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C–H benzylic oxidation promoted by dinuclear iron DBDOC iminopyridine complexes

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ABSTRACT

Several benzofurobenzofuran and methanodibenzodioxocine iminopyridine derivatives have been used as ligands to form mononuclear and dinuclear iron complexes. Complexes **6**, **7**, **8**, **9** and **10** were able to promote the catalytic oxidation of benzylic C–H bonds to ketones in moderate to high yields. The effects of backbone scaffold, nuclearity (mononuclear versus dinuclear) and nitrogen hybridization (iminopyridine versus aminopyridine) were studied. A strong effect on the yields of the nature and position of the substituents in the substrates was observed.

1. Introduction

The selective oxidation of saturated alkanes is a challenging reaction due to the high strength of C–H bond. This transformation can be promoted by homogeneous catalysts [1]. The reaction is of great interest for industry as a means to directly functionalize saturated hydrocarbons [2].

At the end of nineteenth century, Fenton reported an oxidising system based on Fe(II) complexes and hydrogen peroxide [3]. The application of this system allows the oxidation of C–H bonds via the generation of hydroxyl radicals and hence the reaction proceeds with low selectivity and functional group tolerance [4,5].

On the other hand it is well-known that biological systems perform selective oxidation of alkanes under mild conditions. For instance Methane Monooxygenase (MMO) oxidizes methane to methanol [6]. The aliphatic oxidation is catalyzed by two types of enzymes named heme and non-heme proteins [6,7]. These proteins were used as models to develop new iron-based catalytic systems that promoted the oxidation of aliphatic compounds [8–10].

The main drawback in the development of biomimetic ligands is the formation of radicals. Thus the ligand design focused on systems that should be capable to oxidize alkanes selectively avoiding the Fenton type oxidations. Non-heme ligands are more attractive ligands due to their tunability compared to heme ligands [8,9,11].

The first example of a stereospecific alkane hydroxylation promoted by an iron catalyst was reported by Que and co-workers [12]. The reaction was catalyzed by a tris(pyridin-2-ylmethyl) amine (TPA) iron complex. Also in 1997, Nishida and co-workers reported N^1,N^2-dimethyl-N^1,N^2-bis(pyridin-2-ylmethyl)ethane-1,2-diamine (BPMEN) as a convenient ligand system for iron promoted oxidations [13]. Modification of BPMEN resulted in interesting ligands for iron catalyzed C–H bond oxidations [14–16]. The two main structures of tetradentate ligands in iron catalyzed oxidation of alkanes are derived from TPA and BPMEN, having tripodal and linear structures, respectively [17]. 1,4-Dimethyl-7-(pyridin-2-ylmethyl)-1,4,7-triazonane (TACN) resulted in an interesting tetradentate N-donor ligand for the oxidation of alkanes [18,19]. These non-heme ligands are summarized in Fig. 1.

Recently, Bauer and co-workers, reported the use of iminopyridine iron complexes in the oxidation of activated C–H bonds to ketones under mild conditions [23,24]. With this precedent in mind, we considered of interest the application of Fe complexes with large bite angle N-ligands able to form dinuclear complexes as catalyst in the oxidation of C–H aiming at a possible cooperative effect of the two metals.

2. Results and discussion

Our group previously synthesized several imino- and aminopyridine DBDOC and BFBF compounds [25] which were used as ligands in the synthesis of iron mononuclear and dinuclear complexes. Reaction is summarized in Fig. 2.

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Table 1
Selected angles and distances for complex **6**.

Bond distance (Å)			
Fe1–N1	1.965(3)	Fe1–N4	1.965(2)
Fe1–N2	1.956(3)	Fe1–N5	1.948(3)
Fe1–N3	1.961(3)	Fe1–N6	1.946(3)
Angle (°)			
N6–Fe1–N5	85.94(14)	N2–Fe1–N1	81.67(13)
N5–Fe1–N2	86.87(13)	N3–Fe1–N1	94.55(13)
N6–Fe1–N3	90.65(13)	N6–Fe1–N4	91.21(12)
N2–Fe1–N3	96.91(13)	N5–Fe1–N4	93.57(12)
N6–Fe1–N1	93.99(13)	N2–Fe1–N4	93.67(11)
N5–Fe1–N1	90.88(13)	N3–Fe1–N4	81.28(11)

Crystals of complex **6** were grown from CH_3CN:Et_2O (Fig. 3). Complex **6** is composed by two Fe nuclei and two ligands **1** and is a dinuclear complex and present a long distance between both Fe nuclei (over 9 Å).

