

# Iron complexes with nitrogen bidentate ligands as green catalysts for alcohol oxidation

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## ABSTRACT

The iron(II) complexes  $[\text{Fe}(\text{N-N})_3](\text{OTf})_2$  (N-N=2,2'-bipyridine, 1,10-phenanthroline and substituted derivatives) were employed as catalyst precursors for the oxidation of primary and secondary alcohols, including glycerol. The single-crystal structure of  $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$  was determined by X-ray crystallography. The catalytic reactions were performed using either  $\text{H}_2\text{O}_2$  or *tert*-butylhydroperoxide (TBHP) as oxidizing agent, in mild experimental conditions: with all catalysts employed, secondary alcohols were oxidized to the corresponding ketones with up to 100% yields, whereas other substrates gave lower conversions. Indications on the nature of the catalytically active species, which is probably formed via dissociation of a nitrogen ligand from the iron center, were obtained from NMR and ESI–MS spectra.

## 1. Introduction

The recent development of transition-metal promoted organic synthesis has largely focussed on the replacement of catalysts based on precious metals with first row transition-metal compounds. The urgency towards this target lies on the limited availability as well as high price of platinum group metals on one hand and on their relevant toxicity on the other. Among the possible candidates, iron has been emerging as the most attractive substitute due to its large availability, moderate price and low toxicity; last but not least, iron compounds are environmentally benign [1]. The enormous increase of research on iron-based catalysis is witnessed by a growing number of publications, among which some very recent examples concern olefin hydrogenation [2] and epoxidation [3], reduction of carboxylic acid derivatives [4], amination of alcohols [5], alkynes trimerization [6] and diazidation of olefins [7].

Since iron catalysts have a relevant role in biological redox systems, it is not surprising that the most important iron-promoted processes so far developed include oxidation reactions [8]. In particular, regarding the oxidation of alcohols to carbonyl compounds, which is a fundamental transformation in organic synthesis, iron-based catalysts are promising substitutes for the traditional

stoichiometric methods on one hand, and precious metal promoted oxidation on the other. Use of iron catalysts in association with green oxidants such as peroxides, the reduced products of which (alcohols or water) are generally non-toxic [9], is expected to provide highly sustainable oxidation processes.

Apart from early reports of alcohol oxidation catalyzed by iron salts [10], which proved sometimes effective but often poorly selective, more recent papers describe the use of very efficient catalysts based on the association of iron with various polydentate nitrogen-donor ligands [11] including porphyrines [12]. In contrast, examples of alcohol oxidation catalyzed by iron complexes with bidentate ligands with either N or N,O donor atoms are less common [13].

We became interested in the development of iron-based oxidation catalysts which should combine appreciable catalytic activity and selectivity with simple and low-cost catalyst synthesis: in other words, catalyst precursors having cheap, readily available coordinated ligands. In addition, use of Fe(II) low spin complexes would offer the opportunity of gaining information on the evolution of the catalytically active species by means of NMR studies. In fact, the mechanistic details of iron-promoted oxidations are still unclear, in spite of recent efforts to shed light on this subject [14].

A further reason which called our attention towards alcohol oxidation lies in our interest on selective glycerol oxidation, a process of high applicative importance: after developing iridium-based catalysts for the conversion of glycerol to dihydroxyacetone, we recently reported the first example of such reaction

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promoted by an iron catalyst, *i.e.*  $[\text{Fe}(\text{BPA})_2(\text{OTf})_2]$  (BPA = bis(2-pyridinylmethyl)amine) [15].

In the following we describe our results in the oxidation of primary and secondary alcohols, including glycerol, catalyzed by iron complexes with 1,10-phenanthroline, 2,2'-bipyridine and substituted derivatives, using either hydrogen peroxide or TBHP as oxidant in very mild reaction conditions.

## 2. Experimental

### 2.1. General

All the chemicals were reagent grade and were used as received from the commercial suppliers, with the exception of naphthalene, used as GC standard, which was recrystallized from ethanol.

### 2.2. Instrumental

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded either on a Varian 500 spectrometer operating at 500 MHz and 125.68 MHz, respectively, or on a Jeol EX400 spectrometer operating at 400 MHz and 100.4 MHz, respectively; chemical shifts were measured relative to the residual solvent signal. Resonances were assigned with reference to COSY and HSQC spectra.

ESI-MS spectra were obtained by an ion-trap instrument (ESI-MS Bruker Esquire 4000) equipped with an electrospray ion source. The instrument performed with 10.0 psi nebulizer pressure, end-plate offset  $-500\text{ V}$ , capillary 4000 V and capillary exit at 113.3 V. The drying gas ( $\text{N}_2$ ) flow was  $5\text{ L min}^{-1}$  and the spectral range was from  $m/z = 100$  to 1200.

The chemical yields of the catalytic reactions were determined by integration of the  $^1\text{H}$  NMR signals and/or by GC analysis on an Agilent 6850 instrument with helium as carrier gas and a TCD detector.

