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Aquasoluble iron(III)-arylhydrazone-β-diketone complexes: Structure and catalytic activity for the peroxidative oxidation of C_5–C_8 cycloalkanes

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ABSTRACT

The aquasoluble Fe^{III} complexes $[Fe(H_2O)_3(L^1)]\cdot 4H_2O$ (**3**) and $[Fe(H_2O)_3(L^2)]\cdot 3H_2O$ (**4**), bearing the basic forms of 5-chloro-3-(2-(4,4-dimethyl-2,6-dioxocyclohexylidene)hydrazinyl)-2-hydroxy-benzenesulfonic acid (H_3L^1, **1**) and 3-(2-(2,4-dioxopentan-3-ylidene)hydrazinyl)-2-hydroxy-5-nitrobenzenesulfonic acid (H_3L^2, **2**), were synthesized and fully characterized including by X-ray crystal structural analysis. In the channels of the water-soluble 3D networks of **3** and **4**, the uncoordinated water molecules are held by oxygen atoms of the carbonyl and sulfonyl groups, and by the water ligands. The Fe^{III} coordination environment resembles that in the active sites of some mononuclear non-heme iron-containing enzymes. The complexes show a high catalytic activity for the peroxidative oxidation (with aqueous H_2O_2) of C_5–C_8 cycloalkanes to the corresponding alcohols and ketones under mild conditions. The effects of various factors, such as amounts of oxidant, catalyst and HNO_3 additive, were investigated allowing to reach overall yields of ca. 25% and turnover numbers (TONs) up to 290. The catalytic reactions proceed via both oxygen- and carbon-radicals as shown by radical trap experiments.

1. Introduction

Mononuclear non-heme iron-containing enzymes are essential for many biological processes, namely involving substrate oxidation, hydroxylation, halogenation, desaturation and ring-closure [1–8]. The reactivity of such enzymes via Fenton-type chemistry [9] provides the conversion of superoxide anion and hydrogen peroxide to hydroxyl radical [10], reactions essential to initiate lipid peroxidation [11] or to prevent tissue damage [12,13].

Within the large versatility of mononuclear non-heme iron-containing enzymes, in a number of cases their metal centers can display a main structural motif with iron bound by two histidines and a carboxylic acid side chains of a protein, showing an O,N,O-coordination environment. The other coordination sites can be vacant in the resting state (e.g., with labile water molecule ligands) and participate in the oxidation or hydroxylation upon interaction with substrate, oxygen and/or a cofactor (e.g., ketoglutarate) [1,2,5].

A high number of complexes have been prepared to model active sites of mononuclear non-heme iron-containing enzymes [1,8,14], but the syntheses of most of them appear to be rather complicated, expensive and time-consuming. Hence, the design of a simple, cheap and easy to prepare model for such enzymes still constitutes a significant challenge. Good solubility in water, the common solvent in biological processes, is an important feature of the model to be achieved and usually the preparation of water-soluble complexes involves the use of a ligand with a hydrophilic functionality which can be created by attaching a water-solubilizing group, such as sulfonato [15].

Arylhydrazones of β-diketones (AHBD) (Scheme 1, for those of the present study) are compounds which can be easily prepared from relatively cheap starting materials (aromatic amines and beta-diketones) by the easy and well-studied two-step Japp–Klingemann procedure [16,17]. The utilization of an aromatic amine with a sulfo-substituent allows the easy introduction of the water-solubilizing functionality. Further, AHBD compounds contain a O,N,O donor site of high flexibility, which can chelate a number of metal–ions, thus leading to Cu^{II} [18–24], Zn^{II} [25–28], Ni^{II} [19,29], Na^{I} [30], K^{I} [24,29], Pb^{II} [25], Cd^{II} [26] complexes. The preparative procedures for these complexes are usually rather straightforward giving high yields of the final products. It was demonstrated [31] that, in solution, Fe^{III} also interacts with AHBD but, before the current work, Fe^{III}–AHBD complexes in solid phase had not yet been isolated and structurally characterized.

Peroxidative oxidation of alkanes, in particular cyclohexane, is a widely used model to check and compare the activity of the complexes when biomimicking active sites of various oxygenases [32–34]. Moreover, alkane functionalization stands as a challenge for the establishment

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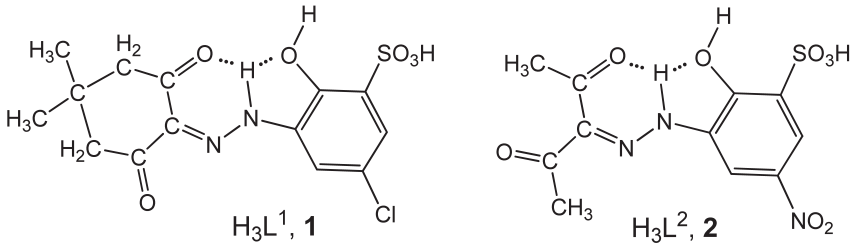


Scheme 1. Arylhydrazones of β-diketones (AHBD) of this work.

of hydrocarbon feedstocks, and new methodologies for C – H bond oxidation can result in synthetic strategies toward more complex and valuable organic products [35–40]. Several Cu^{II}–AHBD complexes have been successfully applied as catalysts for a few oxidation reactions, in particular the peroxidative oxidation of cyclohexane and benzylalcohol [18,21], but Fe^{III}–AHBD compounds have not yet been reported as catalysts for the cycloalkane oxidation.

