Triethylenetetraminehexaacetatoferrato(II)cuprate(II), $[Fe^{II}Cu^{II}(ttha)]^{2-}$: oxidation-induced cross-binuclear metal exchange

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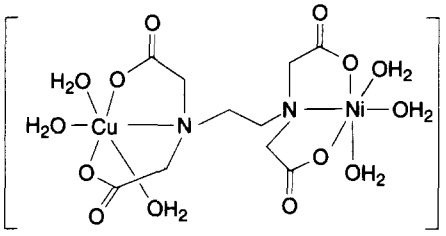
Summary

The heterobinuclear complex $[Fe^{II}Cu^{II}(ttha)]^{2-}$ *(1)* ($ttha^{6-}$ = triethylenetetraminehexaacetate), exhibits the same two-nitrogen per metal coordination of the related homobinuclear $[Cu^{II}_2(ttha)]^{2-}$ complex, but *(1)* has a signature broad single derivative e.p.r. line at $g = 2.11$ with a peak-to-peak width of 182 G. Oxidation to the $[Fe^{III}Cu^{II}(ttha)]^{-}$ complex by either O_2 or H_2O_2 initiates a rapid cross-binuclear metal exchange forming homobinuclear $[Fe^{III}_2O(ttha)]^{2-}$ and $[Cu^{II}_2(ttha)]^{2-}$ products ($t_{1/2}$ *ca* 3.9 s). An isomeric form of $[Fe^{III}Cu^{II}(ttha)]^{-}$, which has three nitrogen donors bound to Cu^{II} and only the remaining iminodiacetate fragment bound to Fe^{III}, rearranges much more slowly ($t_{1/2}$ *ca* 4.8 h).

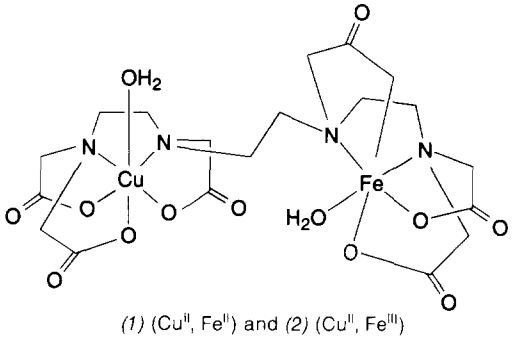
Introduction

Heterobinuclear complexes of polyaminopolycarboxylate ligands were initially observed as kinetic intermediates by Margerum and Bydalek[1] and Margerum and Jones[2] during metal-ion interchange reactions with M′ replacing M in M(edta) complexes. For example, when copper(II) displaces nickel(II) in $Ni(edta)^{2-}$ each metal occupies an iminodiacetate segment of $edta^{4-}$ prior to the rupture of the remaining nickel(II)–nitrogen bond, loss of $Ni(H_2O)^{2+}_6$, and full chelation of the copper(II) centre:



$[Cu^{II}Ni^{II}(edta)]$

Stable binuclear complexes of iron(II), iron(III)[3]; cobalt(II), nickel(II), copper(II)[4]; Zn(II)[5]; chromium(III)[6]; titanium(III)[7]; VO^{2+}[8,9]; vanadium(III)[10]; are more readily formed with triethylenetetraminehexaacetate ($ttha^{6-}$) due to the more extensive chelation at each metal site. Heterobimetallic complexes of copper(II) with iron(II) *(1)* or iron(III) *(2)* are described in this paper:



(1) (Cu^{II}, Fe^{II}) and *(2)* (Cu^{II}, Fe^{III})

Studies of reactions of O_2 with $ttha^{6-}$ binuclear complexes have previously been restricted to homobinuclear complexes of vanadium(III) and iron(II)[10,12]. It has been shown that the mechanisms of oxidation of $[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ with O_2 and H_2O_2 are different[11,12]. The iron(III) oxo-bridged complex, $[Fe_2O(ttha)]^{2-}$, is rapidly formed by O_2 oxidation of $[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ without release of free H_2O_2, O_2^- or HO during the reduction[10,12]. $[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ is oxidized by H_2O_2 by a pathway forming a ferryl entity ($Fe^{IV}O$) at one iron centre of the original extended chain complex[11a]. The fate of the ferryl intermediate is either an internal self-reduction by the pendant iron(II) site, forming the $[Fe_2O(ttha)]^{2-}$ product, or a reduction of the ferryl unit by an additional H_2O_2[11a]. Therefore, H_2O_2 oxidations of iron(II)-polyaminopolycarboxylates exceed consumption of H_2O_2 above a simple 1 H_2O_2:2 iron(II) stoichiometry[11].

The formation of homobinuclear $ttha^{6-}$ complexes with copper(II) and iron(II) prompted our interest in heterobinuclear derivatives of this ligand since heterobinuclear iron/copper species are important in biochemistry. An Fe^{III}–O–Cu^{II} species is proposed for the *met* form of the terminal unit of cytochrome oxidase[13]; a peroxo Fe^{III}–O–O–Cu^{II} intermediate is also proposed during the formation of the Fe^{III}–O–Cu^{II} product[14,15].

Synthetic analogue strategies for preparing iron(II)/copper(II) models of these biometallic centres in other laboratories[16] have focused mainly on iron(III) porphinato complexes bridged through oxygen donors to copper(II) complexes. The copper(II) sites are frequently held for bridging above the axial position of the iron(III) porphyrin as strapped additions to the porphyrin structure[16]. In one case, allowing self-assembly, the copper(II) entity was chelated by the $(aib)_3$ peptide and bridged to the iron centre through the carboxylate terminus of the peptide[17]. Other synthetic complexes intended as iron(III)/copper(II) cytochrome oxidase models have emphasized rigid coplanar assemblies built upon Schiff base and phenoxy chelation[18]. All of the early models[16–18] fail to produce the high antiferromagnetic coupling between iron(III) and copper(II) of the natural cytochrome oxidase *met* form. Only recently have Holm's[13a] and Karlin's[19] groups synthesized iron(III) porphyrins which are linked by oxo bridges to copper(II) complexes of tripodal amine ligands in which the binuclear complexes reproduce the $S = 2$ ground state of the enzyme.

All the successful preparations of synthetic analogues of cytochrome oxidase iron(III)/copper(II) bridged complexes have been prepared in non-aqueous media such as acetone, CH_2Cl_2, CH_3OH/CH_2Cl_2 or toluene, at low temperatures. None of the reported iron(III)/copper(II) bridged complexes has been prepared in which the metal centres are in an environment typical of non-heme iron proteins.

