

Oxidation Catalysis in Clean Technologies for Fine Chemicals

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Abstract

The role of heterogeneous catalysis for the production of fine chemicals is reviewed with particular interest for the oxidation in a wide range of aspects of this kind of processes: reaction of oxygen insertion, oxidative dehydrogenation and nitrogen insertion (with ammonia and oxygen).

In this review are examined the main processes industrially applied and the best research perspectives in the field of heterogeneous oxidation catalysis for the synthesis of fine chemicals. It is an important point of view in relation with the typical parameters of this field of industrial chemistry and in relation with the driving force of environmental friendly technologies (the line guides of green chemistry) to substitute traditional processes. It is examined either the possibility of the use of gas phases, that is better on an economical and plant point of view, with molecular oxygen, nitrous oxide (it is a very specific oxidant, and it is active in mild conditions) and with the technique of short bed reactor to minimise the effects of the consecutive oxidation reaction particularly on aromatic side chains. Or the use of liquid phases, very useful to work in mild conditions with not stable reagents, with hydrogen peroxide and other alternative oxidants such as regenerable organic hydroperoxides. In the liquid phase reactions it is posed a particular interest in the oxidations carried out with the use of metal doped zeolites, with special attention to tiania-silica catalysts such as TS-1 with the new developments of hydrogen peroxide in situ generation; and heteropoly compounds.

Introduction

Nowadays the increasing social pressure on industry to substitute traditional processes by environmentally friendly technologies represents the most important driving force for the development of catalysts for fine chemicals.

Traditionally, fine and speciality chemicals have been produced predominantly using non catalytic organic synthesis; these processes can be characterised as follows:

- Relatively small scale production (5000 t per year)
- Stringent product specifications with high purity requirements
- Multifunctional molecules and materials
- Co-production of large amounts of unwanted products (stoichiometric oxidations with inorganic reagents)
- Utilising of toxic or corrosive reagents
- Multistep processes resulting in lower overall yield of the desired product

In recent years, in this field, there has been a grow-

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ing need for reduction of production price, increasing of product quality and performances, and substantial decreasing of waste. Moreover, the new industrial strategies demand to avoid the use of toxic raw materials and dangerous procedures and to decrease the consume of water and energy.

Since the manufacture of fine chemicals generally utilises thermally instable reagents (heterogeneous catalysts are generally active at high temperature), involves multi-step reactions (with a consequent need of multi-fuctional catalysts) and emploies big molecules that can not enter the catalyst porosity, there are a few problems to applying heterogeneous catalysis to this production.

Despite of this, the development of catalytic process on this field has received increasing attention. Different type of approaches have been used to achieve improved production process:

1. The development of catalyst active at lower temperature
2. The use of supports with large pores
3. The spreading of the active phase on the external surface of a support

4. The developments of new multifunctional catalysts
5. The use of low contact time at high temperature to avoid the decomposition of the product and of the reagents (short bed process)
6. The use of solvents to desorb the products or to orientate the intermediate formation
7. The encapsulation of supporting of homogeneous catalysts

A large number of oxidation reactions made possible by heterogeneous catalysts in principle can be applied to the synthesis of fine chemicals:

1. Reactions of oxygen insertion
 - ♦ Hydroxylation of aromatics
 - ♦ Olefins to epoxides
 - ♦ Alkylaromatics to aldehydes or ketones
 - ♦ Alkanes to alcohols
 - ♦ Amines oxidation
2. Oxidative dehydrogenation
 - ♦ Alcohol to aldehydes
 - ♦ Formation of double bonds
3. Nitrogen insertion with NH_3 and O_2
 - ♦ Ketones to oximes
 - ♦ Hydrocarbons to nitriles

However, quite many problems must be addressed in order to render a catalytic process technically viable, the following are the most important ones:

- Thermal stability of reagents and products (cleavage of C–C bonds)
- Presence of reactions of free radical oxidation
- Dissolution of metals (transformation to homogeneous catalysis) - Leaching

The various type of catalyst and oxidant that can be utilised are outlined in Table 1.

