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New Fe^{II} and Cu^{II} Complexes Bearing Azathia Macrocycles – Catalyst Precursors for Mild Peroxidative Oxidation of Cyclohexane and 1-Phenylethanol

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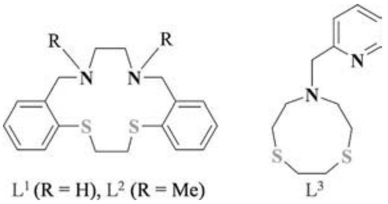
The new mononuclear Fe^{II} and Cu^{II} complexes $[FeCl_2(L^{1,3})]$ [L^1 (**1**), L^3 (**4**)], $[Cu(OTf)_2(L^{1,2})]$ [L^1 (**2**), L^2 (**3**)] and $[Cu(OTf)(L^3)(H_2O)](OTf)$ (**5**) were generated by the treatment of iron(II) chloride or copper(II) triflate in THF solution at ambient temperature with the 14-membered N_2S_2 macrocycles 6,7,13,14,15,16,17,18-octahydrodibenzo(*e*,*m*)-1,4,8,11-dithiadiazacyclotetradecine (L^1), 8,11-dimethyl-5,6,7,8,9,10,16,17-octahydrodibenzo(e,m)-1,4-dithia-8,11-diazacyclotetradecane (L^2), and a new nine-membered NS_2 macrocycle bearing a pendant 2-methylpyridyl arm 7-(2-methylpyridyl)aza-1,4-dithiacyclononane (L^3). Complexes **1**–**5** were characterized by IR spectroscopy, ESI-MS(+), elemental analysis and single-crystal X-ray diffraction (for **2**, **4** and **5**). The oxidation catalytic properties of **1**–**5** were evaluated in two model reactions: (i) the mild oxidation of cyclohexane to cyclohexanol and cyclohexanone by H_2O_2 in MeCN and (ii) the solvent-free oxidation of 1-phenylethanol to acetophenone by *t*BuOOH under low microwave (MW) irradiation power (10 W). The Fe^{II} complexes **1** and **4** exhibited the highest efficiency in both homogeneous oxidation systems, leading to maximum product yields (based on substrate) of up to 21 and 92 % in the oxidation of cyclohexane and 1-phenylethanol, respectively. In the latter transformation, markedly high values of TONs (up to 1200) and TOFs (up to 4200 h^{-1}) were also attained.

Introduction

In contrast to the rich coordination chemistry of simple aza and thioether macrocycles containing three to four donor atoms (e.g., 1,4,7-triaza- and 1,4,7-trithiacyclononanes, 1,4,7,10-tetraaza- and 1,4,7,10-tetrathiacyclododecanes, cyclams and other derivatives),[1–3] the application of the related mixed azathia ligands for the synthesis of metal complexes has been explored to a much less extent.[3,4] However, the combination of both hard N- and soft S-donor atoms in such azathia macrocycles can significantly alter the structural and chemical properties of the resulting metal complexes, thus promoting their specific uses in areas ranging from supramolecular and biological chemistry to molecular magnetism, electrochemistry and homogeneous catalysis.[4,5]

Aiming at studying the coordination chemistry of Fe^{II} and Cu^{II} with azathia macrocycles, we have concentrated on the 14-membered N_2S_2 macrocycle[6] L^1 and its recently reported[7] *N*,*N′*-dimethyl derivative L^2 (Scheme 1) as their use in the synthesis of iron and copper complexes remains poorly explored.[3,8] Another aim of this work was the functionalization of a nine-membered NS_2 macrocycle (7-aza-1,4-dithiacyclononane) with a pendant pyridyl arm (2-methylpyridyl) to obtain a new potentially tetradentate N_2S_2-donor ligand L^3, and to probe its complexation with Fe^{II} and Cu^{II}. The choice of these metals was governed by their relevance in the active sites of various oxygenases and peroxidases,[9] especially those that can oxidize alkanes and other substrates, e.g. methane monooxygenases and cytochromes P450.[10] Although various N- or N,O-macrocyclic complexes of Fe and Cu have been designed and used as bioinspired catalysts,[11] only a limited number of studies have been focused on the application of the related azathia



Scheme 1. Structural formulae of ligands L^1, L^2 and L^3.

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metal complexes in homogeneous catalytic oxidations. Thus, another objective of this study was the evaluation of the oxidation catalytic properties of Fe^{II} and Cu^{II} complexes bearing mixed-donor macrocycles L^1–L^3.

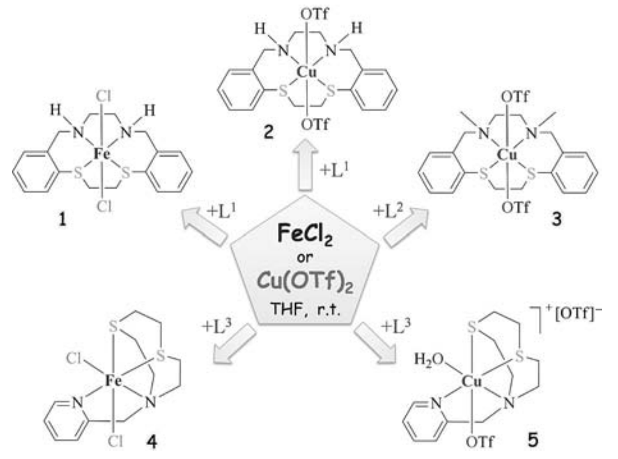
Herein, we describe the synthesis and characterization of a series of mononuclear iron(II) and copper(II) complexes $[FeCl_2(L^{1,3})]$ [L^1 (**1**), L^3 (**4**)], $[Cu(OTf)_2(L^{1,2})]$ [L^1 (**2**), L^2 (**3**)] and $[Cu(OTf)(L^3)(H_2O)](OTf)$ (**5**). Following our interest in the mild oxidative functionalization of alkanes[12] and alcohols,[13] the catalytic behaviour of **1**–**5** was also studied in two homogeneous oxidation reactions, using cyclohexane and 1-phenylethanol as model substrates.

Results and Discussion

Synthesis and Spectroscopic Characterization

To prepare the new iron and copper complexes with macrocyclic azathia ligands, we have selected the 14-membered N_2S_2 macrocycles L^1 and L^2 (Scheme 1), as their application in coordination chemistry is still limited.[3,6–8] For comparative purposes, we have also synthesized a new nine-membered NS_2 macrocycle L^3 bearing a pendant 2-methylpyridyl arm, which can also act as a tetradentate N_2S_2-donor ligand. L^3 has been obtained in 89% yield as a brown oil by the treatment of 7-aza-1,4-dithiacyclononane[14] with 2-picolyl chloride hydrochloride in MeCN in the presence of Na_2CO_3 and $[Bu_4N]Br$. This synthetic procedure is based on a previously described method for a related triaza macrocyclic ligand.[15]

The reactions of iron(II) chloride or copper(II) triflate with L^1 and L^2 in equimolar amounts at ambient temperature in THF led to the isolation of the neutral mononuclear complexes $[Fe(L^1)Cl_2]$ (**1**), $[Cu(OTf)_2(L^1)]$ (**2**) and $[Cu(OTf)_2(L^2)]$ (**3**) (Scheme 2). Similar reactions were carried out with L^3 resulting in the neutral complex $[FeCl_2(L^3)]$ (**4**) and the cationic derivative $[Cu(OTf)(L^3)(H_2O)](OTf)$ (**5**). Although reactions using iron(II) triflate instead of $FeCl_2$ were also attempted, the isolation of analytically pure products was not successful. Compounds **1**–**5** were isolated as air-stable solids in ca. 73–90% yields (based on the metal salt) and characterized by IR spectroscopy, ESI-MS(+), elemental anaylsis and single-crystal X-ray diffraction (for **2**, **4** and **5**). The solution ^1H NMR spectra of **1** and **4** reveal their paramagnetic nature, as expected for the high-spin Fe^{II} chloride complexes.[15,16]



Scheme 2. Synthesis and structural formulae of **1**–**5**.

The IR spectra of **1**–**5** show the typical ν(C–H) and ν(C–X) (X = N, S, C) vibrations due to the presence of the macrocyclic ligands.[17] In addition, the spectra of **1** and **2** show ν(NH) and δ(NH) vibrations with maxima in the ranges of 3183–3038 and 1472–1469 cm^{-1}, respectively. In the Cu^{II} complexes **2**, **3** and **5**, several strong bands in the 1300–1000 cm^{-1} range can be attributed to $\nu(SO_3)$ and $\nu(CF_3)$ vibrations of the triflate moieties.[18] Hence, four highly intense bands in **2** with maxima at 1265, 1223, 1160 and 1032 cm^{-1} can be tentatively assigned to $\nu_{as}(SO_3)$, $\nu_s(CF_3)$, $\nu_{as}(CF_3)$ and $\nu_s(SO_3)$, respectively.[18] Although dry solvents were used for the syntheses, **1**, **4** and **5** show a high affinity to water, adsorbing even traces from solvents and air. Thus, their IR spectra also feature characteristic $\nu(H_2O)$ bands at 3480 (**1**), 3430 (**4**) or 3454 (**5**) cm^{-1}, and δ(OH) at 1629–1633 cm^{-1}.

