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Copper(II) Complexes of Arylhydrazone of 1*H*-Indene-1,3(2*H*)-dione as Catalysts for the Oxidation of Cyclohexane in Ionic Liquids

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Abstract: The copper(II) complexes [CuL(H₂O)₂]·H₂O (**1**) and [CuL(dea)] (**2**) [L = 2-(2-(1,3-dioxo-1*H*-inden-2(3*H*)-ylidene)hydrazinyl)benzenesulfonate, dea = diethanolamine] were applied as catalysts in the peroxidative (with *tert*-butyl-hydroperoxide or hydrogen peroxide) conversion of cyclohexane to cyclohexanol and cyclohexanone, either in acetonitrile or in any of the ionic liquids [bmim][NTf₂] and [hmim][NTf₂] [bmim = 1-butyl-3-methylimidazolium, hmim = 1-hexyl-3-methylimidazolium, NTf₂ = bis(trifluoromethanesulfonyl) imide]. *Tert*-butyl-hydroperoxide led to better product yields, as compared to H₂O₂, with a selectivity directed towards cyclohexanone. The ILs showed a better performance than the conventional solvent for the copper complex **1**. No catalytic activity was observed for **2** in the presence of an IL.

Keywords: catalysis; arylhydrazones; copper; ionic liquids; cyclohexane oxidation

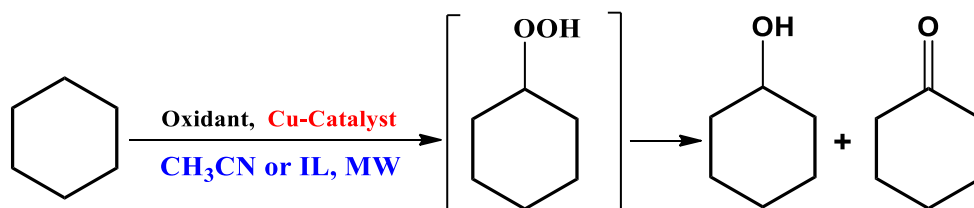
1. Introduction

Due to their intrinsically low reactivity, the oxidation of saturated hydrocarbons under mild reaction conditions is a great challenge in catalysis [1–7]. This is of particular significance to the oxidation of cyclohexane to cyclohexanol and cyclohexanone, in view of the involvement of these products for the production of nylon-6 and nylon-6,6 [8,9].

The conversion of alkanes into valuable products using green oxidants such as molecular oxygen, *tert*-butyl hydroperoxide (TBHP) or hydrogen peroxide is attaining considerable attention, and a variety of transition metals are being applied [1–21].

The usage of ionic liquids (ILs) as solvents in catalysis [22–25] and for cyclohexane oxidation in particular is scarce. Some studies with manganese(III) porphyrins as catalysts in [bmim][PF₆] (PF₆ = hexafluorophosphate) mixed with dichloromethane or acetonitrile showed excellent yields (up to 88%) for the hydroxylation of cyclohexane, cyclooctane, adamantane and tetralin [26], as well as of tetrahydronaphthalene [27]. Examples of transition metal catalysts for the oxidation of cyclohexane include iron scorpionates [28–35], copper(II) terpyridine-based compounds [36], benzene–sulfonate and benzene–carboxylate copper(II) polymers [37,38], and polynuclear copper(II)–arylhydrazone complexes [39], and other metals, such as vanadium [40–46].