While in bulk chemicals manufacture the choice of oxidant is largely restricted to molecular oxygen, the economics of fine chemicals production allow a

broader choice of oxidants. Hydrogen peroxide is the preferred one due to its simplicity of operation but many other organic and inorganic oxygen donors can be utilised (hydroperoxide, N_2O etc.)

The choice of process (liquid phase versus gas phase) is largely dependent on the boiling point and thermal stability of the molecule in question. Where gas phase oxidation with O_2 is feasible this will probably be economically more attractive than other options.

Gas phase oxidation

Gas phase oxidation reactions that have been reported are the following:

- Oxidation with oxygen at very low contact time
- Production of nitriles with NH_3 and O_2
- Oxidation with N_2O

Oxidation with oxygen at very low contact time

The BASF process for the production of citral is an example of the use of a gas phase catalytic oxidation for the production of a fine chemical [1]. The key step of the process involves the gas phase oxidation of isoprenol over a catalyst very similar to the one utilised for methanol oxidation to formaldehyde (based on Ag/SiO_2), see Fig. 1.

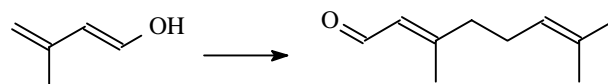


Fig.1. Oxidation of isoprenol.

The epoxidation of non-allylic olefin can be carried out using supported silver catalysts promoted by CsCl salts at low contact time [2].

The epoxidation of butadiene to form epoxybutene marks the first example of an olefin other than ethylene to be selectively epoxidized at steady state and commercially relevant conditions using gas phase oxygen. The epoxidation occurs for unpromoted catalysts but the strength of olefin epoxide adsorption leads to low activity and selectivity as well as catalyst deactivation. The addition of CsCl salts lowers the desorption energy of the olefin epoxide and, in the case of butadiene, increases activity and selectivity from 1% butene conversion and 50% selectivity to 15% conversion and 95% selectivity (reaction conditions: $T=250^\circ\text{C}$, contact time 0,1 s). Some kinetic studies showed the presence of two different catalytic sites;

Table 1

Catalysts and oxidants commonly used in the heterogeneous oxidations for the production of fine chemicals.

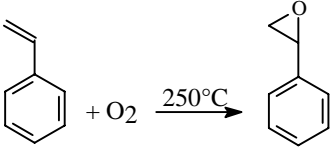
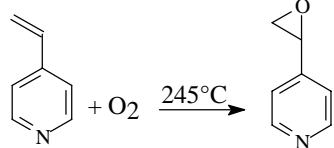
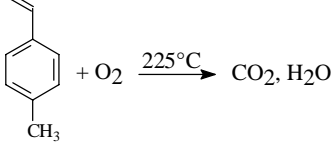
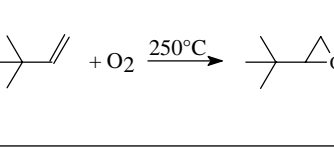
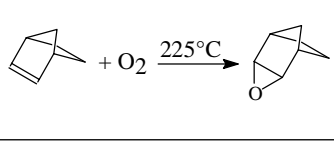
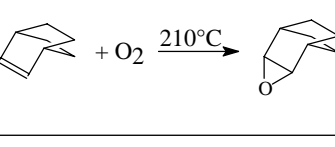
Catalyst	Oxidant
Transition metals dispersed in inert matrix (Es. TS-1)	H_2O_2 /hydroperoxides
Noble metals supported (Es. $\text{Pd}/\text{Al}_2\text{O}_3$; $\text{Pt}/\text{Bi}/\text{C}$; Pd/C)	O_2
Supported polyoxometallates (Es. $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{Al}_2\text{O}_3$)	H_2O_2
Mixed Oxides	$\text{O}_2/\text{N}_2\text{O}$
Encapsulated complex in inert matrix	$\text{O}_2/\text{H}_2\text{O}_2$ /hydroperoxides

one site, the unpromoted compounds, works as the butadiene adsorption site, while the second site, which is promoted, functions as the site for dissociative oxygen adsorption and epoxybutene formation.

Many others non allylic olefins can be epoxidized using these promoted catalysts. Table 2 shows the epoxidation of other olefins using CsCl-promoted Ag/Al₂O₃ catalysts.

