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Mild alkane C–H and O–H oxidations catalysed by mixed-N,S copper, iron and vanadium systems

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ABSTRACT

Reactions of 1,6-bis(2'-pyridyl)-2,5-dithiahexane (Py_2S_2) with different sources of Cu(II), Fe(II) and V(III) afford the corresponding novel complexes [CuCl(Py_2S_2)]Cl (1), [CuCl(Py_2S_2)](CuCl₂) (1'), [Cu($Otf)_2(Py_2S_2$)] (2), [Cu(Py_2S_2)(H_2O)₂](OTf)₂ (2'), [FeCl₂(Py_2S_2)] (3), [Fe(Py_2S_2)(CH_3CN)₂][SbF₆]₂ (4) and [VCl₂(Py_2S_2)]Cl (5), bearing Py_2S_2 as a tetradentate ligand. All the compounds were characterised by IR, ESI-MS, elemental analyses and, in the cases of 1', 2' and 4, the molecular structures were also elucidated by single X-ray crystal diffraction analysis. Complexes 1–5 were evaluated as catalysts or catalyst precursors for the mild peroxidative oxidation of cyclohexane in acetonitrile typically at 25 °C and in the solvent-free oxidation of primary and secondary alcohols under microwave (MW) irradiation. The influences of the type and amount of acid promoter, amounts of oxidant and catalyst, time and temperature, on the product yields and TONs, are investigated.

The iron(II) complexes **3** and **4** are the most active catalysts in the oxidation of cyclohexane with H_2O_2 in a slightly acidic medium, leading to maximum overall yields (based on the alkane) of 38 and 28%, and turnover numbers (TON) up to 950 and 1450, respectively.

Additionally, the Cu and Fe complexes (1-4) proved to be useful catalysts in various MW-assisted alcohol oxidations at 80 °C with *t*-BuOOH. The oxidation of 1-phenylethanol catalysed by the Fe complex **3** in the presence of pyrazine-2-carboxylic acid (co-catalyst) is very fast, giving the acetophenone product (TOF=4470 h⁻¹) in good yield (75%) just after 5 min of reaction time.

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1. Introduction

Recent endeavours to find efficient metal-catalysed oxidative transformations of ubiquitous C–H and O–H bonds are fuelled by the possible direct conversion of largely available alkanes and other constituents of natural gas and petroleum, and possible oxygenated derivatives, to more valuable functionalised products for chemical industry [1–3]. Thus, the development of a selective, chemical, energy- and atom-efficient oxidation process is a key problem to be tackled.

In the biological systems, the activation of O_2 or H_2O_2 occurs in the active site of certain iron-, copper- and vanadium-containing metallobiomolecules that regulate the incorporation of oxygen into natural substrates, allowing for example the natural detoxification of certain xenobiotics [4–8]. The utilisation of peroxides as surrogates of dioxygen has been extensively investigated for the oxidation of various organic substrates [8,9], including amines, sulfides, alkanes, alkenes or alcohols. To date a truly efficient and selective oxidation system has not yet been found and the vast majority of the reported examples show either active, but unselective reactivity patterns, or selective, but often much less active, systems [9,10].

The catalyst models [9–12] for these types of reactions are often based on metal (*e.g.* Fe, Cu or V) complexes with polydentate pyridine-type ligands [13–18], polyamino alcohols [19–21], tris(pyrazolyl)borates and tris(pyrazolyl)methanes [22–24] or macrocyclic amino derived ligands [25]. Despite the fact that sulfur is a naturally occurring donor in the active centre of many metalloenzymes, oxidation catalysts based on all-S or mixed-N,S ligands have been little explored [9,12] if compared to their N- and Oanalogues in view of the concerns arising from their tendency to form sulfoxides or disulfides upon oxidation [4–8,26,27].

We have just reported an efficient $\{FeN_2S_2\}$ catalytic centre that can catalyse at room temperature the oxidation of cycloalkanes to cyclic alcohols and ketones, and of benzene to phenol, in the presence of certain heteroaromatic acids or nitric acid [28].

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Additionaly, Britvosek and co-workers recently reported the use of a series of tetradentate pyridine- and pyrazine-type ligands containing in the backbone unit either nitrogen, oxygen or sulfur donor atoms. In that work, it was found that the formed iron complexes bearing S-ligands, including the *linear* tetradentate ligand 1,6-bis(2'-pyridyl)-2,5-dithiahexane (Py₂S₂), were inactive in the oxidation of cyclohexane under the few experimental conditions tested [29].

Herein, we report the structural and catalytic properties of various novel Cu(II), Fe(II) and V(III) complexes, bearing this N,S-ligand (Py_2S_2), which we find to behave, in acidic medium, as catalyst precursors for the peroxidative oxidations of cyclohexane and alcohols (primary and secondary ones), focusing on the optimisation of the experimental conditions by varying in a systematic way different reaction parameters, such as the type of acid additives, the acid-to-catalyst and the oxidant-to-catalyst molar ratios and the amount of metal catalyst. Furthermore, the influence of microwave irradiation in the solvent-free oxidation by *t*-BuOOH of primary and secondary alcohols is reported and compared with conventional thermal experiments.

2. Experimental

2.1. General methods

Unless stated otherwise, all reactions and operations were carried out at room temperature under dinitrogen, by using standard Schlenk techniques. Solvents were dried and distilled before use and reagents were obtained from commercial sources (Aldrich) and used as received. 1,6-Bis(2'-pyridyl)-2,5-dithiahexane (Py₂S₂) was obtained by reacting 2-(chloromethyl)pyridine hydrochloride with 1,2-ethanedithiol in basic NaOH methanolic media, following a published method [30]. The vanadium complex [VCl₂(Py₂S₂)]Cl (**5**) was prepared according to the general procedure previously described [31] for the related [VX₂(Py₂S₂)]X (X = Br, I).

2.2. Catalyst preparation

2.2.1. $[CuCl(Py_2S_2)]Cl \cdot 0.6 H_2O(1 \cdot 0.6 H_2O)$

To a light yellow solution of Py_2S_2 (100 mg, 0.36 mmol) in MeOH (10 mL) was added CuCl₂ (48 mg, 0.36 mmol). The resulting green solution was stirred in air for 5 h and upon the addition of Et₂O a green precipitate appeared. This precipitate was filtered off, washed thoroughly with Et₂O and dried *in vacuo* to afford **1** as a dark green powder (132 mg, 87%). ESI–MS (positive mode, MeOH): m/z 374 {[CuCl(Py₂S₂)]}+.C₁₄H₁₆Cl₂CuN₂S₂·0.6H₂O (M = 421.68 g mol⁻¹): calcd. C 39.88, H 4.11, N 6.64, S 15.21; found C 39.39, H 3.81, N 6.41, S 15.29. IR (KBr) (selected bands): 3470 (w), 2939 (w), 2900 (w), 1600 (s), 1564 (m), 1482 (m), 1434 (m), 1260 (m), 1025 (m), 931 (m), 772 (vs), 706 (m) cm⁻¹.

