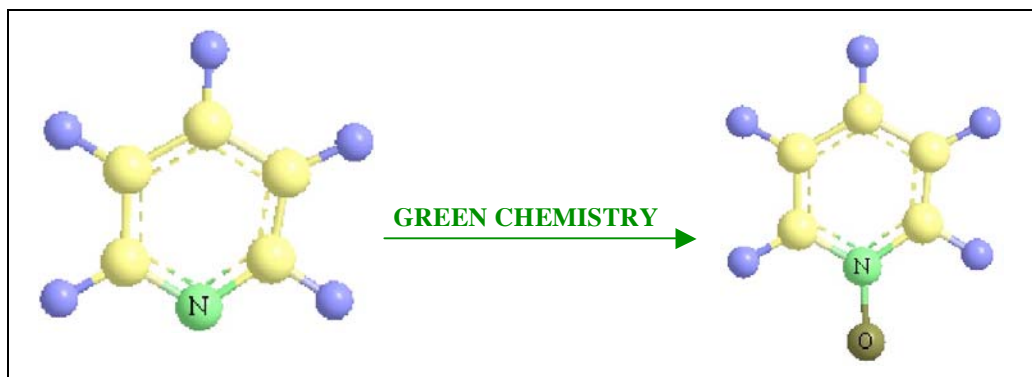


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Environmentally benign oxidation methods satisfy the postulates of green chemistry. Heterocyclic N-oxides have applications in synthetic organic chemistry, chemotherapy and agrochemicals. Synthesis of N-oxides using green oxidants will be attractive over the conventional methods. The presence of the N-oxide group in the azine ring makes it more subject to electrophilic and nucleophilic attack and substantially expands the synthetic approaches for the modification of nitrogen-containing heterocyclics. That is the reason for the increasing interest in the chemistry of heterocyclic N-oxides. Some reactions adopted for oxidation of N-heterocyclics have been discussed. Stereochemical and spectroscopic aspects have been mentioned. It will be advantageous if anchored catalysts are employed for industrial exploitation. Several physicochemical aspects of various methods have been discussed.

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INTRODUCTION

Oxidative reactions are among the most important transformations in synthetic chemistry [1] and offer important methodology for the introduction and modification of functional groups [2]. Environmentally benign and sustainable transformations in organic chemistry are now considered to be basic goals and requirements in the development of modern organic synthesis. To fulfill these goals, reactions should have high atom efficiency along with the use of solvents which are environmentally friendly and be free from dangerous waste. These requirements have led to the introduction of mainly homogeneous liquid phase catalysis into the arena of organic chemistry. During the last two decades there has been a spectacular development in the field and a large number of novel and useful oxidation reactions have been discovered leading to a range of selective and mild processes. These reactions are based on organo-catalysis, metal-catalysis or bio-catalysis. Conventional stoichiometric oxidations using nitric acid, chromic acid and their derivatives, alkyl hydroperoxides, permanganate, osmium tetroxide, and peracids often suffer from high costs, formation of toxic waste or low atom efficiency, providing a strong incentive to develop sustainable catalytic alternatives [3,4]. Homogeneous oxidation catalyst would find more widespread technological application if suitably anchored versions are

available. Immobilization of a homogeneous oxidation catalyst often greatly enhances its lifetime because of the suppression of bimolecular deactivation. Moreover, unprecedented activities and selectivities may be observed, surpassing the performances of the corresponding homogeneous catalyst. Hence we present a green view of the oxidation of N-heterocyclics.

OXYGEN SOURCES

Oxidants whose use is being contemplated include molecular oxygen, hydrogen peroxide, and nitrous oxide where: 1) there is no byproduct, 2) the byproduct is environmentally benign like water or nitrogen, 3) the byproduct can be easily recovered and recycled.