Despite the potential applications of arylhydrazone and their metal complexes, mainly in the oxidation of alkanes and alcohols [39–53], the use of such compounds in catalysis is still an understudied area. In pursuit of our interest in the transition metal-catalysed peroxidative [by *tert*-butyl hydroperoxide (TBHP) or H_2O_2] oxidation of hydrocarbons in ILs [36–39], we have tested a pair of already known [51] copper(II) complexes, viz. $[\text{CuL}(\text{H}_2\text{O})_2] \cdot \text{H}_2\text{O}$ (**1**) and $[\text{CuL}(\text{dea})]$ (**2**), as catalysts for cyclohexane conversion into cyclohexanol and cyclohexanone (Scheme 1), in acetonitrile or in any of the ionic liquids $[\text{bmim}][\text{NTf}_2]$ or $[\text{hmim}][\text{NTf}_2]$ as solvents and under low-power (10 W) microwave irradiation. The favorable effect of microwaves (MWs) in comparison with conventional heating has been recognized in alkane oxidation [54].



Scheme 1. Catalytic oxidation of cyclohexane. IL: ionic liquids; MW: microwave.

The application of ILs in alkane functionalization is still in its infancy, in spite of their attractiveness as a green alternative to volatile organic solvents. Another eventual advantage in using IL is the possibility of recycling [39], which is not the case for the use of conventional solvents. In this work, the imidazolium-based ILs mentioned above are tested in order to try to fill this gap.

Thus, in this study, we intend to achieve the following aims: (i) to apply the known copper(II) complexes based on 2-(2-(1,3-dioxo-1*H*-inden-2(3*H*)-ylidene)hydrazinyl)benzenesulfonate as catalysts for the peroxidative oxidation of cyclohexane, in acetonitrile and in an IL; (ii) to compare the oxidation performance of H_2O_2 and TBHP; and (iii) to recycle the IL + catalyst system after the reaction in order to test its stability.

2. Results and Discussion

2.1. Conventional Medium

Tables 1 and 2 present the results for the peroxidative oxidation of cyclohexane in acetonitrile, using **1** and **2** as catalysts, respectively, and also comprising the studies of the effect of the catalyst and peroxide amounts, type of peroxide and reaction time.

The product yield of the microwave assisted the peroxidative oxidation of cyclohexane depends on the catalyst amount, on the time of reaction, and on the type of oxidant, as expected. For example, the yield of cyclohexanol + cyclohexanone increases when TBHP is used instead of H_2O_2 (Table 1, e.g., compare entries 7 and 15), and the tested catalyst amounts (10^{-4} and $10^{-5} \text{ mol} \cdot \text{L}^{-1}$) when using TBHP also increases with the decrease of the amount of catalyst **1**, probably due to a more extensive overoxidation when using the higher catalyst amount. Upon increasing the reaction time, the yield of product also increases at least up to a maximum of 2 h reaction time. For this reaction time of 2 h and using $1 \times 10^{-5} \text{ mol} \cdot \text{L}^{-1}$ of catalyst **1**, 29.6% yield of total product was obtained using TBHP as oxidant (Table 1, entry 15).

When using H_2O_2 as oxidant, a higher selectivity towards the alcohol is observed, while with TBHP, the amount of this product is lower than that of the ketone (Table 1, entries 9–12), and eventually no alcohol is detected (Table 1, entries 13–16).

It was also observed that with TBHP and a concentration of catalyst **1** of $1 \times 10^{-5} \text{ mol} \cdot \text{L}^{-1}$, TONs above 6×10^3 are attained, reaching 136×10^2 in 2 h (Table 1, entry 15). A TOF value above $120 \times 10^2 \text{ h}^{-1}$ is achieved at the shorter reaction time of 30 min (Table 1, entry 13).

Table 1. Oxidation of cyclohexane to cyclohexanol and cyclohexanone catalysed by **1** ^a.

