Molecular Catalysis 443 (2017) 52–59

Contents lists available at ScienceDirect

Molecular Catalysis

journal homepage: www.elsevier.com/locate/mcat

MCAT

Editor's choice paper

Influence of ligand substitution on molybdenum catalysts with tridentate Schiff base ligands for the organic solvent-free oxidation of limonene using aqueous TBHP as oxidant

Weili Wang[a,b], Dominique Agustin[a,b,*], Rinaldo Poli[a,c]

[a] CNRS, LCC (Laboratoire de Chimie de Coordination), Université de Toulouse, UPS, INPT, 205, route de Narbonne, F-31077 Toulouse, France
[b] Université de Toulouse, Institut Universitaire de Technologie Paul Sabatier – Département de Chimie, Av. Georges Pompidou, BP 20258, F-81104 Castres Cedex, France
[c] Institut Universitaire de France, 1 rue Descartes, 75231 Paris, France

ARTICLE INFO

Article history:
Received 25 July 2017
Received in revised form 5 September 2017
Accepted 29 September 2017

Keywords:
Epoxidation
Molybdenum
Limonene
Solvent-free process
Ligand effect

ABSTRACT

The oxidation of limonene by aqueous TBHP has been analyzed in the presence of molybdenum complexes $[MoO_2L]_2$ as catalysts with five different tridentate ligands L in the absence of organic solvents (greener reaction conditions). The ligands are based on a common salicylidene amino(thio)phenolate, SA(T)P, backbone with differences in the coordination sphere (ONO for L = SAP *vs.* ONS for L = SATP) or in the salicyl moiety functionalization by OH groups for the ONO ligands. The process gives a regioselective endocyclic epoxidation to a kinetically controlled 1:1 mixture of the *cis*-LimO and *trans*-LimO epoxides and/or the isomeric diols *ax*-LimD and *eq*-LimD by the subsequent ring opening in the presence of water, with a product distribution that depends on the ligand, reaction time and temperature. In combination with control experiments of the *cis*/*trans*-LimO ring opening, the investigations demonstrate the catalytic action of the metal complexes in both the epoxidation and the ring opening steps, with the *cis*-LimO stereospecifically producing the *ax*-LimD product and the less reactive *trans*-LimO leading to a 4:3 mixture of *ax*-LimD and *eq*-LimD. The ONS system $[MoO_2(SATP)]_2$ exhibits the highest catalytic activity in both steps.

Introduction

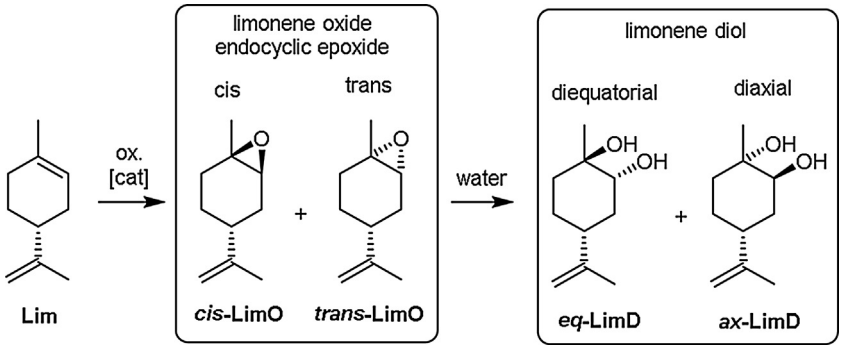
The use of natural feedstock as chemical source is of constantly increasing interest [1]. Terpenes, due to their diverse structures, represent an interesting available ore for several chemical transformations [2]. As an example of terpene, limonene (Lim) is an inexpensive substrate obtained as waste from the orange juice industry [3,4]. The limonene epoxides (LimOs) and diols (LimDs), obtained by oxidation of Lim (Scheme 1), are added-value renewable-based compounds [5,6], with applications in the synthesis of fragrances, flavors, food additives, or compounds with biological and therapeutic activity [7,8]. Both LimO isomers, *cis*-LimO and *trans*-LimO, find applications in medicine [9], metal coatings, varnishes, printing inks, and in natural based polymers [10] but exist in Nature in insufficient quantities to satisfy the needs [11]. Both LimD isomers, *eq*-LimD and *ax*-LimD, generated from the LimOs by epoxide ring opening with water [12], are also precursors of interest for the pharmaceutical industry [13].

The Lim epoxidation may occur at the internal and/or terminal alkene moiety and the presence of water facilitates the epoxide ring opening. In most cases, the main products are *cis*-LimO and *trans*-LimO deriving from the regioselective epoxidation of the endocyclic double bond, which is more reactive because of its higher electron density. The terms *cis* and *trans*, for this family of products, refer to the relative position of the Me and *i*Pr substituents relative to the cyclohexane ring. Although four different stereoisomers may result in principle from the ring opening of *cis*-LimO and *trans*-LimO, only two of them, the diequatorial *cis* isomer (*eq*-LimD) and the diaxial *trans* isomer (*ax*-LimD), have been obtained by this procedure as shown in Scheme 1. Traces of other compounds such as carvone and carveol, resulting from allylic oxidation, may also be observed.

For the non-catalyzed processes leading to endocyclic epoxidation, organic peracids typically yield a 1:1 *cis*/*trans*-LimO mixture [14], whereas N-sulfonyloxaziridines show stereoselectivities in favor of *cis*-LimO [15]. In the extensive literature on metal catalyzed

* Corresponding author at: Université de Toulouse, Institut Universitaire de Technologie Paul Sabatier – Département de Chimie, Av. Georges Pompidou, BP 20258, F-81104, Castres Cedex, France.
E-mail address: dominique.agustin@iut-tlse3.fr (D. Agustin).

http://dx.doi.org/10.1016/j.mcat.2017.09.033
2468-8231/

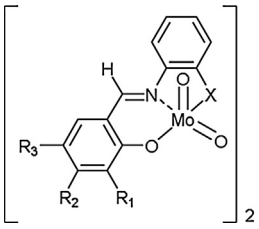


Scheme 1. Oxidation of limonene and potential LimO and LimD products.

Lim epoxidation, the *cis*/*trans* stereoselectivity is rarely indicated. A variety of mononuclear molybdenum catalysts in combination with the TBHP oxidant were reported to yield equimolar amounts of the two isomers [16], while a greater stereoselectivity in favor of the *trans* isomer has been recently reported for a dinuclear Mo catalyst . A mononuclear iron catalyst yields predominantly the *cis*-LimO product [17].

