

Environmentally Friendly Catalytic Methods

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1 Introduction

Increasingly demanding environmental legislation, public and corporate pressure and the resulting drive towards clean technology in the chemical industry with the emphasis on reduction of waste at source will require a level of innovation and new technology that the industry has not seen in many years.¹ Established chemical processes that are often based on technology developed in the first half of the 20th century, may no longer be acceptable in these environmentally conscious days. 'Enviro-economics' will become the driving force behind new products and processes. The cost of cleaning up chemical processes and plants and adopting the best environmental option will be high and could even exceed current R&D expenditure within the European Union. This level of expenditure brings with it an unprecedented opportunity for applied research aimed at developing new and more environmentally friendly chemical processes and for the introduction of new technology.

Catalysts played a major role in establishing the economic strength of the chemical industry in the first half of the 20th century and the clean technology revolution in the industry will provide new opportunities for catalysis and catalytic processes. While the overwhelming majority of chemical processes introduced in the last 50 years depend on catalysis, the market growth potential for catalysis is still considerable and especially in the fine and speciality chemicals industries where catalysts are relatively rarely used or where homogeneous catalysts are difficult to separate and require additional processing stages. Some of the major goals of clean technology in the chemical industry are to increase process selectivity, to maximise the use of starting materials (aiming for 100% atom efficiency), to replace stoichiometric reagents with catalysts and to facilitate easy separation of the final reaction mixture including the efficient recovery (and hopefully reuse) of the catalyst. The use of solid mostly inorganic catalysts often based on common porous support materials promises to go a long way towards achieving these goals in many important chemical processes where current technology is very inefficient or leads to unacceptable levels of waste. Their use is also a good example of 'heterogenisation' whereby the inorganic reagents or catalysts are segregated from the liquid phase facilitating their separation, recovery and reuse.

Supported reagents based on inorganic materials have been known for almost 30 years and the development of the subject is apparent from the steady increase in the number of research articles,

the appearance of several books,^{2–5} the first international symposia and the first industrial applications.⁶ Useful inorganic support materials generally have a large surface area (typically $> 100 \text{ m}^2 \text{ g}^{-1}$) and are often porous. They include zeolites although their microporosity may make them less amenable to liquid phase processes commonly used in fine and speciality chemicals manufacturing, than vapour phase processes (where they are well established) due to poor diffusion rates and pore blockage by larger molecules. Silica gels, aluminas and clays are often used as supports and newer mesoporous inorganic supports such as the MCMs⁷ are likely to become increasingly important in this context.

This review will focus on supported reagent type catalysts based on porous inorganic support materials, and liquid phase organic reactions in which they are used.

2 Supported Reagents

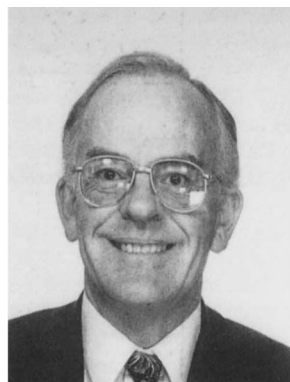
The original principle behind the use of supported reagents was to achieve an increase in the effective surface area and hence activity of potentially useful but insoluble inorganic reagents *via* their dispersion over high surface area inert support materials. The majority of supported reagents reported since then have been stoichiometric^{2,3,8} in their chemistry so that at best only the support material could be recovered and reused. Increasingly, the emphasis has been shifted towards truly catalytic materials, which can involve dispersed acid or basic sites or other reagents that are catalytic in their action or have been rendered catalytic by interaction or reaction with the support. Thus, Brønsted and Lewis acids can be supported (*e.g.* silica- H_3PO_4 , clay- ZnCl_2) as can bases (*e.g.* alumina- NaOH , alumina-KF) but it is also possible to prepare other catalytic supported reagents (*e.g.* supported phase-transfer catalysts) and to prepare catalytic forms of species that are normally stoichiometric in their chemistry (*e.g.* alumina- Cr^{VI}).⁵

The factors likely to be considered in preparing a supported reagent are:

(i) Choice of support material.

(ii) Support pretreatment (including drying to remove loosely bonded water and treatment with aqueous HCl to maximise the coverage of surface OH groups).

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Canada and England, he joined the academic staff at York in 1979. He was appointed to the Chair in Industrial and Applied Chemistry at York in 1994. His research interests cover Clean Synthesis, Supported Reagents, Materials Chemistry and Fluorine Chemistry. He has written or edited four books in these areas and his research has led to awards from the SCI, RSC, RSA, and the EU. He currently holds a Royal Academy of Engineering/EPSRC Clean Technology Fellowship.

Duncan Macquarrie received his BSc and PhD degrees from the University of Strathclyde, Glasgow. In 1985 he moved to the University of York, as a Postdoctoral Fellow under the supervision of Prof. James Clark, researching into the phase transfer catalysis of nucleophilic fluorination reactions. He then moved to Contract Chemicals, where he was a member of the team which developed



the range of Envirocat catalysts. After spells in research at Ciba Geigy (Trafford Park) and R+D at Lonza (Switzerland) he returned to York in October 1995 to take up a position as Royal Society University Research Fellow, where his current research interests are in novel heterogeneous catalysts via chemical surface modification. He is co-author of a book on supported reagents, and is the author of several papers and patents.

