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Green, selective and swift oxidation of cyclic alcohols to corresponding ketones

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ABSTRACT

Cyclohexanol oxidation to cyclohexanone is an important reaction in both organic chemistry and industry. We propose here an efficient, eco-friendly, and general method for oxidizing five- to eight-membered cyclanols used as model substrates, with aqueous hydrogen peroxide (H_2O_2) in the presence of tungstic acid (H_2WO_4) as a catalyst and an ammonium-based ionic liquid (IL) as a co-catalyst under organic solvent-free conditions. Cyclohexanol was found to be the most reactive of the four tested cyclanols. In addition, the role of the IL as a phase transfer catalyst was confirmed by the use of Aliquat 336 and the kinetic of the reaction was significantly improved under microwave or ultrasonic activation, leading to excellent yields in only a few minutes.

1. Introduction

The oxidation of alcohols to their corresponding carbonyl compounds is an important functional transformation in organic synthesis [1]. Among them, cyclohexanone is an excellent solvent widely used in coating processes [2]. Currently the industrial production of cyclohexanone is based on three main processes: (1) the nitric acid oxidation of cyclohexanol [3,4], (2) the two-step process of cyclohexane oxidation by nitric acid [5,6] and (3) the hydrogenation of phenol [7,8]. The two latter processes suffer, respectively, from the generation of a significant amount of cyclohexane by-products, and from the use of an energy-intensive process for the hydrogenation reaction. As regards the cyclohexanol oxidation route, wide use is made of stoichiometric amounts of inorganic oxidants under high temperature in particular chromium(VI) reagents, and environmentally harmful solvents, namely chlorinated hydrocarbons [9].

In the context of Green Chemistry [10], the importance of developing efficient, eco-friendly, highly selective, economical and safe processes in both academia and industry represents a real challenge for the chemistry of the 21st century [11–13]. In accordance with the twelve principles of Green Chemistry, the best oxidants are molecular oxygen or air, but a major limitation of their use is, in many cases, the low selectivity of the associate processes, and the limiting activation of metal catalysts can reduce the opportunities offered by O_2 [14]. In this context, aqueous hydrogen peroxide, H_2O_2, also represents an ideal reactant, with its ability to oxidize organic compounds with a high atom efficiency of 47%, leading to H_2O molecules as the only theoretical co-product [15]. Additionally, it is relatively cheap (<500 US dollar ton^{-1} (35% H_2O_2)) and about 3 million metric tons are produced annually, mainly for use as bleach [15].

Numerous works on the oxidation of alcohols by H_2O_2 are reported in the literature [14,16,17]. In many cases, tungstate complexes are chosen as catalysts to produce to carboxylic acids [18], aldehydes [19,20] or ketones [21,22]. Recently, Chen et al. have explored the effects of the 1-methyl-3-octylimidazolium chloride

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ionic liquid ([C_8mim]Cl) on the selective oxidation of cyclohexanol to cyclohexanone in the presence of WO_3 catalyst (0.6 mol%) [23]. Based on COSMO-RS (COnductor-like Screening MOdel for Real Solvents) calculations, the authors showed that hydrophobic ionic liquids (ILs) tend to be more suitable for the reaction than polar ILs, especially those with a long alkyl chain (*e.g.*, octyl chain).

In recent years, the use of room-temperature ionic liquids (RTILs) as reaction medium has become increasingly attractive [24–26]. The reason is that these ionic solvents display interesting physicochemical properties and can be used advantageously to replace volatile organic solvents (low vapor pressure, air and moisture stabilities, high polarity, etc.). Moreover, ILs display very considerable potential for the improvement of chemical processes, and for the enhancement of reaction rates in organic chemistry [27,28].

In our previous work, we especially studied the effect of different hydrophobic bis(trifluoromethylsulfonyl)imide-based ILs ($[NTf_2]^-$) in the epoxidation of cyclic olefins by H_2O_2 in the presence of a Mn-porphyrin as catalyst [29,30]. It is their low viscosity and chemical stability under oxidation conditions which prompted us to choose them [29–33].

In the present study, we reported the application of these hydrophobic ILs in the oxidation of cyclohexanol to cyclohexanone by H_2O_2, in the presence of metal salts as catalysts. We paid particular attention to the study of the role of each reagent, to better understand the reaction mechanism and to optimise the reaction in terms of efficiency and eco-friendliness. In this context, we investigated the use of ultrasound and microwave as activation methods having major consequences, such as a reduction in reaction time and in energy consumption. The novelty of our contribution lies in the unique combination of the metal salt with a quaternary ammonium-based co-catalyst, under non-conventional activation conditions, to assist an oxidation reaction.

2. Materials

2.1. Materials

1-Methylpyrrolidine, 1-ethylpiperidine, 1-methylimidazole, pyridine, 1-octylchloride, 1-octylbromide, activated charcoal NORIT®, Celite® 545, hydrogen peroxide (30%: wt% solution in water), cyclohexanol (98%), sodium tungstate dehydrate (99%) were purchased from Acros, magnesium sulfate from Chimie-Plus Laboratoires, tungstic acid (99%), cyclopentanol (99%), cycloheptanol (99%), cyclooctanol (99%) and Aliquat® 336 from Sigma-Aldrich, bismuth(III) sulfate (99%) from Alfa Aesar, iron(II) sulfate (99%) and iron(III) nitrate nonahydrate (99%) from Prolabo, dichloromethane and ethyl acetate from Carlo Erba Reagents, $LiNTf_2$ from Solvionic. Chemicals were used without further purification.

^1H NMR spectra were recorded in $CDCl_3$ (Euriso-Top, Saint Aubin, France) at 23 °C using a Bruker DRX300 spectrometer, at 300 MHz and 75.5 MHz for ^1H and ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to tetra-methylsilane (TMS).

Gas chromatography was performed on a GC8000series gas chromatograph from Fisons Instruments using a flame-ionization detector (250 °C) and equipped with an HP1 capillary column (dimethylpolysiloxane, $50\,m \times 0.32\,mm \times 0.52\,\mu m$) from Agilent technologies. The program used an isothermal temperature of 45 °C for 14 min, and then a $30\,°C\,min^{-1}$ ramp for 2 min and at last, an isothermal temperature of 100 °C for 2 min. The 4 µL samples were injected at 275 °C for GC analyses.

