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Recent advances in the partial oxidation of organic molecules using heterogeneous catalysis

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Abstract

With increasing environmental legislation, the synthesis of catalysts that can be easily recovered, give high selectivity and produce low levels of waste is highly desirable. Immobilising an active species on a support material can ease the separation from a reaction, allowing the material to be used again. A constant goal for the selective oxidation of organic substrates is the design of new and improved heterogeneous catalysts. Recent highlights of research towards this goal are reviewed. ©2000 Elsevier Science B.V. All rights reserved.

Keywords: Heterogeneous catalysts; Oxidation; Green chemistry

1. Introduction

The oxidation of organic substrates leads to the production of many functionalised molecules which are of great commercial and synthetic importance [1]. As such, oxidation chemistry is particularly well researched and widely documented [2,3]. The aim of this review is to summarise some of the recent progress made in the use of heterogeneous catalysts for the partial oxidation of organic molecules.

Major industrial products that can be produced by this method include ketones, aldehydes, esters, carboxylic acids, lactones and alcohols.

Various sources of oxygen can be employed. Direct oxidation using organic oxygen donors such as peroxyacids and peroxides is widely used but suffers from the hazardous nature of the reagent and the organic by-products produced. Hydrogen peroxide is a preferred oxidant as it produces only water as a by-product. However, it needs to be handled with care and is generally not as reactive as organic peroxides. Another clean oxidant, capable of highly selective oxidations, is ozone. While it suffers from the disadvantage of requiring specialised equipment for its generation, resulting in high fixed costs, it is likely to become increasingly important in the future as we move toward technologies which are cleaner, producing less waste salts. Another important oxidation method is the use of a so-called sacrificial aldehyde as an oxygen transfer agent which is based on the in situ formation of a peroxyacid. It is a safer option compared to starting with a peroxyacid but it still results in the formation of carboxylic acids which can be marketable products, though are generally considered as waste.

Stoichiometric metal oxidants such as chromates and permanganates are also widely used. Excessive quantities of toxic metals leads to the inevitable production of large amounts of toxic waste which in turn necessitate disposal. The detrimental effects of heavy metals in the environment are well documented and need no further emphasis here. With new environmental legislation to comply to, this classical method of

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oxidation using stoichiometric quantities of metals is no longer acceptable and alternatives must be found [4–6]. As a consequence recent research in the area of catalysis has concentrated on finding alternative methods that will increase selectivity, increase yield and reduce waste [7].

It is evident that the use of molecular oxygen or air in place of other oxidants is clearly desirable on economic and environmental grounds. However, oxygen is a weak, non-selective oxidant and suitable catalysts are required to activate oxygen under mild conditions.

One of the major goals of green chemistry is to develop environmentally acceptable routes to important organic products. Methods by which this can be achieved are increasing product selectivity, aiming for 100% atom efficiency and replacing stoichiometric reagents with heterogeneous catalysts thus allowing easy separation of the catalyst from the product. Increasingly tighter guidelines are being issued concerning the disposal of waste materials, with increasing public and corporate pressure to comply to them. In this respect it was only a matter of time before we saw the principles of making chemistry more environmentally friendly, being applied to oxidation chemistry to give us new and important challenges in research.

The use of a reaction system in which the catalyst is in a different phase to that of the substrate and the products allows easy removal of the catalyst from the reaction mixture via filtration, centrifugation or decantation. This enables easy catalyst recovery and recycle whilst negating the need for a quench or workup step. A heterogeneous catalytically active material can be formed by immobilising active species on or in a support material such as porous silica, titania, or alumina [8,9]. The porosity of such materials can lead to increased reaction selectivity by giving high selectivity to the desired product. This is the ideal situation and can be achieved by the synthesis of chemically modified porous solids or supported reagent catalysts [10].

2. Catalytic materials

One of the greatest breakthroughs in catalysis since the early eighties was the discovery of a family of titanium silicates by chemists at Enichem. The most important member of the family is TS-1. TS-1 is produced hydrothermally from tetraethyl orthosilicate, tetraethyl orthotitanate (Si:Ti ratio typically 30–50), tetrapropylammonium hydroxide and water [11] (as reported in the patent literature [12]). These versatile titanium silicates already have a wide range of industrial applications including epoxide formation, ammoximation and hydroxylation.

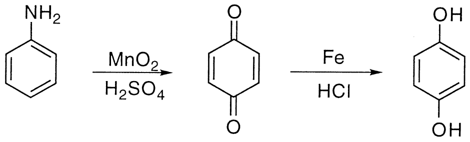

Fig. 1. The preparation of hydroquinone from aniline.

The hydroxylation of aromatics is of particular interest to the chemical industry. Hydroquinone, e.g., which is easily oxidised to quinone, is widely used in the photographic industry. Initially, hydroquinone was produced by the oxidation of aniline using manganate and sulphuric acid. This was then followed by reduction using typically Fe/HCl (Fig. 1).