The iron centres showed an octahedral geometry with angles around 90° and short N–Fe distances, shorter than 2 Å (see Table 1), indicative of low spin complexes [26]. Several isomers could be formed when the present bidentate imine ligands coordinate to iron centres [23]. Complex **6** present the pyridine donors *trans* to one another.

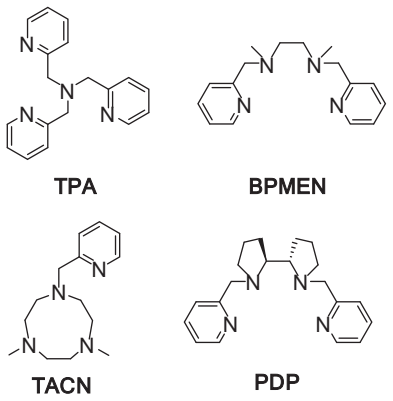


Fig. 1. Non-heme ligands used in C–H iron oxidations. A revolution in the iron catalyzed alkane oxidation was the work reported in 2007 by Chen and White [20]. An iron complex modified with (2*S*,2′*S*)-1,1′-bis(pyridin-2-ylmethyl)-2,2′-bipyrrolidine (PDP) gave rise to a selective catalyst for the hydroxylation of secondary and tertiary C–H bonds. Substrates can be transformed with predictable selectivity based on steric and electronic factors [20–22].

The different complexes were used as catalysts in the oxidation of diphenylmethane **11**. The reaction was optimized using catalyst **6**. Several parameters were shown to influence the reaction and the results of the optimization are summarized in Table 2. First the influence of oxidant loadings was explored. Large excesses of oxidant can contribute to faster catalyst decomposition; it was recently found that amide was formed by oxidation of the iminopyridine, but the amide complex was still active in catalysis [24]. A positive linear relationship between yield and quantity of oxidant was observed (entries 1–3). The usage of an internal standard led to depleted yields and thus an external standard was found to be required. It is suggested that changes in reaction media such as polarity or solubility causing inclusion of the internal standard were responsible for the decreased yields. Due to the decomposition of the metal centres by peroxides slow addition of the peroxide to the system was required [4,5,27,28]. In our case, when the total amount of peroxide was added at the beginning of the reaction (entry 3 versus 5) the conversion decreased and gas evolution was observed. Only pyridine and acetonitrile were tested as solvents (entries 3 and 6). Pyridine proved to be a more suitable solvent but since pyridine can readily coordinate to Fe and act as a good ligand, we decided to use acetonitrile as solvent. From the literature it is known that benzophenone can be prepared with low yields (8%) via a non-metal catalyzed reaction [24].

The reaction evolved quickly in the first 2 h and a chemical yield of 52% was determined. Later the reaction rate decreased and at 4 and 6 h only 68% and 73% yield were obtained. Despite this decrease in activity, the catalyst was still active, as after 20 h yield the reaction had progressed further to 82%. The concentration of ^{t}BuOOH decreased after 4 h due to decomposition, lowering the conversion and the reaction had almost stopped.