Ultrasound was generated by a digital Sonifier® S-250D from Branson ($P_{elec,1} = 11.5\,W$ and $P_{elec,2} = 22.9\,W$). A 3 mm diameter tapered microtip probe operating at a frequency of 20 kHz was used and its acoustic power in water ($P_{acous,1} = 0.787\,W\,mL^{-1}$ and $P_{acous,2} = 1.26\,W\,mL^{-1}$) was determined by calorimetry according to previous work [31].

Microwave irradiations were performed by means of a MicroSynth reactor (35 cm × 35 cm × 35 cm cavity) from Milestone. Temperature was measured and controlled with an optic fiber thermometer (ATC-FO).

2.2. Ionic liquids syntheses and characterizations

Methyloctylpyrrolidinium ([C_8mpyr]Br, [C_8mpyr][NTf_2]), ethyloctylpiperidinium ([C_8epip][NTf_2]), octylpyridinium ([C_8py][NTf_2]) and methyloctylimidazolium ([C_8mim]Cl, [C_8mim]Br, [C_8mim][NTf_2]) based ILs (formula given in Table 1) were synthesized, purified and characterized (^1H and ^{13}C NMR, FTIR, UV–visible, mass spectrometry, cyclic voltammetry, water content, viscosity and density measurements) as described previously [29,30].

Synthesis of [Aliquat][NTf_2] from Aliquat 336 (Fig. 1): Aliquat 336 (2.27 g, 5.6 mmol, 1 equiv.) was added to a solution of $LiNTf_2$ (1.69 g, 5.9 mmol, 1.1 equiv.) in distilled water (50 mL). The mixture was stirred at room temperature under argon for 5 h and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were then washed with water (2 × 10 mL) and with a saturated sodium chloride solution (2 × 10 mL), and then dried over $MgSO_4$. After filtration, the resultant mixture was stirred for 2 h with activated charcoal. Filtration on celite to remove charcoal and evaporation under reduced pressure (rotary evaporator, 2×10^{-3} bar) afforded the colourlessness desired [Aliquat][NTf_2] (Fig. 1b, 2.74 g, 76%).

^1H NMR ($C_{27}H_{54}O_4N_2F_6S_2$, δ ppm, $CDCl_3$, 300 MHz): δ 0.82 (9*H*, m, 3 CH_3), 1.28 (30*H*, m, 15 CH_2), 1.58 (6*H*, m, 3 CH_2), 2.91 (3*H*, m, 1 CH_3), 3.12 (6*H*, m, 3 CH_2); ^{13}C NMR (δ ppm, $CDCl_3$, 75.5 MHz): δ 15.0 (2 C), 15.1, 23.3, 23.6, 23.7, 26.9, 27.2 (2 C), 30.0–30.55 (9 C), 32.7, 32.9, 33.9, 49.4, 62.9 (2 C), 63.9, 121.0 (2 C, $J_{C-F} = 321.2\,Hz$).

2.3. Optimized cyclohexanol oxidation with Aliquat 336

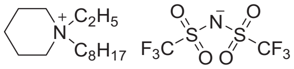
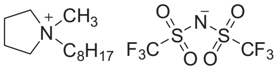
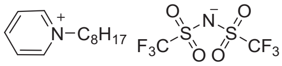
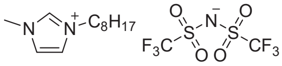
Cyclohexanol (1.04 mL, 10 mmol, 1 equiv.), tungstic acid (58.9 mg, 0.24 mmol, 2.4 mol%), Aliquat 336 (275 mg, 0.68 mmol, 6.8 mol%) and 30% hydrogen peroxide (2.04 mL, 20 mmol, 2 equiv.) were introduced into a glass tube. The mixture was stirred at 90 °C for 30 min. Then, the organic phase was extracted with ethyl acetate (3 × 2 mL) and cyclohexane (2 × 2 mL). The combined organic phases were dried with $MgSO_4$ and analysed by gas chromatography (GC). The same procedure was used from the other substrates: cyclopentanol (0.91 mL, 10 mmol, 1 equiv.), cycloheptanol (1.20 mL, 10 mmol, 1 equiv.) and cyclooctanol (1.32 mL, 10 mmol, 1 equiv.).

Cyclohexanone: $C_6H_{10}O$, δ ppm, $CDCl_3$, 300 MHz): δ 1.73 (2*H*, m, 1 CH_2), 1.86 (4*H*, m, 2 CH_2), 2.36 (4*H*, m, 2 CH_2); **Cyclopentanone** (C_5H_8O, δ ppm, $CDCl_3$, 300 MHz): δ 1.97 (4*H*, m, 2 CH_2), 2.16 (4*H*, m, 2 CH_2); **Cycloheptanone** ($C_7H_{12}O$, δ ppm, $CDCl_3$, 300 MHz): δ 1.49–1.81 (8*H*, m, 4 CH_2), 2.49 (4*H*, m, 2 CH_2); **Cyclooctanone** ($C_8H_{14}O$, δ ppm, $CDCl_3$, 300 MHz): δ 1.28–1.72 (6*H*, m, 3 CH_2), 1.88 (4*H*, m, 2 CH_2), 2.41 (4*H*, m, 2 CH_2).

2.4. Microwave assisted cyclohexanol oxidation with Aliquat 336

Cyclohexanol (1.04 mL, 10 mmol, 1 equiv.), tungstic acid (58.9 mg, 0.24 mmol, 2.4 mol%), Aliquat 336 (275 mg, 0.68 mmol, 6.8 mol%) and 30% hydrogen peroxide (2.04 mL, 20 mmol, 2 equiv.) were introduced into a 50 mL quartz reactor equipped with a 15 bar pressure cap. The mixture was stirred, under microwave irradiation at 90 °C for 2.5 min ($P = 80\,W$). After stopping the microwave

Table 1
Properties of the selected ionic liquids.

ILs	Chemical structure	Density at 20 °C[a]	Viscosity at 20 °C (mPa s)[a]	Water content (ppm)[a]	Saturation water content (ppm)[b]
[C_8epip][NTf_2]		1.27	423.29	721 ± 18	7201 ± 75
[C_8mpyr][NTf_2]		1.27	302.29	1165 ± 14	9970 ± 77
[C_8py][NTf_2]		1.33	167.55	3160 ± 24	19230 ± 104
[C_8mim][NTf_2]		1.31	159.12	483 ± 8	11002 ± 89

[a] Density, viscosity and water content measurements were performed after an exposition of the IL to ambient atmosphere during two days (29% humidity in air).

[b] Saturation water content was measured in the IL phase, saturated with water.

irradiation, the solution was left for about 15 min to reach room temperature. After which, the organic phase was extracted with ethyl acetate and cyclohexane (3 × 2 mL). The combined organic phases were dried with $MgSO_4$ and analysed by GC.