This classical route to hydroquinone suffers from very poor atom utilisation (i.e., a small fraction of the atoms consumed in the process end up in the final product) and leads to the production of enormous volumes of waste. The production of one mole of hydroquinone leads to the production of mole equivalents of ammonium sulphate and iron(II) oxide. More staggering is the production of four mole equivalents of manganese sulphate. This is an example of a process with a poor environmental acceptability factor (high waste to product ratio) made worse by the hazardous nature of the waste [13].

The new TS-1 process involves the direct production of hydroquinone from phenol and hydrogen peroxide (Fig. 2).

The original homogeneous catalysed process gives low conversion as over oxidation and other side reactions lead to the formation of tars. These are signifi-

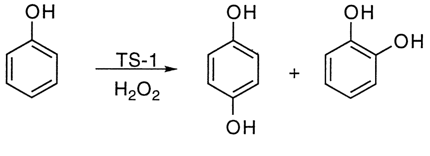

Fig. 2. Hydroxylation of phenol using TS-1 and hydrogen peroxide.

cantly reduced with the use of TS-1. Selectivity to hydroquinone is also higher using TS-1 and can be varied by modification of the catalyst. TS-1 is being used commercially in Italy for the production of catechol and hydroquinone [14]. The TS-1 route highlights a great improvement in atom efficiency and the hydrogen peroxide reacts to produce water which is easy to dispose of, and catechol, which is marketable.

There has also been prolific use of TS-1 in the area of olefin epoxidation. The oxidation of propene to propylene oxide provides an industry with a very important monomer which is used in the production of polyethers for use as non-ionic surfactants. Approximately 3 million tonnes a year are produced. Conventional systems for the production of propylene oxide used >95% hydrogen peroxide to ensure high selectivity to the epoxide and as a method of avoiding the formation of side products. These were typically the diols formed by attack from water. With TS-1, dilute hydrogen peroxide [15] can be used and high selectivity to the epoxide is still achieved. Work is continuing in this area to fully understand the mechanism of epoxidations catalysed by titanium silicates [16,17]. Although selectivity still remains a great asset to TS-1, its microporous nature (pore size ca. 0.55 nm) restricts its use to small molecules. The development of materials with larger porosity including Ti-Beta [18], Ti–MCM-41 [19,20] and titania–silica aerogels [21] have allowed the catalytic epoxidation of more bulky olefins. Epoxides of several species including cyclohexene, cyclododecene, norbornene and limonene have been achieved in high yields.

Corma and coworkers [22] realised that the hydrophilic nature of Ti–MCM-41, reduced its effectiveness for the oxidation of organic molecules using aqueous hydrogen peroxide. In an attempt to create a more hydrophobic material, the surface of Ti–MCM-41 [23] was silylated. Using hexamethyldisilazane as the silylating agent, a hydrophobic material was produced. This showed a greater activity for the epoxidation of cyclohexene compared with the un-silylated material. As the hydrophobic material has a low quantity of surface water, this resulted in higher selectivity to the epoxide. Without surface silylation, hydrolytic ring opening of the epoxide led to the formation of diols. Trimethylsilylation can also be used to give improvements in epoxidation with the use of aqueous hydrogen peroxide [24]. Research has also shown that materials incorporating methylated silicons can be produced in a one step synthesis [25]. Using varying ratios of silicon and titanium, a range of materials was synthesised and tested using the oxidation of cyclohexene with *tert*-butyl hydroperoxide as the oxidant. This new development in titanium silicates enabled around 95% conversion and high selectivity to the epoxide only after 5 h. The authors claim that the results are so far, the best ever obtained for Ti–MCM-41 based oxidations.

Although titanium silicates have proved to be valuable catalysts for the oxidation of alkenes, alkane oxidation using these materials has also been achieved [26]. The preparation of cyclohexanone and cyclohexanol by UV irradiation of cyclohexane, has been achieved with dioxygen at room temperature [27]. Using only TiO_2 as the catalyst, high selectivity is observed for cyclohexanone (82.5%) while the other products, cyclohexanol and CO_2, are produced in yields of only 5 and 12.5%, respectively. A system using a mixture of TiO_2 and TS-1 as a catalyst shows that selectivity to cyclohexanol increases to around 50% while selectivities for CO_2 and cyclohexanone are found to be lower than before. The TiO_2/TS-1 system actually inhibits the conversion of cyclohexanol into cyclohexanone. Since no products were obtained using only TS-1, the product distribution is thought to be due to the shape selectivity that TS-1 provides.

Addition of metal nitrates into the original TS-1 preparation (outlined above) allows the production of titanium silicates containing alkali and alkaline earth metals [28]. Using these as catalysts for the oxidation of *n*-octane it was found that TS-1 containing lithium and sodium were not active for alkane oxidation using aqueous hydrogen peroxide, though washing the material with acid solution can restore the catalytic activity. Magnesium incorporated into TS-1 showed increased substrate conversion compared to the other metal containing materials.