Concerning the selectivity of the ring opening step leading from LimO to LimD, it has been reported that both *cis*- and *trans*-LimO lead to the same *ax*-LimD product under acidic conditions (pH 3) [18], which was attributed to a selective axial nucleophilic attack that can be rationalized by the Fürst-Plattner rule [19]. However, at an only slightly higher pH (4), only *cis*-LimO is opened stereospecifically to yield *ax*-LimD while *trans*-LimO remains unreacted [18]. Further studies have shown that the stereospecific opening of the *cis*-LimO isomer to *ax*-LimD also occurs in the presence of lanthanide [20] or Mo [21] catalysts. This ring opening selectivity has been exploited in some cases as a way to generate isomerically pure *ax*-LimD and/or to kinetically accumulate pure *trans*-LimO from the isomer mixture. The opposite preference for the *trans*-LimO ring opening has been accomplished by use of other conditions such as the use of nucleophilic amines [22], yielding again a *trans*-diaxial addition product, or water in the presence of mercuric reagents at pH 7, which leads, after treatment of an alkoxymercury intermediate with $NaBH_4$, to the stereospecific generation of the *eq*-LimD product [18,23]. The LimO ring opening has also been explored with the use of enzymes. Using the *Rhodotorula glutinis* hydrolytic enzyme, optically pure (1*S*,2*R*,4*S*)-*cis*-LimO was more rapidly and stereospecifically hydrolyzed to (1*S*,2*R*,4*S*)-*ax*-LimD, whereas optically pure (1*S*,2*R*,4*R*)-*trans*-LimO was opened more slowly to yield a mixture of (1*R*,2*R*,4*R*)-*eq*-LimD (65%) and (1*S*,2*S*,4*R*)-*ax*-LimD (35%) [24]. By direct enzymatic oxidation of Lim using a chloroperoxidase enzyme from *Caldariomyces fumago*, the LimD products were directly generated without detection of the LimO intermediates [25]. Only *ax*-LimD was selectively obtained when the procedure was carried out in the absence of KCl and proposed to result from the stereospecific opening of *cis*-LimO, whereas addition of KCl yields a mixture of *ax*-LimD and *eq*-LimD, proposed to derive from a mixture of *cis*-LimO and *trans*-LimO. These enzymatic studies are apparently the only ones highlighting the direct formation of *eq*-LimD by LimO ring opening.

It is also pertinent to highlight that the production of LimO and LimD has typically been accomplished using non-green conditions (oxidants such as peracids [14] and/or organic solvents [26]; or use of mercuric reagents for separation as highlighted above). In order to develop a greener access to these compounds, safer oxidants and non-hazardous conditions are required [27]. Recently, we have reported the solvent-free epoxidation of cyclooctene and cyclohexene catalyzed by different molybdenum [28] and vanadium [29] complexes or by polyoxometalates [30]. The concept was



	X	R_1, R_2, R_3
$[MoO_2(SAP)]_2$	O	H, H, H
$[MoO_2L^a]_2$	O	OH, H, H
$[MoO_2L^b]_2$	O	H, OH, H
$[MoO_2L^c]_2$	O	H, H, OH
$[MoO_2(SATP)]_2$	S	H, H, H

Scheme 2. Pre-catalysts used in this study.

then further applied to terpenic compounds [31]. A particular class of compounds that we have explored in some detail is the salicylidene amino(thio)phenolate family shown in Scheme 2. It was therefore of interest to apply these precatalysts to the Lim epoxidation under simpler and cleaner operating conditions, without organic solvents and with aqueous TBHP as oxidant. Preliminary results on the greener epoxidation of Lim using a few related Mo catalysts, yielding a mixture of *cis*-LimO, *trans*-Limo and *ax*-LimD, have been included in a recent publication . Here, we report a fuller investigation demonstrating how the ligand nature, particularly the presence of the sulfur atom or an OH group in the R_1 position, affects the selectivity and the kinetics of the various transformations.

Results and discussion

Catalyzed limonene oxidation

The results of initial catalytic tests, run with all the pre-catalysts shown in Scheme 2, are collected in Table 1. In the absence of catalyst (run 1), aqueous TBHP leads only to a 7.6% conversion at 80 °C after 4 h, with detected traces of LimOs and LimDs. Using a 0.5% catalyst loading, Lim conversions of 79% (after 4 h with $[MoO_2(SAP)]_2$, run 2) and 93% (after 30 min with $[MoO_2(SATP)]_2$, run 3) demonstrated the catalytic activity of both complexes as well as the greater activity of the sulfur-containing complex. The conversion monitoring for runs 1, 2 and 3 is shown in Fig. 1. The much higher activity for the catalyst with the ONS coordination sphere in Lim oxidation parallels that observed previously for the epoxidation of cyclooctene .

Monitoring the evolution of the various products in runs 2 and 3 revealed additional interesting features (see Fig. 2). For the experiment with $[MoO_2(SAP)]_2$ (Fig. 2, left), the two LimO isomers are initially produced in a ca. 1:1 ratio (13.8% and 15.3% after 60 min), but subsequently the amount of *cis*-LimO slowly decreased (2.6% after 4 h) while that of *trans*-LimO continued to increase (19.8% after 4 h). These data indicate that the rate of *cis*-LimO ring opening exceeds that of its generation at longer reaction times, while *trans*-LimO opens the ring more slowly. At the same time, the *ax*-LimD amount increased from 4.7% to 26.5% while only traces of *eq*-LimD

Table 1
Oxidation of limonene in the presence of various Mo catalysts.[a]

Run	Catalyst	Time (h)	Lim Conv (%)	Selectivity (%)[b]				TON	Highest TOF (h^{-1})[c]
				LimO		LimD			
				Cis	trans	eq	ax		
1	–	4	7.6	5.3	14.5	0.4	6.6	–	–
2	$[MoO_2(SAP)]_2$	4	79	14.6	25.1	2.3	33.5	158	130
3	$[MoO_2(SATP)]_2$	0.5	93	0	0	12.4	40.6	185	371
4	$[MoO_2L^a]_2$	4	90	2.1	4.2	4.1	44.3	180	308
5	$[MoO_2L^b]_2$	4	68	19.0	29.0	1.3	30.3	136	77
6	$[MoO_2L^c]_2$	4	77	10.9	20.8	3.6	35.7	154	110

[a] Reaction conditions: [Mo]/limonene/TBHP = 0.5/100/200, T = 80 °C.
[b] Select = $n_{product}$ formed/n_{Lim} transformed obtained from GC analysis of the organic phase.
[c] TOF is calculated using the time interval with maximum slope in the conversion plot.

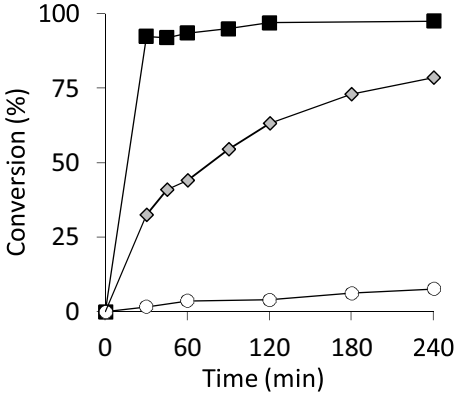
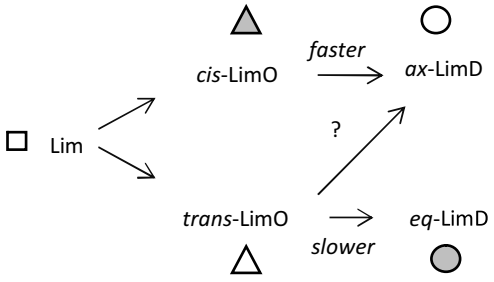


Fig. 1. Kinetic profiles for limonene oxidation: without catalyst (○), with $[MoO_2(SAP)]_2$ (◆), with $[MoO_2(SATP)]_2$ (■). [Mo]/limonene/TBHP = 0.5/100/200, T = 80 °C.

were detected initially and significant amounts are only formed after 3 h.