Thus, we focused this work on the following aims: (i) to prepare, by an easy and convenient way, new water-soluble iron(III)–AHBD complexes with a O,N,O-chelating environment and potentially unsaturated by bearing labile ligands (water molecules); (ii) to demonstrate the viability of the synthesized complexes to mimic oxygenases, in particular alkane peroxidase [1,3,4,6–8,40]. To reach these aims, 5-chloro-3-(2-(4,4-dimethyl-2,6-dioxocyclohexylidene)hydrazinyl)-2-hydroxybenzenesulfonic acid (H_3L^1, **1**) and 3-(2-(2,4-dioxopentan-3-ylidene)hydrazinyl)-2-hydroxy-5-nitrobenzenesulfonic acid (H_3L^2, **2**) (Scheme 1) were chosen as ligand sources to prepare the Fe^{III} complexes, and the peroxidative oxidation of C_5–C_8 cycloalkanes was applied as a model reaction.

2. Experimental

2.1. Materials and instrumentation

The ^1H and ^{13}C NMR spectra were recorded at room temperature on a Bruker Avance II + 300 (UltraShield™ Magnet) spectrometer operating at 300.130 and 75.468 MHz for proton and carbon-13, respectively. The chemical shifts are reported in ppm using tetramethylsilane as the internal reference. The infrared spectra (4000–400 cm^{-1}) were recorded on a BIO-RAD FTS 3000MX instrument in KBr pellets. Carbon, hydrogen, and nitrogen elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. Chromatographic analyses were undertaken by using a Fisons Instruments GC 8000 series gas chromatograph with a DB-624 (J&W) capillary column (flame ionization detector) and the Jasco–Borwin v.1.50 software. The internal standard method was used to quantify the organic products.

2.2. Synthesis of **1**

The synthesis and characterization of **2** were reported earlier [20]; the previously unknown arylhydrazone **1** was synthesized by a modified [41] Japp–Klingemann reaction between the aromatic diazonium salt of 3-amino-5-chloro-2-hydroxybenzenesulfonic acid and 5,5-dimethylcyclohexane-1,3-dione in water–ethanol solution containing sodium hydroxide.

Diazotization: 3-amino-5-chloro-2-hydroxybenzenesulfonic acid (2.24 g, 10 mmol) was dissolved in 50 mL water, and 0.40 g (10 mmol) of NaOH was added. The solution was cooled in an ice bath to 273 K and 0.69 g (10 mmol) of $NaNO_2$ was added; 5.00 mL HCl was then added in 0.5 mL portions for 1 h. The temperature of the mixture should not exceed 278 K.

Azocoupling: NaOH (0.40 g, 10 mmol) was added to a solution of 1.40 g (10 mmol) of 5,5-dimethylcyclohexane-1,3-dione with 50 mL of ethanol. The solution was cooled in an ice bath to ca. 273 K, and a suspension of 3-amino-5-chloro-2-hydroxybenzenesulfonic acid diazonium (see above) was added in three portions under vigorous stirring for 1 h.

H_3L^1 (1). Yield, 75% (based on 5,5-dimethylcyclohexane-1,3-dione), yellow powder, soluble in water, methanol, ethanol, and insoluble in chloroform. Anal. Calcd for $C_{14}H_{15}ClN_2O_6S$ ($Mr = 374.8$): C, 44.86; H, 4.03; N, 7.47. Found: C, 44.65; H, 3.98; N, 7.36%. IR, cm^{-1}: 3504 ν(OH), 3385 ν(NH), 1647 ν(C═O), 1597 ν(C═N). ^1H NMR (300.13 MHz, DMSO-d_6) δ: 1.03 CH_3, 4.03 CH_2, 7.23–7.58 (2H, C_6H_2), 11.30 (s, 1H, Ar – OH), 14.95 (s, 1H, NH). $^{13}C\{^1H\}$ NMR (75.468 MHz, DMSO-d_6) δ: 30.0 ($2CH_3$), 30.3 (C_{ipso}), 51.7 (CH_2), 52.0 (CH_2), 115.6 and 123.0 (2Ar – H), 123.6 (Ar – Cl), 130.8 (Ar – NH – N), 131.3 (Ar – SO_3H), 132.8 (C═N), 141.8 (Ar – OH), 192.8 (C═O), 197.7 (C═O).

2.3. Syntheses of Fe^{III} complexes

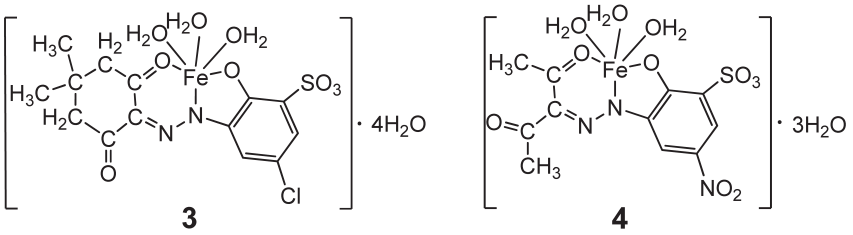
1 mmol of **1** (or **2**) was dissolved in 15 mL water (pH 2), then 1 mmol of $FeCl_3 \cdot 2.5H_2O$ was added. The mixture was stirred at room temperature for 5 min and left for slow evaporation; the greenish-black crystals of the product started to form after ca. 4 d at room temperature; they were then filtered off and dried in air.