Oxidations with molecular oxygen [5], the primary oxidant in biological systems [6], are desirable and are already used in large scale industrial processes [7]. Hydrogen peroxide is also cheap and available from autoxidation in organic solvents such as alkylbenzenes of alkyl anthraquinol [8], H_2 /palladium being used to recycle the quinone formed. It is, however, subject to facile and potentially violent decomposition in the presence of many heavy metals (eq1) and can be highly reactive towards some organic substrates even in the absence of catalyst.



Another problem associated with the use of hydrogen peroxide is the concomitant decomposition of H_2O_2 , which makes the use of a large excess of H_2O_2 necessary to reach full conversion.

Alkyl hydroperoxides are also relatively cheap and are available in large quantities through the autoxidation of hydrocarbons containing a tertiary carbon centre. They are stable species and do not oxidize organic substrates in the absence of a catalyst. Hypochlorites are cheap and readily available as a byproduct of chlorine and caustic alkali production. They are powerful oxidizing agents even in the absence of catalysts. Iodosobenzene is expensive, even though the costly iodo fragment is recyclable. It is available from iodobenzene or by direct aromatic substitution using $(IO)_2 SO_4/H_2SO_4$. It can be an oxidant in its own right without activation by a metal catalyst. The active oxygen content of various oxidants is given below:

Oxidant	Active oxygen content	Waste product
Oxygen (O_2)	100	-
Oxygen(O_2)/reductor	50.0	Water
Hydrogen peroxide	47.0	Water
Nitrous oxide	36.0	Water
Ozone	33.0	Oxygen
Sodium hypochlorite	21.6	Sodium chloride
Peracetic acid	21.1	Acetic acid
tert-butylhydroperoxide	17.8	tert-butylhydroxide
Potassium peroxymonosulphate	10.5	Potassium hydrogen sulphate
{bis(trimethylsilyl)peroxide}	9.0	hexamethyldisiloxane
Iodosobenzene	7.3	Iodobenzene

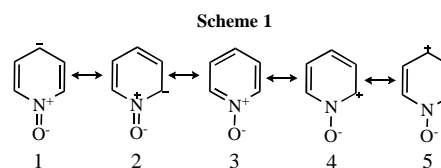
APPLICATIONS OF HETEROCYCLIC N -OXIDES

Compounds containing the N-oxide functionality, where the nitrogen is bound to an unsaturated carbon, have been known for more than a century [9]. Since then the chemistry of N-oxides has become extensive and numerous reactions and methods of preparation have been reported [10]. The chemistry and various applications of heterocyclic N-oxides have attracted many to find methods which follow the postulates of green chemistry. Biological importance of heterocyclic N-oxides is well documented [11]. The pyridine N-oxide derivatives represent a peculiar class of antiviral compound which are promising novel drugs in HIV chemotherapy. Some members exclusively act through inhibition of HIV-1 reverse transcriptase and thus characteristically behave as non-nucleoside reverse transcriptase inhibitors. These compounds have a possible role in the treatment of inflammatory disorders, such as rheumatoid arthritis [12]. A wide variety of pyridine N-oxide derivatives have been found to be inhibitory against feline coronavirus (FIPV strain) and human SARS-CoV (Frankfurt strain-1) in CRFK and simian kidney (Vero) cell cultures,