Silicates incorporating transition metals have also made a dramatic impact on the field of oxidation. Silicate aerogels containing transition metals, ML_n–SiO_2, have been prepared by the sol–gel technique and successfully used for the oxidation of alkyl arenes with anhydrous *tert*-butyl hydroperoxide [29]. Although a range of metal silicates were examined, ones containing cobalt were the most active and selective. The oxidation of ethylbenzene to acetophenone gave 65% conversion and a selectivity of over 99%. Carried out at below reflux and at atmospheric pressure, these results are very encouraging. The same group has also shown that molybdenum silicate is especially active for the selective epoxidation of a range of alkenes using *tert*-butyl hydroperoxide as an oxidant at 50°C [30].

Using a chromium silicate-2 (CrS-2) with hydrogen peroxide [31], the oxidation of thioethers to sulphoxides has been more efficiently achieved. While the TS-1/*tert*-butyl hydroperoxide combination exhibits high selectivity and reactivity for a number of reactions, CrS-2 shows greater conversion in this particular case. Comparing the chromium substituted material with TS-1 it was noted that the oxidation of silyl enol ethers to dicarboxylic acids occurs at a higher rate and selectivity using TS-1. However, when thioethers are subjected to oxidation using 30% H_2O_2 catalysed by CrS-2, it was found that sulphoxidation proceeded in high yields without affecting carbon–carbon multiple bonds. Using a TS-1/H_2O_2 combination, low selectivity was observed and using more sterically hindered thioethers, the reaction did not proceed. CrS-2 is also an active catalyst for the epoxidations of alkenes [32].

The development of chromium substituted aluminophosphate-5 (CrAPO-5) by Sheldon and coworkers [33–35] led to an efficient material for the liquid phase autoxidation of hydrocarbons. In catalysing the autoxidation of cyclohexane at 115–130°C, and 5 bar O_2, (20 bar air) in the presence of a small amount of an alkyl hydroperoxide initiator, cyclohexanone is produced. Tetralin and indane have also been converted to the corresponding ketones, and using a sodium exchanged version of CrAPO-5, ethylbenzene was converted to acetophenone at 130°C using 1 bar O_2. These later oxidations have all been achieved using peroxides in solvent free systems. The catalyst was recycled four times with no observed loss of activity. Although this material appeared to be an excellent catalyst for an extensive range of different oxidations, a more recent publication by the same group has cast doubts on the heterogeneity of the chromium substituted aluminophosphates [36]. The previous notion that the catalysis was taking part in the micropores has been reinterpreted as being due to tiny quantities of leached chromium. By using a bulky substrate (valencene) which is too large to enter the pores of CrAPO-5, oxidation was still shown to occur. This gave evidence to suggest that the catalysis is not occurring in the pores. Backing up this experiment were results obtained using a bulky hydroperoxide (triphenylmethyl hydroperoxide). With α-pinene as the substrate (Fig. 3), no reaction was observed, presumably again due to the small pore size causing steric constraints. Stirring the catalyst with a smaller peroxide (TBHP) followed by filtration of the catalyst, showed that on addition of the substrate to the solution the reaction started. This indicates that in the presence of the peroxide the catalyst is leaching significant quantities of chromium. Stirring the catalyst with the substrate followed by filtration stopped the reaction. However, after filtration at reaction temperature (to avoid readsorption of leached chromium) conversion was still observed to continue. This reinforced the notion that leached chromium is responsible for oxidation.

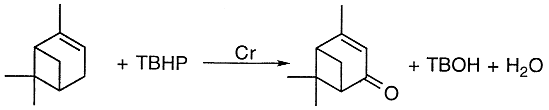

Fig. 3. Conversion of α-pinene with *tert*-butyl hydroperoxide to verbenone using CrAPO-5.

During the so-called hot filtration studies, it was calculated that the large CrAPO-5 crystals leached only 0.3% of their chromium, meaning that the catalyst could be recycled many times without observed loss of activity.

Aluminophosphates containing Mn(III) and Co(III) have also been synthesised and used as catalysts in oxidation reactions [37]. Using benzaldehyde as an oxygen transfer agent at 323 K and 30 bar of pressurised dry air, good conversions were achieved for the epoxidation of cyclohexene, α-pinene, limonene, styrene and hex-1-ene [38].

Transition metal functionalised hydrotalcites have also proved effective catalysts for a range of oxidations. Hydrotalcites are layered mineral materials consisting of cationic Brucite layers separated by layers of anionic species. Various metallic elements can be introduced into the Brucite layer via the substitution of Mg(II) or Al(III) cations at the octahedral sites which are thought to be the active sites of the catalysts. Multi-metallic hydrotalcites consisting of magnesium, aluminium, and iron or copper elements were prepared which catalysed the Baeyer–Villiger oxidation using a combination system of molecular oxygen and benzaldehyde as a sacrificial aldehyde [39]. A range of cyclic ketones have been selectively converted to the corresponding lactones. Highly efficient oxidation of alcohols and aromatic compounds has also been reported using a Ru–Co–Al hydrotalcite [40]. At 60°C with toluene as a solvent and an oxygen atmosphere, a variety of alcohols were converted to the corresponding aldehyde with high yield and selectivity.