$[Fe(H_2O)_3(L^1)] \cdot 4H_2O$ (**3**). Yield, 52% (based on Fe). Calcd. for $C_{14}H_{26}ClFeN_2O_{13}S$ ($Mr = 553.72$): C 30.37, H 4.73, N 5.06. Found C 30.79, H 4.56, N 4.87. IR (KBr), cm^{-1}: 3319 and 3074 (s, br) ν(OH), 1655 (s) ν(C═O) and δ(OH), 1554 (s) ν(C═N).

$[Fe(H_2O)_3(L^2)] \cdot 3H_2O$ (**4**). Yield, 45% (based on Fe). Calcd. for $C_{11}H_{20}FeN_3O_{14}S$ ($Mr = 506.20$): C 26.10, H 3.98, N 8.30. Found C 25.90, H 4.00, N 8.06. IR (KBr), cm^{-1}: 3431 and 3089 (s, br) ν(OH), 1664 (s) ν(C═O), 1629 (s) ν(C═O) and δ(OH), 1591 (s) ν(C═N).

2.4. X-ray measurements

The crystals of **3** and **4** were immersed in cryo-oil, mounted in a Nylon loop, and measured at the temperature of 100 K. The X-ray diffraction data were collected on a Bruker Smart Apex II [42] (**3**) Bruker Kappa Apex II Duo (**4**) diffractometer using Mo Kα radiation ($\lambda = 0.710\ 73$ Å). The *APEX2* program package was used for cell refinements and data reductions. The structures were solved by direct methods using the *SHELXS-97* program with the *WinGX* graphical user interface [43–45]. A semi-empirical multi-scan absorption correction based on equivalent reflections (*SADABS*) [46] was applied to all data. Structural refinements were carried out using *SHELXL-97* [44]. The H_2O hydrogen atoms were located from the different Fourier map but constrained to ride on their parent atom with $U_{iso} = 1.5\ U_{eq}$ (parent atom). Other hydrogen atoms were positioned geometrically and constrained to ride on their parent atoms with $U_{iso} = 1.2–1.5\ U_{eq}$ (parent atom). The crystallographic details are summarized in Table S1. CCDC 851668 and 851669 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



Scheme 2. Schematic representations of complexes **3** and **4**.

2.5. Oxidation of C_5–C_8 cycloalkanes

The reaction mixtures were prepared as follows: to 0.1–10.0 μmol of the complex **3** or **4** contained in the reaction flask were added 4 mL of MeCN, 0–400 μmol of HNO_3, 1.00 mmol of cycloalkane and 2.5–12.5 mmol of H_2O_2 solution (30% in H_2O), in this order. The reaction mixture was stirred for 6 h at room temperature (ca. 298 K) and air atmospheric pressure, then 90 μL of cycloheptanone (as internal standard) and 5.0 mL of diethyl ether (to extract the substrate and the products from the reaction mixture) and 1.0 g of PPh_3 (to reduce the cycloalkanyl hydroperoxide, if formed, to cycloalkanol) [47,48] were added. The resulting mixture was stirred for 15 min, and then a sample taken from the organic phase was analyzed by GC using a FISONS Instruments GC 8000 series gas chromatograph with a DB WAX fused silica capillary column (P/N 123-7032) and the Jasco–Borwin v.1.50 software. Blank experiments were performed and confirmed that no cycloalkane oxidation products (or only traces, below 0.3%) were obtained in the absence of the metal catalyst. In the experiments with radical traps, the carbon radical trap $CBrCl_3$ or TEMPO was used in a stoichiometric amount relative to the substrate (cycloalkane), and the oxygen radical trap Ph_2NH was added in a stoichiometric amount relative to H_2O_2.

3. Results and discussion

3.1. Synthesis and characterization of 1–4

Compound H_3L^1 (**1**) (Scheme 1) was prepared by a modified (see Experimental section) known [39] aqueous diazotization of 3-amino-5-chloro-2-hydroxybenzenesulfonic acid with subsequent coupling with 5,5-dimethylcyclohexane-1,3-dione, while the preparation and characterization of H_3L^2 (**2**) have been reported earlier [20]. The ^{1}H-NMR spectrum of **1** in DMSO-d^6 solution at room temperature shows a signal at δ 14.95 which is assigned [18] to the proton of the protonated nitrogen atom adjacent to the aryl unit (=N–NH–hydrazone form, Scheme 1). The IR spectrum of the isolated compound discloses ν(OH) and ν(NH) vibrations at 3504 and 3385 cm^{-1}, respectively, while ν(C=O) and ν(C=N) are observed at 1647 and 1597 cm^{-1}, correspondingly, supporting the existence of the H-bonded hydrazone structure in the solid state.

Slow evaporation of an aqueous solution (pH 2) of **1** or **2** and Fe^{III} chloride hydrate furnishes greenish-black crystals of the monomeric complex $[Fe(H_2O)_3(L^1)]\cdot 4H_2O$ (**3**) or $[Fe(H_2O)_3(L^2)]\cdot 3H_2O$ (**4**) (Scheme 2, Fig. 1). Elemental analyses support the formulation, while IR spectra reveal 3074 and 3319 (s, br) ν(OH), 1655 (s) ν(C=O) and δ(OH), 1554 (s) ν(C=N) for **3** and 3089 and 3431 (s, br) ν(OH), 1664 (s) ν(C=O), 1629 (s) ν(C=O) and δ(OH), 1591 (s) ν(C=N) cm^{-1} for **4**.