respectively [13]. Their use as protecting groups, auxiliary agents, oxidants, ligands in metal complexes [14-15], for rate enhancement of transition metal catalyzed processes [16], make them very important tool in organic synthesis. Pyridine N-oxides serve as useful oxygen atom transfer agent for alkyl halides [17] and they have been used routinely in the synthesis of high-valent transition- metal and actinide oxo complexes [18-21]. *N*-Methylmorpholine *N*-oxide is used as a reoxidant in the Upjohn procedure for the osmium-catalyzed dihydroxylation [22]. Pyridine *N*-oxides are important as synthetic intermediates in the manufacture of pharmaceuticals and agrochemicals. The antiulcer agent omeprazole is produced from 2,3,5-trimethylpyridine *N*-oxide. Niflumic acid and Pranoprofen are analgesics and anti-inflammatories, which are manufactured from nicotinic acid *N*-oxide, obtained either by N-oxidation of nicotinic acid or by hydrolysis of 3-pyridinecarbonitrile *N*-oxide. Zinc pyrithione, the zinc salt of 2-pyridinethiol *N*-oxide, is a fungicide derived from 2-chloropyridine *N*-oxide [23]. Only recently the donor behaviour of pyridine N-oxides has been successfully harnessed for nucleophilic catalysis [24]. C-H activation by pyridine *N*-oxide with uranium (IV) and thorium (IV) bis(alkyl) complexes have also been reported [25]. Immobilization on pyridine *N*-oxide resins is also reported recently [26]. Theoretical investigations of the N-oxide moiety [27] leading to calculation of linear and non linear optical properties [28], molecular and electric properties [29], have also been carried out. Interestingly, in the nanotechnology field, it has been shown that nanoshampo including carboxylic acid pyridine *N*-oxide is a very powerful hair growth stimulator with a high level of safety [30]. The N-oxides of isoquinolines have been proved to be excellent intermediates for the preparation of many compounds.

THE N-OXIDE MOIETY

Pyridine N-oxide is formally the addition product between pyridine and a sextet oxygen atom. Resonance structures of pyridine *N*-oxide are as follows:



The N-oxide group in pyridine *N*-oxide has both electron-withdrawing and electron donating effects. Consequently, pyridine N-oxide reacts with both electrophiles and nucleophiles, resulting in a more versatile reactivity of the pyridine ring compared to pyridine itself. Nitration of pyridine N-oxide is a typical electrophilic reaction of the N-oxide. Owing to the contribution of resonance structures 4

and **5**, the oxygen atom of the N-oxide group readily undergoes protonation, acylation, allylation, *etc.*

SPECTROSCOPIC PROPERTIES

The spectroscopic properties of pyridine N-oxides are well documented in the literature [31-34].

IR & Raman Spectroscopy. For an isolated pyridine ring hydrogen atom an =CH stretch, in plane bend and out of plane deformation vibrations are observed. The =C-H band is observed at 3052 cm⁻¹. The strong band at 1231 cm⁻¹ and the adjacent absorptions at 1238 cm⁻¹ and 1250 cm⁻¹ are assigned to the N-O stretch, because this vibration is accompanied by a large change in dipole moment and polarizability [35-36]. The band at 1258 cm⁻¹ supports both the assignment to ν (N-O) and the existence of CH.....O-N hydrogen bonding.

In the Raman spectrum bands are observed at 3066 cm⁻¹, 3054 cm⁻¹, 1252 cm⁻¹. The former two bands are assigned to the =C-H stretch and the later to the N-O stretch. The crystal data have shown that there are two different types of =C-H bonds in the crystal [37].

UV Spectra. Analysis of the electronic spectra of pyridine N-oxide results in the conclusion that the HOMO-LUMO excitation leads to intramolecular charge transfer, which is mostly due to the interaction between the N-oxo group and the M- electrons of the conjugated ring [38].

NMR Spectroscopy. Several detailed studies have been made on proton-proton coupling in six-membered aromatic nitrogen containing molecules like pyridine N-oxide, protonated pyridine N-oxide [39-42].

CLASSICAL METHODS IN THE OXIDATION OF N-HETEROCYCLICS

Several reviews on the chemistry of pyridine N-oxides [43], pyrimidine N-oxides [44], and quinoxaline N-oxides [45] have been published. The synthesis and the reactions of pyridine N-oxide has been reviewed recently [46]. A detailed survey was done about the traditional synthetic methods which included ring transformation, classical oxidation using peracids, the use of metalloorganic oxidizing agents and cycloaddition reactions. The reactions of pyridine N-oxide including the deoxygenation, nucleophilic reaction and cycloaddition to N-O bond were studied. The review summarized the unusual oxidizing agents (dimethyldioxirane, oxaziridines) in quantitative conversion and high chemoselectivity, which act as oxygen source for the oxidation of pyridine. Also, the use of pyridine N-oxides for the formation of ion charge transfer compounds which is very important in most of the chemical reaction and cycloaddition of N-O bond with nitrilium salts were studied.

