Iron(III) and copper(II) catalysed cyclohexane oxidation by molecular oxygen in the presence of *tert*-butyl hydroperoxide [1]

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Abstract

In the presence of cyclohexane soluble iron and copper catalysts, *tert*-butyl hydroperoxide selectively oxidises cyclohexane to cyclohexanol and cyclohexanone (with cyclohexene for the copper catalysts). Under reflux for 24 h, the conversions are 4 to 5% (turnover numbers of 70 to 90) and the selectivities above 90%. Under 25 bar of oxygen at 70°C for 24 h, conversions with the iron catalysts are 9% (turnover numbers of up to 166) but the selectivities are below 80%, as large amounts of adipic acid are also formed. The copper catalysts are more selective under these conditions. Using Cu(tma)$_2$ the conversion is 11% (turnover number of 192) and the selectivity is 91%. Reactions in the presence of cyclohexanone show that the iron catalysts deactivate by complexation with the adipic acid formed by its over-oxidation. The copper catalysts rapidly produce cyclohexene at the beginning of the reactions; this is further oxidised to cyclohexen-3-one and cyclohexen-3-ol, thus reducing the catalyst activity for cyclohexane oxidation. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

The significant industrial production of cyclohexane derivatives—10^6 ton/year of cyclohexanone alone—has stimulated studies aiming to find milder, energy-saving conditions for the oxidation of cyclohexane to substitute the classic industrial method [1]. The system currently in use employs cobalt salts, molecular oxygen and temperatures above 150°C, with conversions around 4% and selectivities of 85% [2]. The high energetic demand and the low selectivity warrant the replacement of this method by a more effective catalytic system. Knowledge of the biological oxidation of alkanes catalysed by metalloenzymes has contributed to explaining the role of metallic species in high oxidation states in the cleavage of saturated C–H bonds [3]. Biomimetic metalloporphyrin catalysts, based on the iron complex present in Cytochrome *P*-450, give promising results in se-

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lective oxidation, but their activity decreases rapidly due to the self-destruction of the active species [4]. Biomimetic Gif-systems are able to oxidise secondary CH_2 groups forming mainly ketones [5]. Cyclohexane oxidation using the homogeneous GoAgg^{II} system (ferric chloride with hydrogen peroxide as oxidant) gives 91% efficiency (mol oxidised products/mol peroxide consumed) and a selectivity for cyclohexanone of 94% after 10 h of reaction [6]. The presence of picolinic acid increases the reaction rate but reduces efficiency and selectivity [7]. Using *tert*-butyl hydroperoxide instead of hydrogen peroxide increases the activity; however, in the presence of a copper catalyst, cyclohexane is the principal product [8]. Recently, Barton et al. [9] developed an oxidation system which oxidises cyclohexane in the absence of pyridine and acetic acid using *tert*-butyl hydroperoxide and a cyclohexane soluble iron or copper complex. Here we report our results on cyclohexane oxidation using analogous systems and show that complexes as simple as [bis(ethylenediamine)copper(II)] nitrate give very good results. Furthermore, we present kinetic data for these reactions and show which over-oxidation products are formed and why the systems deactivate during the reactions.

2. Experimental

All reagents and standards used were of analytical grade. Cyclohexane was further purified by washing with concentrated sulphuric acid, water and a 5% sodium hydroxide solution and then distilled. A solution of *tert*-butyl hydroperoxide (TBHP, 86.7%, determined by iodometry) in cyclohexane was supplied by Nitrocarbono, Fe(tma)$_3$ (tris(trimethylacetate)iron(III)) [9] Cu(tma)$_2$ (bis(trimethylacetate) copper(II)) [9], Fe(fod)$_3$ (tris(1,1,1,2,2,3,3–heptafluoro–7,7–dimethyl–4,6–octanodionate)iron(III)) [10] and [Cu(en)$_2$](NO$_3$)$_2$ · 2H$_2$O ([bis(ethylenediamine)copper(II)] nitrate dihydrate) [11] were synthesised as described in the literature.