2.2.2. $[Cu^{II}Cl(Py_2S_2)](Cu^{I}Cl_2)(1')$

Dark green single crystals of 1' were formed by slow diffusion of Et_2O in an equimolar acetonitrile mixture of $CuCl_2$ and Py_2S_2 .

2.2.3. $[Cu(OTf)_2(Py_2S_2)](2)$

Cu(OTf)₂ (130 mg, 0.36 mmol) was added to a light yellow solution of Py_2S_2 (100 mg, 0.36 mmol) in THF (10 mL). The resulting greenish blue mixture was stirred in air for 3 h. The formed precipitate was separated by filtration, washed with Et₂O and dried *in vacuo* (175 mg, 76%). ESI–MS (positive mode, CH₃CN): *m/z* 488 {[Cu(OTf)(Py_2S_2)]}⁺, 339 {[Cu(Py_2S_2)]}⁺. C₁₆H₁₆CuF₆N₂O₆S₄ (M = 638.11 g mol⁻¹): calcd. C 30.12, H 2.53, N 4.39, S 20.10; found C 30.07, H 2.51, N 4.18, S 20.03. IR (KBr) (selected bands): 3479 (w),

2967 (w), 2360 (w), 1605 (m), 1439 (m), 1257 (vs), 1240 (s), 1165 (s), 1032 (vs), 777 (s), 642 (vs), 518 (m) cm⁻¹.

2.2.4. $[Cu(Py_2S_2)(H_2O)_2](OTf)_2(2')$

X-ray quality single crystals of 2' were obtained by slow diethyl ether diffusion over a concentrated solution of 2 in CH₂Cl₂.

2.2.5. $[FeCl_2(Py_2S_2)] \cdot 0.5H_2O(3 \cdot 0.5H_2O)$

A suspension of FeCl₂·4H₂O (431 mg, 2.17 mmol) in CH₃CN (5 mL) was combined with Py₂S₂ (600 mg, 2.17 mmol) and stirred for 5 h under a dinitrogen atmosphere. The resulting yellow powder was filtered off, washed with Et₂O and dried *in vacuo* to yield **3** as a yellow solid (787 mg, 88%). ESI–MS (positive mode, CH₂Cl₂): *m/z* 367 {[FeCl(Py₂S₂)]}⁺, 277 {[Py₂S₂ + H]}⁺. C₁₄H₁₆Cl₂FeN₂S₂·0.5H₂O (M = 412.18 g mol⁻¹): calcd. C 40.80, H 4.16, N 6.80, S 15.56; found C 40.74, H 3.76, N 6.77, S 15.51. IR (KBr) (selected bands): 3429 (m), 3040 (w), 1599 (m), 1479 (s), 1435 (s), 1385 (m), 1161 (m), 1056 (s), 1014 (vs), 886 (s), 773 (vs), 715 (vs), 637 (m) cm⁻¹

2.2.6. $[Fe(Py_2S_2)(CH_3CN)_2][SbF_6]_2(4)$

Ag[SbF₆] (200 mg, 0.58 mmol) was weighted under dinitrogen and then added to a vigorously stirred yellow suspension of 3 (120 mg, 0.29 mmol) in CH₃CN (8 mL) contained in a Schlenk tube which was wrapped with aluminum foil to protect the sensitive silver salts from light. After stirring for 20h the purple solution was filtered several times through Celite and all the solvent was evaporated under an intense dinitrogen stream to furnish a purple powder of complex **4** in quantitative yield. Slow Et₂O diffusion over a concentrated solution of 4 in CH₃CN afforded cubic single crystals after *ca.* 24 h. ESI–MS (positive mode, CH₃CN): m/z567 { $[Fe(Py_2S_2)][SbF_6]$ }⁺, 277 { $[Py_2S_2 + H]$ }⁺, 166 { $[Fe(Py_2S_2)]$ }²⁺. C₁₈H₂₂F₁₂FeN₄S₂Sb₂ (M = 885.87 g mol⁻¹): calcd. C 24.40, H 2.50, N 6.32, S 7.24; found C 24.04, H 2.34, N 5.64, S 7.71. IR (KBr) (selected bands): 3447 (w), 3258 (w), 3197 (w), 2254 (m), 1627 (vs), 1530 (vs), 1466 (s), 1434 (s), 1396 (m), 1256 (m), 1172 (m), 1015 (m), 925 (m), 680 (m) cm^{-1} .

2.2.7. $[VCl_2(Py_2S_2)]Cl(5)$

This compound was prepared according to the general procedure previously described [31] for $[VX_2(Py_2S_2)]X$ (X = Br, I).

2.3. Characterisation techniques

C, H and N elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. Infrared spectra (4000–400 cm⁻¹) were recorded on a Bio-Rad FTS 3000MX instrument in KBr pellets and the wavenumbers are in cm⁻¹. Electrospray mass spectra were performed with an ion-trap instrument (Varian 500-MS LC Ion Trap Mass Spectrometer) equipped with an electrospray (ESI) ion source. For electrospray ionisation, the drying gas and flow rate were optimised for each sample with 35 psi nebuliser pressure. Scanning was performed from m/z = 50 to 1500. The compounds were observed in the positive mode (capillary voltage = 80–105 V).

X-ray quality single crystals of **1**′, **2**′ and **4** were obtained as indicated above. They were mounted in an inert oil within the cold N₂ stream of the diffractometer. Intensity data were collected using a Bruker AXS-KAPPA APEX II diffractometer with graphite monochromated Mo-K α radiation (λ = 0.71073 Å). Data were collected at 150 K using omega scans of 0.5° per frame and a full sphere of data was obtained. Cell parameters were retrieved using Bruker SMART software and refined using Bruker SAINT [32] on all the observed reflections. Absorption corrections were applied using SADABS [32]. The structures were solved by direct methods by using the SHELXS-97 package [33]. Calculations were performed using the WinGX System-Version 1.80.03 [34]. All hydrogen

Crystallographic data and structure refinement details for complexes 1', 2' and 4.

