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# Selective epoxidation of (+)-limonene employing methyltrioxorhenium as catalyst

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#### 1. Introduction

Monocyclic monoterpene hydrocarbons occur in many essential oils and their byproducts. Limonene is one of the most common monoterpenes and a widely used feedstock (30,000 tons per year) [1]. For example, limonene can be found in cosmetics, as fragrance in perfume and as a flavoring to mask the bitter taste of alkaloids. It is used as a precursor of carvone in chemical synthesis and applied as solvent in cleaning products. It exists in two optically active forms: D-limonene, possessing a strong orange smell is the main component of citrus oil, and L-limonene, which is found in pinewood and has a piney, turpentine-like odor [2,3]. Racemic limonene is known as dipentene (Scheme 1).

Terpene oxides such as 1,2-limonene oxide have many applications in synthetic chemistry. They are, in fact, the most important members of the terpene family for the perfume industry and are widely used as raw materials in the manufacture of a range of important commercial products [4,5]. Optically pure epoxides, such as 1,2-limonene oxide and their corresponding 1,2-diols are important building blocks in asymmetric synthesis. They are more

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#### ABSTRACT

This report presents a study of the epoxidation of limonene employing methyltrioxorhenium (MTO) as catalyst. The influence of base ligands, namely t-butylpyridine, 4,4'-dimethyl-2,2'-bipyridine and pyrazole on the catalytic activity was investigated. The choice of the oxidant ( $H_2O_2$  in water or  $H_2O_2$  stabilized by urea) was also examined. The effect of the solvent has been studied in order to determine optimal conditions for the epoxidation of (+)-limonene. The best result was obtained when a molar ratio (+)-limonene:MTO: $H_2O_2$ :t-butylpyridine of 100:0.5:10:150 was used at 25 °C in dichloromethane. 1,2-Limonene oxide was formed with 77% yield and 96% selectivity after 1 h with a TOF of ca. 900 h<sup>-1</sup>. © 2012 Published by Elsevier B.V.

particularly used as chiral precursors [6]. 1,2-Limonene oxide has also being used as a bio-renewable monomer in the formation of biodegradable polymers via copolymerization with  $CO_2$  [1,7].

Epoxidation reactions have been extensively studied in the past. The organic peroxyacids, such as m-chloroperbenzoic acid are still the most widely used epoxidation agents, employing the stoichiometric peracid route. However, they are economically and environmentally undesirable as they produce waste, containing their corresponding acids, and are not selective in the formation of epoxides and their cleaved products, especially in the preparation of acid-sensitive epoxides [8,9]. According to literature reports on limonene epoxidation employing homogeneous catalysts, the formation of 1,2-limonene oxide (1) is challenging, since it competes with the formation of byproducts, for example 8,9-limonene oxide (2) and 1,2-8,9-limonene dioxide (3, also named dipentene dioxide). Moreover, other byproducts such as carvone (4) and carveol (5) are also observed depending on the catalyst used. This problem is different from difficulties encountered during the epoxidation of  $\alpha$ -pinene. In the latter case, the major issue was to decrease the acidity of the rhenium center in order to avoid ring opening of the epoxide [10] (Scheme 2).

The epoxidation of limonene with  $Al_2O_3$  as catalyst leads to rather low conversion (max. 70% after 4 h) and the formation of both monoepoxides and diepoxide [11]. The selectivity towards 1,2-limonene oxide is in the best case around 90%. Cobalt base complexes, employed in the oxidation of limonene, lead to low

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**Scheme 1.** Structures of (S)-(-) and (R)-(+)-limonene.

