Catalytically active centres in porous oxides: design and performance of highly selective new catalysts

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Active centres have been designed on high-area, molecular sieve catalysts which, *inter alia*, can convert n-alkanes to n-alkanols and n-alkanoic acids, cyclohexane to cyclohexanol, cyclohexanone and adipic acid, and n-hexane to adipic acid all using either oxygen or air as oxidants. A number of one-step processes and solvent-free chemical conversions, of paramount importance in the development of clean technology, are also described with catalysts designed (i) to oxidise *p*-xylene to terephthalic acid aerobically, (ii) to effect Baeyer–Villiger reactions with oxygen, and (iii) for the conversion of cyclohexanone to ε-caprolactam under mild conditions. The inner surfaces of mesoporous silicas may also be atomically engineered so as to yield high-performance epoxidation of alkenes at Ti^{IV}-centred active sites, as well as enantioselective hydrogenations of organic species using constrained chiral catalysts.

John Meurig Thomas began his academic career at the University of Wales, first at Bangor then at Aberystwyth where he was Head of Chemistry from 1969 to 1978. He then became Head of the Department of Physical Chemistry, University of Cambridge and Professorial Fellow at Kings College. He succeeded George Porter as Director of the Royal Institution and the Davy Faraday Research Laboratory (1986–1991), where he still does most of his experimental work. His researches have covered wide areas of solid state, surface and materials chemistry, and heterogeneous catalysis and he has received numerous medals and awards for his various contributions. Ten years ago he was knighted for services to chemistry and the popularisation of science. In 1993 he became Master of the oldest college in Cambridge, Peterhouse. In 1999, he was the (first) recipient of the American Chemical Society award for creative research in homogeneous and heterogeneous catalysis.

Robert Raja received his Masters degree in Chemistry at the Birla Institute of Technology and Science and completed his Ph.D. on zeolite mimics of enzymes with Paul Ratnasamy at the National Chemical Laboratory, Pune, India (1997). He was Royal Commission of 1851 Exhibitioner at the Davy Faraday Research Laboratory of the Royal Institution of Great Britain (1997–1999) and is currently a Peterhouse Senior Research Associate at the Department of Chemistry, Cambridge University, working jointly with Brian F. G. Johnson and John Meurig Thomas. His research interest focuses on designing novel microporous and mesoporous catalysts for environmentally benign selective oxidation and hydrogenation processes. He is the author of 30 research publications and is the co-inventor of five International Patents.

1 Introduction

Important milestones in our understanding of catalytically active centres were reached in the mid-1960s with Phillips's determination, by X-ray crystallography, of the structure of lysozyme,[1] and Blow's elucidation, also by X-ray diffraction, of the structure of chymotrypsin,[2] and in particular of the precise environment of the catalytic pockets within these solid enzymes. Not only did knowledge of the structure of the active centres suggest a convincing mechanism for the mode of action of these two catalysts, it transformed the world of enzymology. Ever since that time, protein engineers[3] have become increasingly expert at designing new biological catalysts principally because they know (a) what the precise, atomically-resolved structure of the active centre is in many wild enzymes, and (b) the atomic changes that should be made in the vicinity of the active centre so as to enhance either the enzyme's activity, its selectivity, or both.

It is not possible to use the X-ray approach of protein crystallographers in the study of solid (low surface-area) inorganic heterogeneous catalysts, principally because the bulk of the catalyst contributes vastly more to the diffraction of the X-rays than do the minute numbers of active centres distributed in a random manner at the exterior surface of the solid. When, however, highly microporous or mesoporous solids such as those that possess channels, cavities or cages with diameters in the ranges 4–14 Å (micro) and 15–250 Å (meso) are used as catalyst supports, the atomic structures of the implanted active centres may be retrieved by X-ray-based methods but this time by the use of X-ray absorption fine-structure spectroscopy (XAFS) rather than by X-ray diffraction.[4–8] XAFS as a technique yields detailed local structural information even when the catalyst is non-crystalline.[7–9]

Microporous and mesoporous hosts (see below) may have internal surface areas that are so large—in excess of 1000 m^2 g^{-1}—that, effectively, these solids are best envisaged as possessing three-dimensional surfaces. Either by heterogenizing well-defined organometallic precursors on mesoporous hosts, or by preparing microporous hosts that contain within them adroitly placed potentially active centres, advantage may be taken of special *in situ* methods, described fully elsewhere,[5–9] to determine in atomic detail the nature of the catalytically active sites prior to and during the course of the chemical transformation. Armed with this knowledge, one is in a far better position chemically to modify variants of the original catalysts and thereby to enhance their performance. Knowledge of the atomic architecture of the active centre also facilitates interpretative mechanisms of the catalytic path, a task nowadays greatly aided by invoking reliable computational procedures either of the atomistic or electronic kind. Table 1

takes cognizance of all the above points, and also emphasizes other practical desiderata pertaining to porous (open-structure) oxide catalysts discussed herein.

Table 1 Desiderata for engineered porous oxide catalysts

High activity, high selectivity, longevity and durability

Freedom from restrictions imposed by diffusional considerations (reactants and products)

Capable of facilitating regio-selective, shape-selective and enantioselective processes

Should operate under mild conditions and be environmentally, economically and atom efficient

Should be able to facilitate an increasing number of solvent-free conversions

Possession of isolated, well-defined (single-site) active centres, the atomic architecture of which may be delicately modified

Capability of yielding detailed mechanistic understanding of catalytic action

Between them certain microporous (3.5–14.5 Å apertures) and mesoporous (15–250 Å) oxides satisfy all these desiderata

Close to a half of the elements of the Periodic Table are capable of being incorporated into the framework structures—generally in tetrahedral, but more frequently nowadays in six- or five-fold coordination—of the ever-growing families of microporous and mesoporous materials. In the case of microporous solids, the largest two sub-families are the aluminosilicates and **al**umino**pho**sphates (AlPOs). These are essentially three-dimensional networks of corner-sharing SiO_4 and AlO_4 tetrahedra and of AlO_4 and PO_4 tetrahedra, respectively. Heteroatoms, especially those known to exhibit powerful catalytic properties such as Co^{III}, Mn^{III}, Fe^{III}, Ti^{IV}, may be incorporated substitutionally at regular framework sites. (They may, as in the case of cobalt or manganese, be easier to introduce during preparation as Co^{II} or Mn^{II} ions: they are later convertible, by calcination *in situ*, for example, into their higher-valent forms, Co^{III} and Mn^{III}.) Mesoporous solids, on the other hand, are generally easier to prepare in their pristine state (as SiO_2, GeO_2, TiO_2, *etc.*), and heteroatoms, which serve as the loci of catalytic action, are grafted onto the inner surfaces of the mesopores after synthesis, as described in Section 3 below.

2 Specific examples of designed, characterized and proven microporous catalysts

Although the main thrust of our work is to arrive at new solid inorganic catalysts by engineering appropriate active centres through the principles of solid-state and surface chemistry, we especially aim to produce those catalysts that are important in the context of *clean technology*. The intellectual challenge is to devise strategies for such environmentally desirable objectives as:

- the development of one-step processes and/or solvent-free chemical conversions; and
- to produce oxidation catalysts that use air or oxygen as the oxidant.

In describing below the progress that we have made towards these goals we also recall the salient features of those currently favoured, important processes that need to be replaced either because of their expense, and/or inconvenience, or because they are environmentally (or otherwise) unacceptable.