ESI-MS(+) of all compounds reveal fragmentation with the loss of one Cl (**1** and **4**), OTf (**2** and **3**) or H_2O (in **5**) ligand, in agreement with the detection of the heaviest $[FeCl(L^1)]^+$ (m/z = 421.1), $[Cu(OTf)(L^1)]^+$ (m/z = 542.0), $[Cu(OTf)(L^2)]^+$ (m/z = 570.1), $[FeCl(L^3)]^+$ (m/z = 345.1) and $[Cu(OTf)(L^3)]^+$ (m/z = 466.0) fragments in **1**–**5**, respectively. Further fragmentation pathways typically involve the elimination of the second OTf ligand and the removal of the macrocycle, as confirmed by the presence of the $[Cu(L^{1-3})]^+$ and $[L^{1-3} + H]^+$ fragments with the expected isotopic distribution patterns.[19] The elemental analyses of **1**–**5** are consistent with the proposed formulations (Scheme 2), which are further confirmed (for **2**, **4** and **5**) by single-crystal X-ray diffraction analyses.

X-ray Crystal Structures

$[Cu(OTf)_2(L^1)]$ (2): The molecular structure of **2** (Figure 1, a) is composed of discrete mononuclear units. A highly distorted octahedral environment about the Cu1 atom is filled by one L^1 and two triflate ligands. The donor atoms of L^1 occupy the equatorial positions and adopt *cis*-N_2S_2 coordination with almost equal distances for the pairs of Cu1–N [average 1.994(2) Å] and Cu1–S [average 2.299(1) Å] bonds (Table 1). The binding of L^1 involves the S3–Cu1–S4 [91.49(3)°], N1–Cu1–N3 [87.11(8)°], S3–Cu1–N1 [94.94(6)°] and S4–Cu1–N3 [95.33(6)°] bite angles that approach an idealized value of 90°. The axial sites are occupied by monodentate triflate ligands, which are weakly bound through the long Cu1–O3 [2.636(2) Å] and Cu1–O6 [2.808(2) Å] bonds, defining the most deviated O3–Cu1–O6 angle [146.72(6)°] from the regular octahedral geometry around the Cu1 atom. The binding of both triflate ligands is reinforced by intramolecular N1–H1···O2 [2.978(3) Å, 167.6(1)] and N3–H3···O5 [3.044(3) Å, 164.7(1)°] hydrogen bonds between the NH groups of L^1 and oxygen atoms of

OTf. The packing pattern of **2** is dominated by intermolecular O2···O2^{i} [3.034(2) Å, (i) 1 – *x*, 1 – *y*, 1 – *z*] and O5···O5^{ii} [2.977(3) Å, (ii) 1 – *x*, 1 – *y*, –*z*] short contacts between adjacent triflate moieties, giving rise to houndstooth-like supramolecular 1D chains (Figure 2). In general, the bonding parameters in **2** (Table 1) are comparable to those encountered in Cu^{II} complexes with related N_2S_2 ligands.[8]

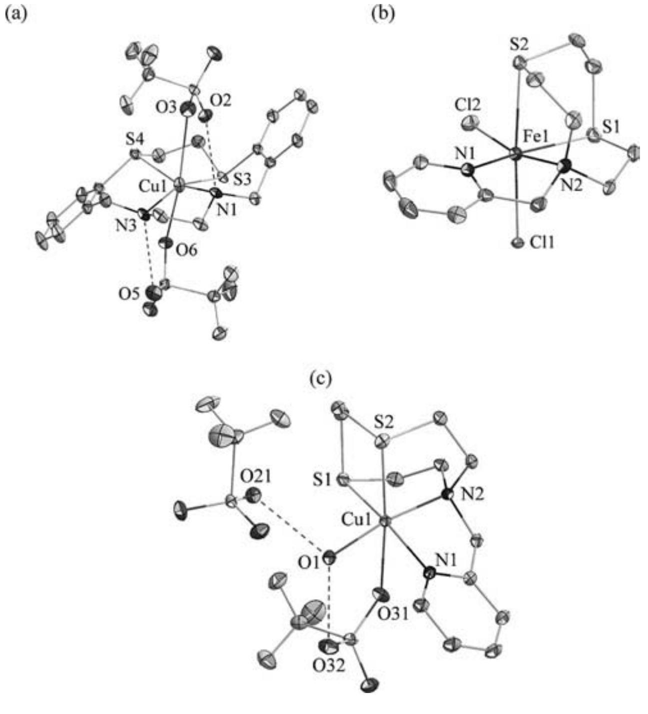


Figure 1. Crystal structures of **2** (a), **4** (b) and **5** (c) with the partial atom labeling scheme. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen bonds are shown as dashed lines. H atoms are omitted for clarity.

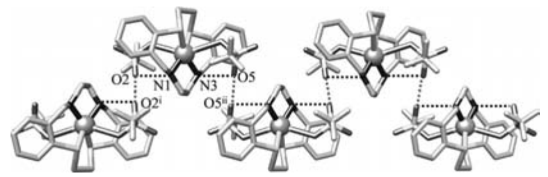


Figure 2. Structural fragment of **2** showing the linkage of adjacent [Cu(OTf)$_2$(L^1)] units through intermolecular O2···O2^{i} [3.034(2) Å, (i) 1 – *x*, 1 – *y*, 1 – *z*] and O5···O5^{ii} [2.977(3) Å, (ii) 1 – *x*, 1 – *y*, –*z*] contacts (red dotted lines), generating a houndstooth-like supramolecular 1D chain. H atoms are omitted for clarity.

Table 1. Selected bond lengths [Å] and angles [°] for **2**, **4** and **5**.

Compound **2**			
Cu1–N1	1.995(2)	S3–Cu1–S4	91.49(3)
Cu1–N3	1.992(2)	O6–Cu1–O3	146.72(6)
Cu1–S3	2.2974(7)	N1–Cu1–O6	121.84(7)
Cu1–S4	2.3007(7)	N1–Cu1–O3	85.20(7)
Cu1–O6	2.808(2)	N3–Cu1–O6	85.21(7)
Cu1–O3	2.636(2)	N3–Cu1–O3	117.76(7)
N1–Cu1–N3	87.11(8)	S3–Cu1–O6	73.18(5)
N1–Cu1–S3	94.94(6)	S3–Cu1–O3	86.47(5)
N1–Cu1–S4	158.61(6)	S4–Cu1–O6	79.55(4)
N3–Cu1–S3	155.76(7)	S4–Cu1–O3	74.84(5)
N3–Cu1–S4	95.33(6)		
Compound **4**			
Fe1–N1	2.141(3)	S1–Fe1–S2	85.18(3)
Fe1–N2	2.328(3)	Cl1–Fe1–Cl2	98.84(3)
Fe1–S1	2.4771(10)	N1–Fe1–Cl1	90.66(8)
Fe1–S2	2.5857(10)	N1–Fe1–Cl2	107.08(8)
Fe1–Cl1	2.4442(9)	N2–Fe1–Cl1	93.03(7)
Fe1–Cl2	2.3625(9)	N2–Fe1–Cl2	167.75(7)
N1–Fe1–N2	75.62(10)	S1–Fe1–Cl1	93.93(3)
N1–Fe1–S1	155.61(8)	S1–Fe1–Cl2	95.86(4)
N1–Fe1–S2	87.19(8)	S2–Fe1–Cl1	172.56(3)
N2–Fe1–S1	80.22(7)	S2–Fe1–Cl2	88.60(3)
N2–Fe1–S2	79.54(7)		
Compound **5**			
Cu1–N1	1.9921(13)	S1–Cu1–S2	89.99(1)
Cu1–N2	2.0338(11)	O31–Cu1–O1	85.11(4)
Cu1–S1	2.3216(4)	N1–Cu1–O31	80.84(4)
Cu1–S2	2.5121(4)	N1–Cu1–O1	90.11(5)
Cu1–O31	2.7925(12)	N2–Cu1–O31	89.24(4)
Cu1–O1	1.9831(11)	N2–Cu1–O1	171.39(5)
N1–Cu1–N2	82.57(5)	S1–Cu1–O31	76.70(3)
N1–Cu1–S1	155.86(4)	S1–Cu1–O1	96.62(4)
N1–Cu1–S2	111.80(4)	S2–Cu1–O31	166.38(3)
N2–Cu1–S1	88.37(4)	S2–Cu1–O1	99.46(3)
N2–Cu1–S2	87.52(3)		