Typically, 0.1 mmol of the iron or copper complex was dissolved in 14.8 g (19 ml; 176 mmol) of cyclohexane in a 50 ml round bottom flask; 10 mmol of *tert*-butyl hydroperoxide was added and the mixture was allowed to react at 70°C under magnetic stirring for 24 h. In the studies under oxygen pressure (25 bar) a 100 ml autoclave was employed and the mixture was also stirred at 70°C for 24 h. After the indicated reaction time, a 0.8 g aliquot of the reaction mixture was collected and diluted with cyclohexane to 4 g (1:4). Approximately 15 mg of cyclooctane (internal standard, weighed with precision of 0.1 mg) was added. In the kinetic studies, a 0.5 g aliquot of the reaction mixture was collected every hour and similarly treated.

The reaction products were analysed using an HP 5890-II gas chromatograph equipped with a 3.0 m stainless steel column packed with 10% Carbowax 20 M on Chromosorb WAW 80/100, coupled to a flame ionisation detector. Cyclohexene (ene), cyclohexanol (ol) and cyclohexanone (one) were quantified using cyclooctane as an internal standard with the appropriate calibration curves. The efficiencies were calculated taking into account that every mol of TBHP consumed produces 1 mol of oxidation products.

The over-oxidation products were identified using a HP 5890-II gas chromatograph coupled to an HP5970b mass spectrometer, using an HP-1 capillary column (25 m × 0.2 mm × 0.33 μm). The semi-quantification of these products was done by area normalisation.

Cyclohexyl hydroperoxide was quantified by gas chromatography using a Carbowax 20 M capillary column of 25 m × 0.2 mm × 0.2 μm coupled to a flame ionisation detector. Cyclohexanol was determined before and after complete reduction of the cyclohexyl hydroperoxide to cyclohexanol with triphenylphosphine. The increase in the quantity of cyclohexanol corresponds to the amount of cyclohexyl hydroperoxide in the sample before reduction [12].

The total hydroperoxide remaining at the end of the reactions was determined by iodometry

[13]. A 1.0 g aliquot of the reaction mixture was diluted with water to give 100 ml. A 25 ml aliquot of this solution was transferred to a 250 ml Erlenmeyer; 10 ml of a 4 mol l^{-1} solution of sulphuric acid, 3 g of potassium iodide and 3 drops of a 3% solution of ammonium molybdate were then added. This mixture was titrated with a standard solution of sodium thiosulphate. The quantity of remaining TBHP was calculated by subtracting the quantity of cyclohexyl hydroperoxide from that of the total hydroperoxide.

3. Results and discussion

In agreement with the results reported by Barton et al. [9], we found that the systems are very efficient at 70°C giving high turnover numbers. In contrast to Barton et al. [9] who used a high concentration of the oxidant and the catalyst (9 mmol of TBHP and 0.2 mmol catalyst per 50 mmol of cyclohexane) and obtained relatively low turnover numbers (typically around 10), we reduced the amount of catalyst to 0.1 mmol and increased the amount of cyclohexane to 176 mmol to obtain higher turnover numbers.

The results obtained at 70°C after 24 h using $[Cu(en)_2](NO_3)_2$ as catalyst are shown in Table 1 as a function of the quantity of oxidant. No oxidation is observed in the absence of TBHP and the turnover numbers increase linearly with the amount of TBHP added. Using 10 mmol of TBHP, we obtained a turnover number of 100 which is significantly higher than the turnover

Table 2
Influence of the different catalysts on cyclohexane oxidation under reflux. Conditions: 19 ml of cyclohexane, 0.1 mmol of catalyst, 10 mmol of *tert*-butyl hydroperoxide, 70°C, 24 h

Product (mmol)	Fe (tma)$_3$	Fe (fod)$_3$	$[Cu(en)_2]$ (NO$_3$)$_2$	Cu (tma)$_2$
Cyclohexene	–	–	2.45	1.78
Cyclohexanone	3.20	3.05	2.34	2.70
Cyclohexanol	3.60	3.37	3.77	3.34
Cyclohexen–3–one	0.03	0.16	0.06	0.24
Cyclohexen–3–ol	0.04	0.22	0.04	0.32
Glutaric acid	0.07	0.06	0.08	0.09
Adipic acid	0.08	0.16	0.13	0.11
Turnover	70	70	89	86
Conversion (%)	4.0	4.0	5.0	4.9
Efficiency (%)	70	70	89	86
Selectivity (%)	97	91	97	91

number of 6 observed by Barton et al. [9] for $Cu(fod)_2$ after 24 h at 60°C.