2.5. *Ultrasound assisted cyclohexanol oxidation with Aliquat 336*

Cyclohexanol (1.04 mL, 10 mmol, 1 equiv.), tungstic acid (58.9 mg, 0.24 mmol, 2.4 mol%), Aliquat 336 (275 mg, 0.68 mmol, 6.8 mol%) and 30% hydrogen peroxide (2.04 mL, 20 mmol, 2 equiv.) were introduced into a glass tube under ultrasonic irradiation (3 mm Ø tapered microtip probe) for 15 min or 60 min. After which, the organic phase was extracted with ethyl acetate and cyclohexane (3 × 2 mL). The combined organic phases were dried with $MgSO_4$ and analysed by GC.

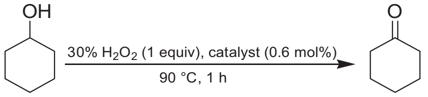
3. Results and discussion

The ability to perform oxidations without the need for a strong oxidant and a toxic catalyst, thus preventing the generation of species which could be potentially harmful to the substrate and/or difficult to remove represents an attractive goal both for multistep synthesis and large scale reactions. With this premise in mind, we turned our attention to the use of catalysts based on tungsten, iron and bismuth metals.

3.1. *Screening of catalysts*

To gain an insight into their catalytic activity, five catalytic systems were monitored: H_2WO_4, $NaWO_4{\cdot}2H_2O$, $FeSO_4$, $Fe(NO_3)_3{\cdot}9H_2O$ and $Bi(SO_4)_3$. Table 2 presents the results obtained in the optimized experimental conditions (90 °C, 1 h).

Table 2
Cyclohexanol oxidation to cyclohexanone catalysed by various metal salts.



Entry	Catalyst[a]	Yield (%)[b]	Selectivity (%)[c]
1	None	0	–
2	H_2WO_4	14	>99
3	$Na_2WO_4{\cdot}2H_2O$	2	>99
4	$FeSO_4$	8	>99
5	$Fe(NO_3)_3{\cdot}9H_2O$	6	>99
6	$Bi_2(SO_4)_3$	1	>99

[a] Reaction conditions: 1 equiv. cyclohexanol, 1 equiv. 30% H_2O_2, 0.6 mol% catalyst, 90 °C, 1 h.

[b] Cyclohexanone GC-yield (based on starting cyclohexanol) measurements.

[c] Selectivity is defined as the percentage of desired cyclohexanone relative to all products obtained.

The best result is obtained in the presence of H_2WO_4 even if the yield in cyclohexanone is low (Table 2, entry 2, 14%). This result tends to confirm the *in situ* formation of the water-soluble $H_2[WO(O_2)_2(OH)_2]$ complex, described by Usui and Sato, from H_2WO_4 and H_2O_2 according to the reaction (1) [18].

$$H_2WO_4 + H_2O_2 \xrightarrow{H_2O} H_2\,[WO(O_2)_2(OH)_2] \tag{1}$$

This complex is known to be efficient for the oxidation of cyclic ketones and alcohols to corresponding carboxylic acids with a minimum reaction time of 20 h in 81 to 99% yields. $Na_2WO_4{\cdot}2H_2O$, FeSO4, $Fe(NO_3)_3{\cdot}9H_2O$ and $Bi(SO_4)_3$ catalysts were also tested but did not lead to significant yield (< 8%). Interestingly, cyclohexanone is obtained solely under these experimental conditions.

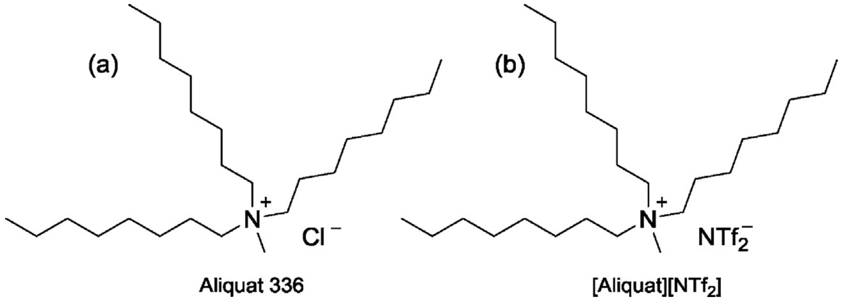
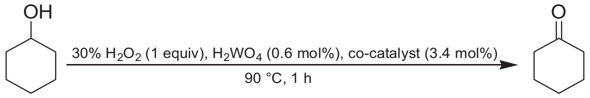


Fig. 1. Chemical structures of (a) Aliquat 336 and (b) [Aliquat][NTf_2].

Table 3
Cyclohexanol oxidation to cyclohexanone with H_2WO_4 and various co-catalysts (ILs).



Entry	Catalyst[a]	Co-catalyst[a]	Yield (%)[b]	Selectivity (%)[c]
1	H_2WO_4	$[C_8mpyr]Br$	37	>99
2	H_2WO_4	$[C_8mpyr][NTf_2]$	50	>99
3	H_2WO_4	$[C_8epip][NTf_2]$	27	>99
4	H_2WO_4	$[C_8py][NTf_2]$	37	>99
5	H_2WO_4	$[C_8mim]Cl$	8	>99
6	H_2WO_4	$[C_8mim]Br$	18	>99
7	H_2WO_4	$[C_8mim][NTf_2]$	58	>99
8	None	$[C_8mim][NTf_2]$	<1	>99
9	H_2WO_4	$[C_8mim][NTf_2]$[d]	35	>99

[a] Reaction conditions: 1 equiv. cyclohexanol, 1 equiv. 30% H_2O_2, 0.6 mol% catalyst, 3.4 mol% co-catalyst, 90 °C, 1 h.

[b] Cyclohexanone GC-yield measurements.

[c] Selectivity is defined as the percentage of desired cyclohexanone relative to all products obtained.

[d] In this case, $[C_8mim][NTf_2]$ was used as solvent; reactions conditions: 1 equiv. cyclohexanol, 1 equiv. 30% H_2O_2, 0.6 mol% catalyst, 5 equiv. $[C_8mim][NTf_2]$, 90 °C, 1 h.