ANCHORED CATALYSIS

The chemical industry is largely based upon catalysis, roughly 85-90% of all products are made through

catalytic processes, and the percentage is increasing steadily.

A catalyst offers an alternative, energetically favourable mechanism to the non catalytic reaction, thus enabling processes to be carried out under industrially feasible conditions of pressure and temperature.

Anchored catalysts are defined as solid or heterogeneous catalysts in which relatively small amounts of catalytically active species, most probably metals, are deposited on the surface of largely inert, porous, and shaped support bodies, like pellets, rings, extrudate and granules [47].

There are many advantages of anchoring a catalyst on a support:

1. Easy separation of the catalyst from the products of the reaction and thus its reuse.
2. Cost effective as the anchored catalyst is only a fraction of the weight of the total catalyst.
3. Larger total active surface area for a given amount of active material in a supported catalyst.
4. Control over the selectivity if the support chosen is chemically inactive to the products of the reaction.
5. Manufacturing a catalyst of a desired shape and size, using a support of similar dimensions. This is an important consideration in the process design as these properties determine the packing density and pressure drop across the reactor.
6. Optimising catalytic performance by choosing the right pore size distribution and the nature of the pores in the catalyst support.

Supports. Alumina, silica, and aluminosilicates with a wide range of alumina to silica ratios, activated carbon, silicon carbide, selected clays, various ceramics, artificial and natural zeolites, and kieselguhr, are some of the commonly used support materials. Polystyrene, polyamines, polyvinyls, polyallyls, polyaminoacids and acrylic polymers are also used [48].

Catalyst preparation methods. Supported catalysts are prepared most commonly by extruding, tableting, or pelletizing or physically mixing the (comulled) solid components, and impregnation of porous shaped support bodies with the catalyst components dissolved in a solvent usually water. In addition, some catalyst are produced and used as powders and granules.

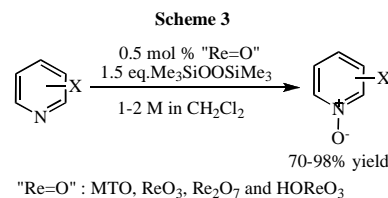
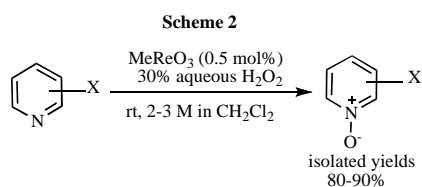
THE CONCEPT OF GREEN CHEMISTRY IN THE OXIDATION OF N-HETEROCYCLICS

Although the above mentioned methods do satisfy the accessibility to N-oxides they do it at the expense of key environmental factors. Most of these suffer from drawbacks such as the use of stoichiometric amount of corrosive acids or toxic metallic compounds those generate undesirable waste [49]. Technology is called "green" if it uses raw materials efficiently, such that the use of toxic and hazardous reagents and solvents can be avoided while

formation of waste or undesirable by-products is minimized [50a,b,c,d]. Catalytic routes often satisfy these criteria. According to Sheldon, the best solvent is no solvent, but if a solvent is unavoidable, then water is a very good candidate [50e]. Sheldon introduced several indicators to measure the efficiency and environmental impact of a reaction. The atom efficiency is the molecular weight of the desired product divided by the total molecular weight of all products. The environmental acceptability of a reaction is expressed in terms of E factor- the weight of waste or undesirable byproduct divided by the weight of the desired product. To assess the environmental impact of the waste generated, Sheldon introduced the environmental quotient, EQ as the E factor multiplied by an unfriendliness quotient, Q, which is assigned a value to indicate how undesirable a byproduct is. Waste prevention is much to be preferred over waste remediation. Environmentally benign oxidants like hydrogen peroxide, molecular oxygen, BSTP {bis-(trimethylsilyl)peroxide}, dioxiranes are to be used in particular for non environmental impacts. *m*CPBA {*meta*-chloroperoxybenzoic acid} seems to be the most common oxidant for most pyridines, but is not reliable for electron deficient pyridines. Hydrogen peroxide on the other hand gives only water as the byproduct and makes the work up easy. Molecular oxygen is an attractive oxidant and development of synthetic methodologies using it as the sole oxidant is a rewarding goal both from environmental and economic points of view [51].