Table 1 Methods of preparing supported reagents

Method	Comments
<i>Impregnation (evaporation)</i> – filling the pores of a support with a solution of the reagent followed by evaporation of the solvent	Widely used Good control over dispersion and loading Requires an appropriate solvent
<i>Precipitation/coprecipitation</i> – of the reagent on to the support	Valuable for poorly soluble reagents Difficult to control
<i>Adsorption from solution</i> – selective removal of the reagent from the solution	Easy to carry out May be inefficient
<i>Intimate solids mixing</i>	Simple to carry out Avoids the use of any other chemical Unlikely to be efficient
<i>Ion exchange</i>	Simple and effective for materials with exchangeable ions (largely zeolites and clays)
<i>Sol-gel techniques</i> – starting from a functionalised silane monomer	Does not require a pre formed support Silane monomer must be synthesised Difficult to control material structure
<i>Silylation of the support</i>	Utilises the known structure of a pre formed support Silane monomer must be synthesised Resulting surface groups can be easily lost
<i>Chlorination and derivatisation of the support</i>	Efficient surface chlorination is quite easy Si-Cl groups are highly reactive Further reaction may require an organometallic

(iii) Reagent loading (often assumed to be at best at monolayer coverage which enables the amount of reagent to be calculated but physisorbed reagents will not be completely dispersed and the loading of chemisorbed functions is in practice, variable, there are also examples where unexpected high loadings or low loadings can apparently be beneficial)

(iv) Method of preparation (see Table 1)

(v) Supported reagent post-treatment (*e.g.* calcination to fix the reagent)

Generally, the aim is to achieve maximum dispersion so as to achieve maximum activity per unit area of support. Other factors may also prove to be important such as ensuring that the reagent is fixed to the support and will not be removed under the conditions of any reaction or separation. For industrial applications, long-term catalyst stability may be more important than initial activity if that early activity is followed by rapid decay.

The successful application of supported reagent catalysts requires a reasonable understanding of the bulk and surface structures of the material. Stability, surface area, porosity and the dispersion and nature of the active sites are all important factors that can critically affect the catalytic value of the supported reagent. Fortunately, there are numerous spectroscopic and non-spectroscopic techniques available for the study of solids and supported surfaces.⁴

The application of supported reagents can be hindered or limited by instability due to

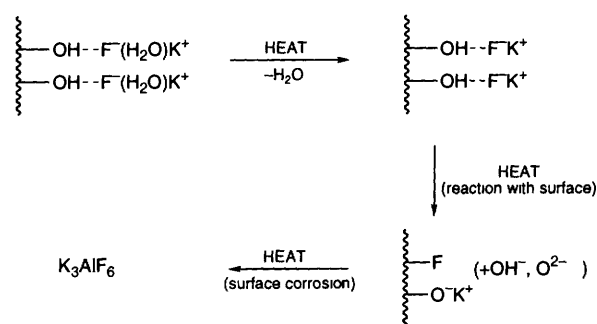
(i) Thermal decomposition of active sites (most common supports are stable up to very high temperatures although a few less

commonly used materials such as some pillared clays may break down at moderate temperatures)

(ii) Reaction of active sites with the atmosphere (solid bases for example, can rapidly adsorb CO₂-forming carbonates)

(iii) Removal of active sites in the course of a reaction (a common problem, which causes contamination of the organic mixture and prevents reuse of the catalyst)

Thermal analysis techniques (TGA, DSC, DTA) can be used to study the thermal stability of supported reagents which generally show a low temperature loss of loosely held water (and other solvent molecules), a gradual loss of chemisorbed water at higher temperatures (from surface hydroxyls), and the thermal decomposition of catalytic sites. Chemisorbed organic functions will normally decompose at *ca.* 300 °C or higher, which is adequate for most liquid phase reactions. Low temperature thermal events from changes to inorganic reagents are less common but can be important [*e.g.* the decomposition of supported Fe(NO₃)₃, the reaction between CuO and the charcoal support or phase changes in supported ZnCl₂]. The thermal behaviour of the superficially simple supported fluorides such as the widely used solid base KF-alumina, is particularly complex and very important (Figure 1).⁹

**Figure 1** Changes in the nature of KF-alumina on heating

While dispersion of the reagent/active sites over the surface of the support material is often only one of several factors affecting the performance of a supported reagent, it remains a very important one. Generally, high surface areas are preferred although the choice of support material is unlikely to depend on that alone. Surface areas of common supports are in the 100–1000 m² g⁻¹ range with the new MCM materials having particularly high values (even to > 1000 m² g⁻¹). Most commonly used support materials are either microporous (pore diameters 3–20 Å) or mesoporous (20–500 Å) with mesoporosity likely to give a reasonable balance between good diffusion rates and useful in-pore effects (*e.g.* high local concentrations of reagent sites to enhance reaction).¹⁰ Zeolites are the best known microporous solids although swelling clays also commonly have interlamellar spacings of less than 10 Å. Pillared clays and non-aluminosilicate molecular sieves (*i.e.* porous solids with regular structures) have pore diameters in the 10–20 Å range. Acid treated clays can contain mesopores as a result of the break up and reorganisation of the aluminosilicate structure (dealumination).¹¹ Until recently mesoporous solids were restricted to amorphous materials with broad pore size distribution (silicas and aluminas). In 1992 the first truly mesoporous molecular sieves were reported.⁷ These 'MCM' materials opened the way to the synthesis of ordered porous solids with high surface areas and tunable pore diameters bridging the zeolites and the common amorphous silicas. Little is known about the use of these materials as supports but the potential is considerable.