### 2.3. Synthesis of the iron complexes

#### 2.3.1. Synthesis of $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$ (1)

A round-bottomed flask was charged with acetonitrile (3 mL) and  $\text{Fe}(\text{OTf})_2$  (0.56 mmol), the yellow solution so obtained immediately turned dark red upon addition of bipy (1.12 mmol). The reaction mixture was stirred at r.t. for 30 min and then concentrated to 1/3 of the initial volume. Addition of diethylether caused precipitation of a dark red solid, which was filtered and washed with ether. Yield 73%.  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  8.56 (d, 2H,  $\text{H}_3$  and  $\text{H}_{3'}$ ), 8.13 (t, 2H,  $\text{H}_4$  and  $\text{H}_{4'}$ ), 7.42 (m, 4H,  $\text{H}_5$  and  $\text{H}_{5'}$ ,  $\text{H}_6$  and  $\text{H}_{6'}$ ).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  160.0 ( $\text{C}_2$  and  $\text{C}_{2'}$ ), 155.0 ( $\text{C}_6$  and  $\text{C}_{6'}$ ), 139.5 ( $\text{C}_4$  and  $\text{C}_{4'}$ ), 128.3 ( $\text{C}_5$  and  $\text{C}_{5'}$ ), 124.8 ( $\text{C}_3$  and  $\text{C}_{3'}$ ).

#### 2.3.2. Synthesis of $[\text{Fe}(\text{phen})_3](\text{OTf})_2$ (2)

Same procedure as for **1** but with ligand phen. Yield 71%.  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  8.65 (d, 2H,  $\text{H}_2 + \text{H}_6$ ), 8.29 (s, 2H,  $\text{H}_5 + \text{H}_6$ ), 7.69 (d, 2H,  $\text{H}_4 + \text{H}_7$ ), 7.63 (dd, 2H,  $\text{H}_3 + \text{H}_8$ ).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  156.2 ( $\text{C}_4 + \text{C}_7$ ), 149.7 (C-N quat.), 137.4 ( $\text{C}_2 + \text{C}_9$ ), 130.5 (C quat.), 128.1 ( $\text{C}_5 + \text{C}_6$ ); 126.0 ( $\text{C}_3 + \text{C}_8$ ).

#### 2.3.3. Synthesis of $[\text{Fe}(\text{DMbipy})_3](\text{OTf})_2$ (3)

Same procedure as for **1** but with ligand DMbipy (DMbipy = 4,4'-dimethyl-2,2'-bipyridine). Yield 80%.  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  8.38 (s, 2H,  $\text{H}_3$  and  $\text{H}_{3'}$ ), 7.21 (br, 4H,  $\text{H}_5$  and  $\text{H}_{5'}$ ,  $\text{H}_6$  and  $\text{H}_{6'}$ ), 2.59 (s, 6H, Me).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  158.9 ( $\text{C}_2$  and  $\text{C}_{2'}$  or  $\text{C}_4$  and  $\text{C}_{4'}$ ), 153.3 ( $\text{C}_5$  and  $\text{C}_{5'}$  or  $\text{C}_6$  and  $\text{C}_{6'}$ ), 151.2 ( $\text{C}_2$  and  $\text{C}_{2'}$  or  $\text{C}_4$  and  $\text{C}_{4'}$ ), 128.3 ( $\text{C}_5$  and  $\text{C}_{5'}$  or  $\text{C}_6$  and  $\text{C}_{6'}$ ), 124.7 ( $\text{C}_3$  and  $\text{C}_{3'}$ ), 20.3 (Me).

#### 2.3.4. Synthesis of $[\text{Fe}(\text{DMphen})_3](\text{OTf})_2$ (4)

Same procedure as for **1** but with ligand DMphen (DMphen = 4,7-dimethyl-1,10-phenanthroline). Yield 75%.  $^1\text{H}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  8.38 (s, 2H,  $\text{H}_2 + \text{H}_9$ ), 7.51 (s, 2H,  $\text{H}_5 + \text{H}_6$ ), 7.44 (s, 2H,  $\text{H}_3 + \text{H}_8$ ), 2.89 (s, 6H, Me).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{CN}$ ,  $25^\circ\text{C}$ ):  $\delta$  156.2 ( $\text{C}_5 + \text{C}_6$ ), 150.4 (C quat.), 148.6 (C quat.), 131.1 (C quat.), 127.5 ( $\text{C}_3 + \text{C}_8$ ), 125.5 ( $\text{C}_2 + \text{C}_9$ ), 18.9 (Me).

### 2.4. X-ray crystal structure analysis

Data collection of **1** was performed at the X-ray diffraction beamline (XRD1) of the Elettra Synchrotron of Trieste (Italy), with a Pilatus 2M image plate detector. The experiment was performed at 100 K (nitrogen stream supplied by an Oxford Cryostream 700) with a monochromatic wavelength of  $0.700\text{ \AA}$  through the rotating crystal method. The diffraction data were indexed, integrated and scaled using program XDS [16]. The structure was solved by direct methods using SIR2014 [17]. Fourier analysis and refinement with the full-matrix least-squares method based on  $F^2$  were performed with SHELXL-2014 [18]. One triflate anion was found disordered over two positions with refined occupancies of 0.850(3)/0.150(3), sharing one oxygen atom. Hydrogen atoms were placed at calculated positions with isotropic U factors equal to 1.2 times the equivalent U factor of the bonded atom.