conversion (40%) and the formation of carvone and carveol as main products [12,13]. Dimethyldioxirane allows the formation of 1,2-limonene oxide with 94% selectivity [14]. However, the conversion remains rather low (71%). Iron-based catalysts employed in the epoxidation of limonene yield a mixture of carvone, carveol and 1,2-limonene oxide [15]. Jacobsen's catalyst allows high conversions of limonene (up to 100%) with a very good selectivity (90%) towards dipentene dioxide [16]. However, employing Nmethylimidazole as additive leads to a decrease in conversion (70%) associated with enhanced selectivity towards 1.2-limonene oxide (74%) [17]. Begué et al. used Mn(OAc)<sub>3</sub>·2H<sub>2</sub>O as catalyst with  $O_2$ /pivalaldehyde as oxidant in perfluoro-2-butyltetrahydrofuran, with 1,2-limonene oxide formed in 96% yield after 1 h [18]. Employing Mo based catalysts in limonene epoxidation leads, in general, to either low conversions or low selectivities towards 1,2-limonene oxide. A microwave-assisted study of the epoxidation of limonene employing [CpMo(CO)<sub>3</sub>CH<sub>3</sub>] as catalyst reports the formation of 1,2-limonene oxide with 93% selectivity at 80% conversion [19]. The best results reported to date are, however, heterogeneously catalyzed processes. For instance, polyoxometalate catalysts lead to the formation of 1,2-limonene oxide with 98% selectivity at 99% conversion after 30 min at room temperature [20]. As seen in the previously published results of the epoxidation of limonene, the main challenge remains to favor the formation of 1,2-limonene oxide in high selectivity. Methyltrioxorhenium (MTO) is well established as an very efficient catalyst for olefin epoxidation reactions [21-23]. Some studies described the reactivity of MTO towards the epoxidation of limonene to 1,2-limonene oxide [24]. The best results known up to date were reported by Rudler et al., reaching a conversion of limonene of 98% and a 1,2-limonene oxide selectivity of 86% after 2 h at 4 °C [25]. However, despite all efforts we were unable to reproduce these results (see Section 2.3). Under the same conditions, we observed several other byproducts besides DPO, and the yield of the main product decreased constantly with the reaction time. Thus, we set out to reinvestigate the optimal conditions for an efficient and selective epoxidation of limonene to 1,2-limonene oxide employing MTO as catalyst. Hydrogen peroxide was chosen as oxidant because of its environmental and economic advantages [5]. Its only drawback, the ring opening of sensitive epoxides at the Lewis acidic Re center, can be overcome by the use of nitrogen containing Lewis bases such as pyridine and derivatives, suppressing the formation of diols by reducing the Lewis acidic properties of MTO [26].

In the present work, the optimal conditions for the regioselective epoxidation of (+)-limonene to 1,2-limonene oxide employing MTO as catalyst were investigated. For this purpose, several monoand bidentate base adducts have been added to MTO. Additionally, the effect of using different oxidants and different reaction media was examined in order to study the optimal reaction conditions for the synthesis of 1,2-limoneneoxide in high selectivity. Under the conditions examined, only dipentene dioxide was detected as byproduct. Another part of the work is dedicated to the study of the conditions favoring the formation of dipentene dioxide. It is of interest to investigate formation conditions of the byproduct in order to optimize the reaction conditions in a way to produce only one single product or one product in very large excess.

#### 2. Experimental

#### 2.1. Starting materials

All commercial products were of the highest grade available and were used as such. A 35% solution of  $H_2O_2$  in water (Aldrich) was used for the catalytic test reactions. (+)-Limonene was obtained from Aldrich. UHP contains 35 wt.%  $H_2O_2$  (Acros Organics). Methyltrioxorhenium was synthesized according to the literature [27].

#### 2.2. Gas chromatography

Gas chromatography was performed using a DB23 column (30 m, 0.25 mm, 0.25  $\mu$ m film thickness). The isothermal temperature profile is 60 °C for the first 2 min, followed by a 10 °C/min temperature gradient to 105 °C for 10 min, then 4 °C/min to 140 °C and finally 10 °C/min to 260 °C. The injector temperature was 320 °C. Chromatography grade helium was used as carrier gas.

#### 2.3. Literature conditions [25]

Limonene (6 mmol) was dissolved in  $CH_2Cl_2$  (5 mL) and cooled to 4 °C. MTO (1 mol%/olefin) and then 150 equiv.  $H_2O_2$  (10% in water) were added to the solution. The reaction was stirred for 2 h, quenched with MnO<sub>2</sub> and analyzed by GC. Result: Conversion limonene = 99%; yield 1,2-limonene oxide = 47%; yield dipentene dioxide = 23%. Moreover, other byproducts (29%), among them 8,9limonene oxide and the corresponding diols of the found epoxides, were observed in the GC spectrum which explain the low 1,2limonene oxide yield obtained compared to the conversion of limonene.