The propensity for formation of $[M_2O(ttha)]^{2-}$ complexes [M = vanadium(III) or iron(III)] led us to attempt the preparation of $[(Fe^{III}–O–Cu^{II})(ttha)]^{3-}$ in aqueous solution at room temperature. Synthetic difficulties with

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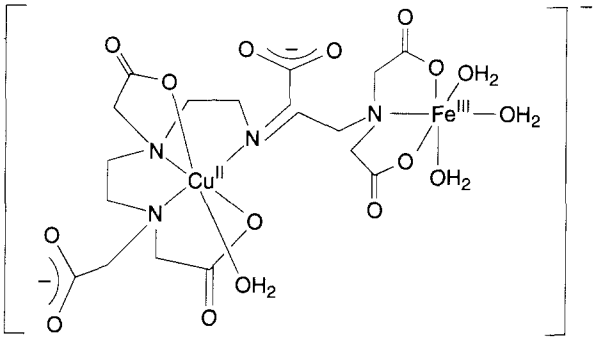
the direct addition of copper(II) to mononuclear $[Fe^{III}(ttha)]^-$ or, conversely, $Fe(H_2O)_6^{3+}$ to $[Cu(ttha)]^{4-}$ prompted us to prepare a precursor $[Fe^{II}Cu^{II}(ttha)]^{2-}$ complex *(1)* as reported herein. In *(1)* each metal centre occupies an 'N_2O_3'-donor environment from the $ttha^{6-}$ ligand. Autoxidation of *(1)* produces a desired $[Fe^{III}Cu^{II}(ttha)]^-$ complex *(2)*. However, this species rapidly undergoes a cross-binuclear metal exchange without demetallation in the pH range of 4–6. The products are the more stable homobinuclear $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)(H_2O)_2]^{2-}$.

An isomeric $[Fe^{III}Cu^{II}(ttha)]^-$ complex *(3)*, in which the copper(II) centre binds to three polyamino-chain donors of $ttha^{6-}$ with the remaining iminodiacetate fragment coordinated to iron(III), also rearranges to the more stable $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)(H_2O)_2]^{2-}$ products. The rate-determining processes involving rearrangement and cross-exchange of *(2)* cannot be the same as with isomer *(3)* because cross-metal exchange for *(2)* is complete in 24s, *cf.* 2 days for *(3)*. These interesting observations are the subject of this paper.



(3)

Experimental

Reagents

H_6ttha was obtained from Sigma; 2,6-Lutidine was obtained from Aldrich. $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ and $Fe(NO_3) \cdot 9H_2O$ were obtained from J. T. Baker; $Cu(NO_3)_2 \cdot 3H_2O$ was supplied by Mallinckrodt. All metal salts were analytical grade. O_2 and Ar gases were supplied by Air Products. Trace O_2 was removed from the Ar by passage through chromium(II) scrubbing towers. Transfers of air-sensitive solutions were carried out with gas-tight syringe techniques, using stainless steel needles. The ttha/metal ion complex solutions were prepared in Ar-purged solvents. Required weights of metal salts were added to the deoxygenated ligand solutions and pH adjusted under Ar with 1 M NaOH or 1 M HCl.

Instrumentation

U.v.–vis. spectra were recorded on a Varian-Cary 118C spectrophotometer. Quartz cells were sealed with rubber septa and flushed with Ar prior to filling with air-sensitive solutions. E.p.r. solution spectra were recorded at room temperature using a quartz flat cell previously purged with Ar. The cell was mounted and tuned in a Varian E-4 instrument. Spectra were recorded over a range of 1000 G, centred at $g = 2.00$. The instrument was calibrated with DPPH in benzene prior to obtaining the spectra of the copper(II) complexes.

pH adjustments were made using a Fisher Accumet Model 810 pH meter and a combination glass/NaCl calomel electrode standardized against Fisher pH buffers.

Preparation of $[Fe^{II}Cu^{II}(ttha)]^{2-}$, (1)

The order of addition of adding Ar-purged $Cu(NO_3)_2 \cdot 3H_2O$ solution to $[Fe^{II}(ttha)]^{4-}$ is essential to avoid the initial presence of $[Cu_2(ttha)]^{2-}$. The 1:1 $[Fe^{II}(ttha)]^{4-}$ complex was prepared by adding the required weight of $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ to an Ar-purged 25.0 cm^3 ttha solution. The final concentration was 7.0–9.5 $\times 10^{-2}$ M upon dilution with copper(II); the pH was adjusted to 4.0. An Ar-purged $Cu(NO_3)_2 \cdot 3H_2O$ solution of 10-fold the iron(II) concentration was then added dropwise *via* a syringe until a 1:1 addition was achieved. Mixing was maintained by Ar gas bubbling throughout the addition; the pH was adjusted slowly to 6.58.

Preparation of $[Fe^{III}Cu^{II}(ttha)]^{2-}$, (3)

An air-exposed $Fe(NO_3)_3$ solution was added dropwise to a $[CuH_2(ttha)]^{2-}$ solution [mixture of isomers *(4)* and *(5)*, as described in the main text] while maintaining the pH below 3.0 in order to prevent precipitation of $Fe(OH)_3$.

Stopped-flow measurements

Stopped-flow data were collected on a Durrum D-110 stopped-flow spectrophotometer interfaced with a DEC-1103 computer for data analysis. The stopped-flow pathlength was 2.00 cm. Data reduction and analysis of the absorbance change at the 470 nm band of $[Fe_2O(ttha)]^{2-}$ were achieved with appropriate first-order kinetic programs[11a]. Reactions were usually followed for seven half-lives and the pseudo-first-order rate constants were averaged with 6–10 runs for a given experimental condition.