Entry	Oxidant	Catalyst Amount (mol L ⁻¹)	Time (min)	Yield % (after PPh ₃) ^b			Total TON ^d	Total TOF ^e (h ⁻¹)	[Alc]/[Keto] ^f
				Cyclo-Hexanone	Cyclo-Hexanol	Total ^c			
1	H ₂ O ₂	1 × 10 ⁻⁴	30	0.8	4.2	5.0	230	460	5.3
2			60	3.8	5.0	8.9	409	409	1.3
3			120	4.4	5.2	9.6	442	221	1.2
4			180	4.7	8.1	12.8	589	196	1.7
5	H ₂ O ₂	1 × 10 ⁻⁵	30	2.3	3.2	5.4	248 × 10	497 × 10	1.4
6			60	2.2	4.5	6.7	308 × 10	308 × 10	2.0
7			120	4.4	4.7	9.1	419 × 10	209 × 10	1.1
8			180	3.7	4.7	8.4	386 × 10	129 × 10	1.3
9	TBHP	1 × 10 ⁻⁴	30	4.7	1.7	6.4	294	588	0.4
10			60	8.4	2.2	10.6	488	488	0.3
11			120	13.0	2.3	15.3	704	352	0.2
12			180	21.7	2.8	24.6	113 × 10	377	0.1
13	TBHP	1 × 10 ⁻⁵	30	13.5	0.0	13.5	621 × 10	124 × 10 ²	0.0
14			60	20.2	0.0	20.2	929 × 10	929 × 10	0.0
15			120	29.6	0.0	29.6	136 × 10 ²	681 × 10	0.0
16			180	17.3	0.0	17.3	796 × 10	265 × 10	0.0
17 ^g	H ₂ O ₂	1 × 10 ⁻⁵	120	trace	0.0	0.0	-	-	-
18 ^g	TBHP	1 × 10 ⁻⁵	120	trace	0.0	0.0	-	-	-
19 ^h	TBHP	4 × 10 ⁻⁴	120	1.6	3.8	5.4	49	24	2.4

^a Reaction conditions, unless stated otherwise: [cyclohexane]₀ = 0.46 mol L⁻¹, [oxidant]₀ = 0.92 mol L⁻¹, additive (H₂SO₄) = 0.019 mol L⁻¹, CH₃CN (3 mL), 50 °C. ^b Based on GC (Gas Chromatography) analysis, after treatment with PPh₃. ^c Values correspond to total yields (moles of products/100 moles of cyclohexane). ^d TON = Total turnover number (moles of product/mol of catalyst). ^e TOF (h⁻¹) = turnover frequency (TON/time). ^f Ratio between the concentrations of cyclohexanol (Alc) and cyclohexanone (Keto). ^g Blank test (no metal catalyst).

^h Cu(NO₃)₂ as catalyst [55].

Table 2. Oxidation of cyclohexane to cyclohexanol and cyclohexanone catalysed by **2** ^a.

Entry	Oxidant	Catalyst Amount (mol L ^{−1})	Time (min)	Yield (%) (after PPh ₃) ^b			Total TON ^d	Total TOF ^e (h ^{−1})	[Alc]/[Keto] ^f
				Cyclo-Hexanone	Cyclo-Hexanol	Total ^c			
1	H ₂ O ₂	1 × 10 ^{−4}	30	1.1	0.3	1.4	64	128	0.3
2			60	1.0	0.5	1.5	69	69	0.5
3			120	1.4	0.9	2.3	106	53	0.6
4			180	2.0	0.8	2.8	129	43	0.4
5	H ₂ O ₂	1 × 10 ^{−5}	30	1.2	0.3	1.5	690	138 × 10	0.3
6			60	3.5	1.7	5.2	239 × 10	239 × 10	0.5
7			120	3.9	2.2	6.1	281 × 10	140 × 10	0.6
8			180	5.4	3.5	8.9	409 × 10	137 × 10	0.6
9	TBHP	1 × 10 ^{−4}	30	17.4	0.0	17.4	800	160 × 10	0.0
10			60	18.4	0.0	18.4	846	846	0.0
11			120	20.0	0.0	20.0	920	460	0.0
12			180	24.5	0.0	24.5	113 × 10	376	0.0
13	TBHP	1 × 10 ^{−5}	30	7.7	0.0	7.7	354 × 10	708 × 10	0.0
14			60	15.2	0.0	15.2	699 × 10	699 × 10	0.0
15			120	15.4	0.0	15.4	708 × 10	354 × 10	0.0
16			180	11.1	0.0	11.1	511 × 10	170 × 10	0.0
17 ^g	H ₂ O ₂	1 × 10 ^{−5}	120	trace	0.0	0.0	-	-	-
18 ^g	TBHP	1 × 10 ^{−5}	120	trace	0.0	0.0	-	-	-