The molecular structures of complexes **3** and **4** have been established by single-crystal X-ray diffraction (Table S1 with the crystal data and structure refinement details) which discloses the coordination of the deprotonated basic $(L^1)^{3-}$ and $(L^2)^{3-}$ species, respectively (Scheme 2, Fig. 1). In spite of the variation of the β-diketone fragment (pentane-2,4-dione in **3** or 5,5-dimethylcyclohexane-1,3-dione in **4**) and of the substituent of the aromatic part (NO_2 in **3** or Cl in **4**), both structures are quite similar, the positive charges of the Fe^{III} ions being compensated by negative charges of N1, O4, O1 (sulfo group oxygen) in **3** and N1, O6, O1 in **4**. The iron atoms in **3** and **4** are 6-coordinated, the Fe–O bond lengths range from 1.9247(9) to 2.0691(10) Å in **3** and from 1.958(4) to 2.029(4) Å in **4**, whereas the Fe(1)–N(1) distance is 2.0998(10) Å in **3** and 2.092(4) Å in **4** (Table S2 with selected bond lengths and angles). The coordination environment of the iron is best described as a distorted octahedron (4+2); one part of $(L^1)^{3-}$ (N1O4O6O8) in **3** and $(L^2)^{3-}$ (N1O5O6O7) in **4**, and the water molecules (O7O9) in **3** and (O8O9) in **4**, the latter being coordinated at axial positions. The iron atom belongs to two fused five- and six-membered metallacycles, Fe1–N1–C5–C6–O4 and Fe1–N1–N2–C7–

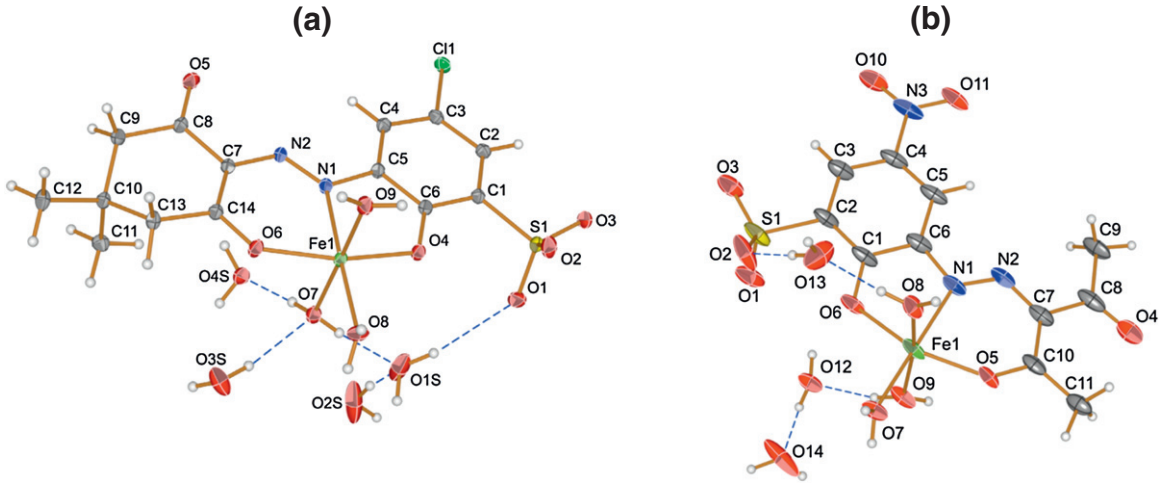
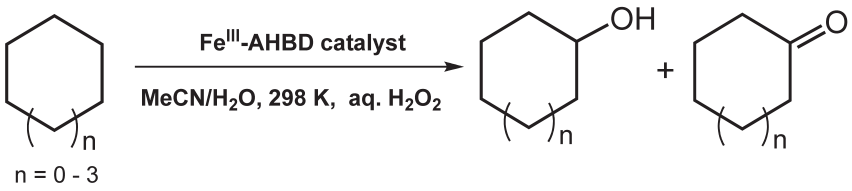


Fig. 1. Thermal ellipsoid plots, drawn at the 50% probability level, of the complexes **3** (a) and **4** (b).



Scheme 3. Oxidation of cyclohexane using **3** or **4** as a catalyst precursor.

C14–O6 in **3**, and Fe1–N1–C6–C1–O6 and Fe1–N1–N2–C7–C10–O5 in **4**. Coordinated water molecules are anti to each other and involved in two hydrogen bonds with the non-coordinated water molecules. The average H$_2$O···O distances of the hydrogen bonds in **3** and **4** fall within the 2.5879(14)–3.6224(13) Å and 2.592(6)–3.058(7) Å ranges, respectively (Table S3), consistent with formation of a strong hydrogen bonding [49,50]. Thus, **3** and **4** show 3D networks with channels, in which water molecules interconnect with carbonyl and sulfonyl oxygen atoms of the ligands and other water molecules. In accord with the geometry of the complexes, the channels incorporating the coordinated water have a nearly quadratic cross-section, whereas those containing the hydrate water molecules have an elongated profile. Moreover, the building blocks of [Fe(H$_2$O)$_3$(L^1)] in **3** and [Fe(H$_2$O)$_3$(L^2)] in **4** are associated in layers separated by water molecules. In the structures of **3** and **4**, the neighboring iron units are positioned in relative proximity to each other (Fe···Fe separation of 5.612 and 5.447 Å, respectively) as a result of their linkage via strong H-bonds (Table S3). In the latter case, the packing structure is determined by the coordination behavior of the water molecules, leading to O–H···O bonded molecular zigzag strands which are further associated by the edge-to-face aromatic interactions.