3. Adsorbed reagents

Traditional supported reagent catalysts consist of reagents adsorbed onto a high surface area support such as alumina, silica [41,42], or a clay [43]. The rationale is that the dispersion of the reagent over the large surface areas would allow more rapid reaction through greater accessibility of the substrates to the reagents. While this is a significant factor, the support material can also have a dramatic influence on the system, often leading to entirely new structures and catalytic centres. These materials are easily prepared and handled, generally allowing more rapid reaction and crucially, an easier workup than the equivalent unsupported reagent [44].

As discussed previously, TS-1 is active for the oxidation of small molecules, but due to its small pore size, larger molecules have difficulty accessing the active sites. This is the case when trying to oxidise bulky sulphides, e.g., Mayoral and coworkers have overcome this difficulty by treating silica gel with $Ti(OPr^i)_4$. This catalyst has previously been used for the epoxidation of alkenes [45] but is also an active catalyst for the oxidation of methyl *p*-tolyl sulphide [46] with hydrogen peroxide and with *tert*-butyl hydroperoxide. The larger pore size of the silica gel allows easy mobility for reagents and products. Reuse of the catalyst showed similar activity, but the product selectivity increased indicating that the recovered catalyst had a different structure. Infra-red analysis showed that the *iso*-propoxy groups had been hydrolysed, therefore, modifying the activity of the titanium centre. Treatment of the original catalyst with diethyl (*R*)-tartrate reduced the catalytic activity though increased selectivity to the sulphoxide. Modification of the original catalyst with (*R*)-tartaric acid gave results that were similar to those obtained using the diethyl (*R*)-tartrate (Fig. 4). However, the reactions carried out with hydrogen peroxide gave an excellent sulphoxide/sulphone ratio with a selectivity of 97%.

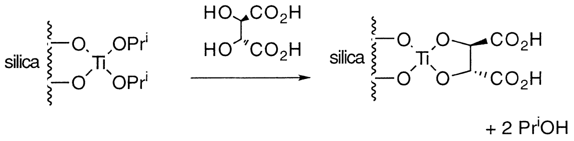

Fig. 4. Proposed reaction of original form of silica supported Ti(IV) catalyst with (*R*)-tartaric acid.

TiO_2 coated silica has also been shown to have value as a support material for V_2O_5 [47]. Stirring an aqueous solution of ammonium metavanadate solubilised with hydrogen peroxide and the titanium grafted silica, yielded an oxidation catalyst. After removal of water by vacuum, the material was dried at 373 K for 16 h. At temperatures of 533–673 K, the oxidation of *o*-xylene with this catalyst yielded phthalic anhydride, *o*-tolualdehyde, phthalide and maleic anhydride.

As has been exemplified here, the grafting of metals onto the surface of an inorganic support can lead to extremely active and selective catalysts. Many high oxidation state metals have previously been shown to be stoichiometric though $KMnO_4$ and $K_2Cr_2O_7$ can be made catalytic if immobilised on alumina [48]. These materials can only be rendered catalytically active if the pH is carefully controlled during the synthesis, otherwise the resulting product is physisorbed and only useful as a stoichiometric oxidant (Fig. 5).

With a typical metal loading of ca. 0.075 mmol g^{-1}, immobilised dichromate has been shown to have activity in the catalytic oxidation of several alkyl aromatics using neat substrates and air as the only consumable oxidant. Utilising atmospheric pressure, temperatures around reflux and no solvent, high selectivities are achieved with water being the only significant side product. This apparently ideal catalytic system has drawbacks. Both the chromium and manganese analogues exhibit a low substrate conversion of only 1 or 2% h^{-1} at reflux, so reaction times are typically long if substantial conversion is to be obtained. Optimisation of the chromium catalysed system has highlighted the importance of optimising the air flow rate, agitator speed and catalyst quantity [49].

By introducing chromium chloride during the gel-preparation for the hydrothermal synthesis of

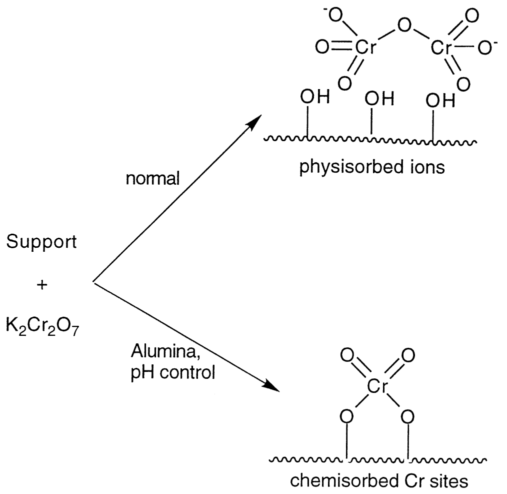

Fig. 5. Supported dichromate is found to be genuinely catalytic when alumina is used as the support and careful pH control is employed.