Interestingly, the Table 2, indicates that the presence of the para-CH₃ group in 4-vinyltoluene, highly reactive towards C-H bond breaking, results in combustion of this olefin.

Table 2
Epoxidation of olefins using CsCl-promoted Ag/Al₂O₃ catalysts.

Epoxidation of olefins using CsCl-promoted, Ag/Al ₂ O ₃ catalysts		
Reaction	Molar Selectivity (%)	Conversion (%)
	95	19
	85	21
	0	100
	95	1.5
	92	43
	36	4

Moreover, the Table 2 shows that norbornene can be selectively epoxidized to norbornene oxide despite of the presence of one C-H bond allylic to the C=C bond. The addition of one additional -CH₂- group in the bridging position, decreasing the puckered geometry of the molecule, results in a dramatic reduction in selectivity and activity.

Production of nitriles with NH₃ and O₂

The ammoxidation of organic substrates is an interesting reaction for the production of fine chemicals. In the case of alkylaromatic ammoxidation, vanadium-based catalysts are usually employed, in particular, V₂O₅ supported on TiO₂ or Al₂O₃ [3].

Table 3 shows the influence of the presence of substituents on the aromatic ring on the selectivity to the nitrile. At low/medium conversion the lower selectivity in nitrile is obtained from p-methoxytoluene, thus with the strongest electron donor group. On the contrary, weak electron donor or acceptor groups (such as methyl or chloro) have higher selectivities. In fact, the presence of a donor group on the aromatic ring, increases the charge density and increases the possibility of the attach of nonselective electrophilic oxygen species leading to combustion.

Table 3
Oxidation of substituted benzene to nitriles.

Alkylaromatic	Selectivity to Mononitrile (%)	Selectivity to Dinitrile (%)	Selectivity to Imide (%)
p-xylene	62	19	
m-xylene	61	12	
o-xylene	15	20	25
p-chlorotoluene	84		
p-methoxytoluene	54		

In the case of the three xylene isomers, the selectivity to dinitrile is practically the same while the selectivity to mononitrile is much lower in the case of o-xylene due to the formation of a third product, the phthalimide that starts after the formation of relatively large amounts of mononitrile. The tuning of the surface oxidation properties of V₂O₅/TiO₂ catalysts can maximise the phthalimide formation [4].

Oxidation with N₂O

Nitrous oxide is a powerful precursor of active

oxygen species that has been known for several years, however, it has recently been the subject of renewed interest. The main advantage of this product lies in the possibility of developing very active oxidising species able to activate molecules under relatively mild conditions.

Liquid phase Oxidation

Heterogeneous catalysts for liquid phase oxidations can be divided into two main categories:

- Oxidation with molecular oxygen on noble metal based catalysts
- Oxidation with hydrogen peroxide on catalyst