We now proceed to highlight our work on:

A the selective oxidation of cyclohexane in air to cyclohexanol, cyclohexanone and adipic acid;
B regio- and shape-selective oxyfunctionalization of n-alkanes in air to yield n-alkanols and n-alkanoic acids;
C conversion of n-hexane to adipic acid in air;

D aerobic oxidation of *p*-xylene to terephthalic acid;
E Baeyer–Villiger reactions using oxygen as the oxidant for conversion of (i) ketones to lactones and (ii) alkenes to epoxides;
F solid-acid-catalyzed dehydrations and oligomerizations, and
G ammoximation of cyclohexanone to yield the oxime and caprolactam.

For a majority of these conversions it has been shown[8,10,11] that free radicals participate in a crucial, spatially constrained manner. One of the key features of our approach[12,13] to the design of the necessary catalysts is to insert (implant) transition metal ions in high oxidation states into the framework of the microporous oxide. These serve as free radical initiators (see, for example, Section E below), but the mean-free path of the radicals is necessarily small (owing to the microporosity of the solid) so that only a limited number of reactions may ensue. Moreover, by astute choice of the dimensions of the pores of the molecular sieve oxide within which the transition metal ion active centres are placed, one may harness the advantages of shape selectivity, whereby only molecules of certain sizes and shapes may reach, or diffuse away from, the active centres. In some instances, where the siting of active centres and the access to them of reactant molecules are sharply defined, it becomes possible to effect regio-selective as well as shape-selective conversions.[10]

A The selective oxidation of cyclohexane to cyclohexanol, cyclohexanone and adipic acid

Apart from its intrinsic importance in the chemistry of C–H activation,[14] the selective oxidation of cyclohexane to yield cyclohexanol and cyclohexanone is the centre-piece of the commercial production of nylon. Many key precursors and products in the polymer industry are generated in costly and polluting processes that also involve the selective oxidation of cyclohexane (Scheme 1).[15] Intermediates such as cyclohexanol
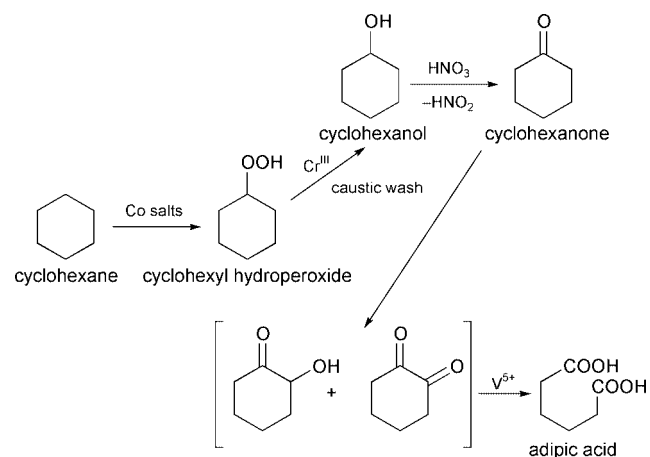
Scheme 1

and cyclohexanone, which, together, are known as K–A oil, are the stepping stones for the production of caprolactam (Scheme 2), which is the monomer for nylon 6, and adipic acid (AA) which is the building block for a series of synthetic polyamide fibres such as nylon 66 and polyurethane resins. Alternate synthetic routes have been developed, such as the one-step oxidation of cyclohexane with either alkyl hydroperoxide as oxidant and a catalyst consisting of cobalt salts,[16,17] or dioxygen as oxidant and a cobalt acetate catalyst in acetic acid.[18] More recent industrial syntheses include homogeneously catalyzed hydrocarboxylation or carboalkoxylation of butadiene.

Because the free radicals generated in the autoxidation of cyclohexane are constrained in space within the interior of the

Scheme 2
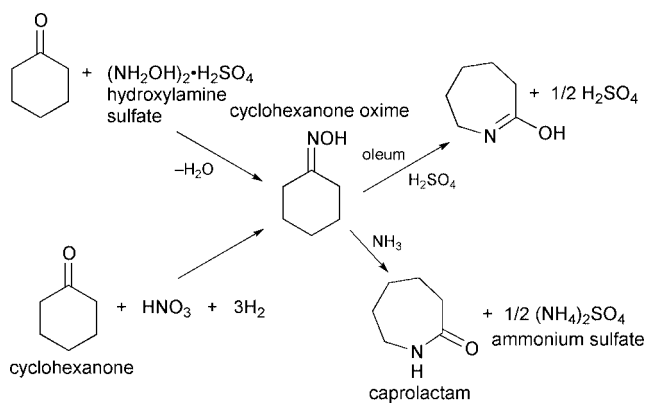
high-area porous catalysts chosen by us, we opted to prepare three distinct kinds of MeAlPO molecular sieve catalysts for this oxidation: $Co^{III}(Mn^{III})AlPO-36$,[19] $Fe^{III}(Mn^{III})AlPO-5$,[20] and $Fe^{III}AlPO-31$[21] (see Fig. 1).

When a few percent of Al^{III} ions in AlPO-36 (pore aperture 6.5×7.5 Å) are replaced by Co^{III} (or Mn^{III}) ions it becomes[19] a good catalyst for cyclohexane oxidation in O_2, the principal products being cyclohexanol and cyclohexanone and small quantities of adipic acid (AA). XAFS measurements show that, in CoAlPO-36, only 50% of the Co^{II} ions present in the framework in the as-prepared state may be raised to the Co^{III} state by calcining in air. In FeAlPO-5, however, (pore aperture 7.3×7.3 Å) all of the iron ions are found (by XAFS) to be in the Fe^{III} state. Indeed, this active site (Fe^{III} in the framework) has an immediate environment almost indistinguishable from that of Fe^{III} in FeZSM-5 (Fig. 2) in which again the Fe^{III} resides in the framework.

We argued that there was merit in designing a MeAlPO molecular sieve catalyst in which the active sites (either Fe^{III} or Mn^{III}) are the same as, but the pores are significantly smaller than, those of MeAlPO-5 analogues. This would mean that, of the reaction intermediates formed within the pores of the catalyst, those that are more sinuous (like AA) would diffuse out readily. MeAlPO-31, in the form of $Fe^{III}AlPO-31$, was therefore selected by us.[21] In effect, we capitalize here on 'product shape-
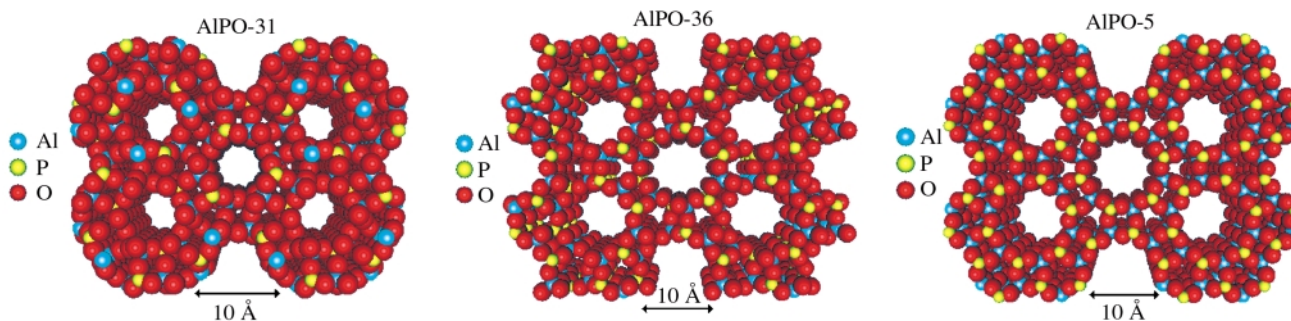