#### 2.4. Epoxidation of (+)-limonene in different solvents

MTO was dissolved in the solvent and the solution was let at  $25 \,^{\circ}$ C or cooled at  $0 \,^{\circ}$ C. The ligand, the 2 standards (mesitylene: 0.5 mL and naphthalene (solution 2 g in 10 mL CH<sub>2</sub>Cl<sub>2</sub>): 0.5 mL),



Scheme 2. Possible products of the oxidation of limonene.

#### Table 1

Summary of the different molar ratio employed in the epoxidation of (+)limonene <sup>a</sup>t-butylpyridine, 4,4'-dimethyl-2,2'-dipyridine, pyrazole <sup>b</sup>H<sub>2</sub>O<sub>2</sub>, UHP <sup>c</sup>CH<sub>2</sub>Cl<sub>2</sub>, MeNO<sub>2</sub>, CHCl<sub>3</sub>, nBuOH or THF.

| <i>T</i> (°C) | Reaction condition: molar ratio |     |                       |                                     |                                      |  |  |  |
|---------------|---------------------------------|-----|-----------------------|-------------------------------------|--------------------------------------|--|--|--|
|               | (+)-Limonene                    | MTO | t-Butylpyr            | idine H <sub>2</sub> O <sub>2</sub> | CH <sub>2</sub> Cl <sub>2</sub> (mL) |  |  |  |
| 25 and 0      | ) 100                           | 1   | 20                    | 300                                 | 6.4                                  |  |  |  |
| 25            | 100                             | 1   | 20                    | 150                                 | 7.1                                  |  |  |  |
| 25            | 100                             | 1   | 20                    | 100                                 | 7.3                                  |  |  |  |
| 25            | 100                             | 1   | 10                    | 150                                 | 7.2                                  |  |  |  |
| 25            | 100                             | 1   | 5                     | 150                                 | 7.2                                  |  |  |  |
| 25            | 100                             | 1   | 0                     | 150                                 | 7.3                                  |  |  |  |
| 25            | 100                             | 0.1 | 2                     | 150                                 | 7.3                                  |  |  |  |
| 25            | 100                             | 1   | 40                    | 300                                 | 6.3                                  |  |  |  |
| 25            | 100                             | 1   | 60                    | 300                                 | 6.1                                  |  |  |  |
| 25            | 100                             | 1   | 20                    | 600                                 | 4.9                                  |  |  |  |
| 25            | 100                             | 1   | 40                    | 600                                 | 4.8                                  |  |  |  |
| 25            | 100                             | 1   | 60                    | 600                                 | 4.6                                  |  |  |  |
| <i>T</i> (°C) | Reaction condition: molar ratio |     |                       |                                     |                                      |  |  |  |
|               | (+)-Limonene                    | MTO | Ligand <sup>a</sup> ( | Oxidant <sup>b</sup>                | Solvent <sup>c</sup> (mL)            |  |  |  |
| 25            | 100                             | 0.5 | 10                    | 150                                 | 7.2                                  |  |  |  |

1 equiv. MTO correspond to 0.06 mmol; 0.5 equiv. MTO correspond to 0.03 mmol; 0.1 equiv. MTO correspond to 0.006 mmol.

and the oxidant ( $H_2O_2$  35% or UHP) were added to the solution. (+)-Limonene was then added to the reaction. Samples were taken after 5 min, 10 min, 15 min, 30 min, 60 min, 90 min, 3 h, 5 h and 24 h. For each sample, 1 mL of the reaction mixture was taken and neutralized by  $MnO_2$ . The mixture was dried over  $MgSO_4$ . 200 µL from the dry solution was taken, 0.5 mL of a solution of 1 mL of methylnaphthalene in 50 mL isopropanol and 0.8 mL of isopropanol were mixed in a vial and analyzed by GC (Table 1).

