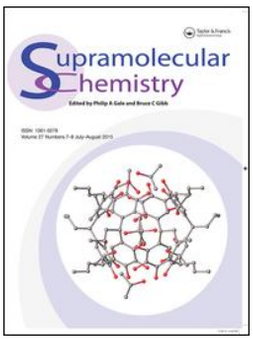

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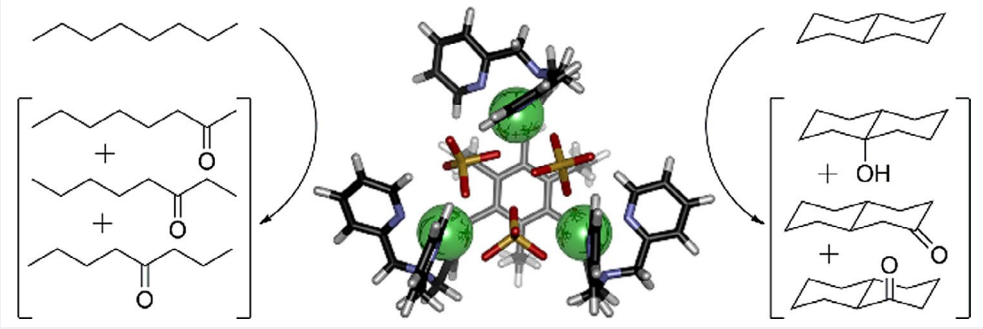
Alkane oxidation catalysed by a self-folded multi-iron complex

Magi Mettry, Melissa Padilla Moehlig, Adam D. Gill and Richard J. Hooley

Department of Chemistry and the UCR Center for Catalysis, University of California Riverside, Riverside, CA, USA

ABSTRACT

A preorganised ligand scaffold is capable of coordinating multiple Fe(II) centres to form an electrophilic CH oxidation catalyst. This catalyst oxidises unactivated hydrocarbons including simple, linear alkanes under mild conditions in good yields with selectivity for the oxidation of secondary CH bonds. Control complexes containing a single metal centre are incapable of oxidising unstrained linear hydrocarbons, indicating that participation of multiple centres aids the CH oxidation of challenging substrates.



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Alkanes; self-assembly; catalysis

1. Introduction

Biological systems perform hydrocarbon oxidations via numerous different enzymatic structures (*1*), from the porphyrin-derived cytochrome P-450 (*2*), galactose (*3*) and methyl monooxygenases (*4*), and the Rieske non-haem iron oxygenases (*5*). Synthetic systems inspired by these active biological catalytic motifs have been applied towards a variety of oxidations including C–H activation (*6*) and late stage introduction of functionality to natural product targets (*7*). In addition to catalytically active sites containing one metal species, various biological processes exploit enzymes that involve multiple metals at the core (*4, 8*). These systems have inspired a number of ligand structures that coordinate multiple metal clusters at the interior (*9*), and have been applied to water splitting and the oxidation of CH bonds. The application of catalytic systems that exploit multiple metal coordination to the oxidation of unactivated hydrocarbons is less common: the majority of studies employ non-haem oxygenase-inspired ligands that provide a tetradentate ligand coordinated to a single Fe(II) centre (*10*). Multi-metal catalysts are more challenging to synthesise, but have potential for greater catalytic activity than their mononuclear counterparts (*11*).

One of the challenges in the creation of ligands capable of complexing multiple metals is the preorganisation of the coordinating motifs. Self-folding has long been exploited in the fields of sensors and supramolecular assembly to confer configurational stability on a flexible system. This self-folding is generally conferred by hydrogen bonding (*12*) or by metal–ligand coordination (*13*). Inspired by these motifs, we sought to create a flexible, self-folding ligand system that could coordinate multiple metals for hydrocarbon oxidation catalysis. The 2,4,6-trisubstituted-1,3,5-triethylbenzene scaffold (Figure 1) is an inviting target to present multiple coordinating motifs in close proximity: this scaffold is well precedented to orient the three ethyl groups to the same face of the aromatic ring, allowing the creation of supramolecular host systems and sensors for cations (*14*), anions (*15*) and saccharides (*16*), among other species. The parent triazide **1** is usually reduced to

CONTACT Richard J. Hooley richard.hooley@ucr.edu

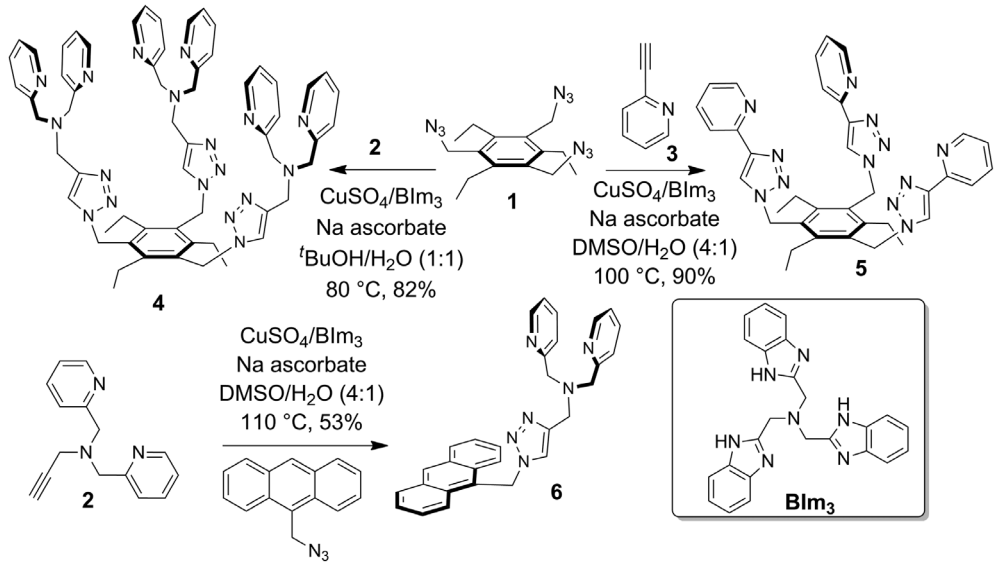


Figure 1. Synthesis of the three Fe-binding ligands used in this study.

