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VOLUME 33:
HETEROGENIZED HOMOGENEOUS CATALYSTS FOR FINE CHEMICALS PRODUCTION

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Foreword: So Why Do We Need Supported Catalysts?

We live in the Oil Age – but not for long. Unlike the Stone Age, Bronze Age or Iron Age, which lasted many thousands of years and, in the case of the Iron Age, is continuing, the Oil Age will extend over only about 150 years. Nehemiah may have discovered oil 2,500 years ago [1], but it was not until the invention of internal combustion engines by Lenoir (1861), Rochas (1860) [2], and especially Otto (1861, 1876 [3]) and their use by Benz and Daimler in cars that oil came to be used as a fuel [4]. Since then, oil has proven to be so useful that massive fortunes have been accumulated by countries where it occurs naturally (even the King in Nehemiah’s day saw its potential: “The king, after verifying the facts, had the place (where the oil was discovered) enclosed and pronounced sacred. To the people on whom the king bestowed it, he granted a part of the considerable revenue he derived from it” [1]) and even wars have been fought over it. Best estimates indicated that, if usage continues at the present rate, readily extractable (so cheap) oil will only last for another 40 years and this projection has hardly changed, since 25 years ago the estimate was 60 years [5]. Gas does not have a much longer lifetime unless methane hydrate can be exploited cheaply but coal will last for several hundred years.

In many ways the diminishing reserves and availability of fossil fuels are a good thing, because the other major problem is that their use immediately or eventually produces carbon dioxide, the major gas implicated in Global Warming and Climate Change, one of the greatest threats to life on earth if it is allowed to proceed unchecked [6]. Use of all the available reserves of oil, gas and coal would lead to unacceptable warming, but their diminishing supply means that there will be a natural end to this source of overheating of the planet.

Although the main use of fossil fuels is for the production of energy in fixed (power stations) or mobile (vehicles) installations, they also find major uses in the production of a vast array of chemical products that allow us the high standard of living we currently enjoy. The petrochemicals industry manufactures all kinds of important chemicals from building blocks for a wide variety of plastics through lubricating and other oils, the main components of shampoos, detergents, soaps, perfumes etc. to drug precursors and agrochemicals, which allow us to feed an ever increasing world population. Without the petrochemical industry we could not sustain life on the planet. We would be cold, hungry, dirty and ill.
However, there is another problem. The industries that rely on petrochemicals, as well as those that do not, sometimes use chemistry that produces large amounts of waste, often more than the amount of the desirable material. This waste must be handled and disposed of – often to toxic land-fill sites at great cost in terms of energy and amenity. Soon there will be few sites left for disposal of this kind. The smaller the amounts of product being manufactured, generally the dirtier is the Chemistry. This is well summed up in the table of E-factors (Table 1) developed by Sheldon [7], which represents the tonnes of waste produced per tonne of product manufactured. The pharmaceutical industry produces drugs of enormous benefit to mankind and very high added value, but it does this with little regard to the elimination of waste.

So this is the major challenge facing us today. How do we produce the very many chemical products upon which we have come to rely, cheaply, cleanly and with diminished use of fossil fuel resources?

Much of the answer lies in catalysis. Catalysis allows chemical reactions to be carried out under milder conditions, thus saving energy. There are three main types of catalyst. Enzymes, which nature has engineered over thousands of years to work in water at room temperature and atmospheric pressure to carry out very highly selective reactions, often selecting one feedstock from a vast array of possibilities and producing only one product with 100% selectivity in terms of chemo-, region-, and stereo selectivity. In other words enzymes can modify a particular molecule in one position to give a single product in which even the chirality is controlled. Unfortunately, the products that nature requires are not always the same as those needed for the vast arrays of feedstocks required by the Chemical Industries, so using enzymes for the kinds of products we need is not always possible. Although enzymes are used in some processes even for fairly large volume products such as the synthesis of lactic acid for the synthesis of polylactide [8], which is a biodegradable replacement for polythene or polystyrene, their very high substrate and product selectivity as well as their often low stability under conditions other than those for which they were optimised (water, room temperature, atmospheric pressure) makes them unsuitable at present for use in the wide range of processes required by the chemical industry. Manmade catalysts have therefore been introduced. These come in two forms; those where the catalyst is in a different phase from the reactants and products (heterogeneous) and those where the catalyst is either dissolved in the products or both are in a solvent, usually an organic compound.