Crystallographic data:  $\text{C}_{32}\text{H}_{24}\text{F}_6\text{FeN}_6\text{O}_6\text{S}_2$ ,  $M = 822.54$ , monoclinic, space group  $C2/c$ ,  $a = 36.417(3)$ ,  $b = 11.123(2)$ ,  $c = 17.554(3)\text{ \AA}$ ,  $\beta = 111.83(3)^\circ$ ,  $V = 6601(2)\text{ \AA}^3$ ,  $Z = 8$ ,  $D_c = 1.655\text{ g/cm}^3$ ,  $\mu(\text{Mo-K}\alpha) = 0.674\text{ mm}^{-1}$ ,  $F(000) = 3344$ ,  $\theta$  range =  $1.19\text{--}28.23^\circ$ . Final  $R1 = 0.0624$ ,  $wR2 = 0.1671$ ,  $S = 1.073$  for 508 parameters and 15945 reflections, 8154 unique [ $R(\text{int}) = 0.0279$ ], of which 7795 with  $I > 2\sigma(I)$ , max positive and negative peaks in  $\Delta F$  map 1.787,  $-1.512\text{ e. \AA}^{-3}$ . CCDC reference number 1473638.

### 2.5. Procedure for the catalytic reactions

#### 2.5.1. Oxidation of alcohols catalyzed by $\text{Fe}(\text{OTf})_2/\text{N-N}$ "in situ"

A round-bottomed flask was charged with the solvent (3.0 mL),  $\text{Fe}(\text{OTf})_2$  (0.050 mmol) and the nitrogen ligand (0.10 mmol). After addition of the substrate (2.5 mmol), the oxidant was added dropwise under stirring, at r.t. After the desired time the reaction mixture was cooled at  $-18^\circ\text{C}$  and subsequently analyzed by GC and/or NMR.

#### 2.5.2. Oxidation of alcohols catalyzed by $[\text{Fe}(\text{N-N})_3](\text{OTf})_2$

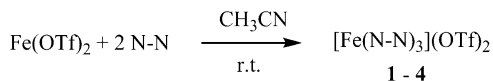
In a round-bottomed flask the solvent (3.0 mL) and the catalyst precursor  $[\text{Fe}(\text{N-N})_3](\text{OTf})_2$  (0.050 mmol) were introduced, followed by the substrate (2.5 mmol). For reactions performed at temperatures higher than r.t., the resulting solution was heated in a thermostatted bath to the desired temperature. Slow addition of the oxidant was then carried out under stirring. After the desired time the reaction mixture was cooled at  $-18^\circ\text{C}$  and subsequently analyzed by GC and/or NMR.

#### 2.5.3. Oxidation of glycerol catalyzed by $[\text{Fe}(\text{N-N})_3](\text{OTf})_2$

Glycerol (2.5 mmol) was introduced into a round-bottomed flask, followed by the solvent (3.0 mL) and the iron catalyst (0.050 mmol). For reactions performed at temperatures higher than r.t., the resulting solution was heated in a thermostatted bath to the desired temperature. The oxidant was then added dropwise under vigorous stirring. After the appropriate time the reaction mixture was cooled at  $-18^\circ\text{C}$  and subsequently analyzed by GC and/or NMR.

### 2.6. Analysis of the reaction mixtures

Qualitative analysis was accomplished by  $^1\text{H}$  and  $^{13}\text{C}$  NMR; the resonances were compared with those of authentic samples



N-N = bipy (**1**), phen (**2**), DMbipy (**3**), DMphen (**4**)

**Scheme 1.** Synthesis of iron precursors.

obtained either by conventional routes or by commercial suppliers. Quantitative evaluation of product distributions was performed by integration of  $^1\text{H}$  NMR signals (in this case the catalytic reactions were performed in a deuterated solvent: acetonitrile- $d_3$ , acetone- $d_6$  or  $\text{D}_2\text{O}$ ) and/or by GC with naphthalene as the internal standard.

### 3. Results and discussion

#### 3.1. Synthesis and characterization of the iron precursors

The oxidation reactions were initially carried out by employing a catalytic system prepared *in situ* from  $\text{Fe}(\text{OTf})_2$  ( $\text{OTf} = \text{CF}_3\text{SO}_3$ ) and two equivalents of 2,2'-bipyridine (bipy) and using 1-phenylethanol as substrate. Oxidant ( $\text{H}_2\text{O}_2$ ) and solvent (acetonitrile) were chosen in agreement with Green Chemistry principles: the latter (classified as “usable” solvent) was selected after exclusion of all “preferred” ones [19] due to poor solubility of reagents and/or competition with substrate. A first series of test reactions thus performed gave promising results, *i.e.* acetophenone was formed in appreciable yield as the only reaction product: these findings prompted us to isolate the Fe/N-N complex which behaved as catalyst precursor. Therefore,  $\text{Fe}(\text{OTf})_2$  was treated on a preparative scale with 2 equivalents of bipy in acetonitrile at r.t., giving a purple-red solution from which, upon addition of diethylether, a dark red solid (**1**) was isolated. The  $^1\text{H}$  NMR spectrum of this product in  $\text{CD}_3\text{CN}$  only showed three resonances, a doublet at  $\delta$  8.56, a triplet at  $\delta$  8.13 and a rather broad signal at  $\delta$  7.42 of area 1:1:2, respectively. The  $^{13}\text{C}$  NMR spectrum was accordingly simple, as it consisted of five signals at  $\delta$  160.0, 155.0, 139.5, 128.3 e 124.8.

