ADVANCED MATERIALS

Advanced Catalysts: Interfaces in the Physical and Biological Sciences

Heterogeneous Catalysis
Molecular Sieves
Biocatalysis
Catalyst Design
Abzymes
Ribozymes

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1. Introduction

It has been established that catalytic materials, one way or another, now account for some 25% of the gross national product (GNP) of the USA. But catalysts have long played a central rôle in the economy of civilized nations. The ancient Greeks and Romans, for example, used biological catalysts (enzymes) for the production of wine and its conversion to vinegar and for the transformation of starch into sugar. They also used alkalis as inorganic catalysts to produce soaps from fats and oils. Nowadays, much of the food we eat and the medicines we take, many of the fabrics and building materials that keep us warm, and almost all the fuels that transport us by road, sea or air are produced by heterogeneously catalyzed reactions. The current world production of ammonia, required as an agricultural fertilizer, is about 120 million tonnes per annum. Owing to the expanding need to feed mankind, this figure is increasing at some 6% per annum. Vitamins and drugs, herbicides and pesticides, as well as a range of foodstuffs including margarine are all the products of catalysis. Catalysts are the cornerstone of the chemical industry, which, in contrast to many other sectors of the (UK) economy, continues to flourish (Figs. 1 and 2).

Most of the catalysts used for commercial processes are heterogeneous, being composed either of metals or alloys (usually supported on high area oxides), of oxides or sulfides, or of microporous, microcrystalline aluminosilicates known as zeolites. Increasingly, biocatalysts such as enzymes, immobilized on high-area solid supports, as well as appropriate micro-organisms are utilized for the production of certain key foodstuffs and pharmaceuticals (Table 1).[3]

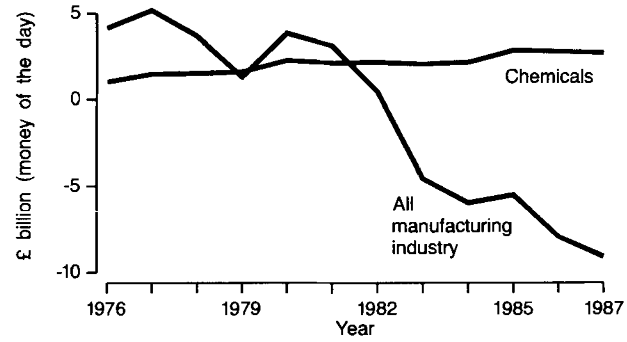

Fig. 1. U.K. Trade balance in chemicals and all manufacturing industry [1].

The first patent encompassing heterogeneous catalysts was taken out by an Englishman named *Peregrine Phillips* who, in 1831, described how sulfuric acid could be manufactured by passing sulfur dioxide and oxygen over finely divid-

Table 1. Current industrial scale applications of immobilized biocatalysts [3].

Application	Enzyme	Microorganism
Steroid conversions	11-β-hydroxylase (EC 1.14.15.4)	*Curvularia lunata*
	Δ'-dehydrogenase (EC 1.3.99.4)	*Arthrobacter simplex*
Glucose isomerization	Xylose (glucose)-isomerase (EC 53.15)	*Actinoplanes sp.* *Arthrobacter sp.* *Bacillus coagulans* *Streptomyces sp.*
Raffinose hydrolysis	α-D-galactosidase (EC 3.2.1.22)	*Mortierella vinaceae*
Starch saccharification	Glucoamylase (EC 3.2.1.3)	*Aspergillus niger*
Lactose hydrolysis	β-D-galactosidase (EC 3.2.123)	*Aspergillus niger*
6-APA from penicillin	Penicillin acylase (EC 3.5.1.11)	*Eschericia coli*
Optical resolution of α-amino acids	Amino acylase (EC 3.5.1.14)	*Aspergillus oryzae*
L-aspartic acid from fumaric acid	Aspartase (EC 4.3.1.1)	Eschericia coli (EC 3.5.2.2)
L-malic acid from fumaric acid	Fumarase (EC 4.2.1.2)	*Brevibacterium ammoniagenes*
D-phenylglycine from D,L-phenylhydantoin	Hydantoinase (EC 3.5.2.2)	*Bacillus brevis*
Acrylamide from acrylonitrile	Nitrilase (EC 3.5.5.1)	*Corynebacterium sp.*
L-phenylalanine	Transaminase (EC 3.6.1.58)	

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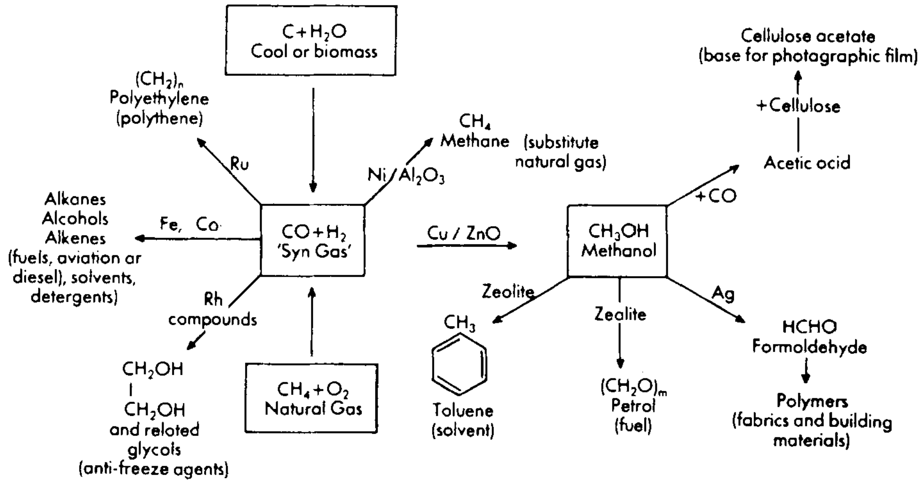

Fig. 2. Synthesis gas (abbreviated 'syngas') is a mixture of carbon monoxide and hydrogen and may be produced either by oxidizing coal or by burning methane. A wide variety of products can be generated from 'syngas' using the appropriate catalyst. Fischer-Tropsch catalysts such as Fe or Co (extreme left) promise to provide (from coal as primary feed-stock) exceptionally clean fuels [2].

ed platinum supported on clay. Platinum continues to play a pivotal rôle in modern catalysis; it serves to isomerize (reform) linear hydrocarbons, such as those initially produced by the (zeolite-catalyzed) cracking of oil, to their branched and aromatic analogs, many of which have high octane ratings. Platinum, and its congener rhodium, also finely divided and supported on alumina and ceria, are the center pieces of the automotive exhaust catalysts, which reduce emissions of undesirable gases into the environment (Table 2). Some forty million auto-exhaust catalytic units were installed on light vehicles in 1988 alone. Over a third of the world's available platinum is now used in auto-exhausts. Platinum is also of central importance in electro-catalysis which is a primary feature of the fuel cell, where electricity is generated directly by the electro-chemical combustion of hydrogen or methanol.