MCM-48, a material which contains about 3 wt.% chromium has been prepared [50]. Initial testing has demonstrated high activity for the oxidative destruction of trichloroethylene using oxygen at 250–400°C.

Permanganate supported on alumina [51] and chromium(VI) oxide supported on wet alumina [52] have been used for the preparation of carbonyl compounds from alcohols again utilising a solvent free system. Simply mixing the finely ground alumina supported permanganate with the alcohols and grinding the mixture for several minutes yields the corresponding carbonyl compound. Interestingly, no over oxidation to carboxylic acid or cleavage of double bonds of α,β-unsaturated alcohols is observed. Microwave radiation has recently been used in combination with chromium trioxide supported on H–Y zeolite [53]. Again the oxidation of alcohols to carbonyl compounds has been reported using a solvent free system. The chromium trioxide and zeolite are simply crushed together in a mortar along with the substrate. High yields and good selectivity to the carbonyl compounds were achieved when radiation was applied for several seconds. These reactions are however, stoichiometric in metal.

Using copper(II) sulphate supported on alumina, Varma et al. [54] have oxidised benzoins, also with the use of microwave radiation (Fig. 6). Using this source of energy, high product yields were obtained in a matter of minutes.

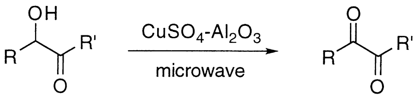

Fig. 6. Oxidation of benzoins using alumina supported copper(II) sulphate.

An intimate mixture of $Fe(NO_3)_3 \cdot 9H_2O$ and HZSM-5 zeolite has also been used for the conversion of alcohols to ketones [55]. The oxidising reagent named ‘zeofen’ has shown high conversions and selectivities using no solvent. The oxidations will also proceed using dichloromethane as a solvent without microwave radiation. Reaction times are longer though high yields are still achieved. Again, all these reactions are stoichiometric in metal.

Although considered as unsafe as the conditions of radiation are not controllable easily, it has been shown that microwave energy can drastically reduce reaction time and enable milder conditions to be used. Whether such an energy source can be considered on an industrial scale for such chemistry is yet to be proven.

The work of Jacobson and coworkers expanded the scope of alkene epoxidation by using chiral manganese Schiff’s base complexes [56]. These enabled asymmetric epoxidation with high stereochemical control. Synthesis of a chiral (salen) Mn(III) which is analogous to that developed by Jacobsen (Fig. 7), has been carried out within the supercages of zeolite Y [57].

Using NaOCl as the oxidant, alkene epoxidations were carried out in dichloromethane at 5°C. By having the active catalyst in a confined environment good enantioselectivity can be achieved. Chiral Mn (salen) complexes have also been supported on clays [58] and used for olefin epoxidation with PhIO as the oxidant at room temperature. The characteristics of the different clays influence the amount and distribution of the com-

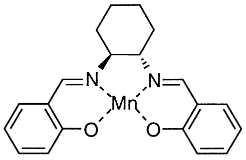

Fig. 7. Chiral (salen) manganese(III) complex.

plex on the surface. Deactivation of these catalysts is a problem and is thought to be due to the decomposition of the salen ligand. Manganese (II) bipyridine complexes immobilised in mesoporous Al–MCM-41 have also shown activity for the oxidation of styrene using iodosylbenzene, hydrogen peroxide and *tert*-butyl hydroperoxide as the oxidants [59].

4. Tethered metal ligand systems

Physisorbing a catalytic site onto a support material has the disadvantage of being sometimes insecure and the active sites can be easily washed off the surface. This can cause loss of activity on reuse, complications due to competing homogeneous catalysis and contamination of the organic product. A possible solution to this problem is to tether the catalytic site to a polymer or support material, by means of covalent, ionic or coordinative bonding.

Palladium [60] bound to an 8% cross-linked chloromethylated styrene–divinylbenzene copolymer via an amino acid type ligand has been used for the oxidation of toluene at 35°C using oxygen at 1 atm. Measuring the rate of oxidation by following the uptake of oxygen, the catalyst was able to be reused three times before rates were observed to fall. Vanadium (V) and chromium (VI) ions have also be immobilised on chemically modified polymers. This involves a 2-picolyl amine ligand [61] bound to a glycidyl methacrylate–ethylene glycol dimethacrylate (GMA–EGDM) copolymer. The vanadium functionalised polymer catalyses Sharpless epoxidation reactions, using a mixture of hydrogen peroxide and *tert*-butyl hydroperoxide while the chromium derivatised polymer can catalyse the oxidation of a range of substrates including 4-hydroxyphenol, α-naphthol and benzylamine to 1,4-benzoquinone, 1,2-naphthaquinone, and benzaldehyde, respectively, using hydrogen peroxide and *tert*-butyl hydroperoxide.