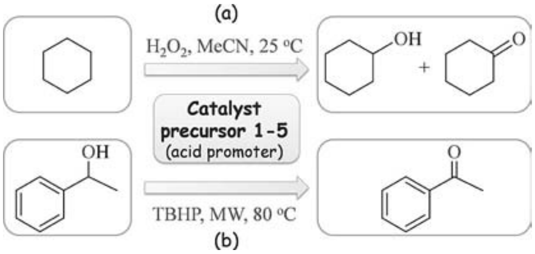
[FeCl$_2$(L^3)] (4): The crystal structure of **4** consists of discrete neutral [FeCl$_2$(L^3)] units (Figure 1, b) in which the six-coordinate iron(II) atom bears one tetradentate macrocycle L^3 and two chloride ligands, giving rise to a distorted octahedral geometry. The equatorial sites are occupied by the S1 and N2 donors from the nine-membered NS_2 ring of L^3, which are *trans* to the N1 atom from the pendant 2-methylpyridyl arm and the Cl2 atom, respectively. The remaining S2 atom of L^3 and the Cl1 ligand lie in axial positions with an S2–Fe1–Cl1 angle of 172.56(3)° (Table 1). As expected, the axial Fe1–S2 [2.5857(10) Å] and Fe1–Cl1 [2.4442(9) Å] bonds are elongated relative to the Fe1–S1 [2.4771(10) Å] and Fe1–Cl2 [2.3625(9) Å] distances. In addition, the Fe1–N2 [2.328(3) Å] bond is significantly longer than the Fe1–N1 [2.141(3) Å] distance, presumably because of a stronger *trans* influence of the Cl2 than the S1 atom. The major deviation from the octahedral geometry concerns the N1–Fe1–S1 angle of 155.61(8)°, whereas the bite angles within the chelate rings of L^3 vary from 75.62(10)° [N1–Fe1–N2] to 85.18(3)° [S1–Fe1–S2]. Most of the bond ing parameters in **4** are comparable with those of iron(II) complexes with related nine-membered N_2S or NS_2 macrocyclic rings.[20]

[Cu(OTf)(L^3)(H$_2$O)](OTf) (5): In contrast to **4**, the crystal structure of **5** comprises a [Cu(OTf)(L^3)(H$_2$O)]$^+$ cation and a triflate anion (Figure 1, c). The Cu1 atom exhibits a distorted octahedral geometry formed by two S and two N donors of L^3, one water (O1) and one monodentate triflate (O31) ligand. The latter, along with the S2 atom of L^3, occupy axial positions and their binding involves long Cu1–

O31 [2.7925(12) Å] and Cu1–S2 [2.5121(4) Å] bonds, and a S2–Cu1–O31 angle of 166.38(3)°. The donor atoms in equatorial sites are connected through normal Cu1–N1 [1.9921(13) Å], Cu1–N2 [2.0338(11) Å], Cu1–S1 [2.3216(4) Å] and Cu1–O1 [1.9831(11) Å] distances, which are comparable to those found in **2** (Table 1) and other Cu^{II} complexes with related NS_2 macrocyclic ligands.[14b,21] In **5**, the geometry of L^3 is similar to that in **4**. Furthermore, the coordinated water molecule O1 acts as a double intramolecular H-bond donor to O atoms of the triflate ligand [O1–H1A···O32: 2.715(2) Å, 168.4(1)°] and the triflate anion [O1–H1B···O21^i: 2.698(2) Å, 158.3(1)°, (i) 2 – *x*, 1 – *y*, 1 – *z*], additionally stabilizing the structure (Figure 1, c).

Mild Peroxidative Oxidation of Cyclohexane

Following our interest in the development of new Fe[22] and Cu[23] catalytic systems for the selective oxidation of alkanes under mild conditions, we tested the catalytic potential of **1**–**5** for the peroxidative oxidation of cyclohexane to cyclohexanol and cyclohexanone (Scheme 3, a). This transformation has been selected as a recognized model and easy to follow reaction.[24] In addition, it generates oxygenate products, which is important as cyclohexanol and cyclohexanone are intermediates in nylon-6,6′ and polyamide-6 production.[25] The catalytic tests were undertaken by reacting cyclohexane at 25 °C in MeCN with aqueous H_2O_2 in the presence of **1**–**5** (0.2 mol-% vs. C_6H_{12}) and an acid additive (optional). Previously, it was found[22,23] that the efficiency of various iron[22] and copper[12d,23] catalytic systems can be dramatically improved upon addition of an acid promoter (additive). Hence, we have investigated the promoting influence of various acids, namely pyrazinecarboxylic (Hpca), nitric, triflic (TfOH) and trifluoroacetic (TFA) acids, and the results are summarized in Table 2. The activity values discussed below concern the total yields, i.e. the sum of the mol-% yields of the two products (cyclohexanol and cyclohexanone) based on cyclohexane. The separate yields of cyclohexanol and cyclohexanone in each run are given in Table S1 (Supporting Information).



Scheme 3. (a) Mild peroxidative oxidation of cyclohexane to cyclohexanol and cyclohexanone. (b) Solvent-free peroxidative oxidation of 1-phenylethanol to acetophenone under MW irradiation.

Table 2. Mild oxidation of cyclohexane by H_2O_2 in the presence of **1**–**5** and different acid additives.[a]

Entry	Acid additive	Total yield [b] [%] **1**	**2**	**3**	**4**	**5**
1	–	2.5	8.3	10.3	12.2	8.6
2	Hpca	17.5	0.4	0.2	15.9 (8.0)[c]	0.2
3	HNO_3	19.2	5.8	7.3	15.8 (7.5)[d]	4.5
4	TfOH	21.3	6.1	6.0	18.0	4.8
5	TFA	20.0	6.0	6.1	16.7	4.1

[a] Reaction conditions (unless otherwise stated): CH_3CN (3.0 mL), cyclohexane (5.0 mmol), catalyst precursor (10 µmol, 0.2 mol-% vs. C_6H_{12}), H_2O_2 (7.0 mmol, 30% in H_2O), acid additive [Hpca (50 µmol), HNO_3, TfOH or TFA (200 µmol)], 6 h reaction time, 25 °C. [b] Moles of products (cyclohexanol + cyclohexanone)/100 mol of cyclohexane determined by GC analysis after treatment with PPh_3. Total TON values (moles of products/moles of catalyst precursor) can be estimated as 5 × total% yield. For yields of cyclohexanol and cyclohexanone in each run see Table S1. [c] MW-assisted (10 W power) reaction (30 min, 50 °C). [d] TBHP (7.0 mmol, 70% in H_2O) was used instead of H_2O_2, reaction at 80 °C for 6 h.

All complexes **1**–**5** act as catalyst precursors for the mild oxidation of cyclohexane (CyH) to cyclohexyl hydroperoxide CyOOH (primary product), cyclohexanol (CyOH) and cyclohexanone (Cy′O), which are the major final products after the autodecomposition of CyOOH and its reduction with PPh_3 (in the latter case giving only CyOH).[26] The iron(II) complexes **1** and **4** exhibit a good activity (yields of up to 21 and 18%, respectively), whereas the copper(II) compounds **2**, **3** and **5** are less active, showing maximum yields of 8–10% (Table 2). Interestingly, the activities of these two groups of catalyst precursors are affected in different ways by the presence of an acid additive. In the systems containing **1** and **4**, the yields of oxygenates increase from 2.5 and 12% to 18–21 and 16–18%, respectively, on addition of various acid promoters. Turnover numbers (TONs) up to 105 and 90 are also achieved with **1**/TfOH and **4**/TfOH, respectively (Table 2, entry 4). These activity levels are comparable or even superior to those exhibited by a variety of iron containing catalysts in the mild oxidation of cyclohexane.[12a,15,16b,23a,23c,27]

In contrast to **1** and **4**, the introduction of various acids to the systems based on the Cu complexes **2**, **3** and **5** results in a reduction of activity (Table 2). This observation is unexpected considering that the majority of the previously reported Cu systems[12d,23] for the peroxidative oxidation of cyclohexane were active only in the presence of an acid promoter. A noteworthy exception concerns a dipicolinate Cu^{II} coordination polymer,[28] the activity of which was also suppressed upon addition of an acid additive.

Although in the systems containing **1** and **4** the yields of oxygenates do not vary significantly with the type of acid additive, it should be mentioned that the highest activity is observed with TfOH, followed by TFA and other acids (Table 2). Hence, higher activities in the presence of acid additives can be associated with a substitution of Cl^- ligands in **1** and **4**. This is confirmed by the ESI-MS(+) analysis of the mixture obtained upon treatment of **4** with HOTf in MeCN, which shows the generation of $[Fe(OTf)(L^3)]^+$ species (*m*/*z* = 459.0), and the intensity of the parent $[FeCl(L^3)]^+$ peak (*m*/*z* = 345.1) significantly decreases. The role of an acid promoter is not yet fully established but can be involved in proton transfer steps leading to the activation of the catalyst precursor through protonation of the macrocyclic ligands with consequent unsaturation of the iron centre, as well as in the enhancement of the oxidizing properties of metal intermediates and hydrogen peroxide and decreasing the eventual catalase activity.[12a,12d,22a,23] Water, a component of the reaction medium, can promote H^+ transfer steps involved in the generation of hydroxy radicals ($HO^·$) from H_2O_2, which act as the H atom abstractor from CyH to afford the easily oxidizable cyclohexyl radical.[12d,12g]

The ability of **2**–**4** to catalyze the oxidation of cyclohexane in acid-free systems is a noteworthy feature, considering that the yields of oxygenates obtained in such systems reach values of 8–12%, which are quite respectable in the field of mild functionalization of alkanes.[24,29] Moreover, all the catalyst precursors show a high selectivity towards cyclohexanol (the main final product) and cyclohexanone, as no other products of the oxidation of cyclohexane were detected.