Fig. 1 Computer graphic representation of the framework structures of the three aluminophosphate molecular sieves used in this work. In the active microporous catalysts a small fraction of the Al^{III} framework ions is replaced by either Co^{III} or Mn^{III} or Fe^{III} ions, which function as the active centres (see text). Diameters of the apertures are: AlPO-31, 5.4 Å; AlPO-36, 6.5×7.5 Å; and AlPO-5, 7.3 Å.
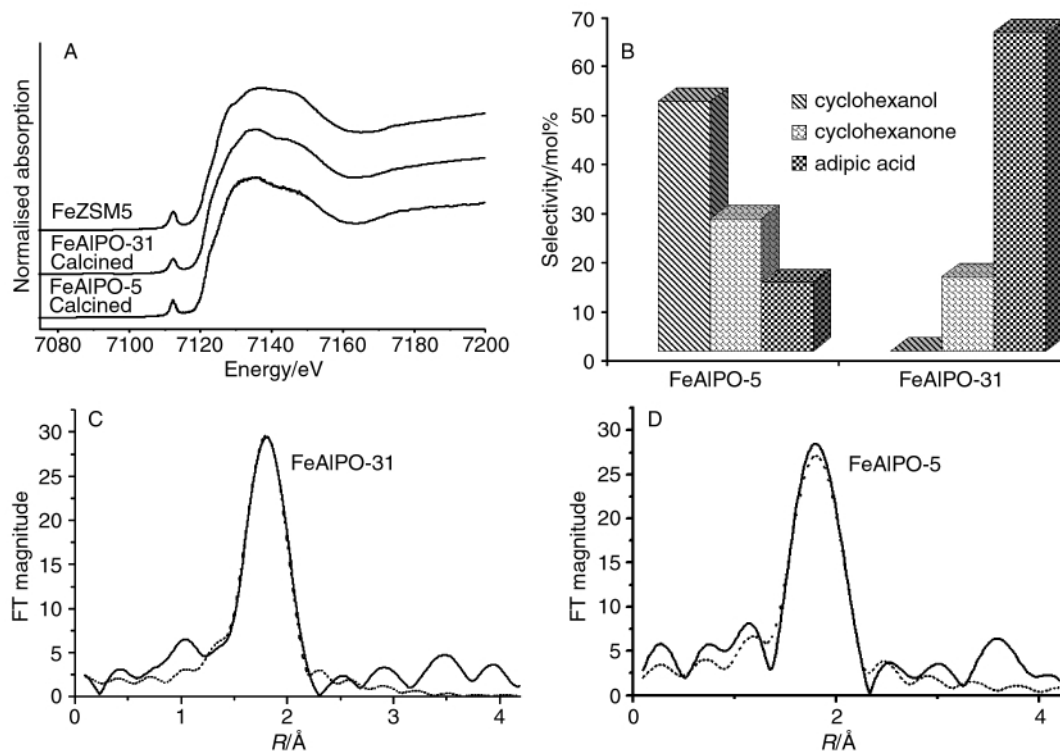

Fig. 2 (A) X-Ray absorption near-edge (XANES) spectra of as-synthesized FeZSM-5 (with framework-substituted Fe^{III} ions) and of calcined FeAlPO-31 and FeAlPO-5. Note the similarities in pre-edge intensities. (B) Bar chart contrasting the product selectivities (at $T = 373$ K, 24 h contact time) of the three principal, selective oxidation products with these two catalysts. (C) and (D) Associated Fourier transform of calcined FeAlPO-31 and FeAlPO-5, respectively (the solid and the dashed curves represent the experimental and calculated data, respectively.

selectivity' (in the same sense as described by Weisz[22] for acid-catalyzed dehydrations of alkanols)—only those products with appropriate molecular dimensions may diffuse easily out of the pores, whereas larger ones formed in the course of the reaction are trapped inside on account of their significantly retarded diffusion. Qualitatively, we may envisage the free radical and molecular intermediates cyclohexanol, cyclohexanone, formed from cyclohexyl hydroperoxide (cHHP) or 2-hydroxycyclohex-anone and 1,2-cyclohexanedione, to be held in the vicinity of the active site until oxidation proceeds further to yield the more mobile and desired linear product AA (see Fig. 3). Because of the more puckered walls of AlPO-31 compared with AlPO-5, and the significantly reduced pore diameter (5.4 Å), we have the constrained environment required for the favoured production of AA (see Fig. 2).

B Regio- and shape-selective oxyfunctionalization of n-alkanes in air

Although linear alkanes are readily oxidized to completion (burnt) at elevated temperatures, they are among the most difficult to oxyfunctionalize at lower temperatures. It is widely acknowledged that the controlled oxyfunctionalization of linear alkanes is one of the major challenges of modern catalysis; and particularly desirable products are those that have been terminally oxidized (hexanoic acid, for example), since these serve as feedstocks for the chemical and pharmaceutical industries. A gleam in the eye of the expert catalyst scientist is to arrive at a catalyst that regiospecifically functionalizes n-alkanes using either air or dioxygen as the oxidant.[23] We have succeeded in doing this (for n-alkane C_nH_{2n+2}, $n = 6$–8, 10, 12) using a carefully designed MeAlPO molecular sieve.[8,10,11,24] Moreover, we have very recently demonstrated how, by judicious modification of the siting of single-site active centres within the same kind of catalyst Co[III]AlPO-18, it also becomes possible to achieve double terminal oxyfunctionalization, thereby enabling n-hexane to be converted in air to AA (see below).

We are certain that Me[III] ions (substituting for Al[III] ones, in the MeAlPO-18) are a *sine qua non* for the catalytic oxidation of the hydrocarbon. If, for example, Mg[II] or Zn[II] ions (or Co[II] or Mn[II] ions) are present in place of Me[III] ions in the MeAlPO, no oxidation ensues.

To achieve single, terminal methyl group attack, one harnesses the fact that the Me[III] ion active site must, during reaction, be readily accessed in a preferential manner by the terminal methyl group of the alkane. One must also ensure that the alkane can gain entry into the interior of the MeAlPO catalyst only by an 'end-on' approach (Fig. 4), otherwise oxyfunctionalization of the CH_2 groups at C_2 and C_3 will occur. [It must be remembered that, all the while during the oxidation, the catalyst and alkanes are swathed in molecular oxygen (Fig. 4) as the latter is so small that it readily reaches the Me[III] and other sites within the molecular sieve catalyst.)

CoAlPO-18 or MnAlPO-18 catalysts are very effective in the regioselective oxidation of n-alkanes. Apart from the qualitative arguments given above for facilitating terminal attack, the quantitative results of energy-minimization (see Fig. 5) yield further insights into, and a deeper understanding of, the regiospecificity.

The computation, which combines Monte Carlo, molecular dynamics and docking procedures,[25] reveals that the terminal methyl group is significantly closer to a tetrahedral framework site than either C_2 or C_3 carbons in the alkane chain. Moreover, the end of the alkane becomes slightly bent, and all this favours oxidation of the terminal (mainly) and penultimate carbon atoms, just as is seen in the experimental results (Fig. 6).

The so-called primary selectivity index (defined as the ratio of concentration of primary products to secondary/tertiary products normalized for the respective number of hydrogens in the alkane molecule) is superior for the Co[III]AlPO-18 and Mn[III]AlPO-18 catalysts than for all previously reported[14,26] inorganic heterogeneous catalysts, even though the latter use sacrificial oxidants such as iodosylbenzene[27] and not air or O_2. It is to be noted[10] that some 70% of the products of oxidation of n-octane after 24 h are the result of oxyfunctionalization of the terminal methyl group for Co[III]AlPO-18 (60% for Mn[III]AlPO-18). Octanoic acid, octan-1-al and octan-1-ol, in descending order, are the principal products of oxyfunctionalization of n-octane.