Data	1′	2'	4
Empirical formula	$C_{14}H_{16}ClCuN_2S_2$, Cl_2Cu	$C_{14}H_{20}CuN_2O_2S_2$, 2(CF ₃ O ₃ S)	C ₁₈ H ₂₂ FeN ₄ S ₂ , 2(F ₆ Sb)
$M_r/g \text{ mol}^{-1}$	509.84	674.12	885.87
crystal system	Triclinic	Monoclinic	Triclinic
space group	P-1 (No. 2)	C2/c (No. 15)	P-1 (No. 2)
a/Å	8.1471(9)	21.7145(8)	12.297(2)
b/Å	10.1037(11)	8.3387(3)	13.773(2)
c/Å	12.8616(14)	13.5446(6)	18.119(3)
$\alpha/^{\circ}$	68.283(6)	90	87.527(11)
β/°	84.602(7)	92.678(2)	87.716(12)
$\gamma/^{\circ}$	67.918(7)	90	69.762(11)
$V(Å^3)$	910.17(17)	2449.85(17)	2875.6(8)
Ζ	2	4	4
$D_{\rm c}/{\rm gcm^{-3}}$	1.860	1.828	2.046
μ (Mo K $lpha$)/mm ⁻¹	3.003	1.325	2.603
R _{int}	0.0449	0.0281	0.0973
No. of collected reflns	8428	13096	27670
No. of unique reflns	3289	3053	10469
Final $R1^a$, $wR2^b$ $(I \ge 2 \sigma)$	0.0412, 0.0832	0.0270, 0.0785	0.1027, 0.2561
GOF on F ²	1.015	1.169	1.057

^a $R1 = \Sigma ||F_0| - |F_c|| / \Sigma |F_0|.$

^b
$$wR2 = \left[\sum \left[w(F_o^2 - F_c^2)^2\right] / \sum \left[w(F_o^2)^2\right]\right]^{1/2}$$

atoms were inserted in calculated positions. Least square refinements with anisotropic thermal motion parameters for all the non-hydrogen atoms and isotropic for the remaining atoms were employed. Table 1 contains the crystallographic parameters for the described crystals. CCDC 819150–819152 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2.4. Catalytic tests

The batch catalytic studies in acetonitrile were performed in a Stem Omni Reactio Station with capacity for 10 reactors (50 mL) with no additional concerns to remove air or moisture prior the reactions. The catalytic investigations under microwave irradiation (10 W) were performed in a focused microwave CEM Discover reactor (10 mL, 13 mm diameter), fitted with a rotational system and an IR detector of temperature. The catalytic reactions were analysed by GC (gas chromatography) using a Fisons Instruments model 8160 gas chromatograph equipped with a DB-WAX (column length: 30 m; internal diameter: 0.32 mm; film: $0.25 \mu \text{m}$) capillary column (helium as a carrier gas) with a FID detector.

2.4.1. Peroxidative oxidation of cyclohexane with aqueous H_2O_2 in acetonitrile

Typical cyclohexane oxidation reactions were carried out in 50 mL screwtop glass reactors (Stem Omni Reactio Station) in air as follows: catalyst 1-5 (0.1-10 µmol), cyclohexane (1-5 mmol), $CH_3CN(3 mL)$ and acid additive (10–1000 μ mol). The reactors were placed on the reaction station and stirred vigorously at a controlled temperature of 25 °C. An aqueous solution of hydrogen peroxide (30%)(1-20 mmol) was then added and the reaction mixture stirred for 6 h. The product analysis was performed as follows: 90 µL of internal standard (cycloheptanone) and 10 mL of diethyl ether (to extract the substrate and the organic products from the reaction mixture) were added. To the obtained mixture was added an excess of triphenylphosphine before GC analysis, in order to reduce the formed cyclohexyl hydroperoxide to the corresponding alcohol, and hydrogen peroxide to water, following a method developed by Shul'pin [35,36]. After stirring the final reaction mixture for 10 min a sample was taken from the organic phase and then analysed by GC.

2.4.2. Peroxidative oxidation of alcohols with aqueous t-BuOOH 2.4.2.1. Conventional method. Oxidation reactions were carried out in air using a 25 mL round-bottom flask equipped with a reflux condenser. Under typical conditions, the catalyst **1–4** (10 μ mol) was placed to the flask, followed by the addition of the alcohol (5 mmol), pyrazine-2-carboxylic acid (Hpca) (50 μ mol) and an aqueous solution of *t*-BuOOH (70%) (10 mmol). In all cases, the reaction solutions were vigorously stirred for 30 min using magnetic bars. The desired reaction temperature (typically 80 °C) was maintained using an oil bath.

2.4.2.2. Microwave-assisted method. Typical oxidation reactions of alcohols were carried out in a sealed Pyrex tube under focused microwave irradiation as follows: alcohol substrate (5 mmol), catalyst **1–4** (10 μ mol) and Hpca (50 μ mol) were introduced into the reactor. Thereafter, an aqueous solution of *t*-BuOOH (70%) (10–15 mmol) was added and finally the cylindrical Pyrex reactor was placed in the microwave reactor. The system was left under stirring and irradiation (10 W) for 5–240 min at 80–120 °C temperature range.

2.4.2.3. Extraction and GC analysis for alcohol oxidations. The reaction mixtures were allowed to cool to room temperature and upon product extraction with 5 mL of CH₃CN, the internal standard 2-octanone (150 μ L) (in the case of the oxidation of linear alcohols), cyclopentanone (150 μ L) (in the case of cyclohexanol oxidation) or benzaldehyde (300 μ L) (in the case of 1-phenylethanol oxidation), was added and the system centrifuged. Then, diethyl ether (10 mL) was taken from the organic phase.

Blank tests indicate that only traces of acetophenone are generated from 1-phenylethanol in the absence of the copper or iron catalyst in the conventional method, while under MW-irradiation the formation of acetophenone does not exceed 6% in a metal-free system.

3. Results and discussion

3.1. Syntheses and spectroscopic characterisation of complexes 1–5

The mixed N,S-compound 1,6-bis(2'-pyridyl)-2,5-dithiahexane (Py_2S_2), bearing two thioether functions, reacted at room temper-



Scheme 1. Syntheses of copper(II) (1,2), iron(II) (3,4) and vanadium(III) (5) complexes.

ature with different Cu(II), Fe(II) and V(III) metal sources *i.e.*, CuCl₂, Cu(OTf)₂ (OTf=OSO₂CF₃), FeCl₂ or [VCl₃(THF)₃], respectively, to originate the corresponding chloro complexes [CuCl(Py₂S₂)]Cl **1**, [FeCl₂(Py₂S₂)] **3** and [VCl₂(Py₂S₂)]Cl **5** (Scheme 1, reactions *a*, *e* and *d*), and the triflate complex [Cu(OTf)₂(Py₂S₂)] **2** (Scheme 1, reaction *b*). The reactions with the Cu(II) salts were in acetonitrile and in air, while those with Fe(II) and V(III) were undertaken under N₂, in CH₃CN or THF, respectively. The di-acetonitrile iron complex [Fe(Py₂S₂)(CH₃CN)₂][SbF₆]₂ **4** was prepared by treating a CH₃CN solution of **3** with two equivalents of silver hexafluoroantimonate (Ag[SbF₆]) under a dinitrogen atmosphere for 20 h at room temperature (Scheme 1, reaction *f*).