Heterogeneous catalysts, usually metals or metal oxides can give dramatic rate accelerations, are stable to high temperature and can easily be separated from the

<table>
<thead>
<tr>
<th>Industry segment</th>
<th>Annual product tonnage</th>
<th>E factor</th>
</tr>
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<tbody>
<tr>
<td>Oil refining</td>
<td>$10^6$–$10^8$</td>
<td>Approx. 0.1</td>
</tr>
<tr>
<td>Bulk chemicals</td>
<td>$10^3$–$10^6$</td>
<td>&lt;1–5</td>
</tr>
<tr>
<td>Fine chemicals</td>
<td>$10^2$–$10^4$</td>
<td>5–50+</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>$10$–$10^3$</td>
<td>25–100+</td>
</tr>
</tbody>
</table>

Table 1  $E$ factors (tonnes of waste generated per tonne of product manufactured [7])
reaction products. Generally their selectivity is low or cannot be tuned very much, although shape selective tuning can occur using microporous solids such as zeolites. Homogeneous catalysts, which generally consist of metal centres surrounded by a variety of ligands on the, other hand are highly versatile, act under mild conditions and can give very high selectivities [9]. By varying the metal centre and the surrounding ligands, the chemo-, region- and stereo-selectivites can be tuned so that a very wide range of different product can be made available. The power of homogeneous catalysis is reflected in the award of Nobel prizes for asymmetric catalysis (Sharpless, Knowles and Noyori, 2001 ) and for alkene metathesis (Schrock, Grubbs and Chauvin, 2005) in the last 10 years.

Despite the huge promise offered by homogeneous catalysts, rather few have been commercialised. One of the main reasons for this arises because they are homogeneous. This means that the reaction products have to be separated from the catalyst and any solvent. Usually this would be done by fractional distillation, but many of the products have rather low volatility and cannot be distilled below the decomposition temperature of the (often) thermally sensitive catalyst. This separation problem and the need to use organic solvents (often volatile organic compounds, VOCs), which can themselves be pollutants.

The huge potential for using homogeneous catalysis for manufacturing a large range of desirable bulk, commodity, speciality, pharmaceutical and agrochemical products awakened scientists to the separation problem from the very early days of homogeneous catalysis research and very many ingenious approaches are being developed [10–13]. These range from biphasic systems in which the catalyst is present in one phase whilst the product is in another to catalysts that are attached to solid supports. There are hybrid systems where the catalyst is dissolved in a thin film of liquid distributed over a solid support and systems where the catalyst can be switched by a stimulus such as heat [14], light or bubbling CO₂ from a phase where the reaction occurs to an immiscible solvent from which the product can be decanted [15–17]. Sometimes the reaction can be carried out in one phase but the mixture separates into two phases on cooling, bubbling CO₂ etc. When two phase reactions are employed, the separation is usually carried out by taking some of the two phase mixture to a gravity separator where the phase containing the organic product is decanted and the catalyst phase returned to the reactor. Two examples where this approach has been commercialised are the Shell Higher Olefins Process where long chain alkenes are prepared by ethene oligomerisation and separated from the catalyst dissolved in polar 1,4-butanediol [18], and the Ruhr Chemie–Rhône Poulenc process for the hydroformylation of propene with the catalyst dissolved in water with which the product butanal is immiscible [19, 20]. These two processes both involve batch continuous processing where some of the reaction mixture is removed from the reactor and treated under quite different conditions from those in the reactor. It would be more desirable to have continuous flow reactions where the substrates and reacting gases are pumped into the reactor containing the dissolved catalyst whilst the products flow out. All the catalyst is in the reactor all the time and is kept under conditions for which it has been optimised. Continuous flow processing of this kind is possible where the reaction products
are volatile under the reaction conditions (e.g. the rhodium catalysed hydroformylation of propene, where the product butanal (b.p. 75°C) distils from the reactor at the reaction temperature (105°C) [21] or in new systems where the catalyst is dissolved in an ionic liquid [22, 23] or a high molecular mass liquid polymer such as polyethylene glycol with the substrates and products being transported out of the reactor using a supercritical fluid [24]. Although such systems can be used for a much wider range of (less volatile) substrates, they have not so far been commercialised.

For supported catalysts, the possibility exists for flow processing since they can be handled like heterogenous catalysts and used in simple flow reactors. In principle, they are very simple to use, but none have so far been commercialised. Although the idea of anchoring homogeneous catalysts onto solid supports was first investigated soon after the development of the new generation of phosphine liganded catalysts (in the 1960s) [25], usually using a modification of the ligand to provide the attachment, leaching of the liquid was always observed to some extent, either because the metal became detached from the linking ligand at some point during the catalytic cycle and so dissolved, or because the ligand itself was somehow cleaved from the support. Nanoparticle formation can also be a cause of leaching. In one case, a rhodium catalyst supported on an anion exchange resin is used for the carbonylation of methanol. It is accepted that leaching occurs and a guard bed is placed further down the reactor flow system [26]. Leached catalyst is trapped by this guard bed, which is eventually used as a replacement catalyst bed, thus reducing the leaching to manageable proportions even for an expensive rhodium based catalyst. In this system, at least some of the catalysis and possibly the majority occurs through the solubilised rather than the supported catalyst.

A key development occurred in 1999 [27], when the group headed by van Leeuwen, Kamer and Reek reported that a rhodium catalyst involving a bidentate ligand which had been modified to include a remote –Si(OEt)₃ group could be incorporated by sol gel processing into silica. A single batch of this catalyst was used for a variety of reactions – mainly hydroformylations in the liquid phase, over a period of 1 year without loss of activity or selective and without observable leaching of rhodium [28]. This development and others have led to a large increase in activity aimed at the development of non-leaching supported catalysts which retain or surpass the activity and selectivity of their homogeneous counterparts [29].