As observed for other Cu and Fe catalytic systems,[22a,22b,23] introduction of a radical trap ($CBrCl_3$ or Ph_2NH) into the reaction mixture results in a considerable suppression of the catalytic activity. This behaviour, along with the formation of cyclohexyl hydroperoxide (typical intermediate product in radical-type reactions) supports a free-radical mechanism[12d,22a,28,30] for cyclohexane oxidation in this study. The formation of intermediate peroxo complexes can also occur upon reaction of **1**–**5** with hydrogen peroxide. In fact, the generation of peroxo species was proven in the cyclohexane oxygenations with the Fe^{II} catalyst precursor $[Fe(OTf)_2(L')]$ [L′ = 1-(2-pyridylmethyl)-4,7-dimethyl-1,4,7-triazacyclononane] that bears an aza macrocyclic ligand closely related to L^3.[15] The dicopper peroxo derivatives supported by 1,4,7-triisopropyl-1,4,7-trithiacyclononane macrocycles have also been reported.[11f,31]

For comparative purposes, we have also tested *tert*-butyl hydroperoxide (TBHP) as an oxidant for the oxidation of cyclohexane catalyzed by **4**, which was less efficient (i.e. 7.5% vs. 16% total yield). A similar yield of 8% is obtained in the MW-assisted oxidation of cyclohexane by the **4**/Hpca/H_2O_2 system. In contrast, TBHP is a better oxidant towards the selective oxidation of 1-phenylethanol to acetophenone in the presence of **1**–**5**, a transformation that is also significantly accelerated by MW irradiation, discussed below.

Microwave-Assisted Solvent-Free Oxidation of 1-Phenylethanol

By switching from an alkane (cyclohexane) to a more reactive alcohol substrate, 1-phenylethanol, we have evaluated the catalytic potential of **1**–**5** for the oxidation of the latter to acetophenone (Scheme 3, b). These tests were performed following our recently developed procedure[13a,13b] for the MW-assisted oxidation of secondary alcohols, namely by reacting 1-phenylethanol with TBHP (70% in H_2O) in the presence of the catalyst precursor **1**–**5** and an acid additive (optional) at 80 °C in a solvent-free medium under MW-irradiation. The influence of various reaction parameters such as the type of acid additive, temperature, time and the amounts of catalyst precursor and oxidant were investigated, and the results are shown in Table 3 and Table 4.

Table 3. MW-assisted solvent-free oxidation of 1-phenylethanol to acetophenone by TBHP catalyzed by **1**–**5**.[a]

Entry	Cat. precursor	Acid additive	Yield[b] [%]	TON (TOF [h^{-1}])[c]
1	**1**	–	15.3	77 (153)
2	**2**	–	38.8	194 (388)
3	**3**	–	22.2	111 (222)
4	**4**	–	20.6	103 (206)
5	**5**	–	23.6	118 (236)
6	**1**	HNO_3	68.4	342 (684)
7	**1**	TFA	71.6	358 (716)
8	**1**	Hpca	74.6	373 (746)
9	**2**	HNO_3	0.9	5 (10)
10	**2**	TFA	1.5	8 (15)
11	**2**	Hpca	1.1	5 (10)
12	**4**	HNO_3	67.4	337 (674)
13[d]	**4**	HNO_3	68.0	340 (680)
14	**4**	TFA	72.2	362 (722)
15[d]	**4**	TFA	85.6	428 (856)
16	**4**	Hpca	75.2	376 (752)
17[d]	**4**	Hpca	92.1	461 (921)

[a] Reaction conditions (unless otherwise stated): 1-phenylethanol (5.0 mmol), catalyst precursor (10 µmol, 0.2 mol-% vs. substrate), acid additive [Hpca (50 µmol), HNO_3 or TFA (200 µmol)], TBHP (10.0 mmol, 70% in H_2O), MW irradiation (10 W power), 30 min reaction time, 80 °C. [b] Moles of acetophenone/100 mol of 1-phenylethanol (GC yield). [c] TON = moles of acetophenone/moles of catalyst precursor; TOF = TON per hour (values in brackets). [d] Reaction was carried out at 100 °C.

Under typical reaction conditions (Table 3), all the catalyst precursors **1**–**5** exhibit some activity in the absence of an acid additive, leading to the yields of acetophenone in the 15–21% and 22–39% ranges for the Fe and Cu catalyzed systems, respectively (entries 1–5). As in the oxidation of cyclohexane, a positive influence of acid additives is only observed when using the iron containing **1** and **4**, whereas the introduction of different acid additives to the most active Cu system with **2** results in almost the full suppression of the catalytic activity (i.e. 1–2% vs. 39% yields, entries 9–11 vs. 2). Bearing these features in mind, **1** and **4** have been used in further tests.

The addition of HNO_3, TFA or Hpca as acid additives to **1** and **4** leads to a remarkable yield increase from 15 and 21% to 68–75 and 67–75%, respectively (Table 3, entries 1, 4, 6–8, 12, 14, 16). In the **4**/TFA and **4**/Hpca systems, the yields of acetophenone can be further augmented to 86 and 92%, respectively, on increasing the reaction temperature from 80 to 100 °C (entries 15, 17). However, further increasing the temperature was not attempted for safety reasons. Given the fact that pyrazinecarboxylic acid (Hpca) shows a slightly stronger promoting effect and is typically required in a lower fourfold amount than that of HNO_3 or TFA to achieve comparable yields, we have selected the **1**/Hpca and **4**/Hpca systems to study the influence of other reaction parameters (Table 4).

Table 4. MW-assisted solvent-free oxidation of 1-phenylethanol to acetophenone by TBHP with the **1**/Hpca and **4**/Hpca systems.[a]

Entry	Cat. precursor/ Hpca [µmol]	TBHP [mmol]	Yield[b] [%]	TON (TOF [h^{-1}])[c]
Catalyst precursor **1**				
1	10/50	5	59.2	296 (592)
2	10/50	7	73.8	369 (738)
3	10/50	10	74.6	373 (746)
4	10/50	15	68.9	345 (690)
5[d]	10/50	10	72.0	360 (1440)
6[e]	10/50	10	70.4	352 (4224)
7	1/5	10	20.0	1000 (2000)
8[d]	1/5	10	13.5	675 (2700)
Catalyst precursor **4**				
9	1/5	10	24.1	1205 (2410)
10	2.5/12.5	10	24.8	496 (992)
11	5/25	10	35.6	356 (712)
12	10/50	10	75.2	376 (752)
13	10/10	10	39.8	199 (398)
14	10/100	10	72.3	362 (724)
15	10/200	10	73.3	367 (734)
16	10/50	5	66.1	331 (662)
17	10/50	7	68.6	343 (686)
18	10/50	15	76.1	381 (762)
19[f]	10/50	10	65.2	326 (54)
20[g]	10/50	–	9.5	48 (96)

[a] Reaction conditions (unless otherwise stated): 1-phenylethanol (5.0 mmol), catalyst precursor **1** or **4** (1–10 µmol, 0.02–0.2 mol-% vs. substrate), Hpca (10–200 µmol), TBHP (5.0–15.0 mmol, 70% in H_2O), MW irradiation (10 W power), 30 min reaction time, 80 °C. [b] Moles of acetophenone/100 mol of 1-phenylethanol (GC yield). [c] TON = moles of acetophenone/moles of catalyst precursor; TOF = TON per hour (values in brackets). [d] 15 min reaction time. [e] 5 min reaction time. [f] Reaction under conventional heating for 6 h. [g] H_2O_2 (10.0 mmol, 30% in water) was used instead of TBHP, reaction at 50 °C.

An interesting feature of the iron(II) systems for the MW-assisted oxidation of 1-phenylethanol is the high oxidant efficiency, as the yields of acetophenone attain values of 59 (**1**/Hpca) and 66% (**4**/Hpca) in an equimolar reaction between the substrate and TBHP (Table 4, entries 1, 16). A 1.4-fold excess of TBHP leads to higher yields of 74 (**1**/Hpca; entry 2) and 69% (**4**/Hpca; entry 17), which slightly increase to maximum values of 75% (entries 3, 12) with a twofold excess of TBHP. A further increase of the oxidant amount (threefold molar excess) results in a similar yield of 76% in the **4**/Hpca system, whereas in the **1**/Hpca system the yield drops to 69% (entries 18, 4) possibly due to the increased water content coming with TBHP. It should be noted that in contrast to TBHP, hydrogen peroxide (30% in H_2O) is not a suitable reagent for the oxidation of 1-phenylethanol, as attested by the low 10% yield of acetophenone with the **4**/Hpca system (entry 20).

Another important feature of **1** and **4** concerns the relatively low loading (0.2 mol-% vs. substrate) necessary to reach high yields of acetophenone (i.e. up to 92%) with substantial TON and TOF values of 461 and 921 h^{-1}, respectively (Table 3, entry 17). Such a catalyst loading is significantly lower to those commonly applied (up to 5 mol-% vs. substrate) in most of the state-of-the-art systems for the oxidation of secondary alcohols.[25a,32,33] Moreover, these iron(II) systems can furnish appreciable yields of acetophenone (20–24%) when operating with a 10-fold reduced amount of **1** and **4** (i.e. 0.02 mol-% vs. substrate), thus giving rise to remarkably high TONs (up to 1205) and TOFs (up to 2410 h^{-1}) (Table 4, entries 7, 9).