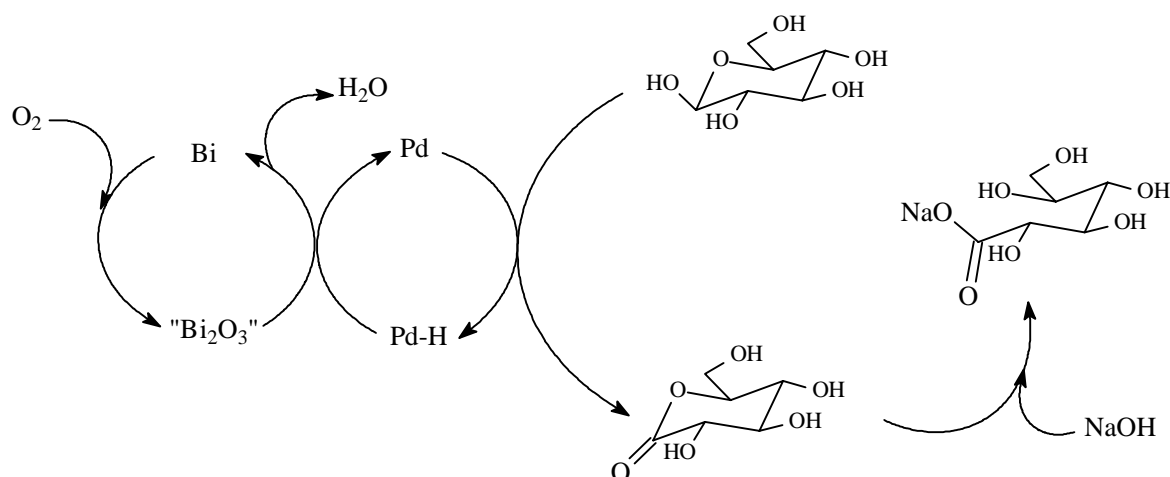


Fig. 2. Oxidation of D-glucose.

The primary oxidation products of Glucose are Gluconic and Glucaric Acid, and from Gluconic Acid, 2-Keto-Gluconic Acid and Glucuronic Acid. The oxidation toward Gluconic Acid can be made very selectively and palladium is preferred over platinum. More recently, bi-(*e.g.* Pd, Bi/C) and trimetallic (Pd, Pt, Bi/C) catalyst have been described that give very high selectivity to Gluconate. Platinum enhances the activity and bismuth the selectivity of the palladium catalyst.

A similar reaction (Fig. 3) is the oxidation of Glycerol to Tartronic Acid; in fact, Glycerol can be selectively converted to Glyceric Acid (Yield 70%) and to Tartronic Acid (Yield 85%) using Pd/C catalysts.

Oxygen, although required to oxidize the adsorbed hydrogen, also acts as a poison for the noble metal. The oxygen tolerance depends on the substrate, the

based on zeolites or supported heteropolyacids

Oxidation with molecular oxygen on noble metal based catalysts

Noble metal oxidation is well suited for the selective conversion of primary hydroxyl or aldehyde groups to carboxylic acid. The oxidation can be viewed as an oxidative dehydrogenation of the substrate by the noble metal, followed by oxidation of the adsorbed hydrogen atoms [5].

One reaction that has been largely studied is presented in Fig. 2, it is the catalytic oxidation of D-glucose with D-gluconate using catalysts based on Pd or Pt on carbon [6,7].

reaction conditions and type of noble metal. Deactivation can be reduced, but not eliminated and due to these problems, despite the enormous effort that has been focused on these metal catalysed oxidative dehydrogenations, very few of these reactions have been reduced to industrial practice.

Oxidation with hydrogen peroxide

Hydrogen peroxide is the most environmentally acceptable (ease of handling, water as by product), high productivity (high active oxygen content) monooxygenation agent. However, its commercial application has been limited by several factors, including;

1. The need for a suitable solvent for both H₂O₂ and the organic substrate
2. The formation of side products through hydrolysis

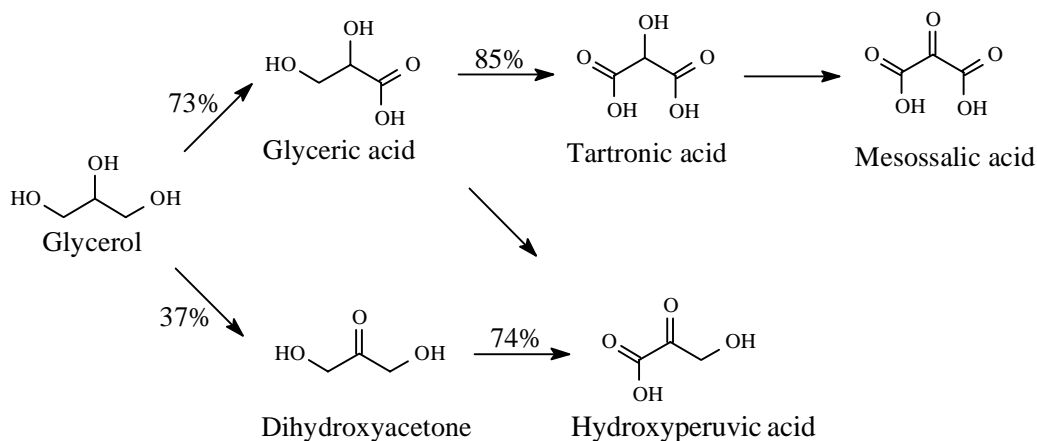


Fig 3. Oxidation of glycerol to Tartronic Acid.