Under these conditions the influence of the different catalysts on the oxidation under reflux were studied, considering also the over-oxidation products. The results, shown in Table 2, reveal that the two iron catalysts have similar behaviour, giving turnover numbers of 70 at conversions of 4% and selectivities towards cyclohexanol and cyclohexanone above 90%, which are higher than the best values reported for 4% conversion in the industrial oxidation [2]. The over-oxidation products are mainly adipic and glutaric acid but also cyclohexen-3-one and cyclohexen-3-ol are observed. The copper catalysts are more active, giving conversions of 5%. They produce cyclohexene as one of the principal products and less cyclohex-

Table 1
Influence of the amount of TBHP on the activity of the system. Conditions: 19 ml of cyclohexane, 0.1 mmol of ($[Cu(en)_2](NO_3)_2$), 70°C, 24 h

TBHP (mmol)	Cyclohexanone (mmol)	Cyclohexanol (mmol)	Cyclohexene (mmol)	Turnover
0	0	0	0	0
1	0.55	0.66	0.20	14
3	0.98	1.25	0.70	29
5	1.67	3.38	1.21	63
7	2.44	4.20	1.51	82
10	2.64	5.23	2.09	100
12	2.96	6.02	2.50	115
15	3.42	6.94	3.14	135

anone than the iron catalysts. The selectivity for the oxidation products is similar to that observed for the iron catalysts and the same over-oxidation products are formed.

The kinetic study of cyclohexane oxidation by $Fe(tma)_3$ under reflux shows that cyclohexanone and cyclohexanol are formed in a 1:1 ratio and that the reaction is practically finished after 24 h (Fig. 1). Increasing the reaction time to 96 h increases the turnover number (TN) by only ca. 10%.

The kinetic study of cyclohexane oxidation by $[Cu(en)_2](NO_3)_2$ under reflux shows that cyclohexanone and cyclohexanol are also formed in a 1:1 ratio. However, an amount of approximately 3 mmol of cyclohexene is observed after 8 h which remains constant throughout the reaction course (Fig. 2). Furthermore, cyclohexanone and cyclohexanol are produced even after 24 h, showing that the copper catalyst is not so easily deactivated. After 120 h a turnover number of 120 is obtained, which corresponds to a cyclohexane conversion of 6.8%.

In the reactions under oxygen pressure, the iron catalysts give reasonably good turnover numbers, with conversions of cyclohexane of 8 to 9%. However, the selectivities towards cyclohexanol and cyclohexanone are reduced to less than 80%, due to over-oxidation forming large amounts of adipic acid (Table 3). The copper catalysts are again better as they give turnover
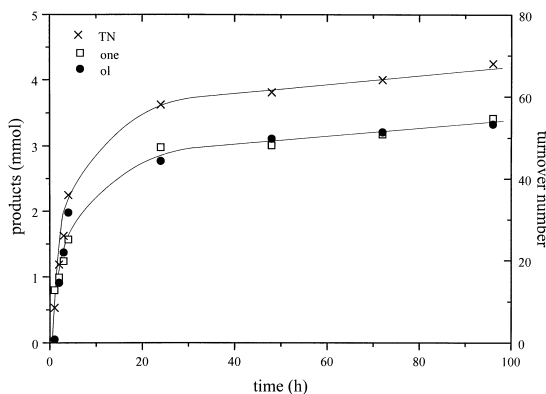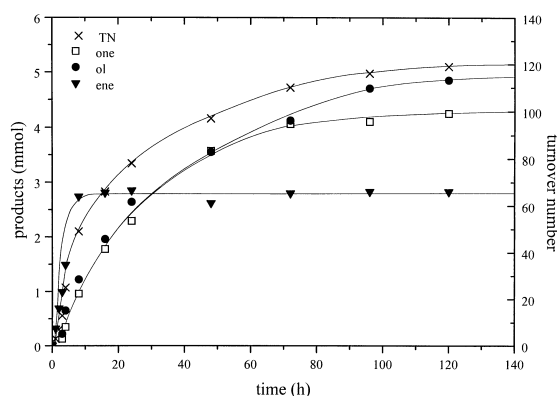

Fig. 2. Cyclohexane oxidation under reflux; catalyst: $[Cu(en)_2](NO_3)_2$.

numbers of 190, which corresponds to 11% conversion. They produce less adipic acid but cyclohexen-3-one as the principal over-oxidation product. $Cu(tma)_2$ gives a very good selectivity of 91% for the principal products.