^a Reaction conditions, unless stated otherwise: [cyclohexane]₀ = 0.46 mol L^{−1}, [oxidant]₀ = 0.92 mol L^{−1}, additive (H₂SO₄) = 0.019 mol L^{−1}, CH₃CN (3 mL), 50 °C. ^b Based on GC analysis, after treatment with PPh₃. ^c Values correspond to total yields (moles of products/100 moles of cyclohexane). ^d TON = Total turnover number (moles of product/mol of catalyst). ^e TOF (h^{−1}) = turnover frequency (TON/time). ^f Ratio between the concentrations of cyclohexanol (Alc) and cyclohexanone (Keto). ^g Blank test (no metal catalyst).

In comparison to **1**, the catalytic activity of **2** is lower (Table 2). However, the yields of the product almost always increase with time and for both types of oxidant. In addition, catalyst **2** is 100% selective for the ketone versus the alcohol by using TBHP as oxidant (Table 2, entries 9–16). The maximum TON value achieved with **2** using TBHP and the lowest tested concentration of the catalyst, 708×10 in 2 h (Table 2, entry 15), is nearly half that achieved with **1** under the same experimental conditions (136×10^2 , Table 1, entry 15).

The catalytic performances of **1** are comparable in terms of yield with those obtained with aqua complexes of iron with arylhydrazone- β -diketone ligands, at room temperature, but using the higher catalyst loading of $\text{ca. } 1 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$, the 1:7.5 substrate/oxidant ratio and 6 h reaction, achieving TON values not higher than 290 [52]. With catalyst **1**, a maximum TON value of 13×10^3 was attained using $1 \times 10^{-5} \text{ mol} \cdot \text{L}^{-1}$ of catalyst **1** and only the 1:2 substrate/oxidant ratio. Similar yields were achieved with copper complexes [55], but for 6 h reaction and the substrate/oxidant ratio of 1:10.

2.2. Unconventional Medium (Ionic Liquid)

In view of the better catalytic performance of **1** relative to **2**, the former catalyst, at the lowest concentration of $1 \times 10^{-5} \text{ mol} \cdot \text{L}^{-1}$, was used for the peroxidative oxidation of cyclohexane and using the ionic liquid [bmim][NTf₂] or [hmim][NTf₂] as solvent. Hydrogen peroxide was kept as the oxidant as it is inexpensive and environmentally friendly. No acidic additive was used. Higher yields of product were achieved in [bmim][NTf₂], reaching 13.9% in 3 h (Table 3, entry 4; compare with Table 1, entry 8). After such a time of reaction, the cyclohexanol/cyclohexanone ratio is similar to that obtained with acetonitrile as solvent, but the TON value is now higher (639×10 against 386×10 ; compare Table 3, entry 4 and entry 8 in Table 1). That ratio reaches a maximum of 2.4 upon 2 h reaction, with cyclohexanol being here the major product; the alcohol yield then decreases with a longer reaction time, while the ketone yield increases (Table 3; compare entries 3 and 4).

Table 3. Oxidation of cyclohexane to cyclohexanol and cyclohexanone catalysed by **1**^a in an IL.