FeAlPO-31

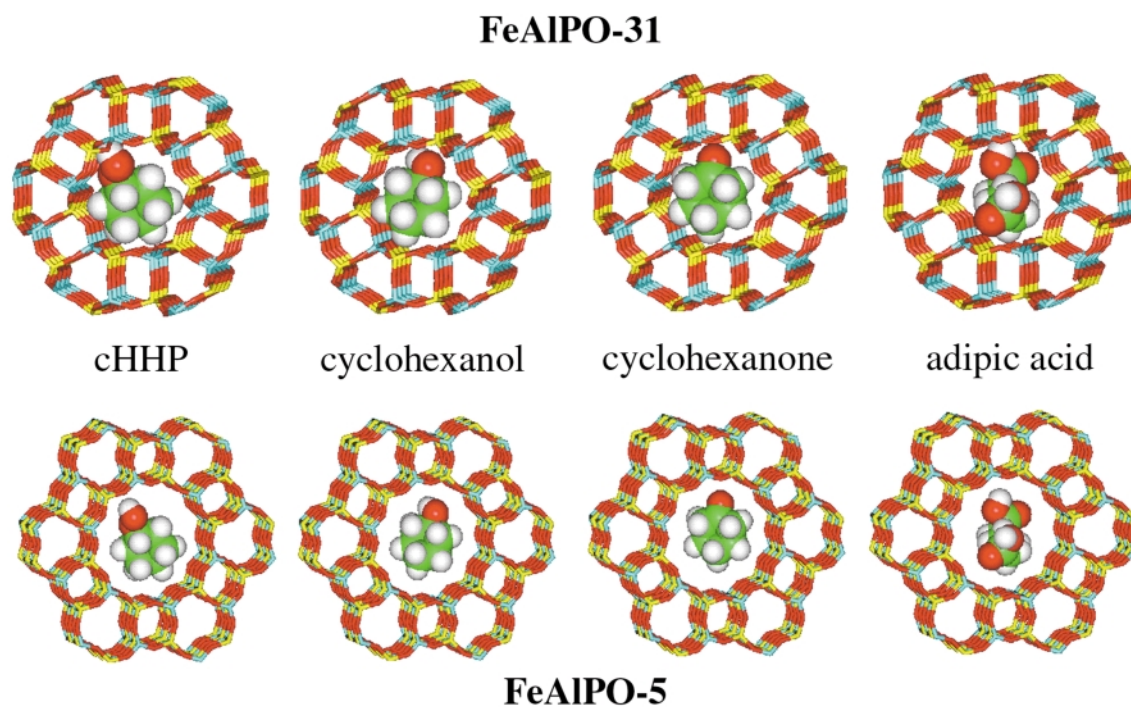cHHP   cyclohexanol   cyclohexanone   adipic acid

FeAlPO-5

Fig. 3 In the autocatalytic oxidation of cyclohexane in air, the main products are cyclohexyl hydroperoxide (cHHP), cyclohexanol, cyclohexanone and adipic acid (AA). In the larger (7.3 Å) FeAlPO-5 catalyst, all products diffuse out freely, whereas in the smaller pore (5.4 Å) FeAlPO-31 catalyst, diffusion out of the solid is much easier for the sinuous adipic acid molecule than for the other three, which fit rather tightly within the pores. This product shape-selectivity explains the results shown in Fig. 2B.
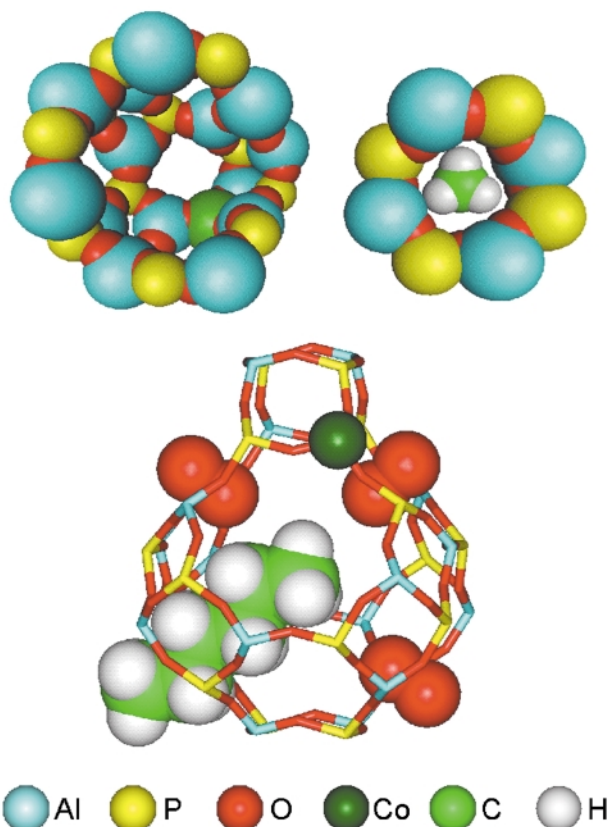
Fig. 4 Views of (left) interior of the chabazitic cage in the $Co^{III}AlPO-18$ catalyst, with the end-on approach of the alkane to the active site emphasized (top right). At the bottom is another view showing the approach to the Co^{III} active site of n-hexane into the chabazitic cage. Oxygen molecules freely enter the cage *via* the other openings.
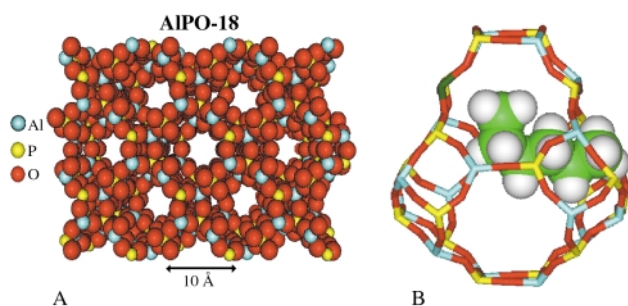

Fig. 5 (A) Computer graphic view of the framework structure of AlPO-18. Each of the intersecting pores, whose openings are shown here, has an array of side pockets possessing a so-called chabazitic structure shown in B. (B) Energy-minimized configuration adopted by n-hexane at 0 K inside the chabazitic cage of the AlPO-18 framework. This configuration was derived from a calculation that combines Monte Carlo, molecular dynamics and docking procedures as described in ref. 25. Note that the terminal methyl group (C_1) is significantly closer to a tetrahedral framework site (and hence to the Me^{III} active centre) than either C_2 or C_3.[10]

C Converting n-hexane to adipic acid (AA) in air

To achieve oxyfunctionalization at both (methyl) ends of n-hexane, a sufficiently large number of framework Co^{III} ions needs to be accommodated on the inner walls of the CoAlPO-18 catalyst in such a manner that two framework Co^{III} ions should be separated by *ca.* 7–8 Å from one another. With the composition $Co_{0.1}Al_{0.9}PO_4$ for the CoAlPO-18 structure (*i.e.* with a Co:P ratio of 0.1, instead of 0.04, as above) there is a high probability for there being two (separated) Co^{III} ions in each cage of the AlPO-18 structure, and for these two ions to be situated opposite one another as shown in Fig. 7.