Table 2. Decrease in emission rates per mile driven since the introduction of auto-exhaust catalysts in the USA.

Pollutant	Percentage Decrease
Carbon Monoxide	86
Nitrogen Oxides	56
Hydrocarbons	84

2. Mechanisms of Catalysis

Much mystery still surrounds our knowledge of how heterogeneous catalysts function. The auto-exhaust catalysts that convert nitric oxide, carbon monoxide and hydrocarbons to harmless products, are less complicated than other multiphasic and multicomponent inorganic catalytic solids. The situation is also less complicated for the so-called uniform heterogeneous catalysts in which all, or almost all, of the atoms in the bulk of the solid participate directly, or are implicated indirectly, in the catalytic processes of the overall reaction.

Examples of uniform catalysts are zeolites, silico-aluminophosphates (SAPO's) – see later – as well as certain clays and pillared clays. In all these cases, the active sites are uniformly distributed in the bulk of the solid. Because of the microporosity of these structures, however, the active sites are accessible only to gaseous reactant species of the requisite size and shape. Uniform heterogeneous catalysts, primarily because their structures may be elucidated by the traditional techniques (especially X-ray crystallography) applicable to the study of bulk solids, are therefore very well characterized in comparison with heterogeneous catalysts consisting of supported or multiphasic solids.[4, 5] Detailed discussions of how catalysts function have been given elsewhere.[4, 6]

The zeolitic and SAPO-based catalysts frequently function in a dual manner. First, they provide, at specific (active) sites within the accessible pores, protons that are effectively the catalytic agents. Second, their well-defined porosity, in which the apertures in the form of cages and channels – at the internal surface of which the active sites are situated – permit access to those reactants that are of the requisite size. This shape-selectivity for the reactants, is often accompanied by a similar shape-selectivity for the products, since only those generated species that are small enough are able to diffuse out from the interior of the catalyst.

Uniform heterogeneous catalysts possessing zeolitic character are much more akin to enzymes in their mode of action than to the multiphasic inorganic solids, typified by the ammonia synthesis catalyst (which consists of iron and the oxides of potassium, silicon, aluminum and combinations thereof[7]) or by the iron–potassium based industrial catalysts for the conversion of ethylbenzene to styrene. This catalyst has recently been shown[8] by in situ X-ray diffraction study to contain Fe_3O_4, $KFeO_2$ and $K_3Fe_{22}O_{34}$.

Paradoxically, much more is known about the structure of the active sites in enzymes than those in metallic or oxide catalysts, even though their overall structures and constituent parts are substantially more complicated than those of the metals and oxides in extensive industrial and laboratory-scale use. Enzymes generally have active sites which consist of pockets, or clefts, the lining of which contain the crucial set of amino acids, in the right sequence and conformation required to 'process' the reactant species.[4]

3. Trends in the Design of New Catalysts

In addition to the logical extensions and improvements that are being pursued for existing catalysts, there is also intense activity focused on the creation of radically new ones. Not only are there advances occurring in heterogeneous catalysis, which has hitherto dominated the commercial scene, there are nowadays significant developments in biocatalysis, in homogeneous catalysis and in the evolution of fundamentally new types of catalysts. Some of these are rooted in the inorganic, inanimate world, others very firmly in the biological and animate.

3.1. New Heterogeneous Catalysts

Table 3 highlights the areas currently attracting considerable attention both at the fundamental and applied level.

Table 3. Current trends in the evolution of heterogeneous catalysts.

Tailored Solids
- Development of stereoselective catalysts based on pretreated metals (e.g. Ni, Pt) and on immobilized transition-metal complexes.
- Membrane (e.g. metal alloy) catalysts for single-stage synthesis.
- Molecular sieves in which cage and channel dimensions are controlled.
- Development of new oxide-based solids capable of the sacrificial loss of structural oxygen for selective oxidation of hydrocarbons
- Schottky-junction (metal on oxide) catalysts [a]
- Fine-tuning of Fischer-Tropsch catalysts (based on Fe, Co, Ru) so as to generate ultra-clean hydrocarbons from CO + H_2 mixture derived from coal.

Photocatalysts
- Design and preparation of solids, the electronic band-gap of which are engineered (as in the fields of semiconductor physics and opto-electronics)
- Quantum solids (ultra fine particles in 20 to 500 Å diameter range) with and without enclathration.

Electrocatalysts
- New designs and components for fuel cells (for energy generation).
- Derivatized electrodes (for sensors and other analytical purposes).

[a] See J. C. Frost's discussion on junction effects in catalysts for methanol synthesis (*Nature London 334* (1988) 577).

Stereoselective catalysts, which are capable of producing an enantiomeric excess of a given species from a prochiral precursor, are of growing importance. Chirality, after all, holds sway in living processes and is hence of enormous relevance in the quest for catalysts needed for the generation of pharmaceuticals. Until about the early 1960s, access to enantiomerically enriched compounds from prochiral reactants was thought to be realizable only by biological or enzymatic methods.[9] However, at least a decade earlier, some fascinating Japanese work[10] had indicated that a special preparation consisting of metallic palladium supported on silk served as a heterogeneous catalyst for the asymmetric reaction involving the hydrogenation of oximes and ketones. Since that time Ziegler-Natta catalysts for the asymmetric polymerization of olefins, as well as specially modified Raney-nickel heterogeneous catalysts, have been used extensively for asymmetric conversions. Of late so-called Lindlar catalysts,[10, 11] in which the surface of the palladium is modified by the deliberately added lead 'impurities', have been extended to encompass Pd-Pb alloys, which function as efficient means of effecting stereoselective hydrogenations for the synthesis of insect sex pheromones.[12]

The scope for tailoring metal catalysts by pre-adsorbing upon their surfaces bulky organic molecules which create prochiral cavities for the incoming reactant is obviously considerable. *Wells* et al.[13] have re-examined the Orito reaction[14] in which platinum, modified by the presence of presorbed cinchonidine (a member of the cinchona alkaloids), becomes active for the stereoselective hydrogenation of an α-ketoester (e.g. methyl pyruvate) to an optically active product (e.g. *R*-(+)-methyl-lactate, Fig. 3). My colleagues and I[15] have explored, by computer graphics (see Fig. 4), the way in which this stereoselective process might proceed. The plausible assumption here is that cinchonidine forms an ordered, well spaced out array of interstices in the sorbed layer. The interstices permit ingress of the methyl pyruvate in a preferred fashion so as to pre-ordain the formation of a given stereo product.