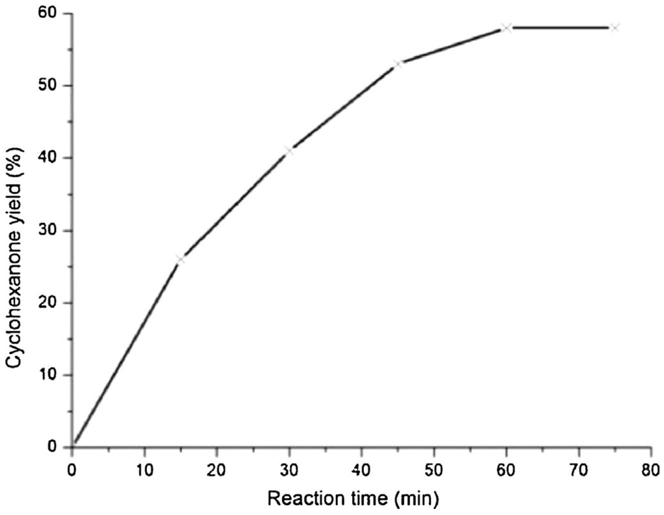


Fig. 2. Kinetic monitoring of the cyclohexanol oxidation to cyclohexanone (Reaction conditions: 1 equiv. cyclohexanol, 1 equiv. 30% H_2O_2, 0.6 mol% H_2WO_4, 3.4 mol% $[C_8mim][NTf_2]$, 90 °C).

3.2. *Screening of ionic liquids*

Based on the results reported by Chen et al. in the presence of WO_3 catalyst and a chloride based IL, we studied the influence of the use of an IL as co-catalyst (amount of 3.4 mol%) on the oxidation of cyclohexanol catalysed by H_2WO_4. The corresponding yields obtained with non-aromatic ($[C_8mpyr]Br$, $[C_8mpyr][NTf_2]$, $[C_8epip][NTf_2]$), and aromatic ($[C_8py][NTf_2]$, $[C_8mim]Cl$, $[C_8mim]Br$, $[C_8mim][NTf_2]$) ILs (see formula in Table 1) are summarized in Table 3. A blank oxidation experiment carried out in the absence of the catalyst showed a very slow rate (Table 3, entry 8) leading to less than 1% of cyclohexanone after 1 h of reaction, suggesting that H_2O_2 is not able to oxidize cyclohexanol in the absence of tungstic acid.

In the conditions detailed in Table 3, the oxidation of cyclohexanol is totally selective to cyclohexanone (>99%). Cyclohexanone is obtained in 58%, 50%, 37%, 37% and 27% yields, respectively, when the co-catalyst is $[C_8mim][NTf_2]$, $[C_8mpyr][NTf_2]$, $[C_8py][NTf_2]$, $[C_8mpyr]Br$ and $[C_8epip][NTf_2]$. No effect of the aromaticity of the IL cation is observed. However, the anion of the IL seems to be of great importance and the best conversion is obtained with $[NTf_2]^-$ in comparison to halide-based ILs. Entries 5, 6 and 7 (Table 3) show that the ketone yield increases with the size of the anion, for the imidazolium cation: $[C_8mim][NTf_2] > [C_8mim]Br > [C_8mim]Cl$. The same result is observed with pyrrolidinium as the cation (Table 3, entries 1 and 2): 50% yield is obtained when $[NTf_2]^-$ is the anion compared to 37% with bromide as the anion. On the basis of these results, we could suspect an influence of the anion size, since the $[NTf_2]^-$ anion is the largest, but also an influence of the great stability against oxidation of bis(trifluoromethylsulfonyl)imide based ILs, compared to the tested halide based ILs [33–36].

For the same anion, the evolution of the yield as a function of the IL cation follows the increasing order: $[C_8epip][NTf_2] < [C_8py][NTf_2] < [C_8mpyr][NTf_2] < [C_8mim][NTf_2]$. As is indicated in Table 1, the correlation between this evolution and physicochemical properties such as the density, viscosity and water content of ILs is difficult to establish clearly. For example, $[C_8py][NTf_2]$ and $[C_8mim][NTf_2]$ which present comparable viscosities of 167.55 and 159.12 mPa s^{-1}, respectively (Table 1), produce very different results for the oxidation of cyclohexanol. More precisely, $[C_8mim][NTf_2]$ is 1.6 times more efficient than $[C_8py][NTf_2]$, leading, respectively, to 37% and 58% yields (Table 3, entries 4 and 7). In addition, Table 1 shows that the hypothesis that the water content in ILs could improve the transfer between aqueous phase and IL phase is not confirmed since $[C_8py][NTf_2]$, which is more hygroscopic than $[C_8mim][NTf_2]$, does not lead to the best yield in ketone (Table 3, entry 4, 37%). However, the less hygroscopic IL, $[C_8epip][NTf_2]$, leads to an even lower 27% yield (Table 3, entry 3). $[C_8mim][NTf_2]$ presenting as it does the best result for cyclohexanol oxidation, was selected as the IL for the following experiments.

At this stage, no clear correlation between IL structure and the yield obtained has been identified. Other ILs are currently being studied in our laboratory to establish the relationship between IL structure and oxidation efficiency.

Moreover, a control experiment was carried out in the absence of any catalyst (Table 3, entry 8) showing that no reaction occurred when the IL was used as sole catalyst. This result proves the evidence that the catalytic effect of ILs on the cyclohexanol oxidation is negligible. When the IL is used in excess, as a solvent, the reaction is also less efficient and a mere 35% yield is obtained in $[C_8mim][NTf_2]$ (Table 3, entry 9). These results lead us to suspect a co-catalyst role of for the IL, which improves H_2WO_4 catalytic activity. This synergy between ILs and metal has already been observed several times previously in the field of catalysis [37,38].

3.3. *Kinetic monitoring of the reaction*

The kinetic monitoring of the reaction in the presence of the most efficient IL ($[C_8mim][NTf_2]$, Table 3, entry 7, 58%) was performed for 75 min in order to determine the optimum reaction time. Fig. 2 shows that after 1 h, the reaction is completed. Various methods of H_2O_2 addition were investigated (unique, continuous or portionwise additions) but no improvement was observed, showing that the end of the reaction is not caused by H_2O_2 decomposition. In this case, it seems that the maximum of the catalyst oxidation system efficiency was reached after this time.