This book brings together contributions from leaders in the field of research into supported homogeneous catalysts. It takes a broad view, covering soluble and insoluble supports, supported liquid phase catalysis and membrane imbedded catalysts. Some Chapters concentrate on the design and synthesis of the supports and on the attachment of the catalysts to the supports, whilst others concentrate on specific types of applications of the supported catalysts or on studies aimed at identifying the exact nature of the supported species. However, the commercialisation of catalysts does not only depend upon the catalyst and the support, but also in the reaction engineering that allows the Chemistry to be carried out to its fully optimised potential. One chapter of the book discusses the challenges and some solutions for the engineering of supported catalysts, whilst another addresses progress made in modelling homogeneous catalysts on supports. Finally, a most important chapter discusses the major
Factors that must be taken into account when considering using supported catalysts in commercial processes. The various possible pitfalls are explored and the reasons why a fully homogeneous system was preferred over a supported analogue for the synthesis of the enantiopure herbicide (S)-metolachlor are discussed.

The majority of the contributors to the book are members of NANO-HOST an Initial Training Network set up by the European Commission under the auspices of the Marie Curie actions to train young people in the area of supported catalysis and to encourage them to be flexible and mobile within the European Community. Funding for these Networks is extremely competitive so the presence of NANO-HOST indicates the importance placed on the development of supported catalysts by the European Commission. The work of all the authors has been integrated through the European Network of Excellence, IDECAT, which seeks to facilitate integration of scientists working in all branches of catalysis. NANO-HOST sprung from IDECAT, which has also spawned the European Research Institute of Catalysis, for the continued development of catalysis in Europe.

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Preface

The design of green and economically feasible processes for the production of fine chemicals is certainly one of the major needs and biggest challenges for a sustainable development of our planet. Catalysis contributes substantially to this goal by providing comparatively lower impact technologies and further in the recent years several efforts have been exerted aimed at broadening the scope of the catalysts, increasing their accessibility and efficiency, lowering their costs and ensuring their reuse.

This book collects the contributions of some of the leading scientist working in the field of the heterogenization of homogeneous chemical catalysts. The snapshot we get is a clear evidence of the level of expertise and sophistication reached with this methodology. The fascinating world of “heterogenized catalysis” is perfectly introduced in Chapter 1, where the differences and the advantages of the approach, compared to the two traditional disciplines of homogeneous and heterogeneous catalysis, are illustrated. The following chapters focus on the solid support materials, either inorganic, organic, dendrimer or nanosized, to show their subtle, often determining influence on the catalyst performance and how the mastered elaboration of new materials may be used as a tool to tailor and improve this. Selected examples of application reported in Chapters 9–11 testify the versatility and the potential of the method. No surprise that most processes are carried out in an enantioselective fashion. This is a prerogative of molecular catalysts which, coupled with the easy handling and recycling typical of immobilized systems, favourably differentiate heterogenized catalysts from the conventional heterogeneous ones. To this end, particularly evocative is the possibility to engineer enzyme-mimicking solid catalysts, as properly described in Chapter 2. The contributes dealing with membranes and reactors were purposefully included to provide insights of the technological opportunities and solutions offered by the heterogenization of homogeneous catalysts. Further, clear distinction of immobilized molecular systems is their possibility to enable both a systematic design of new catalysts and an easier characterization of the active sites, compared to the classical heterogeneous catalysts. Chapters 12 and 13 are paradigmatic in this sense.

Nevertheless, despite the above advantageous features and the progresses achieved by academia in this research area, with a few notable exceptions [1], examples of the use of heterogenized catalyst in industrial processes are still rare. This issue is critically analyzed in the “industrial” viewpoint reported in Chapter 7.
In conclusion, the main aim of the book was to provide the reader not only with an update on the state-of-the-art of the heterogenization of molecular catalysts, but also to offer a guide on the basic concepts behind this emerging, multidisciplinary technology which integrates several of the subdivision of chemistry, at the border of physics and chemical engineering; to assess the critical points in the field and, at the same time, to indicate the future perspectives and possible strategies. Our feeling is that the target was fully achieved. Likely, this is the first text in which the subject is treated comprehensively in all its essential facets. Therefore, we are confident that this book will be a helpful companion and deliver key hints to those, in the academia and in the industry, who decide to move their research interests in this direction.

Finally, we wish to thank the Authors of this volume for their enthusiasm and care in drawing up their contribution, all people at Springer’s office, London for their precious assistance and the IDECAT (www.idecat.org) and NANO-HOST (www.nano-host.eu) Networks for providing substantial inputs to the topic of the book.

Pierluigi Barbaro and Francesca Liguori

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Chapter 1
Fine Chemicals Synthesis Through Heterogenized Catalysts: Scopes, Challenges and Needs

Duncan Macquarrie

Abstract The development of new, highly efficient heterogenized catalysts is an active and important area in fine chemicals production. Many opportunities present themselves in terms of the significant developments in the tailoring of solid supports, which allow a rich variety of surface functionalities and properties, along with unprecedented control of physical features such as porosity, pore connectivity and high surface area. Key challenges include making full use of this palette of materials in the drive towards sustainable manufacturing. The knowledge base in materials chemistry and catalysis, coupled with ever-improving techniques to analyse catalytic materials and the reactions they promote will provide a sound foundation for future research and applications in this area.