the corresponding triamine for further derivatisation, but **1** itself is ideally suited to the introduction of multiple *N*-coordinating arms by copper (I) catalysed alkyne-azide cycloaddition (CuAAC) chemistry: the triazoles formed upon CuAAC can provide an extra coordination site for metal binding, simplifying the synthesis of multiply coordinating ligands (*13*).

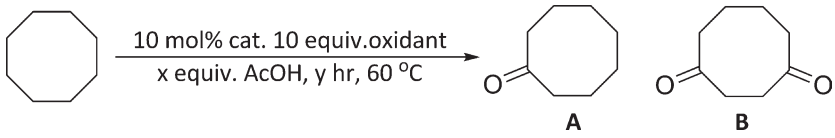
2. Results and discussion

We initially focused on the application of two core components, scaffold **1** (accessed from azidation of commercially available 1,3,5 tris(bromomethyl)-2,4,6-triethyl-benzene (*17*)) and bis-pyridyl alkyne **2**. CuAAC coupling of **1** and **2** should give rise to ligand **4**, displaying three tetradentate coordinating groups around the central triethylbenzene scaffold. The synthetic challenge is to confer complete derivatisation of **1** under CuAAC conditions: synthesis of strongly coordinating ligands via metal-catalysed reactions is often complicated by irreversible formation of metal–ligand complexes with the catalyst. To minimise leaching of Cu from the catalyst mixture into the product, we employed the tetradentate BIm_3 as cocatalyst (Figure 1) (*18*). Even in the presence of the activating BIm_3 ligand:$CuSO_4$ system, the reaction required elevated temperatures in a ^tBuOH:H_2O mixture to achieve good yields.

The strong metal-binding properties of the ligand were evident: complete removal of Cu salts from **4** required four separate washings with an aqueous solution of NaEDTA, and purification by column chromatography in neutral alumina, followed by recrystallisation from CH_2Cl_2. Two other ligand systems were synthesised as controls: tris-pyridyl triazine **5** (synthesised by CuAAC coupling between **1** and 2-pyridylacetylene **3**) displays the basic scaffold with fewer coordinating groups, whereas ligand **6** is a singly coordinating version of **4**. These ligands were synthesised in an analogous, although much simpler manner to **4**. Heating at 100 °C in a 4:1 DMSO:H_2O mixture gave good yields of both **5** and **6** (reaction in ^tBuOH yielded only starting material), and a single EDTA wash was sufficient to remove residual copper ions.

The strong Cu binding properties of **4** were encouraging, and suggested that ligand **4** would be capable of coordinating metal ions that would confer catalytic activity on the system, notably Fe salts. Ligand **4** was combined with three equivalents of $FeSO_4$ in a 1:1 mixture of CH_2Cl_2:MeOH, and catalyst **4**·$Fe_3(SO_4)_3$ was isolated by simple filtration after 30 min stirring. The recovered yield of **4**·$Fe_3(SO_4)_3$ was high, indicating that all three Fe(II) ions were coordinated to the ligand. The initial tests of the activity of the **4**·$Fe_3(SO_4)_3$ complex towards hydrocarbon oxidation were performed on cyclooctane, an unactivated hydrocarbon that is nonetheless relatively simple to oxidise due to torsional strain release upon reaction. Our previous hydrocarbon oxidation catalysts had performed adequately in a CH_3CN:H_2O solvent mixture, and *t*-butyl hydroperoxide (TBHP) was the most effective oxidant (*13*). As can be seen in Table 1, 10% **4**·$Fe_3(SO_4)_3$ was an effective catalyst for the oxidation of cyclooctane to cyclooctanone. Maximal conversion (84%) was achieved after 24 h at 60 °C, although the best selectivity was achieved at lower conversions, as small amounts of over oxidation product 1,4-cyclooctanedione were formed upon prolonged oxidation. The preference for 1,4-cyclooctanedione is due to stereoelectronic effects (*13*). Other solvents such as water or anhydrous acetonitrile were less effective, due to the relative insolubility

Table 1. Optimisation of oxidation conditions with **4**·$Fe_3(SO_4)_3$.[a]



Oxidant	Time (hr)	Eq. AcOH	Yield (%)	%**A**	%**B**
^{t}BuOOH	2	0	29	29	0
^{t}BuOOH	6	0	50	50	0
^{t}BuOOH	18	0	56	56	0
^{t}BuOOH	24	0	84	74	10
^{t}BuOOH	24	2	86	73	13
^{t}BuOOH	24	5	80	74	6
^{t}BuOOH	24	10	80	74	6
H_2O_2	24	0	0	0	0
NMO	24	0	53	53	0

[a]1:1 MeCN:H_2O as solvent, product yields determined by GC analysis.