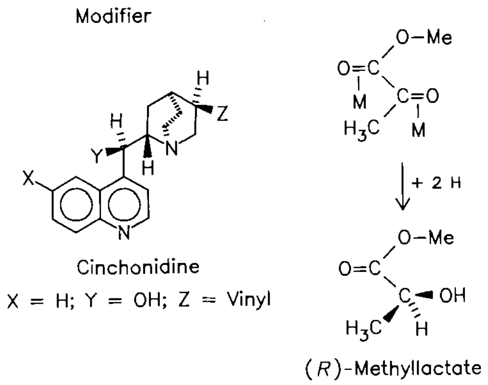

Fig. 3. Cinchonidine preadsorbed on a platinum catalyst favors the hydrogenation of a co-adsorbed α-ketoester to the optically active *R*-methyl lactate [13].

Membrane catalysts such as those based on palladium or on binary alloys of palladium with one of a dozen or more other metals – Al, Ti, Ni, Cu, Mo, Ru, Rh, Ag, In, W, Re and

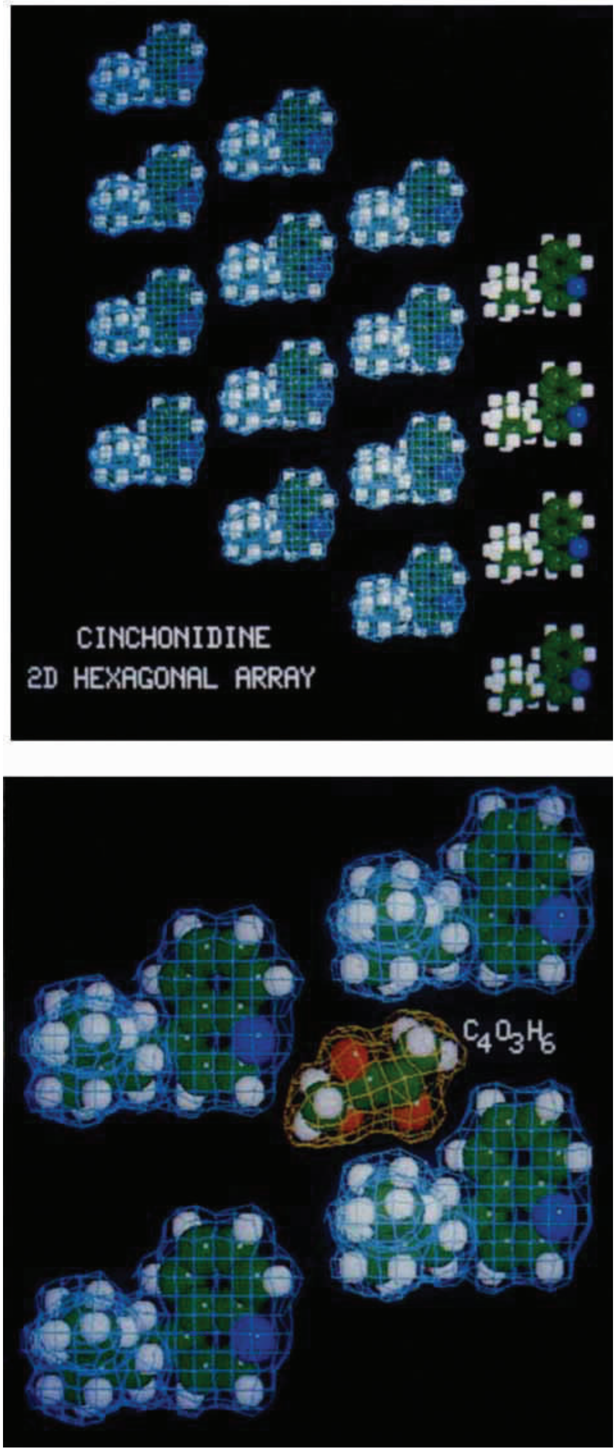

Fig. 4. (a) Schematic illustration of the way in which cavities in the ordered monolayer of cinchonidine (on a platinum surface, which is not shown) may serve as centers where a prochiral reactant may be stereo-preferentially adsorbed as in (b). This preordains the production of an enantiomeric excess of the methyl lactate formed by catalytic reduction on the modified metal surface. (After *Barnaby Smith* et al. [15]).

Pt – are permeable to hydrogen but not to the organic compounds which are to be hydrogenated. Hydrogen transfer through such membrane catalysts which are in the form of foils or thin-walled tubes, provides a new method of influencing the addition or removal of hydrogen. The Soviet scientist *Gryaznov*[16] has carried out pioneering studies of this new type of catalyst, which has already been brought to commercial use in the one-stage production of vitamin K_4, as shown in Figure 5.

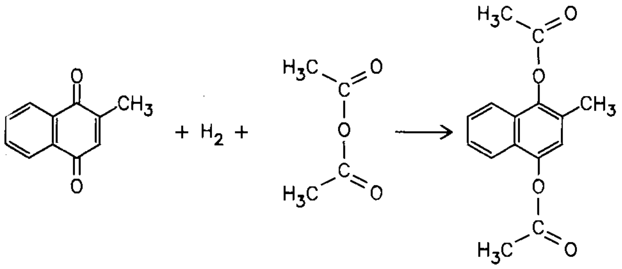

Fig. 5. One-stage production of Vitamin K_4 on a permeable palladium membrane catalyst [16].