1.1 Introductory Remarks

The synthesis of fine chemicals through the use of heterogenized catalysts has been an active research field for several decades. Over about the same period, the chemical industry has been enormously reliant on the use of solid catalysts, in particular the zeolites (3D crystalline solids with pore sizes below 1 nm) for the conversion of crude oil into a range of small molecules. These high temperature, gas phase processes run continuously and are amongst the largest volume chemical processes in existence. The enormous thermal stability, robustness and high acidity of the zeolite catalysts employed, combined with their very well defined crystalline nature means that they are extremely effective and highly selective catalysts. Part of this selectivity comes from the fact that, in a crystalline material, active sites are always situated in the same environment and therefore always have the same activity and selectivity (although transport processes taking substrate to, and product from, the...
active sites may restrict the frequency of their utilisation). A second major contributor to their selectivity comes from the fact that their pore dimensions are often more or less the same size as the substrates/products that are involved in the reaction, leading to the notion of shape selectivity, crucial in the formation of $p$-xylene with a sufficiently high purity (>99.9%) for use in terephthalic acid production. Such selectivity is well beyond normal chemoselectivity. The crystalline nature of the zeolites also means that they can be very well characterised and therefore a thorough understanding of their behaviour is possible.

In stark contrast, there is a distinct lack of solid catalysts or continuous processes in the predominantly solution phase world of fine chemicals. Catalysts are used frequently, but (with the exception of hydrogenation reactions, where e.g. Pd/C or Pt/Al$_2$O$_3$ are commonly utilised as catalysts) are almost always homogeneous. This gives them the benefit of being typically discrete, well-characterised molecules (although these molecules may or may not actually be the true catalytic species) where rational modifications can be made and the consequences readily measured. Additionally, diffusion is typically excellent – not always the case with a porous solid, where transport through the (often narrow) pore system can be the rate determining step.

Despite this partial lack of utilisation by the wider community, there has been a considerable amount of research carried out into heterogenized catalysts and catalysis using them. In particular, recent years have seen a resurgence in activity for a range of reasons. These reasons include the increased awareness of clean, efficient processing and the establishment of Green Chemistry as a fundamental part of designing a process [1], with catalysis being very much central to its fundamental principles [2,3], and the very significant breakthroughs in the design and synthesis of very well designed inorganic solids such as the MCM-41 and SBA-15 series of silicas [4,5], both of which have well-defined porosity in the mesoporous range and narrow pore size distributions. The larger pores that these families of materials have allow the conversion of fine chemicals, the vast majority of which are too small to fit into the sub-nanometre pores of the zeolites. Crucially, for heterogenized catalysts, the pores are also large enough to accommodate bound catalytic units. Furthermore, these (or their precursors) can be incorporated during the silica synthesis itself [6,7].

### 1.2 Scope: What is a Heterogenized Catalyst?

A heterogenized catalyst can be viewed as a homogeneous catalyst attached typically (but not always) via a covalent tether to an insoluble support. Some, such as those based on polymers such as polystyrene or chitosan, can have solubility under some conditions (solvent, pH, etc.), but the majority are based on 3-D inorganic polymers such as silica.

This combination of two species (catalyst plus support) means that the catalyst exists in (usually close) proximity to a solid surface, which may itself have catalytically active groups or groups that can interact with the catalyst in a beneficial or detrimental manner. For example, the slightly acidic nature of the silica surface can be beneficial in acid–base catalysts – the Knoevenagel reaction works unusually well on aminopropyl silicas [8], where the weak acid/weak base combination aids
the reaction. On the other hand, more strongly basic systems such as guanidines have their basicity reduced by interaction with the silica surface, and optimal activity is obtained when the surface is passivated to eliminate acidity [9,10]. Similarly, there may be a requirement to modify the catalyst to provide a binding group which can attach to the surface. This may modify the basic chemistry of the catalyst to a degree and must be taken into account, especially when considering changes to the activity or selectivity which may be noticed in a comparison between the homogeneous and heterogeneous equivalents. Attachment of other catalytic groups to the same surface can lead to bifunctional catalysts; attachment of other, non-catalytic, groups has been shown to lead to rate enhancements in several cases. Behind all this is the requirement to have the correct distribution of groups (uniformly distributed and well spaced out to minimise interactions between groups or, alternatively, to have them clustered together to maximise interactions between groups or to increase the local “concentration” of groups). This is important whether the catalyst is monofunctional or multifunctional, with two or more active different sites – positioning of the sites throughout the material is an important consideration, but is not always straightforward to either measure or to achieve.

1.3 Why Heterogenize a Homogeneous Catalyst?

Given the potentially more complex nature of the heterogenized catalyst, and the likelihood that it may be more difficult to prepare, one must naturally ask why this additional effort is justified. There are several reasons. Firstly, the heterogenized catalyst is almost certainly more easily recovered, and therefore reuse becomes more realistic (although reactivation may be required). Therefore less waste is generated, and expensive, difficult-to-obtain components such as ligands or scarce metals can be effectively recovered and reused. This also has the effect of making the isolation and purification of product easier, as catalyst residues have been easily removed.