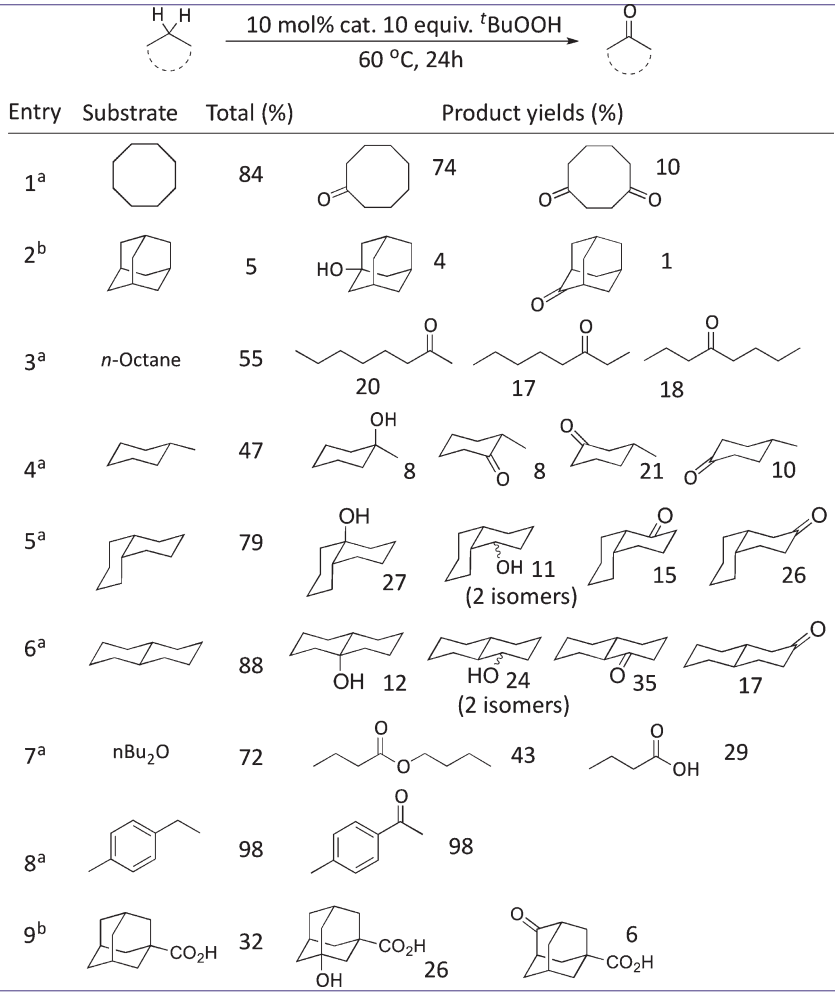
of either reactant or **4**·$Fe_3(SO_4)_3$. The presence of acetic acid as additive in this system proved unnecessary: although carboxylic acids have been shown to increase reactivity or provide directing effects in other tetra-nitrogen ligand: Fe(II) systems (*7*), we saw minimal yield enhancement in the presence of excess AcOH (entries 5–7). The nature of the stoichiometric oxidant was important: use of fewer than 10 eq. TBHP led to lower conversions, and 30% H_2O_2 was an ineffective oxidant. Interestingly, the weaker oxidant *N*-methylmorpholine *N*-oxide (NMO) conferred reactivity on the system (entry 9), although less effectively than TBHP. No reaction was seen with molecular O_2 as oxidant.

Having optimised the reaction conditions, the scope of the process was tested with more challenging hydrocarbon substrates (Table 2). The **4**·$Fe_3(SO_4)_3$ complex was an effective oxidant for a variety of unstrained, unactivated cyclic hydrocarbons: adamantane, methylcyclohexane and *cis*- and *trans*-decalin were all oxidised in moderate to good yields. The reactions were clean, and only the oxidation products and reactants were observed: the yields described in Table 2 also correspond to conversions. Most excitingly, linear alkanes such as *n*-octane were susceptible to oxidation by **4**·$Fe_3(SO_4)_3$, challenging targets that are unreactive to other self-folded multi-metal oxidation catalysts (*13*). The reaction was not highly selective, but did show some unusual regiochemical outcomes. Most C–H activations show strong selectivity for 3º substrates (*6*), although there are examples of systems that favour 2º oxidation (*19*). Here, the **4**·$Fe_3(SO_4)_3$ complex shows selectivity (albeit moderate) for 2º C–H bonds. Oxidation of methylcyclohexane (entry 4) gives a 5:1 selectivity for the various ketone isomers over 3º oxidation, with little selectivity between the 1,2-, 1,3- and 1,4-methylcyclohexanone products seen.

Cis-decalin (entry 5) displays a 2:1 selectivity towards 2º oxidations, with the terminal ketone product most favoured. In the case of *trans*-decalin (entry 6), the overall conversion was high (88%), but a greater proportion of secondary oxidation occurred (2°:3° ratio = 4.4:1). Five major oxidation products were formed (in similar yields): the expected ketone and tertiary alcohol products, plus small amounts of 2° alcohol products were observed. Essentially, no selectivity between the 2° oxidation products was observed, as would be expected. This lack of positional selectivity was also observed for the oxidation of *n*-octane: 2-, 3- and 4-octanone were all formed in essentially identical yields. Only adamantane-carboxylic acid (entry 9) showed significant selectivity for 3° over 2° C–H oxidations, an observation attributed to the increase in ring strain upon incorporation of the ketone into the tricyclic scaffold. No appreciable directing effect is observed from the COOH group, and the oxidation selectivity appears to be dominated by substitution. Other substrates were applied to test the functional group tolerance of catalyst **4**·$Fe_3(SO_4)_3$. Activated C–H bonds were very easily oxidised: 4-ethyltoluene was rapidly oxidised in excellent yield, and complete selectivity was observed for ketone formation. Dibutyl ether provided the corresponding ester in 43% yield, along with a small amount of hydrolysis product.