Entry	Oxidant	Time (min)	Yield (%) (after PPh ₃) ^b			Total TON ^d	Total TOF ^e (h ^{−1})	[Alc]/[Keto] ^f
			Cyclohexanone	Cyclohexanol	Total ^c			
[bmim][NTf ₂]								
1	H ₂ O ₂	30	3.6	5.2	8.8	405 × 10	810 × 10	1.4
2		60	4.4	5.9	10.3	474 × 10	474 × 10	1.3
3		120	3.5	8.5	12.0	552 × 10	276 × 10	2.4
4		180	6.1	7.8	13.9	639 × 10	213 × 10	1.3
[hmim][NTf ₂]								
5	H ₂ O ₂	30	0.0	0.0	0.0	0	0	n.d.
6		60	0.0	0.0	0.0	0	0	n.d.
7		120	0.11	0.10	0.21	97	49	0.9
8		180	0.18	0.16	0.34	156	52	0.9

^a Reaction conditions, unless stated otherwise: [cyclohexane]₀ = 0.46 mol L^{−1}, [H₂O₂]₀ = 0.92 mol L^{−1}, [cat] = $1 \times 10^{-5} \text{ mol L}^{-1}$, IL (2 mL), 50 °C. ^b Based on GC analysis, after treatment with PPh₃. ^c Values correspond to total yields (moles of products/100 moles of cyclohexane). ^d TON = Total turnover number (moles of product/mol of catalyst). ^e TOF (h^{−1}) = turnover frequency (TON/time). ^f Ratio between the concentrations of cyclohexanol (Alc) and cyclohexanone (Keto).

By using [hmim][NTf₂] as solvent, a very low yield of 0.34% was obtained after 3 h (Table 3, entry 8), much lower than those observed for [bmim][NTf₂] and even acetonitrile (13.9%, Table 3, entry 4; 8.4%, Table 1, entry 8). This difference in yield may eventually be due to the higher viscosity of [hmim][NTf₂] relative to [bmim][NTf₂] (26.2 mPa·s for the former and 20.4 mPa·s for the latter, at 323.15 K) [56].

The performance of catalyst **1** after recycling is presented in Table 4, which clearly indicates a severe loss of activity.

Table 4. Recycling of the system **1** + [bmim][NTf₂]^a.

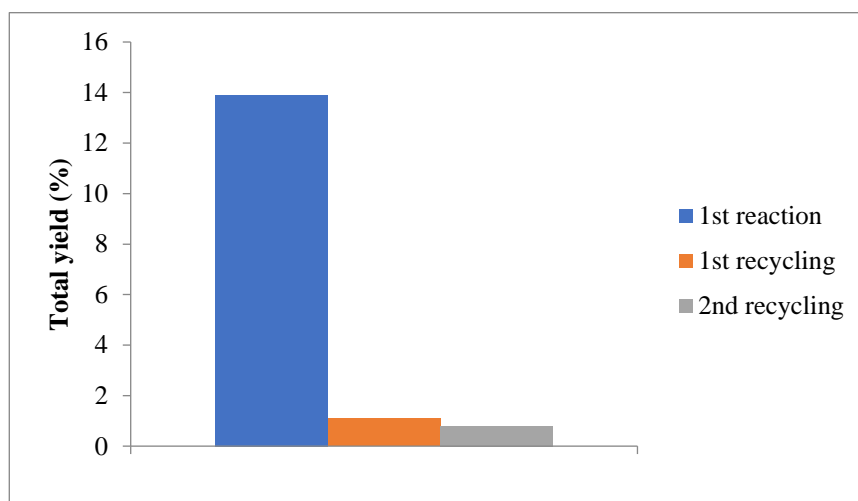
Entry	Yield (%) (after PPh ₃) ^b			Activity (%)	Total TON ^d	Total TOF (h ^{−1}) ^e	[Alc]/[Keto] ^f
	Cyclohexanone	Cyclohexanol	Total ^c				
1	6.1	7.8	13.9	100	639 × 10	213 × 10	1.3
2	0.3	0.8	1.1	8	638	213	2.7
3	0.5	0.3	0.8	6	464	155	0.6