The initial observation of *ax*-LimD as the predominant diol in solution while only the *cis*-LimO intermediate is being consumed at significant rate suggests that the faster ring opening of *cis*-LimO leads selectively to this product. This observation is consistent with previous literature reports. On the other hand, the slower generation of *eq*-LimD suggests that this isomer results from the slower ring opening of *trans*-LimO. We are unaware of other contributions where the direct generation of *eq*-LimD from metal-catalyzed Lim epoxidation has been highlighted (see also the Introduction). Whether the ring opening of *trans*-LimO is selective or leads to both



Scheme 3. Selectivities for the LimO ring opening.

diol products cannot be established from these data (see Scheme 3), but will be detailed later.

Concerning the experiment with $[MoO_2(SATP)]_2$ (Fig. 2, right), only traces of the intermediate epoxide compounds were detected, even at short reaction times, whereas the two isomeric diols were rapidly produced in large amounts. A greater amount of *eq*-LimD is generated relative to run 2, although the *ax*-LimD isomer remains the prevalent product. These results suggest that not only the epoxidation step but also the ring opening step is metal catalyzed. These results are in line with a previous report, in which a $[MoO_2Cl_2L]$ complex (L = β-ketophosphonate derived from camphor) was shown to catalyze the stereospecific ring opening of *cis*-LimO to yield *ax*-LimD, whereas *trans*-LimO remained essentially unreacted [21]. The catalytic activity of $[MoO_2(SAP)]_2$ and $[MoO_2(SATP)]_2$ in the LimO ring opening has been further confirmed by separate investigations of the ring opening of *cis*- and *trans*-LimO by water (see further details in the next section).

The mass balance (*cis*-LimO + *trans*-LimO + *eq*-LimD + *ax*-LimD + residual Lim) is low in both experiments: 80% after 2 h

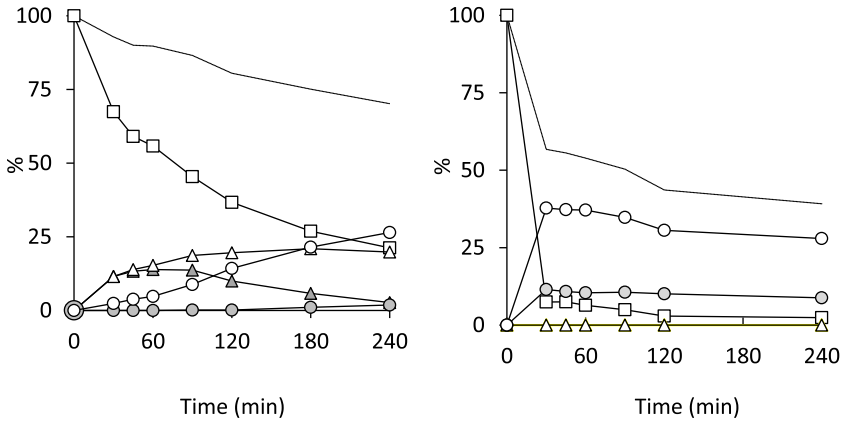


Fig. 2. Kinetic profile for the limonene oxidation catalyzed by $[MoO_2(SAP)]_2$ (left), $[MoO_2(SATP)]_2$ (right): [Mo]/limonene/TBHP = 0.5/100/200, T = 80 °C. Mass balance (. . .), limonene (□), *cis*-LimO (▲), *trans*-LimO (△), *eq*-LimD (●), *ax*-LimD (○).

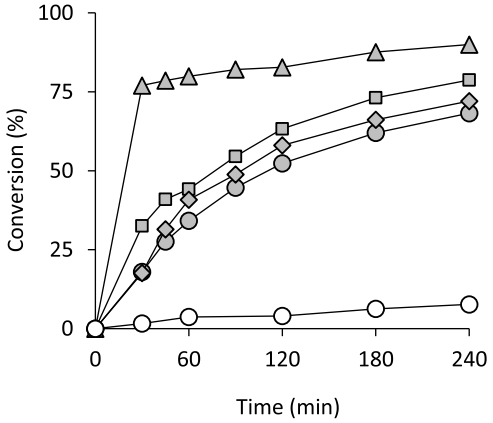


Fig. 3. Kinetic profile for limonene oxidation: without catalyst (–), with $[MoO_2(SAP)]_2$ (■), with $[MoO_2L^a]_2$(▲), with $[MoO_2L^b]_2$ (●), with $[MoO_2L^c]_2$(◆). [Mo]/limonene/TBHP = 0.5/100/200, reaction time = 4 h, T = 80 °C.

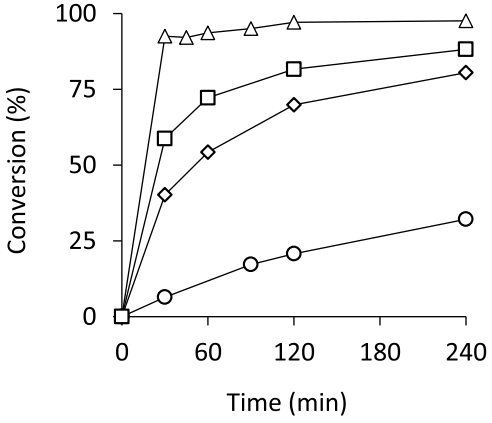


Fig. 5. Influence of temperature on the $[MoO_2(SATP)]_2$-catalyzed limonene oxidation: 30 °C (○), 50 °C (◊), 60 °C (□), 80 °C (△). Conditions: [Mo]/limonene/TBHP = 0.5/100/200.

and 70% after 4 h for run 2; 56% after 0.5 h for run 3. This loss of material can be attributed to the further oxidative transformations of the LimD isomers to non-volatile products. Traces of carvone and carveol, plus other unidentified products, were also visible in the gas-chromatogram for both runs and were not quantified but could be estimated as <5%, hence could not account for the lack of mass balance. The final reaction mixture consisted of a single phase in each case, presumably because the organic compounds and the water originating from the TBHP reagent solution, which generates two phases at the beginning of the reaction, are progressively compatibilized by the LimD and *t*BuOH products.