As alluded to above, there may be advantages in terms of beneficial chemistry from the support (or indeed shape/size selectivity considerations) which make the catalyst more effective when heterogenized. Catalysts which are deactivated by dimerisation or agglomeration can be effectively isolated on a surface, maintaining their activity for longer.

More than one catalyst can be present in the reaction mixture at the same time, allowing for multi-stage reactions to be carried out in one pot, simplifying further the processing (so-called telescoped synthesis). These catalysts may be on the same solid support, or on different supports. Examples of these are given later in the chapter.

Solid catalysts can also be fixed in reactors such as fixed or fluidised bed reactors, flow reactors, membrane reactors etc. Here, the reactants are flowed over/through a bed or film of catalyst with reaction and separation being achieved simultaneously. There are many advantages to such technology (which, as stated earlier, is standard practice in gas-phase catalytic chemistry). Examples of such systems are known, and more will be said about them later.

Thus, it can be seen that, with a correctly designed catalyst, excellent rates and selectivities may be achieved, although this may be limited by diffusion constraints
which can make heterogeneously catalysed reactions slower than their homogeneously catalysed counterparts. Nonetheless, the many advantages in terms of product isolation which arise due to the solid nature of the catalyst (easy separations, better recovery and reuse, flow systems, etc.) can outweigh this often slower reaction, making the overall process faster. Indeed, one of the major hurdles in the use of heterogenized catalysts by the wider synthetic community is that we, as chemists are very good at thinking in terms of optimising reactions, but rarely think in terms of the process as a whole, meaning that product isolation is often an afterthought. On a larger scale, this then represents a major problem, and many scale-up campaigns are blighted by difficulties in efficiently isolating pure product.

1.4 Methods of Heterogenization

There are several possible routes to heterogenize a catalyst. The most common of these is the covalent attachment of a catalyst to a solid surface (or via co-polymerisation with a suitable non-active monomer), although non-covalent interactions can be used as well. Each route has benefits and disadvantages in terms of generality, complexity and the range of conditions that can be used successfully. The major methodologies for heterogenization are summarised below.

1.4.1 Covalent Binding of Catalyst

Examples of covalent binding of the catalytic group to the support include both organic polymers, such as those formed from the copolymerisation of styrene with a substituted styrene, as well as inorganic polymers formed from the sol-gel polymerisation of e.g. tetraethoxysilane and an organically functionalised trialkoxysilane.

The functional groups introduced via this route may be the catalysts themselves or may be anchor points which are then subsequently reacted with a suitably functionalized catalyst unit. It should be noted that the Y-CAT unit can often be directly attached to the pre-formed polymer. In the case of silicas, this is actually still a far more common route than the sol-gel co-condensation route in Fig. 1.1 and appears to give materials with subtly different properties. Here, the silica is functionalised with XSi(OMe)₃ with further reaction on X if required. The direct attachment of Y-CAT units to organic polymers is less common.

What should be borne in mind is that the ratio of the two (or more) monomers is typically far from 1:1. The functional monomer rarely makes up more that 10 mol% of the total, and is often significantly lower than this. In the final product, the distribution (and accessibility) of the functional groups must be defined, and this is often difficult. It is fair to say that more progress has been made for the organic polymers than for the inorganic systems in this respect. A further challenge is often met when X needs to be functionalised. Incomplete functionalisation is often not straightforward, and this means that the loading of catalyst is less than expected and...
there are X groups remaining on the surface which may influence the behaviour of the system. However, incomplete functionalisation is often due, at least in part, to variable accessibility of the functional groups at different parts of the structure, and this probably means that those sites which are readily functionalised are also those which are most likely to be accessible to the substrates during the catalytic reaction itself. Therefore, a partial functionalisation should favour the sites that will play the major part in the process. Nonetheless, there is an argument that the non-accessible sites are wasted, and that improved accessibility by better design of the material/polymer architecture is desirable. Implicit in this is the fact that there are generally a range of different sites in which a catalytic unit might be heterogenized, meaning that there may well be a spread of selectivities and activities.

### 1.4.2 Ionic Heterogenization

Ionic materials may be readily heterogenized by forming an ion pair with a charged group on the surface of a support. This has been achieved with of the simplest
examples being aminopropyl silica, which can be protonated and used to heterogenize ionic catalytic units. Examples include heteropolyacid salts [11], but other acid functionalised systems could be immobilised too. Clearly, the catalysts should be used and re-isolated/reactivated under conditions where ion exchange is not possible, otherwise leaching and loss of material will be encountered. Augustine’s group have demonstrated that heteropolyacids directly adsorbed on alumina can effectively tether a range of organometallic catalysts [12].