Reactive reagents notably hydroxides and fluorides will corrode the surfaces of common support materials so that the actual surface species present may be more complex than might be expected (see Figure 1 for example) and surface areas can be much reduced. Even the simplest methods of supported reagent preparation can give good dispersion of most reagents as witnessed by techniques such as electron microscopy, X-ray diffraction and where the reagent is amenable, diffuse reflectance Fourier transform infra red (FTIR) spectroscopy.

One of the most interesting features of supported reagent chemistry which has become particularly significant in recent years, is that the activity of the composite material (A_{SR}) is not usually a simple sum of the component parts ($A_S + A_R$). The value of this in catalysis is when $A_{SR} > A_S + A_R$.

This increase in activity is a result of a synergistic effect between the reagent and the support. The exact nature of this effect when it occurs is variable. In extreme cases it can be due to actual reaction between the support and the reagent such as in the case of some supported fluorides.⁹ In other cases it is more subtle with an increase in the number of available sites and/or the local in-pore concentration of sites (mini reaction vessels) being responsible such as is the case for supported zinc chloride.¹⁰

The nature of an adsorbed reagent can be investigated by numerous techniques. Diffuse reflectance FTIR and magic angle spinning (MAS) NMR spectroscopies are especially popular. The useful information that can be obtained by such studies includes

(i) Identification of the surface species (*e.g.* to confirm that the original reagent is intact or to identify new species formed *via* support–reagent reaction)

(ii) Information on the strength of the interaction between the support and the reagent

(iii) Identification of sites including Lewis and Brønsted acid sites and determination of their relative strength (*e.g.* through the use of spectroscopic titration techniques such as those based on the use of pyridine⁴)

(iv) Determination of any changes to the bulk support structure as a result of corrosion of the support by attack of the reagent

Through the use of spectroscopic and non-spectroscopic techniques it is possible not only to understand the behaviour of supported reagent catalysts but also to help optimise their performance in organic reactions

3 Catalysis using Supported Reagent Solid Acids^{2,3,5}

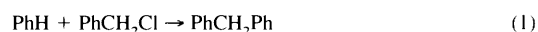
Solid acids are the most widely studied and commonly used heterogeneous catalysts. They are used in many important large-scale vapour phase manufacturing processes such as catalytic cracking (X and Y zeolites), alkylation (zeolites, $\text{SiO}_2\text{-H}_3\text{PO}_4$), and paraffin isomerisations (chlorinated Pt– Al_2O_3) with the scale of larger reactions exceeding 10^9 kg per year. All solid acids are characterised by the presence of surface protons or coordinatively unsaturated cationic centres which give Brønsted or Lewis acidity. The number of acid sites gives the total surface acidity while their structure determines the acid strength. Lewis and Brønsted acid sites are often present together and may be sufficiently strong to justify the term 'solid superacids' ($H_0 < -12$) which can enable the catalysis of demanding reactions such as transformations of alkanes.

Suitable solid acid catalysts for reactions under more moderate conditions than typical petrochemical type reactions and in the liquid phase, include those based on clays, silicas and zeolites. In many cases they are sought as replacements for inexpensive liquid or soluble acids such as H_2SO_4 , HF and AlCl_3 and relatively low cost solids are required. The environmental unacceptability of using large volumes of corrosive acids and of the waste resulting from the work-up of such reactions, which usually requires the neutralisation/decomposition of the acid, is a strong driving force for developing environmentally friendly processes based on solid acids. The range of acid-catalysed liquid phase reactions is enormous and includes Friedel–Crafts reactions, halogenations, and nitrations with relevance to almost all sectors of the fine, speciality and intermediates chemical industries.

Friedel–Crafts reactions probably represent the most important range of 'named' reactions in organic chemistry. They include acylations, benzoylations, alkylations and sulfonylations giving an enormous range of useful products including ketones, alcohols, alkyaromatics and sulfones. Many batch processes operating in a very large number of companies use AlCl_3 as the soluble acid catalyst.⁶ The reagent is inexpensive and very reactive being one of the most powerful Lewis acids. Unfortunately, it is difficult to handle

being readily hydrolysed by water (and therefore unstable to the atmosphere) giving health and safety, and storage problems. The work-up reactions using AlCl_3 present further problems with the usual water quench creating an acidic, aluminium-rich waste stream. The problem is particularly acute with reactions involving products that are capable of acting as Lewis bases such as ketones which complex the AlCl_3 . In these cases, at least stoichiometric quantities of AlCl_3 are required, indeed in the case of sulfone-forming reactions, up to three mole equivalents are used to ensure good conversion. The quantity of waste generated in these reactions greatly exceeds the amount of product.¹ Other problems with AlCl_3 'catalysed' reactions include lack of selectivity with polyalkylation being a particular problem. Alternative homogeneous reagents fare little better. Hydrogen fluoride has useful activity but presents its own special hazards due to its extremely corrosive nature.