In general, the coordination (O$_5$NFe) environment of the Fe^{III} center in **3** and **4** resembles that in the active site of, e.g., the peroxidase *Desulfovibrio vulgaris* [10], among others mononuclear non-heme iron enzymes [1,3,4,6–8]. As has been mentioned, the enzymes share a common structural motif in which two histidines and one carboxylate occupy a trigonal face of the metal coordination sphere [2]. This facial triad is proposed to anchor the Fe^{III} center in the active site, leaving the remaining coordination sites available for binding exogenous ligands such as cofactor, substrate, and/or H$_2$O$_2$ [6]. Such an arrangement allows the enzyme to juxtapose reactants to facilitate catalysis. In addition, it has been suggested that ligating anionic exogenous ligands may prime the iron center for binding and activating O$_2$ or H$_2$O$_2$, presumably by altering the redox potential of the metal center [3]. Thus, we applied the synthesized Fe^{III}–AHBD complexes as model catalysts for the peroxidative oxidation of cycloalkanes with H$_2$O$_2$.

3.2. Catalytic activity of complexes 3 and 4

To prove the viability of the Fe^{III} complexes **3** and **4** as peroxidase models, their catalytic activity in the oxidation of cyclohexane, a model reaction to test and compare activities of oxidase biomimicking complexes, was tested. In accord, **3** and **4** exhibit good catalytic activities in the oxidation of that alkane to a cyclohexanol and cyclohexanone mixture, by aqueous hydrogen peroxide in acidic medium at room temperature (Scheme 3, n = 1), with a total yield of ca. 25% and turnover number (TON) values up to 290 mol of products per mole of catalyst, for a single batch (Table S4). Both **3** and **4** catalyst precursors display a high selectivity toward cyclohexanone (the main final product) and cyclohexanol, as no other products of the oxidation of cyclohexane were detected. The obtained maximum yields are higher than those reported for mono-, di-, tetra- and polynuclear Cu^{II}–AHBD species under similar conditions (Table S5) [18,21].

A positive effect is observed upon addition of nitric acid as an additive. In the absence of acid, the oxidation proceeds with overall yields not higher than 7%. The addition of the acid promoter (up to a HNO$_3$: catalyst molar ratio of 10:1) leads to a remarkable yield growth for both **3** and **4** (up to 25%, Fig. 2). A high promoting effect of that acid on the oxidation of alkanes (and other substrates), catalyzed by various iron, copper or vanadium complexes [40,51–60], has previously been recognized [36–39,47,48]. The role of HNO$_3$ is conceivably associated with (i) the activation of the metal center by further unsaturation upon protonation of the anionic basic ligand, (ii) the enhancement of oxidative properties of metal complexes, (iii) the stabilization of oxidant and promotion of peroxo (or hydroperoxo)-complexes formation [32].

The effect of the H$_2$O$_2$ amount on the overall yield is depicted in Fig. 3. The increase of the n(H$_2$O$_2$)/n(catalyst) molar ratio up to 750 (which corresponds to the H$_2$O$_2$:substrate molar ratio of 7.5:1.0) leads to an enhancement of the yield up to 23% or 25%, for **3** or **4**, respectively. However, further increase of the oxidant amount results in a significant yield drop, eventually due to the increase of the water content in the reaction mixture, resulting in lowering of alkane solubility, and/or to overoxidation reactions at higher H$_2$O$_2$ amounts.

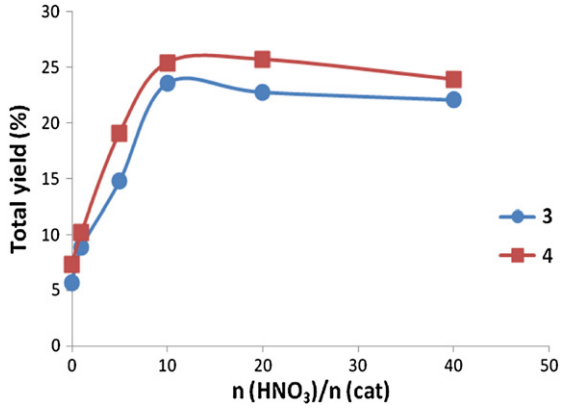


Fig. 2. Effect of nitric acid-to-catalyst molar ratio on the total (cyclohexanol and cyclohexanone) yield, in the peroxidative oxidation of cyclohexane. Reaction conditions: CH$_3$CN (4 mL), C$_6$H$_{12}$ (1 mmol), H$_2$O$_2$ (7.5 mmol), catalyst (10 μmol), nitric acid additive (0–400 μmol), 25 °C, 6 h.

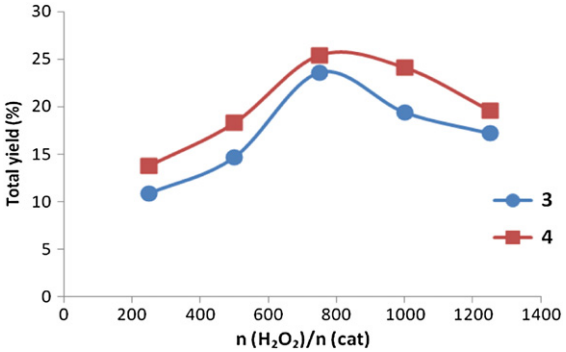


Fig. 3. Effect of the oxidant-to-catalyst molar ratio on the total (cyclohexanol and cyclohexanone) yield, in the peroxidative oxidation of cyclohexane. Reaction conditions: CH$_3$CN (4 mL), C$_6$H$_{12}$ (1 mmol), H$_2$O$_2$ (2.5–12.5 mmol), catalyst (10 μmol), acid additive (100 μmol), 25 °C, 6 h.