Finally different oxidants were tested in the iron catalyzed oxidation of diphenylmethane to benzophenone (Fig. 4). The best oxidant for this reaction was found to be *tert*-butyl hydroperoxide **13** which gave 73% yield after 6 h. Cumene hydroperoxide **14** was found to be a less suitable oxidant as only 15% yield was obtained. Surprisingly, hydrogen peroxide **15** gave the lowest yield of all tested oxidants, only 10%, which is most likely due to fast decomposition of hydrogen peroxide by the metal catalyst [4,5,27,28]. *meta*-Chloroperbenzoic acid (*m*-CPBA, **16**) gave yields of up to

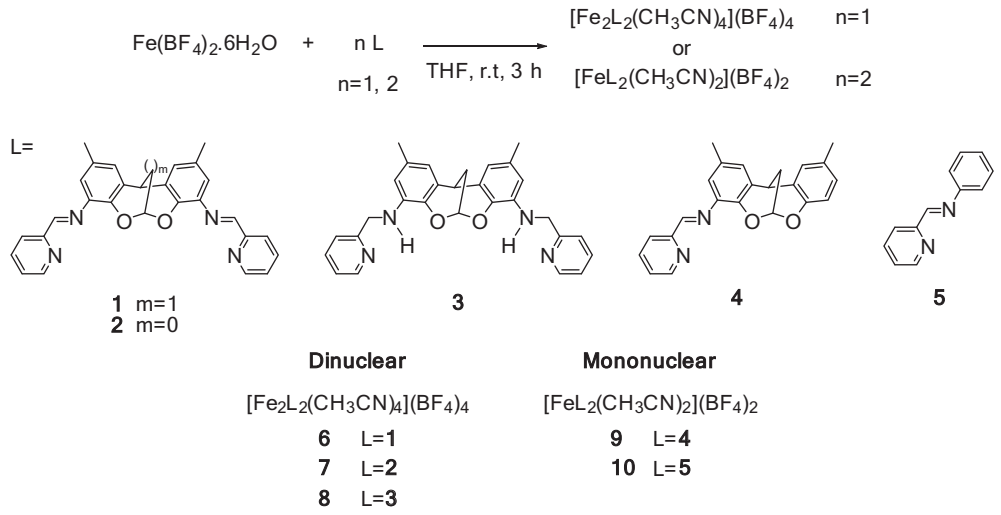


Fig. 2. Synthesis of mononuclear and dinuclear complexes with ligands **1**–**5** and catalysts **6**–**10**.

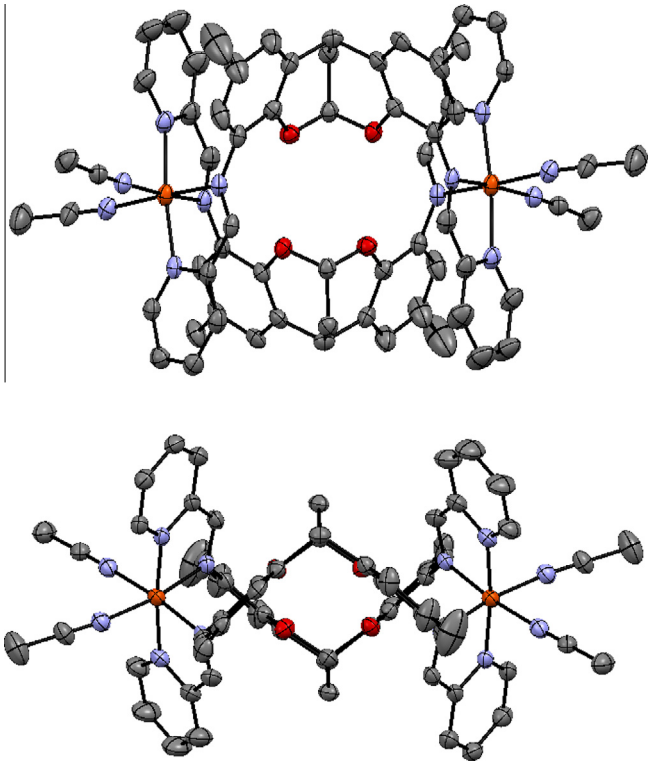
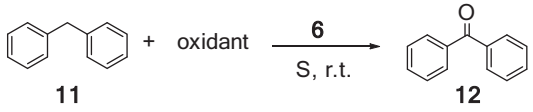


Fig. 3. ORTEP-plots (thermal ellipsoids shown at 50% probability levels) of complex **6**. Non-relevant hydrogen atoms and tetrafluoroborate counterions have been omitted for the sake of clarity.

Table 2
Diphenylmethane oxidation: optimization of reaction conditions.