Palladium-based binary alloys consisting of yttrium have also recently been used,[17] as membrane catalysts, for the production of hydrocarbons from synthesis gas ($CO + H_2$ mixtures). Recognizing that palladium surfaces are remarkably efficient catalysts for the trimerization of acetylene to benzene[18] and the synthesis of thiophene[19] from adsorbed acetylene and sulfur[20] (see Fig. 6), it ought to be feasible to so design a system, consisting of a membrane catalyst based on this metal, capable of selectively synthesizing partially hydrogenated aromatic and heterocyclic compounds.

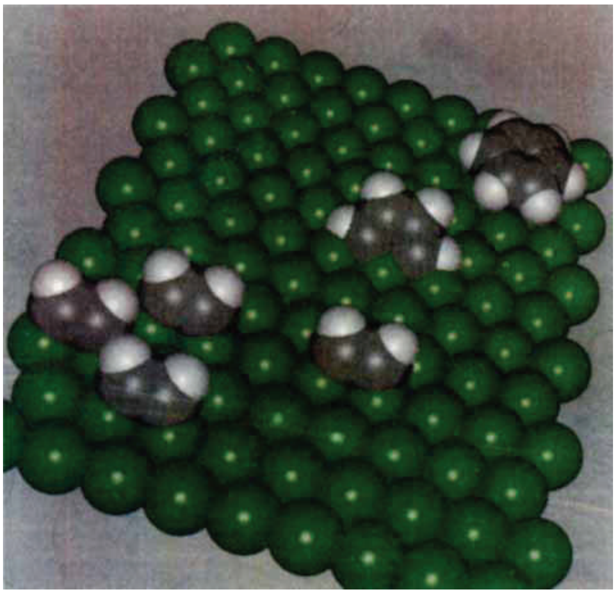

Fig. 6. Schematic illustration, after *Gellman* [19], showing how a close-packed surface of palladium metal catalyzes the trimerization of acetylene, via intermediates, to benzene.

Molecular sieve catalysts are already widely used[4, 20–23] in the hydrocracking of oil and petrol, in the synthesis of petrol from methanol, in alkylations and isomerizations; and their increasing rôle in laboratory-scale synthesis and conversions continues to expand.[23-25] A selection[25-27] (taken from other publications) of interesting catalytic reactions, of value in the production of fine chemicals, is shown in Figure 7.

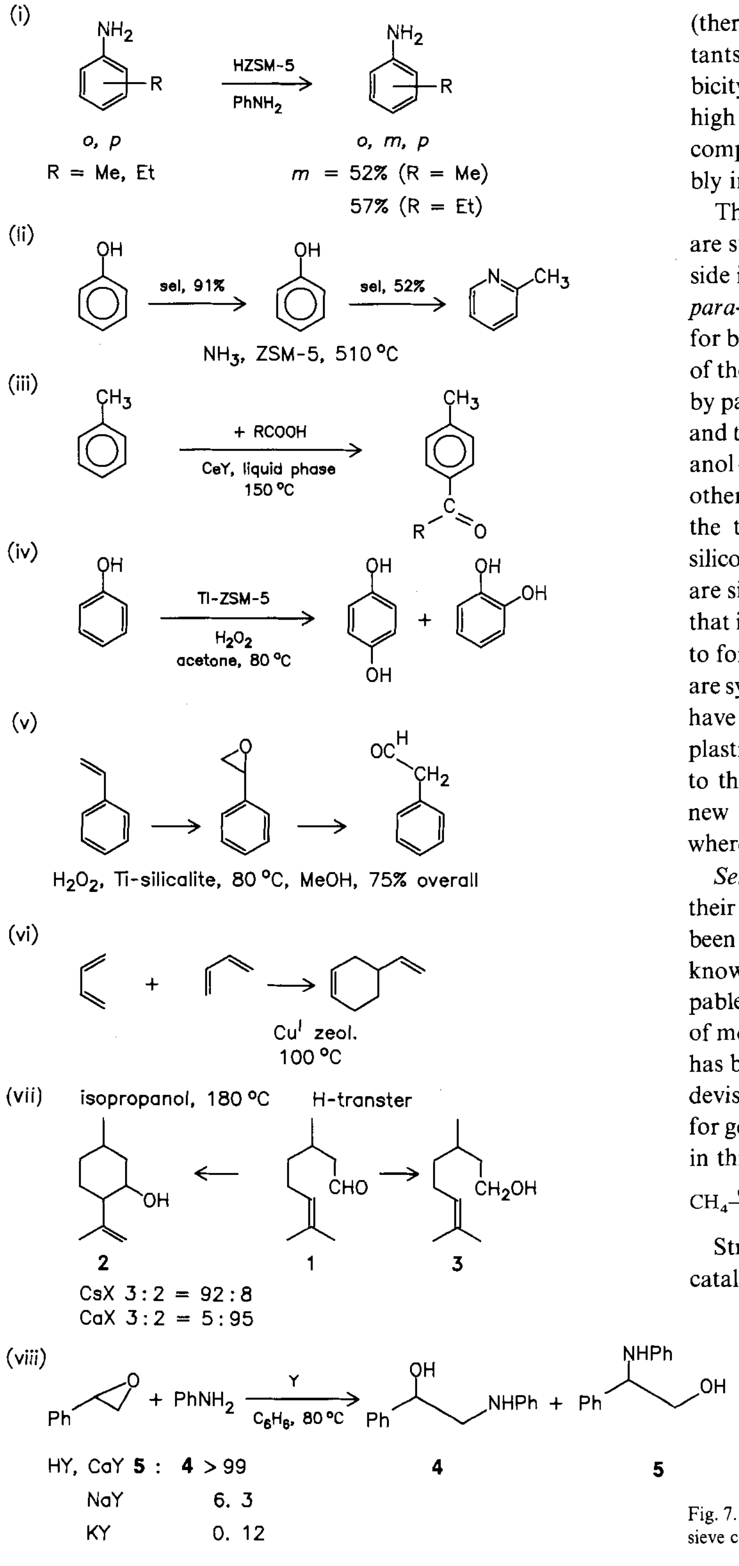

Fig. 7. A selection of some of the organic reactions catalyzed by molecular sieve catalysts. (After *Van Bekkum* [25] and *Thomas* and *Theocharis* [24])

These and other reactions, for which the appropriate microporous solid catalyst has yet to be developed, are or will be rendered possible through the special characteristics of zeolitic solids viz: a sharp, well-defined pore-size distribution; good thermostability; adjustable Brønsted or Lewis acidity; a wide range of exchangeable cations of different radius or polarizability; adjustable size and morphology (thereby allowing scope to modify diffusion times of reactants and products); adjustable hydrophilicity or hydrophobicity (according to whether the Si/Al ratio is low (1.0) or high (> 20) respectively) an ability to accommodate metal complexes, some of which are so bulky as to require assembly inside the cavities and channels.