3.4. *Influence of the amounts of oxidant, catalyst and ionic liquid*

We then studied the effect of the amounts of oxidant, and catalyst on the oxidation of cyclohexanol. Fig. 3 shows that regardless of the amount of catalyst used, the best yields are obtained with 2 equivalents of H_2O_2. With additional amounts of oxidant, the

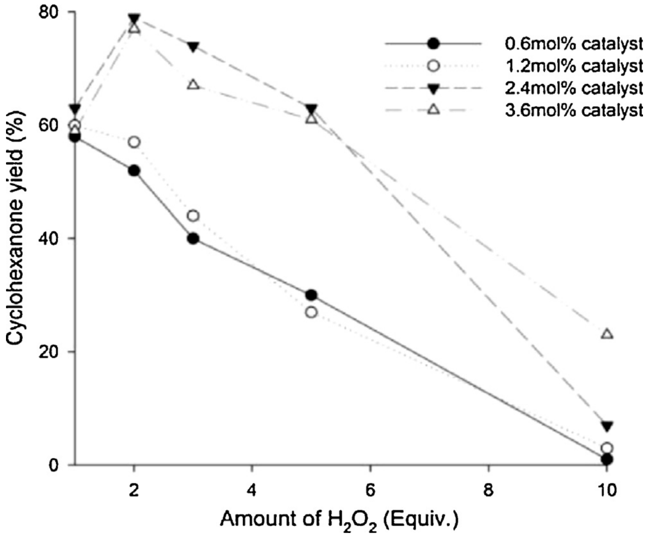
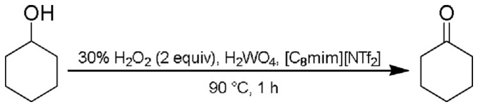


Fig. 3. Cyclohexanol oxidation to cyclohexanone as a function of H_2O_2 and H_2WO_4 amounts (Reaction conditions: 1 equiv. cyclohexanol, 30% H_2O_2, H_2WO_4, 3.4 mol% $[C_8mim][NTf_2]$, 90 °C, 1 h).

Table 4

Cyclohexanol oxidation to cyclohexanone as a function of amount of H_2WO_4 and $[C_8mim][NTf_2]$.



Entry	H_2WO_4 (mol%)[a]	$[C_8mim][NTf_2]$ (mol%)[a]	Yield (%)[b]	Selectivity (%)[c]
1	2.4	5.1	78	>99
2	2.4	6.8	82	>99
3	2.4	8.5	76	>99
4	3.6	5.1	70	>99
5	3.6	6.8	71	>99
6	3.6	8.5	78	>99

[a] Reaction conditions: 1 equiv. cyclohexanol, 2 equiv. 30% H_2O_2, H_2WO_4 catalyst, $[C_8mim][NTf_2]$ IL, 90 °C, 1 h.

[b] Cyclohexanone GC-yield measurements.

[c] Selectivity is defined as the percentage of desired cyclohexanone relative to all products obtained.

yields of cyclohexanone decrease, and this up to 3% when using 10 equivalents of oxidant and 0.6 mol% of catalyst (Fig. 3).

When 2 equivalents of oxidant are used, the increase of in the catalytic charge to 2.4 mol% produces an increase in yield of up to 79%. The increase from 2.4 mol% of H_2WO_4 to 3.6 mol% did not result in better results. The influence of the percentage of $[C_8mim][NTf_2]$ on the yield and the selectivity in cyclohexanone when 2 equivalents of 30% H_2O_2 are used was studied for 2.4 and 3.6 mol% of catalyst. Table 4 confirms that the reaction is totally selective in cyclohexanone and that the optimal catalytic charge is 2.4 mol% of H_2WO_4. In addition, when using 6.8 mol% of co-catalyst, an interesting 82% yield is obtained in only 1 h of reaction (Table 4, entry 2). In conclusion, the best conditions for this oxidative system, which reproduced in the following experiments, are 2 equivalents of H_2O_2 and 2.4 mol% of catalyst.

In pursuit of our efforts to reduce the environmental impact of the reaction, we attempted to replace some of the toxic extraction solvents previously used (such as dichloromethane) by more eco-friendly ethyl acetate. In this connection, ethyl acetate is ranked as one of the best solvents according to the EHS indicator proposed by Capello et al. [39] The EHS indicator takes environmental, safety and health impacts into account to classify the solvents. The extraction yields of cyclohexanone are comparable regardless of the solvent used (97% with ethyl acetate/cyclohexane and 99% with dichloromethane) after 4 cycles of extraction. E-factor calculation, including the work-up procedures, leads to a value of 50 which is comparable to the values obtained in the fine chemicals industry [40]. Optimization of the work-up procedures will be addressed in further work in order to minimize waste production and increase the amounts of reagents in the process.

Table 5

Oxidation of various cyclic alcohols to corresponding ketones.

Entry	Substrate[a]	Yield (%)[b]	Selectivity (%)[c]
1	C_5H_9OH	51 (48)[d]	>99
2	$C_6H_{11}OH$	82 (79)[d]	>99
3	$C_7H_{13}OH$	69 (65)[d]	>99
4	$C_8H_{15}OH$	72 (69)[d]	>99

[a] Reaction conditions: 1 equiv. cycloalkohol, 2 equiv. 30% H_2O_2, 2.4 mol% H_2WO_4 catalyst, 6.8 mol% $[C_8mim][NTf_2]$ IL, 90 °C, 1 h.

[b] Cycloketone GC-yield measurements.

[c] Selectivity is defined as the percentage of desired ketone relative to all products obtained.

[d] Isolated yields.

3.5. *Oxidation of various cyclanols*

Optimized conditions were then used to oxidized a variety of cyclic alcohols using H_2O_2/H_2WO_4 in $[C_8mim][NTf_2]$. A perusal of data in Table 5 shows the following order of reactivity among cycloalcohols: cyclohexanol > cyclooctanol > cycloheptanol > cyclopentanol. This result is surprising and unexpected in a cyclic system, which is classically governed by the I-strain effect and where cyclohexanol should be the least reactive [41]. However, the same order of reactivity, contrary to the I-strain concept, has already been observed in the Tl(III) oxidation of cyclanols [42]. It was attributed to a different type of mechanism operating in cyclohexanol oxidation, where a radical path seems to be the preferred one, as it is a strain-free system.

Interestingly, the oxidation of each cyclic substrate proceeded selectively to ketone formation and no other side product was detected *via* GC and NMR analyses. In addition, isolated yields (Table 5) and NMR spectra confirmed that no degradation occurred during the reaction. In addition, ^1H NMR analysis was performed before and after the extraction step to show that the experimental conditions of the cyclic alcohols oxidation only give rise to the corresponding ketones (>99% selectivity).