The kinetic study shows that $Fe(tma)_3$ under oxygen pressure produces cyclohexanone and cyclohexanol continuously but looses its activity already after 20 h (Fig. 3). The catalyst $[Cu(en)_2](NO_3)_2$ produces 5 mmol of cyclohexene in 4 h which stays constant during the reaction course. Cyclohexanone and cyclohexanol are produced for 20 h after which the system is deactivated (Fig. 4).

Table 3
Influence of the different catalysts on cyclohexane oxidation under oxygen pressure (25 bar). Conditions: 19 ml of cyclohexane, 0.1 mmol of catalyst, 10 mmol of *tert*-butyl-hydroperoxide, 70°C, 24 h

| Product (mmol)	Fe $(tma)_3$	Fe $(fod)_3$	$[Cu(en)_2]$ $(NO_3)_2$	Cu $(tma)_2$
Cyclohexene	–	–	4.93	4.94
Cyclohexanone	5.92	5.37	5.25	5.33
Cyclohexanol	7.05	6.30	5.23	7.22
Cyclohexen–3–one	0.76	0.77	1.91	1.21
Cyclohexen–3–ol	0.37	0.39	0.55	0.24
Glutaric acid	0.53	0.52	0.23	0.05
Adipic acid	1.94	1.34	0.86	0.24
Turnover	166	147	190	192
Conversion (%)	9.4	8.4	10.8	10.9
Efficiency (%)	164	147	190	192
Selectivity (%)	78	79	81	91

Fig. 1. Cyclohexane oxidation under reflux; catalyst: $Fe(tma)_3$.
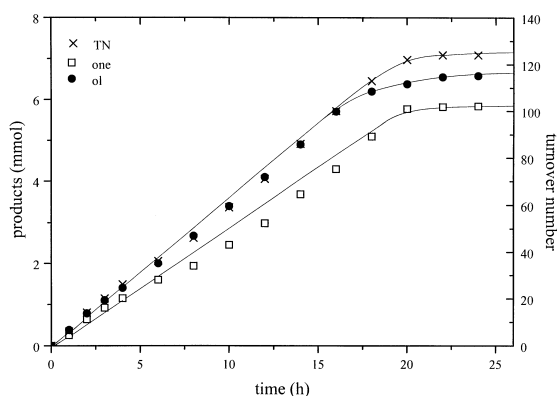
Fig. 3. Cyclohexane oxidation under oxygen pressure; catalyst: Fe(tma)$_3$.

The TBHP is totally consumed after 24 h for all catalysts studied. The reaction can be restarted by addition of further TBHP. However, the amount of additionally formed oxidation products is small and large amounts of over-oxidation products, mainly cyclohexen-3-one, cyclohexen-3-ol and adipic acid are observed. In order to understand these results, we performed reactions in the presence of the oxidation products, adipic acid, additional ligand and *tert*-butanol. The results are shown in Fig. 5. It can be seen that for the iron catalyst the formation of the principal oxidation products is strongly suppressed by cyclohexanone, cyclohexene and adipic acid. As the iron catalyst does not produce cyclohexene, cyclohexanone is the principal reason for its deactivation. It is
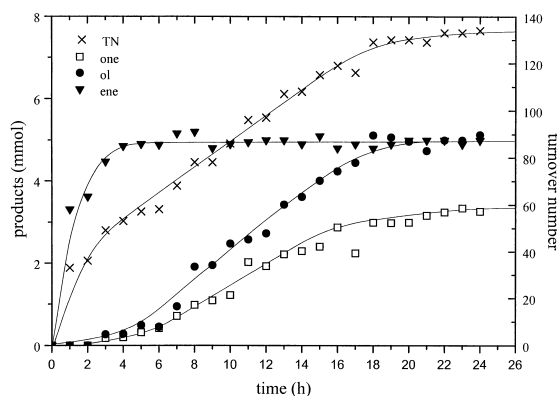