Solid acid supported reagents based on inexpensive inorganic solids notably clays and silica show promise as Friedel–Crafts catalysts as do some modified zeolites. Many clays have been investigated including bentonites, vermiculites, halloysites, and kaolinites. Ion-exchanged clays can show much improved activity over the raw materials and especially those based on acid treated clays such as the commercial material K10 (which can itself be a useful solid Brønsted acid). The activity of ion-exchanged clays is very dependent on the cation so that in the benzylation of benzene using benzyl chloride for example (1), the order is $\text{Fe}^{\text{III}} > \text{Zn}^{\text{II}} > \text{Cu}^{\text{II}} > \text{Zr}^{\text{IV}} >$



$\text{Ti}^{\text{IV}}\text{Ta}^{\text{V}} > \text{Al}^{\text{III}} > \text{Co}^{\text{II}} > \text{K10} > \text{Nb}^{\text{V}}$ ¹² The order does not correspond to the order of Lewis acidities for homogeneous cations with the low activity for Al^{III} (very active in solution) and the high activity for Zn^{II} (weakly active in solution) being especially noteworthy. It is likely that at least part of the activity is due to the polarisation of water molecules by the cations within the highly polarising environment of the interlamellar regions of the clays. At best, ion exchanged clays can show activities in reaction (1) 20 times greater than the simple acid-treated clay. Selectivity to the monoalkylated product was little improved by ion exchange with only 57% isolated diphenylmethane from the fastest reaction and never better than 66%. Alcohols and alkenes can also be used as alkylating agents but the rates of reaction are significantly reduced and the orders of activity of the clay are not the same, although the Ti^{IV} exchanged clay in particular is active with all of the alkylating agents. It is also important to note that these catalysts are reusable at least to some extent.

Perhaps the greatest breakthrough in the use of solid acid catalysts in Friedel–Crafts reactions came with the discovery that supported (as opposed to ion exchanged) zinc chloride on K10 was an extremely active and reusable catalyst for benzylation reactions such as (1).¹³ The activity is several orders of magnitude greater than that of the ion-exchanged materials with the model reaction being complete in minutes at room temperature and giving a particularly high yield of diphenylmethane (80%). Like the ion-exchanged materials, the activity of the K10 supported reagents does not correlate with solution phase activities of the reagents so that supported ZnCl_2 and CuCl_2 are especially active while supported AlCl_3 is a poor catalyst. 'Clayzic' has been the subject of intense research since its discovery in 1989 and also forms the basis of an industrial catalyst. It is a particularly striking example of a supported reagent that is considerably more active than its constituent parts and this is in part explained by a structural change to the support. Acid treatment of the montmorillonite clay causes a breakdown in the lamellar structure and the creation of mesopores which are occupied by the ZnCl_2 (Figure 2).¹⁰ Thermal activation of clayzic results in further structural changes but the catalytic activity of the material does not correlate with its surface area¹⁴ – a good example of a supported reagent catalyst where surface area is not the most important factor. Spectroscopic titration of the active sites on clayzic reveal the presence of weak Lewis acid sites but little Brønsted acidity (K10 itself shows Brønsted acid sites only),¹⁰ indeed mesoporous silica supported ZnCl_2 which can be as active as clayzic, can be a pure solid Lewis acid. The remarkable activity of supported ZnCl_2 cannot be

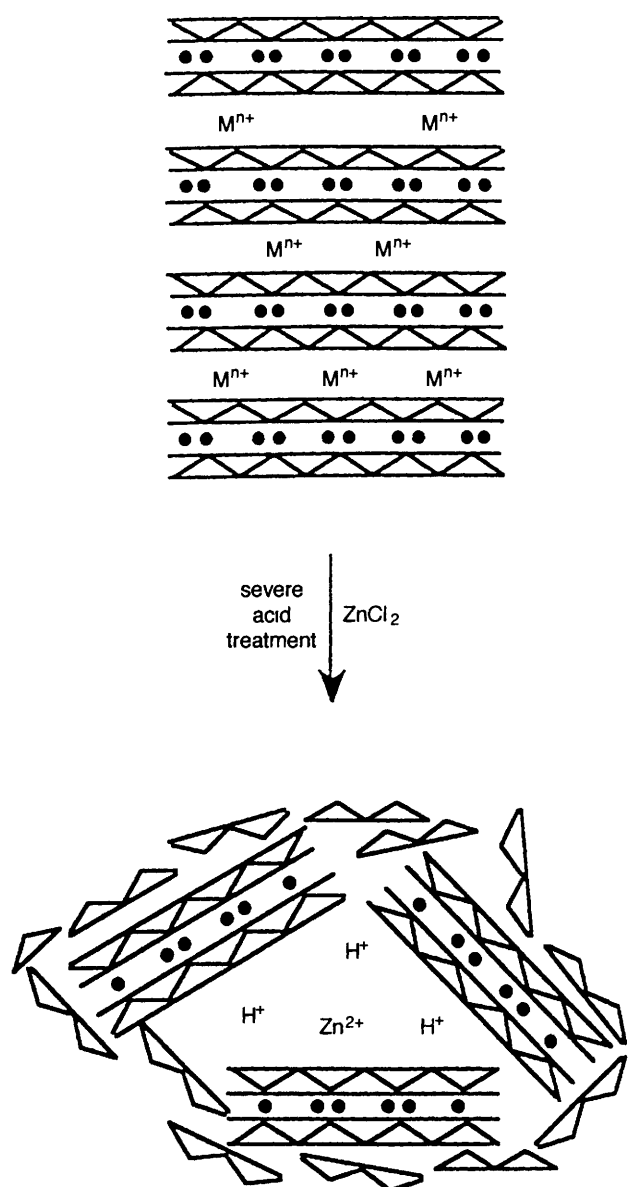


Figure 2 Structural representation of the formation of clayzic

due to strong acid sites – rather it is likely to be due to a high concentration of sites within the constrained in-pore environments

