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COMMUNICATION

Hydrocarbon Oxidation Catalyzed by a Cheap Nonheme Imine-based Iron(II) Complex

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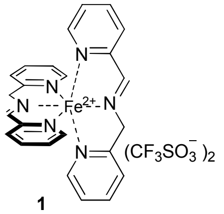
Nonheme iron complex 1 is easily obtained by one-pot assembly of cheap and commercially available starting materials. This complex effectively catalyzes the oxidation of a number of non-activated C-H bonds by H_2O_2 with high turnover numbers and good selectivity.

The last decade has witnessed the disclosure of a promising path towards non-activated C-H bond oxidation.[1] A great impulse to this research topic came from several studies on nonheme iron oxygenase models, which were demonstrated to exhibit enzyme-like activity.[2] Subsequently, some iron complexes of abiotic ligands have been prepared and shown to be good catalysts of the hydroxylation of non-activated C-H bonds with high yields and selectivities.[3]

These catalysts use the cheap and abundant iron (II) as the metal center and the environmentally friendly H_2O_2 as the oxidant. Efficient ligand design is crucial for both activity and selectivity. The most active complexes prepared so far consist of tetra- and pentadentate amine and/or pyridine based ligands arranged in a *cis-alpha* topology around the iron center. The ligand should be quite rigid and sterically encumbered in order to obtain high selectivities.[3,4] Effective ligands developed so far are either commercially available but expensive, or require multistep syntheses.

Despite the large use of imine ligands in organometallic chemistry,[5] the number of examples in which imine ligands are employed as nonheme iron catalysts are scanty.[6,7] Since imines are very easily prepared by simple mixing of the parent primary amine and carbonyl compound in a proper solvent,[8] we became interested in exploring the possibility of Fe(II)-catalyzed oxidations using imine-based ligands with a very simple structure.

In this communication we report on the in situ one-pot preparation of complex **1** from cheap and commercially available precursors, and show that this complex catalyzes with high efficiency the oxidation of hydrocarbon by H_2O_2.



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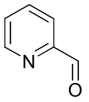

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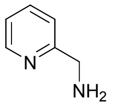

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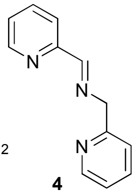

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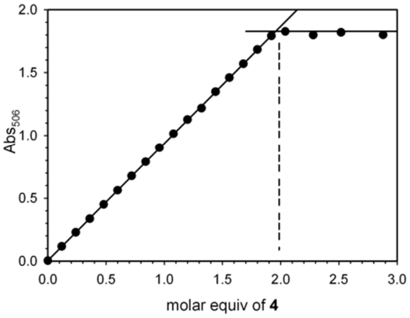


Fig. 1. Titration of 0.5 mM $Fe(CF_3SO_3)_2$ with preformed **4** in CH_3CN at 25 °C followed at 506 nm. Saturation is reached after addition of 2 mol equiv of ligand.

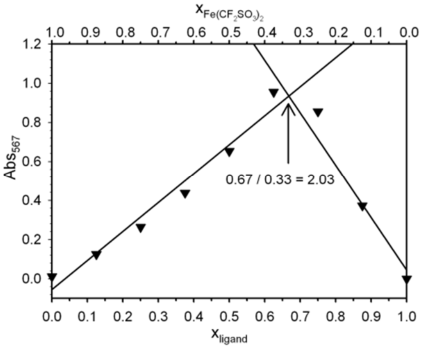
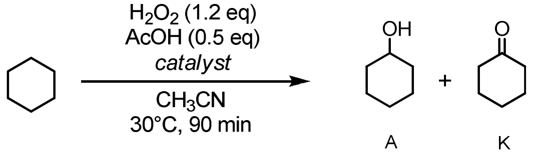


Fig. 2. Job plot for complexation between **4** and $Fe(CF_3SO_3)_2$ in CH_3CN at 25 °C followed at 567 nm. Maximum is reached for a 1:2 $Fe(CF_3SO_3)_2$ to **4** stoichiometry.