Both Cu and Fe complexes **1–4** were obtained as air-stable solids, whereas the V complex **5** is very sensitive to O_2 and moisture, converting likely into high-valent oxo-vanadium derivatives [31]. All the complexes have been fully characterised by IR, ESI⁺–MS and elemental analyses, and, in the case of **4**, also by X-ray structural diffraction analysis (Fig. 1c). Crystallisation attempts of **1** and **2** afforded also $[Cu^{II}Cl(Py_2S_2)](Cu^{I}Cl_2)$ **1**' and $[Cu(Py_2S_2)(H_2O)_2](OTf)_2$ **2**', respectively, which have been char-

acterised only by X-ray analyses (Fig. 1a and 1b). Compound 1' possesses a $Cu^{I}Cl_{2}^{-}$ counter-ion, which was conceivably formed upon Cu^{II} reduction by the "soft" dithioether Py₂S₂ ligand [37,38]. In the case of the aqua derivative **2**', the two water ligands (from the moisture present in the crystallisation solvent) displaced the weakly coordinating triflate (OTf⁻) anions. The ESI⁺–MS spectra of the complexes reveal typically the [MX(Py₂S₂)]⁺ peak with the expected isotopic patterns.

3.2. X-ray crystal structures of complexes 1', 2' and 4

The molecular structures of $[Cu^{II}Cl(Py_2S_2)](Cu^{I}Cl_2)$ (1'), $[Cu(Py_2S_2)(H_2O)_2](OTf)_2$ (2') and $[Fe(Py_2S_2)(CH_3CN)_2][SbF_6]_2$ (4) were determined by X-ray crystallography and are shown in Fig. 1, while the selected distances and angles are listed in Tables 2 and 3.

In complex **1**' the copper ion exhibits a five-coordinate distorted trigonal bipyramidal conformation, but the metal centres in **2**' and **4** display six-coordinate octahedral geometries, with the chelating ligand adopting a *cis*- α configuration. The bond lengths of all three compounds lie in expected characteristic ranges [17,29]. A



Fig. 1. ORTEP diagrams of (a) [CuCl(Py₂S₂)]⁺ (cation of 1'), (b) [Cu(Py₂S₂)(H₂O)₂]²⁺ (dication of 2') and (c) [Fe(Py₂S₂)(CH₃CN)₂]²⁺ (dication of 4) showing the atom labelling scheme. The hydrogen atoms and counter ions were omitted for clarity.

Selected bond lengths (Å) and angles (°) for complexes $[CuCl(Py_2S_2)](CuCl_2)(1')$ and
$[Cu(Py_2S_2)(H_2O)_2](OTf)_2 (2').$

Complex 1'	
Cu1-S1 2.4317(12) Cu1-N1	1.996(4)
Cu1-S2 2.4363(13) Cu1-N2	1.995(4)
Cu1-Cl1 2.2733(13)	
Cl1-Cu1-S1 128.59(5) S2-Cu1-N2	84.27(12)
Cl1-Cu1-S2 140.18(5) Cl1-Cu1-N1	93.06(11)
S1-Cu1-S2 91.21(4) Cl1-Cu1-N2	92.89(11)
S1-Cu1-N1 84.74(10) N1-Cu1-N2	174.03(15)
S1-Cu1-N2 91.15(10)	
S2-Cu1-N1 91.48(11)	
Complex 2 ′	
Cu1-S1 2.5073(6) Cu1-O10	2.1543(15)
Cu1–N1 2.0091(15)	
S1-Cu1-S1 ⁱ 87.02(2) S1-Cu1-N1	83.66(4)
S1–Cu1–O10 177.49(5) S1–Cu1–N1 ⁱ	90.57(4)
S1 ^{<i>i</i>} -Cu1-O10 91.08(5) S1 ^{<i>i</i>} -Cu1-N1 ^{<i>i</i>}	83.66(4)
010–Cu1–O10 ^{<i>i</i>} 90.87(9) 010–Cu1–N1	98.00(6)
N1–Cu1–N1 ^{<i>i</i>} 172.05(8) O10 ^{<i>i</i>} –Cu1–N1	87.60(5)
O10 ⁱ -Cu1-N1 ⁱ	98.00(6)

Symmetry code to generate equivalent atoms: (i) 1 - x, y, 3/2 - z.

relevant difference in the structures of these complex cations concerns the $-S-CH_2$ -pyridyl moiety which, for **1**', is almost plane ($C_{pyridyl}-C_{pyridyl}-C-S$ torsion angle of *av*. 172.56°), while for the other cations it is markedly twisted. Indeed, for **2**' this torsion angle is of 142.78° and for **4**, which presents two independent complex units in the asymmetric unit, that parameter assumes the average values of 145.64° for the Fe1 containing cation, and 151.79° for the Fe2 one. Additionally, the angles between the planes of the two pyridyl rings are also quite different, taking values of 84.86° (**1**'), 67.17° (**2**') or 53.73° and 56.77° (**4**, Fe1 and Fe2 cations, respectively).

3.3. Catalytic results

The catalytic study focused on the use of cyclohexane and various alcohols, mainly 1-phenylethanol, as model substrates for the investigation of the catalytic properties of the Cu(II) (**1**,**2**), Fe(II) (**3**,**4**) and V(III) (**5**) complexes bearing the bis-pyridyl dithioether ligand, under mild oxidations using hydrogen peroxide (H_2O_2) and *tert*-butyl hydroperoxide (*t*-BuOOH) as oxidants.

Table 3

Selected bond lengths (Å) and angles (°) for the two independent molecules of $[Fe(Py_2S_2)(CH_3CN)_2][SbF_6]_2~({\bf 4}).$

Ι		II	
Fe1-S11	2.249(6)	Fe2-S21	2.244(5)
Fe1-S12	2.249(5)	Fe2-S22	2.245(6)
Fe1-N31	1.999(14)	Fe2-N41	2.017(17)
Fe1-N51	1.952(16)	Fe2-N61	1.973(15)
Fe1-N11	1.954(18)	Fe2-N21	1.944(17)
Fe1-N12	1.940(16)	Fe2-N22	1.937(17)
S11-Fe1-S12	90.9(2)	S21-Fe2-S22	89.9(2)
S11-Fe1-N31	89.7(5)	S21-Fe2-N41	84.2(5)
S11-Fe1-N51	85.4(5)	S21-Fe2-N61	89.8(5)
S11-Fe1-N11	178.3(5)	S21-Fe2-N21	178.4(6)
S11-Fe1-N12	90.2(5)	S21-Fe2-N22	91.8(5)
S12-Fe1-N31	85.0(5)	S22-Fe2-N41	93.4(4)
S12-Fe1-N51	89.1(6)	S22-Fe2-N61	84.3(4)
S12-Fe1-N11	90.6(5)	S22-Fe2-N21	89.8(5)
S12-Fe1-N12	178.8(5)	S22-Fe2-N22	178.3(6)
N11-Fe1-N12	88.3(7)	N21-Fe2-N22	88.6(7)
N11-Fe1-N31	89.7(7)	N21-Fe2-N41	94.3(7)
N11-Fe1-N51	95.4(7)	N21-Fe2-N61	91.7(8)
N12-Fe1-N31	94.6(7)	N22-Fe2-N41	87.2(6)
N12-Fe1-N51	91.4(7)	N22-Fe2-N61	95.2(6)
N31-Fe1-N51	172.3(7)	N41-Fe2-N61	173.6(7)



Scheme 2. Oxidation of cyclohexane with H_2O_2 catalysed by Cu (1,2), Fe(3,4) or V (5) compounds.