The kinetic profiles for the same oxidation processes in the presence of the precatalysts $[MoO_2L^{a–c}]_2$ (runs 4–6) are shown in Fig. 3 in comparison with those of runs 1 and 2. The conversion after 4 h was very good for each catalyst (see Table 1), in the order $[MoO_2L^a]_2$ (90%) > $[MoO_2(SAP)]_2$ (79%) ~ $[MoO_2L^c]_2$ (77%) > $[MoO_2L^b]_2$ (68%). The $[MoO_2L^a]_2$ complex (R_1 = OH) exhibited a much higher activity than the other pre-catalysts. The initial *cis*/*trans* ratio for the LimO intermediates for the experiments with the $[MoO_2L^b]_2$ and $[MoO_2L^c]_2$ complexes was similar (ca. 1:1, see Fig. 4) to that observed for the experiment with $[MoO_2(SAP)]_2$ (Fig. 2), whereas the most active $[MoO_2L^a]_2$ catalyst yields an initial *cis*/*trans* ratio of ca. 1:2 (Fig. 4). Once produced, the LimO isomers

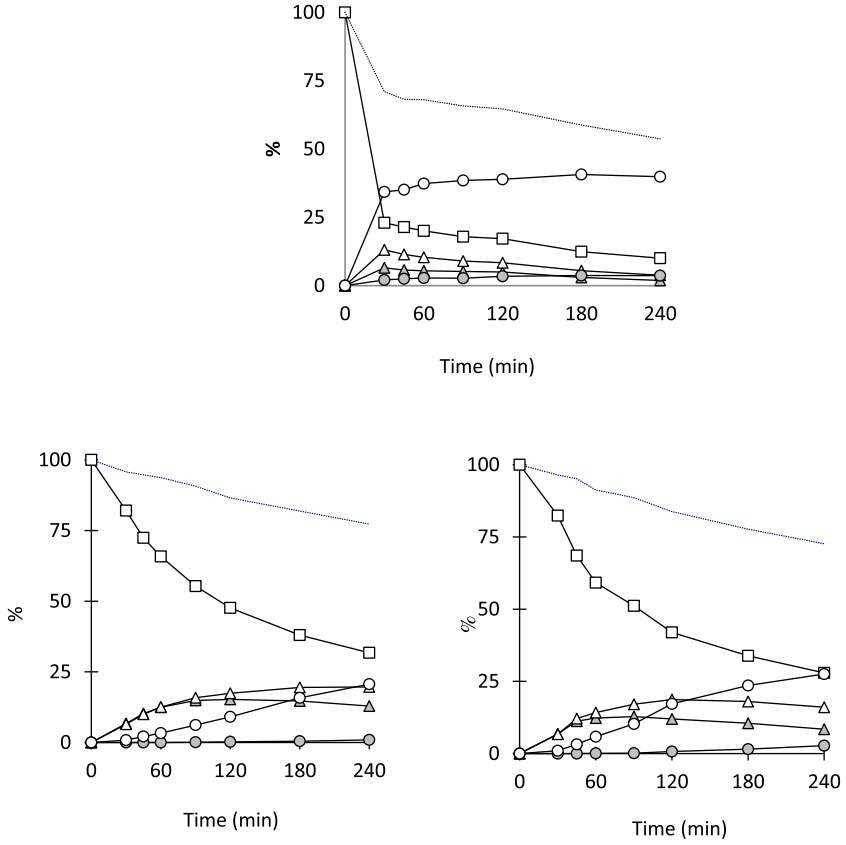


Fig. 4. Kinetic profile for the limonene oxidation catalyzed by $[MoO_2L^a]_2$ (up), $[MoO_2L^b]_2$ (down left), $[MoO_2L^c]_2$ (down right),: [Mo]/limonene/TBHP = 0.5/100/200, T = 80 °C. Mass balance (. . .), limonene (□),-LimO *cis*-LimO (▲), *trans*-LimO (△), *eq*-LimD (●), *ax*-LimD (○).

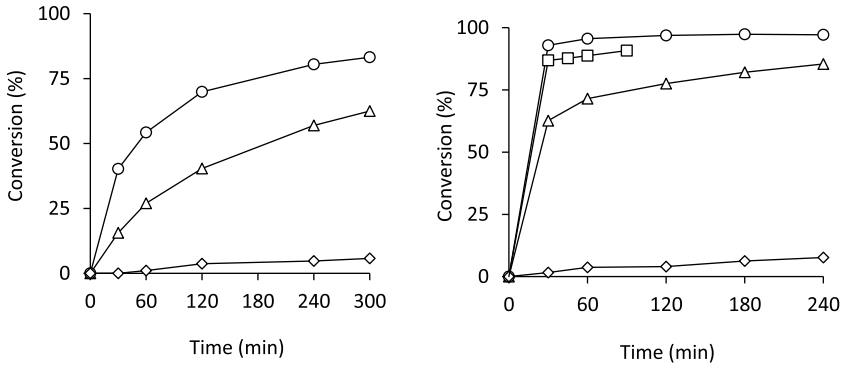


Fig. 6. Influence of the catalyst loading on the $[MoO_2(SATP)]_2$-catalyzed limonene oxidation at 50 °C (left) and 80 °C (right): [Mo]/limonene/TBHP = ×/100/200, x = 0 (◊), 0.1 (△), 0.25 (□), 0.5 (○).

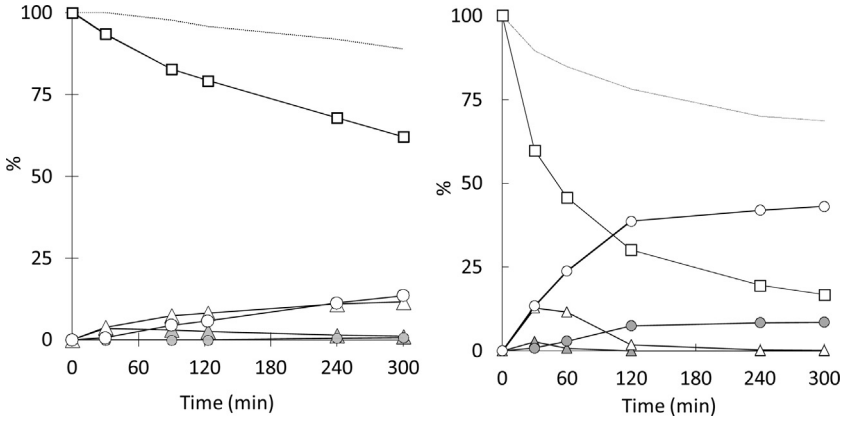


Fig. 7. Kinetic profile for the limonene oxidation catalyzed by $[MoO_2(SATP)]_2$ at 30 °C (left) and 50 °C (right): [Mo]/limonene/TBHP = 0.5/100/200. Mass balance (. . .), limonene (□), *cis*-LimO (▲), *trans*-LimO (△), *eq*-LimD (●), *ax*-LimD (○).

are consumed to yield the two LimD products, mainly the axial isomer. The ring opening data are also in line with the behavior reported above for the parent $[MoO_2(SAP)]_2$ pre-catalyst: rapid for *cis*-LimO with selective formation of *ax*-LimD and slower for *trans*-LimO (see further details later). In addition, the LimD selectivity correlates with the Lim conversion, with the relative amount of the minor *eq*-LimD product increasing with the rate of Lim conversion. These data further confirm that the epoxide ring opening process is, like the epoxidation, metal-catalyzed and that the better epoxidation catalyst is also a better ring opening catalyst. The same trends for the epoxide/diol selectivity vs. the rate of conversion, although quantitatively less pronounced, have also been previously observed for the oxidation of cyclohexene catalyzed by the same ONO complexes but no conclusion concerning the epoxide ring opening catalysis was made . The Green metrics for these catalyzed reactions have been analyzed in terms of the influence of catalyst and temperature on the LimO and LimD production (See SI).