Although recent studies have described the quantitative oxidation of cyclopentanol using solid-supported catalysts [43,44], our results are highly promising given than, by using our system, cyclopentanol oxidation proceeds in 1 h (Table 5, entry 1) instead of 8 to 24 h for the systems described in the literature [43,44]. In addition, the catalytic system ($H_2WO_4/[C_8mim][NTf_2]$) used is very simple and easily available. Finally, very few studies have reported the oxidation of cycloheptanol. For example, Kwong et al. oxidized this substrate with a 97% yield and an excellent selectivity, but they used a more complex and expensive Mn(V)-based catalyst ($(PPh_4)_2[Mn(N)(CN)_4]$), compared to tungstic acid catalyst [45]. Patil et al. selectively and efficiently oxidized cycloheptanol and cyclooctanol to the corresponding ketones with 86% and 87% yields, respectively, using HBr/H_2O_2 in dioxane [46], which is a non-benign solvent in terms of safety, health and the environment [39]. Moreover, the reactions described in their work were completed in 8 h compared to the 1 h required in our work. In addition, separation by column chromatography was required [46]. Pillai and Sahle-Demessie described the selective oxidation of cyclopentanol, cyclohexanol and cycloheptanol in acetonitrile over

Table 6
Cyclohexanol oxidation to cyclohexanone using non-conventional methods.

Entry	Activation method	Reaction time (min)[a]	Temperature (°C)[b]	Yield (%)[c]
1	US (20 kHz, $P_{elec,1}$)[d]	60	58	23
2	US (20 kHz, $P_{elec,2}$)[e]	60	58	42
3	US (800 kHz, $P_{elec,3}$)[f]	60	52	51
4	MW (80 W)[g]	30	90	94

[a] Reaction conditions: 1 equiv. cyclohexanol, 2 equiv. 30% H_2O_2, 2.4 mol% H_2WO_4 catalyst, 6.8 mol% [C_8mim][NTf_2] ionic liquid.

[b] Macroscopic average temperature

[c] Cyclohexanone GC-yield measurements.

[d] 3 mm in diameter tapered microtip probe, $P_{elec,1}$ = 11.5 W, $P_{acous,1}$ (water) = 0.787 W mL^{-1}.

[e] 3 mm in diameter tapered microtip probe, $P_{elec,2}$ = 22.9 W, $P_{acous,2}$ (water) = 1.26 W mL^{-1}.

[f] 50 mm in diameter cup-horn system, $P_{elec,3}$ = 31.0 W, $P_{acous,3}$ (water) = 1.72 W mL^{-1}, temperature maintained by cooling.

[g] 30 min microwave irridiation, P = 80 W.

a vanadium phosphorous oxide catalyst using H_2O_2 with yields of 68%, 44% and 61% yields [47]. Unfortunately, the reactions required 4 h for completion, such as when using polyoxymetalate complex for the selective oxidation of cyclohexanol and cyclooctanol in the presence of H_2O_2 as oxidant [48,49]. In conclusion, our system is selective, safe and swift for the oxidation of various cyclanols composed of 5, 6, 7 and 8 atoms of carbon.

3.6. *Influence of activation methods*

In previous studies, we demonstrated improvements to the epoxidation of olefins by using non-conventional methods such as ultrasound [29–32]. In the present work, we have investigated the effect of both ultrasound (US) and microwave (MW) irradiations on the oxidation of cyclohexanol (Table 6). Low and high frequency ultrasound assisted procedures were used with no success compared to experiments conducted under silent conditions. Mere 23% yields were obtained at 20 kHz ($P_{elec,1}$ = 11.5 W) (Table 6, entry 1) and 42% were obtained when the electric power was twice as high (Table 6, entry 2). However, this input power is huge for such a low reaction volume, rendering the method inefficient in terms of energy usage. At 800 kHz, the yield reached only 51% (Table 6, entry 3) and the temperature of the reaction medium was difficult to control. In this oxidation reaction, based on preliminary experiments, the physical and chemical effects of ultrasound do not appear to improve either yields or reaction time. By cons, microwave irradiation is effective and an excellent 94% yield was reached in a reaction time two times lower (Table 6, entry 4, only 30 min). Microwaves improve the heat of the reaction and probably promote the *in situ* formation of $H_2[WO(O_2)_2(OH)_2]$, which seems to be temperature dependent [18]. The improvement by microwave was discussed by Bogdal and Lukasiewciz for the oxidation of alcohols using aqueous hydrogen peroxide and commercial tetrabutylammonium hydrogen sulfate [50]. In the latter study, the cyclohexanol oxidation under microwave led to cyclohexanone in a 77% yield in 10 min. Loupy et al. have also reported several examples explaining how the microwave activation can promote certain reactions [51,52].

3.7. *Determination of the role of the ionic liquid*

Based on Bogdal's and Lukasiewciz's works [50], we suspected a role as a phase transfer agent for our IL. To confirm this hypothesis, we replaced the [C_8mim][NTf_2] by *N*-methyl-*N*,*N*-dioctyloctan-1-ammonium chloride (Fig. 1a), also called Aliquat 336 and commonly used as a phase transfer agent [53–55]. This choice was motivated by the structure of this quaternary salt which is close to that of the IL we used, in terms of lipophilic chain lengths. To identify the effect of the [NTf_2]$^-$ anion, we also synthesized and tested *N*-methyl-*N*,*N*-dioctyloctan-1-ammonium bis(trifluoromethylsulfonyl)imide, noted [Aliquat][NTf_2] (Fig. 1b), by anion metathesis from Aliquat 336 in presence of $LiNTf_2$ salt. The oxidation experiments performed in the presence of Aliquat 336 and [Aliquat][NTf_2], under classical conditions and/or under microwave irradiation are summarized in Table 7.

In the presence of Aliquat 336, the oxidation of cyclohexanol to cyclohexanone is almost quantitative after 1 h of reaction under conventional heating at 90 °C (Table 7, entry 3). Moreover, the yield is already 87% after 15 min of reaction (Table 7, entry 1) whereas 60 min are required to reach a 82% yield in the presence of [C_8mim][NTf_2] (Table 4, entry 2). Under these conditions, the kinetic of the reaction is faster than in the presence of the most efficient IL, and only 30 min are necessary to produce a quantitative oxidation of cyclohexanol (Table 7, entry 2).

These results highlight the role as a phase transfer agent of the IL acting as a co-catalyst. The aliphatic cation of Aliquat is more efficient than the cyclic cations of the ILs we used. In addition, Table 7 shows that the associated anion also plays an important role in Ø phase transfer**:** in 1 h of reaction only a 61% yield was obtained

Table 7
Cyclohexanol oxidation in presence of the Aliquat phase transfer agent.