As a promoter, Hpca is typically required in a fivefold molar excess over the catalyst precursor. An equimolar amount of Hpca is not enough to reach the optimum yields, whereas higher loadings (i.e. a 10- or 20-fold molar excess) lead to comparable results (Table 4, entries 12–15). The role of Hpca is presumably in the activation of the metal catalyst precursors e.g. by protonation of L^1 and L^3, or through its coordination to the iron centre. The good promoting behaviour of Hpca was previously recognized for other Fe containing catalytic systems.[22a,26b,27a,27b,27d]

The relevance of MW irradiation concerns the dramatic acceleration of the oxidation. In contrast to the oxidation of 1-phenylethanol under conventional heating (maximum 65% yield after 6 h; entry 19), even higher yields of acetophenone can be achieved at much shorter reaction times (5–30 min) when applying a very low MW irradiation power (10 W). Although under typical conditions in the **1**/Hpca system, the acetophenone yield of 75% (TOF = 746 h^{-1}) is attained after 30 min of MW irradiation, the reaction time can be further reduced to 5 min, resulting in a comparable yield of 70% with a remarkably high TOF of 4224 h^{-1} (Table 4, entry 3 vs. 6). It should also be mentioned that very high selectivities (> 98%) are typically observed in our MW-assisted oxidations, as confirmed by mass balances.

Although the investigation of the mechanism of the catalysis lies outside the scope of this work, on the basis of previous studies[13a,13b] and experiments with radical traps resulting in the suppression of the catalytic activity, we propose that the MW-assisted oxidation of 1-phenylethanol proceeds by a free-radical mechanism with the participation of *t*BuO· and *t*BuOO· radicals.[13b,34]

A noteworthy feature of our MW-assisted oxidations is the use of a very weak MW irradiation (10 W). This contrasts with most of the MW-assisted organic reactions reported to date, which require a much higher power of MW irradiation (typically above 200 or even 500 W).[35] Furthermore, apart from high yields and TOFs (up to 92% and 4200 h^{-1}, respectively), an important feature of the **1**/Hpca and **4**/Hpca systems is that they are solvent-free. This contrasts with the common use of organic solvents or costly ionic liquids in many state-of-the-art methods for the oxidation of alcohols.[32,33,35b,36]

Conclusions

This work has extended the application of mixed 14-membered N_2S_2 azathia macrocycles L^1 and L^2 in coordination chemistry, resulting in new mononuclear complexes **1**–**3**. In addition, a new nine-membered NS_2 macrocyclic ligand L^3 with a pendant 2-methylpyridyl arm has been generated and used to prepare the Fe^{II} and Cu^{II} complexes **4** and **5**, respectively. Compounds **1**–**5** broaden the limited family of macrocyclic azathia complexes of iron and copper and represent rare examples of derivatives that find application in homogeneous oxidation catalysis.

As **1**–**5** are not intact in the course of the catalytic reactions, they act as catalyst precursors for the mild and selective oxidations of two different classes of substrates including an alkane (cyclohexane) and an alcohol (1-phenylethanol). Inclusion of various acid additives has revealed a significant activity enhancement in systems with **1** and **4**, whereas the activity of copper(II) complexes **2**, **3** and **5** is reduced by the addition of an acid. Hence, **1** and **4** are more efficient in both cyclohexane and 1-phenylethanol oxidations and exhibit comparable levels of activity, in spite of being based on different macrocyclic ligands.

This study also widens the scope of MW irradiation applied to oxidative transformations[35] and extends the range of catalytic systems that it can be applied to. Their activity is drastically accelerated by a low MW irradiation power (10 W), achieving good yields of acetophenone (up to 92%) in the solvent-free oxidation of 1-phenylethanol, in addition to remarkably high values of TONs (up to 1200) and TOFs (up to 4200 h^{-1}).

The features observed here will be accounted for in further research focused on the extension of both synthetic and catalytic areas by widening the type of azathia macrocycles and metal complexes used, as well as by broadening the substrate versatility of the catalytic transformations. Moreover, the use of an aqueous MeCN medium under mild conditions in the case of the cycloalkane oxidation with H_2O_2, and the use of low power MW irradiation in a solvent-free system in the alcohol oxidation, are significant steps towards the development of green catalytic systems in those fields.

Experimental Section

Materials and Methods: Unless stated otherwise, all reactions and operations were carried out at ambient temperature (ca. 25 °C) under dinitrogen using standard Schlenk techniques. Solvents were dried and distilled before use, and reagents were obtained from commercial sources (Aldrich) and used as received. L^1 and L^2 were prepared according to the procedure described by Fritz et al.,[7] and 7-aza-1,4-dithiacyclononane[14] (the starting material for L^3) was obtained by a modification of the literature method.[14b]

C, H, N and S elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. ^1H and $^{13}C\{^1H\}$ NMR spectra were measured with Bruker Avance II 300 or 400 (UltraShield^{TM} Magnet) spectrometers at ambient temperature. ^1H and ^{13}C chemical shifts (δ) are expressed in ppm relative to Me_4Si, and *J* values are given in Hz. IR spectra (4000–400 cm^{-1}) were recorded with a Bio-Rad FTS 3000MX instrument as KBr pellets, and wavenumbers are given in cm^{-1}. ESI-MS were run with a 500-MS LC Ion Trap instrument (Varian Inc, Alto Palo, CA, USA) equipped with an ESI source. Scanning was performed from m/z = 50 to 1500. The fragmentations of compounds were observed in the positive mode (capillary voltage = 80–105 V). GC analyses were undertaken with a Fisons Instruments GC 8000 series gas chromatograph with a DB-624 (J&W) capillary column (FID detector) and Jasco-Borwin v.1.50 software.

7-(2-Methylpyridyl)-7-aza-1,4-dithiacyclononane (L^3): A Schlenk flask was charged with 2-picolyl chloride hydrochloride (500 mg, 3.05 mmol), 7-aza-1,4-dithiacyclononane (500 mg, 3.06 mmol) and anhydrous CH_3CN (10 mL). Na_2CO_3 (1.1 g) and tetrabutylammonium bromide (40 mg, 0.12 mmol) were added, and the resulting suspension was heated to reflux under N_2 for 20 h. The mixture was cooled to ambient temperature and filtered. The solid inorganic salts collected were washed with CH_2Cl_2 and then discarded. The combined organic fractions were evaporated under reduced pressure to afford a brown oil, which was treated with CH_2Cl_2 (100 mL) and H_2O (100 mL), followed by the adjustment of pH to 13 with 3 M aqueous KOH. After stirring for 1 h, the layers were separated and material in the aqueous phase was extracted into CH_2Cl_2 (3 × 100 mL). The combined organic fractions were dried with anhydrous Na_2SO_4, and the solvent was removed at reduced pressure to yield L^3 as a brown oil (700 mg, 89%). ^1H NMR ($CDCl_3$, 400 MHz, 298 K): δ = 8.54 (d, J = 4.4 Hz, 1 H, pyH_α), 7.68 (t, J = 7.6 Hz, 1 H, pyH_γ), 7.46 (d, J = 7.6 Hz, 1 H, pyH_β), 7.19–7.17 (m, 1 H, pyH_β), 3.86 (s, 2 H, pyCH_2N), 3.19 (s, 4 H, SCH_2CH_2S), 3.07–3.05 (m, 4 H, N$CH_2$$CH_2$S), 2.75–2.73 (m, 4 H, N$CH_2$$CH_2$S) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, 298 K): δ = 159.55 (pyC_q), 149.49 (pyC_α), 136.74 (pyC_γ), 123.76 and 122.48 (pyC_β), 63.38 (pyCH_2N), 58.13, 35.20 and 33.28 (CH_2CH_2) ppm. ESI–MS(+) (CH_2Cl_2): m/z = 255.1 $[L^3 + H]^+$.

$[FeCl_2(L^1)]$ (1): Anhydrous $FeCl_2$ (77 mg, 0.61 mmol) was added to a stirring solution of L^1 (200 mg, 0.61 mmol) in THF (5 mL). The reaction mixture was stirred at ambient temperature for 5 h under N_2 and then concentrated to half of the initial volume. The addition of Et_2O (5 mL) resulted in the formation of a precipitate, which was collected by filtration, washed with Et_2O and dried in vacuo to give **1** as a yellow solid (204 mg, 73%). $C_{18}H_{26}Cl_2FeN_2O_2S_2$ (**1**·$2H_2O$, 493.3): calcd. C 43.83, H 5.31, N 5.68, S 13.00; found C 43.91, H 5.08, N 5.59, S 12.51. IR (KBr): $\tilde{\nu}$ = 3480 (w), 3038 (w), 2960 (w), 2925 (w), 2870 (w), 1629 (m), 1472 (m), 1442 (s), 1307 (m), 1384 (m), 1082 (m), 956 (m) and 769 (vs) cm^{-1}. ESI-MS(+) (MeCN): m/z = 421.1 $[FeCl(L^1)]^+$, 331.2 $[L^1 + H]^+$.

$[Cu(OTf)_2(L^1)]$ (2): A solution of $Cu(OTf)_2$ (221 mg, 0.61 mmol) in THF (5 mL) was added to a stirring solution of L^1 (200 mg, 0.61 mmol) in THF (5 mL). The reaction mixture was stirred at ambient temperature for 5 h and then concentrated to half of the initial volume. The addition of Et_2O (10 mL) resulted in the formation of a fine precipitate, which was collected by filtration, washed with Et_2O and dried in vacuo to give **2** as a green solid (350 mg, 83%). $C_{20}H_{22}CuF_6N_2O_6S_4$ (692.2): calcd. C 34.70, H 3.20, N 4.05, S 18.53; found C 34.71, H 3.03, N 3.88, S 18.42. IR (KBr): $\tilde{\nu}$ = 3183 (w), 2920 (w), 2860 (w), 1629 (w), 1469 (m), 1421 (w), 1265 (vs), 1223 (vs), 1160 (s), 1032 (vs), 996 (m), 767 (s) and 637 (vs), 576 (m) and 517 (m) cm^{-1}. ESI-MS(+) (MeCN): m/z = 542.0 $[Cu(OTf)(L^1)]^+$, 394.1 $[Cu(L^1)]^+$, 331.2 $[L^1 + H]^+$. X-ray quality single crystals of **2** were obtained by slow diffusion of diethyl ether into a concentrated MeCN solution of **2**.