In order to better understand the catalytic epoxidation and epoxide ring opening for this substrate, additional experiments were carried out for the more active $[MoO_2(SATP)]_2$ systems at variable temperature and catalyst loading (Table 2 and Figs. 5–7). A temperature increase without catalyst leads to greater Lim transformation although the conversion and selectivity remained poor (runs 9 and 12). With 0.5% molar ratio $[MoO_2(SATP)]$ and 2 eq TBHP per substrate in the 30–80 °C range, the Lim conversion after 4 h increased dramatically, from 36% at 30 °C after 5 h to 93% at 80 °C after 30 min (runs 8, 11 and 15; Fig. 5). At both 50 °C (runs 6–11) and 80 °C (runs 12–15) the conversion becomes faster as expected upon increasing the catalyst loading, see also Fig. 6.

The results of the individual intermediates and products monitoring at 30 and 50 °C are shown in Fig. 7. At the end of the catalytic runs, the LimO intermediates (mainly the *trans* isomer) could be detected only at temperatures up to 50° when in the presence of catalyst. Interestingly, while the *cis*-LimO was the main epoxide product in the absence of catalyst at 50 °C, the selectivity was inverted in the presence of catalyst in favor of *trans*-LimO, probably because of the faster catalyzed ring opening of *cis*-LimO opening (mainly yielding *ax*-LimD as already discussed above). The highest *eq*-LimD yield was observed in the presence of catalyst at 80 °C (run 15).

The effect of the TBHP/substrate ratio has also been investigated, both at 50 °C and at 80 °C, with a 0.5% loading of the $[MoO_2(SATP)]$ catalyst (Table 3). Lowering the TBHP amount leads, as expected, to a slower conversion (*cf.* run 16 with run 11 of Table 2 and run 17 with run 15 of Table 2). It is of interest to note that this also results in a slight decrease of the *eq*-LimD selectivity and an increase of the *ax*-LimD selectivity.

Catalyzed limonene oxide ring opening

As shown in the previous section, the Lim epoxidation produced LimOs and/or LimDs in a catalyst- and temperature-dependent process and there is clear evidence that the more active epoxidation catalysts (e.g. the SATP complex) also have higher activity in the ring opening process. It was therefore of interest to carry out more detailed investigations on the catalyzed epoxide ring opening process. For this purpose, both a commercial LimO isomer mixture (*cis*/*trans* = 47:53) and the pure individual isomers have been investigated (Table 4).

Table 2
Influence of temperature and catalyst loading for limonene epoxidation catalyzed by $[MoO_2(SATP)]_2$.[a]

Run	T (°C)	time (h)	X (%)	Lim Conv. (%)	Selectivity (%)[b]				TON	TOF (h^{-1})[c]
					LimO		LimD			
					Cis	trans	eq	ax		
7	30	5	0	3.2	9.4	9.4	1.6	5.6	–	–
8			0.5	36	3.7	32.2	1.7	35.3	70	26
9	50	5	0	5.3	10.4	0.6	0.6	5.8		
10			0.1	62.5	0.3	20.3	4.6	42.2	627	312
11			0.5	83	0.1	10.4	5.8	50	166	161
12	80	4	0	7.7	5.2	14.3	0.4	6.5		
13		2	0.1	85	0	0	7.9	72.9	850	1042
14		0.5	0.25	87	0	0	11.4	46.3	348	1743
15		0.5	0.5	93	0	0	12.4	40.6	185	371

[a] [Mo]/limonene/TBHP = ×/100/200.[b]
[b] Select = $n_{product}$ formed/n_{Lim} transformed obtained from GC analysis of the organic phase.
[c] TOF is calculated using the time interval with maximum slope in the conversion plot.

Table 3
Influence of the TBHP amount on the $[MoO_2(SATP)]_2$-catalyzed limonene epoxidation.[a]

Run	T (°C)	Time (h)	y	Conversion (%)	Selectivity (%)[b]				TON	TOF[c] (h^{-1})
					LimO		LimD			
					cis	*trans*	*eq*	*ax*		
16	50	5	110	61	0	4.9	9.5	58.5	123	109
17	80	0.5	150	89	0	0	12.2	47.4	178	357

[a] Conditions: [Mo]/limonene/TBHP = 0.5/100/y. Reaction time = 4 h. T = 50 °C.
[b] Select = $n_{product}$ formed/n_{Lim} transformed obtained from GC analysis of the organic phase.
[c] TOF is calculated using the time interval with maximum slope in the conversion plot.

Table 4
Ring opening of limonene oxides catalyzed by molybdenum complexes.[a]

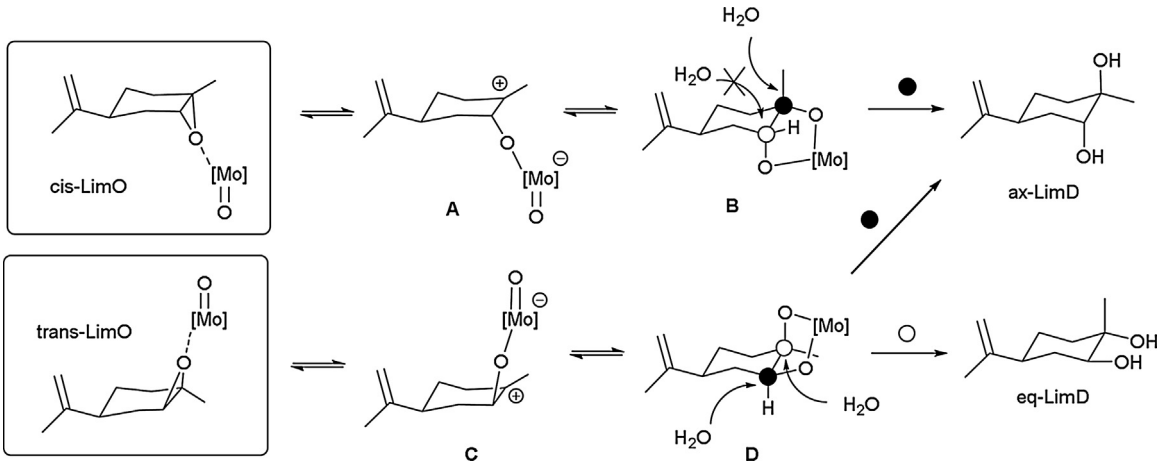
Run	substrate	Time (h)	catalyst	Conv (%)		LimD selectivity[b] (%)		TON	TOF (h^{-1})[c]
				cis	*trans*	eq	ax		
18	LimO	4	No catalyst	60.7	12.0	11.7	58.7	–	–
19	mixture[d]	4	$[MoO_2(SAP)]_2$	93.3	26.2	2.6	58.5	119	45
20		0.5	$[MoO_2(SATP)]_2$	100	100	12.1	45.0	200	400
21	*cis*-LimO	4	No catalyst	13.5		0	6.4	–	–
22		4	$[MoO_2(SAP)]_2$	26.9		0	28.4	52	27
23		0.5	$[MoO_2(SATP)]_2$	100		0	25.3	200	400
24	*trans*-LimO	1.5	$[MoO_2(SATP)]_2$		100	15.8	20.8	200	130

[a] [Mo]/limonene/TBHP = 0.5/100/200; T = 80 °C.
[b] Select = $n_{product}$ formed/$n_{LimO(cis+trans)}$ transformed obtained from GC analysis of the organic phase.
[c] TOF is calculated using the time interval with maximum slope in the conversion plot.
[d] Commercially available sample (*cis*/*trans* = 47/53).