The channel dimensions of the well-known zeolite ZSM-5 are such that, when methanol is catalytically dehydrated inside its pores, only monocyclic aromatics (benzene, toluene, *para*-xylene, etc.) are produced. The channels are too small for bicyclics such as naphthalene to form. This is the essence of the synthesis of petrol from natural gas – methane, which by partial oxidation is first converted to a CO + H_2 mixture and then, catalytically, over a copper-based catalyst to methanol – now operating in New Zealand.[30] By assembling another type of molecular sieve, known as SAPO-34, in which the tetrahedrally-coordinated framework constituents are silicon, aluminum and phosphorus, the channel dimensions are significantly smaller than those of ZSM-5 (see Fig. 8) so that it is not now possible for even the monocyclic aromatics to form. Instead olefins such as propene and other α-olefins are synthesized. This is an important advance as the α-olefins have a variety of end uses: components of solvents, textiles, plastics, plasticizers and surfactants. More details pertaining to the general principles of the design of new zeolites and new AlPO-based molecular sieve catalysts are given elsewhere.[4, 31, 32]

Selective oxidation catalysts, especially those that release their own structural oxygen in a sacrificial fashion, have been known for some time. Of late, however, an increased knowledge of the solid-state chemistry of solids that are capable of accommodating large, steady-state concentrations of mobile vacancies created by the loss of structural oxygen has been acquired. This will make it increasingly possible to devise novel solids capable of catalyzing reactions that have, for good reasons, been regarded as very difficult to cope with in this way. One such example is:

$$CH_4 \xrightarrow{(O)} C_2H_6 + C_2H_4 + C_2H_2 + \text{other products}$$

Strenuous efforts will continue to be made to devise new catalysts for other reactions in which there is an abundance

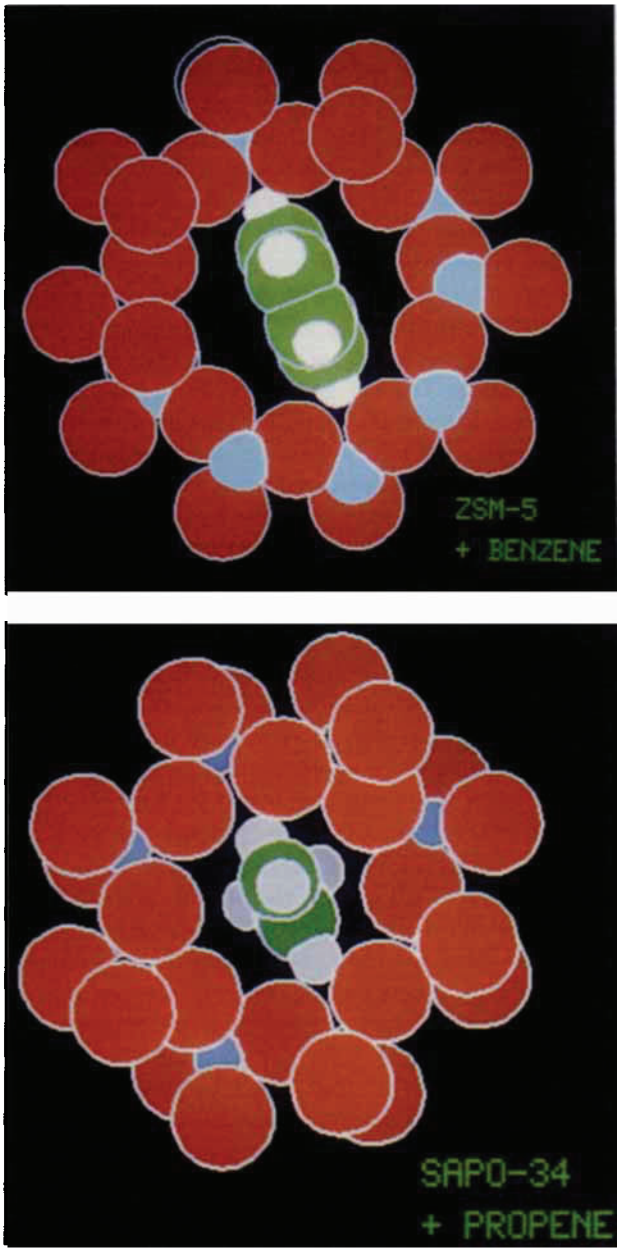

Fig. 8. When methanol is catalytically dehydrated over a molecular sieve (acid) catalyst, the nature of the products is governed by the dimensions of the channels. (a) Over a ZSM-5 catalyst, the channels are large enough to permit the formation of benzene. (b) Over a SAPO-34 (acid) catalyst, which has smaller pores, the dehydration yields only alkenes such as propene. (After *Yan Xu* and *Barnaby Smith*, unpublished).

of reactants e.g. nitrogen to nitrates, carbon dioxide to formates and fossil material to more useful hydrocarbons. Insofar as producing clean hydrocarbons (for fuels or packaging material) is concerned, there in renewed interest in Fischer-Tropsch catalysis based on iron, cobalt or ruthenium. Thus, coal or natural gas, when gasified to $CO + H_2$ mixtures, can be satisfactorily purged of sulfur, nitrogen and other environmentally harmful heteroatoms. Using catalytic systems such as the Shell middle distillate process, which by Fischer-Tropsch catalysis converts the $CO + H_2$ mixtures to a suite of hydrocarbons of controllable ranges of molecular weight, an abundance of high-quality hydrocarbons is created. Recognizing that world coal supplies will persist for many more centuries, this is an important development.