#### 3. Results and discussion

#### 3.1. Background

The epoxidation of olefins employing MTO as catalyst has been extensively studied [28-33]. The influence of different ligands, oxidants and solvents on the activity of MTO was reported in some detail for a variety of substrates [34-36]. The most commonly applied oxidant for the epoxidation of olefins utilizing MTO as catalyst is aqueous hydrogen peroxide. It is an efficient oxidant, cheap and environmentally friendly since the only byproduct formed is water. However, the  $MTO/H_2O_2$  system can lead to the formation of diols by ring opening of the epoxide at the Re center, due to its strong Lewis-acidic character [37]. This is particularly the case for acid-sensitive epoxides. It was shown that the ring opening can be prevented when the Lewis acidity of Re(VII) is reduced by coordination of  $\sigma$ -donor ligands to Re, which are typically aromatic N-bases, such as for example pyridine derivatives [28,29,37]. The Lewis base adducts of MTO inducing the best activity in olefin epoxidation are pyridine based such as t-butylpyridine or 4,4'-dimethyl-2,2'bipyridine [34,38,39]. Pyrazole was also described as an efficient Lewis-base additive [40,41]. To avoid water as solvent, anhydrous hydrogen peroxide adducts, e.g. UHP (urea hydrogen peroxide) can be applied [35,36]. The solvents are also known to have an influence on the activity of the catalytically active complexes. The most efficient solvents in the epoxidation of olefin employing MTO as catalyst are non- or weakly coordinating solvents such as CH<sub>2</sub>Cl<sub>2</sub> and CHCl<sub>3</sub> not competing with Lewis-base and substrate for coordination sites [28,42,43]. The preliminary study on the epoxidation of limonene described in this paper was thus undertaken with these reactants.



Fig. 1. Kinetics of the oxidation of (+)-limonene.

3.2. Epoxidation of (+)-limonene: formation of 1,2-limonene oxide

3.2.1. Oxidation of (+)-limonene, determination of the byproducts

The formation of 1,2-limonene oxide (LO) and byproducts is investigated. For this purpose, the molar ratio (+)-limonene:MTO:t-butylpyridine: $H_2O_2$  of 100:1:20:300 is applied in  $CH_2Cl_2$  at 25 °C.

As depicted in Fig. 1, under the applied conditions the formation of 1,2-limonene oxide (LO) is fast at the beginning of the reaction. The yield of 1,2-limonene oxide reaches a maximum after 15 min and then decreases. The byproduct observed during the epoxidation of (+)-limonene (L) employing MTO as catalyst is dipentene dioxide (DPO). Other byproducts, e.g. 8,9-epoxide or (+)-limonene diol, were not observed.

#### 3.2.2. Optimization of the reaction conditions

The synthesis of 1,2-limonene oxide is optimized employing MTO as catalyst, t-butylpyridine as Lewis base adduct and aqueous hydrogen peroxide as oxidant in  $CH_2Cl_2$ . The influence of the concentration of each reactant is investigated as well as the effect of temperature.

3.2.2.1. Temperature influence. Applying a molar ratio (+)-limonene:MTO:t-butylpyridine: $H_2O_2$  of 100:1:20:300 in  $CH_2Cl_2$  leads to slower oxidation of (+)-limonene at 0 °C than at 25 °C (see Fig. 2). The temperature was decreased in an attempt to avoid the formation of the diepoxide.

From the structure of (+)-limonene, it is possible to deduce that the oxidation of the (1–2) double bond is easier than the (8–9) double bond. Moreover, the activity of the catalytic complex decreases with lower temperature. This property could have lead to the only formation of 1,2-limonene oxide avoiding the epoxidation of the second double bond, which cannot be easily oxidized at low temperature. However, as depicted in Fig. 1, the selectivity towards 1,2-limoneneoxide is not improved at lower temperature. At the highest yield of 1,2-limonene oxide under both conditions (30 min for T=0 °C and 15 min for T=25 °C), the selectivity towards LO is higher at 25 °C (S=77% for 25 °C and S=60% for 0 °C). This temperature is therefore applied in all following experiments.