1.4.3 Supported Liquid Phase

This technique was introduced in 1989 by the group of Davis and is a cross between liquid–liquid biphasic catalysis and solid–liquid biphasic catalysis [13]. The key concept is the immobilisation of a thin film of liquid (the first examples were water, but others such as ionic liquids have been used [14,15]) on the surface and within the pores of a solid support. A catalyst is then dissolved in the liquid layer. The key requirement for heterogeneous catalysis is then that the catalyst does not leach out into the surrounding organic solution, putting restrictions on the nature of the solvent used (it should have very low water miscibility and should not dissolve the catalyst or any intermediates in the catalytic cycle). There can be issues with the synthesis of a catalyst with the correct solubility which may restrict the utility or the green credentials of a system in some cases, but in other instances, where the solubility of the catalyst suits the basic notion, then this may be a very promising avenue to explore.

1.4.4 Ship in a Bottle

A few examples are available for this method whereby a catalyst is prepared inside a cage-like pore such that the dimensions of the catalyst precursors are such that relatively free diffusion in and out of the pore is possible, but the catalyst itself is too large to escape from the pore, and is thus permanently entrapped. Porphyrins and related structures have been prepared within the pores of the larger zeolites and used with some success, but the limitations on diffusion of substrates and products and the constraints of their interaction with the catalyst means that this approach is not particularly common. Nonetheless, good results can be obtained, albeit more slowly than with homogeneous catalysis, as in the example provided by Ferreira et al. where alkenes can be selectively and effectively oxidised to epoxides by a ship in a bottle Ni–Salen complex within zeolite X or Y [16]. While reaction was slower, selectivity and conversion were good, and indeed improved somewhat upon reuse. It was noted that the distribution of active catalytic groups appeared to be mostly centred close to the external surface with less catalyst deep within pores.
1.4.5 **Entanglement**

This method has been used in the case of nanoparticle catalysts. Nanoparticles are very prone to agglomeration, and heterogenization is one technique that has been used to reduce the prevalence of this phenomenon. While this often takes the form of a covalent tether, a different, non-covalent, approach can sometimes be successful. Many polysaccharides form gels under appropriate conditions, and these can be used to entrap nanoparticles such that the nanoparticles are tangled up in a network of H-bonded polysaccharide strands. This reduces the tendency of the nanoparticles to diffuse and coalesce, meaning that their activity as catalysts is maintained for longer. Indeed, one of the benefits of this approach is that the polysaccharide can effectively reduce the metal salts that are often precursors, meaning that the nanoparticles can be produced in-situ without an additional reductant. This simplifies the procedure enormously, as the reduction takes place without the need for a separate reductant, therefore meaning that there are no side products from the reduction which must be removed [17].

The key features of these different methods of heterogenization are given in Table 1.1 below.

<table>
<thead>
<tr>
<th>Type of attachment</th>
<th>Key features</th>
<th>Pros/cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covalent attachment</td>
<td>One or more covalent bonds between catalyst and support</td>
<td>Generally stable link and more than one route to form catalysts. Requirement for covalent attachment can add complexity and may alter nature of catalyst.</td>
</tr>
<tr>
<td>Ionic attachment</td>
<td>Electrostatic attraction between catalyst and support</td>
<td>Ideal for charged catalyst, easily carried out. Catalyst must stay charged throughout catalytic cycle, conditions must not allow ion exchange.</td>
</tr>
<tr>
<td>Supported liquid phase (SLP)</td>
<td>Thin film of catalyst on high surface area solid</td>
<td>Relatively simple to carry out with catalyst soluble in SLP. Otherwise modification of catalyst required to make it soluble in SLP but insoluble in bulk liquid medium. Similar requirements for SLP.</td>
</tr>
<tr>
<td>Ship in a bottle</td>
<td>Physical constraint</td>
<td>Effective immobilisation but restricted range and diffusion difficult.</td>
</tr>
<tr>
<td>Entanglement</td>
<td>Physical restriction on the movement and coalescence of catalyst</td>
<td>Simple to do, and polysaccharides generally inexpensive. Need for interaction between catalyst precursor and polymer. Thermal stability probably limited.</td>
</tr>
</tbody>
</table>
The vast majority of heterogenized catalysts have been prepared either on organic polymeric supports such as modified polystyrenes, or on silicas. Both types of support are widely available and are relatively easily functionalised to give stably bound groups, either by C–X bond formation on e.g. a phenyl ring or by S₂ reaction of an aryl -CH₂Cl in the case of a functionalised polystyrene, or by the attachment of trialkoxy silanes to the surface of a silica. Several of these are commercially available, and many complex groups can be attached via some of the simpler amine, halide or isocyanate functionalities that can be bought. The Si–O–Si unit is relatively stable under most conditions (especially where all three alkoxy groups are converted to Si–O–Si) and therefore stable catalysts can be produced. Grafting to the surface of a pre-formed silica is the more frequently used route to these materials, but the direct sol-gel synthesis is also an attractive approach. The materials produced by each route are usually broadly similar, but rarely identical, and it is worth using both routes to find which give the better system.

The early 1990s saw an explosion in the area of mesoporous silicas, with unprecedented control over porosity being achieved, along with exceptional surface areas. The templated methods which were developed during this period have led to a great leap in the range of materials available as catalyst supports. About a decade later, there was a second significant jump forward in the choice of highly tunable, regularly structured materials, which has been much less fully exploited in catalysis. This second step forward came about via the findings by Ryoo and co-workers, that carbon replicates of SBA-15 materials could be produced which preserved the structural features of the SBA-15, by filling the pores with carbon precursors, forming the carbon within the pores and then etching the silica away, leaving behind the so-called CMK materials [18]. These mesoporous carbons created great interest, as the vast majority of carbons prepared up to that point had been predominantly microporous.