Results and discussion

Copper(II)- and zinc(II)-(ttha) complexes

When copper(II) is constrained to the N_2O_4 donor set of the $hedta^{3-}$ ligand its e.p.r. spectrum exhibits a well-resolved, four-line pattern with copper hyperfine splitting ($A_{Cu} = 63$ G; Figure 1E). The ligand-field spectrum of $[Cu(hedta)]^-$ exhibits one $^2T_{2g} \leftarrow {}^2E_g$ transition at 718 nm ($\varepsilon = 60\ M^{-1}\ cm^{-1}$). The copper(II) complexes of $ttha^{6-}$ exhibit more complicated spectra due to additional rotational drag of the molecule which leads to broadening of the lines and a partially immobilized e.p.r. spectrum. If the second binding site is populated by a paramagnetic centre there is an additional dipolar paramagnetic effect[4c]. These two effects are seen in the spectrum of $[Cu_2(ttha)]^{2-}$ (Figure 1D) where a single smooth derivative spectrum appears at $g = 2.08$ with a peak-to-peak width of 139 G. By comparison, the $[Cu^{II}Zn^{II}(ttha)]^{2-}$ complex exhibits an immobilized spectrum, but still shows line splitting associated with a single copper(II) site (Figure 1A). Both $[Cu_2(ttha)]^{2-}$ and $[Cu^{II}Zn^{II}(ttha)]^{2-}$ have an active copper(II) chromophore with a ligand field transition of 725 nm (Figure 2A and B); the $[Cu_2(ttha)]^{2-}$ complex is twice as intense as anticipated for non-interacting optical sites ($\varepsilon = 125\ M^{-1}\ cm^{-1}$). When only one copper(II) per $ttha^{6-}$ ligand is present both the e.p.r. and ligand-field

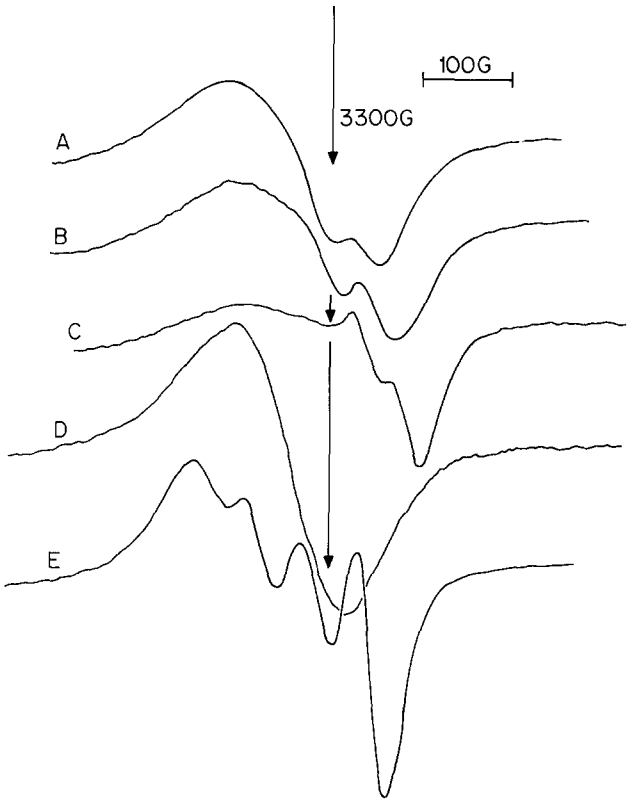
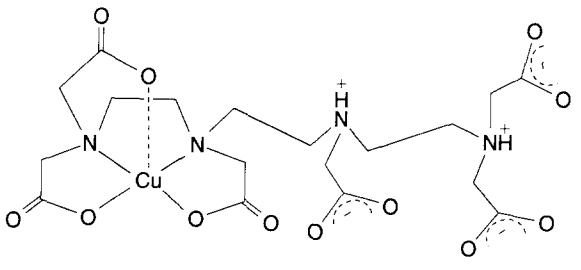


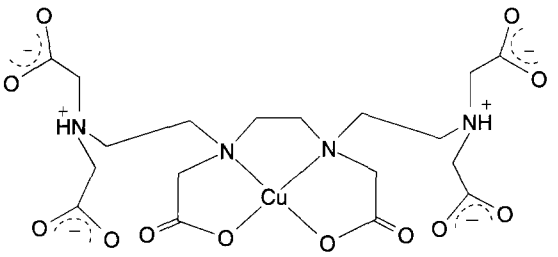
Figure 1. Room temperature e.p.r. spectra of mononuclear and bimetallic polyaminocarboxylate complexes (RG = receiver gain; tc = time constant). (A) $[CuZn(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 7.0, RG = 8.0×10^3, tc = 3.0 s; (B) $[CuH_2(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 3.62, RG = 8.0×10^3, tc = 3.0 s; (C) $[Cu(ttha)]^{4-} = 5.00 \times 10^{-3}$ M, pH = 10.14, RG = 8.0×10^3, tc = 3.0 s; (D) $[Cu_2(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 4.98, RG = 8.0×10^3, tc = 1.0 s; (E) $[Cu(hedta)]^{-} = 9.09 \times 10^{-3}$ M, pH = 4.8, RG = 3.2×10^3, tc = 1.0 s. Other settings for all spectra: mod. freq. = 9.481 GHz; mod. amp. = 12.4 G; power = 30.0 mW; scan time = 4.0 min.

spectra are pH dependent. At lower pHs (*ca* 4.0) where the formulation $[CuH_2(ttha)]^{2-}$ may be given on the basis of the pK_as of $ttha^{6-}$, two species are possible, both with λ_{max} *ca* 725 nm, $\varepsilon = 60\ M^{-1}\ cm^{-1}$. One isomer *(4)* has copper(II) at the terminal site, equivalent to its position in $[Cu_2(ttha)]^{2-}$[4]; another isomer is the more symmetric central placement with the terminal nitrogens as non-coordinated iminodiacetate units bearing the two protons *(5)*:



(4)

Either structure has an N_2O_4 environment for the copper centre. However, the terminally occupied isomer *(4)* has a statistical and an electrostatic advantage. The similarity in e.p.r. spectra of $[CuH_2(ttha)]^{2-}$ (Figure 1B) and $[CuZn(ttha)]^{2-}$ (Figure 1A) strongly suggest that *(4)* is the favoured isomer. When the pH is increased to



(5)

8.2 or above, the deprotonation of either isomer causes a closure of one nitrogen base, forming *(6)* with an N_3O_3 donor set for copper(II). Complex *(6)* has a structure analogous to *(3)* with a proton instead of iron(III) on the pendant iminodiacetate nitrogen fragment. The N_3O_3 ligand field of *(6)* is at a higher energy ($\lambda_{max} = 675$ nm). The structure of *(6)* in this pH range is analogous to the 1:1 $[Cu^{II}(dtpa)]^{3-}$ complex of Sievers and Bailar[20], which exhibits its d–d transition at 660 nm. The more compact structure produces less rotational drag, and the e.p.r. spectrum of *(6)* at pH 10.14 shows more resolved copper hyperfine lines ($A_{Cu} \simeq 47$ G; Figure 1C).