The observed (moderate) selectivity in hydrocarbon oxidation is consistent with a sterically bulky multi-Fe catalyst. 3° C–H bonds are weaker and more easily oxidised: even moderate selectivity for 2° C–H oxidation requires limited access to the more crowded 3° sites, something enhanced by bulky ligands around the active metal sites. In addition, the selectivity for the distal oxidation product of cis-decalin corroborates this theory. Interestingly, no isomerisation was observed in the bridgehead 3º oxidation product of *cis*-decalin. The radical rebound mechanism usually present in non-haem Fe-catalysed oxygenations forms radical intermediates (*6*), which leads to isomerisations of strained bridgehead C–H bonds (*20*). This is not observed here: no *trans*-decalin products are observed from *cis*-decalin reactants (see Supporting Information for

Table 2. Scope of unactivated hydrocarbon oxidation with **4**·$Fe_3(SO_4)_3$.



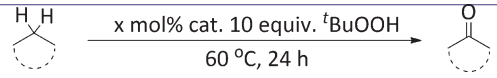
[a]reaction performed in 1:1 MeCN: H_2O.
[b]reaction performed in 1:1 EtCN: H_2O.

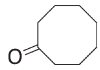
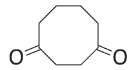
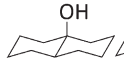
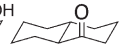
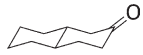
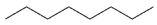
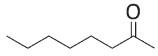
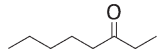
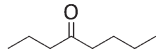
comparison between the GC traces). We have no reason to suggest a different mechanism in this case: presumably recombination merely happens before isomerisation.

In contrast to the effective oxidation performance of the multi-iron complex **4**·$Fe_3(SO_4)_3$, the two control complexes **5**·$FeSO_4$ and **6**·$FeSO_4$ were less active (Table 3). There was little difference between complexes **5**·$FeSO_4$ and **6**·$FeSO_4$ for relatively simple substrates: the obtained yields for cyclooctane and *trans*-decalin oxidation were similar for the two catalysts, and only slightly lower than those for the folded **4**·$Fe_3(SO_4)_3$. The catalytic power of **4**·$Fe_3(SO_4)_3$ is illustrated by the more challenging substrates, however: no products were observed at all for the oxidation of *n*-octane with either **5**·$FeSO_4$ or **6**·$FeSO_4$. Whereas, simple, cyclic substrates can be oxidised by single Fe centres, only the self-folded, multi-metal catalyst **4**·$Fe_3(SO_4)_3$ is capable of oxidising linear, unactivated hydrocarbons. This behaviour is not simply due to a greater concentration of Fe in the system: the complete lack of reactivity of **5**·$FeSO_4$ or **6**·$FeSO_4$ towards *n*-octane indicates that **4**·$Fe_3(SO_4)_3$ is greater than the sum of its parts, and that participation between the Fe centres is necessary for optimal catalytic activity for challenging substrates.

The improved reactivity of the multi-metal coordinating ligand **4** led us to investigate the structure of the pre-catalyst complex formed upon addition of $FeSO_4$ to ligand **4.** Accurate analysis of the **4**·$Fe_3(SO_4)_3$ complex structure was challenging, however. We were unable to access X-ray quality crystals of **4**·$Fe_3(SO_4)_3$, or indeed of any complexes between **4** and other Fe(II) salts (e.g. ClO_4^-, Cl^- or OAc^-). The **4**·$Fe_3(SO_4)_3$ complex was weakly paramagnetic and gave rise to broad NMR spectra, but determination of the coordination stoichiometry was possible by MS analysis (see Figure 2(a) and Supporting Information). The parent ion $[\mathbf{4}\cdot Fe_3(SO_4)_2\cdot H_2O\cdot OH]^+$ is the largest *m/z* species observed, and the other major ionic species correspond to the loss of one or more sulfate ions and formation of iron-oxo species under the ionisation/injection conditions. The weakly coordinated sulfate ions and associated water molecules are easily lost upon ionisation, but the **4**·Fe_3 core with

Table 3. Scope of unactivated hydrocarbon oxidation with monometal complexes **5**·$FeSO_4$ and **6**·$FeSO_4$.[a]



Substrate	Cat. loading	Total (%)	Product yields (%)			
						
	10% **5**•$FeSO_4$	74	69	5		
	30% **5**•$FeSO_4$	72	72	0		
	10% **6**•$FeSO_4$	53	53	0		
	30% **6**•$FeSO_4$	47	47	0		
						
	10% **5**•$FeSO_4$	28	1	8	11	8
	30% **5**•$FeSO_4$	19	2	2	8	7
	10% **6**•$FeSO_4$	38	5	3	13	17
	30% **6**•$FeSO_4$	27	4	2	10	11
						
	10% **5**•$FeSO_4$	0	0	0	0	
	30% **5**•$FeSO_4$	0	0	0	0	
	10% **6**•$FeSO_4$	0	0	0	0	
	30% **6**•$FeSO_4$	0	0	0	0	

[a]1:1 MeCN:H_2O solvent.