Clayzic has been used to catalyse various Friedel–Crafts reactions including those of aromatic substrates with alkyl halides, aldehydes and alcohols. In the commercial manufacture of diphenylmethanes for example, product yields of over 75% can be achieved by using this catalyst, which is also easily recovered and can be reused.¹ Use of homogeneous AlCl_3 leads to product yields of less than 50% and the work-up procedure is difficult and destroys the AlCl_3 . Other applications include the preparation of benzothiophenes by cyclisations of phenylthioacetals (normal catalysts can cause extensive polymerisation of the thiophenes and the pores in clayzic are believed to favour the desired intramolecular cyclisation at the expense of the polymerisation – Figure 3),¹⁵ and the olefination of benzaldehyde (involving a previously unknown reaction mechanism – Figure 4)¹⁶

Interestingly, when two or more possible substrates are present,

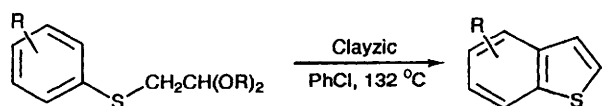


Figure 3 Formation of benzothiophenes using clayzic

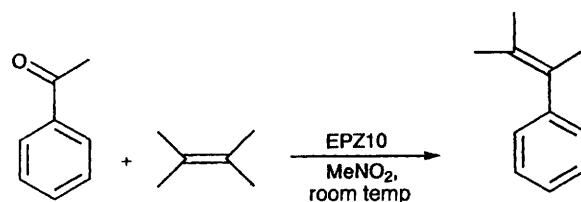
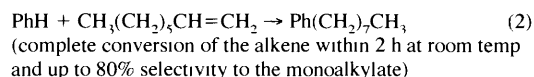


Figure 4 Olefination of benzaldehyde using clayzic (in its commercial form 'EPZ10')

reaction occurs first with the more polar substrate whatever its normal relative reactivity. Thus, with a mixture of an alcohol and an alkyl halide, the alcohol will always react first although the alkyl halide is more reactive.¹⁷ The discrimination can be more subtle so that for haloaromatics, the order of activity in clayzic-catalysed alkylations is $\text{PhBr} > \text{PhCl} > \text{PhF}$, PhH , which parallels the polarisability of the substrate although it is the exact opposite of the activities in solution phase reactions.¹⁸ These observations are consistent with the presence of highly polar pores in the catalyst and with molecular sieving on the basis of molecular polarity/polarisability.

The widespread use of AlCl_3 in Friedel–Crafts and other acid-catalysed reactions along with its environmental unacceptability makes it an obvious target for heterogenisation *via* a supported reagent. Early attempts to prepare an active form of supported aluminium chloride had limited success with promising results in vapour phase processes such as long chain alkane isomerisations and hydrocarbon cracking reactions, but poor activity in liquid phase reactions.¹⁹ More recently, a new form of the supported reagent has been prepared and found to be highly active in some liquid phase Friedel–Crafts reactions.²⁰ Mesoporous silica and acid-treated montmorillonite supported aluminium chloride (prepared by reaction of the support with either AlCl_3 or RAlCl_2 in an aromatic solvent) is particularly effective in catalysing the reactions of alkenes with aromatics such as that of oct-1-ene with benzene, eqn (2) – remarkably the activity of the solid acid is comparable to



that of homogeneous AlCl_3 , but its selectivity towards monoalkylation is significantly superior. Greater selectivity is also observed in the dodecene–benzene reaction with the desired 2-alkyl isomer (this isomer gives the best emulsibility characteristics in detergency applications) being produced in 47% yield (32% with homogeneous AlCl_3 , 13–20% with HF). As with clayzic and other supported reagents, the optimum pore size is at the low end of the mesoporous range (*ca* 70 Å). Alkyl halides also react quite well with aromatics in the presence of supported aluminium chloride so that dichloromethane for example reacts with benzene to give diphenylmethane in a yield of 62% after 2.5 h at 40 °C. A comparison of supported aluminium chloride with supported zinc chloride, two of the more promising solid acids for Friedel–Crafts alkylations would suggest that the former is considerably more active (strong Brønsted and Lewis acid sites are revealed by spectroscopic titration) but the latter is an extremely useful mild Lewis acid catalyst.

Supported reagents have been used rather less to catalyse aromatic halogenations although zeolites have been proved to give enhanced *para*-selectivity in, for example, the chlorination and bromination of alkylaromatics (up to 75% in the chlorination of toluene using elemental chlorine²¹ and up to 95% in the bromination of toluene using elemental bromine²²).

Aromatic nitration, a particularly wasteful and hazardous industrial process, has benefited relatively little from the use of supported reagents with very low conversions usually accompanying any good isomer selectivities (*e.g.* using zeolites) or good conversion and selectivity requiring inconvenient reaction times at high dilution. The combination of the H^+ form of zeolite beta and acetyl nitrate as the nitrating agent can, however, give good selectivities (*e.g.* 79% *para* for toluene) in fast reactions.²³

Numerous other typically acid-catalysed reactions have been

successfully carried out in the presence of supported reagent-type solid acids where the solids have replaced conventional acids such as mineral acids, AlCl_3 , BF_3 and FeCl_3 , among others. Some of the more interesting recent examples include the single-pot synthesis of methyl *tert*-butyl ether from *tert*-butyl alcohol and methanol using dodecatungstophosphoric acid supported on clay²⁴ and the use of pillared acid-activated clays for Brønsted catalysed processes such as alkene alkylations and alcohol dehydrations²⁵.

It is also worth noting the early successes emerging from studies on the use of MCM type materials as solid acids²⁶ – this area seems likely to develop quickly.