$[Cu(OTf)_2(L^2)]$ (3): A solution of $Cu(OTf)_2$ (503 mg, 1.39 mmol) in THF (3 mL) was added to a stirring solution of L^2 (500 mg, 1.39 mmol) in THF (10 mL). The mixture became cloudy after a few seconds, and a dark green precipitate started to form. The resulting suspension was stirred for 5 h and the precipitate was collected by filtration. The precipitate was washed with THF and Et_2O and dried in vacuo to yield **3** as a green solid (890 mg, 89%). $C_{22}H_{26}CuF_6N_2O_6S_4$ (720.3): calcd. C 36.69, H 3.64, N 3.89, S

17.81; found C 36.55, H 3.89, N 3.60, S 17.99. IR (KBr): ṽ = 2985 (w), 2920 (w), 1632 (m), 1469 (m), 1258 (s), 1163 (s), 1031 (vs), 759 (s), 639 (vs), 575 (m) and 518 (m) cm^{-1}. ESI-MS(+) (CH_2Cl_2): m/z = 570.1 $[Cu(OTf)(L^2)]^+$, 421.2 $[Cu(L^2)]^+$, 359.2 $[L^2 + H]^+$.

$[FeCl_2(L^3)]$ (4): A solution of anhydrous $FeCl_2$ (55 mg, 0.43 mmol) in THF (3 mL) was combined with a solution of L^3 (109 mg, 0.43 mmol) in THF (3 mL) and stirred overnight under N_2. A yellowish solid precipitated and the solvent was removed by a cannula. The precipitate was washed with Et_2O and dried in vacuo to give **4** as a yellow solid (150 mg, 90%). $C_{12}H_{18.5}Cl_2FeN_2O_{0.25}S_2$ (**4**·$0.25H_2O$, 385.7): calcd. C 37.37, H 4.83, N 7.26, S 16.63; found C 37.20, H 4.76, N 6.92, S 16.52. IR (KBr): ṽ = 3430 (m), 2957 (m), 2920 (m), 2853 (m), 1630 (m), 1603 (s), 1477 (s), 1430 (vs), 1307 (m), 1082 (m), 956 (m) and 769 (vs) cm^{-1}. ESI-MS(+) (CH_2Cl_2/MeOH): m/z = 345.1 $[FeCl(L^3)]^+$. X-ray quality single crystals of **4** were obtained by slow diffusion of diethyl ether into a concentrated MeCN solution of **4**.

$[Cu(OTf)(L^3)(H_2O)](OTf)$ (5): A solution of $Cu(OTf)_2$ (156 mg, 0.43 mmol) in THF (3 mL) was combined with a solution of L^3 (109 mg, 0.43 mmol) in THF (3 mL) and stirred overnight under N_2. The addition of Et_2O (20 mL) caused the immediate precipitation of a solid, which was collected by filtration and dissolved in CH_2Cl_2 (10 mL). This solution was evaporated to dryness in vacuo, affording **5** as a fine greenish blue powder (210 mg, 77%). $C_{14}H_{20}CuF_6N_2O_7S_4$ (634.1): calcd. C 26.52, H 3.18, N 4.42, S 20.23; found C 26.18, H 3.12, N 4.18, S 20.64. IR (KBr): ṽ = 3454 (m), 3038 (w), 2986 (w), 2928 (w), 1633 (m), 1613 (m), 1442 (m), 1274 (vs), 1252 (vs), 1172 (s), 1029 (vs), 771 (m), 640 (vs), 574 (m) and 518 (m) cm^{-1}. ESI-MS(+) (CH_2Cl_2): m/z = 466.0 $[Cu(OTf)(L^3)]^+$, 317.1 $[Cu(L^3)]^+$, 255.1 $[L^3 + H]^+$. X-ray quality single crystals of **5** were obtained by slow diffusion of diethyl ether into a concentrated MeCN/MeOH solution of **5**.

X-ray Crystallography: X-ray quality single crystals of **2**, **4** and **5** were obtained as indicated above. They were mounted in inert oil within the cold N_2 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[37a] on all the observed reflections. Absorption corrections were applied using SADABS.[37a] The structures were solved by direct methods using SHELXS–97 and refined with SHELXL-97 programs.[37b] Calculations were performed using the WinGX System–Version 1.80.03.[37c] All hydrogen atoms were inserted in calculated positions. Crystal data and details of data collection for **1**, **4** and **5** are reported in Table 5.

CCDC-809154 (for **1**), -809155 (for **4**) and -809156 (for **5**) contain 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.

Peroxidative Oxidation of Cyclohexane by H_2O_2: Typical cyclohexane oxidation reactions were carried out under atmospheric pressure in 50 mL screwtop glass reactors (Stem® Omni Reacto Station) without removal of air or moisture. The reactors were filled with the catalyst precursor **1**–**5** (10 µmol), cyclohexane (5.0 mmol), CH_3CN (3 mL) and an acid additive (50–200 µmol) and placed in the reaction station. The mixtures were stirred vigorously at 25 °C. An aqueous solution of hydrogen peroxide (30%) (7.0 mmol, 0.71 mL) was then added and the reaction mixture was stirred for 6 h at 25 °C. 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. This mixture was treated with an excess of triphenylphosphane before GC analysis to reduce cyclohexyl hydroperoxide to cyclohexanol and hydrogen peroxide to water following a method developed by Shul'pin.[26] After stirring the final reaction mixture for 10 min, a sample was taken from the organic phase and analyzed by GC.

GC analyses of the aqueous phase revealed the presence of traces (less than 0.1%) of oxidation products. Blank experiments were also performed with different amounts of H_2O_2 and other reagents, and confirmed that no cyclohexane oxidation products (or only traces, below 0.4%) were obtained in the absence of the metal catalyst precursor. Furthermore, the formation of chlorocyclohexane in the reactions catalyzed by **1** and **4** was not observed.

Peroxidative Oxidation of 1-Phenyletheanol by *t*BuOOH. MW-Assisted Method: The catalytic tests under MW irradiation were per-

Table 5. Crystal data and structure refinement details for **2**, **4** and **5**.

	2	**4**	**5**
Empirical formula	$C_{20}H_{22}CuF_6N_2O_6S_4$	$C_{12}H_{18}Cl_2FeN_2S_2$	$C_{14}H_{20}CuF_6N_2O_7S_4$
M_r [g mol^{-1}]	692.18	381.15	634.10
Crystal system	triclinic	orthorhombic	triclinic
Space group	$P\bar{1}$	$2_12_12_1$	$P\bar{1}$
Temperature [K]	150(2)	150(2)	150(2)
a [Å]	9.7709(9)	8.4818(13)	9.3128(3)
b [Å]	11.1332(11)	12.1005(19)	11.4488(4)
c [Å]	13.7123(11)	14.694(2)	11.6596(4)
α [°]	89.105(5)		71.559(1)
β [°]	75.572(5)		75.526(2)
γ [°]	65.292(4)		88.667(1)
V /Å^3	1305.7(2)	1508.1(4)	1139.78(7)
Z	2	4	2
D_c [g cm^{-3}]	1.761	1.679	1.848
μ(Mo-K_α) [mm^{-1}]	1.240	1.617	1.414
Reflections collected	17866	14200	23733
Unique reflections	4624	4178	9021
R_{int}	0.0250	0.0589	0.0282
Final $R1$[a], $wR2$[b] ($I \geq 2\sigma$)	0.0287, 0.0722	0.0377, 0.0804	0.0286, 0.0775
GOF on F^2	1.058	1.034	1.078

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$.

formed in a focused MW CEM Discover reactor (10 mL, 13 mm diameter), fitted with a rotational system and an IR temperature detector. Typical oxidation reactions were carried out in a sealed Pyrex tube under focused MW-irradiation as follows: 1-phenylethanol (5.0 mmol), catalyst precursor **1**–**5** (1–10 µmol) and an acid additive (5–200 µmol) were introduced into the reactor. An aqueous solution of TBHP (5.0–15.0 mmol, 70% in H_2O) was added, and the cylindrical Pyrex reactor was placed in the MW reactor. The system was left stirring under irradiation for 5–240 min within the 40–100 °C temperature range.

Caution! Although no problems were encountered in this work, reactions of TBHP or H_2O_2 with organic compounds at elevated temperatures may be explosive. Such tests should be performed with due care.

After the reaction, the mixture was allowed to cool. A power of 10 W was selected for all experiments, as it was previously found[13a] that 5 W is not sufficient to maintain the desired reaction temperature, and a higher power (e.g. 20 W) does not improve the product yield.