^a Reaction conditions, unless stated otherwise: [cyclohexane]₀ = 0.58 mol L^{−1}, [H₂O₂]₀ = 1.15 mol L^{−1}, [cat] = 1 × 10^{−5} mol L^{−1}, IL (2 mL), 50 °C, reaction time = 180 min. ^b Based on GC analysis, after treatment with PPh₃. ^c Values correspond to total yields (moles of products/100 moles of cyclohexane). ^d TON = Total turnover number (moles of product/mol of catalyst). ^e TOF (h^{−1}) = turnover frequency (TON/time). ^f Ratio between the concentrations of cyclohexanol (Alc) and cyclohexanone (Keto).

For homogeneous catalysis, the main industrial process exhibits yields of 4–10% of KA (ketone + alcohol) oil (cyclohexanol + cyclohexanone) with a maximum 85% selectivity at 150 °C [57]. The present study shows a visible improvement, both in yield and in using milder conditions. Other homogeneous Cu(II) complexes of arylhydrazone published previously led to overall yields up to 34% and TONs up to 42 [58]. For Cu(II) complexes of pyrazole the obtained yields were up to 58% and TONs up to 108 × 10 in 30 min reaction time at 100 °C [59]. In our study, our TONs are higher.

The peroxidative oxidation of cyclohexane catalyzed by polynuclear copper(II) complexes of arylhydrazone with H₂O₂, was also carried out in [bmim][BF₄], in which a yield of 29.5% was achieved, at 90 min reaction and the same temperature as used here, but with 10^{−3} mol·L^{−1} of catalyst [39], which is two orders of magnitude higher than that used in our work.

Regarding the effect of the IL as the reaction medium, we note that the interaction of the scorpionate iron(II) catalyst [FeCl₂(Tpm)] (Tpm = hydrotris(pyrazol-1-yl)methane) with the IL 1-butyl-3-methylimidazolium dicyanamide ([bmim][N(CN)₂]) was investigated using theoretical DFT calculations [28]. They indicate the coordination of the dicyanamide anion to form the neutral associate [bmim][FeCl₂{N(CN)₂}(Tpm)], which accounts for the effective retention of the catalyst by the IL, without appreciable loss upon recycling. In the current case of the copper(II) complexes [CuL(H₂O)₂]·H₂O (**1**) and [CuL(dea)] (**2**), the interaction of the copper sites with the NTf₂[−] anion of the IL is expected to be weaker for steric reasons in view of the bulkiness of this anion, which does not allow the prevention of catalyst leaching. This can account, at least in part, for the ineffective catalyst recycling, as it is shown in Figure 1. The possible formation of inactive copper compounds (e.g., copper oxido species) can also contribute to such behaviour.

**Figure 1.** Recycling of the IL + catalyst **1** system.

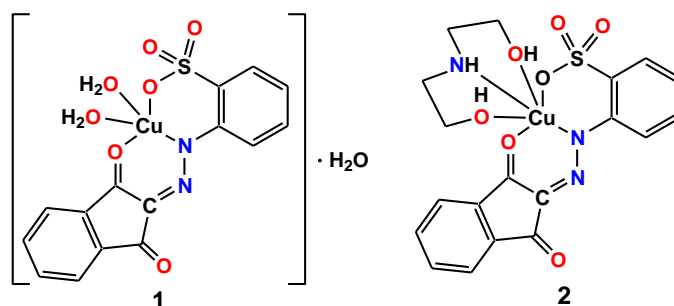
3. Experimental Section

3.1. Materials and Equipment

All chemicals were obtained from commercial sources and used as received. All the catalytic work was performed in a Microwave Synthesis Reactor (Anton Paar, Graz, Austria) at 50 °C. Chromatographic analyses were undertaken by using a Fisons Instruments GC 8000 (Fisons Instruments SpA, Rodano, Italy) series gas chromatograph with a DB-624 (J&W) capillary column (Agilent, Santa Clara, CA, USA) (flame ionization detector) (temperature of injector: 230 °C) and the Jasco-Borwin v.1.50 software (ChromatographyForum, Ashford, UK) (temperature range 100–180 °C). The internal standard method was used to quantify the organic products (see below for details).