Formation of imine ligand **4** is complete within 40 min upon addition of equimolar amounts of pyridine-2-carbaldehyde **2** and 2-aminomethylpyridine **3** (33 mM) in CD_3CN solution at room temperature. The aldehydic ^1H NMR signal of **2** (9.98 ppm) disappears at the expense of the imine signal of **4** at 8.50 ppm (see Figure S1, ESI). When $Fe(CF_3SO_3)_2$ is added to the solution, the latter instantaneously becomes purple-coloured. UV-Vis titration of 0.5 mM $Fe(CF_3SO_3)_2$ with preformed ligand **4** in CH_3CN and the related job plot (Figures 1 and 2), definitely demonstrate that complex **1** has a 1:2 iron(II) to **4** stoichiometry as previously suggested in the literature for a similar complex having perchlorate counterion.[9] Furthermore UV-Vis spectra demonstrate that when compounds **2** and **3** and $Fe(CF_3SO_3)_2$ are added at the same time in solution at concentrations as low as

0.50, 0.50 and 0.25 mM respectively, complex **1** is instantaneously formed, showing that the rate of imine formation is significantly enhanced by the iron (II) template (compare Figure S3a with S3b, ESI).

Complex **1** was tested as a catalyst in the oxidation of a series of hydrocarbon substrates by H_2O_2. A first series of reactions was carried out on cyclohexane (Scheme 1) with the aim at choosing the optimal ligand/Fe(II) molar ratio for efficient catalysis (see entries 1-5 of Table 1 and Figure 3). In these experiments only the concentration of ligand **4** was varied.[‡] When only $Fe(CF_3SO_3)_2$ was present in solution, similar amounts of cyclohexanol and cyclohexanone were obtained in very low yields (entry 1). The best results were observed for a 2:1 ligand **4** / Fe(II) molar ratio (entry 4).



Scheme 1

Table 1. Oxidation of cyclohexane to cyclohexanol (A) and cyclohexanone (K) by H_2O_2 in CH_3CN at 30 °C in the presence of $Fe(CF_3SO_3)_2$ and imine ligand **4** unless otherwise stated.[a]

entry	$Fe(CF_3SO_3)_2$[b]	Ligand **4**[b]	A[c]	K[c]	A+K[d]
1	2.5	-	1.4 ± 0.2	1.7 ± 0.2	3 (2.0)
2	2.5	1.2	4.2 ± 0.2	9.3 ± 0.3	13 (8.8)
3	2.5	2.5	14 ± 1	9.1 ± 0.3	23 (13)
4	2.5	5.0	13 ± 1	17 ± 1	30 (19)
5	2.5	10	11 ± 1	6.2 ± 0.2	17 (9.2)
6[e]	2.5	5.0	13 ± 1	17 ± 1	30 (19)
7[f]	2.5	5.0	14 ± 1	14 ± 1	28 (17)
8	0.5	1.0	8.3 ± 0.3	5.4 ± 0.2	13 (36)
9[g]	1.0	2.0	18 ± 1	15 ± 1	33 (48)
10	5.0	10.0	13 ± 1	14 ± 1	27 (8.2)
11	1.0	[h]	1.3 ± 0.2	1.5 ± 0.2	3 (4.3)

[a] Cyclohexane (0.51 mmol), hydrogen peroxide (0.61 mmol, 120 mol%), acetic acid (0.25 mmol, 50 mol%). [b] mol% referred to the substrate amount. [c] GC % yields are referred to the initial amount of cyclohexane. Average from two or three independent determinations. [d] Turnover number (TON) in brackets. [e] Hydrogen peroxide 1.02 mmol (200 mol%). [f] in the absence of acetic acid. [g] An additional loading of the same amounts of H_2O_2, $Fe(CF_3SO_3)_2$ and **4** into the reacted mixture gave the following results: A, 11%; K 32%. [h] 2-picolinic acid added as a ligand (4 mol%) instead of **4**.