3.2.2.2. Influence of the oxidant concentration. Again, a molar ratio (+)-limonene:MTO:t-butylpyridine: $H_2O_2$  of 100:1:20:X is applied in  $CH_2Cl_2$  at 25 °C.

The kinetics of the epoxidation of limonene depicted in Fig. 3-1 show how important it is to stop the reaction after a certain time to obtain the best ratio of yield vs selectivity towards 1,2-limonene oxide. In the case of the molar ratio MTO:oxidant 1:150, the selectivity towards 1,2-limonene oxide is optimal (100%) after 10 min, however, the yield is low (45%). If the reaction is stopped after



Fig. 2. Kinetics of the epoxidation of limonene at: (1) 0 °C and (2) 25 °C (yields are determined by GC analysis).

30 min, good yields of 1,2-limonene oxide can be reached (75%), however the selectivity is already beyond its optimum (77%). Stopping at the time with the best selectivity/yield ratio is therefore a prerequisite. In this example, the optimal time is 15 min with 63% yield and 92% selectivity towards 1,2-limonene oxide. The optimal time for the molar ratio MTO:H<sub>2</sub>O<sub>2</sub> 1:300 and 1:100 are respectively 15 min and 2 h. The yield and selectivity showed in Fig. 3-2 are taken for each condition at this optimal time.

The oxidant concentration leading to the highest yield is  $MTO:H_2O_2$  1:150 (Fig. 3-1). The selectivity reaches also a maximum when a ratio  $MTO:H_2O_2$  of 1:150 is used (Fig. 3-2). A higher concentration of oxidant enhances the activity of the catalytic system. As shown in Fig. 3-1, the formation of 1,2-limonene oxide is faster during the first 15 min. In the case of a 1:300 ratio, however, after 15 min, the yield of 1,2-limonene oxide already decreases due to byproduct formation. In the case of a 1:100 ratio, the formation of LO and DPO are both slow. Consequently, the MTO:H<sub>2</sub>O<sub>2</sub> ratio of 1:150 leads to the highest yield and selectivity within a reasonable time reaction and is thus applied for the following experiments.

3.2.2.3. Influence of the ligand concentration. It is known that the activity of the catalytic system increases, within certain border lines, with the quantity of the Lewis base adduct [34,38]. The ligand is useful to prevent the formation of byproducts forming due to the Lewis acidity of the rhenium center [26]. The influence of ligand concentration on the regioselectivity of the formation of 1,2-limonene oxide is therefore important to be determined. For this purpose, a molar ratio (+)-limonene:MTO:t-butylpyridine:H<sub>2</sub>O<sub>2</sub> of 100:1:X:150 was applied in CH<sub>2</sub>Cl<sub>2</sub> at 25 °C.

The activity of the catalytic system increases when the concentration of the Lewis base increases from 1:5 to 1:20 [40]. However, the activity of the examined catalytic system is better when no Lewis base adduct is added than for MTO:ligand ratios of 1:5 and 1:10. The  $MTO/H_2O_2$  in some cases oxidizes the N-base ligand to N-oxide. This reaction, however, is usually slower than the olefin

epoxidation [40,44]. The complex formed by the N-oxide ligand with MTO is also catalytically less active than the N-base-MTO adduct. It is therefore important to use a significant excess of the Lewis base adduct. As depicted in Fig. 4, the highest yield and selectivity towards 1,2-limonene oxide are reached when a molar ratio MTO:t-butylpyridine of 1:20 is applied. When no Nbase adduct is added to the reaction, besides dipentene dioxide several other byproducts could be observed. It can reasonably be assumed that the byproducts are 8,9-limonene oxide and the corresponding diols to the found epoxides. The latter observation shows that employing the N-base adduct prevents the formation of other byproducts. A MTO:t-butylpyridine ratio of 1:20 leads also to a fast formation of dipentene dioxide since the yield of 1.2-limonene oxide begins to decrease early (30 min). As a consequence, a high concentration of Lewis base adduct favors the formation of 1,2-limonene oxide. The optimal 1,2-limonene oxide yield was obtained after 15 min with a yield of 63% and a selectivity of 92%. Finally, the concentration of t-butylpyridine was increased to a MTO:t-butylpyridine ratio of 1:40. Yield and selectivity towards 1,2-limonene oxide, however, decrease at this latter ratio. Consequently, the ratio MTO:t-butylpyridine of 1:20 appears to lead to the formation of 1,2-limonene oxide with the highest yield and selectivity.