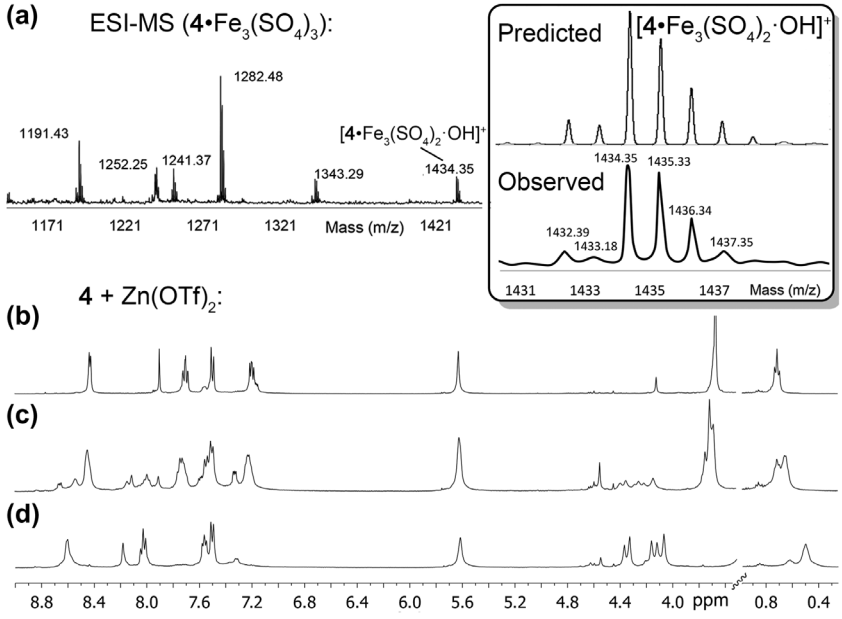


Figure 2. Metal coordination properties of ligand **4**. (a) ESI-MS spectrum of the **4**·$Fe_3(SO_4)_3$ complex; ^{1}H NMR spectra (298 K, DMSO-d_6) of the titration of $Zn(OTf)_2$ into **4**, (b) ligand **4** alone, (c) **4** + 1 equiv. $Zn(OTf)_2$, and (d) **4** + 3 equiv. $Zn(OTf)_2$.

attached anions is detectable, and the isotope pattern matches that of a three Fe-containing system. Elemental analysis explains some of the issues with crystal growth: ICP analysis of a microcrystalline sample of **4**·$Fe_3(SO_4)_3$ was performed, and corroborated the proposed stoichiometry **4**·Fe_3, but the microcrystalline samples contained a mix of three and four Fe centres (see Supporting Information). C–H–N combustion analysis was also consistent with this mixture of two stoichiometries, and traces of a four Fe complex were observed. No evidence of a four Fe species was observed in the MS analysis, however, suggesting that weak coordination is possible in the solid state with a fourth Fe centre, but the most stable structure in solution (and upon ionisation in MS) is **4**·$Fe_3(SO_4)_3$.

Further evidence for the favoured binding stoichiometry containing three metal ions was obtained by ^{1}H NMR analysis of an analogous **4**·Zn_3 complex (Figure 2(b)–(d)). While the coordination modes of Zn^{II} and Fe^{II} can obviously

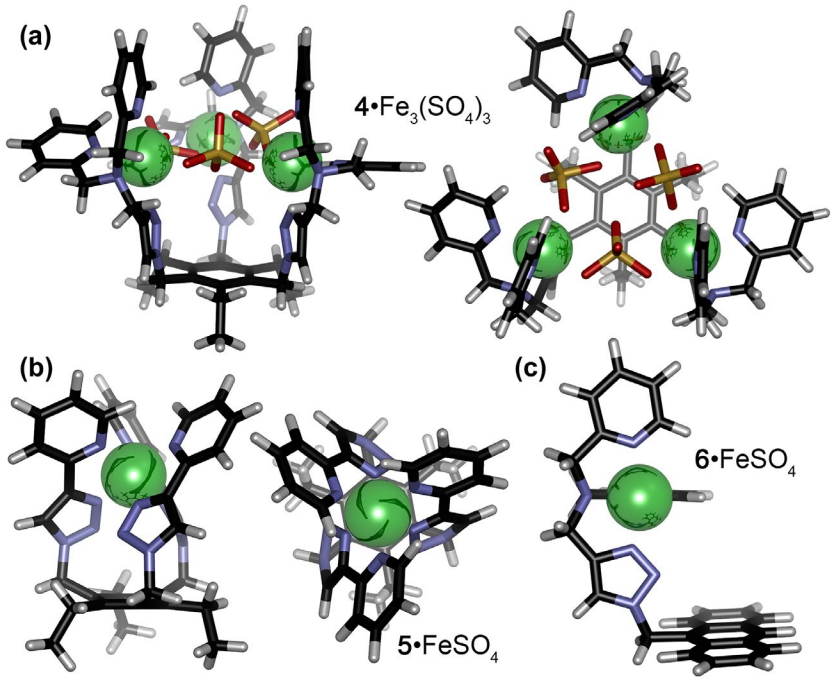


Figure 3. (Colour online) Minimised models of the Fe-ligand catalyst complex structures: (a) **4** + 3 x $FeSO_4$, (b) **5** + $FeSO_4$, (c) **6** + $FeSO_4$ (SPARTAN, Hartree-Fock forcefield, counterions in (b) and (c) omitted for clarity).

vary, Zn^{II} can act as a suitable diamagnetic surrogate of Fe^{II}, to shed light on the complex structure formed. Upon addition of one equiv. $Zn(OTf)_2$ to a solution of **4** in DMSO-d_6, multiple species can be seen in the NMR spectrum: after addition of three equivalents, only a single species is present, displaying reduced symmetry and diastereotopic methylene protons between 4.0 and 4.5 ppm, suggesting that all six pyridyl groups are coordinated to the Zn (II) ions. No further change is observed upon adding excess Zn (II). MALDI-MS analysis of the **4**·Zn_3 complex was also performed (see Supporting Information), and the parent [**4**·Zn_3·$(OTf)_5$]$^+$ ion was the only species observed.