One may expect that, with our increased knowledge of the factors that influence the magnitude of the electronic band gaps of solids, and the preparative requirements for their production, important developments are likely in the field of photocatalysis. With the practice of band-gap engineering, well established in the design and preparation of solids for specific optoelectronic purposes, it would be surprising if new photocatalysts were not developed in the near future. In this connection, the realization that very finely divided solids (such as the binary III–V and II–VI semiconductors) possess band gaps larger than those of their bulk analogs offers further scope for the preparation of new photocatalysts, especially when they can be stabilized by enclathration inside zeolitic or analogous hosts.

3.2. New Homogeneous Catalysts

Whilst it is not the aim of this review to encompass homogeneous catalysts, a few comments are in order since renewed efforts are now underway to improve methods of immobilizing homogeneous catalysts on inert, durable and large surface area solids. The performance of all homogeneous catalysts could, in principle, be improved by anchoring them on to an appropriately derivatized microporous solid. More often than not, however, the support tends to diminish the effectiveness of the dispersed catalyst, either by reducing its turnover frequency or its selectivity. The supreme advantage that immobilization confers, whether it be on inorganic[33] or polymeric[34] supports, however, is the ease of separating product from reactant.

Some of the materials that ought to be relatively easy to tether to an appropriate solid surface are the metal complexes. And it is these very materials that have recently shown extraordinary efficiency as entioselective catalysts in the important field of chiral synthesis. The work of *Noyori*[9] and others[35, 36] testifies to the significance of asymmetric reactions generally. Among other things, we note that impressive entioselectivities, rivaling those attained via the use of enzymes, have been achieved using metal-complexes.

It is convenient to illustrate the strategy employed by reference to the recent elegant work of *Pfaltz*,[35] who has introduced transition-metal semicorrins, schematized in Figure 9. The C_2-symmetry of these transition-metal complexes ($M = Co^{II}$, Ni^{II}, Pd^{II} or Cu^{II}, as well as other ions) is readily apparent. The chirality elements are dictated by the size and nature of the R groups, which are in close proximity to the coordination center.

With the aid of Figures 10 and 11 we see how these semicorrin complexes function as enantioselective catalysts. Assuming that the transition state of the enantioselectivity-

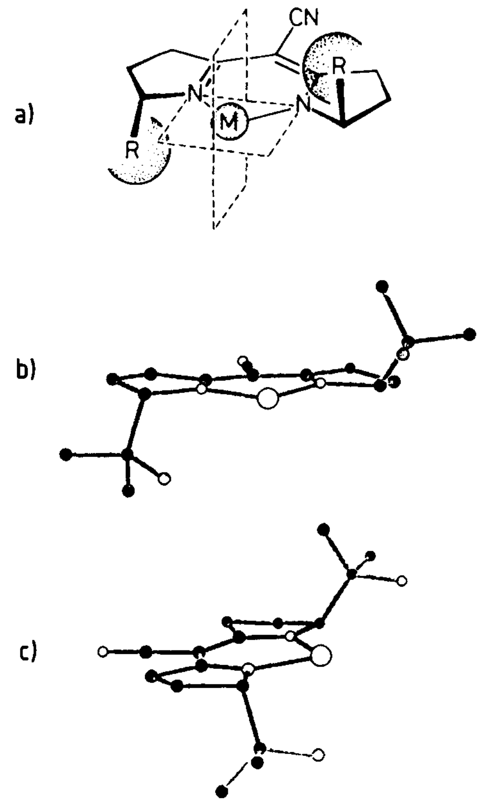

Fig. 9. The C_2-symmetry of the semicorrin ligand is illustrated in (a). The two substituents, R, at the stereogenic centres are held in close proximity to the coordination center (metal M) by the rigid framework of the semicorrin ligand. (b) and (c) represent molecular models when R is a $C(OH)(CH_3)_2$ group. (After *Pfaltz* [35]).

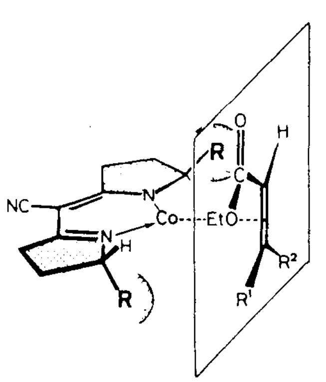

Fig. 10. The transition state for the (semicorrinato) cobalt-catalyzed reduction of α,β-unsaturated carboxylic esters is thought [35] to be of this kind.

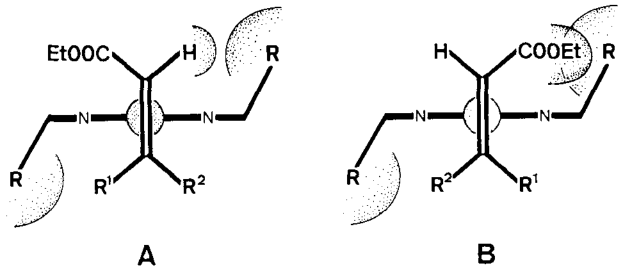

Fig. 11. Illustration of the possible origin of enantioselection. For steric reasons the transition state, represented by B, is forbidden, and that shown in A is likewise preferred [35].

determining step resembles the hypothetical π-complex depicted in Figure 10, the observed selectivity may be rationalized in the following manner. The ester group occupies a sterically unencumbered site of the coordination sphere, whereas the olefinic H-atom is placed in a sterically more crowded environment (Fig. 11 A). However, the transition structure leading to the opposite enantiomer (Fig. 11 B) is expected to be considerably destabilized owing to steric repulsion between the ester group and the adjacent substituent of the semicorrin ligand.

When such elegant design can be introduced to fashion powerful homogeneous catalysts of this kind, there will be a great incentive to devise a 'tea-bag' version[37] of the immobilized catalyst, where the active catalyst may rattle around in its (molecular) container, be accessible to the reactant, and from which product may be washed away so as to regenerate the original catalyst.