Fig. 8 summarizes the results of the selective oxidation experiments and, in particular, highlights the contrast in catalytic performance—especially in regard to production of
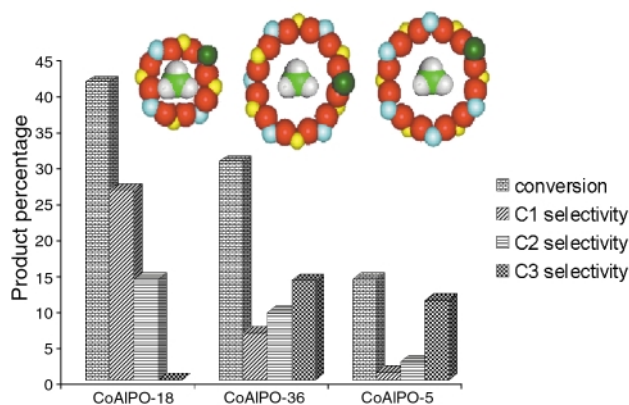

Fig. 6 Bar chart showing the regio-selective oxyfunctionalization of n-hexane when exposed to air and a $Co^{III}AlPO-18$ catalyst. 65% of the products are oxyfunctionalized at the terminal methyl (C_1), and 34% at the penultimate methylene (C_2) carbons, in marked contrast to what occurs under identical conditions (373 K, 1.5 MPa, 24 h) with CoAlPO-36 and CoAlPO-5 catalysts.
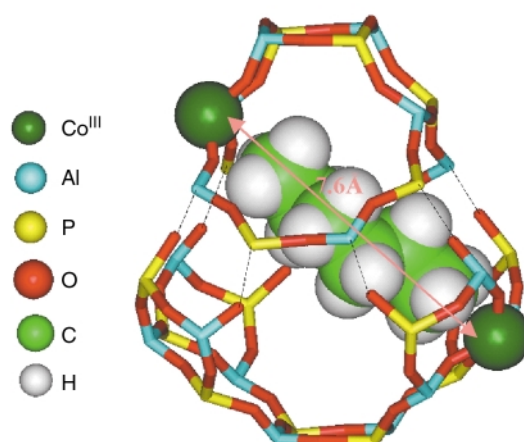

Fig. 7 With two Co^{III} ions at the opposite vertices of the chabazitic cage in CoAlPO-18 (as occurs when the composition is close to $Co_{0.1}Al_{0.9}PO_4$), their separation distance (*ca.* 7.6 Å) is similar to that which separates the two terminal methyl groups in n-hexane. This maximizes the occurrence of oxyfunctionalization of the alkane to form adipic acid (see text and Fig. 8)
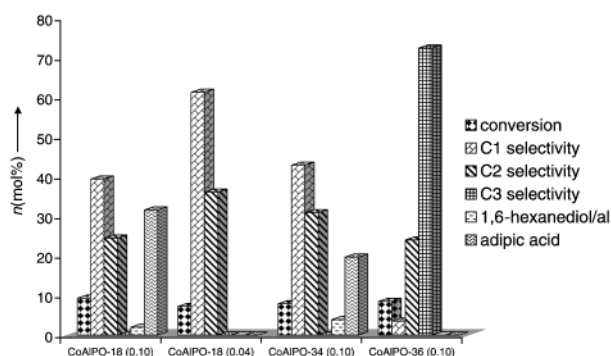

Fig. 8 A low ratio of Co:P (*e.g.* 0.04) in the CoAlPO-18 catalyst yields essentially no adipic acid, whereas a high one (*ca.* 0.10) yields substantial quantities. The closely similar CoAlPO-34 catalyst (which is structurally identical to CoAlPO-18 in its chabazitic cages and pore dimensions) also yields adipic acid with a high (0.10) Co:P ratio. CoAlPO-36, on the other hand, which has no chabazitic cages and has larger pores than CoAlPO-18 or CoAlPO-34, and which therefore exerts no shape selectivity, produces no adipic acid.

adipic acid—of low and high Co:P ratios for CoAlPO-18 (*i.e.* 0.04 and 0.10, respectively). It is to be noted that CoAlPO-34, which is very similar structurally to CoAlPO-18 (they each have chabazitic cages), exhibit broadly similar catalytic performance

when the Co:P ratio is 0.10. But CoAlPO-36, which has a much larger pore aperture (6.5 × 7.5 Å) is markedly different from both CoAlPO-18 and CoAlPO-34.

Detailed kinetic studies (described elsewhere[10,28]) are also informative, especially when compared with those reported earlier for CoAlPO-18 with a Co:P ratio of 0.04. With a Co:P ratio of 0.10, for both CoAlPO-18 and CoAlPO-34 catalysts, hexan-1-ol is the major product during the initial stages of the reaction, but this is subsequently converted to hexan-1-al and hexanoic acid. After 5 h, hexane-1,6-diol, hexane-1,6-dial and traces of adipic acid appear in the reaction mixture as well as the three principal products (hexan-1-ol, hexan-1-al and hexanoic acid) observed earlier.[10]

It is noteworthy that there is no decrease in the hexanoic acid selectivity, but at prolonged contact times (10–24 h) there is a steady decrease in the concentration of both hexane-1,6-diol and hexane-1,6-dial, and a concomitant build-up in the production of AA. Evidently, the production of AA arises as a result of the further oxidation of the hexane-1,6-diol and hexane-1,6-dial. Further, when hexanoic acid was taken as the substrate (instead of n-hexane), using CoAlPO-18 (0.10) as catalyst, we did not observe any conversion to AA. With a Co:P ratio of 0.04, the CoAlPO-18 catalyst, under identical conditions, does not produce hexane-1,6-diol or hexane-1,6-dial or any detectable AA. This active adipic acid-producing CoAlPO-18 catalyst, with a Co:P ratio of 0.10, is remarkably stable and there is no leaching of the cobalt ions (see Section 4) during catalysis.

D Terephthalic acid from p-xylene

Textile and synthetic fibres such as saturated polyesters (Terylene) are made from terephthalic acid, which is currently produced commercially by the oxidation of p-xylene using aggressive reagents such as bromine, and acetic acid as solvent (Scheme 3).[15] In 1992, the worldwide demand for terephthalic
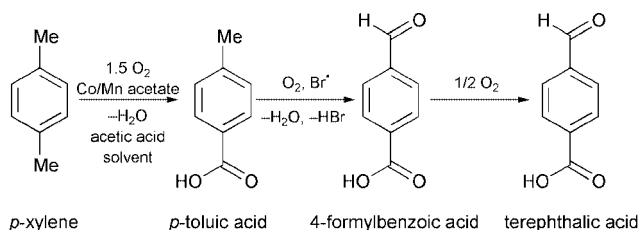
Scheme 3

acid was 12.6×10^6 tonnes and textile and industrial fibres accounted for 75% of this demand.[29] Various salts of cobalt and manganese can be used as homogeneous catalysts and the bromine source is usually HBr, NaBr or tetrabromoethane. The highly corrosive bromine–acetic acid environment requires the use of titanium-lined equipment.

Our approach to the design of suitable catalysts for this important reaction again relies on the use of a microporous molecular sieve in which the active sites are Co^{III} or Fe^{III} ions in framework sites substituting for Al^{III} ions. These catalysts operate under solvent-free conditions without the need for corrosive activators and solvents such as bromine or acetic acid. Their mode of operation also relies on shape-selective, free-radical processes of a spatially constrained kind. Moreover, all such oxidation catalysts designed by us require only benign oxidants (dioxygen or air), and consist of inexpensive, readily preparable, Co^{III}(Fe^{III})–AlPO-36 or Co^{III}(Fe^{III})–AlPO-5.