The epoxidation of the *trans*/*cis* LimO mixture confirms that *cis*-LimO is opened faster than *trans*-LimO, whether in the presence or absence of catalyst. The rate of the transformation increases in the order: no catalyst (run 18) < $[MoO_2(SAP)]_2$ (run 19) < $[MoO_2(SATP)]_2$ (run 20). Both LimO isomers are opened faster by the more active $[MoO_2(SATP)]_2$ catalyst (*cf.* runs 19 and 20). The greater catalytic activity of the ONS ligand in ring opening is confirmed by the study of the isomerically pure *cis*-LimO (*cf.* run 22 and 23), which results in the stereospecific production of *ax*-LimD. Only the most active $[MoO_2(SATP)]_2$ catalyst was tested in the opening of pure *trans*-LimO (run 24): in spite of the more sluggish ring opening of this isomer, quantitative conversion could be achieved after 1.5 h. This run confirms that the *eq*-LimD isomer results from the opening of *trans*-LimO, but the product ratio is still in favor of the ax-LimD isomer. The mass balance suggests that either other reactions also occur, or that the LimD products are partially transferred in aqueous phase.

The separate investigations of pure *cis*-LimO and *trans*-LimO provide additional useful information on the stereochemistry of the ring opening process. None of the *eq*-LimD was generated by the ring opening of *cis*-LimO, either with or without catalyst (runs 21–23). Thus, both non-catalyzed and catalyzed *cis*-LimO ring openings lead stereospecifically to the *ax*-LimD isomer, in agreement with previous reports.[18,21,24] However, the ring opening of pure *trans*-LimO (run 24) provides a mixture of *ax*-LimD and *eq*-LimD in a ca. 4:3 ratio. To the best of our knowledge, this is the first report of the metal-catalyzed opening of *trans*-LimO. Interestingly, the stereoselectivity of this Mo-catalyzed ring opening process is quite similar to that reported for the opening catalyzed by the hydrolytic enzyme *Rhodotorula glutinis* (65:35) [24].

In terms of mechanistic interpretation, the generation of the *eq*-LimD product cannot result by an effect of the Mo complex identical to that proposed for Hg^{2+} in the selective generation of this diol from *trans*-LimO, for two reasons: *i*) the Hg^{2+} reagent accelerates



Scheme 4. Proposed mechanism for the Mo-catalyzed ring opening of the LimO isomers.

the opening of *trans*-LimO relative to *cis*-LimO, whereas the Mo catalyst leads to faster opening of the *cis* isomer; *ii*) the Hg^{2+}-promoted opening of the *trans*-LimO is stereospecific, leading solely to *eq*-LimD, whereas the Mo catalyst generates a mixture of both LimD isomers. Indeed, the action of Hg^{2+} was rationalized though a conformational change induced by the interaction between the soft Hg^{2+} ion and the isopropenyl substituent, which is not possible for the Lewis-acidic Mo^{VI} center because this d^0 metal ion has no affinity toward C=C unsaturations. We can rather invoke a mechanistic scheme with formation of Mo^{VI}-glycolate intermediates (see Scheme 4), based on that proposed by Cole-Hamilton et al. and supported by NMR investigations of the catalyst-substrate interactions [21]. Activation of the epoxide by the Lewis acidity of the mononuclear 5-coordinate $[MoO_2L]$ complex would result in equilibria with a molybdate-substituted carbocation and a Mo-glycolate intermediate (**A** and **B** from the *cis* isomer; **C** and **D** for the *trans* one). These intermediates are then attacked by water at the more substituted C atom with inversion of configuration. The smaller catalytic activity of the previously used camphor-based $[MoO_2Cl_2L]$ catalyst [21] did not allow the stereoselectivity of the water addition to **D** to be established. Indeed, formation of intermediate **D** itself was not considered possible. We now find that the greater catalytic activity of $[MoO_2(SATP)]$ (and to a certain extent also the other catalysts containing the SAP, L^a, L^b and L^c ligands) allows sufficiently rapid access to this intermediate. While the reactivity of the tertiary C atom in intermediate **B** dominates and leads to the selective generation of the *trans*-diaxial *ax*-LimD product, the lower reactivity of the same ring C atom in intermediate **D** allows competitive attack at the secondary C atom with production of a mixture of the two LimD products.

Conclusions

Lim epoxidation is catalyzed very efficiently by $[MoO_2L]_2$ with salicylidene amino(thio)phenolate ligands, particularly $[MoO_2(SATP)]_2$. These complexes promote not only the Lim regioselective endocylic epoxidation to yield both *cis*- and *trans*-LimO isomers in a kinetically controlled 1:1 ratio, but also the subsequent epoxide ring opening in the presence of water to obtain a mixture of *ax*- and *eq*-LimD. The high activity of the $[MoO_2(SATP)]_2$ precatalyst promotes the efficient ring opening of the less reactive *trans*-LimO isomer, which is shown to proceed unselectively to a mixture of *ax*- and *eq*-LimD by analogy with a previous report of hydrolytic enzymatic ring opening, whereas the more reactive *cis*-LimO is stereospecifically opened to *ax*-LimD.

Experimental part

Materials and methods

All manipulations were carried out in air. Water was deionized twice before use. Organic solvents (ethanol, methanol, diethylether: synthesis grade, Aldrich) were employed as received without any purification. All molybdenum complexes were synthesized as previously described . Limonene (98% Aldrich), the LimO mixture (Aldrich cis/trans 47/53, 98%), ax-LimD (Aldrich, 98%)) and TBHP (70% in water, ACROS) were used as received. The pure *cis*-LimO, *trans*-LimO and eq-LimD were synthesized according to literature procedure [18,22,23]. The catalytic reactions were monitored by gas chromatography on an Agilent 6890A chromatograph equipped with an FID detector, a HP5-MS capillary column (0.30 m × 0.25 mm × 0.25 m) and an autosampler, or on a Fisons GC 8000 chromatograph equipped with an FID detector and with a SPB-5 capillary column (30 m × 0.32 mm × 0.25 m). Authentic samples of all reactants and products were used for calibration. The Lim conversion and the formation of LimOs and limDs were calculated from the calibration curves (r^2 = 0.999) and an internal standard.