3.3. Enzyme Catalysis

It has long been recognized[38, 39] that enzymes have great potential as catalysts for use in synthetic organic chemistry; and their importance in this, and other contexts, is underlined by the processes enumerated in Table 1. Increasingly, a number of small-scale syntheses of materials used in analytical procedures (such as derivatized, biological sensors), in research and as chiral building blocks (synthons) for the production of pharmaceuticals and fine chemicals, is under development. An important trend is the change in technology for the production of enzymes – partly because of improved methods from classical microbiology, and partly because of the viability of genetic engineering, in particular site-selective mutagenesis – for their stabilization and manipulation now makes these catalysts practical for far broader use than hitherto in large-scale synthetic organic chemistry.[38]

The main impetus for biotransformation studies, using enzyme catalysts as center pieces, has been the continued growth in demand for enantiomerically pure compounds. In this context, advantage is taken of the high stereospecificity of the actual reactions catalyzed. Advantage is also taken of the regioselectivity of enzyme-catalyzed reactions. Examples may be found in the selective esterification of dicarboxylic acids, the selective hydrolysis of compounds containing ester functions (e.g. sugar esters) and the selective reduction of compounds containing multiple carbonyl groups.[39]

For the materials scientist, one of the significant messages here is that enzymology is now playing a growing rôle in governing the strategies for the modification of materials derived from fermentation synthesis. Another is the exigent need to evolve more satisfactory means of immobilizing some of the several dozen or so commercially available and useful enzymes, as well as the many more that have recently come to light but which are not yet so readily obtainable.

3.4. Trends in Biocatalysis

Because most enzymes operate effectively under mild conditions (pH usually between 6.5 and 8.5 and at around room temperature) it is often possible to assemble complex systems containing multiple enzymes operating in sequence or in parallel to achieve multi-step processing of the reactants. The work of *Knowles* and *Whitesides* et al.[40] on the synthesis of ribulose 1,5-diphosphate (RuDP), an important substrate in plant biochemistry constitutes a nice example. The point of chief technical interest here is the final conversion of 6-phosphogluconate to RuDP. The kinase that converts ribulose-5-phosphate to RuDP is oxygen sensitive. Thus, the in situ regeneration of NAD from NADH required in the conversion of 6-phosphogluconate to ribulose-5-phosphate cannot be carried out using an oxygen-based regeneration system. The regeneration is, however, conveniently carried out anaerobically using the α-ketogluconate/glutamate dehydrogenase system. This part of the synthesis requires the cooperative action of four enzymes: 6-phosphogluconate dehydrogenase and 5-phosphoribulokinase for the principal conversions, and glutamate dehydrogenase and acetate kinase for in situ regeneration of cofactors.

It may be seen, therefore, that multi-enzyme 'cocktails' constitute a useful way of producing novel biocatalysts. However, there are other ways forward; and these are summarized in Table 4.

Table 4. Current topics and trends in biocatalysis.

Use of: (i) Multi-enzyme systems
(ii) 'Whole cells' and micro-organisms, (e.g. Bacteria such as *Methylococcus capsulatus* (Bath) and baker's yeast).
Antibodies as enzymes (abzymes) [a].
RNA as enzymes (ribozymes) [b].
Genetic and chemical modification of enzymes (protein engineering).
Man-made (miniature) enzymes.

[a] See P. G. Schultz et al. *Angew. Chem. Int. Ed. Engl. 27* (1988) 1172; *Angew. Chem. 100* (1988) 1227. [b] See T. R. Cech, *Nature 339* (1989) 507, for a discussion of the idea that RNA molecules may exhibit catalytic activity.

It is often not necessary to extract an enzyme or a collection of enzymes from the living cell. The latter may be used as such; and whole cell catalysts are nowadays in quite common use, either in their suspended or immobilized state, on an inert solid (often derived from a heat-treated clay). In microbial biotechnology, one uses the microbes as such to catalyze a highly specific chemical change. Both ICI[41] and Shell[42] have put to good industrial use the microbial catalytic conversion (fermentation) of benzene and some of its derivatives to *cis*-3,5-cyclohexdiene-1,2-diol (Fig. 12).

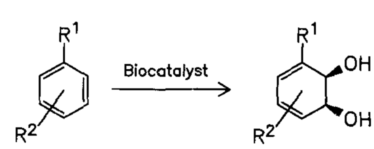

Fig. 12. The process of dioxygenation of substituted benzene (where R_1 and R_2 may, for example, be CF_3 and H respectively) is catalyzed using soil bacteria [42].

Certain enzyme systems, operating in vivo, catalyze hydrooxylations, epoxidations and related oxidation reactions with selectivities unparalleled by any other procedure. They are of great value in the oxidative functionalization of steroids and other hydrocarbons (using fungal systems).

There is a bacterium, known as *Methylococcus Capsulatus* (Bath),[43] a soluble methane monooxygenase, that converts methane to methanol at room temperature. Its mode of action, in particular its regio- and stereo-selectivity, when catalyzing the conversion of cyclohexanes consists of at least three components.

Though other microorganisms have been used to catalyze the (bio) reduction of ketones, it has recently been reported[45] that baker's yeast efficiently catalyzes the reduction of $Cr(CO)_3$-complexed aromatic ketones. Increased enantiomeric excess, over that achieved by other catalysts, and kinetic resolution of planar chiral complexes is feasible with the yeast (Fig. 13).

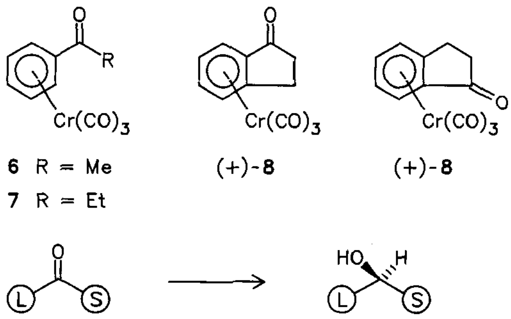

Fig. 13. Aromatic ketones, such as those shown in (1) to (3) when complexed with chromium carbonyl, undergo enantioselective reduction using baker's yeast [45]. The (*S*)-alcohol is always obtained preferentially, indicating that the reduction follows the so-called Prelog rule (Scheme 1; the large substituent L represents the aromatic group)

Abzymes (or catalytic antibodies) have appeared on the scene very recently. Their existence arises because of a question posed more than a decade ago: Can antibodies be made to serve as enzymes? (The term abzymes is a hybrid of *a*nti*b*odies and en*zymes*).

