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Synthesis and structure study of some catecholase-mimetic iron complexes

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Abstract

The biomimetic dioximatoiron complexes $[Fe(Hdmed)]^+$ and $[Fe(H_2dmdt)]^{2+}$ act as catecholase models but the latter also catalyzes the intradiol cleavage of 3,5-di*tert*-butylcatechol. This remarkable selectivity was ascribed to the stable, hydrogen-bonded, macrocyclic coordination sphere of $[Fe(Hdmed)]^+$, precluding bidentate catechol binding, as opposed to the less stable, mobile structure of $[Fe(H_2dmdt)]^{2+}$. This hypothesis is supported by the structures of $[Fe(Hdmed)]^+$ and $[Fe(H_2dmdt)]^{2+}$ determined by X-ray diffraction in 1 M methanol solution. This study is a demonstrative example for the capabilities of the X-ray diffraction technique applied for complexes in the solution phase. The characteristic bond lengths of the complex and the number of solvent molecules in the solvation shell have been determined. To examine the structure of the complexes, gas phase density functional geometry optimizations were performed by using the ADF-2004.01 and GAUSSIAN-98 packages. The PCM methodology was applied to estimate the effect of solvent on the relative energetics of the low-spin and high-spin electronic states of the complexes. The calculations confirmed that the electronic ground state corresponds to the triplet state for both complexes.

Keywords: Iron(II) complexes; Cathecolase mimetic action; X-ray diffraction; Structure of complexes; Solution structure

1. Introduction

There is continuing interest in the biomimetic catalytic activity of transition metal complexes, which may serve as structural and functional models for various metalloenzymes [1–4]. The published studies are aimed at gaining mechanistic information on the details of the corresponding enzymatic reactions. In the modelling approach metalloenzymes are regarded as metal complexes embedded in the protein structure. It is therefore convenient to investigate low molecular mass complexes with the objective of obtaining structural information on reactivity patterns transferable with some reservations to the enzyme [5–8].

We have been interested in the modelling of the metalloenzymes catechol oxidase (catecholase), catechol dioxygenase and phenoxazinone synthase. These enzymes play vital roles in the metabolism of aromatic compounds, which are first converted to phenols and then to catechols. Catechol oxidases convert catechols to *o*-benzoquinones (Scheme 1), catechol dioxygenases catalyze the oxidative cleavage of the same substrates with oxygen insertion (Scheme 2). The related phenoxazinone synthase transforms 2-aminophenols to 2-amino-3*H*-phenoxazin-3-one (Scheme 3). $[Co(Hdmg)_2(Ph_3P)_2]$, cobaloxime(II), and $[Fe(Hdmg)_2(MeIm)_2]$, ferroxime(II), act as functional catecholase [9–11] and phenoxazinone synthase models [12]. They have rigid H-bonded structures, which favour a two-step H-atom transfer mechanism exhibiting a kinetic isotope effect (KIE) [13,14].

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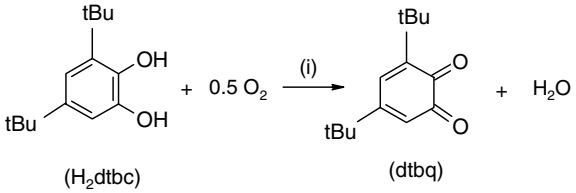
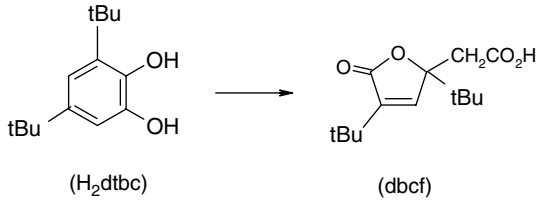
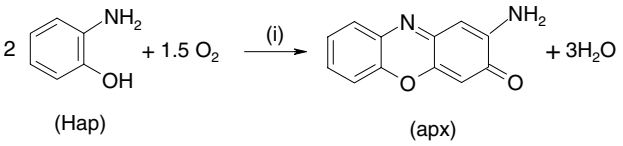


Scheme 1. Catechol oxidase activity: conversion of 3,5-di*tert*-butylcatechol (H_2dtbc) to the corresponding *o*-benzoquinone (dtbq) (i = $[Co(Hdmg)_2(Ph_3P)_2]$ or $[Fe(Hdmg)_2(MeIm)_2]$; 20 °C) [9–11].



Scheme 2. Catechol dioxygenase activity: formation of the cleavage product 3,5-di*tert*-butyl-5-carboxymethyl-2-furanone (dbcf) [5,8].



