An Iron(III) Complex with 2-[Bis(2-pyridylmethyl)aminomethyl]-4-nitrophenol as an Intradiol Dioxygenase Model Compound

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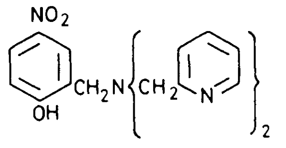
An iron(III) complex with 2-[bis(2-pyridylmethyl)aminomethyl]-4-nitrophenol catalysed the oxidative cleavage of 3,5-di-t-butylcatechol to give the corresponding *cis,cis*-muconic acid anhydride, and showed a spectral change similar to that of pyrocatechase as observed in its reaction towards catechols.

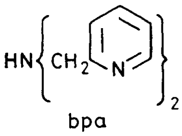
The intradiol dioxygenases, such as pyrocatechase and protocatechuate 3,4-dioxygenase, catalyse the cleavage of catechols to yield *cis,cis*-muconic acid.[1] Most of these enzymes contain high-spin iron(III) in the active site and are characterized by a strong absorption band centred at *ca.* 450 nm (ε/Fe 3000). When a substrate is bound to the enzyme, the band is broadened, accompanied by a significant increase in absorbance in the range 550—700 nm.[2,3] Recent resonance Raman spectroscopy and EXAFS experiments on protocatechuate 3,4-dioxygenase have shown the presence of phenol (from a tyrosine residue) and imidazole (histidine residue) groups in the co-ordination site.[4,5] In an attempt to elucidate the reaction mechanism of pyrocatechase, several iron(III) complexes with complexans[6] or Schiff bases[7] have been prepared as model compounds. Some of them can catalyse the oxidative cleavage of catechols in alkaline solution.[6] However, none of them have mimicked the enzyme in both the catalytic activity and spectral behaviour with catechols.

In this study we have prepared an iron(III) complex with 2-[bis(2-pyridylmethyl)aminomethyl]-4-nitrophenol, and found that this complex shows a reactivity and a spectral behaviour similar to those of pyrocatechase.

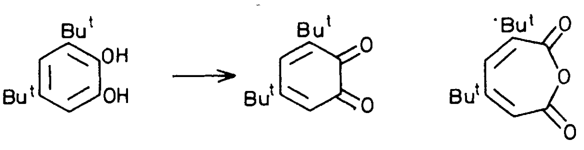
The ligand (abbreviated as Hbpnp) was prepared in the following manner. A tetrahydrofuran (THF) solution contain-



Hbpnp



bpa



(1) 40%

(2) 10%

ing 2-chloromethyl-4-nitrophenol (5 mmol) was added to a THF solution of *N,N*-bis(2-pyridylmethyl)amine (bpa), (5 mmol) at room temperature. To this solution triethylamine (5 mmol) was added, and the mixture was heated under reflux for 2 h. After cooling, the triethylamine hydrochloride separated was filtered off, and the filtrate was evaporated to obtain a syrup which was used for the preparation of the metal complex without further purification.

The iron(III) complex Fe(bpnp)Cl$_2$ was obtained by leaving a methanol solution containing FeCl$_3$ (1 mmol), Hbpnp (1 mmol), and triethylamine (1 mmol) at room temperature for 24 h, and the violet needles deposited were recrystallized from a nitromethane–methanol solution. The complex Fe(bpa)Cl$_3$ was also obtained as yellow needles by a similar method to the above.†

The magnetic moments are 5.9 μ_B at room temperature for both of the complexes, indicating that these complexes are of the high-spin type. The e.s.r. spectrum of Fe(bpnp)Cl$_2$ shows only one sharp signal at *g ca.* 4.3, implying high-spin iron(III) in a rhombic field.[8] In the cyclic voltammograms [in dimethylformamide (DMF), 20 °C], a single redox process corresponding to the Fe^{3+}/Fe^{2+} couple was observed for both complexes, giving $E_{1/2}$ [= $(E_{\text{anode}} + E_{\text{cathode}})/2$] at −0.53 and −0.43 V (*vs.* Fc$^+$/Fc)‡ for Fe(bpa)Cl$_3$ and Fe(bpnp)Cl$_2$, respectively.

Oxidative cleavage of 3,5-di-t-butylcatechol to form *cis,cis*-muconic acid anhydride (**2**), was readily achieved in the presence of Fe(bpnp)Cl$_2$ when a nitromethane solution containing the substrate (1 mmol) and the complex (0.02 mmol) was left in air at room temperature for 4 days. The product (**2**), was isolated by column chromatography on silica gel using CHCl$_3$ as eluant,[10] and was identified by elemental analysis, m.p. (93 °C), and its absorption spectrum.[11] It is clear that the iron(III) complex acted as a catalyst in this reaction, because the amount of (**2**) obtained was more than five times (in mol) that of the iron(III) complex present, and (**2**) was not obtained in the absence of Fe(bpnp)Cl$_2$ under the same experimental conditions. The mixture of Fe(bpnp)Cl$_2$ and (**1**) in nitromethane did not give (**2**), suggesting that the muconic acid anhydride was obtained directly from 3,5-di-t-butylcatechol, not from (**1**), as reported for a ruthenium complex.[12] No formation of muconic acid anhydride was observed in mixtures of Fe(bpnp)Cl$_2$–catechol in DMF, and Fe(bpa)Cl$_3$–catechol in methanol.

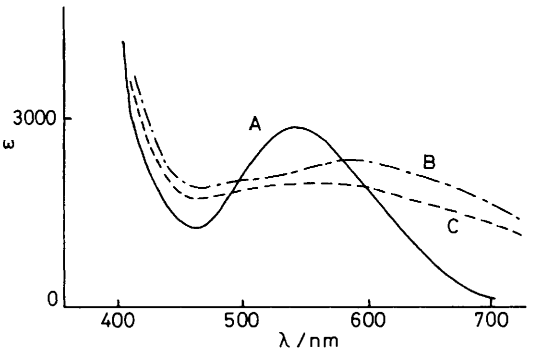


Figure 1. Absorption spectra in nitromethane-methanol (1 : 1) solution at 288 K. The spectrum induced by the addition of 3,5-di-t-butylcatechol was similar to curve C. A: Fe(bpnp)Cl$_2$; B: Fe(bpnp)Cl$_2$ + protocatechuic acid (ratio 1 : 10); C: Fe(bpnp)Cl$_2$ + 4-t-butylcatechol (ratio 1 : 10).

The absorption spectrum of Fe(bpnp)Cl$_2$ is shown in Figure 1. The strong band (ε/Fe 3000) at 550 nm is assigned to the charge-transfer transition from the phenolate oxygen to iron(III), since such a band is not observed for Fe(bpa)Cl$_3$. When a catechol, such as protocatechuic acid or 4-t-butylcatechol, was added to a solution of Fe(bpnp)Cl$_2$, the absorption band at 550 nm was broadened with an increase of absorbance in the range 660—750 nm, as shown in Figure 1. This behaviour resembles that of pyrocatechase. When protocatechuic acid or 4-t-butylcatechol was added to a solution of Fe(bpa)Cl$_3$, which has no absorption band in the visible region, a new absorption band appeared at 700 or 800 nm. These spectral changes must be due to the co-ordination of catechol to the iron(III) ion.

Although the mechanism for the formation of muconic acid anhydride is not known at present, we conclude that Fe(bpnp)Cl$_2$ is the first iron(III) complex which mimics pyrocatechase in both the reactivity and spectral behaviour of catechols.

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† Satisfactory elemental analyses (C,H,N, and Fe) were obtained.

‡ The potentials were referenced to that of ferrocene (Fc) (ref. 9).