3.2.2.4. Influence of the catalyst concentration. A molar (+)limonene:MTO:t-butylpyridine: $H_2O_2$  ratio of 100:X:20:150 is applied in dichloromethane at 25 °C (Fig. 5).

The activity of the system appears to be best at the lowest applied concentration of 0.1 mol% catalyst. At higher concentration most likely not all catalyst molecules are involved in the reaction. Additionally, a catalyst concentration of 1 mol% leads to fast byproduct formation since the catalyst molecule not involved in olefin epoxidation may instead promote its transfer to diepoxide. An optimal selectivity and yield (96 and 76%) is reached with 0.5 mol% catalyst after 1 h.



**Fig. 3.** Influence of the oxidant concentration on the (1) yield; (2) highest selectivity of (+)-1,2-limonene oxide at yield<sub>optimal</sub>. Molar ratio MTO:H<sub>2</sub>O<sub>2</sub> (a) 1:300/ $t_{opt}$  = 15 min; (b) 1:150/ $t_{opt}$  = 15 min; (c) 1:100/ $t_{opt}$  = 2 h.



**Fig. 4.** Influence of the ligand concentration on the (1) yield; (2) highest selectivity of 1,2-limoneneoxide at yield<sub>optimal</sub>. Molar ratio MTO:t-butylpyridine: (a) 1:20/t<sub>opt</sub> = 15 min; (b) 1:10/t<sub>opt</sub> = 30 min; (c) 1:5/t<sub>opt</sub> = 1 h; (d) 1:0/t<sub>opt</sub> = 15 min.

3.2.2.5. Influence of the oxidant  $H_2O_2$  vs UHP. A molar (+)limonene:MTO:t-butylpyridine:oxidant ratio of 100:0.5:10:150 is applied in dichloromethane at 25 °C.

Fig. 6 shows a feature which is quite different compared to the epoxidation of  $\alpha$ -pinene [26]. As for  $\alpha$ -pinene, employing MTO:UHP as catalytic system does not decrease the velocity of the epoxidation compared to the catalytic system MTO:H<sub>2</sub>O<sub>2</sub> but increases the selectivity towards the desired epoxide. In case of (+)-limonene epoxidation, the catalytic system MTO:UHP is less efficient than MTO:H<sub>2</sub>O<sub>2</sub> (Fig. 6-1). This decrease in catalytic activity can be explained by the fact that UHP is not soluble in most organic solvents. The access of the oxidant and the formation of the catalytic species are consequently slower. The selectivity towards 1,2-limonene oxide formation is not enhanced when UHP is used as oxidant (Fig. 6-2). The highest yield (77%) and selectivity (96%) are observed when aqueous hydrogen peroxide is used as oxidant.

3.2.2.6. Ligand influence. t-Butylpyridine, 4,4'-dimethyl-2,2'-bipyridine and pyrazole are applied as ligands. A molar ratio (+)-limonene:MTO:ligand:H<sub>2</sub>O<sub>2</sub> of 100:0.5:10:150 is applied in dichloromethane at 25 °C.

It is known that N-base adduct such as t-butylpyridine and 4,4'-dimethyl-2,2'-bipyridine can be oxidized to the corresponding N-oxide by the MTO/H<sub>2</sub>O<sub>2</sub> system [40,44]. Pyrazole was found to be a good alternative to the pyridine-based ligand since it is not easily oxidized by MTO/H<sub>2</sub>O<sub>2</sub> and its MTO adducts shows good reactivity towards epoxidation activity[41]. As seen in Fig. 7-1, both 4,4'-dimethyl-2,2'-bipyridine and pyrazole lead to a somewhat higher rate of 1,2-limonene oxide formation than t-butylpyridine. However, as depicted in Fig. 7-2, the use of t-butylpyridine as N-base adduct leads to the best selectivity towards 1,2-limonene oxide and allows the highest product yield. Hence, in the following, t-butylpyridine was used as additive.