In order to unambiguously characterize compound **1** suitable crystals were grown by slow diffusion of *n*-hexane into a concentrated solution of **1** in acetonitrile. As shown in Fig. 1, in spite of the stoichiometry employed (bipy/Fe=2) the resulting complex was  $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$ , a well-known compound previously prepared by a different procedure [20]. The octahedral complex presents Fe–N bond distances in the range 1.959(2)–1.973(2) Å, in agreement with values measured in the numerous reported  $[\text{Fe}(\text{bipy})_3]^{2+}$  derivatives having different counterions.

By the same procedure three more iron complexes were synthesized (see Scheme 1), each one having a different coordinated nitrogen ligand: thus, compounds  $[\text{Fe}(\text{phen})_3](\text{OTf})_2$  (phen = 1,10-phenanthroline) (**2**),  $[\text{Fe}(\text{DMbipy})_3](\text{OTf})_2$  (DMbipy = 4,4'-dimethyl-2,2'-bipyridine) (**3**) and  $[\text{Fe}(\text{DMphen})_3](\text{OTf})_2$  (DMphen = 4,7-dimethyl-1,10-phenanthroline) (**4**) were obtained and characterized on the basis of their NMR spectra (see Section 2).

#### 3.2. Oxidation of 1-phenylethanol (PE) with $\text{H}_2\text{O}_2$ catalyzed by $[\text{Fe}(\text{N-N})_3](\text{OTf})_2$

Using compound **1** as catalyst precursor, oxidation of PE with hydrogen peroxide was performed in acetonitrile solution. The results reported in Table 1 (entries 1–4) show that the yield of acetophenone after 30 min increased by increasing the reaction temperature, ranging from 17% at 25 °C to 66% at 70 °C. After 30 min the conversion no longer increased. However, after 1 h a second addition of hydrogen peroxide promoted the overall conversion to a final 85% (Table 1, entry 5).

**Table 1**

Oxidation of 1-phenylethanol (PE) to acetophenone with  $\text{H}_2\text{O}_2$  catalyzed by  $[\text{Fe}(\text{L})_3](\text{OTf})_2$ .<sup>a</sup>

Entry	L	T (C°)	solvent	t (min)	$[\text{H}_2\text{O}_2]/[\text{sub}]$	Yield (%)
1	bipy	25	$\text{CH}_3\text{CN}$	30	2	17
2	“	40	“	30	2	47
3	“	55	“	30	2	55
4	“	70	“	30	2	66
5	“	55	“	120	2+2	85
6	phen	25	“	30	2	16
7	“	55	“	30	2	50
8	DMPhen	55	“	30	2	48
9	DMBipy	55	“	30	2	39
10	phen	25	acetone	0.5	2	16
11	“	“	“	24	“	38
12	“	“	“	48	2+2	61
13	bipy	25	“	0.5	2	15
14	“	“	“	24	“	37
15	“	“	“	48	2+2	60
16	“	50	“	0.5	2	34
17	“	“	“	24	“	34

<sup>a</sup> Experimental conditions:  $[\text{Fe}] = 1.7 \times 10^{-2} \text{M}$ ;  $[\text{sub}]/[\text{Fe}] = 50$ ;  $\text{H}_2\text{O}_2(\text{aq})$  30%.

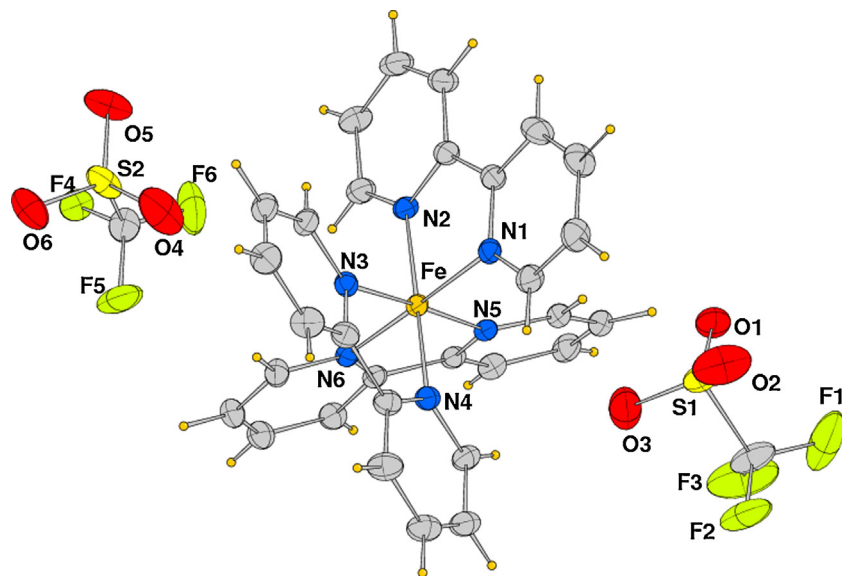
Catalytic reactions carried out using **2**, **3** or **4** as catalyst precursor under the same experimental condition gave similar results (see Table 1, entries 6–9). Therefore, in the process under investigation the different properties of the nitrogen ligands in terms of donor abilities [21] do not appear to influence the catalytic performance of the active species.