Scheme 3. Phenoxazinone synthase activity: transformation of 2-aminophenol (Hap) to 2-amino-3*H*-phenoxazin-3-one (i = $[Co(Hdmg)_2(Ph_3P)_2]$ or $[Fe(Hdmg)_2(MeIm)_2]$; 20 °C) [12].

Throughout this paper H_2dmg is dimethylglioxime.

Catechol dioxygenases usually exhibit catechol oxidase (catecholase) activity too, but the reverse is not true: catecholases and models do not necessarily act as catechol dioxygenases [1–8]. This raises the interesting question of what structural features are required for the catecholase versus catechol dioxygenase activity.

In this work we make an attempt to approach this problem by comparing the structures of two dioximatoiron(II) complexes $[Fe(Hdmed)]^+$ and $[Fe(H_2dmdt)]^{2+}$ and their catechol oxidase versus dioxygenase activities. The structure of these catalyst complexes will be determined by X-ray diffraction in methanol solution.

2. Experimental

2.1. Synthesis of ligands and catalyst complexes

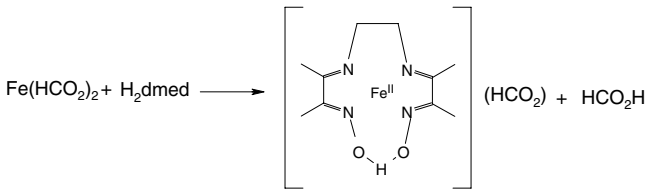
Ligands: H_2dmed, {HON=C(CH_3)C(CH_3)=NCH_2CH_2N=C(CH_3)C(CH_3)=NOH}, was made by the condensation of diacetyl monoxime (dm) with ethylenediamine (ed), whereas H_2dmdt {HON=C(CH_3)C(CH_3)= NCH_2-CH_2}$_2$NH was prepared from dm and diethylenetriamine (dt) by literature methods [15a]. The ligand names were generated by joining the abbreviations for the condensation partners. White crystalline materials were obtained in both cases.

The iron(II) complexes of H_2dmed and H_2dmdt were synthesized according to the reactions in Schemes 4 and 5, respectively.

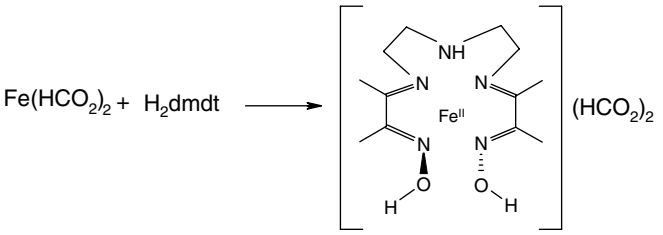
Procedure: 388.9 mg of H_2dmdt (1.44 mmol) or 325.8 mg of H_2dmed (1.44 mmol) was placed in a Schlenk vessel under nitrogen atmosphere, followed by the addition of 263.1 mg (1.45 mmol) of $[Fe^{II}(HCO_2)_2(H_2O)_2]$. The solid mixture was dissolved at ambient temperature in 20–30 cm^3 ethanol (a.g.), previously bubbled out with a stream of nitrogen. After stirring the solutions for 20–30 min, the methanol was evaporated with a rotary pump. 600 mg of the resulting solid complex was dissolved in 1.5 cm^3 methanol and then filtered. Homogeneous 1.0 mol dm^{-3} solutions were used for X-ray measurements. Table 1 contains the physical properties of the examined solutions.

The solids were purified by dissolution in MeOH, slow evaporation of some solvent and separation of the solid. The resulting solids gave satisfactory microanalyses for the formulas corresponding to Schemes 3 and 4. It should be noted that the four-coordinate $Hdmed^-$ forms a pseudo-macrocycle, stabilized by intramolecular hydrogen bonding around iron(II) in $[Fe(Hdmed)](HCO_2)$, conferring extra stability on the complex. On the other hand, no such stabilization is apparent for $[Fe(H_2dmdt)](HCO_2)_2$, in which both oxime groups remain unionized and are not involved in hydrogen bonding.

The high solubility of the iron complexes in MeOH prevented crystallization from this solvent for single-crystal X-ray diffraction studies, but at the same time allowed to carry out X-ray scattering measurements in methanol solution. Attempts at crystallization using anions other than formate, such as BPh_4^-, BF_4^-, PF_6^-, Br^-, Cl^-, ClO_4^- also failed. The detailed results on the structure of $[Fe(Hdmed)](HCO_2)$ and $[Fe(H_2dmdt)](HCO_2)_2$ have been determined by X-ray diffraction in methanol solution and are reported in the following sections of this paper.



Scheme 4. Synthesis of $[Fe(Hdmed)](HCO_2)$.



Scheme 5. Synthesis of $[Fe(H_2dmdt)](HCO_2)_2$.