- of the primary product
3. The inhibiting effect of water on reaction kinetics
 4. The hazards associated with handling concentrated or anhydrous hydrogen peroxide
 5. The ready decomposition of hydrogen peroxide
 6. The prize and availability

Despite these problems, two catalytic processes that use hydrogen peroxide as an oxidant have become well established. (i) two phase catalysis using heteropoly compounds, and (ii) liquid phase catalytic oxidation using titanium silicalite or other metal-containing microporous materials.

Liquid phase oxidation on catalyst based on supported heteropolyacids

In oxidation reactions carried out with hydrogen peroxide as the primary oxidant, the heteropoly-compounds studied most intensively are those based on tungsten, owing to its properties in the formation of metal-peroxo species. The tungsten in the primary structure has often been partially replaced with other transition metal ions in the research for catalysts that can oxygenate the organic substrate with specificity

and do not catalyse the parallel decomposition of hydrogen peroxide. A considerable amount of homogeneous chemistry has been carried out in the presence of hydrogen peroxide utilising these catalysts; however, immobilisation of metal complex onto either polymer or high surface area inorganic oxides offers several advantages and a few examples of supported catalytic systems have also been reported.

A system which has been extensively studied is the epoxidation of cyclic alkenes with H_2O_2 in the presence of supported phosphotungstic acid [8]. Table 4 shows some results obtained in *t*-butanol at 80°C over 5 hours of reaction run (support $\gamma-Al_2O_3$).

The fact that the cyclic alkenes have greater reactivity respect to linear alkenes indicates that the substrate had no difficulty in reaching the active site on the catalytic surface; this behaviour is complementary to titanium silicalite catalyst which is more effective towards the epoxidation of linear alkenes.

Immobilised polyoxometallates were also tested in the oxidation of Penicilin-G potassium salt to the sulphoxide and in the oxidation of benzenethiol to the sulphonic acid, see Fig. 4.

Table 5 shows the results obtained at room tem-

Table 4
Oxidation of cyclic olefins.

Substrate	Product	Conversion %	Selectivity %
Cyclooctene	Cyclooctene oxide	98	98
Cyclohexene	Cyclohexene oxide	29	63
Cycloheptene	Cycloheptene oxide	54	90
Cyclopentene	Cyclopentene oxide	30	87
1-Octene	1-Octene oxide	5	100

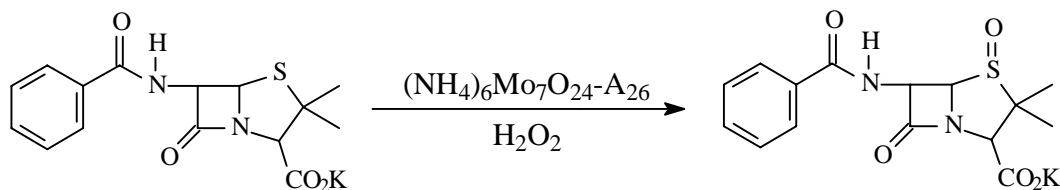


Fig. 4. Liquid phase oxidation of thio group.

perature or sub-ambient conditions in water or water/ alcohol mixtures for the oxidation of Penicillin-G.

Table 5

Activity of heteropoly compounds in the oxidation of Penicillin G.

Catalysts	Solvent	Temperature (°C)	Conversion (%)	Selectivity (%)
None	H ₂ O	20	12	80
H ₄ PMo ₁₁ O ₄₀ -Al ₂ O ₃	H ₂ O	20	69	49.3
H ₃ PW ₁₂ O ₄₀ -Al ₂ O ₃	H ₂ O	20	96	75.3
H ₄ PMo ₁₁ O ₄₀ -Al ₂ O ₃	PrOH/H ₂ O	-10	31	70.3
H ₃ PW ₁₂ O ₄₀ -Al ₂ O ₃	PrOH/H ₂ O	-10	74.4	65
(NH ₄) ₆ Mo ₇ O ₂₄ -A ₂₆ beads	H ₂ O	20	96	78
TS-1 - ZSM-5	H ₂ O	20	10	50
(NH ₄) ₆ Mo ₇ O ₂₄ unsupported	H ₂ O	20	100	69

The (NH₄)₆Mo₇O₂₄ - A₂₆ system was found to be the most efficacious catalyst screened while the titanium silicalite was found to be particularly poor for such transformation probably due to its relatively small pore size.