$[Fe^{II}Cu^{II}(ttha)]^{2-}$ complex

When iron(II) serves the role as the second metal ion bound to $ttha^{6-}$, a new species with $\lambda_{max} = 725$ nm, $\varepsilon = 98\ M^{-1}\ cm^{-1}$ (Figure 2C) is obtained. That this species is the $[Fe^{II}Cu^{II}(ttha)]^{2-}$ complex *(1)*, and not due to a mixture of $[Fe_2(ttha)(H_2O)_2]^{2-}$ and $[Cu_2(ttha)]^{2-}$ is clearly shown by its unique e.p.r. spectrum near $g = 2$ (Figure 3D) compared to $[Cu_2(ttha)]^{2-}$ (Figures 3A and 1D). $[Fe^{II}Cu^{II}(ttha)]^{2-}$ has e.p.r. parameters of $g = 2.11$ and a peak-to-peak width of 182 G. Also, the e.p.r. spectrum of a synthetic mixture of $[Cu_2(ttha)]^{2-}$ and

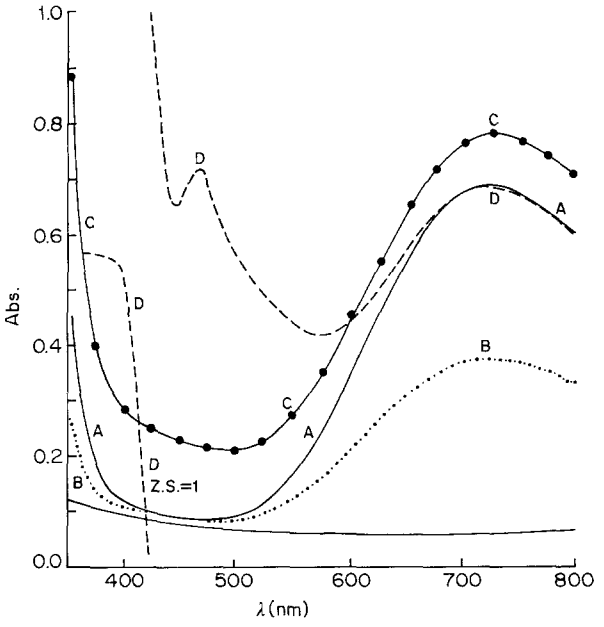


Figure 2. Vis. spectra of bimetallic $ttha^{6-}$ complexes at 25 °C. (A) $[Cu_2(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 4.34; (B) $[Cu^{II}Zn^{II}(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 7.28; (C) $[Fe^{II}Cu^{II}(ttha)]^{2-} = 7.41 \times 10^{-3}$ M, pH = 6.35; (D) $[Cu_2(ttha)]^{2-} = [Fe_2O(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 5.02; $[Fe_2O(ttha)]^{2-}$ was produced by dissolving its Me_2dabco^{2+} salt into the $[Cu_2(ttha)]^{2-}$ solution of (A).

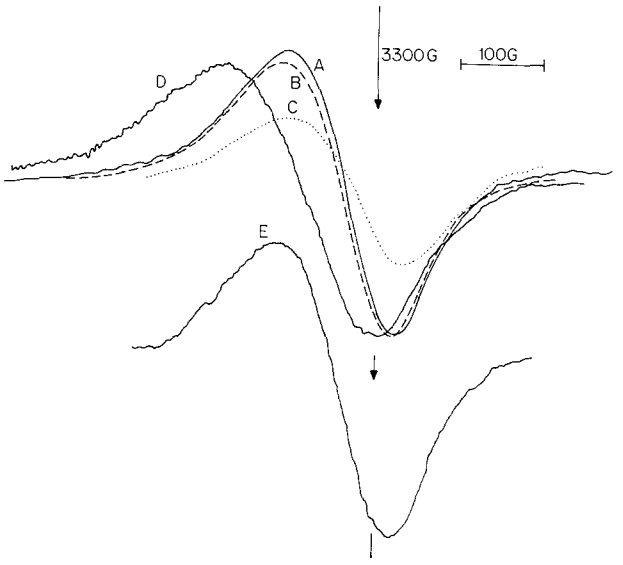


Figure 3. Room temperature e.p.r. spectra of bimetallic ttha^{6-}-complexes of copper(II) and iron(II) or iron(III) (RG = receiver gain). (A) $[Cu_2(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 4.34, RG = 4.0×10^3; (B) $[Cu_2(ttha)]^{2-} = [Fe_2O(ttha)]^{2-} = 5.00 \times 10^{-3}$ M (synthetic mixture), pH = 4.98, RG = 4.0×10^3; (C) $[Cu_2(ttha)]^{2-} = [Fe_2(ttha)]^{2-} = 2.50 \times 10^{-3}$ M (synthetic mixture), pH = 3.24, RG = 8.0×10^3; (D) $[Cu^{II}Fe^{II}(ttha)]^{2-} = 5.00 \times 10^{-3}$ M, pH = 4.74; RG = 8.0×10^3; (E) Autoxidation products of solution D at 12.0 min bubbling of O_2, RG = 8.0×10^3 (note spectrum matches that of solution B when the RG is 8.0×10^3 for *E versus* 4.0×10^3 for B as required by the stoichiometry. Other e.p.r. settings for all spectra: mod. freq. = 9.482 GHz, mod. amp. = 12.5 G, power = 30.0 mW, time constant = 1.0 s, scan time = 4.0 min.

$[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ shows the same *g* and peak-to-peak width as $[Cu_2(ttha)]^{2-}$ above (Figure 3C). Therefore, the equilibrium in Equation 1 lies either to the left or metal exchange forming the homobinuclear species occurs very slowly. Similarly, formation of the heterobinuclear complex is also slow *via* metal exchange from the homobinuclear complexes:

$$2[Fe^{II}Cu^{II}(ttha)]^{2-} \rightleftharpoons [Cu_2(ttha)]^{2-} + [Fe_2(ttha)(H_2O)_2]^{2-} \quad (1)$$

When air or O_2 is admitted to the solution of $[Fe^{II}Cu^{II}(ttha)]^{2-}$ autoxidation occurs (Figure 4). Incremental addition of air, followed by spectral scans, show a significant decrease in absorbance initially at 725 nm band and a steady growth of a 470 nm feature (Figure 4). Changes are also readily detected with e.p.r. The product solution spectrum (Figure 3E) obtained at 4 min is identical to the synthetic mixture of $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)]^{2-}$ (Figure 3B). The u.v.–vis. spectrum of the autoxidation products of *(1)* is also identical to the synthetic mixture of $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)]^{2-}$ (Figure 2D).