Nature, it is believed, utilizes no more than about 30 to 40 thousand enzymes to effect all the bewildering range of coupled processes responsible for the teaming manifestations of life. So far as practical applications—outside of life cycles—are concerned, the limitation of enzymatic catalysis is that there are so few enzymes compared with the enormous numbers of scientifically important chemical reactions which one seeks to catalyze. Antibodies, like enzymes, are proteins. Their structural features complement, in a literal sense, those of the antigenic sites of intruder species. They have the ability to recognize foreign substances, and are of breathtaking diversity. The immune system, which is where antibodies are generated, is able to make over a 100 million different kinds of antibodies.

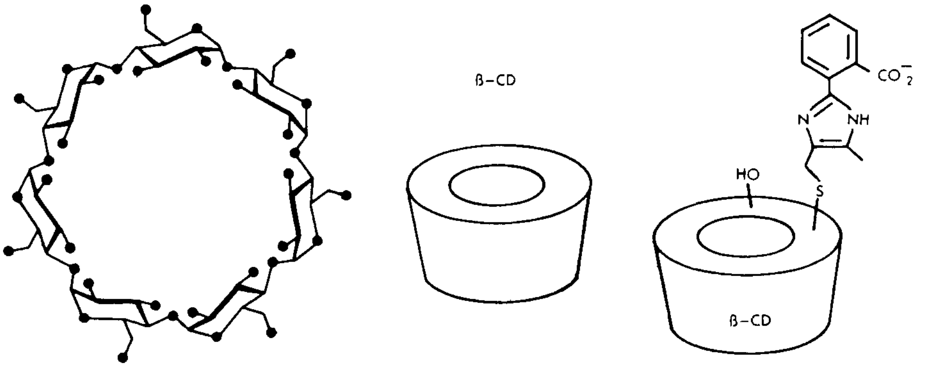

Fig. 14. A miniature enzyme, which rivals the performance of chymotrypsin, has been fashioned by *Bender* et al. [47], from a β-cyclodextrin, which consists of seven sugar units and serves as the receptacle to accommodate (recognize) the substrate molecule. The functional groups grafted on to the rim of the cyclodextrin are the same as those that line the active site of the chymotrypsin. The nature of the active site was determined by X-ray crystallography as in the classic study of lysozyme by *Phillips* [48].

Both antibodies and enzymes exert their influences in much the same way: by binding to other molecules. The question therefore naturally arises: Can one capitalize upon the similarity of antibodies and enzymes (as molecular recognizers) to make the former act as biocatalysts? If so, the door is opened to an almost limitless range of new catalysts. However, antibodies, in their normal rôle, do not catalyze chemical transformations. The way in which they have been recently 'cultured' to function as catalysts, is by feeding the immune system with a stable structural analog of the transition-state through which a particular reactant molecule must pass to be transformed. The antibody will then bind that 'transition state' and its precursor, enabling the free energy with which antibodies bind to their targets to be harnessed in a catalytic process. This kind of abzyme chemistry is in its infancy. But it is already clear that it has a major rôle to play in biological and medical science.

Rationally modified enzymes may be produced by means of site-directed mutagenesis. Such enzymes possess significantly different surface charges, pH-activity profiles and (often) high catalytic activities as well as altered specificities compared with their parental analogs. The serine protease subtilisin (from *Bacillus amyloliquefaciens*)[46] has been 'engineered', by site-directed mutagenesis so as to effect all the above-mentioned changes. The human enzyme called tissue-type plasminogen activator has recently been modified by mutagenesis so as to increase its effectiveness in dissolving blood clots. These are pointers for directions that may be taken in the design and assembly of rationally modified enzymes, i.e. to go from the so-called wild to the mutant state.

There is a radically different route that may also be followed, and that entails the assembly of a miniature enzyme, rivaling the performance of the parent which it mimicks. *Bender* et al.[47] have constructed a miniature biological catalyst (see Fig. 14) which has a performance that closely matches that of chymotrypsin. Chymotrypsin itself is a large (MW 24,800 Daltons) and complicated (245 amino acids) enzyme, the function of which is to catalyze the hydrolysis of a variety of esters and amines. From an X-ray analysis of its structure, the constituents of its active site—the lining, as it were, of the pocket into which the reactant falls upon being bound by the catalyst—were determined. This reveals which chemical constituents are essential for the catalytic action. But an engineered miniature catalyst must also be efficient in capturing the reactant: it has to possess accessible pockets of the right size to accommodate the reactant but not too securely, for the reasons given earlier. *Bender* et al. took advantage of the carbohydrates known as cyclodextrins, which are themselves the products of enzymatic decomposition of starch. The α, β, and γ-cyclodextrins have, respectively, six, seven and eight sugar units (Fig. 14) and on a molecular scale they are like truncated cones or bottomless empty buckets. They also have remarkable receptor properties for a range of guests. It is also rather easy to graft small side-groups on to their rim. The net result is an artificial or miniature enzyme, provided the side-groups that are grafted onto the rim are those present, in the right sequence, at the active site in chymotrypsin itself.

The future of catalysts rests, quite clearly, not on the use of one family of structures, or on one type of catalytic system. It is instead bound up with a rich diversity of disciplines that incorporate major strands of endeavor ranging from solid-state science (physics and chemistry) on the one hand, through to biological, and medical science (encompassing microbiology and enzymology) on the other. The materials scientist and chemical engineer confronted with the task of evolving new systems for catalytic conversion needs to be a polymathic individual capable of roaming freely, and with discrimination, through this vast field of endeavor.

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Materials for the Next Millenium

By Ernest D. Hondros* and Edward Bullock *

Consumption Trends
Technico-Economics
European Performance
Materials Development

1. Introduction – The Materials Spectrum

The materials that make up the things which surround our daily lives and which are taken so much for granted are the product of a highly sophisticated and interactive chain of processes. The mineral-based materials in particular, extracted from the earth as raw ores are converted into alloys, composites and fine ceramics by techniques which call on the utmost ingenuity of man. The complexity of the basic, interactive, scientific disciplines involved in the production of modern, advanced materials is illustrated in Figure 1. The whole spectrum from the minerals in the earth to the formed material component, which has been finely tuned to closely specified properties to meet the requirements of a particular application, is shown.

The intricacy and breadth of such an interdependent chain of processes has evolved over many centuries to meet the immediate needs of society. Progress in materials utilization has largely determined the advance and ascendancy of soci-

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