Our molecular sieve catalysts are effective for the aerobic oxidation of p-xylene, the main products being toluic acid, 4-formylbenzoic acid (4-carboxybenzaldehyde) and terephthalic acid, leaving the benzene ring virtually untouched. 4-Formylbenzoic acid is a troublesome impurity and, because of its structural similarity to terephthalic acid, it co-crystallizes with the latter and becomes trapped and inaccessible for

completion of the oxidation.[30] We find that AlPO-36-based catalysts, containing up to 10 atom% of transition metal ions (Co^{III}, Mn^{III}, Fe^{III}, etc.), suppress the formation of 4-formylbenzoic acid and increase the selectivity for terephthalic acid. As in the case of Co^{III}AlPO-18, containing ca. 10 atom% of Co^{III} ions in the framework (see Section C), one might envisage oxyfunctionalization occurring simultaneously at both methyl ends of p-xylene, which could well be the reason for the higher selectivity of the Co^{III}AlPO-36 (0.10) catalyst for terephthalic acid (see Fig. 9) compared to Co^{III}AlPO-36 (0.04).[31] Owing to the low solubility of terephthalic acid in p-xylene (and since no co-solvents are used) most of it precipitates as it forms.[32]
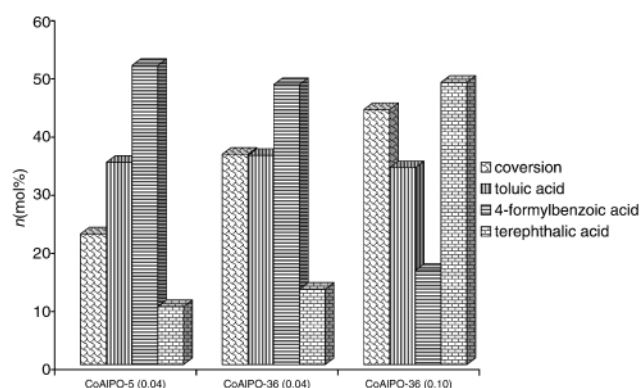
Fig. 9 CoAlPO-36, with a high Co:P ratio (ca. 0.10) is a good catalyst for the aerial oxidation of p-xylene to terephthalic acid (see text).

E Baeyer–Villiger reactions using oxygen as the oxidant

A reaction of great commercial importance is that devised more than a century ago by Baeyer and Villiger[33] who showed how cyclic ketones could be converted into lactones using a powerful oxidant, such as peroxomonosulfuric acid, H$_2$SO$_5$, otherwise known as Caro's acid. This reaction plays a central role in applications that span antibiotics, steroids and numerous aspects of agrochemistry. For environmental and other reasons the use of H$_2$SO$_5$, or alternatives such as (the potentially explosive) 90% H$_2$O$_2$, is frowned upon (where not banned); and some have turned to the use of milder forms of H$_2$O$_2$ in the presence of inorganic materials such as methyl-trioxorhenium.

Our approach (Fig. 10) relies[34] on Mn^{III} (or Co^{III})-framework-substituted MeAlPOs, in which air (or O$_2$) and a
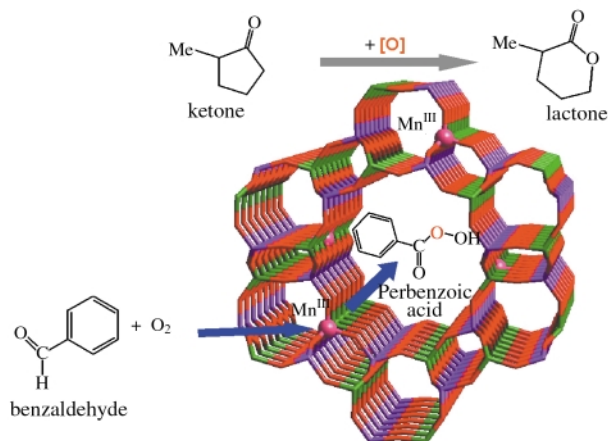
Fig. 10 Graphical representation of a Mn^{III}AlPO-36 molecular sieve catalyst showing the Baeyer–Villiger oxidation of a cyclic ketone to the corresponding lactone. In place of the conventional aggressive oxidants such as H$_2$SO$_5$, here, perbenzoic acid is formed in situ from benzaldehyde in the presence of O$_2$ assisted by the Mn^{III} active sites. (After Thomas et al.[15])

sacrificial aldehyde are used. These constituents produce in situ, a percarboxylic acid (e.g. perbenzoic acid), and this functions as

an environmentally successful oxygen donor to convert the ketone to the corresponding lactone. [A similar approach, again using a sacrificial aldehyde, serves to epoxidize a range of alkenes in O_2 (air), with the same kind of molecular sieve catalyst employing a Mn^{III} (or Co^{III}) active site in its framework.[35]]

Insofar as catalytic epoxidations are concerned, as with Baeyer–Villiger reactions with ketones, the centre-piece of our heterogeneous catalytic conversion is MeAlPO-36 (with Me ≡ Mn^{III} and Co^{III}). In both cases, we exploit the easy autoxidation of aldehydes to promote the *in situ* formation of peroxy acids.[36]

Benzaldehyde molecules may freely enter the large internal areas of MeAlPO-36 thereby generating[37] first PhCO· and then PhCOOO· radicals, which, from the sequence of steps shown below, lead to the formation of perbenzoic acid and the alkene

PhCHO	+	Mn^{III}	→	PhCO·	+	H^+	+	Mn^{II}
PhCO·	+	O_2	→	PhCOOO·				
PhCOOO·	+	PhCHO	→	PhCOOOH	+	PhCO·		
PhCOOOH	+	PhCHO	→	2 PhCOOH				
PhCOOO·	+	C_6H_{10}	→	$C_6H_{10}O$	+	PhCOO·		
PhCOOOH	+	C_6H_{10}	→	$C_6H_{10}O$	+	PhCOOH		
PhCOO·	+	PhCHO	→	PhCOOH	+	PhCO·		
PhCOOOH	+	Mn^{II}	→	PhCOO·	+	OH^-	+	Mn^{III}
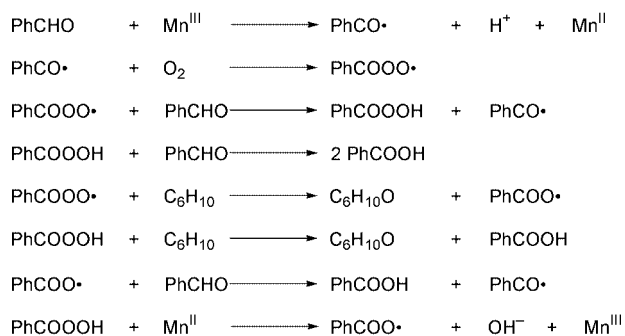
oxide—in our case[35] cyclohexene oxide. This free-radical-based epoxidation of cyclohexene [and other alkenes such as α-(+)-pinene, *R*-(+)-limonene and styrene] is mechanistically quite distinct from the radical-free epoxidation of alkenes using alkyl hydroperoxides and titanosilicate catalysts (which is described in Section 3A, below).

F Solid acid-catalyzed reactions

As described elsewhere,[38] solid acid catalysts are urgently required in the petrochemical and other industries to replace such environmentally aggressive and widely used liquid acids as HF, H_3PO_4 and H_2SO_4. Following the lead given by the Union Carbide group[39] on the use of metal-ion- and silicon (framework)-substituted AlPOs as Brønsted acid catalysts, our colleague Jiesheng Chen and one of us[40] found that many MeAlPO-18 molecular sieves (M ≡ Zn^{II}, Mg^{II}, Co^{II}, Ni^{II}, *etc.*) were extremely effective, shape-selective catalysts for the dehydration of methanol to olefins. Moreover, they could be readily prepared in a state of high phase purity.[40] Such are the dimensions of the cavities and locations of the active sites—loosely attached protons to framework oxygen atoms in the vicinity of the metal ions (Me) {or of the Si^{IV} ions that substitute for framework P^V ions}[41] as shown in Fig. 11—that there is room inside this molecular sieve acid catalyst for the production of only ethene, propene and traces of butene. Because of the spatial restrictions, no aromatic molecules, such as those produced using H^+-ZSM-5 catalysts, can be formed. This is an example of transition-state shape-selectivity.