$[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)]^{2-}$ complexes formed in the $[Fe^{II}Cu^{II}(ttha)]^{2-}/O_2$ reaction were separated by ion-exchange on AG1-4X resin. The $[Cu_2(ttha)]^{2-}$ readily moves with 0.10 M NaCl, as does the authentic complex; the $[Fe_2O(ttha)]^{2-}$ ion was removed by 2.0 M NaCl. Its spectral features are $\lambda_{max} = 470$ nm, ε/Fe = 63 M^{-1} cm^{-1}, and a shoulder at 510 nm as reported previously[11a].

The course of the autoxidation by saturated O_2 solution proceeds as shown in Scheme 1. An estimate of $t_{1/2}$ for the oxidation process was made on the basis of complete

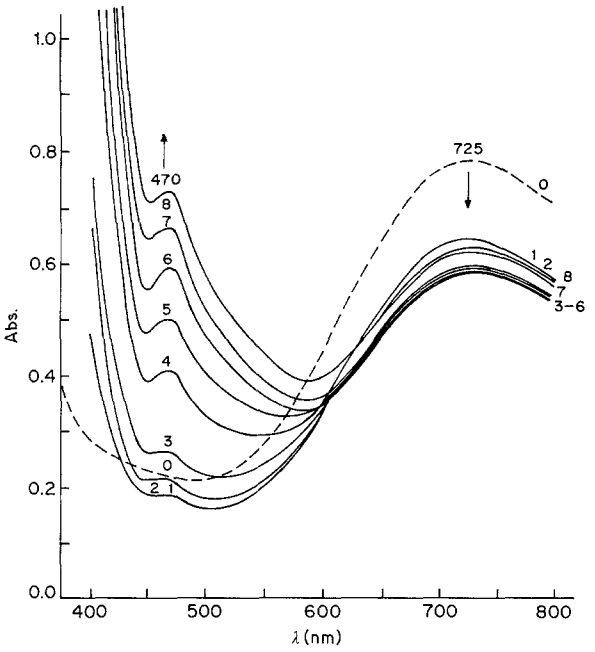
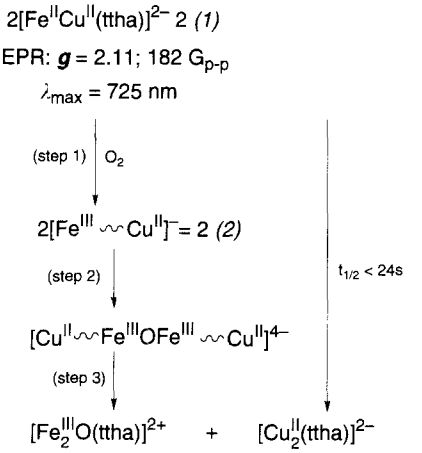


Figure 4. Pulsed addition of O_2 as air to $[Fe^{II}Cu^{II}(ttha)]^{2-}$ *[(1)]*. $[Fe^{II}Cu^{II}(ttha)]^{2-}_i = 7.40 \times 10^{-3}$ M. (0) under Ar; (1) stirred with air for 10.0 min, sealed and scanned; (2)–(7) stirred 2.0 min, sealed and scanned; (8) after 6.0 h.

reaction within the earliest time to record the e.p.r. spectrum after admitting O_2 ($t_{1/2} < 24$ s). A tetrametallic species of anionic charge 4^- would also be compatible with the final u.v.–vis. spectrum (Figure 2D), but not with the final e.p.r. Furthermore, the anion exchange experiment shows the products to be the homobinuclear $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)]^{2-}$ complexes. In these schemes the symbol M ~ M′ is adopted to designate the ttha^{6-} ligand structure bridging two metal centres in an extended chain configuration.



$\lambda_{max} = 470$ nm, 510 nm (sh): $\lambda_{max} = 725$ nm;AG1-4X2 M NaCl elutes: E.P.R.: $g = 2.08$; 139 Gp–p; AG1-4X0.10 M NaCl elutes.

Scheme 1.

Isomeric [$Fe^{III}Cu^{II}$(ttha)] complex (3)

A 1.00×10^{-2} M solution of the iron(III) derivative exhibited its copper(II) d–d transition at 725 nm when prepared by $Fe(NO_3)_3$ addition (as described in the Experimental section) at pH *ca* 3. Adjustment of the pH in the range of

6.50–8.67 gave a new species with a broad maximum near 700 nm for the copper(II) d–d transition and a very slight shoulder at 470 nm for an iron(III) chromophore; the solution was khaki green. A trace amount of $Fe(OH)_3$ was removed by filtration prior to obtaining the spectrum. However, the majority of the iron(III) was retained in solution (*ca* 1.0×10^{-2} M). Therefore, iron(III) must be coordinated. The iron(III) competes for the available N-donors of the $ttha^{6-}$ ligand with the copper(II) centre. In the absence of iron(III), $[Cu(ttha)]^{4-}$, *ca* pH 7, is fully converted to a single species with λ_{max} at 675 nm, indicative of an N_3O_3 donor set. Since the maximum near 700 nm is very broad for the $Fe^{III}Cu^{II}$ species at pH *ca* 7, it suggests that two complexes of copper(II) are present, one with three nitrogen donors *(3)* (λ_{max} *ca* 675 nm) and one with two nitrogens *(2)* (λ_{max} *ca* 725 nm). The maximum near 700 nm shifts towards 675 nm in the first 10 min of the reaction, indicating that the dominant species at pH 7 is isomer *(3)* after 10 min, *(2)* having decayed to exchanged products. Species *(3)* slowly rearranges to give the homobinuclear products $[Fe_2O(ttha)]^{2-}$ and $[Cu_2(ttha)]^{2-}$ in 82% yield after two days. The remaining 18% of iron(III) is lost to demetallation as $Fe(OH)_3$ in a competitive reaction. This also supports the iron(III) being bound more weakly at an iminodiacetate site of species *(3)*, as a greater fragment as in *(2)* of the $ttha^{6-}$ does not allow demetallation.