In all catalytic reactions above described the final conversion was attained within 30 min from the addition of  $\text{H}_2\text{O}_2$ : such findings were ascribed to the well-known iron-catalyzed hydrogen peroxide decomposition [22]. With the aim of discouraging such decomposition, another series of catalytic tests was performed in a different reaction medium: thus, acetonitrile was replaced by acetone, which is known to have a beneficial effect on oxidations with  $\text{H}_2\text{O}_2$  as it stabilizes the peroxide releasing it gradually [23]. As a matter of fact, at r.t. if on one hand after short reaction times the same conversions were obtained in acetone and acetonitrile (compare entries 10 with 6 and 13 with 1 in Table 1), on the other hand the oxidation performed in acetone proceeded for longer reaction times (Table 1, entries 11 and 14); also in this case, further addition of  $\text{H}_2\text{O}_2$  gave new impulse to the catalytic reaction (Table 1, entries 12 and 15). However, when higher reaction temperatures were employed no beneficial effect of using acetone was observed (Table 1, entries 16 and 17).

#### 3.3. Oxidation of 1-phenylethanol with TBHP

A series of catalytic reactions was performed using *tert*-butylhydroperoxide (TBHP) in place of  $\text{H}_2\text{O}_2$ : such replacement proved beneficial to the outcome of the reactions. In the presence of complex **1** at 55 °C the reaction yields after 30 min with  $\text{H}_2\text{O}_2$  and TBHP were 55% and 79%, respectively. Moreover, at 25 °C with all catalytic precursors **1–4** the reactions performed with TBHP produced acetophenone with conversions around 80% after 2 h (Table 2, entries 1, 3, 5, and 7) whereas in all cases 100% conversion was achieved after 24 h (Table 2, entries 2, 4, 6, and 8). Replacement of acetonitrile with acetone as reaction medium caused no significant differences in the final conversion. Thus, with the catalytic systems under investigation TBHP behaved as a more efficient oxidant than hydrogen peroxide, giving complete conversion at r.t., in contrast with lower yields obtained with  $\text{H}_2\text{O}_2$  even at higher temperatures. In our previous studies on iron-promoted oxidation [15] we had found a reverse trend, as hydrogen peroxide behaved as more efficient oxidant.

Use of a single equivalent of TBHP also gave conversions above 80% (Table 2, entry 9). Notably, even at increased  $[\text{sub}]/[\text{Fe}]$  ratios



**Fig. 1.** Asymmetric unit of complex **1** (Ortep drawing, 50% probability ellipsoid). Coordination bond distances (Å) Fe-N(1)=1.973(2), Fe-N(2)=1.960(2), Fe-N(3)=1.965(2), Fe-N(4)=1.959(2), Fe-N(5)=1.965(2), Fe-N(6)=1.9598(19).

conversions of 90% or higher were obtained (Table 2, entries 10, 11).

The stability of the catalyst was then examined, by adding new loads of both substrate and TBHP after complete oxidation of the initial amount of PE: after two such additions complete oxidation was again observed, and even a forth load of substrate and oxidant gave formation of acetophenone in 90% yield (see Table 2 entries 2 and 12–14).

Interestingly, when the catalytic reaction with complex **1** was repeated in the presence of 3 equivalents of added bipy we observed a dramatic drop in acetophenone yield (6% in 2 h); an analogous reaction carried out with compound **2** and added phen gave the same result (compare entries 1 with 15 and 3 with 16 in Table 2). These findings indicate that the catalytically active species is formed *via* dissociation of one nitrogen chelating ligand from the iron center: such process is depressed by the presence of added ligand, with consequent loss of catalytic activity.

### 3.4. Oxidation of primary and secondary alcohols catalyzed by $[Fe(bipy)_3](OTf)_2$

The substrate scope of the catalytic reactions in the presence of complex **1** was examined with a series of primary and secondary

alcohols, as well as an unsaturated alcohol and a diol. In this investigation both hydrogen peroxide and TBHP were tested as oxidizing agents. A selection of the results is reported in Table 3: the catalytic system was effective for oxidation of nearly all examined substrates. First of all, a comparison between oxidation of the model secondary and primary alcohols, *i.e.* PE and benzyl alcohol, shows that with the latter substrate – which was oxidized to benzaldehyde – the extent of oxidation was lower, independently on the choice of the oxidant (compare entries 1 and 2, 3 and 4 in Table 3). On the other hand, a catalytic reaction performed by using an equimolar mixture of these two compounds showed no substrate selectivity, as in the final reaction mixture both acetophenone and benzaldehyde were present in an approximate 2:1 ratio.

Aliphatic primary alcohols were oxidized only in traces to the corresponding aldehydes, whereas an allylic alcohol (cinnamyl alcohol) was converted to the corresponding unsaturated aldehyde (cinnamaldehyde) with appreciable yield (see Table 3 entries 7, 10 and 6, respectively).

