Hydroxylation of alkanes by molecular oxygen with dinuclear Fe^{II} macrocyclic complexes as catalysts

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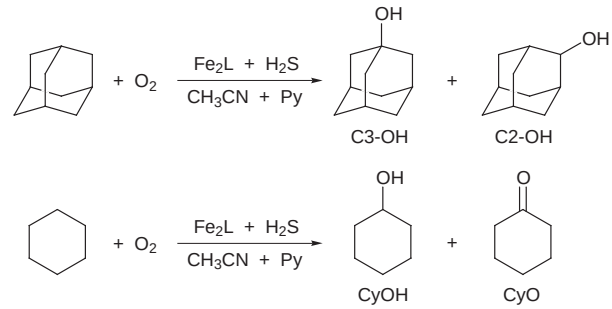
The iron(II) complexes of two new macrocyclic ligands: [24]RBPyBC (L24), a 24-membered macrocycle containing phenol, pyridine and amino donor groups, and [30]RBBPyBC (L30), a 30-membered macrocycle containing phenol, bipyridine, and amino donor groups, were found to be effective for the hydroxylation of alkanes, including cyclohexane and adamantane, with H_2S as a two-electron reductant.

The synthesis, characterization, and metal-binding properties of two new macrocyclic ligands [24]RBPyBC (L24) and [30]RBBPyBC (L30) have been reported,[1–3] and the stabilities of their mixed-valence dinuclear iron(II,III) chelates were described. It has now been discovered that the dinuclear iron(II) complexes of these ligands catalyze the hydroxylation of the hydrocarbons cyclohexane and adamantane in the presence of a two-electron reductant (H_2S) and thus may serve as functional models of methane monooxygenase.

Methane monooxygenase is known to contain a binuclear iron active center[4] and has been mimicked by a number of dinuclear model complexes,[5] but in most cases an oxidant such as H_2O_2 or ROOH was used. Descriptions of model systems containing porphyrin ligands in which the oxidant was molecular oxygen have been published.[6] Of the model systems that have molecular oxygen as an oxidant and do not contain porphyrin ligands are the GIF systems of Barton *et al.*,[7] an O_2/Zn/HOAc system of Christou *et al.*[5] and of Kitajima *et al.*,[8] and the present work.

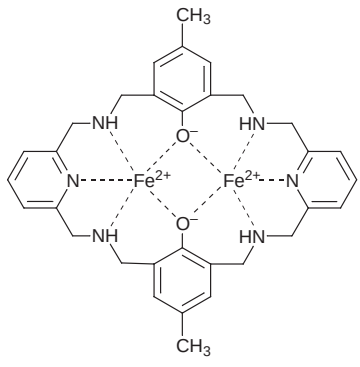
The new dinuclear iron(II) complexes of the macrocyclic ligands designated above, L24 and L30, are indicated below by **1** and **2**, respectively. These dinuclear Fe^{II} complexes are believed to react with oxygen to form a diiron–peroxide intermediate. The active species may decay to a dinuclear Fe^{III} complex with an oxo bridge, releasing an oxygen atom for insertion (hydroxylation) of a hydrocarbon. In the presence of a two-electron reductant the dinuclear Fe^{III} species may revert back to the dinuclear Fe^{II} complex to complete the catalytic cycle.



Scheme 1 Oxidation of adamantane and cyclohexane by molecular dioxygen with diiron complexes as catalysts

The overall oxidation reactions are shown in Scheme 1, which shows the organic substrates and reaction products. The results obtained for the hydroxylation of adamantane and cyclohexane are summarized in Tables 1 and 2. Typical oxidation reaction procedures were as follows: at room temperature and atmospheric pressure, 0.10 mmol of free macrocyclic ligand L24 or L30 was dissolved in 40 ml of CH_3CN. $FeCl_2{\cdot}4H_2O$ (0.20 mmol) was added to initiate iron complex formation. After the mixture was stirred for 10 min, the solution turned dark violet signifying the formation of the dinuclear iron complexes Fe_2L24, **1**, or Fe_2L30, **2**. While stirring was continued, 20 mmol cyclohexane or adamantane was added, then 1.0 ml pyridine was added. Hydrogen sulfide (2 ml min^{-1}) and dioxygen (20 ml min^{-1}) were simultaneously passed through the solution. After successive 2 h periods, the reaction mixture was filtered from the deposited sulfur and the solution was analyzed.

An aliquot (1.0 ml) was taken from the reaction solution and added to an aqueous NaOH solution (5%, 2 ml) at 0 °C. The products were extracted with diethyl ether (3 × 5 ml) and dried over $MgSO_4$. A naphthalene solution (1.0 ml, 0.080 M in diethyl ether) was added as an internal standard. The organic products were quantitatively analyzed by gas chromatography.