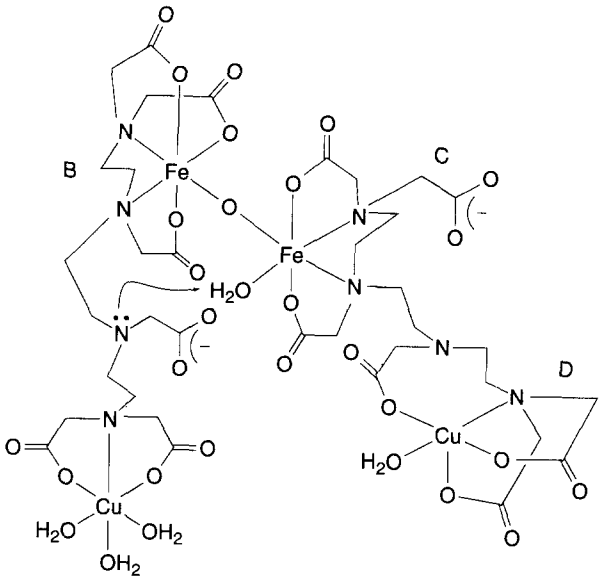
The rearrangement of *(3)* to its homobinuclear products was not followed kinetically due to the light scattering problems with co-production of the $Fe(OH)_3$. However, the slow progress of this reaction differs significantly from the $[Fe^{III}Cu^{II}(ttha)]^-$ complex prepared via autoxidation of *(1)*. The failure of the direct addition of iron(III) to $[CuH_2(ttha)]^{2-}$ to provide a clearly discernible $[Fe^{III}Cu^{II}(ttha)]^-$ complex, in which each metal site retains two nitrogen donors, precluded further detailed study. However, the spectral observations of a second short-lived $[Fe^{III}Cu^{II}(ttha)]^-$ complex *(2)* in which each metal is coordinated by two N-donors (*e.g.* λ_{max} 725 nm for this isomer) is required to explain the initial spectral changes. But the yield of *(2)* by the direct addition pathway of iron(III) to $[CuH_2(ttha)]^{2-}$ is uncertain, and the presence of isomer *(3)* as the major product *via* this route precludes a feasible study of the kinetic behaviour of *(2)*. These complications prompted the study of *(1)* and its autoxidation reaction, since it was observed that *(1)* produced oxidation products without parallel demetallation.

The decay of species *(2)* in these solutions will generate $[Fe_2O(ttha)]^{2-}$ which absorbs at 470 nm. The initially formed $[Fe_2O(ttha)]^{2-}$ chromophore from *(2)* would mask the appearance of an oxo-bridged 4^- anion as a precursor to the final homobinuclear products (Equation 2), prepared *via (3)*.

$$2(3) \rightleftharpoons [Cu^{II}\text{wwww}Fe^{III}OFe^{III}\text{wwww}Cu^{II}]^{4-} \quad (2)$$

This 4^- species would differ from the related one presented in Scheme 1 in that the copper(II) sites retain three nitrogen donors for the 4^- ion in Equation 2, but would have only two nitrogen donors for copper(II) in the species of Scheme 1. The much more rapid conversion of complex *(2)* compared to *(3)* suggests that the rate determining step in forming homobinuclear products probably occurs with rupture of a Cu—N bond to provide a good nucleophile to attack and stabilize the incipient $[Fe_2O(ttha)]^{2-}$ complex. The rate-determining step for *(3)* is most likely the rearrangement of *(3)* to *(2)*, followed by the rapid metal-ion exchange, or the change of the tetranuclear species derived from *(3)* into the tetranuclear species derived from *(2)*, followed by rapid metal exchange.

It is feasible to consider a sequence of reaction steps which involve only the rupture of glycinato moieties at one metal site and the transfer of this same free glycinato fragment of $ttha^{6-}$ to the opposite metal–metal partner within the tetranuclear complex. If the reaction sequence begins with rupture of an interior glycinato arm away from the copper(II) end of the complex (site A) the same freed glycinato unit is poised to act as a nucleophile toward the iron(III) centre on the parallel branch (site C). The nature of the first tetranuclear activated fragment is shown here for purposes of visualization:



A

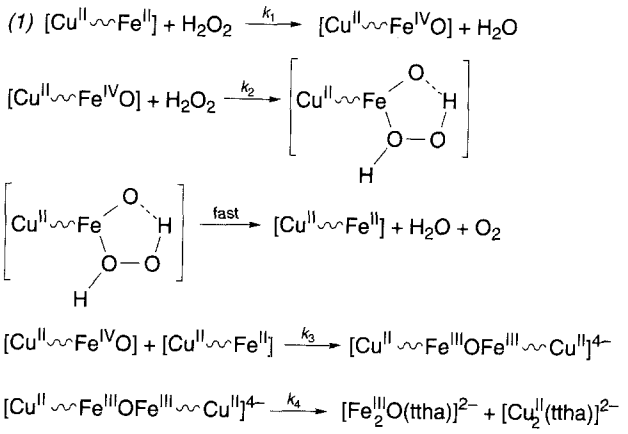
Energetically, this will trade one new glycinato fragment at the iron(III) site (C) for one it originally has from its own $ttha^{6-}$ chelation. The liberated glycinato functionality of $ttha^{6-}$ from the cross-iron(III) complex can act as a nucleophile to the first copper(II) centre which has reduced in its extent of chelation (site A). The residual glycinato fragment at site C from the original $ttha^{6-}$ may then rupture to provide the second nucleophile N-donor to attack the copper(II) centre at site A. The displaced iminodiacetate fragment from site A on the fully liberated $[Fe^{III}_2O(ttha)]^{2-}$ isomer then needs only to displace the water ligands on the iron(III) intermediate to complete formation of $[Fe^{III}_2O(ttha)]^{2-}$. In this manner the iron(III) (C) and copper(II) (A) sites are able to follow a 'walking mechanism' between the two $ttha^{6-}$ ligands without dissociation as free metal ions which would hydrolyse or precipitate in the medium.

During the proposed process it is noteworthy that only the initial loss of the glycinato fragment at site A of the copper(II) complex will be a high energy process which is not compensated for by rapid bond formation with a second metal site, or steps which are energetically equivalent in bonds broken and bonds formed. The proposed sequence is essentially similar to the postulates of Margerum and Bydalek[1] and Margerum and Jones[2] for metal ion exchange with [M(edta)M'] complexes except that the leaving metal ions are not liberated to the solvent in the cross-binuclear exchange reaction for $[Fe^{III}Cu^{II}(ttha)]^-$ complexes.