4 Oxidation Catalysis using Supported Reagents

The partial oxidation of organic substrates provides routes to a wide range of important functionalised molecules including alcohols, aldehydes, ketones, epoxides and carboxylic acids. Traditional methods of oxidation often involve the use of stoichiometric quantities or large excesses of poisonous high oxidation state chromium, manganese and osmium reagents. Environmental and economic factors make the use of these reagents increasingly unacceptable. Oxidation processes based on lower oxidation state transition metals such as Co^{II} , Mn^{II} and Cu^{II} in acetic acid media are also known and some are catalytic in the metal using molecular oxygen as the consumable oxidant, but the conditions are often harsh, the reagent mixture is corrosive (bromide is used as a promoter), and the chemistry is rarely selective. Environmentally acceptable catalytic partial oxidations of inexpensive substrates (including hydrocarbons) that operate under moderate conditions in the liquid phase (most suitable for many of the industrial beneficiaries) with a high degree of selectivity are clearly desirable.^{1,6}

A large number of supported reagents have been used in the liquid phase partial oxidation of organic substrates.^{2,3,5} The low cost of the support (commonly chromatographic materials such as silica gel), the mesoporosity of many of these supports, and the other general advantages of supported reagents (ease of handling, use and recovery, low toxicity and the avoidance of solvents) make them very attractive in the context of clean synthesis. However, in oxidations, supported reagents have generally acted as stoichiometric reagents being effectively dispersed forms of traditional oxidants.⁸ There are notable exceptions to this which promise much for the future of supported reagent oxidation catalysis. These are the new molecular sieves which incorporate active metal centres (notably Ti and V) in their structures, and chemically modified support materials which have active metal centres on their surfaces.⁵

While established aluminosilicate zeolites have proved popular in high temperature oxidation processes,^{1–3} their value in selective oxidations typically carried out in the liquid phase is less. There has, however, been considerable early success in the use of other molecular sieves notably the titanium silicates such as TS-1 which are already being used in commercial units.²⁷ The catalysts are synthesised from typical sol-gel preparations involving tetraethyl-orthotitanate and tetraethylorthosilicate. High Si/Ti ratios minimise titanium centres with titanium nearest neighbours, and maximise activity. The pore diameter of TS-1 is only 5.5 Å which is very restrictive in terms of accessible substrates and products but despite this, it has been successfully used in the hydroxylation of aromatics, the epoxidation of alkenes, in ammoxidation, amine oxidation and the oxidation of alcohols and thioethers. In the hydroxylation of toluene for example, the selectivity to *para*-cresol is an impressive 81% (Figure 5). The most important application for TS-1 to date is probably the hydroxylation of phenol, giving mixtures of hydroquinone and catechol. This represents a very clean option giving excellent conversion to product and very little waste. The TS-1 process is not only cleaner than the alternatives (avoiding the use of strong acids or soluble transition metal catalysts) it also outperforms them, particularly in terms of conversion (because of the much lower amounts of tars which result from side reactions and overoxidation). Catalytically active Si–O–Ti sites can also be formed *via* treatment of preformed silica with an active source of Ti such as TiF_4 .

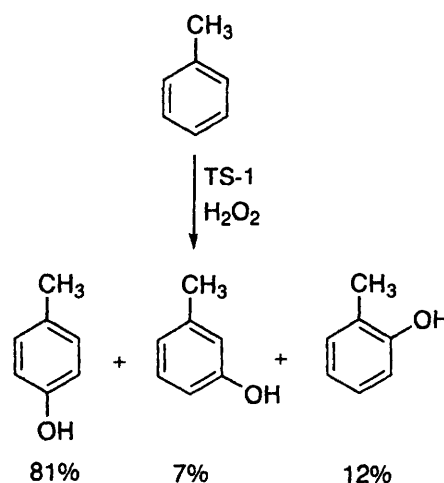


Figure 5 Hydroxylation of toluene catalysed by TS-1

Vanadium silicate molecular sieves are capable of selectively oxidising 4-chlorotoluene to 4-chlorobenzaldehyde using hydrogen peroxide as the source of oxygen in acetonitrile solvent (Figure 6).²⁸

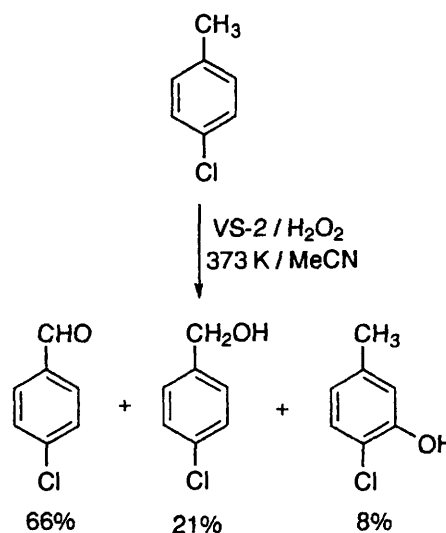


Figure 6 Oxidation of chlorotoluene catalysed by a vanadium silicate

Vanadium has also been incorporated into the structure of MCM materials to give efficient catalysts for the oxidation of large molecules such as cyclodecane with hydrogen peroxide.²⁹ Molecular sieves containing structural chromium can also be active in oxidations notably those of amines to nitro compounds using *tert*-butyl hydroperoxide as the oxidant.³⁰