Entry	Phase transfer agent	Activation method	Reaction time (min)[a]	Yield (%)[b]
1	Aliquat 336	Conventional heating (90 °C)[a]	15	87
2	Aliquat 336	Conventional heating (90 °C)[a]	30	97
3	Aliquat 336	Conventional heating (90 °C)[a]	60	97
4	[Aliquat][NTf_2]	Conventional heating (90 °C)[a]	60	61
5	Aliquat 336	Microwave irradiation (80 W)[c]	3	86
6	Aliquat 336	Microwave irradiation (80 W)[d]	2.5	94
7	[Aliquat][NTf_2]	Microwave irradiation (80 W)[d]	2.5	22
8	None	Microwave irradiation (80 W)[d]	2.5	18
9	Aliquat 336	Ultrasound (20 kHz, $P_{elec,1}$)[e]	15	98
10	Aliquat 336	Ultrasound (20 kHz, $P_{elec,1}$)[e]	7.5	94
11	[Aliquat][NTf_2]	Ultrasound (20 kHz, $P_{elec,1}$)[e]	15	33
12	None	Ultrasound (20 kHz, $P_{elec,1}$)[e]	15	40

[a] Classical conditions: 1 equiv. cyclohexanol, 2 equiv. 30% H_2O_2, 2.4 mol% H_2WO_4 catalyst, 6.8 mol phase transfer agent, 90 °C. Macroscopic average temperature.

[b] Cyclohexanone GC-yield (based on starting cyclohexanol) measurements.

[c] 3 min pulsed microwave irradiation, P = 80 W (0.5 min) and P = 0 W (0.25 min) and the reaction was continued for 5 min after stopping the MW, 90 °C.

[d] 2.5 min continuous microwave irradiation, P = 80 W and the reaction was continued for 15 min after stopping the MW, 90 °C.

[e] 3 mm in diameter tapered microtip probe, $P_{elec,1}$ = 11.5 W, $P_{acous,1}$ (water) = 0.787 W mL^{-1}.

in the presence of [Aliquat][NTf_2] (Table 7, entry 4) instead of the 97% obtained in the presence of Aliquat 336, where the anion is a chloride (Table 7, entry 3). As far as Ø biphasic oxidation with aqueous H_2O_2 is concerned, the use of lipophilic quaternary ammonium salts is crucial for the process [50]. However, the association of the $[NTf_2]^-$ anion with the ammonium salt produces a phase transfer agent whose lipophilicity is excessive. Other ILs are currently being tested in our laboratories with the aim of improving the corresponding yields.

3.8. Optimized conditions in the presence of Aliquat 336

We next turned our attention to the possible contribution of microwave or ultrasound to the kinetic of the reaction in the presence of Aliquat 336. Following 3 min of pulsed irradiation and a 5 min break, a promising 84% yield was obtained (Table 7, entry 5). Under 2.5 min continuous irradiation followed by a 15 min break, the reaction is almost quantitative (Table 7, entry 6). In the absence of Aliquat 336, the yield is low (Table 7, entry 7), thereby showing the synergic effect of the phase transfer agent and the microwave irradiation.

The same trends are observed using low frequency ultrasound (20 kHz), since 94% and 98% yields are obtained after 7.5 and 15 min of irradiation (Table 7, entries 9 and 10), respectively, in the presence of Aliquat 336. The synergic effect produced by the US/Aliquat 336 combination is confirmed by the low yield of 40% obtained under ultrasound but without the phase transfer agent. Compared to conventional heating (P_{elec} = 200–267 W mL^{-1}), the ultrasound (P_{elec} = 4 W mL^{-1}) and microwave (P_{elec} = 27 W mL^{-1}) assisted processes are more economical in terms of energy consumption and reaction time (30 min *vs.* 15 min under ultrasound and 2.5 min under microwave).

4. Conclusion

As a conclusion, our work describes the efficient oxidation of five- to eight-membered cyclanols using H_2O_2/H_2WO_4 in the presence of a co-catalyst. Cyclohexanol was found to be the most reactive of the four tested cyclanols. This unexpected reactivity was attributed to a different type of mechanism operating in cyclohexanol catalytic oxidation where a radical path could be the preferred one. Further investigations are required to fully understand the mechanisms involved in this system.

Additionally, the role of the IL as a phase transfer agent was confirmed by the use of Aliquat 336 in the reaction, leading to best results in only 30 min of reaction at 90 °C for the different selected substrates. Performing well-controlled oxidations without the need for a strong oxidant and a toxic catalyst represents an attractive goal, both for multistep synthesis and large scale reactions. The method we describe is general, efficient, and rapid and could be used for catalytic oxidation of more complex alcohols. The originality of the method lies in this unique system combining a metal salt with a quaternary ammonium-based co-catalyst, under non-conventional activation conditions, to make green, efficient and swift an oxidation reaction. We are currently investigating the design of a specific IL to improve phase transfer and increase yields.

The use of Aliquat 336 associated with a non-conventional method such as microwave or ultrasound led to excellent yields after only 2.5–15 min of irradiation, thereby decreasing reaction times and energy consumption compared to conventional conditions. Based on the improvements enabled by this oxidative system, we are currently developing a challenging process to directly convert cyclohexanol into adipic acid in our laboratories.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.apcata.2014.03.033.