Oxidation of $Fe^{II}Cu^{II}(ttha)^{2-}$ (1)

When complex *(1)* at 3.84×10^{-3} M is oxidized in 2,6-lutidine/2,6-lutidinium perchlorate buffer (pH = 7.00, $\mu = 0.050$, $T = 25.0\,^{\circ}C$) only one increasing absorbance change is detected at 470 nm when either O_2 at half-saturation (6.25×10^{-4} M) or if H_2O_2 at 1.92×10^{-3} M is used as the oxidant. The solubility limitation on $[O_2]$ in water, and the small change in absorbance if the concentration of *(1)* is decreased to achieve pseudo-first-order reaction conditions in $[O_2]$, prevented detailed mechanistic studies by the stopped-flow method with O_2 as the oxidant. However, several observations suggestive of the mechanism in Scheme 1 were obtained. Under clearly second-order reaction conditions, where the ratio of the molar reducing equivalents from *(1)* to oxidizing equivalents from O_2 was 1.54, a strictly first-order absorbance increase at 470 nm was detected by stopped-flow methods. The rate constant was $0.18 \pm 0.01\ s^{-1}$ for the process yielding the final absorbance. Given that the reaction conditions in $[(1)]$ and $[O_2]$ are second order, and that formation of the tetranuclear *(4)*-intermediate is almost certainly a second-order process in $[(2)]$, it seems most likely that the process being measured spectrophotometrically is the rearrangement step 3 in Scheme 1. The value of the rate constant for this rate-determining step ($0.18\ s^{-1}$) is consistent with the e.p.r. observations wherein the half-life of the reaction was observed to be less than 24 s (determination limited by mixing and spectral procedures). The stopped-flow method is consistent with an O_2 oxidation-induced metal exchange process for *(2)* with $t_{1/2} = 3.9$ s.

Studies were also carried out using H_2O_2 as the oxidant. When H_2O_2 is present at a 2 iron(II): H_2O_2 stoichiometry, sufficient to allow complete oxidation of iron(II) to iron(III) by a Fenton-like one-electron hydroxyl radical chain pathway, it was observed (Figure 5) that only half of the iron(II) is consumed by H_2O_2. The remainder may be readily oxidized by bubbling with O_2 (*cf.* Figure 5B and D). This behaviour is the same as that observed when H_2O_2 reacts with $[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ [11a] and with other iron(II)-polyaminopolycarboxylate complexes of the $edta^{4-}$ family[11b]. These results are evidence for the formation of ferryl intermediates in the course of the oxidation of *(1)* by H_2O_2[11]. Since the copper(II) and iron(II) chromophores of *(1)* are spectrally and chemically independent, it is reasonable to assume that the reaction steps involving the oxidation of the open-chain $[Cu^{II}Fe^{II}(ttha)]^{2-}$ complex adopt many of the features known for $[Fe^{II}_2(ttha)]^{2-}$. Therefore, it is anticipated that the minimum number of reaction channels shown in Scheme 2, which is an appropriate modification of the reported sequence for the $[Fe^{II}_2(ttha)]^{2-}/H_2O_2$ reaction[11b]. Unlike $[Fe^{II}_2(ttha)]^{2-}$ the formation of an internally bridged oxo complex, $[(Cu^{III}OFe^{III})(ttha)]^{2-}$, is precluded on the evidence that no species with copper(III) character is indicated as an intermediate, and the final Cu-containing complex is $[Cu^{II}_2(ttha)]^{2-}$, not a copper(III) complex.



Scheme 2.

When the oxidation of *(1)* by H_2O_2 was examined at 470 nm by the stopped-flow method two separate processes were detectable. The first yields an absorbance increase; the second has a slower, smaller absorbance decrease. The first process exhibits a rate saturation with increasing $[H_2O_2]$. Our instrumentation utilized an absorbance fitting routine that eliminates a need to know the actual first absorbance maximum value, but it imposes a first-order treatment on a time domain where competitive reactions must occur. Such a forced fit may obscure the true rate dependence for $[(1)]$ in the first reaction. Fitting to first order for the early reaction revealed that rate

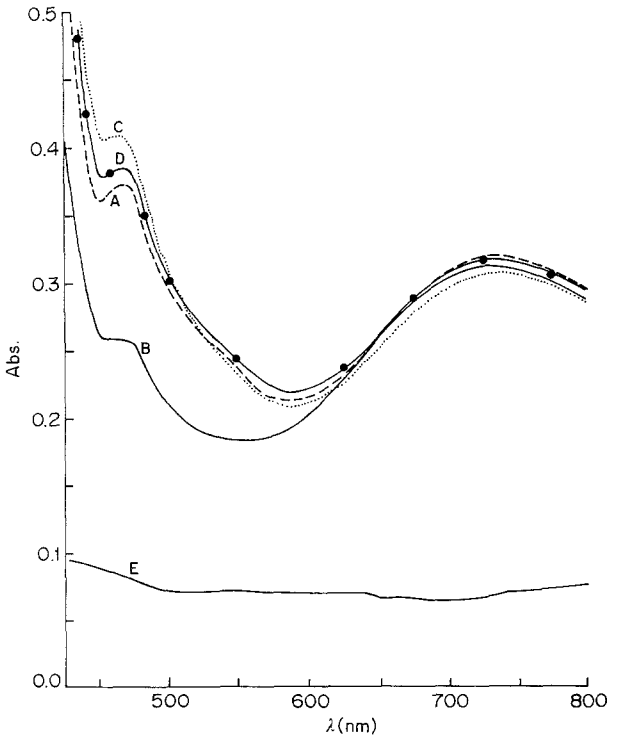


Figure 5. Oxidation products of $[Fe^{II}Cu^{II}(ttha)]^{2-}$ $[(1)]$. $[Fe^{II}Cu^{II}(ttha)]^{2-}_i = 4.12 \times 10^{-3}$ M. (A) *(1)* oxidized by O_2 saturation; (B) *(1)* plus H_2O_2 at 2 iron(II):H_2O_2 under Ar; (C) *(1)* plus H_2O_2 at iron(II):H_2O_2 under Ar; (D) solution B bubbled with O_2 for 14 min; $\mu = 0.050$, $T = 25.0\,^{\circ}C$, pH = 7.0, lutidine buffer; (E) 1.00 cm cell H_2O blank.