Kureshy et al. [62] highlighted the use of Schiff's base ligands to complex metal ions and produced a range of Mn (salen) complexes tethered to polymers. In catalysing chiral epoxidation of styrene, these materials exemplify the range of oxidations that can be achieved with polymer immobilised metals. Sherrington and coworkers [63–65] have produced several other polymer supported manganese Schiff's base complexes which have also exhibited activity in catalysing epoxidation reactions using *m*-chlorobenzoic acid as the oxidant. Schiff's base ligands can host a range of metal species, for instance VO^{2+} can be complexed and used for the hydroxylation of benzene at 65°C using hydrogen peroxide [66]. Sutra and Brunel [67] reported the preparation of an MCM-41 bound manganese(III) Schiff's base complex formed by the derivatisation of grafted 3-chloropropyl triethoxysilane. Although no catalysis was reported, the methodology provided new scope for immobilising potentially active complexes.

Also using the approach of grafting silanes onto silica, Kurusu [68] has shown that catalysts immobilised on silica gel and montmorillonite could be easily synthesised and used as oxidation catalysts. By reacting grafted 3-aminopropyl trimethoxy silane with salicylaldehyde, a material was formed that allowed metals to be complexed. As well as studying this Schiff's base ligand, the ligating effects of (*N*,*N*-dimethyl-3-aminopropyl) trimethoxysilane and *N*-(aminoethyl) aminopropyl trimethoxysilane were investigated. Although removal of any unbound metal was not reported, the immobilised copper and iron Schiff's base catalysts showed activity for the oxidation of cyclohexane and ethylbenzene at 90°C using oxygen, hydrogen peroxide and a solvent consisting of 45% acetic acid. The montmorillonite based materials could be recycled.

We have recently reported the formation of an imprinted chromium Schiff's base complex on a silica surface [69]. Condensation of salicylaldehyde and 3-aminopropyl trimethoxy silane followed by complexation with Cr^{3+} in the form of chromium(III) acetate leads to the formation of a stable metal complex in solution (Fig. 8). Imprinting of this complex onto silica allows the formation of an immobilised chromium(III) catalyst which shows high activities for the oxidation of several alkyl aromatics (Table 1).

Using only air as the oxidant, neat substrate and a typical working temperature of around reflux, the process is remarkably clean and requires little workup to isolate the required products. The catalyst has proved to be surprisingly stable.

Using a nickel derivative of this imprinted catalyst, high yields have been achieved for the Baeyer–Villiger oxidation of cyclohexanone at room temperature

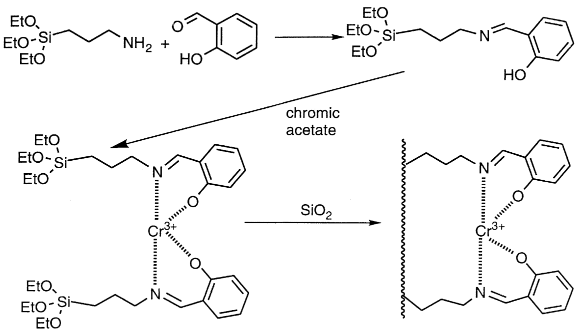

Fig. 8. Preparation of imprinted chromium(III) Schiff's base complex.

Table 1
Oxidation of alkylaromatics using an imprinted supported Cr(III) catalyst

Substrate	*T* (°C)	Product(s)	Yield (24 h, %)
Ethylbenzene	130	Acetophenone	50
p-Xylene	138	*p*-Toluic acid	29
		Terephthalic acid	5
o-Xylene	145	*o*-Toluic acid	7
p-Chlorotoluene	130	*p*-Chlorobenzoic acid	12

using a sacrificial aldehyde and oxygen. These results are comparable with those using a previously reported immobilised nickel complex [70] though different solvent effects are observed for the catalysts. The immobilised nickel complex consists of a diaromatic chain featuring a terminal acetate group [71] (Fig. 9). Fully characterised by solid state ^{13}C NMR and diffuse reflectance infra-red, this supported ligand has been used to tether a range of metal acetates.

For the oxidation of cyclohexane to ϵ-caprolactone, the thermally activated (105°C, 24 h) immobilised nickel complex achieves ca. 98% conversion in benzene after only 3.5 h, whereas the imprinted nickel catalyst shows similar conversion after 7 h. The imprinted catalyst exhibits a faster rate when the reaction is carried out in 1,2-dichloroethane.

Both of these catalytic systems involve the use of dioxygen and a sacrificial aldehyde as an oxygen transfer agent. The combination of catalyst, oxygen and aldehyde allows the formation of an active peroxyacid in situ [72–74]. Peroxyacids are hazardous to handle and lose activity on storage, so the generation of alternative oxidants in situ is an important part of clean technology [75]. However, by forming carboxylic acid as a by-product, a potential waste product is created.

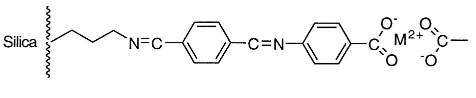

Fig. 9. Organophilic immobilised metal complex.