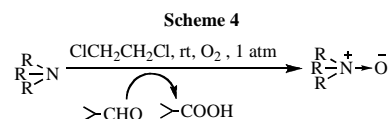
Sharpless and coworkers designed an efficient method by using catalytic amounts of methyltrioxorhenium (MTO), 30 % aqueous hydrogen peroxide as the stoichiometric oxidant for the N-oxidation of pyridines [52]. Earlier, they had showed that addition of 3-cyanopyridine improves the MTO catalyzed epoxidation of terminal alkenes with 30% aqueous hydrogen peroxide [53]. On further investigation they were able to establish that MTO was a quite stable catalyst for N-oxidation. N-oxidation of electron deficient pyridines was also achieved with pretty good yield.

Sharpless and coworkers reported N-oxidation catalyzed by various inorganic rhenium derivatives using bis-(trimethylsilyl)peroxide (BTSP). Oxidation of methylisonicotinate by BTSP in presence of MTO or various inorganic rhenium derivatives such as ReO_3 , Re_2O_7 and HOREO_3 gave high yields of its N-oxide while ReCl_3 and NaOREO_3 gave only trace amounts of oxidation products even after several days [54]. The optimal water content for the reaction was found to be between trace amounts to 15 mol%, higher contents led to lower conversions.

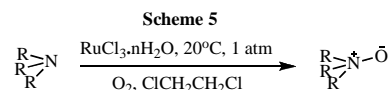


Perrhenic acid was used as a source of both rhenium and water. *para* or *meta* substituents did not significantly effect the reaction course while *ortho* analogues showed peculiar characteristics depending on their nature. Both electron rich and electron deficient pyridines also gave high yield of their N-oxides. A simple workup (filtration or distillation), environmentally friendly oxidant (BTSP), makes the method attractive. However, the rhenium oxides being water sensitive undergo changes in presence of water and cannot be reused. The use of dichloroethane doesn't adapt to present circumstances.

Bir Sain *et al* reported the N-oxidation using molecular oxygen/2-methylpropanal system [55]. Molecular oxygen/ aldehyde (in the absence of catalyst) system has been studied in detail for various oxidations like epoxidation of olefins [56], oxidation of secondary alcohols [57] and sulphides [58]. N-oxidations have been achieved in nearly quantitative yields. Oxidation was done with a series of aldehydes (aliphatic, aromatic, and heterocyclic).



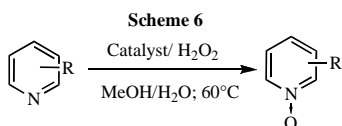
Continuing their work with molecular oxygen as the sole oxidant Bir Sain *et al*, have conducted N-oxidation with ruthenium trichloride [59].



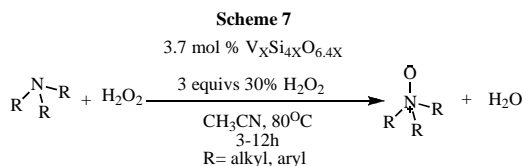
Ruthenium with a wide scope of oxidation states has been used as a versatile catalyst for a large number of organic transformations. Among the catalysts studied dichlorotris(triphenylphosphine)ruthenium(II) was found to be the most efficient catalyst. The probable reaction mechanism involves the formation of oxo ruthenium species from ruthenium and molecular oxygen followed by oxygen transfer to tertiary nitrogen, which yields the corresponding N-oxide. The reaction is carried out under mild conditions to make the work up easy. For the N-oxidation of 4-picoline to their corresponding N-oxide dichloroethane was found to be the best solvent.