References

[1] L. Wang, J. Li, Y. Lv, G. Zhao, S. Gao, Appl. Organomet. Chem. 26 (2012) 37.
[2] D. Glowacz-Czerwonka, M. Kucharski, J. Appl. Polym. Sci. 99 (2006) 1083.
[3] M. Jhansi, L. Kishore, K.A. Anand, A. Kumar, Catal. Commun. 10 (2008) 285.
[4] Y.H. Chang, T. Jiang, B.X. Han, L.A. Gao, R. Zhang, Z.M. Liu, W.Z. Wu, Ind. Eng. Chem. Res. 42 (2003) 6384.
[5] L. Liu, Y. Li, H.B. Wei, M. Dong, J.G. Wang, A.M.Z. Slawin, J.P. Li, J.X. Dong, R.E. Morris, Angew. Chem. Int. Ed. 48 (2009) 2206.
[6] R. Kumar, S. Sithambaram, S.L. Suib, J. Catal. 262 (2009) 304.
[7] S.G. Shore, E.D.C. Park, M.A. Kean, J. Mol. Catal. A: Chem. 212 (2004) 291.
[8] H.Z. Liu, T. Jiang, B.X. Han, S.G. Liang, Y.X. Zhou, Science 326 (2009) 1250.
[9] D. Santhanaraj, C. Suresh, P. Vijayan, N. Venkatathri, K. Shanthi, React. Kinet. Mech. Catal. 99 (2010) 439.
[10] P.T. Anastas, J.C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, Oxford, 1998.
[11] H.-J. Federsel, Acc. Chem. Res. 42 (2009) 671.
[12] E.S. Beach, Z. Cui, P.T. Anastas, Energy Envrion. Sci. 2 (2009) 1038.
[13] R.A. Sheldon, Chem. Soc. Rev. 41 (2012) 1437.
[14] J.-E. Backvall, Modern Oxidation Methods, second ed., Wiley-VCH, Weinheim, Germany, 2010.
[15] R. Noyori, M. Aoki, K. Sato, Chem. Comm. (2003) 1977.
[16] K. Sato, M. Aoki, R. Noyori, Science 281 (1998) 1646.
[17] C.M. Starks, C.L. Liotta, M.E. Halpern, Phase-Transfer Catalysis: Fundamentals, Applications, and Industrial Perspectives, Chapman & Hall, Inc., London, UK, 1994.
[18] Y. Usui, K. Sato, Green Chem. 5 (2003) 373.
[19] K. Sato, J. Takagi, M. Aoki, R. Noyori, Tetrahedron Lett. 39 (1998) 7549.
[20] S.K. Maiti, K.M. Abdul Malik, R. Bhattacharyya, Inorg. Chem. Comm. 7 (2004) 823.
[21] K. Sato, M. Aoki, J. Takagi, R. Noyori, J. Am. Chem. Soc. 199 (1997) 12386.
[22] W. Zhao, Y. Ding, B. Ma, W. Qiu, Synth. Commun. 4 (2012) 554.
[23] L. Chen, T. Zhou, L. Chen, Y. Ye, Z. Qi, H. Freund, K. Sundmacher, Chem. Commun. 47 (2011) 9354.
[24] N.V. Plechkova, K.R. Seddon, Chem. Soc. Rev. 37 (2008) 123.
[25] H. Olivier-Bourbigou, L. Magna, D. Morvan, Appl. Catal., A: Gen. (2010) 1.
[26] J.P. Hallett, T. Welton, Chem. Rev. 111 (2011) 3508.
[27] P. Wasserscheid, T. Welton, Ionic Liquids in Synthesis, second ed., Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2008.
[28] N. Plechkova, R. Rogers, K. Seddon, Ionic Liquids: From Knowledge to Application, in: ACS Symposium Series, American Chemical Society, Washington, DC, 2010.
[29] G. Chatel, C. Goux-Henry, A. Mirabaud, T. Rossi, N. Kardos, B. Andrioletti, M. Draye, J. Catal. 291 (2012) 172.
[30] G. Chatel, C. Goux-Henry, N. Kardos, J. Suptil, B. Andrioletti, M. Draye, Ultrason. Sonochem. 19 (2012) 390.
[31] G. Chatel, L. Leclerc, E. Naffrechoux, C. Bas, N. Kardos, C. Goux-Henry, B. Andrioletti, M. Draye, J. Chem. Eng. Data 57 (2012) 3385.
[32] G. Chatel, R. Pflieger, E. Naffrechoux, S.I. Nikitenko, J. Suptil, C. Goux-Henry, N. Kardos, B. Andrioletti, M. Draye, ACS Sustainable Chem. Eng. 1 (2013) 137.
[33] K.-P. Ho, W.-L. Wong, L. Lee, K.-M. Lam, T. Chan, K.-Y. Wong, Chem. Asian J. 5 (2010) 1970.
[34] T. Yim, H.Y. Lee, H.-J. Kim, J. Mun, S. Kim, S.M. Oh, Y.G. Kim, Bull. Korean Chem. Soc. 28 (2007) 1567.
[35] R.G. Evans, O.V. Klymenko, C. Hardacre, K.R. Seddon, R.G. Compton, J. Electroanal. Chem. 556 (2003) 179.
[36] S. Sowmiah, V. Srinivasadesikan, M.-C. Tseng, Y.-H. Chu, Molecules 14 (2009) 3780.
[37] P. Wasserscheid, W. Keim, Angew. Chem. Int. Ed. 38 (2000) 3772.
[38] Q. Zhang, S. Zhang, Y. Deng, Green Chem. 13 (2011) 2619.
[39] C. Capello, U. Fischer, K. Hungerbühler, Green Chem. 9 (2007) 927.
[40] R.A. Sheldon, Chem. Ind. (London) (1992) 903.
[41] H.C. Brown, R.S. Fletcher, R.B. Johannesen, J. Am. Chem. Soc. 73 (1951) 212.
[42] V.S. Skiniva, V. Venkatasubramanian, Proc. Indian Acad. Sci. 91 (1982) 467.
[43] W. Zhao, Y. Ding, B. Ma, W. Qiu, Synth. Commun. 42 (2012) 554.
[44] X. Wang, G. Wu, W. Wei, Y. Sun, Transition Met. Chem. 35 (2010) 213.
[45] H.-K. Kwong, P.-K. Lo, K.-C. Lau, Chem. Commun. 47 (2011) 4273.
[46] R.D. Patil, G. Joshi, S. Adimurthy, Ind. Eng. Chem. Res. 49 (2010) 8100.
[47] U.R. Pillai, E. Sahle-Demessie, Appl. Catal., A: Gen. 276 (2004) 139.
[48] J. Wang, L. Yan, G. Li, X. Wang, Y. Ding, J. Suo, Tetrahedron Lett. 46 (2005) 7023.

[49] D. Sloboda-Rozner, P.L. Alsters, R. Neumann, J. Am. Chem. Soc. 125 (2003) 5280.
[50] D. Bogdal, M. Lukasiewciz, Synlett 1 (2000) 143.
[51] S. Deshayes, M. Liagre, A. Loupy, J.-L. Luche, A. Petit, Tetrahedron 55 (1999) 10851.
[52] A. de la Hoz, A. Loupy, Microwaves in Organic Synthesis, third ed., Wiley-VCH, Weinheim, Germany, 2012.
[53] C. Venturello, E. Alneri, M. Ricci, J. Org. Chem. 48 (1983) 3831.
[54] P.L. Anelli, C. Biffi, F. Montanari, S. Quici, J. Org. Chem. 52 (1987) 2559.
[55] E.V. Dehmlow, Angew. Chem. Int. Ed. 16 (1977) 493.