Conventional Method: For comparative purposes, several tests were also carried out with conventional heating in air using 25 mL round-bottomed flasks equipped with a reflux condenser. Under typical conditions, the catalyst precursor (10 µmol) was placed into the flask, followed by the addition of 1-phenylethanol (5.0 mmol), an acid additive (200 µmol) and TBHP (10.0 mmol, 70% in H_2O). In all cases, the reaction mixtures were vigorously stirred for 30 min with magnetic stirrers. The desired reaction temperature (typically 80 °C) was maintained with an oil bath.

Extraction and GC Analyses: In the methods mentioned above, the reaction samples (after cooling to ambient temperature) were treated with 5 mL of MeCN and 300 µL of benzaldehyde (GC internal standard). The aliquots were placed into Eppendorf vials and centrifuged. Diethyl ether was added to dilute the sample followed by GC analyses. Blank tests indicate that only traces of acetophenone were generated in the absence of metal catalyst precursor in the conventional method, whereas under MW irradiation the formation of acetophenone does not exceed 6% in the metal-free system.

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[1] a) L. F. Lindoy, *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, **1990**; b) *Macrocyclic Chemistry: Current Trends and Future Perspectives* (Ed.: K. Gloe), Springer, **2005**; c) *N4-macrocyclic Metal Complexes* (Eds.: J. H. Zagal, F. Bedioui, J.-P. Dodelet), Springer, **2006**.

[2] a) X. Y. Liang, P. J. Sadler, *Chem. Soc. Rev.* **2004**, *33*, 246; b) K. P. Wainwright, *Coord. Chem. Rev.* **1997**, *166*, 35; c) S. R. Cooper, *Acc. Chem. Res.* **1988**, *21*, 141; d) P. Chaudhuri, K. Wieghardt, *Prog. Inorg. Chem.* **1987**, *35*, 329; e) S. G. Murray, F. R. Hartley, *Chem. Rev.* **1981**, *81*, 356.

[3] See the Cambridge Structural Database (CSD, version 5.31, August 2010): F. H. Allen, *Acta Crystallogr., Sect. B* **2002**, *58*, 380.

[4] For reviews, see: a) J. P. Danks, N. R. Champness, M. Schroder, *Coord. Chem. Rev.* **1998**, *174*, 417; b) G. Reid, M. Schroder, *Chem. Soc. Rev.* **1990**, *19*, 239; c) L. F. Lindoy, G. V. Meehan, I. M. Vasilescu, H. J. Kim, J.-E. Lee, S. S. Lee, *Coord. Chem. Rev.* **2010**, *254*, 1713.

[5] For selected examples, see: a) M. Mameli, V. Lippolis, C. Caltagirone, J. L. Capelo, O. N. Faza, C. Lodeiro, *Inorg. Chem.* **2010**, *49*, 8276; b) M. Mameli, M. C. Aragoni, M. Arca, M. Atzori, A. Bencini, C. Bazzicalupi, A. J. Blake, C. Caltagirone, F. A. Devillanova, A. Garau, M. B. Hursthouse, F. Isaia, V. Lippolis, B. Valtancoli, *Inorg. Chem.* **2009**, *48*, 9236; c) Y. Yan, Y. Hu, G. P. Zhao, X. M. Kou, *Dyes Pigm.* **2008**, *79*, 210; d) D. A. Medvetz, K. D. Stakleff, N. Schreiber, P. D. Custer, K. Hindi, M. J. Panzner, D. D. Blanco, M. J. Taschner, C. A. Tessier, W. J. Youngs, *J. Med. Chem.* **2007**, *50*, 1703; e) M. W. Glenny, M. Lacombe, J. B. Love, A. J. Blake, L. F. Lindoy, R. C. Luckay, K. Gloe, B. Antonioli, C. Wilson, M. Schroder, *New J. Chem.* **2006**, *30*, 1755; f) M. Shamsipur, T. Poursaberi, M. Rezapour, M. R. Ganjali, M. F. Mousavi, V. Lippolis, D. R. Montesu, *Electroanalysis* **2004**, *16*, 1336; g) C. A. Grapperhaus, M. Li, A. K. Patra, S. Poturovic, P. M. Kozlowski, M. Z. Zgierski, M. S. Mashuta, *Inorg. Chem.* **2003**, *42*, 4382; h) A. H. Alberts, J.-M. Lehn, D. Parker, *J. Chem. Soc., Dalton Trans.* **1985**, 2311.

[6] L. F. Lindoy, R. J. Smith, *Inorg. Chem.* **1981**, *20*, 1314.

[7] G. Fritz, B. Steinfeld, B. Kersting, *Z. Naturforsch. B* **2007**, *62*, 508.

[8] R. Bentfeld, N. Ehlers, R. Mattes, *Chem. Ber.* **1995**, *128*, 1199.

[9] a) L. Que Jr., W. B. Tolman, *Nature* **2008**, *455*, 333; b) J. T. Groves, *J. Inorg. Biochem.* **2006**, *100*, 434; c) H. M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T. N. Bhat, H. Weissig, I. N. Shindyalov, P. E. Bourne, *Nucleic Acids Res.* **2000**, *28*, 235.

[10] a) R. Balasubramanian, S. M. Smith, S. Rawat, L. A. Yatsunyk, T. L. Stemmler, A. C. Rosenzweig, *Nature* **2010**, *465*, 115; b) R. A. Himes, K. Barnese, K. D. Karlin, *Angew. Chem. Int. Ed.* **2010**, *49*, 6714; c) R. A. Himes, K. D. Karlin, *Curr. Opin. Chem. Biol.* **2009**, *13*, 119; d) M. Merkx, D. A. Kopp, M. H. Sazinsky, J. L. Blazyk, J. Muller, S. J. Lippard, *Angew. Chem.* **2001**, *113*, 2860; *Angew. Chem. Int. Ed.* **2001**, *40*, 2782; e) I. Schlichting, J. Berendzen, K. Chu, A. M. Stock, S. A. Maves, D. E. Benson, B. M. Sweet, D. Ringe, G. A. Petsko, S. G. Sligar, *Science* **2000**, *287*, 1615; f) E. I. Solomon, U. M. Sundaram, T. E. Machonkin, *Chem. Rev.* **1996**, *96*, 2563.

[11] For selected reviews, see: a) I. Siewert, C. Limberg, *Chem. Eur. J.* **2009**, *15*, 10316; b) S. Friedle, E. Reisner, S. J. Lippard, *Chem. Soc. Rev.* **2010**, *39*, 2768; c) E. A. Lewis, W. B. Tolman, *Chem. Rev.* **2004**, *104*, 1047; d) M. Costas, M. P. Mehn, M. P. Jensen, L. Que Jr., *Chem. Rev.* **2004**, *104*, 939; e) E. Y. Tshuva, S. J. Lippard, *Chem. Rev.* **2004**, *104*, 987; f) P. Gamez, P. G. Aubel, W. L. Driessen, J. Reedijk, *Chem. Soc. Rev.* **2001**, *30*, 376.

[12] For recent examples, see: a) Y. Y. Karabach, M. F. C. Guedes da Silva, M. N. Kopylovich, B. Gil-Hernández, J. Sanchiz, A. M. Kirillov, A. J. L. Pombeiro, *Inorg. Chem.* **2010**, *49*, 11096; b) A. M. Kirillov, J. A. S. Coelho, M. V. Kirillova, M. F. C. Guedes da Silva, D. S. Nesterov, K. R. Gruenwald, M. Haukka, A. J. L. Pombeiro, *Inorg. Chem.* **2010**, *49*, 6390; c) M. V. Kirillova, A. M. Kirillov, A. J. L. Pombeiro, *Chem. Eur. J.* **2010**, *16*, 9485; d) M. V. Kirillova, Y. N. Kozlov, L. S. Shul'pina, O. Y. Lyakin, A. M. Kirillov, E. P. Talsi, A. J. L. Pombeiro, G. B. Shul'pin, *J. Catal.* **2009**, *268*, 26; e) M. V. Kirillova, A. M. Kirillov, A. J. L. Pombeiro, *Adv. Synth. Catal.* **2009**, *351*, 2936; f) M. V. Kirillova, A. M. Kirillov, M. L. Kuznetsov, J. A. L. Silva, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, *Chem. Commun.* **2009**, 2353; g) M. L. Kuznetsov, A. J. L. Pombeiro, *Inorg. Chem.* **2009**, *48*, 307.

[13] For recent examples, see: a) P. J. Figiel, M. N. Kopylovich, J. Lasri, M. F. C. Guedes da Silva, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, *Chem. Commun.* **2010**, *46*, 2766; b) P. J. Figiel, A. M. Kirillov, M. F. C. Guedes da Silva, J. Lasri, A. J. L. Pombeiro, *Dalton Trans.* **2010**, *39*, 9879; c) M. V. Kirillova, A. M. Kirillov, D. Mandelli, W. A. Carvalho, A. J. L. Pombeiro, G. B. Shul'pin, *J. Catal.* **2010**, *272*, 9; d) P. J. Figiel,

A. M. Kirillov, Y. Y. Karabach, M. N. Kopylovich, A. J. L. Pombeiro, *J. Mol. Catal. A* **2009**, *305*, 178.

[14] a) A. S. Craig, R. Kataky, R. C. Matthews, D. Parker, G. Ferguson, A. Lough, H. Adams, N. Bailey, H. Schneider, *J. Chem. Soc. Perkin Trans. 2* **1990**, 1523; b) A. J. Blake, J. P. Danks, I. A. Fallis, A. Harrison, W. S. Li, S. Parsons, S. A. Ross, G. Whittaker, M. Schroder, *J. Chem. Soc., Dalton Trans.* **1998**, 3969.