Although it was reported [29] that the related iron complex $[Fe(OTf)_2(Py_2S_2)]$ was inactive in the oxidation of cyclohexane with H_2O_2 in acetonitrile, in that study it was not investigated the possible effect of additives and only a few experimental conditions were tested.

In the current work, under our conditions, the catalytic activity of 1-5 was disclosed. At the initial stage of our study, we screened all the complexes 1-5 in the presence of various acid additives and with the purpose to find the most active system (complex/acid) in the oxidation, with H₂O₂ at 25 °C, of cyclohexane (CyH) to cyclohexyl hydroperoxide (CyOOH), cyclohexanol (CyOH) and cyclohexanone (Cy' = 0) (Scheme 2). Under our typical conditions, *i.e.* 10 µmol catalyst, 200 µmol of acid additive, 5 mmol CyH, 7 mmol H_2O_2 (25 °C, 6 h), the primary product of the cyclohexane oxidation is CyOOH, as revealed by the quite different amounts of cyclohexanol and cyclohexanone in the GC analyses before and after quenching the reaction with an excess of triphenylphosphine (PPh₃), which quantitatively reduces CyOOH to CyOH, following a method developed by Shul'pin [35,36]. Thus, all catalytic runs were analysed after the addition of PPh₃ for accurate determination of the final oxygenated products, *i.e.* CyOH and Cy' = 0.

3.3.1. Effect of different acid additives

The dramatic role of certain additives, in particular acids, on the activity in oxidation catalysis of various transition metal complexes, *e.g.* of Cu, Fe and V, is well known [20,21,35,36,39–42]. Vanadium centres combined with different heteroaromatic [41], sulfuric and oxalic [42] acids as co-catalysts can be very active in peroxidative oxidations of cyclic, linear and branched saturated hydrocarbons. In several bioinspired Fe-catalysed oxidations of alkanes, alkenes and other organic molecules, the addition of acetic acid (typically 50–100 equivalents relatively to the Fe catalyst) resulted in significant improvements of activity and selectivity [15,18,43–45].

Recently, we have also reported an ${FeN_2S_2}$ catalytic system that exhibited a good activity in the oxidation of cycloalkanes and benzene in the presence of certain heteroaromatic acids or nitric acid [28].

Hence, the catalytic oxidations of cyclohexane by complexes **1–5** were examined in the presence of different acid additives, such as pyrazine-2-carboxylic acid (Hpca), nitric acid (HNO₃), hydrochloric acid (HCl), triflic acid (HOTf), acetic acid (AcOH) and trifluoracetic acid (TFA) (Table 4).

In the absence of acid, the overall yields (CyOH and Cy' = O) (after treatment with PPh₃) are practically equal (4-5%) for the reactions catalysed by complexes **2**, **3** and **5**, what contrasts with

Table 4	
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Effect of different acids on the oxidation of cyclohexane catalysed by 1-5.ª

Entry	Acid	n(acid)/n(catalyst)	Overall yield ^{b,c} (%)				
			1	2	3	4	5
1	-	0	9.8(1.8 ^d)	4.3	4.8	1.3	4.0
2	Hpca	5	0.2	0.5	13.8(12.9 ^e)(13.5 ^f)	17.1	11.0(12.7 ^g)
3	HNO ₃	20	6.2	4.4	$18.0(4.2^{d})$	16.7	7.2
4		40	5.7	6.9	16.5	14.6	9.8
5		100	3.0	5.1	10.6	9.3	12.6
6	HCl	20	7.1	14.5	6.6	4.5	8.5
7		40	6.3	3.8	1.0	1.8	7.4
8	HOTf	20	7.9	6.2	13.9	22.9	7.5
9	AcOH	20	11.8	5.2	3.3	1.0	4.8
10	TFA	20	7.3	5.0	20.2(22.1 ^g)	11.3	5.7

^a Reaction conditions (unless stated otherwise): CH₃CN (3 mL), cyclohexane (5 mmol), catalyst (10 µ.mol), H₂O₂ (7 mmol), reaction time (6 h), temperature (25 °C). ^b Molar yield (%) based on cyclohexane, *i.e.* number of moles of product per 100 moles of substrate, determined by GC after treatment with PPh₃; molar yields (%) based

on H₂O₂, if required, can be estimated as TON \times 100 \times n(catalyst)/n(H₂O₂).

^c Cyclohexanol and cyclohexanone (after treatment with PPh₃).

^d Reaction carried out in the presence of diphenylamine (DPA) (5 mmol).

 $^{e}\,$ Controlled addition of $H_{2}O_{2}$ during 15 min.

^f Controlled addition of H₂O₂ during 5 h.

^g Reaction carried out at 40 °C.

Table 5

Effect of the acid promoter-to-catalyst molar ratio on the oxidation of cyclohexane catalysed by 3.^a

Entry	Acid	n(acid)/n(catalyst)	Yield ^b (%)	Yield ^b (%)		
			СуОН	Cy' = 0	Overall ^c	
1		0	2.3	2.5	4.8	24.0
2		1	6.5	0.2	6.7	33.5
3		5	17.0	1.7	18.7	93.5
4	HNO ₃	10	17.1	1.5	18.6	93.0
5		20	14.6(4.0 ^e)	3.4(10.8 ^e)	18.0(14.8 ^e)	90.0
6		40	14.8	1.7	16.5	82.5
7		1	5.8	0.4	6.2	31.0
8		5	12.9	0.9	13.8	69.0
9	TFA	10	15.8	1.3	17.1	85.5
10		20	18.6(4.5 ^e)	$1.6(10.6^{e})$	20.2(15.1 ^e)	101.0
11		40	17.0	1.3	18.3	91.5

^a Reaction conditions: CH₃CN (3 mL), cyclohexane (5 mmol), catalyst (10 µmol), acid additive (0–400 µmol), H₂O₂ (7 mmol), reaction time (6 h), temperature (25 °C).

^b Molar yield (%) based on cyclohexane, *i.e.* number of moles of product per 100 moles of substrate, determined by GC after treatment with PPh₃.

^c Cyclohexanol and cyclohexanone (after treatment with PPh₃).

^d Turnover number (moles of product per mol of metal catalyst).