Perhaps the very first attempt to bring together the advantages of homogeneous and heterogeneous catalyst

by means of a support was done by Kulkarni *et al* for the oxidation of N-heterocycles [60-61]. 30% dilute H_2O_2 (1:2 or 1:4 *M*) was used as the oxidant. The redox titanium catalyst {TS-1 (titanium silicate), Ti-ZSM-5(30), Ti-MCM-41} was supported on molecular sieves: ZSM-5 ($SiO_2/Al_2O_3=30$), MCM-41. The Ti-ZSM-5(30) was synthesized by post-synthetic modification of HZSM-5(30). TS-1 was prepared according to the procedure reported in the literature. The use of redox metals like titanium, iron, vanadium, and chromium is of advantage as they provide shape selective oxidation properties. The structured Silica (Ti-MCM-41) offer great advantage over modified Silica gels because the former can be shape selective. The aqueous or methanol medium made the reaction very attractive and eco-friendly. A large number of substrates, pyridines, substituted pyridines, picolines, halo-pyridines, cyano-pyridines, vinyl-pyridines, and pyrazines were subjected to oxidation. Routine characterization with, solid state NMR, XRD, IR were used for characterization of the catalyst. Product analysis was done with 1H NMR, FT-IR, Mass spectroscopy, melting point. The high activity of TS-1 is due to the large number of site isolated titanium active centers per unit volume. Water is the only byproduct. Ti-ZSM-5(30) catalyst showed good yields for electron-donating groups. Pyrazines formed both mono- N-oxide and N,N-dioxide because of the small pore size of zeolites. Turn over number of the catalyst has not been mentioned. The catalyst can be recycled and reused for specified number of runs. The focus has been on quantitative yields.



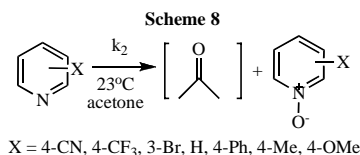
Punniyamurthy *et. al* studied the N-oxidation of tertiary amines over silica supported vanadium catalyst ($V_xSi_{4x}O_{6.4x}$) with 30% hydrogen peroxide as the oxidant [62]. The catalyst prepared was recyclable and was reused without loss of activity.



Very recently Fatemeh .F. B. *et al.* were successful in demonstrating the N-oxidation using hydrogen peroxide as oxidant and Preyssler's anion, $[NaP_5W_{30}O_{110}]^{-14}$ as the catalyst. Acidities of heteropolyacids can be compared with those of super acids. Preyssler's anion, $[NaP_5W_{30}O_{110}]^{-14}$ one of the largest anions known for the

potential application as catalyst. The heteropolyacid has the advantages like strong Bronsted acidity with 14 acidic protons, high thermal stability, high hydrolytic stability, safety, separability, corrosiveness, high oxidation potential, and greenness [63]. The position of COOH group in nicotinic, picolinic, quiniolic acids plays an important role in the product type. The catalyst can be recycled due to the non degradation in the structure of Preyssler's anion. The catalyst is very much active in the biphasic system (hydrogen peroxide: non polar solvent and Preyssler's catalyst), and oxidizes pyridine-carboxylic acids to the corresponding pyridine N oxides with decarboxylation at 2-position. The substrate type, solvent and reaction time as well as catalyst type are important factors. The solvents used were toluene, benzene and carbon tetrachloride.

The only attempt so far to study the kinetics and solvent effects has been done by Baumstark *et al.* [64]. Dimethyldioxirane was used as the oxidant and acetone and mixed solvents (Carbon tetrachloride/acetone, acetonitrile or methanol) system were used. They reported the first kinetic data for the N-oxidation [Scheme 8].