[15] A. Company, L. Gómez, M. Güell, X. Ribas, J. M. Luis, L. Que Jr., M. Costas, *J. Am. Chem. Soc.* **2007**, *129*, 15766.

[16] a) A. L. Gott, P. C. McGowan, T. J. Podesta, M. Thornton-Pett, *J. Chem. Soc., Dalton Trans.* **2002**, 3619; b) J. England, R. Gondhia, L. Bigorra-Lopez, A. R. Petersen, A. J. P. White, G. J. P. Britovsek, *Dalton Trans.* **2009**, 5319.

[17] K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 5th ed., Wiley, New York, **1997**.

[18] D. H. Johnston, D. F. Shiver, *Inorg. Chem.* **1993**, *32*, 1045.

[19] W. Henderson, J. S. McIndoe, *Mass Spectrometry of Inorganic, Coordination and Organometallic Compounds: Tools – Techniques – Tips*, Wiley, **2005**.

[20] a) V. A. Grillo, L. R. Gahan, G. R. Hanson, R. Stranger, T. W. Hambley, K. S. Murray, B. Moubaraki, J. D. Cashion, *J. Chem. Soc., Dalton Trans.* **1998**, 2341; b) U. Heinzel, A. Henke, R. Mattes, *J. Chem. Soc., Dalton Trans.* **1997**, 501.

[21] a) M. Arca, A. J. Blake, V. Lippolis, D. R. Montesu, J. McMaster, L. Tei, M. Schroder, *Eur. J. Inorg. Chem.* **2003**, 1232; b) H. Weller, L. Siegfried, M. Neuburger, M. Zehnder, T. A. Kaden, *Helv. Chim. Acta* **1997**, *80*, 2315.

[22] a) R. R. Fernandes, M. V. Kirillova, J. A. L. da Silva, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, *Appl. Catal. A* **2009**, *353*, 107; b) D. S. Nesterov, V. N. Kokozay, V. V. Dyakonenko, O. V. Shishkin, J. Jezierska, A. Ozarowski, A. M. Kirillov, M. N. Kopylovich, A. J. L. Pombeiro, *Chem. Commun.* **2006**, 4605; c) M. N. Kopylovich, A. M. Kirillov, A. K. Baev, A. J. L. Pombeiro, *J. Mol. Catal. A* **2003**, *206*, 163.

[23] a) K. R. Gruenwald, A. M. Kirillov, M. Haukka, J. Sanchiz, A. J. L. Pombeiro, *Dalton Trans.* **2009**, 2109; b) Y. Y. Karabach, A. M. Kirillov, M. Haukka, M. N. Kopylovich, A. J. L. Pombeiro, *J. Inorg. Biochem.* **2008**, *102*, 1190; c) C. Di Nicola, Y. Y. Karabach, A. M. Kirillov, M. Monari, L. Pandolfo, C. Pettinari, A. J. L. Pombeiro, *Inorg. Chem.* **2007**, *46*, 221; d) A. M. Kirillov, M. N. Kopylovich, M. V. Kirillova, E. Y. Karabach, M. Haukka, M. F. C. G. da Silva, A. J. L. Pombeiro, *Adv. Synth. Catal.* **2006**, *348*, 159; e) A. M. Kirillov, M. N. Kopylovich, M. V. Kirillova, M. Haukka, M. F. C. G. da Silva, A. J. L. Pombeiro, *Angew. Chem.* **2005**, *117*, 4419; *Angew. Chem. Int. Ed.* **2005**, *44*, 4345.

[24] U. Schuchardt, D. Cardoso, R. Sercheli, R. Pereira, R. S. da Cruz, M. C. Guerreiro, D. Mandelli, E. V. Spinace, E. L. Pires, *Appl. Catal. A* **2001**, *211*, 1.

[25] a) *Ullmann's Encyclopedia of Industrial Chemistry*, 6th ed., Wiley-VCH, Weinheim, Germany, **2002**; b) *Encyclopedia of Chemical Technology*, 5th ed., Kirk-Othmer, Wiley, New York, **2004**.

[26] a) G. B. Shul'pin, *Mini-Rev. Org. Chem.* **2009**, *6*, 95; b) G. B. Shul'pin, *J. Mol. Catal. A* **2002**, *189*, 39; c) G. B. Shul'pin, *C. R. Chim.* **2003**, *6*, 163.

[27] a) G. V. Nizova, B. Krebs, G. Süss-Fink, S. Schindler, L. Westerheide, L. G. Cuervo, G. B. Shul'pin, *Tetrahedron* **2002**, *58*, 9231; b) G. B. Shul'pin, G. V. Nizova, Y. N. Kozlov, L. G. Cuervo, G. Süss-Fink, *Adv. Synth. Catal.* **2004**, *346*, 317; c) J. England, G. J. P. Britovsek, N. Rabadia, A. J. P. White, *Inorg. Chem.* **2007**, *46*, 3752; d) V. B. Romakh, B. Therrien, G. Süss-Fink, G. B. Shul'pin, *Inorg. Chem.* **2007**, *46*, 3166; e) T. F. S. Silva, E. C. B. A. Alegria, L. M. D. R. S. Martins, A. J. L. Pombeiro, *Adv. Synth. Catal.* **2008**, *350*, 706; f) S. Tanase, P. Marques-Gallego, W. R. Browne, R. Hage, E. Bouwman, B. L. Feringa, J. Reedijk, *Dalton Trans.* **2008**, 2026; g) G. Trettenhahn, M. Nagl, N. Neuwirth, V. B. Arion, W. Jary, P. Pochlauer, W. Schmid, *Angew. Chem.* **2006**, *118*, 2860; *Angew. Chem. Int. Ed.* **2006**, *45*, 2794.

[28] M. V. Kirillova, A. M. Kirillov, M. F. C. Guedes da Silva, A. J. L. Pombeiro, *Eur. J. Inorg. Chem.* **2008**, 3423.

[29] a) A. E. Shilov, G. B. Shul'pin, *Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes*, Kluwer Academic Publishers, Dordrecht, The Netherlands, **2000**; b) A. E. Shilov, G. B. Shul'pin, *Chem. Rev.* **1997**, *97*, 2879; c) G. B. Shul'pin, *Org. Biomol. Chem.* **2010**, *8*, 4217.

[30] M. V. Kirillova, A. M. Kirillov, P. M. Reis, J. A. L. Silva, J. J. R. Fraústo da Silva, A. J. L. Pombeiro, *J. Catal.* **2007**, *248*, 130.

[31] J. A. Halfen, S. Mahapatra, E. C. Wilkinson, S. Kaderli, V. G. Young Jr., L. Que Jr., A. D. Zuberbühler, W. B. Tolman, *Science* **1996**, *271*, 1397.

[32] a) G. Tojo, M. Fernández, *Oxidation of Alcohols to Aldehydes and Ketones: A Guide to Current Common Practice*, Springer, New York, **2006**; b) I. W. C. E. Arends, R. A. Sheldon, in: *Modern Oxidation Methods* (Ed.: J.-E. Bäckvall), Wiley-VCH, Weinheim, Germany, **2004**, pp. 83–118.

[33] a) R. A. Sheldon, I. W. C. E. Arends, G.-J. Ten Brink, A. Dijksman, *Acc. Chem. Res.* **2002**, *35*, 774; b) R. A. Sheldon, I. W. C. E. Arends, A. Dijksman, *Catal. Today* **2000**, *57*, 157; c) M. Besson, P. Gallezot, *Catal. Today* **2000**, *57*, 127; d) J. Muzart, *Tetrahedron* **2003**, *59*, 5789.

[34] G. Rothenberg, L. Feldberg, H. Wiener, Y. Sasson, *J. Chem. Soc. Perkin Trans. 2* **1998**, 2429.

[35] a) O. C. Kappe, D. Dallinger, S. Murphree, *Practical Microwave Synthesis for Organic Chemists*, Wiley-VCH, Weinheim, Germany, **2008**; b) V. Polshettiwar, R. S. Varma, *Acc. Chem. Res.* **2008**, *41*, 629; c) D. Dallinger, C. O. Kappe, *Chem. Rev.* **2007**, *107*, 2563; d) *Microwave Assisted Organic Synthesis* (Eds.: J. P. Tierney, P. Lidström), Blackwell Publishing/CRC Press, Oxford, **2005**; e) *Microwaves in Organic Synthesis* (Ed.: A. Loupy), Wiley-VCH, Weinheim, Germany, **2002**.

[36] a) D. Betz, P. Altmann, M. Cokoja, W. A. Herrmann, F. E. Kühn, *Coord. Chem. Rev.* **2011**, *255*, 1518; b) *Ionic Liquids in Synthesis* (Eds.: P. Wasserscheid, T. Welton), vol. 2, Wiley-VCH, Weinheim, Germany, **2008**; c) S. F. Liu, J. Xiao, *J. Mol. Catal. A* **2007**, *270*, 1; d) P. J. Dyson, T. J. Geldbach, *Metal Catalysed Reactions in Ionic Liquids*, Springer, **2005**.

[37] a) Bruker, *APEX2 & SAINT*, AXS Inc., Madison, WI, **2004**; b) G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112; c) L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837.

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