Success in designing shape-selective, microporous solid-acid catalysts consists in building a molecular sieve, the pore apertures and cage dimensions of which function as spatial constraints for the production of bulky hydrocarbons, but which still favour the generation of the light olefins alluded to above. By careful choice of structure-directing agents (SDAs), a new, shape-selective, microporous MAlPO solid acid catalyst, known as DAF-4, having a framework structure essentially the same as that of the naturally occurring zeolitic mineral levyne was produced.[42] In its Co^{II}-substituted form, DAF-4 transforms methanol with greater than 75% conversion at 350 °C into
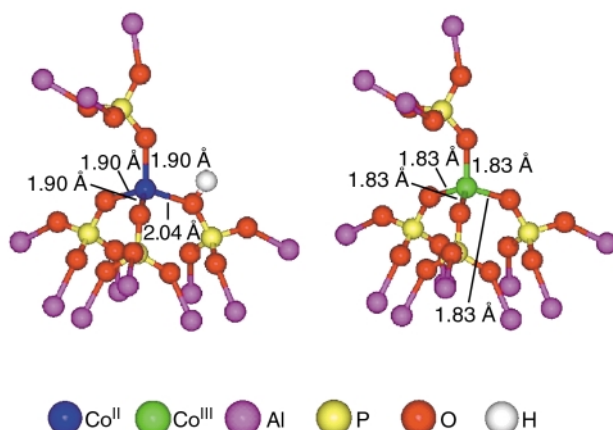

Fig. 11 The Brønsted acid active centre in Co^{II}AlPO-18 consists of the Co^{II} ion (shown in blue) together with its nearby proton (white) loosely bound to an adjacent framework oxygen. (When this acid catalyst is calcined in oxygen, the Co^{II} ion is converted to Co^{III} which is the redox active centre.[5])

ethene and propene, with a selectivity of *ca.* 60% and *ca.* 20% for the two alkenes, respectively.

There are many points of similarity between catalytic reactions in microporous sieves on the one hand and enzymatic reactions on the other, shape-selectivity being the most prominent common feature. Further points of comparison have been made in a recent study[43] with Harris and his group involving the (solid)-acid-catalyzed oligomerization or cyclo-dimerisation of 3-hydroxy-3-methylbutan-2-one, hereafter abbreviated as HMB.

HMB is a stable liquid at ambient temperature. In acidic solutions, however, HMB readily undergoes reaction to generate a variety of products including the cyclic dimer (see Scheme 4) and the dehydrated reactant MeCOC(Me)=CH_2. The
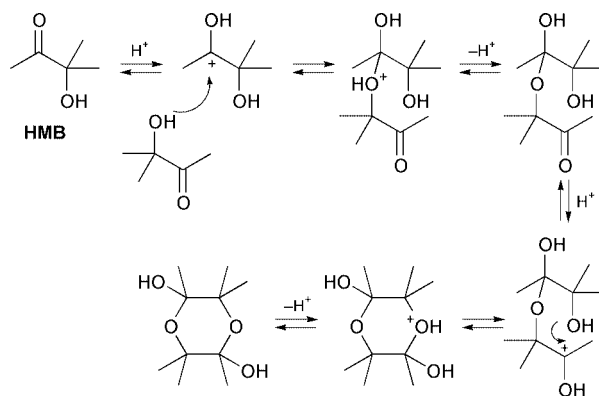
Scheme 4

precise nature and distribution of the products varies significantly depending on the solvent and conditions used for the proton-catalyzed solution-state reaction. However, when HMB is incorporated within the channels of a synthetic zeolite, ferrierite, only one product (established by ^{13}C solid state MAS NMR) is observed together with some unreacted HMB. A plausible mechanism for the Brønsted acid-catalyzed cyclo-dimerisation is shown in Scheme 4. Harris and coworkers[43] have recently made a comparison of the proton-catalyzed bimolecular reaction observed in the cyclo-dimerization of HMB and other monomers with the mode of action of triosephosphate isomerase.

G Ammoximations: ε-caprolactam from cyclohexanone

For completeness, we should also mention the ability possessed by our designed Me^{III}AlPO-36 and Me^{III}AlPO-5 molecular sieve catalysts in effecting ammoximations. The reaction of

cyclohexanone with hydroxylamine (in its sulfate or phosphate form) is the best known method for the production of cyclohexanone oxime, and its subsequent Beckmann rearrangement to ε-caprolactam is an important, industrially used reaction. About 90% of ε-caprolactam world-wide is produced by using the above-mentioned conventional cyclohexanone process. However, large-scale industrial processes for the production of ε-caprolactam (monomer for nylon 6), employing cyclohexanone as the starting material, invariably produce large quantities of ammonium sulfate as by-products (see Scheme 2), which are undesirable. In 1990, the world-wide production of ε-caprolactam reached 3 million metric tons.

Fig. 12 summarizes the results of our ammoximation experiments using cyclohexanone in the presence of ammonia
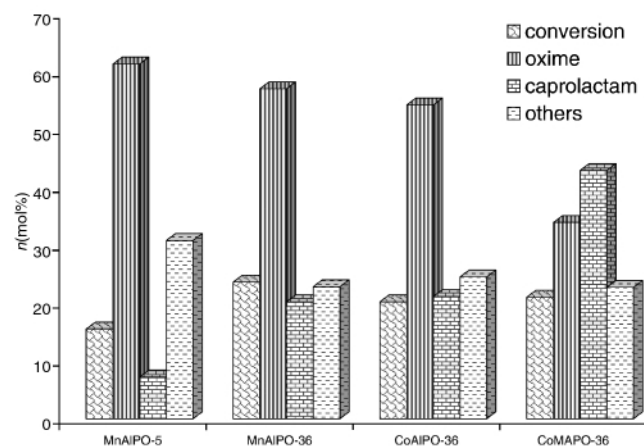

Fig. 12 Bar chart showing the relative performance of various transition metal ion (framework)-substituted molecular sieve catalysts in the conversion of cyclohexanone to its corresponding oxime and ε-caprolactam. The best catalyst is the bifunctional one (CoMAPO-36) which has both redox- and Brønsted acid-active sites.

and H_2O_2 [O_2 or *tert*-butyl hydroperoxide (TBHP) can also be used as oxidants], and MnAlPO-5 or Mn(Co)-AlPO-36 as catalysts, to produce the corresponding cyclohexanone oxime and ε-caprolactam. The ketone (cyclohexanone) is first oxidized in the presence of the 'redox' (Co^{III}, Mn^{III}) ions and ammonia to the oxime (cyclohexanone oxime). The Brønsted acid sites in the molecular sieves catalyze the subsequent Beckmann rearrangement of cyclohexanone oxime to ε-caprolactam. Interestingly, the (deliberate) introduction of acid centres (in the form of Mg^{II} or Zn^{II}, during synthesis, and typified by CoMAPO-36 in Fig. 12), further enhanced the selectivity for ε-caprolactam, thereby bringing out the bifunctional ability possessed by our catalysts.