Entry	Solvent	Oxidant eq.	Yield[a] (%)
1	ACN	4	30
2	ACN	6	49
3	ACN	8	73
4[b]	ACN	8	57
5[c]	ACN	8	65
6	Py	8	80

0.3 mmol of **11**, 0.015 eq. of **6**, oxidant ^{t}BuOOH in 0.5 mL of solvent, 6 h and r.t. Slow addition of oxidant over 30 min, every 5 min.

[a] Chemical yield determined by GC using *o*-dichlorobenzene as external standard.

[b] Internal standard.

[c] Fast addition of oxidant.

34% and this moderate conversion was attributed to the low solubility of the oxidant in the reaction media (410 mg in 0.5 mL of solvent).

Several substrates were screened, along with different Fe complexes. A schematic representation of the reaction is shown in Scheme 1.

The results obtained in the oxidation of diphenylmethane **11** with different iron catalyst are summarized in Table 3. Low to moderate conversions were obtained. The best yields were achieved with complex **6**, up to 73% (entry 1). The nature of the backbone was found to influence the activity, with catalyst **7** giving

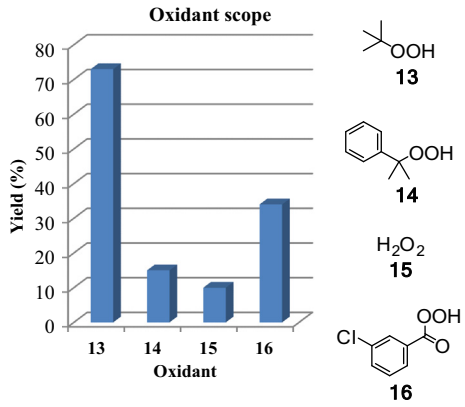
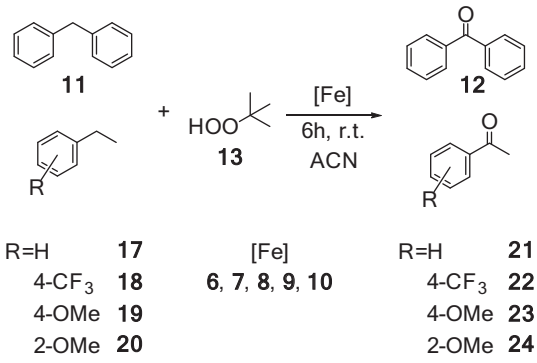


Fig. 4. Oxidant scope in the catalytic oxidation of **11**. Reaction conditions: 0.3 mmol of **11**, 0.015 eq. of **6**, in 0.5 mL of ACN, 6 h and r.t. Slow addition of oxidant, over 30 min, every 5 min. Chemical yield determined by GC using *o*-dichlorobenzene as external standard.



Scheme 1. Substrate and catalyst scope in iron catalyzed oxidation of benzylic C–H bonds.

Table 3
Diphenylmethane oxidation with iron complexes.

Entry	Catalyst	Chemical yield[a] (%)
1	**6**	73
2	**7**	50
3	**8**	20
4	**9**	41
5	**10**	49

0.3 mmol of **11**, 0.015 eq. of **6**, oxidant ^{t}BuOOH in 0.5 mL of ACN, 6 h and r.t. Slow addition of oxidant over 30 min, every 5 min.

[a] Chemical yield determined by GC using *o*-dichlorobenzene as external standard.

lower conversions (entry 2). The complex with aminopyridine **8** gave lower yields, 20%, probably due to the nature of the ligand. Monomeric species (entries 4 and 5) were found to perform similarly.

The conversion was affected by the electronic properties of the N-donor. For example, complex **8** containing the amino derivative was the worst catalyst for this transformation with only 20% yield (entry 3). It is known from literature that secondary amines can be oxidized in the presence of iron and oxidant [29,30], thus they are less stable than imine complexes and the conversion decreased for these ligands.