While original forms of supported reagents involving high oxidation state metal oxidants were stoichiometric, *e.g.* KMnO_4 -silica and $\text{K}_2\text{Cr}_2\text{O}_7$ -silica, genuinely catalytic materials derived from the reaction of dichromate and permanganate with alumina were reported in 1989.³¹ The materials are prepared from aqueous solution by careful control of pH and other reaction conditions. The concentrations of metal centres at the support surface are very low and while their identity is unknown, a surface structure for the supported chromium species, based on chemically bonded Cr^{VI} has been suggested as part of a proposed mechanistic pathway in catalytic oxidations (Figure 7). The supported chromium catalyst is active in alkyl benzene oxidations using only air as the source of oxygen and the neat substrate as the reaction medium – the ideal system from an environmental point of view. In a typical oxidation, that of ethylbenzene to acetophenone, the only other product is water and the catalyst can be used in very small quantities and is reusable. The major drawback with the catalyst and the manganese analogue are their low activities – rates of oxidation of alkylaromatics of only

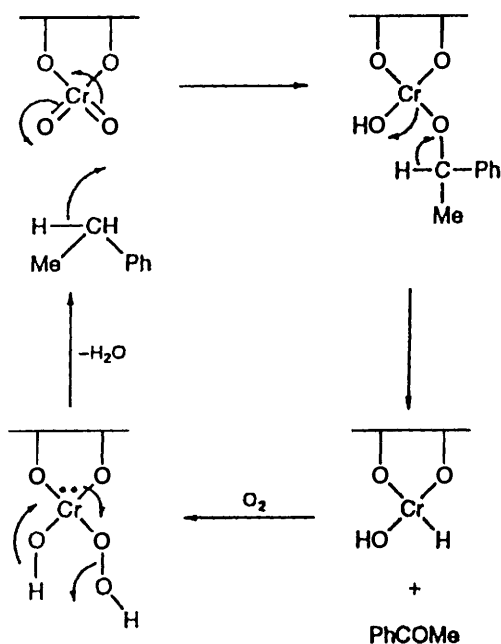


Figure 7 Possible mechanism for oxidations catalysed by supported chromium (VI)

1–2% h⁻¹ are possible at > 100 °C so that prohibitively long reaction times are required for good overall substrate conversions

Recent reports of oxidation catalysts based on chemically modified support materials that can complex metal ions with useful redox properties including cobalt, copper and iron may well represent a way forward in this field. Such materials can be more robust than simpler metal–support materials and can show activity very similar to their homogeneous analogues. Effective catalysts include cobalt immobilised on silica which has been derivatised with carboxylic acid functions (Figure 8).³² This will catalyse the epoxidation of

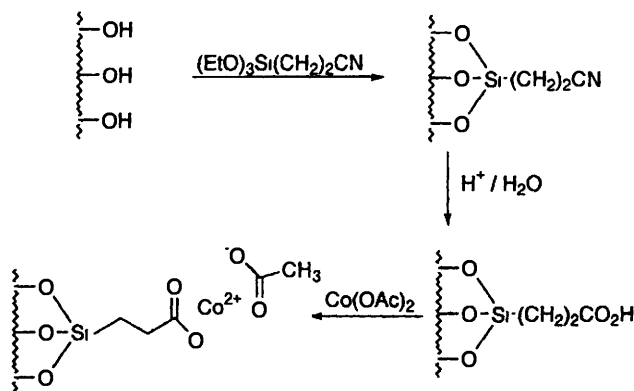


Figure 8 Formation of a supported cobalt catalyst based on a chemically modified silica

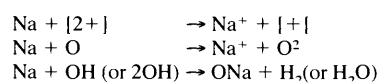
alkenes using air and a sacrificial aldehyde. Significant features of the catalysis include the high selectivity normally leading to the epoxide product only (diols, commonly formed in homogeneous peracid reactions are not observed) and the ability of the catalyst to retain its metal ion even under harsh conditions.

5 Catalysis using Supported Reagent Solid Bases^{2–5}

In contrast to the areas of heterogeneous oxidation catalysis and solid acid catalysis, the use of solid base catalysis in liquid phase reactions has not seen the same level of major breakthroughs. This is partly because the negative environmental impact of chemical processes using conventional acids and metal oxidants has attracted

more attention than those based on such as NaOH. Base catalysis is, however, widely used both on a laboratory and industrial scale, and the handling, separation, treatment and disposal of basic reagents and basic waste can all be troublesome.

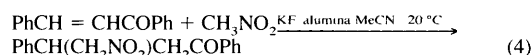
Several different supports have been used for preparing solid bases, with alumina based catalysts being the most widely studied in organic synthesis. Most common basic reagents have been supported including alkali metals (*e.g.* alumina–Na and silica–K), alkali metal hydroxides (*e.g.* alumina–KOH) and metal alkoxides (*e.g.* xonolite–KOBu^t). Zeolite materials that have been exchanged with alkali metal cations and Cs⁺ in particular can also act as solid bases being particularly useful for higher temperature vapour phase processes. Of these some of the more interesting are the immobilised alkali metals which can be prepared in a variety of ways including treatment of the support with a solution of the metal in liquid ammonia. The solids are often brightly coloured which is due to the formation of colour centres of one electron donor character.