Aliphatic secondary alcohols (2-butanol, cyclopentanol and cyclohexanol) were oxidized to the corresponding ketones with comparable yields (Table 3, entries 8, 9, and 11); finally, 2,3-butandiol was converted to a 1:1 mixture of the corresponding ketoalcohol and diketone (Table 3 entry 12).

**Table 2**

Oxidation of 1-phenylethanol (PE) to acetophenone with TBHP catalyzed by  $[Fe(L)_3](OTf)_2$ .<sup>a</sup>

Entry	L	[L]/[Fe(L) <sub>3</sub> (OTf) <sub>2</sub> ]	t (h)	[sub]/[Fe]	Yield (%)
2	–	–	24	–	100
3	phen	–	2	–	84
4	–	–	24	–	100
5	DMBipy	–	2	–	89
6	–	–	24	–	100
7	DMPPhen	–	2	–	78
8	–	–	24	–	100
9 <sup>b</sup>	bipy	–	24	–	85
10	–	–	24	100	100
11	–	–	24	250	90
12	–	–	24	50 + 50	100
13	–	–	24	3 × 50	100
14	–	–	24	4 × 50	90
15	–	3	2	50	6
16	phen	3	2	–	4

<sup>a</sup> Experimental conditions: [Fe]=1.7 × 10<sup>2</sup> M; TBHP(aq) 70%; [TBHP]/[sub]=2; T=25 °C.



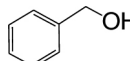

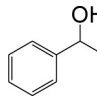
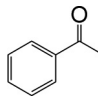
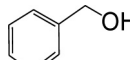

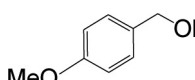
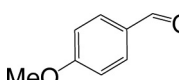
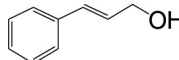
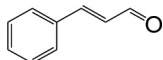
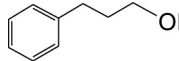
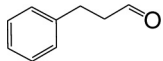




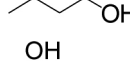




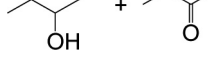
<sup>b</sup> [TBHP]/[sub]=1.

### 3.5. Oxidation of glycerol catalyzed by $[Fe(bipy)_3](OTf)_2$

As already mentioned in the Introduction, the selective oxidation of glycerol is a process of extremely high importance, all the possible products being of interest from an industrial point of view. The first step of this process is the oxidation of either one primary hydroxyl group to give glyceraldehyde or the secondary hydroxyl group forming dihydroxyacetone (DHA) (see Scheme 2), the latter product being the most desirable one in terms of commercial value. We recently showed that iron can catalyze this process with selective formation of DHA, as proved by the results obtained with  $[Fe(BPA)_2](OTf)_2$  (BPA = bis(2-pyridinylmethyl)amine) [15].

The results discussed in the previous paragraph indicate a preference of the catalytic systems under investigation towards oxidation of secondary alcohols in comparison to primary ones: thus, compounds **1–4** appeared potentially suitable catalysts for the selective oxidation of glycerol to DHA.

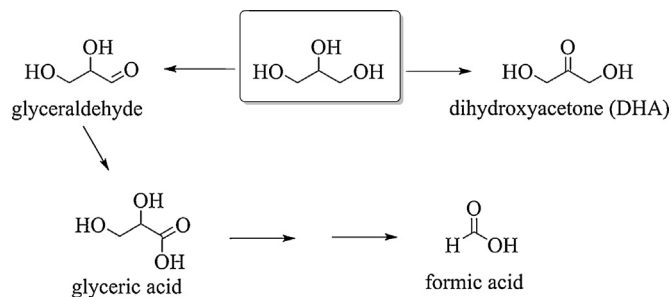
**Table 3**  
Oxidation of alcohols catalyzed by  $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$ .<sup>a</sup>

Entry	Substrate	Product	Yield (%)
1 <sup>b</sup>			55
2 <sup>b</sup>			35
3			100
4			52
5			49
6			66
7			2
8			52
9			55
10			2
11			47
12			23 <sup>c</sup>

<sup>a</sup> Experimental conditions:  $[\text{Fe}] = 1.7 \times 10^2 \text{ M}$ ;  $[\text{sub}]/[\text{Fe}] = 50$ ;  $\text{ox} = \text{TBHP}(\text{aq}) 70\%$ ;  $[\text{ox}]/[\text{sub}] = 2$ ;  $T = 25^\circ \text{C}$ ;  $t = 24 \text{ h}$ .

<sup>b</sup>  $T = 55^\circ \text{C}$ ;  $\text{ox} = \text{H}_2\text{O}_2(\text{aq}) 30\%$ ;  $t = 30 \text{ min}$ .

<sup>c</sup> yields 11% ketoalcohol and 12% diketone.

**Scheme 2.** Products of glycerol oxidation.

Therefore, we carried out a series of reactions with complexes **1–4** as catalyst precursors and glycerol as substrate. (see selected results in Table 4). The final reaction mixtures using acetonitrile as solvent and either hydrogen peroxide or TBHP as oxidant contained DHA as the main product albeit in yields not exceeding 4%, along with traces of other products (glycerinaldehyde, glycolic acid) (see entries 1–5 in Table 4).