The reaction was found to be first order with respect to each of the reagents; second order overall. The Hammett plot of the substituted pyridines yielded an excellent fit with sigma values with a rho of -2.91 ± 0.13 ($r = 0.995$). The rho value is in agreement with that previously reported in the Hammett study of substituted pyridine N-oxidation by peroxybenzoic acid ($\rho = -2.35$, 25°C) in 50:50 dioxane/water [65]. The effect of solvent polarity on the oxidation of {X = 4-CF₃ in (Scheme-8)} by dimethyldioxirane was studied under pseudo first order conditions at 23°C. Here again preferential N-oxidations (when the substrate contains olefinic or aldehydic group) was observed. Polar, protic solvents significantly enhanced the rate of N-oxidation. The oxidation of substituted pyridines occurs *via* an SN^2 mechanism, rather than an electron transfer. The costs of dioxiranes need to be kept in mind while using it as the oxidant.

Biomimetic N oxidations with hydrogen peroxide as oxidant using flavin [66], manganese porphyrin [67] as catalyst have been reported in search of greener technologies.

STEREOCHEMISTRY OF HETEROCYCLIC N- OXIDES

An oxygen atom directly attached to the ring nitrogen atom can decrease the inversion rate to the extent that the nitrogen atom is almost "locked" in a chiral configuration,

and introduces a source of optical activity [68]. The inversion rate, and the effect of the substituents on it, varies from one hetero atom to another. The oxygen atom also undergoes inversion, but it is not as interesting as the nitrogen atom because it is divalent. In the last few years there is an increasing interest on the synthesis and the use of related optically active pyridine N-oxides as chiral controllers for asymmetric reactions [69]. So far no work has been reported with supported catalysts.

CONCLUSION

In research involving catalysis the vital issue of catalytic integrity, recovery and recycling efficiency should always be kept in mind. For better processes, new catalysts need to be developed. Beyond the description of the practical utility of the new catalyst, significant inroads into the mechanism of oxidant and substrate activation is key to the understanding of catalytic activity and selectivity.

Much progress has been made in understanding how to create and use catalysts, but the design and preparation of practical catalysts still relies on the application of known facts and intuition to trial and error methods. A catalytic system designed only by theoretical considerations may not be practical.

In a typical design experiment, an element known to be catalytically active towards a certain type of reaction must be correctly combined with a support material considered to be suitable because of its chemical and physical properties. The catalyst must be evaluated under conditions considered feasible for the reaction. If the experiment is successful, that is, if the catalyst produces conversion of the reactant and with adequate selectivity to the desired product, then the experimental catalyst may be a candidate for further development. If there is inadequate activity, an attempt to obtain greater catalyst surface area may be made, or a different catalytically active element may be tried. If selectivity is poor, the catalyst support or the reaction conditions must be changed. Once a promising combination has been found, the process of developing the catalyst becomes reiterative, and a large number of variables must be optimized. Statistical methods can be of great value in optimization, but they are not particularly useful in the design or discovery phase. Today, much catalyst research is centered on improving or modifying existing catalytic systems.

In addition to developing satisfactory catalysts, the designer also may have to develop a catalyst support or work with a support manufacturer to achieve this. In industry, catalyst manufacturers either form symbiotic relationships with support manufacturers or become experts in support design and manufacture themselves. There have been a number of industrial acquisitions and

joint ventures formed to exploit just such a relationship. It is quite clear from the works that have been reported that the focus has been only on the quantitative aspects of N oxidation.

All volatile organic solvents are toxic to some degree. Excessive vapour inhalation of the volatile chlorinated solvents, and the central nervous system depression that results, is the greatest hazard for industrial use of these solvents. Therefore it would be preferable, if possible, to carry out these reactions in aqueous media or organic media with a low environmental load.