This is in accordance with complex **1** being the pre-active species in the catalytic event. Reaction of this octahedral complex with H_2O_2 would lead to a Fe^{III}-OOH species eventually transformed into an active oxo-complex able to carry out cyclohexane oxidation.[10] It is likely that complex **1** temporarily looses one of the six coordination legs to host hydrogen peroxide. Alternatively the latter could occupy a seventh site in the inner metal ion coordination sphere, as suggested by Bauer et al in the activation of the analogous saturated amine-based iron complex.[11]

Figure 4 shows the time evolution of cyclohexane oxidation products (conditions of entry 4 in Table 1). Cyclohexanone is clearly formed by further oxidation of the initial cyclohexanol product. Thus, a Russell-type termination mechanism involving free hydroxyl radicals should be confidently ruled out.[12]

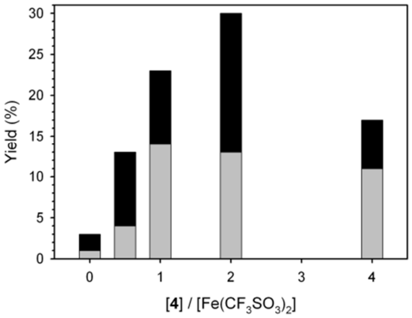


Fig. 3. Yields for oxidation of cyclohexane to cyclohexanol (grey) and cyclohexanone (black) as a function of ligand **4** / $Fe(CF_3SO_3)_2$ molar ratio. Reaction condition as reported in Table 1.

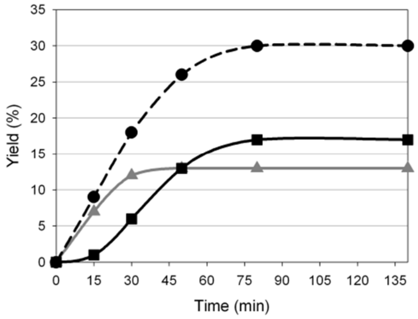


Fig. 4. Time evolution for production of cyclohexanol (triangles) and cyclohexanone (squares) as a function of time (data points related to entry 4 of Table 1). Total yield is given by circles.

Further experiments were carried out at varying amounts of oxidant, catalyst and additive as reported in Table 1 (entries 6-11). The presence of acetic acid as an additive[3] is not determinant for the catalytic efficiency (compare entry 4 with 7) although in its presence a slightly higher selectivity towards cyclohexanone was observed. No improvement was obtained on increasing catalyst (entry 10) or oxidant (entry 6) loading, but enhanced catalytic efficiency in terms of turnover number (TON) was observed when a smaller catalytic amount (1%) was added (entry 9).Whereas a further decrease in catalyst loading definitely led to lower conversions (entry 8), the total yield of oxidation products somewhat increased as a consequence of a subsequent addition of catalyst and oxidant[3a,f] (see footnote g to Table 1). A marked dependence of catalytic efficiency on catalyst concentration may be the result of auto-oxidative wasting processes which become important at high catalyst concentration.

Some pyridin-2-yl based iron and manganese complexes have been recently reported to be oxidized by H_2O_2 to 2-picolinic acid,[13] which then becomes the effective ligand in the catalytic active species. The absence of a time lag in the formation of cyclohexanol (Figure 4) and, more importantly, the negligible catalytic activity observed when 2-picolinic acid was added as a ligand instead of **4** (compare entry 11 with entry 9 in Table 1), definitely rule out any significant role of 2-picolinic acid in our catalytic system.

Next we turned our attention to the oxidation of other benchmark hydrocarbons in order to compare the catalytic activity and selectivity of **1** with other nonheme iron (II) complexes and iron (II) triflate salt (Fenton chemistry).

With all of the investigated substrates, conversions and selectivities turn out to be much higher in the presence of complex **1** than with the free iron (II) salt (compare Table 2 with Table S1, ESI).

Adamantane was converted into oxidation products, adamantanols and adamantanone, in 29% yield with a total TON of 29 (Table 2, entry 1). The latter value is significantly higher than the TONs reported in the literature, ranging from 4.9 to 8.4, for other nonheme iron complexes.[14,15] The 3°/2° selectivity observed (9.4) is in line with the results obtained with other nonheme iron catalysts[7,14,15] even though is significantly lower than that provided by the very selective Py-TACN complex developed by Costas and coworkers (30).[16]

In the oxidation of (*d*)-menthyl acetate the main product was the tertiary alcohol deriving from the oxidation of the most reactive C-H bond with retention of configuration, as previously observed in the oxidation with the White's complex.[14] However, the selectivity was lower, the main oxidation product accounting for about half of total product yields (entry 2).