As well as being an active catalyst for the Baeyer–Villiger oxidation, this organophilic material can bind a range of first row transition metals, a variety of which have shown activity as catalysts for the oxidation of alkylaromatics (especially chromium) at reflux using a solvent free system and air as the oxidant. Using an oxygen atmosphere, dichloromethane as a solvent and *iso*-butyraldehyde, the epoxidation of cyclohexene has also been achieved. Using cyclohexene as a model substrate, rates of epoxidation have been measured at 28 and 26.5% h^{-1} for the nickel (II) and copper (II) catalysts, respectively. In comparison, we earlier reported a novel approach of tethering metal acetates to a silica surface via derivatisation of a grafted cyanoethyl silane (Fig. 10).

An active epoxidation catalyst was discovered when cobalt acetate was bound to the supported acetate function [76]. When used with a combination of molecular oxygen and a sacrificial aldehyde (typically *iso*-butyraldehyde), useful conversions of several alkenes to epoxides were achieved at room temperature. These important synthetic intermediates are more commonly achieved with peracids often leading to ring opening and the formation of diols. The immobilised cobalt catalyst is highly selective to the epoxide and no side products are observed. Obvious advantages of this system are the absence of toxic reagents and excess metal waste. The catalyst retains

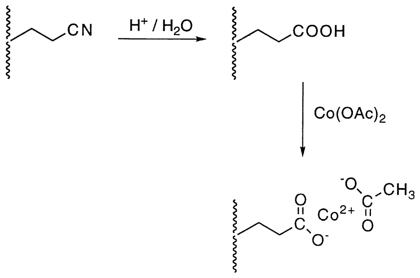

Fig. 10. Formation of a supported cobalt catalyst based on a chemically modified silica.

its metal ions under the harsh reaction conditions and has been shown to be active on reuse.

Surface grafting of (3-glycidyloxypropyl) trimethoxysilane offers another method of supporting an active functional group onto a support. The tethered epoxide can be easily ring opened to enable the build-up of ligating molecules. This methodology has been used to support a triazacyclononane function [77]. To create a ligand for metal ions, the *secondary* amine groups of the triazacyclononane were further reacted with propylene oxide. As this ring opens, a hydroxyl group is formed β to the nitrogen creating a species capable of binding metal ions. This synthesis has the added advantage that the initial opening of the immobilised epoxide also creates a hydroxy group. When used to complex manganese ions, this material has been found to be active in the epoxidation of styrene and cyclohexene. This is one of the few examples of a catalytically active, non-aromatic manganese complex which is covalently immobilised on an inorganic support. Epoxidation has also been achieved with the use of iron(III) porphyrins [78] using iodosylbenzene in dichloromethane. The heterogeneous reactions are significantly slower (ca. tenfold) than reactions catalysed by the homogeneous analogue.

5. Supported oxidants

The use and development of sacrificial aldehydes and peroxyacids as oxygen transfer agents has grown considerably over the last few years. Their use however, is hindered because of the requirement of at least stoichiometric amounts of aldehydes, resulting in the production of a large amount of waste carboxylic acid. In some cases the acid can be marketed, though it is generally considered and treated as waste. Although recycling of these acids back to peroxyacids is possible, the process is complex and involves treatment with hydrogen peroxide in the presence of concentrated acids. Hydrogen peroxide can be considered a more environmentally friendly reagent, as water is the only side product of its decomposition although aqueous hydrogen peroxide can give low rates of reaction and more concentrated solutions are hazardous. Generally because of the aforementioned drawbacks, the use of peroxyacids and sacrificial aldehydes are not popular on an industrial scale.

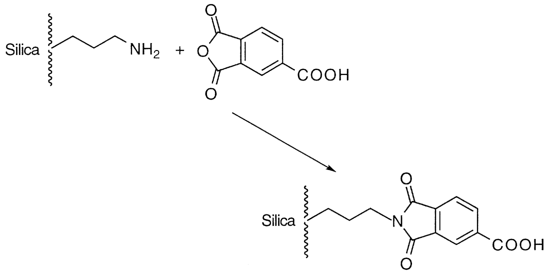

Fig. 11. Condensation between supported amine function and anhydride to produce an immobilised carboxylic acid.

The work of Sherrington et al. [79] has shown that it is possible to securely attach peracids to inorganic supports and Solvay Interox have investigated condensation of surface bound amine functions with anhydrides as a way of synthesising surface bound carboxylic acids [80,81] (Fig. 11). Conversion of these to peroxyacids was achieved using hydrogen peroxide and methanesulphonic acid.

These have found uses not only in organic synthesis, but also as reagents for disinfection and waste water treatment.

The preparation of a new ultra high-loading silica supported peroxyacid [82] via the production of a previously reported sol–gel material [83] has recently been reported from our laboratory. Formed from 2-cyanoethyl triethoxysilane and tetraethyl orthosilicate, the sol–gel material was then treated with aqueous sulphuric acid to yield a supported carboxylic acid. Further treatment with methanesulphonic acid and hydrogen peroxide yielded an immobilised peroxyacid (Fig. 12).