The control ligands **5** and **6** were simpler in their coordination motifs, and MS/NMR analysis showed the presence of only a single Fe ion when either **4** or **5** were complexed with $FeSO_4$, as expected. Interestingly, loss of the anthracenyl group via C–C cleavage was observed in ESI-MS analysis of **6**·$FeSO_4$, which did not occur for the multimetal **4**·$Fe_3(SO_4)_3$ complex. ICP analysis was consistent with a monomeric coordination of $FeSO_4$ (see Supporting Information).

The expected complex structures of **4–6** with $FeSO_4$ were analysed by molecular modelling, and the structures shown in Figure 3. The minimised structure of **4**·$Fe_3(SO_4)_3$ shows the possibility of sulfate templation of the structure. The difficulty in crystallisation of the **4**·$Fe_3(SO_4)_3$ complex indicates that this is not a static structure in solution, and there will be an appreciable amount of flexing of the three 'arms' when dissolved, but the three Fe(II) centres are positioned in close proximity to each other, with two vacant (or weakly sulfate/solvent coordinated) *cis* sites present on each metal that can be easily displaced by stoichiometric oxidant. This structure (especially the plan view in Figure 3(a)) also suggests the possibility of a coordinating a fourth Fe^{II} ion atop the bridging sulfates, which would explain the presence of a small excess of $FeSO_4$ in the solid state analysis. Single-arm ligand **6** forms a similar coordination environment around a single Fe(II) ion, maintaining the weakly coordinated *cis* positions at the metal centre. Ligand **5** appears more restricted, however, and all six coordinating nitrogens can access the Fe centre, presumably limiting its catalytic ability.

3. Conclusions

A new preorganized ligand scaffold has been shown to coordinate multiple Fe(II) centres, forming an electrophilic C–H oxidation catalyst. This catalyst is capable of oxidising unactivated C–H bonds including simple, linear alkanes under mild conditions in good yields. The catalyst shows selectivity for the oxidation of secondary over tertiary CH bonds. Maximal activity is only obtained for the multi-iron complex: control complexes containing single metal centres are incapable of oxidising unstrained linear hydrocarbons, indicating that participation of multiple centres is required for the oxidation of challenging substrates. Further investigations into self-folding scaffolds for multi-metal coordination are underway in our laboratory.

4. Experimental section

4.1. General information

^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 300 or Inova 400 spectrometer. Proton (^{1}H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane ($Si(CH_3)_4$, $\delta = 0$), and referenced internally with respect to the protio solvent impurity. Carbon (^{13}C) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane ($Si(CH_3)_4$, $\delta = 0$), and referenced internally with respect to the solvent ^{13}C signal (either $CDCl_3$ or DMSO-d_6). Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. All other materials were obtained from Aldrich Chemical Company, St. Louis, MO and were used as received. Solvents were dried through a commercial solvent purification system (SG Water, Inc.). Electrospray mass spectra were recorded on an Agilent 6210 LC TOF mass spectrometer using electrospray ionisation and processed with an Agilent MassHunter Operating System. MALDI mass spectra were obtained using a PE Biosystems DE-STR MALDI TOF spectrometer operating in refractive mode at 2100 eV. Molecular minimisations were performed using Hartree-Fock calculations of equilibrium geometry at ground state with basis set 3–21G using SPARTAN. The minimisations started from initial geometry with total charge neutral.

4.2. Synthesis of new compounds

Synthesis of 1,3,5-tris(azidomethyl)-2,4,6-triethylbenzene 1. Adapted from a literature procedure (*21*): In a 25-ml round bottom flask equipped with a stir bar 1,3,5-trisbromomethyl-2,4,6-trimethyl-benzene (1.0 g, 2.3 mmol) and sodium azide (18 mL, 0.5 M in DMSO, 9.0 mmol) were combined. The reaction mixture was stirred for 24 h at room temperature. The solution was then diluted in 100 ml H_2O and extracted with dichloromethane. The organic layer was dried with Na_2SO_4, filtered, and the solvent removed under reduced pressure to yield **1** as a white solid (621 mg, 84%) ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.50 (6H, s), 3.86 (q, J = 7.7 Hz, 6H), 1.25 (t, J = 7.7 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 130.0, 47.9, 23.2, 15.7.