Following on from this discovery came the finding that these carbons could, in turn, serve as 3-D templates for a range of different oxides, with the same porosity and surface area as the original SBA-15. while some oxides and sulfides can be prepared directly using SBA-15 as a hard template, this is limited to those which are stable to the conditions required to etch away the silica (alkali or HF). For other systems, the use of a CMK material as template can get round this problem, as the removal of carbon requires different conditions. This reverse templating (Fig. 1.2) can be used to provide a range of highly structured mesoporous materials which were previously impossible, or at least very difficult to synthesise by more direct routes [19].

In addition to these systems, other potential solids for functionalisation are available, although currently under-exploited. Two examples are the periodic mesoporous organosilicas (PMOS) pioneered by Inagaki [20], which are prepared from bis-silanes, where the two trialkoxysilane groups are linked by a typically short and non-functionalised organic bridge such as a phenylene or –CH₂CH₂–. Catalytic groups can be subsequently attached, or can be incorporated in the sol-gel synthesis medium, as was done by Sullivan, who prepared a very active base catalyst using this approach [21].

Organically functionalised aluminium phosphonates have been prepared by Vioux’s group, using a co-condensation of M(OR)₃ and phosphonic acids, leading
to Ti, Zr, and Al organohybrids [22,23]. Such an approach should be amenable to extension, using the relative simplicity of the three component coupling between phosphites, aldehydes and amines.

It is clear from the examples in this chapter that the surface of the support material can have a significant impact on the chemistry that takes place at the catalytic site, and that controlling/designing this environment is therefore a very important facet of the overall design of an optimal catalyst. Therefore, the choice of support should be made bearing in mind and drawing upon the wide range of possible supports that is now available. The biomass-derived systems described below are also of great interest and further extend the choice of support available.

### 1.6 Challenges and Needs

There are many challenges to be met and needs to be fulfilled in the area of heterogenized catalysis towards the production of fine chemicals. There is a much wider range of choices available in many ways than there has been before, and some of these, such as the remarkable advances in the synthesis of and structural control over mesoporous solids in particular open up many possibilities to enhance catalysts and their operation. Other challenges are very fundamental, and include the need to move from petrochemical feedstocks to biomass-derived feedstocks.
It is important not to lose sight of the fact that there are likely to be difficulties with the sustainable supply of other elements, and that we need to conserve resources very carefully.

### 1.6.1 Green Chemistry

The principles of green chemistry highlight very well some of the challenges, opportunities and needs of a good heterogenized catalyst. Green chemistry is a way of looking at chemistry, focussing on developing products and processes which have as little impact on the environment as possible. Of the twelve principles of green chemistry (Table 1.2) several are directly applicable to the concept of heterogenized catalysts. Indeed, catalysis itself is a fundamental aspect, with energy requirements being reduced and the scope for higher selectivity bringing better yields of the desired product (and an increased likelihood of recovering unconverted starting material). Clearly improvements in the separation of the catalyst after reaction has benefits in terms of the recovery of catalyst, reducing catalyst waste and allowing reuse in subsequent reactions. An easily recoverable catalyst will also make the isolation of product (and starting material) easier. All these benefits can help substantially to minimise the waste generated by a process.

However, one aspect of waste reduction must also be borne in mind, and that is the waste generated during catalyst preparation. This is often overlooked.

<table>
<thead>
<tr>
<th>Principle</th>
<th>Waste: processing/energy: health/environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>Prevention of waste better than clean-up</strong></td>
<td>Waste</td>
</tr>
<tr>
<td>2. Design of safer chemicals</td>
<td>Health/environment</td>
</tr>
<tr>
<td>3. <strong>Less hazardous syntheses</strong></td>
<td>Health/environment</td>
</tr>
<tr>
<td>4. Use renewable feedstocks</td>
<td>Waste, health/environment</td>
</tr>
<tr>
<td>5. <strong>Employ catalysis where possible</strong></td>
<td>Waste, processing/energy</td>
</tr>
<tr>
<td>6. <strong>Reduce the use of derivatives and auxiliaries where possible</strong></td>
<td>Waste, processing/energy</td>
</tr>
<tr>
<td>7. Employ atom efficient procedures in the design of synthesis</td>
<td>Waste, processing/energy</td>
</tr>
<tr>
<td>8. Use safer solvents and reaction media</td>
<td>Processing/energy, health/environment</td>
</tr>
<tr>
<td>9. <strong>Design processes for energy efficiency</strong></td>
<td>Processing/energy</td>
</tr>
<tr>
<td>10. Design processes/products for degradation/design for end of life</td>
<td>Waste, health/environment</td>
</tr>
<tr>
<td>11. Real-time analysis and monitoring of processes</td>
<td>Processing/energy</td>
</tr>
<tr>
<td>12. Carry out inherently safer chemistry</td>
<td>Health, processing/energy</td>
</tr>
</tbody>
</table>
(and its impact reduces as catalyst turnover number increases) but it must form a fundamental part of the design and execution of heterogenized catalyst synthesis.

