is protonated and does not bind to the metal ion, as evidenced by the crystal-structure determinations below. Both 1 and 2 are insoluble in common solvents. The solubilities of 1 and 2 in water were estimated by ICP-AE (Inductively Coupled Plasma-Atomic Emission) to be 0.2 and 0.03 µg/mL, respectively.

The X-ray crystal analysis of 1 revealed that the FeII ion is coordinated in a distorted octahedral geometry defined by six oxygen atoms from four different H-Norf ligands (Figure 1). Two H-Norfs afford one 4-oxo and one carboxyl oxygen to bind FeII to form two six-membered rings and one equatorial plane defined by O(1), O(2), O(1A) and O(2A), while the apical positions are occupied by two oxygen atoms [(O3B) and O(3C)] from two different carboxylates of H-Norf. Thus, the carboxylate group of H-Norf in 1 clearly binds in a bidentate manner and links the Fe(H-Norf)2 unit to form a 2D framework, as shown in Figure 1 (bottom). The framework core, composed of the 4-oxo and the 3-carboxyl oxygen atoms, is like a small 2D square grid. The N atom of the piperidyl ring in 1 loses its coordination capacity as a result of protonation. The crystal packing view also indicates that the anions (sulfate) and water are intercalated between two adjacent layers (see Supporting Information). There are also many hydrogen bonds, such as those between water and sulfate (2.547 Å), and water and the protonated N atom (2.711 Å), that hold two adjacent layers together.

The apical positions in 2 (Figure 2), unlike those in 1, are occupied by two N atoms [N(1) and N(2)] of piperidyl rings,
resulting in the formation of a 2D square grid with a cavity dimension of $13.538 \times 13.538 \text{ Å}$. The coordination environment around Fe$^{II}$ in 2 is also slightly distorted octahedral with an equatorial plane defined by O(2), O(3), O(2A) and O(3A) from two different Norfs. Unlike in 1, the carboxylate group of Norf in 2 acts as monodentate ligand, and one of the O atoms of the carboxylate group is uncoordinated. This mode of bonding is similar to that of Zn(Norf)$_2$$\cdot$4H$_2$O.$[6h]$

Studies of the magnetic susceptibility of 1 versus temperature (Figure 3) show strong antiferromagnetic coupling between 20 K and 300 K and a weak ferromagnetic phenomenon at lower temperatures (5–20 K). In contrast, 2 shows a weak ferromagnetic interaction throughout this whole temperature range. This is in good agreement with the shorter distance between the Fe ions in 1 than in 2. At room temperature the value of $\chi_{mol}T$ for 1 is discontinuous around 15 K, which is indicative of a magnetic phase-transition originating from a spin-canting phenomenon as a consequence of neighboring spin units of iron being aligned in a canted antiparallel manner.$[7]$ The magnetization of 1 at 5 K performed up to 50 kOe (Figure 4) shows that the field dependence of the magnetization departs from linearity. A hysteresis loop at very low magnetic field range ($< 2000 \text{ Oe}$) was obtained. When the magnetic field was cycled, a remnant magnetization of about 0.3 $\mu_B$ and a coercive field of about 130 Oe were observed as a result of magnetic ordering at this temperature. This observation shows that 1 is a hard magnet material.

In conclusion, the reaction products of H-Norf with iron$(\text{III})$ were found to be mainly dependent upon the pH of the solutions. In basic solution, the product is a 2D square network involving the coordination of the N atom of the piperidyl ring to iron$(\text{III})$, while in weakly acidic solution the product is also a 2D framework with a $\mu_3$-carboxylate coordination mode.

**Experimental Section**

**Compound 1:** Samples of 1 mmol of (NH$_4$)$_2$Fe(SO$_4$)$_2$·6H$_2$O and 2 mmol of H-Norf were thoroughly mixed in a mortar with a pestle, and placed in thick-walled Pyrex tubes (ca. 20 cm long; pH = 5.8 in the solution). After addition of 0.5 mL of EtOH and 1.5 mL of H$_2$O, the tube was frozen with liquid N$_2$ evacuated under vacuum and sealed with a torch. The tube was heated at 105 °C for one day to give pale-yellow block crystals (0.454 g) in 55% yield based on H-Norf. C$_{32}$H$_{40}$F$_2$FeN$_6$O$_{12}$S (826.61): calcd. C 46.45, H 4.84, N 10.12, Fe 8.51, S 12.16; found C 46.25, H 4.84, N 10.13, Fe 8.49, S 12.12.

**Compound 2:** Samples of 1 mmol of (NH$_4$)$_2$Fe(SO$_4$)$_2$·6H$_2$O and 2 mmol of H-Norf were thoroughly mixed in a mortar with a pestle, and placed in thick-walled Pyrex tubes (ca. 20 cm long; pH = 5.8 in the solution). After addition of 0.5 mL of EtOH and 1.5 mL of H$_2$O, the tube was frozen with liquid N$_2$ evacuated under vacuum and sealed with a torch. The tube was heated at 105 °C for one day to give pale-yellow block crystals (0.454 g) in 55% yield based on H-Norf. C$_{32}$H$_{40}$F$_2$FeN$_6$O$_{12}$S (826.61): calcd. C 46.45, H 4.84, N 10.12, Fe 8.51, S 12.16; found C 46.25, H 4.84, N 10.13, Fe 8.49, S 12.12.
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