Table 1. Absorbance changes of $Cu^{II}Fe^{II}(ttha)^{2-}$ with excess H_2O_2 in 2,6-lutidine buffer (pH = 7.00, $\mu = 0.050$, $T = 25\,^{\circ}C$)

$[H_2O_2]_{ex}$ (M)	k_{obs}, Reaction 1* (s^{-1})	A_∞	k_{obs}, Reaction 2 (s^{-1})	$A_{\infty 2}$
9.6×10^{-4}	0.340 ± 0.020	0.362	Not observed	–
0.110	0.793	0.842	–	–
0.147	0.786	0.770	0.103 ± 0.020	0.711
0.221	0.802	0.847	0.062 ± 0.020	0.726

saturation was essentially complete when $[H_2O_2]$ was in a 290-fold excess and slightly less than half-maximal at 1.26 H_2O_2:[complex] (Table 1). Saturation in the rate with increasing $[H_2O_2]$ is consistent with the competition of H_2O_2 in forming a ferryl intermediate needed to produce the tetranuclear intermediate and the suppression in rate, *via* step 2 of Scheme 2, in which H_2O_2 also destroys the same ferryl intermediate. The slower process has a first-order rate constant of $0.083 \pm 0.021\ s^{-1}$ which is similar, but not identical, to the value found for the O_2 oxidation of *(1)* for the rearrangement reaction (k_4); *i.e.* 0.083 *cf.* $0.18\ s^{-1}$.

In studies of the oxidation of $[Fe^{II}_2(ttha)(H_2O)_2]^{2-}$ it has been shown that oxo-bridged species formed between iron(III) centres on adjacent ligating polyaminopolycarboxylates in a less strained configuration than for the side-on bridge arrangement in $[Fe^{III}_2O(ttha)]^{2-}$ have higher extinction coefficients[11a]. Therefore, a decrease in absorbance would be anticipated for the k_4 step. This is evidence that the last spectral change most likely correlates with the final step of Scheme 2. If the slow step properly measures the rate of the rearrangement pathway it may be that the small differences between the O_2 rate data and H_2O_2 rate data reflect different mechanistic steps which form the respective tetranuclear species for Schemes 1 and 2. In the O_2 case, if the $Cu^{II}Fe^{III}$ complex *(2)* is the first iron-oxidized species, the tetranuclear species is formed by a bimolecular reaction of two $[Cu^{II}\text{wwm}Fe^{III}OH]^{2-}$ entities, accounting for iron(III)-aqua hydrolysis at pH 7. By contrast, the k_3 step in Scheme 2 requires only substitution on an iron(II)-aqua site by the ferryl partner to establish the oxo-bridged tetranuclear complex. The formation of the tetranuclear oxo-bridged species from *(2)* = $[Cu^{II}\text{wwm}Fe^{III}OH]^{2-}$ requires substitution, proton transfer and dehydration steps which may be slower than the final rearrangement, yielding homobinuclear ions[21].

The details of the H_2O_2 oxidation of *(1)* have not been pursued, given the complex number of reaction channels and parallel contaminant hydroxyl radical chain reactions (usually 6–8% of the reactivity) which are also known for iron(II)-polyaminocarboxylate/H_2O_2 reactions[11]. It is clear that the H_2O_2 oxidation of *(1)* retains the central features already known for the H_2O_2 oxidation of $[Fe^{II}_2(ttha)]^{2-}$. Since the main goal of finding a $[Cu^{II}OFe^{III}(ttha)]^{3-}$ complex in aqueous solution is inevitably eliminated by the cross-binuclear metal exchange process, a knowledge of the full kinetic details of the H_2O_2 oxidation of *(1)* appears to be beyond a reasonable time investment to obtain more than a qualitative support for Scheme 2.

Conclusions

The heterobinuclear $[Cu^{II}Fe^{II}(ttha)]^{2-}$ *(1)* complex is stable to cross-binuclear metal exchange reactions. Complex *(1)* has been shown to have a characteristic e.p.r. spectrum which, although similar to $[Cu_2(ttha)]^{2-}$, is uniquely characteristic of the heterobinuclear species. Complex *(1)* may be oxidized by either O_2 or H_2O_2, ultimately forming copper(II)iron(III)-containing complexes *(2)* in which the metal centres each have two nitrogen donors, as in *(1)*. These complexes rapidly rearrange ($t_{1/2}$ *ca* 3.9 s) by a cross-binuclear metal exchange reaction *via* tetranuclear intermediates to produce the homobinuclear products $[Cu^{II}_2(ttha)]^{2-}$ and $[Fe^{III}_2O(ttha)]^{2-}$. An isomer of *(2)* in which the coordination of the copper(II) site has three nitrogen donors and the iron(III) site but one nitrogen donor *(3)* is much slower to rearrange to the homobinuclear products. The coordination of the iron(III) centre in the iminodiacetate fragment of *(3)* is less stable to hydrolysis than the analogue *(2)* with two nitrogen donors of $ttha^{6-}$ attached to iron(III). Hydrolysis leading to precipitation of $Fe(OH)_3$ competes with the slower cross-binuclear metal exchange process for *(3)*. The metal exchange reaction for *(3)* is over 4430 times slower than *(2)*, and a rearrangement involving breaking a Cu^{II}—N bond in *(3)* and the formation of *(2)*, which rapidly reacts to give homobinuclear products, seems the most likely pathway for metal exchange on *(3)*.

Perhaps the most obvious outcome of these metal exchange reactions of complexes *(2)* and *(3)* is the fact that iron(III) strongly prefers formation of μ-oxo bridged complexes to another iron(III), even in a second complex, compared to formation of an oxo or hydroxy bridge to copper(II) within its own ligand structure.

An explanation of this effect is that high-spin d^5 iron(III) gains superexchange with a second iron(III) centre, stabilizing $[Fe^{III}_2O(ttha)]^{2-}$[21c]. The superexchange between high-spin d^5 and high-spin d^9 configurations must be much smaller and, therefore, cannot strongly stabilize a $[Cu^{II}OFe^{III}(ttha)]^{3-}$ complex. We have recently reported that the low-spin d^5 ruthenium(III) analogue, $[Ru^{III}_2O(ttha)]^{2-}$, is unstable and rapidly aquates into the extended chain form of the ruthenium(III) complex[22]. Thus, superexchange is an important component of oxo-bridged binuclear ion complexes of polyaminopolycarboxylates. Since species such as *(2)* and *(3)* cannot gain much stability between iron(III) and copper(II) from superexchange, but can gain stability within the homobinuclear derivatives, there is a driving force to achieve the homobinuclear $[Fe^{III}_2O(ttha)]^{2-}$ product at the expense of the heterobinuclear complexes. This also explains the apparent stability of *(1)* with respect to rapid metal exchange processes. The iron(II) site gains no advantage in forming the homobinuclear complexes; thus, the heterobinuclear species is stable long enough to identify its unique e.p.r. signature.

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