^e GC analysis carried out before the addition of PPh₃.

the very weak activity of **4** (*ca.* 1%) and a moderate activity of **1** (*ca.* 10%, TON = 49). The addition of the heteroaromatic acid Hpca has a divergent effect on the various catalytic systems. The oxidations catalysed by the Cu complexes **1** and **2** are inhibited by Hpca, while a marked yield growth is observed for the Fe **3** and **4**, and V **5** catalysed reactions, in accord with previous reports [21,25,46–50] of the co-catalytic effect of Hpca and other acids for different systems. In general, we observe that the addition of acid to the Cu systems **1** and **2** does not influence significantly the overall yield, except for enhanced catalytic activity of the system **2**/HCl (*ca.* 15% yield).

The vanadium catalyst **5** showed its maximum activity in the presence of Hpca and for the higher tested amounts of HNO₃, *ca.* 11% and 13%, respectively.

A positive effect was displayed by both iron complexes **3** and **4** in the presence of any acid additive, except for high acid-tocatalyst molar ratios and for AcOH (inhibition effect). Among all the catalyst/acid systems surveyed, the iron **3**/TFA and **4**/HOTf combinations exhibited the highest activities, 20% (TON = 101) and 23% (TON = 115) yields, respectively.

Performing the reactions at 40 °C for the systems **3**/TFA (Fe) and **5**/Hpca (V) lead only to a slight enhancement of activity from *ca.* 20 to 22% and from *ca.* 11 to 13%, respectively (Table 4, entries 2 and 10).

The influence of the H_2O_2 addition rate to **3**/Hpca (Table 4, entry 2) was also investigated, but the yields obtained for the single and controlled 15 min and 5 h additions are comparable (*ca.* 13–14%). This suggests that no major decomposition of the peroxide to H_2O and O_2 occurs in the beginning of the reaction and that the rate of addition does not alter considerably the reaction efficiency.

Based on these results, we selected the best catalytic systems, *i.e.* the iron **3**/TFA and **4**/HOTf, and attempted the optimisation of the acid and oxidant amounts, and the obtained results are summarised in Tables 5 and 6, and Figs. 2 and 3 (see also in Supplementary data – Tables S1 and S2).

3.3.2. Effect of acid amount and time

Since the amounts of the oxygenated products are expected [19-21,28,43-45] to depend on the quantity of the acid promoter, in search for the optimal conditions we varied the acid promoter-to-catalyst molar ratio in the oxidations catalysed by **3** and **4**. Tables 5 and 6 show the variation of the CyOH and Cy' = O yields under various acidic conditions and in Fig. 2 is depicted the dependence of the overall yield as a function of the acid amount.

The oxidation of cyclohexane by the system $3/HNO_3$ has the maximum overall yield and TON (*ca.* 19% and 94, respectively) (Table 5, entry 3) for the considerably low amount of 50 µmol of HNO₃ (acid-to-catalyst molar ratio = 5) and remains practically



Fig. 2. Overall yields in the Fe-catalysed oxidation of cyclohexane by (a) **3** and (b) **4** as function of the amounts of nitric (●, circles), trifluoroacetic (■, squares) and triflic (♦, diamonds) acid promoters. Reaction conditions: CH₃CN (3 mL), CyH (5 mmol), H₂O₂ (7 mmol), catalyst (10 µmol), acid additive (0–400 µmol), 25 °C, 6 h.

constant (19–17%) for higher acid-to-catalyst molar ratios (Table 5, entries 4–6). In the presence of TFA a higher acid-to-catalyst molar ratio of 20 is required to reach the maximum activity (overall yield of 20% and TON of 101) (Table 5, entry 10). Furthermore, the sharp differences observed in the GC analyses, concerning the yields of CyOH and Cy' = 0, before and after the treatment of the reaction mixture with triphenylphosphine (PPh₃) (Table 5, entries 5 and 10), hints at the formation of cyclohexyl hydroperoxide (CyOOH) as the major product of these oxidations. The appreciable deviation of the overall yields, before and after the addition of PPh₃, results from the likely decomposition of CyOOH under the GC conditions into other products (*e.g.* adipic acid) [51] rather than only CyOH and Cy' = 0 [35,36].

In the case of the di-acetonitrile complex 4, we found that nitric acid (HNO₃) and triflic acid (HOTf) are the most favourable acids and their relative amounts were optimised (*ca.* 10 and 20 acid-to-catalyst molar ratios, respectively) as summarised in Table 6 and depicted in Fig. 2b.

The oxidation catalysed by **4** proceeds more efficiently in the presence of the very strong acid HOTf, but is more sensitive to the variation of the acid relative amount. For a HOTf/**4** molar ratio of 20 the very good overall yield of 23% (TON = 115) was attained (Table 6,

entry 10), which dropped to less than half for a 2-fold increase of the triflic acid content. The yields of Cy' = 0 remain in the 2–3% range for acid amounts of 50–200 µmol (which correspond to acid-to-catalyst ratios of 5–20), but, for higher HNO₃ amounts, a *ca.* 2-fold increase of Cy' = 0 content is observed (4.6%, Table 6, entry 6), and for both systems (**4**/HNO₃ and **4**/HOTf) an overall yield drop is then observed. The cyclohexane oxidations catalysed by **4**/HOTf were also performed for different reaction times of 1, 3, 6, 12 and 24 h (Table 6, entries 10–14). The CyOH yield remains invariant after 6 h (*ca.* 20%), whereas only a slight increase is observed for the Cy' = O yield upon prolonged reaction times (12 and 24 h) (Table 6, entries 13 and 14), thus resulting in a hardly noticeable enhancement of the overall yield.

3.3.3. Effect of oxidant amount

The influence of the H_2O_2 concentration in the product distribution for the cyclohexane oxidation is shown in Fig. 3 and Table S1 (Supplementary data). It should be pointed out that these experiments were carried out using only 1 mmol of CyH and 10 µmol of Fe catalysts **3** or **4** (*i.e.* 1.0 mol%) and that the maximum overall yields of *ca.* 38% and 28%, respectively, were achieved for a peroxide-to-catalyst molar ratio of 500 (which corresponds to



Fig. 3. Dependence of the CyOH (♦, diamonds), Cy' = O (●, circles) and overall (■, rectangles) yields on the oxidant-to-catalyst molar ratio in the oxidation of cyclohexane catalysed by (a) 3 and (b) 4. Reaction conditions: CH₃CN (3 mL), CyH (1 mmol), H₂O₂ (0–20 mmol), catalyst (10 µmol), acid additive (200 µmol), 25 °C, 6 h.

Effect of the acid promoter-to-catalyst molar ratio on the oxidation of cyclohexane catalysed by $\mathbf{4}^{a}$

Entry	Acid	n(acid)/n(catalyst)	Yield ^b (%)			TONd
			СуОН	Cy′ = O	Overall ^c	
1		0	0.8	0.5	1.3	6.5
2		1	1.6	0.4	2.0	10.0
3	UNO	5	10.1	2.4	12.5	62.5
4	HINO ₃	10	14.3	2.6	16.9	84.5
5		20	14.5	2.2	16.7	83.5
6		40	10.0	4.6	14.6	73.0
7		1	1.2	0.4	1.6	8.0
8		5	6.8	1.8	8.6	43.0
9		10	15.7	2.5	18.2	91.0
10 ^e		20	6.9	1.3	8.2	41.0
11 ^f	HOTf	20	15.5	2.1	17.6	88.0
12		20	20.3	2.6	22.9	115
13 ^g		20	20.7	3.4	24.1	121
14 ^h		20	20.3	4.1	24.4	122
15		40	7.5	2.0	9.5	47.5

^a Reaction conditions (unless stated otherwise): CH_3CN (3 mL), cyclohexane (5 mmol), catalyst (10 μ mol), acid additive (0–400 μ mol), H_2O_2 (7 mmol), reaction time (6 h), temperature (25 °C).