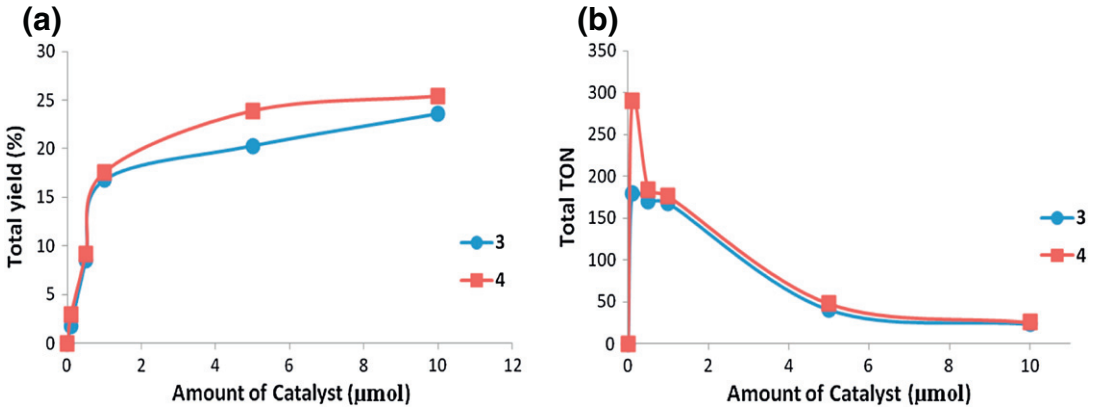


Fig. 4. Effects of the amounts of catalysts **3** and **4** on the total (cyclohexanone and cyclohexanol) yield (a) and TON (b), in the peroxidative oxidation of cyclohexane. Reaction conditions: CH_3CN (4 mL), C_6H_{12} (1 mmol), H_2O_2 (7.5 mmol), $n(HNO_3)/n(cat) = 10$, 25 °C, 6 h.

The catalyst amount also plays a significant role and its increase leads to a yield enhancement (Fig. 4(a)), e.g., from 2.9% to 25% for the respective amounts of 0.1 and 10 μmol of catalyst **4** (corresponding to catalyst-to-substrate molar ratios of $1 \cdot 10^{-4}$ and $1 \cdot 10^{-3}$, respectively). On the other hand, a decrease of the catalyst amount below the typical value of 10 μmol results in enhancements of the overall TON (Fig. 4(b)), e.g., from 25 up to 290 for catalyst **4**, the maximum TON corresponding to the catalyst amount of 0.1 μmol (substrate/catalyst molar ratio of 10,000).

The cyclohexane oxidation appears to proceed mainly by mechanisms that involve both carbon-centered and oxygen-centered radicals (the former upon homolysis of an alkane C–H bond), since very pronounced decreases in product yields occur when the reactions are carried out in the presence of either a carbon-radical trap such as $CBrCl_3$ or TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) or an oxygen-radical trap such as Ph_2NH. In fact, the use of $CBrCl_3$ almost completely suppresses the formation of cyclohexanol and cyclohexanone (Table S4, entries 29 and 32) when used in excess relative to the alkane, whereas the presence of TEMPO leads to 77–84% suppression of activity (Table S4, entries 30 and 33) for a stoichiometric amount in relation to the alkane. The use of Ph_2NH (stoichiometric amount relative to H_2O_2) leads to a lowering of the activity of ca. 86–92% (Table S1, entries 31 and 34). Thus, the pronounced yield drops verified for cyclohexane oxidations when containing free radical scavengers corroborate the involvement of radical pathways that can compete with metal-based oxidations catalyzed by other Fe^{III} complexes with N,O– or O,O– ligands [18,32–34].

The oxidation of other C_5–C_8 cycloalkanes was also tested with previously optimized reaction parameters. Both compounds **3** and **4** catalyze the oxidation of cycloalkanes (Table 1) to the corresponding alcohols and ketones. The maximum total yields of products are achieved in the oxidation of C_5H_{10} (17%), C_6H_{12} (25%), C_7H_{14} (17%) and C_8H_{16} (13%). In the case of cyclooctane a lower yield is observed (Table 1, entries 7 and 8), probably due to substantial sterical hindrance. In all cases, catalyst **4** shows a slightly higher activity over the complex **3**.

4. Conclusions

In this work, an easy and straightforward synthesis of new aquasoluble Fe^{III} complexes bearing sulfonate-functionalized AHBD ligands was performed by simple reaction of an iron salt with the corresponding AHBD in water (pH 2) and under air at room temperature. To our knowledge, they are the first Fe^{III}–AHBD complexes to be structurally characterized. Moreover, they display catalytic activity (overall yields of alcohols and ketones up to 25% with TONs up to 290) in the peroxidative oxidation of C_5–C_8 cycloalkanes, thus extending for the first time the application of Fe^{III}–AHBD complexes to this type of catalytic reactions. These proceed via both oxygen- and carbon-radicals as shown by experiments with radical traps.

These Fe^{III} catalysts (or catalyst precursors) are more active for such a peroxidative oxidation than the other known AHBD complexes with different metals, and the study deserves to be extended to the syntheses of Fe^{III} complexes with other aquasoluble AHBD ligands and their expected applications as oxidation catalysts for various types of substrates, mimicking the functions of iron-oxidases.