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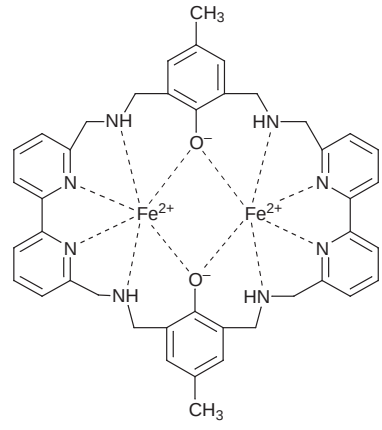

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Table 1 Oxidation of adamantane by molecular oxygen with diiron complexes as catalysts and hydrogen sulfide as reductant[a]

Catalyst	Time/h	C3-OH/ mmol	C2-OH/ mmol	C3-OH/ C2-OH	Turnover
Fe_2L24	2	0.099	0.29	0.37	3.7
	4	0.867	0.749	1.16	16.2
	6	1.13	0.882	1.28	20.1
	8	1.27	1.05	1.21	23.2
	10	1.51	1.22	1.24	27.3
	20	2.38	2.13	1.12	45.1
Fe_2L30	2	0.360	0.355	1.01	7.2
	4	0.502	0.400	1.26	9.0
	6	0.621	0.492	1.26	11.1
	8	0.782	0.574	1.36	13.6
	10	0.79	0.642	1.24	14.4
	12	0.850	0.719	1.18	15.7

[a] Reaction conditions: $FeCl_2$ (0.20 mmol), ligand (0.10 mmol), adamantane (20 mmol), pyridine (1.0 ml), and CH_3CN (40 ml) at 25 °C. Oxygen and hydrogen sulfide were purged through the solution. Turnover is based on mmols of the products per mmol of the catalyst used.

Table 2 Oxidation of cyclohexane by molecular oxygen with diiron complexes as catalysts and hydrogen sulfide as reductant[a]

Catalyst	Time/h	CyOH/ mmol	CyO/ mmol	CyOH/ CyO	Turnover
Fe_2L24	2	0.96	0.50	1.92	14.6
	4	1.38	0.70	1.97	20.8
	6	1.61	0.73	1.94	24.4
	8	1.85	0.99	1.87	28.4
	10	2.06	1.04	1.98	31.0
	12	2.33	1.26	1.85	35.9
Fe_2L30	2	0.64	0.60	1.07	12.4
	4	0.89	0.83	1.07	17.2
	6	1.10	1.04	1.06	21.4

[a] Reaction conditions: $FeCl_2$ (0.20 mmol), ligand (0.10 mmol), cyclohexane (20 mmol), pyridine (1.0 ml), and CH_3CN (40 ml) at 25 °C. Oxygen and hydrogen sulfide were purged through the solution. Turnover is based on mmols of the products per mmol of the catalyst used.

The mmols of products = $P_{product}/P_{naphthalene} \times 40$ ml $\times$ 0.080 M. The turnovers = the sum of mmols of products/mmol of catalyst. The turnover numbers show that these macrocyclic iron complexes are several times more effective as hydroxylating catalysts for cyclohexane than are the μ-oxo dinuclear iron complexes containing a tris(pyrazol-1-yl)borate ligand described by Kitajima *et al.*[8b] The effectiveness in the catalytic oxidation of adamantane is approximately at the same level as Kitajima's catalyst.[8b] Thus the dinuclear macrocyclic iron(II) complexes described in this paper are among the most effective functional models of methane monooxygenase reported thus far.

The oxidation of cyclohexane gives cyclohexanol and cyclohexanone. The turnovers are 24.4 after 6 h for the 24-membered macrocyclic diiron complex as a catalyst, or 21.4 after 6 h with the 30-membered macrocyclic complex. The ratios of cyclohexanol to cyclohexanone are 1.9 and 1.1 for **1** and **2**, respectively, during the whole period of time of the oxidation reactions. This result shows that the mechanisms of oxidation are similar but slightly different for the two catalysts.

The recent stability studies of dinuclear and mononuclear Fe^{II} and Fe^{III} complexes of the ligand indicate the dinuclearity of the complexes under reaction conditions. Accordingly, the electronic spectra of the reaction mixture before and after the reactions show the same characteristic absorption bands that are attributed to hydroxo dinuclear iron complexes. Thus, we suggest that the active center is a diiron species and the reaction mechanism probably resembles that of MMO.

H_2S serves as both an electron and a proton donor, the equivalent of NADH in MMO systems. The diiron(II) complex can be regenerated from the oxidized diiron(III) complex with H_2S as a two electron reductant to produce a sulfur precipitate which was analyzed quantitatively after the experiment.

In the control experiments for the oxidation of cyclohexane, the turnover is 1.1 in 8 h with Fe^{II} as a catalyst and is 1.7 in 8 h with pyridine as a ligand. Significantly, the turnover is 28.4 in 8 h with the use of the macrocyclic ligand. Autoxidation is clearly ruled out by comparison with these turnover numbers.

It is interesting that the oxidation of adamantane produces only hydroxylation products. The ratio of tertiary adamantanol to secondary adamantanol is around 1.2 for both catalysts. No ketonization product is observed even when the turnover is 45.1 after 20 h. A similar result was obtained by Kitajima *et al.*,[8b] who reported only a trace of ketonization product. This result seems to imply a difference in the mechanisms of oxidation of cyclohexane and adamantane.

The turnover numbers show that the iron complex of the 24-membered macrocycle is a better catalyst for these oxidation reactions than that of the 30-membered macrocycle.

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Notes and References

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