Recently ionic liquids have become popular as new solvents in organic synthesis [70]. The properties such as miscibility with organic compounds, non-coordinating nature, excellent chemical and thermal stability, ease of reuse, negligible vapour pressure make them attractive towards future developments using them as solvents or catalysts. Homogeneous catalyst can be isolated in a phase, separate from that containing most of the reactants, for example, by the use of liquid-liquid two-phase systems. In such systems, the catalyst are confined in a polar liquid phase in which the organic products are poorly soluble. In such biphasic catalysis aqueous [71] or fluoruous [72] phases can be used. The advantages of homogeneous catalysis can be realised without the disadvantages of expensive separation of catalyst from products. Most catalytic applications of ionic liquids involve a biphasic or multiphasic system.

As mentioned the principle of anchoring a catalyst into a solid support can also be extended to the oxidation of N-heterocyclics.

Kinetics is the key discipline of catalysis. Kinetics is the tool to investigate and describe catalytic reactivity. It provides us with the tools to link the microscopic world of reacting molecules to the macroscopic world of industrial reaction engineering. Kinetic studies links directly to reactivity. Kinetics of individual molecules, called reaction dynamics takes into account:

a) the effect of orientation of molecules in a collision that results in a favourable reaction,

b) the distribution of energies over a molecules various degrees of freedom,

provides a channel to quantum mechanics leading to a conclusion about reaction feasibility. Kinetics through the thermodynamic parameter-temperature accounts for the average energy content of all the molecules participating in the reaction. Kinetics describes the behavior of large ensembles of molecules during a reaction. Therefore kinetics of N-oxidation needs to be studied in detail for reactivity prediction. The reaction time those have been reported need to be kept at a very reasonable rate.

Biopolymers (biodegradable polymers) can be distinguished according to the source from which they come from:

1) Natural polymers: Polymers coming from natural sources. Examples include Polysaccharides, proteins, lipids, natural rubbers.

2) Synthetic polymers: polymers synthesized from crude oil. Examples include aliphatic polyesters, aromatic polyesters, polyvinyl alcohols, and modified polyolefins.

Biopolymers keep a special place in green chemistry and have been exploited as supports in catalysis. Biodegradability, high sorption capacity, stability of metal anions, shape selectiveness (gel beads, membranes, fibers, hollow fibres, sponges) and chemical and physical versatility make them ideal for anchored catalysis. Biopolymers like alginate [73], gelatin [74], starch [75], and chitosan [76] have been used as supports in some catalytic processes.

As the most important skeletal component in plants, the polysaccharide cellulose is an almost inexhaustible polymeric raw material with fascinating structure and properties. Hydrophilicity, chirality, biodegradability, broad chemical modifying capacity, formation of semi crystalline fibre morphologies, makes it suitable for application in catalysis [77]. Optical activity, strong affinity towards transition metals, conformation, and flexibility has made chitosan a suitable candidate for the application as supports in catalysis [78]. Biotechnologies and genetic engineering will revolutionize the design and production of biodegradable materials, eventually molding materials for catalysis. Materials based on natural fibers (flax, hemp, paper, etc.) have also a promising future.

The relationship between the structure of a molecule and its physical properties can be understood by finding a quantitative structure-property relationship (QSPR). The same strategy can be used to relate chemical reactivity, catalytic ability, and bioactivity of pyridine compounds with their structure. Although such a prediction is still in its formative stage, existing results have been encouraging [79].

Modern computational modelling techniques can be applied at a number of different levels to heterogeneous catalytic systems, paving the way to a more efficient approach to catalyst optimization. Both methods, in computational modelling, those treat the catalyst using atomic/molecular forcefields (Molecular Mechanical-Classical Monte Carlo, Classical Molecular Dynamics) and those which deal with electronic structure (Quantum

Mechanical-Hartree-Fock theory, Density Functional Theory), can be used in collaboration with experimental methods to give insight into structures and processes occurring at a level of atomic/electronic detail otherwise inaccessible [80].

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