**Table 4**  
Oxidation of glycerol catalyzed by  $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$ .<sup>a</sup>

Entry	Solvent	T (°C)	t (h)	Oxidant	[ox]/[sub]	DHA yield (%)	FA yield (%)
1	CH <sub>3</sub> CN	25	24	H <sub>2</sub> O <sub>2</sub>	2	2	0
2	"	55	0.5	H <sub>2</sub> O <sub>2</sub>	2	1	0
3	"	25	24	TBHP	2	2	0
4	"	55	0.5	TBHP	2	3	0
5	"	70	2	TBHP	2	4	0
6	H <sub>2</sub> O	70	2	H <sub>2</sub> O <sub>2</sub>	1	5	22
7	"	70	2	H <sub>2</sub> O <sub>2</sub>	2	4	49
8	"	70	2	TBHP	2	2	6

<sup>a</sup> Experimental conditions:  $[\text{Fe}] = 1.7 \times 10^2 \text{ M}$ ;  $[\text{sub}]/[\text{Fe}] = 50$ ; oxidant: H<sub>2</sub>O<sub>2</sub> (aq) 30% or TBHP (aq) 70%; DHA = dihydroxyacetone; FA = formic acid.

Other catalytic tests were performed using water in place of acetonitrile as reaction medium, in association with H<sub>2</sub>O<sub>2</sub> as oxidizing agent: such modification caused an increase of the overall conversion, however the major product was now formic acid (FA), with yields of DHA not exceeding 5% (Table 4, entries 6 and 7). At variance, reactions carried out in water with TBHP gave lower yields in both FA and DHA (Table 4, entry 8). Notably, FA is a valuable product both as hydrogen carrier [24] and as convenient source of C1 raw material for the chemical industry [25]; formation of FA as the main product of iron-catalyzed oxidation of glycerol was very recently reported by our group [26].

In conclusion, association of iron(II) with bipy, phen or their substituted derivatives does not produce efficient catalysts for the selective oxidation of glycerol to DHA, in contrast to that of ligand BPA.

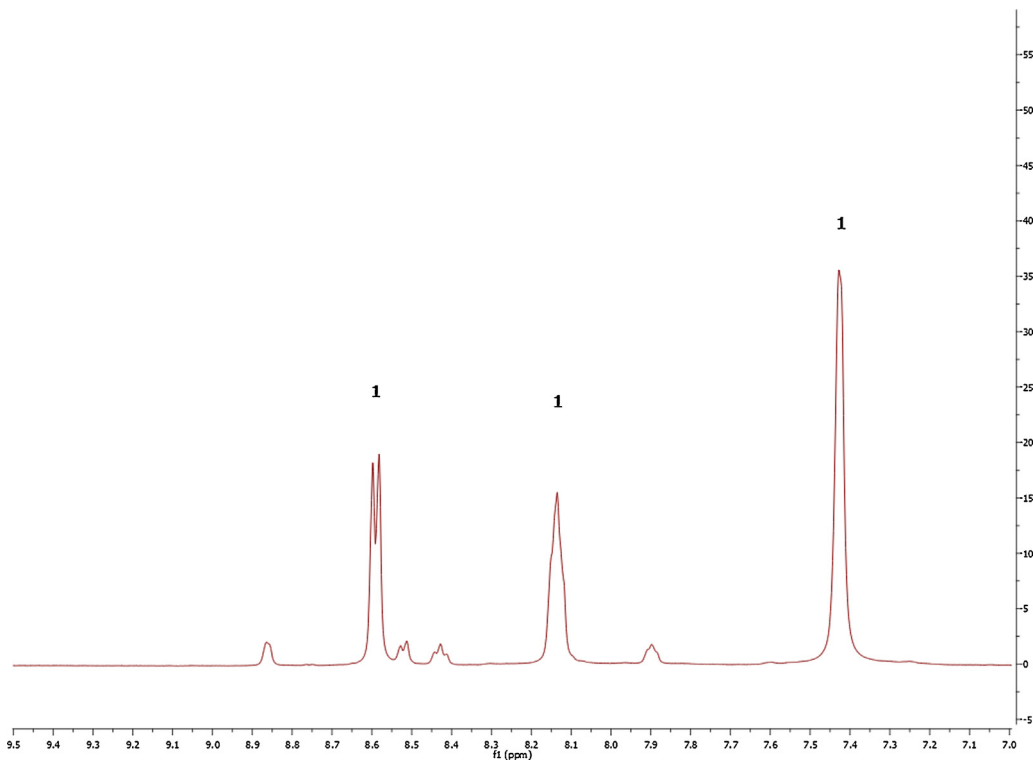
### 3.6. NMR and ESI-MS studies of the oxidation of PE catalyzed by $[\text{Fe}(\text{bipy})_3](\text{OTf})_2$

With the aim of following the evolution of the iron precursors in the course of the catalytic process, the NMR spectra of samples prepared for this purpose were recorded before, during and after completion of the oxidation reaction.