Catalytic procedure

In a typical experiment, limonene (1 equiv) and catalyst (x equiv, see tables) were mixed together in air in a round bottom flask. Acetophenone was added as internal standard. The flask was then immersed in a thermostated bath set at the desired temperature (see Tables) and magnetically stirred. After thermal equilibration, aqueous THBP (70% in water, y equiv see tables) was added to the mixture, starting the reaction. Samples were periodically withdrawn and quenched by the addition of MnO_2, followed by the addition of diethylether and removal of the manganese oxide and residual water by filtration through silica before GC analysis.

Acknowledgements

We acknowledge the Centre National de la Recherche Scientifique (CNRS) and the Institut Universitaire de France (IUF) for financial support, the Université Paul Sabatier and its Institut Universitaire Technologique for the facilities and the Chinese Scholarship Council for the fellowship of W.W. No.201208370239.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.mcat.2017.09.033.

References

[1] (a) G.A. Cordell, T.L.G. Lemos, F.J.Q. Monte, M.C. de Mattos, J. Nat. Prod. 70 (2007) 478–492;
L. Filiciotto, A. M. Balu, J. C. Van der Waal, R. Luque, Catal Today (2017) proofs online http://dx.doi.org/10.1016/j.cattod.2017.03.008;
(b) A. Arbenz, L. Averous, Green Chem. 17 (2015) 2626–2646;
(c) I.K.M. Yu, D.C.W. Tsang, Bioresour. Technol. 238 (2017) 716–732;
(d) A.K. Kumar, S. Sharma, Bioresources and Bioprocessing 4 (2017) 7;
(e) G. Chatel, K. De Oliveira Vigier, F. Jérôme, ChemSusChem 7 (2014) 2774–2787;
(f) P. Spannring, P.C.A. Bruijnincx, B.M. Weckhuysen, R.J.M. Klein Gebbink, Catal. Sci. Technol. 4 (2014) 2182–2209;
(g) C.O. Tuck, E. Perez, I. Horvath, R. Sheldon, M. Poliakoff, Science 337 (2012) 695–699;
(h) J. Kudakasseril Kurian, G. Raveendran Nair, A. Hussain, G.S. Vijaya Raghavan, Renew. Sust. Energ. Rev. 25 (2013) 205–219;
(j) L. Wu, T. Moteki, A.A. Gokhale, D.W. Flaherty, F.D. Toste, Chemistry 1 (2016) 32–58;
(k) F.D. Pileidis, M.-M. Titirici, ChemSusChem 9 (2016) 562–582;
(l) V. Negro, G. Mancini, B. Ruggeri, D. Fino, Bioresour. Technol. 214 (2016) 806–815;
(m) E.V. Gusevskaya, ChemCatChem 6 (2014) 1506–1515;
(n) T.I.J. Dugmore, J.H. Clark, J. Bustamante, J.A. Houghton, A.S. Matharu, Top. Curr. Chem. 375 (2017) 46;
(o) M.P. Adhikari, R. Adhikari, R.G. Shrestha, R. Rajendran, L. Adhikari, P. Bairi, R.R. Pradhananga, L.K. Shrestha, K. Ariga, Bull. Chem. Soc. Jpn. 88 (2015) 1108–1115;
(p) V.S. Sikarwar, M. Zhao, P. Clough, J. Yao, X. Zhong, M.Z. Memon, N. Shah, E.J. Anthony, P.S. Fennell, Energy Environ. Sci. 9 (2016) 2939–2977;
(q) A. Scoma, S. Rebecchi, L. Bertin, F. Fava, Crit. Rev. Biotechnol. 36 (2016) 175–189.

[2] (a) W. Schwab, C. Fuchs, F.-C. Huang, Eur. J. Lipid Sci. Technol. 115 (2013) 3–8;
(b) N. Ravasio, F. Zaccheria, M. Guidotti, R. Psaro, Top. Catal. 27 (2004) 157–168;
(c) J.L.F. Monteiro, C.O. Veloso, Top. Catal. 27 (2004) 169–180.

[3] G.A. Burdock, Fenaroli's Handbook of Flavor Ingredients, 3rd ed., CRC Press, Boca Raton, 1995, p.107.

[4] (a) R.A. Sheldon, in: F.E. Harkes (Ed.), Catalysis of Organic Reaction, USA, 1998;
(b) R.A. Sheldon, in: G. Centi, F. Trifiro (Eds.), New Developments in Selective Oxidation, Elsevier, Amsterdam, 1990.

[5] R. Ciriminna, M. Lomeli-Rodriguez, P. Demma Cara, J.A. Lopez-Sanchez, M. Pagliaro, Chem. Commun. 50 (2014) 15288–15296.

[6] (a) K.A.D. Swift, Top. Catal. 27 (2004) 143–155.

[7] (a) J.M. Derfer, M.M. Derfer, Encyclopedia of Chemical Technology Kirk-Othmer, vol. 22, third ed., Wiley, New York, 1978, p. 709;
(b) E. Herrero, S. Casuscelli, J. Fernandez, C. Poncio, M. Rueda, O. Oyola, Molecules 5 (2000) 336–337;
(c) K. Bauer, D. Garbe, H. Surburg, Common Fragrance and Flavor Materials, Preparation, Properties and Uses, Wiley VCH, New York, 1997.

[8] (a) D. Comins, L. Guerra-Weltzien, J.M. Salvador, Synlett (1994) 972–974;
(b) W. Chrisman, J.N. Camara, K. Marcellini, B. Singaram, C.T. Goralski, D.L. Hasha, P.R. Rudolf, L.W. Nicholson, K.K. Borodychuk, Tetrahedron Lett. 42 (2001) 5805–5807;
(c) H. Lebel, E.N. Jacobsen, J. Org. Chem. 62 (1998) 9624–9625.

[9] (a) S.K. Kulkarni, A. Dhir, Prog. Neuropsychopharmacol. Biol. Psychiatry 31 (2007) 1248–1254;
(b) T. Umezu, Pharmacol. Biochem. Behav. 64 (1999) 35–40;
(c) A.A.C. de Almeida, J. Pereira Costa, R.B.F. de Carvalho, D. Pergentino de Sousa, R. Mendes de Freitas, Brain Res. 1448 (2012) 56–62.

[10] (a) C.M. Byrne, S.D. Allen, E.B. Lobkovsky, G.W. Coates, J. Am. Chem, Soc 126 (2004) 11404–11405;
(b) A. Corma, S. Iborra, A. Velty, Chem. Rev. 107 (2007) 2411–2502;
(c) O. Hauenstein, M. Reiter, S. Agarwal, B. Rieger, A. Greiner, Green Chem. 18 (2016) 760–770;
(d) E. Hosseini Nejad, A. Paoniasari, C.G.W. van Melis, C.E. Koning, R. Duchateau, Macromolecules 46 (2013) 631–637.

[11] Jd. Moraes, A.A. Almeida, M.R. Brito, T.H. Marques, T.C. Lima, D.P. Sousa, E. Nakano, R.Z. Mendonça, R.M. Freitas, Planta Med. 79 (2013) 253–258.