For example, we have demonstrated the potential to recover and reuse template in the synthesis of organically modified mesoporous silicas [24]. Here, the organically modified silica is prepared by a co-condensation of tetraethoxysilane and an organo triethoxysilane in aqueous ethanol at room temperature. 1-Aminododecane is used as a template to direct the pore structure of the material. After reaction, the solid organosilica is filtered and the template removed by ethanol extraction. This gives the product and an ethanol solution of template, which can be used directly (by addition of the appropriate amount of water) in a further synthesis. The more commonly used quaternary ammonium templates can be recovered, but this requires ion exchange and is less straightforward, generating more waste.

A rigorous life-cycle or ecodesign approach is, however, the best way to really define the environmental impact of a given synthesis. However, this is a complex and difficult task, and has rarely been carried out for such systems. A recent paper by Baccile has been published [25], which investigates the synthesis of silica sol-gel materials from an ecodesign perspective. There are a number of suggested routes forward in terms of designing the preparation of silica-based materials covering the source of silica (with TEOS being particularly wasteful due to its synthesis as well as its utilisation – silicates are significantly less of a problem, but are often less amenable to well-controlled syntheses of materials), the nature and conditions of the preparation route, and the use of structure directing agents, all of which can have a significant impact on the overall impact of the preparation. Clearly, the efficiency with which these catalytic materials are used has a similarly significant impact, and therefore design of catalyst synthesis and use must both be considered.

1.6.2  Biomass as Catalyst Support – Towards Sustainable Catalysts

Given the conclusions outlined above, the use of renewable and sustainable raw materials is a major challenge facing the whole of society, and heterogenized catalysts must play a role here too. This means that heterogenized catalysts must be developed that can efficiently convert biomass-derived feedstocks into useful chemicals, but that the catalysts as far as possible should also be derived from renewable and sustainable sources.

1.6.2.1  Biosilicate(s) as Sources of Silica

While silica is thought of as a simple inorganic chemical, it does in fact play an important biological role in many plants, including grasses and related species, as
a structure stabilising agent. Silica therefore forms a considerable proportion of the ash derived from the combustion of biomass. Given that much waste from food processing is burnt to recover energy (e.g. rice hulls, which can have up to 20% by weight silica, [26,27]) and that increasing quantities of biomass is being co-fired in power stations to meet renewable energy targets, it is likely that silica could be obtained from these waste sources and converted into supports for heterogenized catalysts. Examples of such an approach have already started to appear, and some silicas and zeolites have been prepared from bio-silica(te)s. The highly structured mesoporous silica, MCM-41, has been prepared using rice hull ash as a source of silica [28]. Silicas with mesopores have been produced using rice hull ash (rich in silica(te)s) and glycerol as a processing aid [29]. This approach has also been successfully utilised in the synthesis of the zeolite ZSM-5, where Al was obtained from natural clinoptilolite [30].

The varying composition of these bio-derived silica sources is a challenge, as they contain a varying amount of carbon, and also of alkali metal salts such as sodium and potassium. Additionally, the history of the sample is important, in particular whether it has been heated, how long for and to what temperature. All these factors will influence the ease of recovery of the silica in a form suitable for catalyst/support manufacture.

1.6.2.2 Polysaccharide-Derived Support Materials

The use of polysaccharides has been alluded to earlier as a stabilising system for nanoparticles. Almost a decade ago, we developed catalysts heterogenized onto expanded starch, a material with a much higher surface area than native starch, which proved to be useless in this respect. While the expanded catalysts were very active for a series of reactions [31], they suffered from a lack of storage stability. Partial carbonisation of these materials (before attachment of catalyst) led to materials with properties of both starch and carbon, the blend of properties being dependent on the temperature of carbonisation. This led to a series of catalyst supports, which have become known as starbons, and which have much better stability, while maintaining the high surface area and mesoporosity of the initial expanded starches [32]. Recently, this approach has been extended to include other polysaccharides (Fig. 1.3) [33].

Chitosan is a polysaccharide derived from the shells of crustaceans, in which calcium carbonate, proteins and chitin are combined to form the protective shell. Chitin can be converted, by deacetylation, to chitosan, a polysaccharide made up of 2-aminoglucose units. Chitosan has found application in the adsorption of metal ions from water, meaning that it has a natural affinity for such potentially catalytic species. However, the stability of such species is relatively low, and catalytic activity is often poor, meaning that the attachment of ligand systems is preferred to bind the metal more strongly and to enhance its activity. This amine functionality makes it very unusual as a polysaccharide, but is also ideal for attaching catalytic units. Indeed, much of the heterogenization of catalysts on silica employs coupling with aminopropyl-functionalised silicas, and it appears that very similar methods can be directly translated to chitosan (Fig. 1.4).
Fig. 1.3 Preparation and characteristics of starbon

Fig. 1.4 Complexes of chitosan, illustrating strategies for attachment of catalytic units to the polymer backbone