Synthesis of 9-anthracenylmethyl azide. Adapted from a literature procedure (*22*), 9-Anthracenemethanol (1.50 g, 7.40 mmol) was dissolved in dichloromethane (30 mL). $SOCl_2$ (810 µL, 11.1 mmol) was then added at 0 °C. After mixing for 2 h, the solvent was removed under vacuum. The resultant residue was redissolved in DMF (10 mL), and sodium azide (0.77 g, 12.0 mmol) was added. The reaction mixture was heated for 4 h at 60 °C, cooled to room temperature and diluted with 50 mL water. The mixture was then extracted with ethyl acetate. The organic layer was separated, dried with Na_2SO_4, filtered and the solvent removed under reduced pressure to yield 9-anthracenylmethyl azide as a yellow solid (1.70 g, 97% yield). CAUTION: organic azides are explosive, and should be handled carefully. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (1H, s), 8.28 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 8.4 Hz, 2H), 7.59 (t, J = 8.0 Hz, 2H), 7.50 (t, J = 8.0 Hz, 2H), 5.33 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.4, 130.7, 129.3, 129.0, 126.9, 125.2, 123.5, 46.4; EIMS: found 233.1 [M^+] calculated for $C_{15}H_{11}N_3$: 233.1.

Synthesis of N,N-bis(2-pyridylmethyl)-N-propargylamine 2. N,N-bis(2-pyridylmethyl)-N-propargylamine was synthesised according to literature procedures (*23*). Di-(2-picolyl)amine (10.0 mmol, 1.08 mL) was dissolved in MeCN (20 mL). K_2CO_3 (40 mmol, 5.4 g) was added to the solution followed by dropwise addition of propargyl bromide (80% in toluene, 10 mmol, 1.09 mL). The reaction mixture was stirred for 24 h before being diluted with dichloromethane. The diluted reaction mixture was filtered to remove K_2CO_3, and then washed with dichloromethane before being concentrated under vacuum. N,N-bis(2-pyridylmethyl)-N-propargylamine was isolated as yellow oily solid (2.28 g, 96%) from an alumina column eluted by EtOAc in dichloromethane (0% - 40%). After purification, the solvent was rapidly removed by rotary evaporation and the product was stored under nitrogen. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.57 (d, J = 4.2 Hz, 2H), 7.66 (td, J = 1.2, 7.8 Hz, 2H), 7.52 (d, J = 7.8 Hz, 2H), 7.17 (td, J = 5.4, 7.2 Hz, 2H), 3.93 (4H, s), 3.43 (d, J = 2.4 Hz, 2H), 2.30 (t, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 149.5, 136.7, 123.4, 122.3, 73.9, 59.7, 42.79; HRMS (ESI): calcd. (M + Na^+) 260.1164, found 260.1159.

Synthesis of hexapicolyl ligand 4. In a sealed tube flushed with nitrogen, 1,3,5-tris(azidomethyl)-2,4,6-triethylbenzene **1** (50 mg, 0.15 mmol), *N,N*-bis(2-pyridylmethyl)-*N*-propargylamine **2** (180 mg, 0.76 mmol), $CuSO_4 \cdot 5H_2O$ (12 mg, 0.05 mmol), sodium ascorbate (18 mg, 0.09 mmol), BIm_3 co-catalyst (19 mg, 0.05 mmol), and 2 mL of 1:1 ^{t}BuOH:H_2O were added. The reaction mixture was stirred for 24 h at 80 °C. The solvent was removed under vacuum, redissolved in dichloromethane (20 mL) and added to an aqueous solution of Na_2EDTA (15 mL). This mixture was stirred for 1 h to remove any bound copper from the ligand. The organic layer was separated, dried with Na_2SO_4, filtered and the solvent removed under reduced pressure to yield a brown, tar-like substance (130 mg, 82% yield). The ligand was purified via rapid flash chromatography with an alumina column eluted by EtOAc in dichloromethane (0–40%). The product was then recrystallized from CH_2Cl_2 under a nitrogen atmosphere. After purification, the product was stored under nitrogen. CAUTION: organic azides are explosive, and should be handled carefully. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (dt, J = 4.7, 1.4 Hz, 6H), 7.61(td, J = 7.6, 1.8 Hz, 6H), 7.51 (td, J = 7.8,

1.2 Hz, 6H), 7.45 (s, 3H), 7.11 (ddd, *J* = 7.4, 4.9, 1.4 Hz, 6H), 5.62 (s, 6H), 3.76 (s, 6H), 3.75 (s, 12H), 2.80 (q, *J* = 7.4 Hz, 6H), 0.92 (t, *J* = 7.3 Hz, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 158.9, 148.8, 146.2, 144.2, 136.4, 129.6, 123.2, 122.7, 121.9, 59.3, 48.4, 47.8, 23.5, 15.2. ESI-TOF [MNa^+] calcd 1061.5616, found 1061.5734.

Synthesis of 4·$Fe_3(SO_4)_3$. In a dry two-dram vial flushed with nitrogen, **4** (100 mg, 0.16 mmol) was dissolved in dichloromethane (1 mL). In a separate two-dram vial $FeSO_4·7H_2O$ (48 mg, 0.17 mmol) was dissolved in MeOH (1 mL). The two solutions were combined and sonicated for 5 min before collecting a brown precipitate (221 mg, 92%). mp:>250 °C (decomp). ESI-TOF [**4**·$Fe_3(SO_4)_2·H_2O·OH]^+$ calcd 1061.5616, found 1061.5734. Elemental Analysis: Theoretical ($C_{60}H_{66}Fe_4N_{18}O_{16}S_4$): C: 43.76, H: 4.04, N: 14.31. Theoretical ($C_{60}H_{66}Fe_3N_{18}O_{12}S_3$): C: 48.20, H: 4.45, N: 16.86. Found: C: 45.07, H: 4.39, N: 15.22. ICP analysis (Fe): 3.76%. NMR analysis: The broadness of the ^{1}H NMR spectrum limited accurate spectral assignments due to the paramagnetic nature of the complex, and so the peaks are not transcribed here. See Supporting Information for spectral data.