[12] (a) C.K. Modi, J.A. Chudasam, H.D. Nakum, D.K. Parmar, A.L. Patel, J. Mol. Catal. A Chem. 395 (2014) 151–161;
(b) A.M.A. Santa, J.C.G. Vergara, S. Palacio, I. Catal. Today 133–135 (2008) 80–86.

[13] M. Blair, K.L. Tuck, Tetrahedron: Asymmetry 20 (2009) 2149–2153.

[14] (a) W.F. Newhall, J. Org. Chem. 24 (1959) 1673–1676;
(b) W.F. Newhall, J. Org. Chem. 29 (1964) 185–187;
(c) W. Knoll, C. Tamm, Helv. Chim. Acta 58 (1975) 1162–1171.

[15] (a) F.A. Davis, J.C. Towson, D.B. Vashi, R. Thimmareddy, J.P. McCauley, M.E. Harakal, D.J. Gosciniak, J. Org. Chem. 55 (1990) 1254–1261;
(b) F.A. Davis, R. Thimmareddy, J.P. McCauley, R.M. Przeslawski, M.E. Harakal, P.J. Carroll, J. Org. Chem. 56 (1991) 809–815.

[16] (a) R. Clarke, M. Gahagan, R.K. Mackie, D.F. Foster, D.J. Cole-Hamilton, M. Nicol, A.W. Montford, J. Chem. Soc., Dalton Trans. (1995) 1221–1226;
(b) J.A. Brito, S. Ladeira, E. Teuma, B. Royo, M. Gomez, Appl. Catal. A 398 (2011) 88–95.

[17] D. Clemente-Tejeda, A. López-Moreno, F.A. Bermejo, Tetrahedron 69 (2013) 2977–2986.

[18] M. Blair, P.C. Andrews, B.H. Fraser, C.M. Forsyth, P.C. Junk, M. Massi, K.L. Tuck, Synthesis (2007) 1523–1527 (and references cited therein).

[19] (a) A. Fürst, P.A. Plattner, Helv. Chim. Acta 32 (1949) 275–283;
(b) E.E. Royals, J.C. Leffingwell, J. Org. Chem. 31 (1966) 1937–1944.

[20] P.C. Andrews, M. Blair, B.H. Fraser, P.C. Junk, M. Massi, K.L. Tuck, Tetrahedron: Asymmetry 17 (2006) 2833–2838.

[21] L. Salles, A.F. Nixon, N.C. Russell, R. Clarke, P. Pogorzelec, D.J. Cole-Hamilton, Tetrahedron: Asymmetry 10 (1999) 1471–1476.

[22] D. Steiner, L. Ivison, C.T. Goralski, R.B. Appell, J.R. Gojkovic, B. Singaram, Tetrahedron: Asymmetry 13 (2002) 2359–2363.

[23] M.J. van der Werf, H. Jongejan, M.C.R. Franssen, Tetrahedron Lett. 42 (2001) 5521–5524.

[24] C. Weijers, Tetrahedron: Asymmetry 8 (1997) 639–647.

[25] S. Aguila, R. Vasquez-Duhalt, R. Tinoco, M. Rivera, G. Pecchi, J.B. Alderete, Green Chem. 10 (2008) 647–653.

[26] (a) A.A. Valente, I.S. Goncalves, A.D. Lopes, J.-E. Rodriguez-Borges, M. Pillinger, C.C. Romao, J. Rocha, X. Garcia-Mera, New J. Chem. 25 (2001) 959–963;
(b) P. Oliveira, M.L. Rojas-Cervantes, A.M. Ramos, I.M. Fonseca, A.M. Botelho do Rego, J. Vital, Catal. Today 118 (2006) 307–314;
(c) N. Mizuno, S. Hikichi, K. Yamaguchi, S. Uchida, Y. Nakagawa, K. Uehara, K. Kamata, Catal. Today 117 (2006) 32–36;
(d) C.C.L. Pereira, S.S. Balula, F.A. Almeida Paz, A.A. Valente, M. Pillinger, J. Klinowski, I.S. Goncalves, Inorg. Chem. 46 (2007) 8508–8510;
(e) T.R. Amarante, P. Neves, C. Tomeí, M. Abrantes, A.A. Valente, F.A. Almeida Paz, M. Pillinger, I.S. Gonçalves, Inorg. Chem. 51 (2012) 3666–3676;
(f) T.R. Amarante, P. Neves, A.A. Valente, F.A. Almeida Paz, A.N. Fitch, M. Pillinger, I.S. Gonçalves, Inorg. Chem. 52 (2013) 4618–4628;
(g) Z. Strassberger, E.V. Ramos-Fernandez, A. Boonstra, R. Jorna, S. Tanase, G. Rothenberg, Dalton Trans. 42 (2013) 5546–5553;
(h) A. Gallo, C. Tiozzo, R. Psaro, F. Carniato, M. Guidotti, J. Catal. 298 (2013) 77–83;
(i) J. Mlodzik, A. Wroblewska, E. Makuch, R.J. Wrobel, B. Michalkiewicz, Catal. Today 268 (2016) 111–120;
(j) A. Wroblewska, E. Makuch, P. Miadlicki, Catal. Today 268 (2016) 121–129.

[27] R.A. Sheldon, Green Chem. 7 (2005) 267–278.

[28] (a) J. Morlot, N. Uyttebroeck, D. Agustin, R. Poli, ChemCatChem 5 (2013) 601–611;
(b) W. Wang, T. Vanderbeeken, D. Agustin, R. Poli, Catal. Commun. 63 (2015) 26–30;
(c) W. Wang, J.-C. Daran, R. Poli, D. Agustin, J. Mol. Catal. A 416 (2016) 117–126;
(d) J. Pisk, D. Agustin, J.C. Daran, V. Vrdoljak, R. Poli, Adv. Synth. Catal. 353 (2011) 2910–2914;
(e) J. Pisk, B. Prugovečki, D. Matković-Čalogović, R. Poli, D. Agustin, V. Vrdoljak, Polyhedron 33 (2012) 441–449;
(f) J. Pisk, B. Prugovečki, D. Matković-Čalogović, T. Jednačak, P. Novak, D. Agustin, V. Vrdoljak, RSC Adv. 4 (2014) 39000–39010;
(g) V. Vrdoljak, J. Pisk, D. Agustin, P. Novak, J. Parlov Vuković, D. Matković-Čalogović, New J. Chem. 38 (2014) 6176–6185.

[29] (a) C. Cordelle, D. Agustin, J.C. Daran, R. Poli, Inorg. Chim. Acta 364 (2010) 144–149;
(b) J. Pisk, J.-C. Daran, R. Poli, D. Agustin, J. Mol. Catal. A: Chem. 403 (2015) 52–63.

[30] B. Guérin, D. Mesquita Fernandes, J.-C. Daran, D. Agustin, R. Poli, New. J. Chem. 37 (2013) 3466–3475.

[31] (a) M. Loubidi, D. Agustin, A. Benharref, R. Poli, C. R. Chim. 17 (2014) 549–556;
(b) M. Cindric, G. Pavlovic, R. Katava, D. Agustin, New J. Chem. 41 (2017) 594–602.