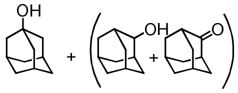
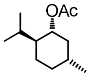
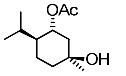
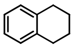
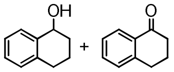
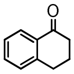
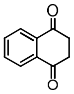
Finally, we investigated the efficiency of catalyst **1** in the oxidation of the benzylic position of tetraline (entry 3). As expected on the basis of the presence of the activated benzylic C-H bonds, the products 1-tetralol and 1-tetralone were formed with a higher conversion with respect to the oxidation of aliphatic hydrocarbons. The efficiency of our catalyst was found to be very sensitive to electronic effects as shown by the drop of catalytic activity in the oxidation of α-tetralone, due to the presence of the deactivating electron withdrawing carbonyl group (entry 4).

Conclusions

To sum up, we have shown that nonheme imine-based iron(II) complex **1,** easily prepared in situ from cheap and commercially available starting materials, is a promising catalyst for the oxidation of hydrocarbons by H_2O_2 with a good activity, even at low catalyst loadings as low as 1%. In terms of turnover number, the catalytic efficiency of complex **1**, compares well with that of the majority of non-heme iron complexes reported so far in the literature.[2b,c,6,14,15,17]

The study of the catalytic activity in the oxidation of hydrocarbons promoted by other imine-based iron(II) complexes is currently underway in our laboratory.

Table 2. Oxidation of hydrocarbons by H_2O_2 catalyzed by the imine complex **1** in CH_3CN at 30 °C. Yields are average of two or three runs. TON are reported in brackets.

Entry	Substrate	Products	Total yield
1[a,b]		 22 ±2 444444447 ±2444444444	29 (29)
2[c,d]		 8±1	15 (15)
3[b,e]		 15±1 (6.0)44428±1 (22)44444	43 (28)
4[b,e]		 5±1 (4.0)	5 (2.0)

[a] Conditions: $Fe(CF_3SO_3)_2$ (1.5 µmol, 1 mol%), **2** (3.0 µmol, 2 mol%), **3** (3.0 µmol, 2 mol%), adamantane (150 µmol), H_2O_2 (180 µmol, 120 mol%), AcOH (75 µmol, 50 mol%). [b] GC yields. [c] Conditions: $Fe(CF_3SO_3)_2$ (5.1 µmol, 1 mol%), **2** (10.2 µmol, 2 mol%), **3** (10.2 µmol, 2 mol%), (*d*)-menthyl acetate (508 µmol), AcOH (254 µmol, 50 mol%), H_2O_2 (610 µmol, 120 mol%). [d] ^{1}H-NMR yield. Only yield of the main product is reported. [e] Conditions: $Fe(CF_3SO_3)_2$ (13 µmol, 2.5 mol%), **2** (26 µmol, 5 mol%), **3** (26 µmol, 5 mol%), substrate (508 µmol), H_2O_2 (1.16 mmol, 200 mol%), AcOH (254 µmol, 50 mol%).

Notes and references

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† Electronic Supplementary Information (ESI) available: [^{1}H-NMR and UV-Vis spectra, details of oxidation procedures, results related to oxidation reactions carried out in the presence of $Fe(CF_3SO_3)_2$ alone]. See DOI: 10.1039/b000000x/

‡ Ligand, $Fe(CF_3SO_3)_2$ and additive were one shot added to the acetonitrile substrate solution at the beginning of the reaction while H_2O_2 was added over a period of 15 min through a syringe-pump. The reaction mixture was then left under stirring at 30 °C for additional 75 min.

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Graphical abstract

An imine-based iron complex, prepared in situ from iron (II), pyridine-2-carbaldehyde and 2-aminomethylpyridine effectively catalyzes hydrocarbon oxidation at low loadings.