The catalytic oxidation was extended to ethylbenzene derivatives, the results of which are summarized in Fig. 5. Ethylbenzene is a more challenging substrate than diphenylmethane as it is less

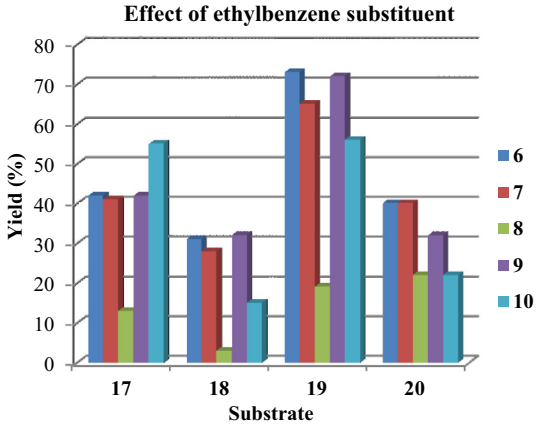


Fig. 5. Effect of substituents in ethylbenzene in iron catalyzed oxidation of benzylic C–H bonds. Reaction conditions: 0.3 mmol of substrate, 0.015 eq. of **6**, oxidant ^{t}BuOOH in 0.5 mL of ACN, 6 h and r.t. Slow addition of oxidant, over 30 min, every 5 min. Chemical yield determined by GC using *o*-dichlorobenzene as external standard.

activated towards oxidation. A similar trend was observed, iminopyridine complexes were more active than aminopyridine complexes. Likewise for **11**, no cooperative effect was observed as mononuclear and dinuclear complexes oxidize ethylbenzene to acetophenone **21** with comparable yields. Electronic effects were observed for substituents in the *para* position, substrates **18** and **19**. Thus EDG activated the substrate towards oxidation due to an increase of electron density of the ring and **19** was converted with up to 75% yield, which is very close to **11** which contains two aryl groups and is doubly activated. On the contrary, EWD groups in the substrates gave only 32% yields. The most hindered substrate, **20** gave lower yields and the best catalytic system gave only 40% (Fig. 4). Two different effects could explain this behaviour: (a) the steric hindrance could block the approach of the substrate to the iron centre and (b) the intermediate alcohol may coordinate as a chelate to the Fe catalyst, slowing down the reaction.

3. Conclusions

In summary, several iminopyridine and aminopyridine iron complexes were applied in the catalytic oxidation of benzylic C–H bonds. This reaction offered moderate to high yields which were highly affected by electronic and steric properties of the substrate; EWG containing and sterically demanding substrates were the most difficult to oxidize. As general trend the best catalyst was the dinuclear complex **6** containing ligand **1**. No cooperative effect between the iron nuclei was observed. The results presented in this work are comparable to those previously reported in literature [23,24].

4. Experimental

4.1. General considerations

Solvents were purchased from Sigma–Aldrich as HPLC grade and dried with an SPS system of ITC-inc. Reagents were used as commercially available. Gas chromatographic analyses were run on a Hewlett-Packard HP 5890A instrument (split/splitless injector, J&W Scientific, IA, 25 m column, internal diameter 0.25 mm, film thickness 0.33 mm, carrier gas: He, F.I.D. detector) equipped with a Hewlett-Packard HP 3396 series II integrator.

4.2. Synthesis of Fe complexes

A Schlenk tube was charged with $Fe(BF_4)_2{\cdot}6H_2O$ (34 mg, 0.1 mmol). Then 3 mL of dry THF and 0.1 mL of TEOF (0.6 mmol) were added. The solution was stirred for 30 min and it became light purple. Ligand was added (0.1 mmol) to the stirring solution. The resulting solution was allowed to stir during 3 h. Then 10 mL of dry diethyl ether were added and the solution was filtered and dried. The resulting solid was clean 3 times with diethyl ether and dried under vacuum.

$[Fe_2 1_2(CH_3CN)_4](BF_4)_4$, ***6***. Yield: 74% ^{1}H NMR (400 MHz, CD_3CN) δ = 10.50 (s), 9.68 (s), 7.31 (s), 6.35 (s), 6.06 (s), 5.15 (s), 3.67 (s), 3.45 (s), 3.25 (s), 1.30 (s), 1.15 (s), 0.91 (s). $C_{66}H_{60}B_4F_{16}Fe_2N_{12}O_4{\cdot}4H_2O$ (1616.41): Calc. C, 49.05; H, 4.24. Found C, 48.81; H, 4.24%.