Tables listing crystallographic data, atomic coordinates, bond lengths and bond angles, anisotropic displacement parameters, hydrogen

Table 1
Peroxidative oxidation of cycloalkanes (C_5–C_8) to the corresponding alcohols and ketones.[a]

Entry	Cycloalkane	Catalyst	Yield of products (%)[b]		
			Alcohol	Ketone	Total[c]
1		**3**	7.4	8.1	15.5
2		**4**	6.5	10.2	16.7
3		**3**	11.3	12.3	23.6
4		**4**	10.8	14.6	25.4
5		**3**	7.9	9.0	16.9
6		**4**	7.6	9.5	17.1
7		**3**	6.1	6.7	12.8
8		**4**	5.4	7.9	13.3

[a] Reaction conditions: catalyst (10 μmol), cycloalkane (1 mmol), H_2O_2 (7.5 mmol), $n(HNO_3)/n(cat) = 10$ in acetonitrile (4 mL), 25 °C, 6 h.
[b] Moles of product/100 mol of cycloalkane.
[c] Yield of products.

coordinates and isotropic displacement parameters, torsion angles, hydrogen bonds and some catalytic results can be found on line at http://dx.doi.org/10.1016/j.jinorgbio.2012.05.008.

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References

[1] Iron-Containing Enzymes, in: S.P. de Visser, D. Kumar (Eds.), Versatile Catalysts of Hydroxylation Reactions in Nature, Royal Society of Chemistry, Cambridge, 2011.
[2] S.V. Kryatov, E.V. Rybak-Akimova, Chem. Rev. 105 (2005) 2175–2226.
[3] M.M. Abu-Omar, A. Loaiza, N. Hontzeas, Chem. Rev. 105 (2005) 2227–2252.
[4] M. Costas, M.P. Mehn, M.P. Jensen, L. Que Jr., Chem. Rev. 104 (2004) 939–986.
[5] E.I. Solomon, T.C. Brunold, M.I. Davis, J.N. Kemsley, S. Lee, N. Lehnert, F. Neese, A.J. Skulan, Y. Yang, J. Zhou, Chem. Rev. 100 (2000) 235–349.
[6] X. Shan, L. Que Jr., J. Inorg. Biochem. 100 (2006) 421–433.
[7] J.M. Bollinger Jr., C. Krebs, J. Inorg. Biochem. 100 (2006) 586–605.
[8] Y. Mishina, C. He, J. Inorg. Biochem. 100 (2006) 670–678.
[9] L.D. Slep, F. Neese, Angew. Chem. Int. Ed. 42 (2003) 2942–2945.
[10] D.M. Kurtz Jr., J. Inorg. Biochem. 100 (2006) 679–693.
[11] G. Minotti, S.D. Aust, Chem. Phys. Lipids 44 (1987) 191–208.
[12] S.D. Aust, Bibl. Nutr. Diem 43 (1989) 266–277.
[13] M.C.R. Symons, J.M.C. Gutteridge, Free Radicals and Iron: Chemistry, Biology, and Medicine, Oxford University Press, 1998.
[14] Y. Suh, M.S. Seo, K.M. Kim, Y.S. Kim, H.G. Jang, T. Tosha, T. Kitagawa, J. Kim, W. Nam, J. Inorg. Biochem. 100 (2006) 627–633.
[15] M.N. Kopylovich, K.T. Mahmudov, M. Haukka, P.J. Figiel, M. Archana, J.A.L. da Silva, A.J.L. Pombeiro, Eur. J. Inorg. Chem. 27 (2011) 4175–4181.
[16] H.C. Yao, J. Org. Chem. 29 (1964) 2959–2963.
[17] E.V. Shchegol'kov, Y.V. Burgart, O.G. Khudina, V.I. Saloutin, O.N. Chupakhin, Russ. Chem. Rev. 79 (2010) 31–61.
[18] M.N. Kopylovich, K.T. Mahmudov, M.F.C. Guedes da Silva, M.L. Kuznetsov, P.J. Figiel, Y.Y. Karabach, K.V. Luzyanin, A.J.L. Pombeiro, Inorg. Chem. 50 (2011) 918–931.
[19] J. Marten, W. Seichter, E. Weber, Z. Anorg. Allg. Chem. 631 (2005) 869–877.
[20] A.M. Maharramov, R.A. Aliyeva, K.T. Mahmudov, A.V. Kurbanov, R.K. Askerov, Russ. J. Coord. Chem. 35 (2009) 704–709.
[21] M.N. Kopylovich, A.C.C. Nunes, K.T. Mahmudov, M. Haukka, T.C.O. Mac Leod, L.M.D.R.S. Martins, M.L. Kuznetsov, A.J.L. Pombeiro, Dalton Trans. 40 (2011) 2822–2836.
[22] C. Enrique, M. Quiros, J.M. Salas, A. Garca, J.D. Martin, J. Cryst. Spectrosc. Res. 23 (1993) 407–410.
[23] M.N. Kopylovich, K.T. Mahmudov, M. Haukka, K.V. Luzyanin, A.J.L. Pombeiro, Inorg. Chim. Acta 374 (2011) 175–180.
[24] M.N. Kopylovich, Y.Y. Karabach, K.T. Mahmudov, M. Haukka, A.M. Kirillov, P.J. Figiel, A.J.L. Pombeiro, Cryst. Growth Des. 11 (2011) 4247–4252.
[25] Y. Gao, X. Yang, J. Zhang, G. Li, H. Zhang, J. Coord. Chem. 63 (2010) 3413–3422.