^b Molar yield (%) based on cyclohexane, *i.e.* number of moles of product per 100 moles of substrate, determined by GC after treatment with PPh₃.

^c Cyclohexanol and cyclohexanone (after treatment with PPh₃).

^d Turnover number (moles of product per mol of metal catalyst).

^e Reaction time: 1 h.

f Reaction time: 3 h.

- g Reaction time: 12 h.
- h Reaction time: 24 h.

the H_2O_2 -to-substrate molar ratio of 5:1). Further increasing the H_2O_2 amount results in a lower activity, conceivably associated to overoxidation reactions and diminished alkane solubility due to the higher water content of the reaction medium. Both iron(II) systems **3**/TFA and **4**/HOTf show a similar behaviour (Fig. 3a and b, respectively) in relation to the H_2O_2 amount. Despite the labile acetonitrile ligands in complex **4**, the chloride system **3**/TFA displays a significantly higher activity.

3.3.4. Effect of catalyst amount

The effect of the catalyst amount on the overall yield and TON was also investigated and is illustrated in Fig. 4 and Table S2 (Supplementary data). In the case of the **3**/Hpca system, the maximum TON of 950 (corresponding to 9.5% of overall product yield) was achieved at 25 °C for a substrate-to-catalyst molar ratio of 10,000, while for **4**/HOTf even higher TONs of 1450 and 1190 (corresponding to 3 and 12% of overall yields) were obtained for substrate-to-catalyst molar ratios of 50,000 and 10,000 (Fig. 4 and Table S2).



Fig. 4. Effect of the amount of catalysts precursors **3** (black bars) and **4** (grey bars) on the turnover number (TON) in the catalytic oxidation of cyclohexane. Reaction conditions: CH_3CN (3 mL), CYH (5 mmol), H_2O_2 (7 mmol), catalyst (0–10 μ mol), catalyst/acid additive molar ratio (1/20), 25 °C, 6 h.

The maximum yields and turnover values reported with these systems based on mononuclear Fe **3** and **4** complexes are among the best ones reported so far in the oxidation of cyclohexane under mild conditions ($25 \,^{\circ}$ C) and are comparable to those obtained with a few polynuclear iron and copper species [19,20,52,53].

3.3.5. Microwave-assisted solvent-free peroxidative oxidation of alcohols

The catalytic performance of the Cu(II) and Fe(II) complexes was also surveyed in the oxidation of different alcohols. The studies were based on a recent procedure reported by some of us [54,55], by using a very low power of microwave irradiation to accelerate the solvent-free oxidation of primary and secondary alcohols with aqueous *t*-BuOOH in the presence of the catalysts **1–4** and using Hpca as additive. Various alcohols were tested as substrates, including 1-phenylethanol and various C₆ alcohols (linear and cyclic), and, as expected, the yields are much higher than those achieved for cyclohexane oxidation, in view of the higher reactivity of the O–H bonds. The ketones are the only oxidation products obtained from these MW-assisted transformations and the high selectivities observed (typically > 98%) were confirmed by mass balances.

The copper(II) complexes 1 and 2 catalyse poorly the peroxidative oxidation of 1-phenylethanol under MW at 80°C, leading, respectively, to 29 and 13% yields of acetophenone after 30 min (Table 7, entries 2 and 4). Once again, Hpca demonstrated an inhibitory effect on the Cu-catalysed reactions and, in particular for the oxidation of 1-phenylethanol, a significant yield drop from ca. 29% to 3% was observed for the 1/Hpca system (Table 7, entries 2 and 3). In contrast, the efficiency of the iron-catalysed oxidations is dramatically improved by Hpca and 76% yield of acetophenone is obtained after 30 min at 80 °C. The reaction is very fast; in fact after 5 min the maximum yield is nearly reached (75%, Table 7, entry 11). Moreover, the reaction strongly depends on the temperature and at 120 °C the maximum yield of 80% was attained after 15 min (Table 7, entry 8). Using lower catalyst loadings (i.e. 1 µmol, which corresponds to a substrate-to-catalyst molar ratio of 5000), the maximum TON of 835 and TOF of $8580 h^{-1}$ (Table 7, entries 10 and 12), corresponding to yields of 17 and 14%, were achieved for the short reaction times of 15 and 5 min. The oxidation of 1-phenylethanol by 3/Hpca under conventional thermal heating (80°C) is much less efficient furnishing the acetophenone product in 26% yield after 30 min (compare Table 7, entries 6 and 13). Somehow unexpectedly, the di-acetonitrile Fe complex 4 exhibited a much lower activity than the related dichloro-complex 3, leading to the acetophenone yield of only 22%.

The activity of the **3**/Hpca system in the oxidation of other alcohols is rather modest since only moderated yields were obtained in the oxidation of cyclohexanol (36%, Table 7, entry 15), 1-hexanol (16%, Table 7, entry 18), 2-hexanol (28%, Table 7, entry 16) and 3hexanol (32%, Table 7, entry 17) for the extended reaction time of 240 min at 80 °C.

As mentioned above, the addition of pyrazine-2-carboxylic acid (Hpca) has an opposing effect on the Cu and Fe systems, since it acts as strong inhibitor for both cyclohexane and 1-phenylethanol Cucatalysed oxidation reactions (compare entries 1 and 2 in Table 4 and entries 2 and 3 in Table 7) and as a potent co-catalyst in the case of Fe-catalysed oxidations, *e.g.*, *ca.* 15-fold yield boosts were observed in the oxidation of 1-phenyethanol upon addition of Hpca (compare entries 5 and 6 in Table 7).