The transformation of benzenethiol (Fig. 5) using immobilised heteropolyacids is interesting because the homogeneous metal catalysed system generally gives poor yields of sulphonic acids due to preferential formation of disulphide compounds. Some results obtained in *t*-butanol at 80°C over 5 hours are presented in Table 6.

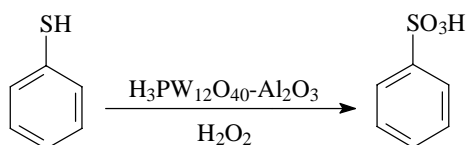


Fig. 5. Oxidation of benzenethiol to sulphonic acid.

Little work has been reported on the use of metal(IV) phosphates as oxidation catalysts; nevertheless they are potentially interesting catalytic species since certain forms possess regular layer struc-

Table 6

Oxidation of benzene thiol with heteropolyacids.

Catalysts	Conversion (%)	Yield (%)
None	100	42
H ₃ PW ₁₂ O ₄₀ -Al ₂ O ₃	100	96
H ₄ SiW ₁₂ O ₄₀ -Al ₂ O ₃	100	69

Reaction run at 80°C in *t*-butanol over 5 hours.

tures with strong acidic properties. The Baeyer-Villiger reaction, in Fig. 6, is of considerable synthetic use for the shortening of carbon chains, hydroxylating aromatic rings, converting carbocycles to heterocycles and opening up cyclic arrays to prepare functionalized chains or rings.

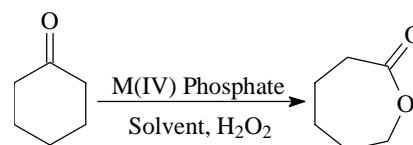


Fig. 6. Baeyer Villiger reaction with heterogeneous catalyst.

Some results obtained in this reaction utilising metal(IV) phosphates indicates that these products appear to be excellent catalyst for the preparation of esters under relatively mild conditions [8].

Liquid phase oxidation on catalyst based on zeolites

The most important example of this kind of catalysis is the TS-1 [9]. This is a catalyst employed in many processes, some examples are reported in Fig. 7, for its very interesting qualities in the liquid phase oxidations with hydrogen peroxide or organic hydroperoxides (particularly t-BuOOH, ter-butyl hydroperoxide). This catalyst was formerly made for the cyclohexanone ammoximation to cyclohexanone oxime, with ammonia and hydrogen peroxide by EniChem researchers.

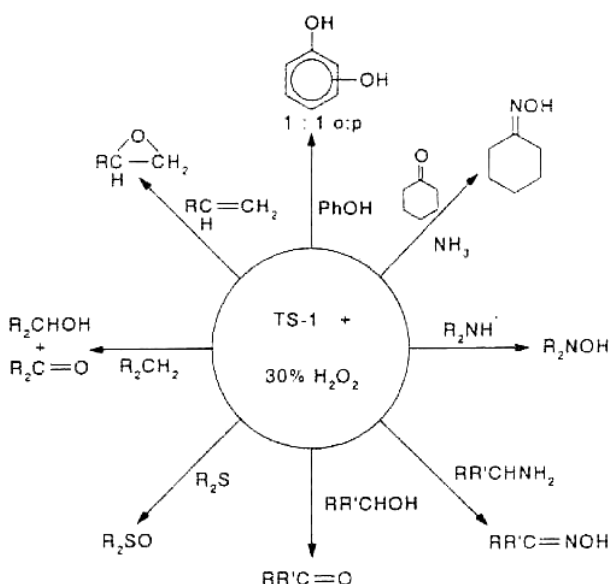


Fig. 7. TS-1 catalyzed reactions.