In a first experiment we followed the oxidation of cyclohexanol with TBHP in the presence of complex **1**: the starting solution was prepared in CD<sub>3</sub>CN with a lower substrate concentration ( $[\text{sub}]/[\text{Fe}] = 10$ ) than that usually employed, in order to identify more clearly the resonances of the iron complexes (the same reason motivated the choice of a substrate which has no resonances in the aromatic region). The NMR spectra of the solution were recorded in three moments, with reference to addition of TBHP: (i) before the addition, (ii) 1 h after the addition and (iii) 24 h after the addition (the sample was stored at  $-18^\circ \text{C}$  overnight).

<sup>1</sup>H and <sup>13</sup>C NMR spectra of sample (i) displayed the resonances of complex **1** and those of the substrate, whereas the absence of signals assignable to cyclohexanone indicated that no aerobic oxidation had taken place. In sample (ii) the catalytic reaction was underway, the <sup>1</sup>H NMR spectrum showed very broad signals attributable to the presence of paramagnetic iron intermediates. Finally, in the <sup>1</sup>H NMR spectrum of sample (iii) rather narrow signals were once more observed, indicating that no paramagnetic species were present in significant amount: besides the signals of cyclohexanone the spectrum comprised those of complex **1**, accompanied by smaller resonances at  $\delta$  8.86, 8.52, 8.43 and 7.90, referable to a new iron/bipy compound (**5**) (see Fig. 2), which we were unable to identify due to its very low concentration.

In order to gain further indications on the evolution of the iron precursor we acquired the ESI-MS spectra of samples (i) and (iii). The mass spectrum of sample (i) showed a major peak at  $m/z$  184, assignable to  $\text{Fe}(\text{bipy})_2^{2+}$ , accompanied by a smaller signal at  $m/z$  262 correspondent to  $\text{Fe}(\text{bipy})_3^{2+}$ ; a very small peak at  $m/z$  361 assignable to  $\text{Fe}(\text{bipy})(\text{OTf})^+$  was also present. Sample (iii), obtained



**Fig. 2.**  $^1\text{H}$  NMR spectrum ( $\text{CD}_3\text{CN}$ ) of the final reaction mixture of oxidation of cyclohexanol catalyzed by **1**.

at the end of the catalytic reaction, had MS signals identical to those observed for sample (i), but for the absence of the peak of  $\text{Fe}(\text{bipy})_3^{2+}$  at  $m/z$  262. Notably, in both samples no other signals assignable to further iron complexes were detected.

When the same NMR analysis above described was repeated using the same three-steps procedure, but in the presence of added bipy ( $[\text{bipy}]/[\mathbf{1}] = 3$ ), the spectra of samples (i) and (iii) showed a single notable difference, *i.e.* the absence in the final solution of the signals of the new iron species **5**.

These findings, in association with the results of the catalytic reactions discussed in the previous paragraph, support the hypothesis of dissociation of one bipy from complex **1** to give the catalytically active species, to which the iron species **5** present in the final solution is probably related. Conversely, in the presence of free bipy the dissociation of one ligand from the iron center is repressed, resulting in nearly complete suppression of the catalytic activity (see Table 2, entry 15) and in the consequent absence of complex **5** in the final reaction mixture. As a matter of fact, formation of the catalyst *via* dissociation of a nitrogen chelating ligand from the precursor was previously proposed in iron-catalyzed processes [27].

With regard to the nature of the catalytically active species, the very broad signals observed in the NMR spectra 1 h after addition of the peroxide suggest the formation of paramagnetic iron species in higher oxidation state. It is well known that in oxidation reactions the presence of iron in association with  $\text{H}_2\text{O}_2$  may give rise to the classical free radical mechanism, with indiscriminate, poorly selective reactivity, as opposed to metal-based mechanism, *i.e.* the desirable catalysis. When iron complexes with nitrogen polydentate ligands are used as catalysts, such reactions are believed to occur via a metal-based mechanism, whereas hydroxyl radicals do not seem to be involved [11a,b,14a,20,28]. According to mechanistic studies, initial reaction of the iron precursor with hydrogen peroxide gives an iron-peroxo, which in turn is transformed into a  $\text{Fe}(\text{IV})$  or  $\text{Fe}(\text{V})=\text{O}$  complex, the likely catalytically active species.

Support to this hypothesis was provided by trapping high-valent iron-oxo intermediates at low temperature [29].

#### 4. Conclusions

The iron compounds **1–4** with coordinated bipy, phen or substituted derivatives proved to be efficient catalysts for the oxidation of primary and secondary alcohols with hydrogen peroxide or TBHP. Although the ability of iron complexes to catalyze this reaction has been well documented, the present work introduces as catalyst precursors well characterized compounds in which with iron is associated to simple nitrogen bidentate ligands, at variance with most examples of iron oxidation catalysts previously reported with coordinated polydentate ligands which must be synthesized by a multi-step procedure. In spite of the preferred oxidation of secondary alcohols observed, selective oxidation of glycerol to DHA was not attained. The evolution of the iron precursor in the course of the catalytic reaction, monitored by NMR and ESI-MS, provided support to the hypothesis of formation of the catalytically active species via dissociation of one nitrogen ligand. Notably, the catalytic reactions here described are all examples of sustainable processes in terms of choice of catalyst (both metal and ligand), nature of oxidant and solvent as well as experimental conditions.

#### Acknowledgement

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.molcata.2016.05.023>.

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