The active catalytic species in our reaction mixtures could not be discovered, but by reacting Hpca with the Cu and Fe complexes we attempted to shed light into the type of complexes formed. Hence, we studied the reactivity of the chloro-complexes of Cu 1 and Fe 3 with Hpca (2 equivalents) and attempted to use the formed species as catalysts for comparison with the corresponding 1/Hpca and 3/Hpca systems. The reaction of copper(II) 1 with Hpca

Solvent-free and MW-assisted oxidation of different alcohols with t-BuOOH catalysed by 1-4.^a

Entry	Substrate	Catalyst	Time (min)	Product	Yield ^{b,c} (%)	TONd	TOF (h ⁻¹) ^e
1		-	30		6.5	_	-
2 ^f		1	30		29.3	147	293
3		1	30		2.6	13.0	26.0
4 ^f		2	30		12.7	63.5	127
5 ^f		3	30		4.9	24.5	49.0
6		3	30		76.3	382	763
7 ^g		3	30		3.2	16.0	32.0
	OH CH ₃			CH ₃			
8 ⁿ		3	15		80.1	401	1602
9		3	15		75.4	377	1508
10 ¹		3	15		16.7	835	3340
11		3	5		74.5	373	4470
12		3	5		14.3	715	8580
13		3	30		26.3	132	263
14		4	30		22.4	112	224
15	ОН	3	240	0	35.9	180	44.9
16	OH	3	240	○ ↓	28.3	142	35.4
17	OH	3	240	o IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	31.7	159	39.6
18 ^k	V∕∕OH	3	240	ОН	15.9	79.5	19.9
19 ^{к,1}		3	240		16.7	83.5	20.9

^a Reaction conditions (unless stated otherwise): substrate (5 mmol), catalyst **1-4** (10 µmol), Hpca (50 µmol), t-BuOOH (10 mmol, aq. 70%), reaction time (30 min), MW irradiation (10 W power), temperature (80 °C).

^b Molar yield (%) based on substrate, *i.e.* number of moles of product per 100 moles of substrate, determined by GC.

^c In all reactions, selectivity was >98%.

^d Turnover number (moles of product per moles of metal catalyst).

^e Turnover frequency (TON per hour).

^f Reaction carried out in the absence of Hpca.

^g Reaction carried out in the presence of diphenylamine (DPA) (5 mmol).

^h Reaction performed at 120 °C.

ⁱ Catalyst loading of 1 µmol and 5 µmol of Hpca.

^j Reaction carried out under conventional thermal heating at 80 °C during 30 min.

^k Traces of hexanal were detected (<1%).

¹ *t*-BuOOH amount of 15 mmol.

in MeOH afforded after 2 h a light blue insoluble precipitate, which was isolated by filtration and thoroughly washed with methanol and diethyl ether. The elemental analysis of this compound reveals a very low percentage of sulfur (<2%) and is consistent with the tentative formulation of [Cu(pca)₂] (with methanol) as the main product. In accord, the ESI⁺–MS and IR spectra show peaks at m/z 340, assigned to [Cu(pca)₂(MeOH)]⁺, and 1637 cm⁻¹ [ν (CO)], respectively. These observations support the replacement of the ligated Py₂S₂ by two chelating pca⁻ ligands.

In the case of the iron(II) **3** complex, although we failed to isolate a pure compound, the equimolar reaction with Hpca in MeOH resulted in a dark red solution and its ESI⁺–MS spectrum shows a fragment at m/z 455 that tentatively can be attributed to $[Fe(Py_2S_2)(pca)]^+$.

The above pale blue solid obtained from the reaction of **1** with Hpca was tested as catalyst for the MW assisted oxidation of 1-phenylethanol with *t*-BuOOH and, as expected, a very low yield (2%) was obtained, thus confirming the very low activity of copper centres bearing pyrazine-2-carboxylate (pca^-) ligands.

3.3.6. Type of mechanism and role of acid additives

Albeit a detailed mechanistic study on the oxidation pathways for both alkane and alcohol oxidations was not within the objectives of this work, we conducted some experiments in the way to envisage the nature of the oxidizing species and the type of mechanism for some of the above metal catalyst/acid additive systems.

The addition of an acid additive is beneficial for both Fe- and V-catalysed oxidation reactions and does not affect significantly the product yields obtained with the Cu systems. The acid promoter is believed to accelerate these reactions by improving the oxidation properties of the complexes, by creating unsaturation of metal centres and allowing the formation of tentative M-OOH peroxo intermediates that by homolysis produce the active hydroxyl and peroxyl radicals, likely to attack the organic substrate (Habstraction) [21,35,49,50,56]. Thus, the formation of cyclohexyl hydroperoxide (CyOOH) as the major product in the oxidation of cyclohexane and the pronounced yield drops verified for both cyclohexane (Table 4, entries 1 and 3) and 1-phenylethanol (Table 7, entry 7) oxidations when containing free radical scavengers (such as diphenylamine) corroborate the hypothesis involvement of radical pathways that can compete with more selective metal-based oxidants commonly involved in related Fe bis-pyridyl type systems [12-18.43-45].

The acid promoter structure has a relevant effect on the investigated oxidations and the obtained results suggest a possible influence of the ionisation degree of the acid co-catalyst on the catalytic activity for related acids [57–59]. Indeed, the performances of the iron systems **3**/TFA and **4**/TFA are far superior to those of 3/AcOH and 4/AcOH, which use acetic acid as additive instead of the stronger trifluoroacetic acid (compare entries 9 and 10, Table 4).

4. Conclusion

In the present work, we evaluated a series of copper(II), iron(II) and vanadium(III) complexes bearing a N₂S₂-type ligand as catalyst precursors for the oxidation of cyclohexane and various alcohols under mild conditions, using H₂O₂ and *t*-BuOOH as oxidants. It was found that the addition of an acid promoter produces opposing effects on the Cu- or Fe-/V-based systems and that minor modifications in the type of acid co-catalyst used can influence greatly the catalytic activity and the oxygenated product distributions.

From all the catalysts screened, the iron-based systems 3/TFA and 4/HOTf are the most promising ones and their activities are comparable to state-of-the-art systems for both cyclohexane and 1-phenyethanol oxidations, thus demonstrating that S-containing ligands can also be used to broaden the collection of oxidation catalysts precursors, despite of the concerns regarding their stability in the harsh oxidizing conditions. To this regard, it should be underlined the importance not only of the catalyst precursor structure but also of the reaction conditions to develop an efficient catalytic system, since in an previous study an analogous iron triflate complex bearing Py₂S₂ failed as a catalyst for cyclohexane oxidations with H₂O₂ [29].

Very good vields are achieved for both cyclohexane (maximum yield of ca. 38% and TON up to 1450) and 1-phenylethanol (maximum yield of ca. 80% and TOF up to 8580) oxidations.

The 1-phenylethanol oxidation with t-BuOOH occurs very rapidly under microwave (MW) irradiation and, just after 5 min, ca. 75% of all substrate is converted to acetophenone.

The experimental results evidence the extensive involvement of radical species, namely HO[•], R[•] and ROO[•], as confirmed by the large formation of CyOOH in the cyclohexane oxidation reaction and by the pronounced yield drop when diphenylamine (radical trapping agent) was added to both cyclohexane and 1-phenylethanol oxidations.

Given the promising results obtained with these pyridine thioether systems, further studies will be devoted to the syntheses of novel N,S-ligands and complexes, and the peroxidative oxidation investigations will be pursued under different conditions, namely by extending our studies under MW irradiation to other types of oxidation reactions and substrates.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.apcata.2011.05.035.

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