3.2.2.7. Solvent influence. In the epoxidation of olefins, the solvent plays a crucial role. In this study, the influence of  $CH_2Cl_2$ ,  $CHCl_3$ , THF and MeNO<sub>2</sub>, which are often used in olefin epoxidation, was studied. Additionally, the alcohol n-butanol is also used to study the influence of a one-phase system, which could be of practical interest as well. For this purpose, the molar ratio (+)-limonene:MTO:t-butylpyridine:H<sub>2</sub>O<sub>2</sub> of 100:0.5:10:150 is applied in different solvents at 25 °C.

In n-butanol as well as in nitromethane, the formation of 1,2limonene oxide is fast (5 min) but the yield does not increase significantly any more (Fig. 8-1). Selectivity towards 1,2-limonene oxide is ca. 60% for both solvents, however, due to byproduct formation the conditions are not very promising. An explanation for the fast activity decrease when n-butanol is used is the presence of a one-phase system. As mentioned before, the system MTO/H<sub>2</sub>O<sub>2</sub> catalyzes the transformation of t-butylpyridine to t-butylpyridine-N-oxide. In a two phase system, the N-oxide adduct dissolves in the water phase, avoiding the formation of less active MTO/N-oxide base adduct. In the case of a onephase system, a MTO/N-oxide base adduct is formed leading to an activity decrease (see Fig. 8-1). CH<sub>2</sub>Cl<sub>2</sub> is the solvent allowing the highest activity of the catalytic system followed by CHCl<sub>3</sub> and THF (Fig. 8-1). As depicted in Fig. 8-2, the latter order is maintained for the selectivity towards the 1,2-limonene oxide.

## 3.3. Epoxidation of (+)-limonene: formation of 1,2–8,9-limonene dioxide (DPO)

Parallel to the experiments on 1,2-limonene oxide formation, some experiences are executed to synthesize the byproduct dipentene dioxide in high yield and selectivity. Despite the main goal of this work being to synthesize the mono-epoxide in high selectivity,



**Fig. 5.** Influence of the catalyst concentration on the (1) yield; (2) highest selectivity of 1,2-limonene oxide at yield<sub>optimal</sub>. (a) 1 mol% MTO/*t*<sub>opt</sub> = 15 min; (b) 0.5 mol% MTO/*t*<sub>opt</sub> = 1 h; (c) 0.1 mol% MTO/*t*<sub>opt</sub> = 1 h30.



Fig. 6. Effect of the different oxidants on the (1) yield; (2) highest selectivity of 1,2-limonene oxide at yield<sub>optimal</sub>. (a) Hydrogen peroxide/t<sub>opt</sub> = 1 h; (b) UHP/t<sub>opt</sub> = 2 h.



**Fig. 7.** Effect of the different Lewis bases on (1) yield; 2) (highest selectivity of 1,2-limonene oxide at yield<sub>optimal</sub>. (a) *t*-Butylpyridine/*t*<sub>opt</sub> = 1 h; (b) pyrazole/*t*<sub>opt</sub> = 30 min; (c) 4,4'-dimethyl-2,2'-bipyridine/*t*<sub>opt</sub> = 30 min.



**Fig. 8.** Effect of the different solvents on the (a) yield; (b) highest selectivity of 1,2-limonene oxide at yield<sub>optimal</sub>. (a)  $CH_2Cl_2/t_{opt} = 1$  h; (b)  $CHCl_3/t_{opt} = 1$  h; (c)  $THF/t_{opt} = 4$  h; (d)  $nBuOH/t_{opt} = 30$  min; (e)  $MeNO_2/t_{opt} = 30$  min.

it is of interest to investigate the conditions which can lead to the formation of the byproduct dipentene dioxide in high yields and selectivity.