$[Fe_2 2_2(CH_3CN)_4](BF_4)_4$, **7**. Yield: 65%. ^{1}H NMR (500 MHz, Acetonitrile-d_3) δ = 9.35–8.66 (m), 8.60–7.86 (m), 7.85–7.19 (m, 0H), 7.11–6.63 (m), 5.12 (m), 3.37–2.07 (m), 1.27 (s). $C_{64}H_{56}B_4F_{16}Fe_2N_{12}O_4{\cdot}4H_2O$ (1516.41): Calc. C, 48.40; H, 4.06. Found C, 48.56; H, 4.24%.

$[Fe_2 3_2(CH_3CN)_4](BF_4)_4$, ***8***. Yield: 71%. ^{1}H NMR (500 MHz, CD_3CN) δ = 8.54 (s), 8.01 (s), 7.99 (s), 7.92 (s), 6.57 (s), 6.32 (s), 6.07 (s), 4.76 (bs), 3.92 (s), 2.26 (s), 2.22 (s). $C_{66}H_{68}B_4F_{16}Fe_2N_{12}O_4{\cdot}4H_2O$ (1624.29): Calc. C, 48.80; H, 4.72. Found C, 48.52; H, 4.62%.

$[Fe4_2(CH_3CN)_2](BF_4)_2$, ***9***. Yield: 71% ^{1}H NMR (500 MHz, Acetonitrile-d_3) δ = 8.73 (d, J = 17.8 Hz), 8.35 (s), 7.78 (s), 7.15 (d, J = 30.8 Hz), 6.97–6.77 (m), 4.90 (s), 3.78 (d, J = 114.6 Hz), 2.70–2.07 (m), 1.34 (s). $C_{50}H_{46}B_2F_8FeN_6O_4{\cdot}3H_2O$ (1616.41): Calc. C, 55.69; H, 4.86. Found C, 55.35; H, 4.89%.

4.3. Catalytic tests

A Schlenk tube was charged with the substrate (0.3 mmol) and the catalyst (4.5 μmol) dissolved in ACN (0.5 mL). The oxidant tBuOOH (0.32 mL, 70 wt% in H_2O, 2.4 mmol) was slowly added within 30 min, and then solution was shaken for 6 h at room temperature. 0.2 mL of the solution were dissolved in 1 mL of DCM and the yield was determined by GC. After that 1 μL of solution was injected to a GC (Pressure = 111.7 KPa of He, T oven-initial = 50 °C during 0 min, ramp temperature 15 °C/min, Final oven temperature = 200 °C during 10 min, T inj = Tdet = 250 °C). Conditions were different for diphenylmethane (Pressure = 111.7 KPa of He, T oven-initial = 100 °C during 0 min, ramp temperature 25 °C/min, T oven-final = 320 °C during 10 min, T-inj = T-det = 250 °C).

4.4. X-ray crystallography

Measurements were made on a Bruker-Nonius diffractometer equipped with a APPEX 2 4 K CCD area detector, a FR591 rotating anode with Mo Kα radiation, Montel mirrors as monochromator and a Kryoflex low temperature device (T = −173 °C). Full-sphere data collection was used with w and j scans. Programs used: Data collection APEX2 V. 1.0-22 (Bruker-Nonius 2004), data reduction SAINT+Version 6.22 (Bruker-Nonius 2001) and absorption correction SADABS V. 2.10 (2003).

Empirical formula	$C_{72}H_{69}B_4F_{16}Fe_2N_{15}O_4$
Formula weight	1667.36
Space group	*P*4(2)/*n*
Unit cell dimensions	
a (Å)	23.7118(19)
α (°)	90.00
b (Å)	23.7118(19)
β (°)	90.00
c (Å)	3.5686(14)

(*continued on next page*)

γ (°)	90.00
U (Å^3)	7628.9(12)
Z, D_{calc}	4, 1.452 mg/m^3
M (mm^{-1})	0.478
F(000)	3416
Reflections collected	44832
Independent reflections	9123 [R_{int} = 0.1428]
Parameters	721
R_1, wR_2 [$I > 2\sigma(I)$]	0.0965, 0.2319
R_1, wR_2 (all data)	0.1660, 0.2641
Largest peak/hole (e Å^{-3})	0.777 and −0.638

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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.ica.2014.12.016.