TS-1 is a zeolite with MFI structure like ZSM-5, there is not aluminium inside and a little amount of silicon is statistically substituted with titanium during the synthesis, in this manner it is possible to obtain a great dispersed titanium, in fact it is possible to find on the surface of the catalyst only isolated titanium atoms, it is important because any cluster formation (anatase or rutile phases) brings to the decomposition of the peroxide. Instead the presence of isolated atoms of titanium allows the co-ordination of oxygen atoms in an activated form able to oxidize many substrates.

Many other structures than MFI zeolites were used

for the incorporation of titanium some examples are: zeolites beta and Y, ALPO zeolites and mesoporous structures like MCM-41 and MCM-48, particularly the last two examples were prepared to obtain catalysts able to oxidize bulky molecules that can not enter inside the MFI little pores.

The new perspective of this catalysis is the in-situ production of hydrogen peroxide with the introduction of noble metal atoms (platinum or palladium) in the structure, it can react with oxygen to produce the peroxide.

One of the main application of TS-1 catalyst is the phenol hydroxylation, to make diphenols, it is presented in Fig. 8, most of all catechol and hydroquinone, this process became very important in the industrial chemistry because it is very clean and there is a isomer selectivity toward catechol and hydroquinone with about no production of resorcinol (the meta isomer). Another key feature of this process is the possibility of control the catechol to hydroquinone ratio by changing the reaction conditions. For this kind of reactions were tested some different catalysts and the best was TS-1 (see Table 7) [10]

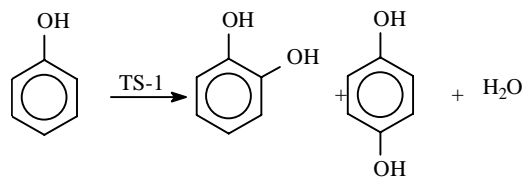


Fig. 8. Phenol hydroxylation over TS-1 catalyst.

Table 7

Diphenols production. Yield on a hydrogen peroxide basis.

Catalysts	Yield to diphenols (%)	Catechol/Hydroquinone
TS-1	80.8	1.2
ZSM-5	>1	-
Al-TS-1	81.0	1.18
Ga-TS-1	77.5	1.38
Fe-TS-1	<10	-

Reactor charge: 112.0 g of phenol; 20.8 g of acetone; 27.2 g of water; 5.6 g of catalyst; 16 g of hydrogen peroxide (60% in water) added over 45 minutes. Temperature 98°C; reaction time 1 h 45 min.

Another important use of TS-1 catalyst is the production of propylene oxide, by the hydrogen peroxide peroxidation in liquid phase of propylene [11] and the use of TS-1 in the production of much kind of epoxides

from double bond structures [12]. It is important to underline the greater activity of TS-1 on linear double bonded molecules than on cyclic ones, maybe for the little channel dimensions of MFI like catalysts.

The most important application of TS-1 catalyst, Fig. 9, at least from a scientific point of view, is the ammoximation of cyclohexanone to cyclohexanone oxime with ammonia and hydrogen peroxide, in liquid phase at low temperature [13]. This process has very interesting characteristics in fact it has very high conversion of cyclohexanone (close to 99%) and selectivity to cyclohexanone oxime (very close to 99.5), moreover this process has the important task of the avoiding of the production of inorganic salts as by products, typical of the classical process.

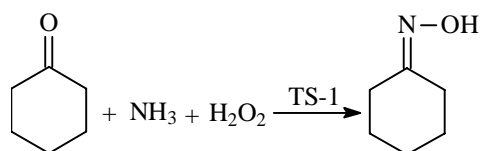


Fig. 9. Cyclohexanone ammoximation over TS-1 catalyst with hydrogen peroxide and ammonia.