Titration and porosimetry of these materials has indicated that active site yields can be at a concentration as high as 3.5 mmol g^{-1} and that the surface areas can be in excess of 1000 $m^2\,g^{-1}$. The solid peracids also appear to be stable under anhydrous conditions at room temperature. This material is highly active and selective for the epoxidation of alkenes and the

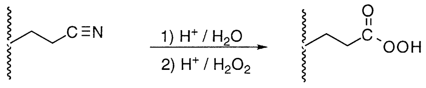

Fig. 12. Formation of an immobilised peroxyacid from cyano-derivatised silica.

yields on reuse (after recovery and reoxidation with acidic hydrogen peroxide) are comparable with those obtained originally.

Other recent advances in solid state synthesis offer some interesting possibilities for the future. The preparation of metalloporphyrinosilicas by hydrolysis and polycondensation, or cocondensation with tetraethoxysilane allow iron porphyrins to be encapsulated within a robust silica backbone [84]. These new materials are efficient catalysts for the epoxidation of cyclooctene and the hydrolysis of alkanes. The ever increasing research into new support materials including sol–gel and MCM development is leading to a greater understanding into the role of the inorganic support. Our recently reported highly fluorinated materials derived from amide formation between perfluorocarboxylic acids and aminopropyl trimethoxysilylated silica may also point the way towards more hydrophobic materials. This could be advantageous when considering mass transport of non-polar substrates and polar oxidation products in a typical reaction mixture [85].

Recent advances to rate enhancement in heterogeneous catalysis has recently been reviewed by Hutchings [86].

Biomimetic oxidation studies have also been explored with on going research into simulating enzyme active sites to promote oxidation of organic substrates. Successful alkane oxidation has been achieved using $[Fe_2O(OAc)(tris((1\text{-methylimidazol-2-yl})methyl)amine)_2]^{3+}$ in the presence of *tert*-butyl hydroperoxide and oxygen [87]. This structural model of methane monooxygenase has shown activity as a homogeneous catalyst in the oxidation of a range of alkanes. Cytochrome *P*-450 catalyses the oxidation of various organic compounds in many living organisms and has attracted particular attention because of its efficiency as a strong oxidising agent. Murahashi and Komiya [88] have simulated the enzymatic function of cytochrome *P*-450 with transition metal complexes enabling biomimetic oxidations of amines, amides, β-lactams, alcohols, phenols, and hydrocarbons by using a ruthenium catalyst and peroxide. The use of sacrificial aldehydes with such biomimetic systems has also been discussed.

Miki and Furuya [89] have synthesised an active hydroxylation catalyst by mimicking the active site of methane monooxygenase on a silica surface. This mononuclear iron carboxylate complex immobilised and isolated on a modified silica surface catalyses the oxidation of hexane to a mixture of hexan-1-ol, -2-ol and -3-ol using mercaptan, acetic acid, triphenylphosphine and molecular oxygen at ambient conditions. It is thought that this highly selective hydroxylation occurs via reductive dioxygen activation. The unique properties of the complex provides oxygen ligation in a hydrophobic microenvironment analogous to the active site of an enzyme deep within a protein cavity.

6. Conclusions and future directions

The last few years have seen the development of a large number of heterogeneous catalysts for use in nearly every aspect of oxidation, with a growing number being considered for commercial use in industrial processes. While serendipitous discoveries will continue to be made, our understanding of the problems associated with clean synthesis and of the nature of solid catalysts will enable an increasingly more logical approach to the subject. With a reduction in waste production being of utmost concern, catalyst stability and selectivity are important issues.

An area of growing importance is concerning the surface modification [90,91]. Here, surfaces are modified typically by binding of organic molecules onto the support material covalently. Within the field of chromatography this methodology has been researched for several years, but has always been hampered by the relative instability of the bonded phases under reaction conditions. There are still many problems in obtaining adequate proof that a supposed heterogeneous catalyst is actually operating in a truly heterogeneous manner. Sheldon et al. [92] has highlighted that the conventional practice of recycling a heterogeneous catalyst without observing any significant loss of activity is by no means proof of heterogeneity. It appears now common place for true heterogeneity to be tested by filtering the catalysts at the reaction temperature (before completion of the reaction) and testing the filtrate for activity. Though this seems an ideal test, examination of the mixture for leached catalyst and a true understanding of the catalysts role is vital to confirm heterogeneity. As awareness grows concerning the prevention of leaching from catalysts, newer methods are being developed which are capable of yielding more stable materials. One possible method of value is via the chlorination of silica (carried out most efficiently using a fluidised bed reactor), followed by nucleophilic substitution of a chloride with an organometallic reagent (typically RMgX or RLi) giving relatively stable surface species based on surface Si–C bonds [93]. Sol–gel techniques also provide suitable methods for incorporating metal ions [94] and firmly attached organic functions. Further developments in surface architecture will pave the way for the heterogenisation of more stable and elaborate catalytic functions.

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