3.2. Synthesis of the Catalysts

The synthesis and characterization of both copper(II) catalysts (Scheme 2) were reported earlier [51] and are therefore not discussed here.



Scheme 2. Copper catalysts used in this work [51].

3.3. Oxidation of Cyclohexane and Products Analysis

Cyclohexane oxidations were carried out in a microwave (MW) reactor. Typically, 3 mL of acetonitrile was used (in the experiments with this solvent), to which the solid catalyst was added, and the solution was stirred to ensure the total dissolution of the catalyst. Then, the substrate (cyclohexane) was added to the reaction mixture (initial cyclohexane concentration in the reaction solution of 0.46 mol L⁻¹), followed by the acid additive (concentrated H₂SO₄, 5 µL, 0.094 mmol) and the reaction started upon the addition of the oxidant (aq. 30% or 50% H₂O₂ or aq. 70% TBHP) in one portion (initial concentration in the reaction solution of 0.92 mol L⁻¹). Other acidic additives were tested, such as HNO₃, but no product was detected. The reaction was subjected to microwave irradiation (10 W) for variable periods of time and at a temperature of 50 °C (for comparison with other works, which have also used this temperature).

In the experiments with the ionic liquid ([bmim][NTf₂] or [hmim][NTf₂]), 2 mL of IL was used instead of NCMe, and the same reaction conditions mentioned above were applied, except for the fact that, in this case, no acidic additive was used and only aq. H₂O₂ was applied as oxidant. After the reaction with IL, 0.500 mL of distilled water was added and the mixture stirred to ensure the extraction of the products to the aqueous phase. A further amount of distilled water was added after the analysis, but no additional product was extracted.

The products were identified by GC, by the comparison of the retention times with those of commercial products. Cyclopentanone (0.05 mL) was used as an internal standard. The amount of formed product was estimated by comparing the retention times and peak areas of the reaction species with the ones of commercially available products. An example of yield calculation is presented in Supplementary Materials. PPh₃ was added to the samples, to ensure that all the cyclohexylhydroperoxide present in the mixture was converted to cyclohexanol [60–62]. Upon each PPh₃ addition, a little effervescence occurred. When no more effervescence was observed, the addition of PPh₃ was stopped.

4. Conclusions

In the present work, it was observed that catalyst **1** is more active than **2**, in accordance with its lower coordination number and the presence of two labile water ligands. Moreover, *tert*-butyl-hydroperoxide, a stronger oxidant than H₂O₂, gives rise to higher product yields, and with a higher selectivity towards cyclohexanone instead of cyclohexanol. With [bmim][NTf₂], good results were achieved, but only with catalyst **1**, even with a small catalyst amount and with the weaker oxidant H₂O₂. By increasing the cation chain length (use of [hmim][NTf₂]), the product yield sharply decreases. Although the higher viscosity of the latter IL may have an effect, further studies with ILs with cations with different sizes must be undertaken to understand the effect of the IL size.

Supplementary Materials: The following are available online at <http://www.mdpi.com/2073-4344/8/12/636/s1>, Figure S1. Example of GC chromatogram; Figure S2. Calibration line for cyclohexanone; Table S1. Species areas.

Author Contributions: G.A.O.T. did the synthesis of the complexes, the catalytic tests and wrote the majority of the paper; A.P.C.R. did the plan of the catalytic studies and wrote the discussion of the catalytic results; M.F.C.G.d.S. solved the complexes structures by X-ray diffraction; K.T.M. helped in the complexes synthesis and wrote a part of the introduction; L.C.B. gave general revision; A.J.L.P. did the final revision of the paper.

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Conflicts of Interest: The authors declare no conflicts of interest.

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