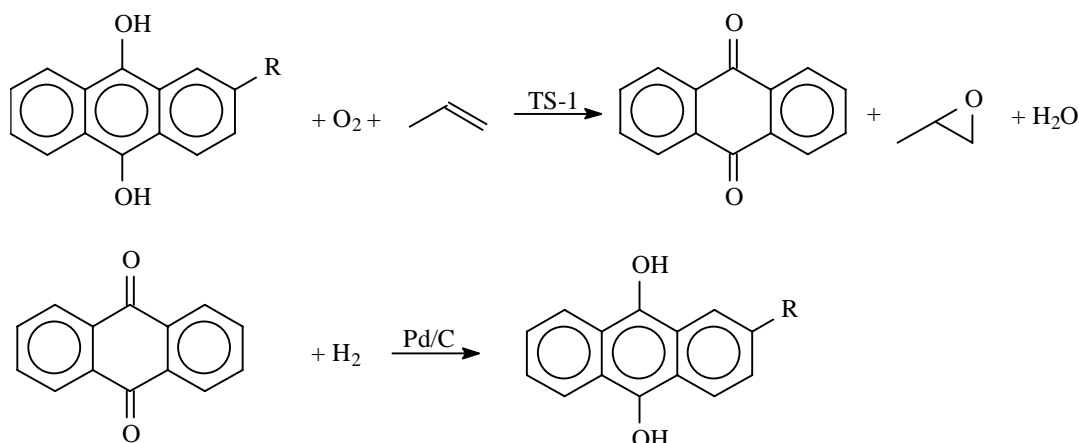


Fig. 10. Propylene epoxidation over TS-1 with the in-situ generation of hydrogen peroxide.

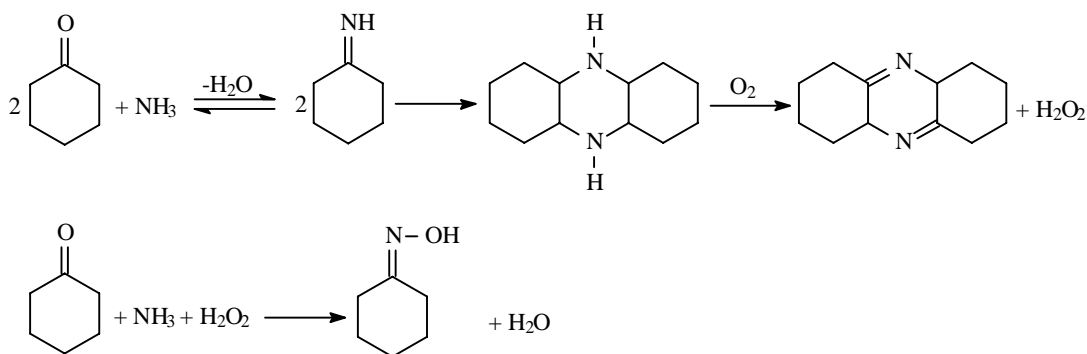


Fig. 11. Cyclohexanone ammoximation with in-situ production of hydrogen peroxide.

Hydrogen peroxide in-situ generation

The newest aim in the research about the titanium silicalite structures is the in situ production of hydrogen peroxide to avoid the costs and the risks connected to the use and the movement of this kind of reagent. This in situ production is made by the incorporation of noble metals, like platinum or palladium, in the TS-1 structure, if oxygen is refluxed inside the reactor there is the production of hydrogen peroxide, another way in Fig. 10 is the use of the couple of anthraquinone and hydroanthraquinone for example in the industrial process for the propylene epoxidation, where the regeneration of the oxygen source is made out of the epoxidation reactor with a palladium based catalyst.

A similar technique is used in the cyclohexanone ammoximation, in this case part of the cyclohexanone is used to produce hydrogen peroxide (Fig. 11).

Conclusions

At present there is an increasing attention to the

heterogeneous catalysis applied to fine chemical synthesis because it allows a very low environmental cost.

Solid catalysts make possible a wide variety of oxidation reactions at a low cost, these reactions can be the classical stoichiometric reactions carried out since many years in the industrial chemistry and new kinds of reactions that could open new synthetic perspectives in the future. It is very important the use of alternative oxidants with interesting characteristics to avoid the use of pollutant stoichiometric oxidisers such as mineral acids.

Finally it is very important to underline the fact that it seems to be possible the creation of new processes that are environmental friendly and with interesting characteristics in an industrial point of view.

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