Synthesis of trispyridyl ligand 5. In a 10-ml round bottom flask equipped with a stir bar was combined with $CuSO_4·5H_2O$ (23 mg, 0.09 mmol), sodium ascorbate (36 mg, 0.18 mmol) and 1,3,5-tris(azidomethyl)-2,4,6-triethylbenzene **1** (100 mg, 0.31 mmol) in 4 mL of 4:1 DMSO:H_2O. To this mixture was added 2-ethynyl pyridine **3** (97 µL, 0.92 mmol) and the reaction mixture was stirred for 24 h at 100 °C. After being cooled to room temperature, 15 mL of water was added and the resulting grey precipitate was collected by vacuum filtration. The crude precipitate was dissolved in dichloromethane and washed with an aqueous solution of Na_2EDTA. The organic layer was dried with Na_2SO_4, filtered, and the solvent removed under reduced pressure to yield **5** as a grey solid (175 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.46 (d, *J* = 4.5 Hz, 3H), 8.18 (d, *J* = 7.9 Hz, 3H), 8.08 (s, 3H), 7.76 (td, *J* = 7.8, 1.5 Hz, 3H), 7.21 (dd, *J* = 6.8, 5.2 Hz, 3H), 5.73 (s, 6H), 2.84 (q, *J* = 7.4 Hz, 6H), 1.00 (t, *J* = 7.5 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 150.1, 149.0, 148.2, 146.9, 137.3, 129.8, 123.1, 121.8, 120.6, 48.2, 23.8, 15.5. ESI-TOF [MH^+] calcd 637.3259, found 637.3227.

Synthesis of 5·$FeSO_4$. In a dry two-dram vial flushed with nitrogen, **5** (25 mg, 0.04 mmol) was dissolved in MeOH (1.5 mL). In a separate 2-dram vial $FeSO_4·7H_2O$ (65 mg, 0.24 mmol) was dissolved in MeOH (1 mL). The two solutions were combined and sonicated for 5 min before collecting a brown precipitate (30 mg, 97%). ESI-TOF [**5**·$Fe(HSO_4)]^+$ calcd 881.2, found 881.4. NMR analysis: The broadness of the ^{1}H NMR spectrum limited accurate spectral assignments due to the paramagnetic nature of the complex, and so the peaks are not transcribed here. See Supporting Information for spectral data.

Synthesis of dipicolyl ligand 6. In a sealed tube was combined with 9-anthracenylmethyl azide (100 mg, 0.43 mmol), *N,N*-bis(2-pyridylmethyl)-*N*-propargylamine (160 mg, 0.64 mmol), $CuSO_4·5H_2O$ (32 mg, 0.13 mmol), sodium ascorbate (42 mg, 0.25 mmol), BIm_3 co-catalyst (52 mg, 0.13 mmol), and 10 mL of 4:1 DMSO:H_2O. The reaction mixture was stirred for 24 h at 110 °C before removing the solvent and redissolving in dichloromethane (20 mL) and adding an aqueous solution of Na_2EDTA (15 mL). This mixture was stirred for 1 h to remove any bound copper from the ligand. The organic layer was separated, dried with Na_2SO_4, filtered and the solvent removed under reduced pressure to yield a brown solid (90 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.56 (s, 1H), 8.34 (d, *J* = 4.5 Hz, 2H), 8.28 (d, *J* = 8.7 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.61 (m, 2H), 7.40 (m, 2H), 7.45 (td, *J* = 7.6, 1.6 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 5.9 Hz, 1H), 6.97 (dd, *J* = 6.4, 5.2 Hz, 2H), 6.47 (s, 2H), 5.30 (s, 1H), 3.69 (d, 4H), 2.58 (s, 2H).^{13}C NMR (125 MHz, $CDCl_3$): *δ* 158.19, 148.7, 136.6, 131.4, 131.2, 130.8, 129.7, 129.4, 129.3, 127.6, 125.7, 125.4, 124.0, 123.5, 123.1, 122.9, 122.1, 59.4, 48.8, 46.4, 41.0. ESI/APCI [MH^+] calcd 470.22, found 471.0.

Synthesis of 6·$FeSO_4$. In a dry two-dram vial flushed with nitrogen, **6** (40.0 mg, 0.038 mmol) was dissolved in MeOH (1.5 mL). In a separate 2-dram vial $FeSO_4·7H_2O$ (30 mg, 0.192 mmol) was dissolved in MeOH (1 mL). The two solutions were combined and sonicated for 5 min before collecting a brown precipitate (21 mg, 90% yield). ESI-TOF [**6**·$Fe(SO_4)·H_2O·H]^+$ calcd 643.13, found 643.48. ICP analysis (Fe): 1.64%. The broadness of the ^{1}H NMR spectrum limited accurate spectral assignments due to the paramagnetic nature of the complex, and so the peaks are not transcribed here. See Supporting Information for spectral data.

General procedure for oxidation reactions. In a 0.3-mL conical vial, catalyst (4 µmol, 10 mol%) was dissolved in 0.25 mL solvent (1:1 MeCN:H_2O). ^{t}BuOOH (0.40 mmol, 10 equiv.), and substrate (0.04 mmol, 1 equiv.) were added. The reaction mixture was stirred for 24 h at 60 °C. Aliquots were taken and passed through a silica gel pipet plug with ether before being analysed by GCMS. All yields are based on GCMS analysis via integrative comparison to an internal standard. Product identification was determined by comparison to authentic samples via fragmentation pattern matching in MS.

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