These materials have been referred to as solid superbases (estimated $H > 37$) and they are capable of promoting reactions of hydrocarbons such as the isomerisation of 5-vinylbicyclo[2.2.1]hept-2-ene to 5-ethylidenebicyclo[2.2.1]hept-2-ene (used as a comonomer in the production of synthetic rubber).⁵

Surprisingly, perhaps the most widely studied supported reagent solid base in the context of organic synthesis is not based on a conventional base. Attempts to support ionic fluorides and hence render them more active for nucleophilic fluorinations have been largely unsuccessful but have led to the discovery of remarkably useful solid bases.^{4,5,9} Simple metal fluorides such as KF are known to be weak bases but their dispersion over a support is not enough to explain the often powerful basicity exhibited by KF–alumina, for example. The surface chemistry is in fact quite complex (see Figure 1) and oxide and hydroxide sites are likely to contribute to the basic properties. When at their most active, supported fluorides are capable of adsorbing large quantities of carbon dioxide from the atmosphere which reduces their activity through the formation of surface carbonates. These facts help to explain the diversity of claims in the literature over their activity which has been variously described as weakly basic, strongly basic and even superbasic.¹

Supported fluorides have been used in a wide range of typically base catalysed reactions (Table 2) as well as several stoichiometric reactions. KF–alumina is certainly the most widely studied although important variables such as loading and supported reagent post-treatment remain contentious issues. The basic catalyst is especially effective in carbon–carbon bond forming Michael reactions (*e.g.* reaction 4) and it is interesting to note that some of these have



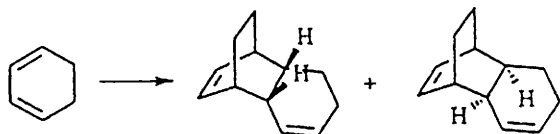
been translated into continuous flow reactions based on fixed catalyst beds.

Table 2 Some of the reactions catalysed by KF–alumina

Reaction	Example
Oxidation of alkylaromatics	Ph ₂ CH ₂ → PhCO
Alkylations	PhOH + MeOH → PhOMe
Condensations	EtCHO + MeNO ₂ → EtCHOHCH ₂ NO ₂
Rearrangements	ArCH ₂ CH=CH ₂ → ArCH=CHMe
Michael reactions	AcCH=CH ₂ + EtNO ₂ → Ac(CH ₂) ₂ CHMeNO ₂
Additions	CHCl ₃ + <i>m</i> O ₂ NC ₆ H ₄ CHO → <i>m</i> O ₂ NC ₆ H ₄ CH(OH)CCl ₃

6 Other Supported Reagent-catalysed Reactions and Future Trends

Numerous other types of supported reagents (including those based on organic polymers which are beyond the scope of this review) have been developed and applied to liquid phase organic reactions. These include catalysts for Diels–Alder reactions which enable the reaction to be applied beyond the normal electron rich dienes and electron poor dienophiles, and in some cases allow the use of water as the solvent (a particularly important goal in clean synthesis)^{2,3,5} Perhaps the best solid catalyst for these reactions is Fe³⁺ – montmorillonite which can result in a dramatic improvement in reaction rates (e.g. see Figure 9)



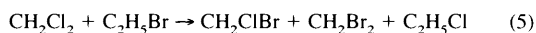
Conditions

Fe³⁺ – K10 clay, *p*-Bu' C₆H₄OH (10%), 0 °C 1h
200 °C, 20 h, no catalyst

Isolated product
yield (%)
77
30

Figure 9 Diels–Alder reaction catalysed by Fe³⁺ – montmorillonite

Apart from solid acid catalysed halogenations, other supported reagents have been used in halogenation reactions. These include supported phase transfer catalysts such as alumina–Bu₄PBr which will catalyse the halogen scrambling reactions between haloalkanes, eqn (5). The immobilisation of phase transfer catalyst may



intuitively seem surprising but the concept of 'triphase catalysis'³³ has in fact been known for some 20 years. The insoluble supported catalyst can act very effectively at the organic–aqueous interface and offers the usual advantages of supported reagents, notably easy separation and reuse. It is often physically difficult (due to very good solubility in most solvents, and limited thermal stability) and rarely economic to recover a soluble phase transfer catalyst. These facts have restricted their use and added to the waste generated from chemical processes.

Chemically fixing a catalytic structure such as an organometallic complex to a support material is a simple illustration of 'heterogenisation' whereby the useful properties exhibited by the catalyst in solution are hopefully maintained in the solid base. Apart from applications relevant to acid catalysis and oxidation catalysis outlined earlier, the principle has been successfully applied to other important reactions in the liquid phase such as hydrogenation, asymmetric reduction and the deprotection of acetals^{2,3,5}. Very significantly, the direct grafting of an organometallic complex onto the inner walls of a mesoporous silica has recently been used to prepare, *via* removal of the organic ligands by calcination, a new form of supported Ti⁴⁺. This method is superior to other, more conventional forms of grafting, as it does not lead to undesired titano–oxospecies. The catalyst is active in epoxidations with *tert*-butyl hydroperoxide as the oxidant³⁴.

Supported reagent type catalysts have already proved their value in many organic reactions as environmentally friendly replacements for established reagents and catalysts that through their corrosive or toxic nature, or difficulty in separation and recovery from reactions lead to unacceptable chemical waste. The scope of these catalysts in liquid phase reactions is expanding on many fronts and commercial catalysts and industrial processes based on their use are now a reality³⁵. 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. Much remains to be done including improvements in catalyst activity, selectivity and stability particularly in areas such as Friedel–Crafts acylation,

nitration and base catalysis. Process engineering aspects of the subject such as separation techniques and the translation of batch-type processes to continuous processes are also very important issues. There are many interesting new developments emerging including the availability of controlled pore materials that may enable the right balance between activity and selectivity in liquid phase reactions to be achieved. Chemical surface modification also has much to offer and research into ways of achieving high surface coverage and robust structures is very important if the catalytic potential of these materials is to be fully realised. The way is clear for a greener future!

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