References

[1] A.E. Shilov, G.B. Shul'pin, Chem. Rev. 97 (1997) 2879.
[2] J.F. Brazdil, Top. Catal. 38 (2006) 289.
[3] H.J.H. Fenton, J. Chem. Soc., Trans. 65 (1894) 899.
[4] J. Prousek, Pure Appl. Chem. 79 (2007) 2325.
[5] C. Pavan, J. Legros, C. Bolm, Adv. Synth. Catal. 347 (2005) 703.
[6] S. Friedle, E. Reisner, S.J. Lippard, Chem. Soc. Rev. 39 (2010) 2768.
[7] F.P. Guengerich, Chem. Res. Toxicol. 14 (2001) 611.
[8] L. Que, W.B. Tolman, Nature 455 (2008) 333.
[9] M. Costas, K. Chen, L. Que, Coord. Chem. Rev. 202 (2000) 517.
[10] M. Costas, Coord. Chem. Rev. 255 (2011) 2912.
[11] A. Correa, O. García, Chem. Soc. Rev. 37 (2008) 1108.
[12] C. Kim, K. Chen, J. Kim, L. Que, J. Am. Chem. Soc. 7863 (1997) 5964.
[13] T. Okuno, S. Ito, S. Ohba, Y. Nishida, Dalton Trans. (1997) 3547
[14] L. Gómez, I. Garcia-Bosch, A. Company, J. Benet-Buchholz, A. Polo, X. Sala, X. Ribas, M. Costas, Angew. Chem., Int. Ed. 48 (2009) 5720.
[15] L. Gómez, M. Canta, D. Font, I. Prat, X. Ribas, M. Costas, J. Org. Chem. 78 (2013) 1421.
[16] M. Canta, D. Font, L. Gómez, X. Ribas, M. Costas, Adv. Synth. Catal. 356 (2014) 818.
[17] K. Chen, L. Que, Chem. Commun. (1999) 1375
[18] A. Company, L. Go, M. Gu, X. Ribas, J.M. Luis, J. Am. Chem. Soc. 129 (2007) 15766.
[19] G. Roelfes, M. Lubben, R. Hage, L. Que, B.L. Feringa, Chem. Eur. J. 6 (2000) 2152.
[20] M.S. Chen, M.C. White, Science 318 (2007) 783.
[21] M.C. White, Science 335 (2012) 807.
[22] M.S. Chen, M.C. White, Science 327 (2010) 566.
[23] P. Shejwalkar, N.P. Rath, E.B. Bauer, Dalton Trans. 40 (2011) 7617.
[24] M. Lenze, E.T. Martin, N.P. Rath, E.B. Bauer, ChemPlusChem 78 (2013) 101.
[25] O. Martínez-Ferraté, Synthesis of Dinuclear Complexes. From Ligand Design to Catalysis, Universitat Rovira i Virgili, 2013. http://www.tesisenred.net/handle/10803/126531.
[26] S.C. Bart, E.B. Lobkovsky, E. Bill, K. Wieghardt, P.J. Chirik, Inorg. Chem. 46 (2007) 7055.
[27] M.D. Godbole, M.P. Puig, S. Tanase, H. Kooijman, A.L. Spek, E. Bouwman, Inorg. Chim. Acta 360 (2007) 1954.
[28] N. Carvalho, A. Horn, O. Antunes, Appl. Catal., A Gen. 305 (2006) 140.
[29] A. Machkour, D. Mandon, M. Lachkar, R. Welter, Eur. J. Inorg. Chem. 2005 (2005) 158.
[30] J. Larsen, K.A. Jsrgensen, J. Chem. Soc., Perkin Trans. 2 (1992) 1213.