A systematic study of the formation of dipentene dioxide during the investigation of 1,2-limonene oxide synthesis shows that a highly active catalytic system favors the byproduct formation. Therefore, high concentrations of Lewis base adduct and oxidant should allow high yield formation of dipentene oxide. Dichloromethane was applied with a catalyst concentration of 1 mol%. In the following experiments, the effect of the concentration of either t-butylpyridine or aqueous hydrogen peroxide on the oxidation of (+)-limonene was studied.

As depicted in Table 2, the formation of dipentene oxide is favored when the concentration of Lewis base adduct increases from a MTO:ligand ratio 1:20 to 1:60. As seen in the previous paragraph, the yield of dipentene dioxide increases with the oxidant concentration between the molar ratio 1:100 and 1:300. However, this relation does not apply when the oxidant concentration is too high (Table 3). The formation of dipentene oxide competes with other byproducts when the molar ratio  $MTO:H_2O_2$  of 1:600 is applied leading to lower dipentene oxide yields.

The conditions leading to the formation of dipentene dioxide in highest yield and selectivity are found applying a molar ratio (+)-limonene: MTO:t-butylpyridine: $H_2O_2$  of 100:1:40:300 in dichloromethane at 25 °C.

Table 2

Influence of Lewis base adduct concentration towards the formation of dipentene dioxide.

| Conditions: mo | lar ratio | Yield <sub>max</sub> DPO | Time (h) |     |    |
|----------------|-----------|--------------------------|----------|-----|----|
| (+)-Limonene   | MTO       | t-Butylpyridine          | $H_2O_2$ |     |    |
| 100            | 1         | 20                       | 600      | 55% | 24 |
| 100            | 1         | 40                       | 600      | 70% | 24 |
| 100            | 1         | 60                       | 600      | 83% | 24 |

#### Table 3

Influence of oxidant concentration towards the formation of dipentene dioxide.



Fig. 9. Kinetics of the oxidation of (+)-limonene to dipentene dioxide.

As depicted in Fig. 9, the formation of 1,2-limonene oxide is very fast at the beginning. The yield of 1,2-limonene oxide reaches a maximum after only 5 min and then decreases significantly during the first 3 h of the reaction. After 24 h 1,2-limonene oxide is nearly entirely converted. Dipentene dioxide is obtained in 90% yield and 90% selectivity after 24 h. 2% of the impurities is 1,2-limonene oxide, the other 8% could not be unambiguously determined. However, it can reasonably be assumed that the byproducts are again 8,9-limonene oxide and the corresponding diols of the found epoxides.

#### 4. Conclusion

Optimal conditions for the epoxidation of (+)-limonene employing MTO as catalyst were established. To reach optimal 1,2limonene oxide formation (high activity, selectivity and yield) MTO has to be applied in not too high concentrations to avoid secondary reactions of 1,2-limonene oxide (most prominent is diepoxide formation). When the Lewis base ligand/MTO ratio is too high or too low, byproduct formation also begins to dominate. With low Lewis base concentrations epoxide ring opening reactions are favored due to the Lewis acidity of the system. t-Butylpyridine turned out to be optimal amongst the examined Lewis bases, it applied together with H<sub>2</sub>O<sub>2</sub> as oxidant in a two phase system with dichloromethane as organic phase at room temperature (25 °C). Under these conditions, the highest selectivity towards 1,2-limonene oxide is obtained with a ratio of (+)-limonene:MTO:t-butylpyridine:H<sub>2</sub>O<sub>2</sub> of 100:0.5:10:150. Under these conditions 1,2-limonene oxide is formed in 77% yield with 96% selectivity after 1 h.

For dipentene dioxide formation, the optimal condition is reached with a catalyst concentration of 1 mol% with enhanced ligand and oxidant concentration. The highest yield and selectivity are obtained with a (+)-limonene:MTO:t-butylpyridine:H<sub>2</sub>O<sub>2</sub> ratio of 100:1:40:300 at 25 °C. Dipentene dioxide is formed under these conditions in 90% yield and selectivity after 24 h.

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