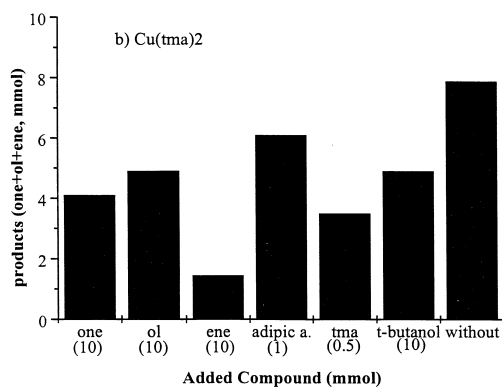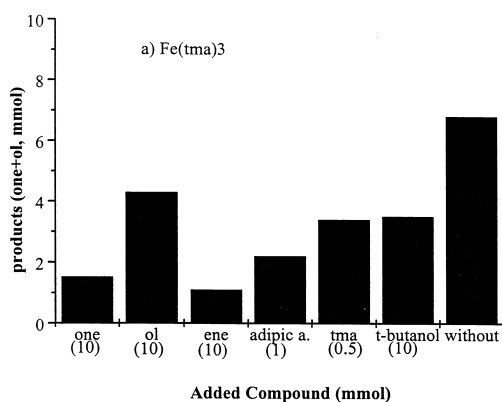Fig. 4. Cyclohexane oxidation under oxygen pressure; catalyst: [Cu(en)$_2$](NO$_3$)$_2$.

Fig. 5. Influence of oxidation and over-oxidation products on the catalytic activity of (a) Fe(tma)$_3$; (b) Cu(tma)$_2$ under reflux.

further oxidised to adipic acid which complexes the catalyst thus deactivating already in small quantities its active site.

On the other hand, the active site of the copper catalyst is not blocked by adipic acid; cyclohexanone has, therefore, only a small influence on its catalytic activity. However, the reaction is strongly suppressed by cyclohexene. As this is easily over-oxidised to cyclohexen-3-one and cyclohexen-3-ol, it is consumed after a certain reaction time at a rate similar to its formation and its concentration remains constant. This means, however, that less catalyst is available for cyclohexane oxidation, which explains why the copper catalyst shows reduced activity after a certain reaction time.

The oxygenated products are formed by the well known free radical process [14–16] in

which molecular oxygen adds to the cyclohexyl radical. The formation of cyclohexene in the presence of the copper catalysts is due to the fact that copper(II) captures cyclohexyl radicals forming by β-elimination cyclohexene, copper(I) and a proton [17]. In order to confirm that the *tert*-butoxy radical abstracts hydrogen from cyclohexane, we performed two kind of experiments. Substitution of the *tert*-butyl hydroperoxide by 2-methyl-1-phenylprop-2-yl hydroperoxide forms large quantities of acetone ($> 40\%$ of the converted hydroperoxide) and products obtained by reaction of the benzyl radical, thus confirming that the hydroperoxide reacts with the catalyst to form the 2-methyl-1-phenylprop-2-oxy radical which suffers extremely rapid β-scission to form acetone and the benzyl radical [15]. Utilisation of di–*tert*–butyl peroxyoxalate, which decomposes at 70°C to form *tert*-butoxy radicals and carbon dioxide [18], gives, in the absence of a catalyst and under reaction conditions, cyclohexanol and cyclohexanone in a 1:1 ratio, as observed in the reaction with *tert*-butyl hydroperoxide.

4. Conclusions

Tert-butyl hydroperoxide very efficiently oxidises cyclohexane in the presence of cyclohexane soluble copper and iron catalysts. The copper catalysts are more selective, furnishing 90% of the principal oxidation products at conversions higher than 10%. This corresponds to concentrations of up to 0.9 mol l^{-1} which, to the best of our knowledge, are higher than those reported in the literature for a selectivity of 90%. The iron catalysts deactivate by overoxidation of cyclohexanone to adipic acid which complexes the active center. The copper catalysts deactivate more slowly and do not overoxidise cyclohexanone but further oxidise cyclohexene to cyclohexen-3-one and cyclohexen-3-ol. Other catalysts should be found which do not produce cyclohexene nor lose their activity in the presence of carboxylic acids, thus allow-

ing higher turnover numbers without loss of the good selectivity found at 70°C.

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