[26] Z. Li, G. Mei, H. Zhang, G. Li, W. Wang, Z. Zhang, Inorg. Chim. Acta 363 (2010) 2616–2623.
[27] G. Mei, Z. Li, H. Zhang, G. Li, X. Meng, Synth. React. Inorg. Met.-Org., Nano-Met. Chem. 40 (2010) 163–169.
[28] M.N. Kopylovich, T.C.O. Mac Leod, K.T. Mahmudov, M.F.C.G. Guedes da Silva, A.J.L. Pombeiro, Dalton Trans. 40 (2011) 5352–5361.
[29] M.N. Kopylovich, K.T. Mahmudov, M.F.C.G. Guedes da Silva, A.M. Kirillov, A.J.L. Pombeiro, Dalton Trans. 40 (2011) 12472–12478.
[30] J. Marten, W. Seichter, E. Weber, Supramol. Chem. 22 (2010) 163–171.
[31] R.A. Aliyeva, F.M. Chyragov, K.T. Mahmudov, Russ. J. Inorg. Chem. 49 (2004) 1458–1460.
[32] G.B. Shul'pin, Org. Biomol. Chem. 8 (2010) 4217–4228.
[33] J. England, C.R. Davies, M. Banaru, A.J.P. White, G.J.P. Britovsek, Adv. Synth. Catal. 350 (2008) 883–897.
[34] J. England, R. Gondhia, L. Bigorra-Lopez, A. Petersen, A.J.P. White, G.J.P. Britovsek, Dalton Trans. (2009) 2337–2344.
[35] G. Dyker, Handbook of C–H Transformations, vol. 1–2, Wiley-VCH, Weinheim, 2005.
[36] J.A. Labinger, J.E. Bercaw, Nature 417 (2002) 507–514.
[37] H.M.L. Davies, J.R. Manning, Nature 451 (2008) 417–424.
[38] R.G. Bergman, Nature 446 (2007) 391–393.
[39] K. Godula, D. Sames, Science 312 (2006) 67–72.
[40] A.E. Shilov, G.B. Shul'pin, Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes, Kluwer Academic Publishers, Dordrecht, The Netherlands, 2000.
[41] M.N. Kopylovich, K.T. Mahmudov, M.F.C. Guedes da Silva, L.M.D.R.S. Martins, M.L. Kuznetsov, T.F.S. Silva, J.J.R.F. Silva, A.J.L. Pombeiro, J. Phys. Org. Chem. 24 (2011) 764–773.
[42] Bruker AXS, APEX2—Software Suite for Crystallographic Programs, Bruker AXS, Inc., Madison, WI, USA, 2009.
[43] M.C. Burla, M. Camalli, B. Carrozzini, G.L. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna, J. Appl. Cryst. 38 (2005) 381–388.
[44] G.M. Sheldrick, Acta Cryst. A64 (2008) 112–122.
[45] L.J. Farrugia, J. Appl. Cryst. 32 (1999) 837–838.
[46] G.M. Sheldrick, SADABS—Bruker Nonius Scaling and Absorption Correction, Bruker AXS, Inc., Madison, Wisconsin, USA, 2008.
[47] G.B. Shul'pin, J. Mol. Catal. A: Chem. 189 (2002) 39–66.
[48] G.B. Shul'pin, C. R. Chim. 6 (2003) 163–178.
[49] P. Gilli, L. Pretto, V. Bertolasi, G. Gilli, Acc. Chem. Res. 42 (2009) 33–44.
[50] G. Gilli, P. Gilli, The Nature of the Hydrogen Bond: Outline of a Comprehensive Hydrogen Bond Theory, Oxford University Press, Oxford, 2009.
[51] G.S. Mishra, A.J.L. Pombeiro, J. Mol. Catal. A: Chem. 239 (2005) 96–102.
[52] A.M. Kirillov, M.N. Kopylovich, M.V. Kirillova, Y.Y. Karabach, M. Haukka, M.F.C.G. da Silva, A.J.L. Pombeiro, Adv. Synth. Catal. 348 (2006) 159–174.
[53] G.B. Shul'pin, G.S. Mishra, L.S. Shul'pina, T.V. Strelkova, A.J.L. Pombeiro, Catal. Commun. 8 (2007) 1516–1520.
[54] G.S. Mishra, J.J.R.F. da Silva, A.J.L. Pombeiro, J. Mol. Catal. A: Chem. 265 (2007) 59–69.
[55] C.D. Nicola, Y.Y. Karabach, A.M. Kirillov, M. Monari, L. Pandolfo, C. Pettinari, A.J.L. Pombeiro, Inorg. Chem. 46 (2007) 221–230.
[56] M.V. Kirillova, A.M. Kirillov, M.F.C.G. da Silva, A.J.L. Pombeiro, Eur. J. Inorg. Chem. (2008) 3423–3427.
[57] G.S. Mishra, E.C.B. Alegria, L.M.D.R.S. Martins, J.J.R.F. da Silva, A.J.L. Pombeiro, J. Mol. Catal. A: Chem. 285 (2008) 92–100.
[58] C.D. Nicola, F. Garau, Y.Y. Karabach, L.M.D.R.S. Martins, M. Monari, L. Pandolfo, C. Pettinari, A.J.L. Pombeiro, Eur. J. Inorg. Chem. (2009) 666–676.
[59] T.F.S. Silva, G.S. Mishra, M.F.G. da Silva, R. Wanke, L.M.D.R.S. Martins, A.J.L. Pombeiro, Dalton Trans. 38 (2009) 9207–9215.
[60] J.A.L. Silva, J.J.R.F. Silva, A.J.L. Pombeiro, Coord. Chem. Rev. 255 (2011) 2232–2248.