3 Atomically engineered active sites in mesoporous solids

Here we demonstrate how to design and characterize high-performance catalysts for four distinct categories of reaction: the epoxidation of alkenes, solvent-free hydrogenations of unsaturated organic species, a novel kind of enantioselective hydrogenation, and selective oxidation (including oxidative dehydrogenation). Since these conversions employ mesoporous catalysts (with pore diameters upwards of 30 Å), quite bulky organic molecules (many of which could not gain access to the active centres inside the microporous catalysts discussed so far in this review) may be processed. Moreover, all the desiderata enumerated in Table 1, with the exception of regio- and shape-selective processes that are easier to effect with microporous, molecular sieve catalysts are achievable with mesoporous silicas onto the three-dimensional surface areas of which active sites have been grafted as described below.

A Titanosilicate epoxidation catalysts

The catalytic conversion of propylene to propylene oxide over Ti/SiO₂ catalysts in the presence of *tert*-butyl hydroperoxide (TBHP) is an industrially important epoxidation that accounts for an annual production of more than a million tons of propylene oxide worldwide.[23] From the outset,[44] there has been much speculation as to both the nature of the active site and the mechanism of this reaction and other selective oxidations effected by titanium-centred catalysts.[45] Five years ago, one of us and his colleagues set out[46] to prepare single-site, Ti^{IV}-centred, silica-based catalysts by reacting titanocene dichloride in the presence of triethylamine with the silanol groups that line (see Fig. 13) the inner walls of mesoporous silica. After
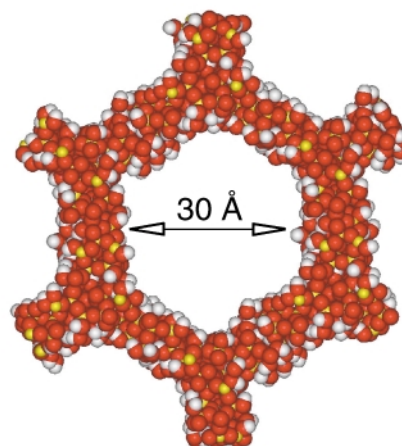

Fig. 13 Computer graphic representation of a single mesopore in MCM-41 silica (red, oxygen; yellow, silicon; white, hydrogen).

subsequent calcining in oxygen, all the organic residue in the silica-bound titanocene was driven off; and XAFS analysis showed that the structure of the active site is as shown in Fig. 14.
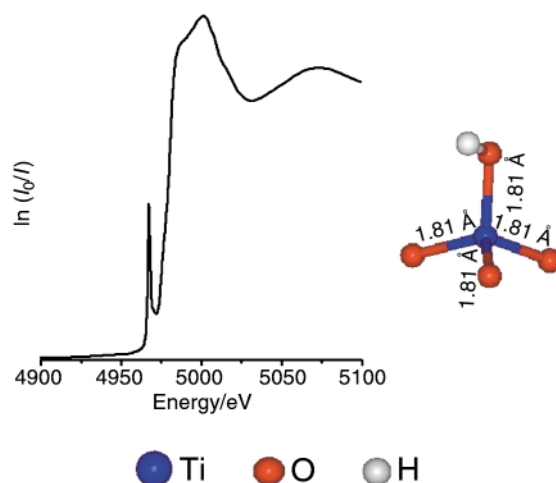

Fig. 14 Ti K-edge XANES of a Ti↑MCM-41 epoxidation catalyst after calcination. Both the XANES and EXAFS data (latter not shown) point to the tripodally attached titanyl group as the (Ti^{IV}-centred) active site.[47]

Both the XANES and EXAFS results for this catalyst revealed that isolated Ti^{IV}-centred active sites, composed of a tripodally-linked titanol groups, abound on the catalyst surface. There are no signs of Ti–O–Ti linkages, nor of any titanyl (T=O) groups of the kind proposed[44] earlier, either of a three- or five-coordinated kind. Detailed comparisons (of XAFS data) with several other local Ti^{IV}-centred oxygen environments leave no doubt[47–49] that the active sites in our highly active (so-called[48] Ti↑MCM-41) catalyst are four-coordinated. There are no 6-coordinated Ti^{IV}-centred sites present in the as-prepared catalyst. Thomas and Sankar also recorded[7,47,49] XAFS data

during the course of operation of the Ti ↑ MCM-41 catalyst in the epoxidation of cyclohexene to its epoxide with TBHP, a convenient test reaction. Significantly, the coordination shell of the original, 4-coordinated Ti^{IV} active sites expands to six during catalysis. And, whereas four of the surrounding oxygens are at distances strictly comparable to those in the pristine active site, in the reactive state there are two additional oxygens situated further away. This fact flatly contradicts the mechanism of epoxidation proposed earlier:[44] a more realistic picture is one in which, just prior to the act of epoxidation, the Ti^{IV}-centred active site is in six-fold coordination. This is compatible with the radical-free picture of epoxidation that we established previously.[48] Our method of preparing highly active titanosilicate catalysts from a titanocene precursor has been shown[50] recently to be ideally suited for the one-pot conversion of citronellal into isopulegol epoxide (see Scheme 5).

Scheme 5
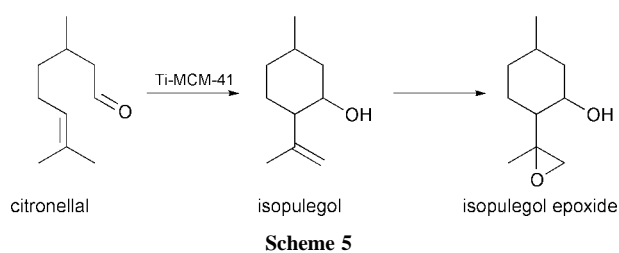
Knowing the structure of the active site, we may set about boosting its catalytic activity by altering its immediate environment. This can be done by replacing[51] one of the silicons in the tripodally attached Ti^{IV} centre by germanium. The resulting catalyst, with a modified active site, exhibits an activity for the epoxidation of cyclohexene that surpasses that of the original catalyst, which, in turn, is superior to that of the catalyst prepared according to the procedure employed for the industrial preparation. There is clearly a favourable electronic influence in proceeding from ⩾(SiO)$_3$Ti–OH to ⩾(SiO)$_2$(GeO)Ti–OH.

It is a fortunate fact that titanosilsesquioxanes,[52] in which the Ti occupies one of the eight vertices of the cube formed by alkyl-substituted Si$_7$O$_{11}$ moieties, are soluble in organic solvents, and that they also function as good, homogeneous epoxidation catalysts.[53] Moreover, the immediate environment of the Ti^{IV}-centred active sites in these soluble catalysts may also be readily probed using the XAFS technique.

Significantly, the performance of the heterogeneous and homogeneous Ti^{IV}-centred epoxidation catalysts are quantitatively very similar,[54] both in the un-enhanced and promoted states, caused by juxtaposing germanium in place of silicon. Furthermore, the fact that the turnover frequency in absolute terms (number of moles of the alkene epoxidized by the active site in unit time) is essentially the same for the heterogeneous as it is for the homogeneous (titanosilsesquioxane) catalyst lends independent proof (beyond the structural one based on EXAFS) that our designed titanosilicate catalysts are indeed 'single-site' ones.

B Engineered active centres for selective hydrogenations: encapsulated bimetallic nanocatalysts for solvent-free reactions

An inherent advantage possessed by mesoporous silicas, of the type exemplified in Fig. 13, is that it is readily possible to insert into such pores mixed-metal carbonylates that are quite bulky, or to graft onto their inner walls carefully constructed, chirally biased large metal complexes. In a collaboration with Johnson and his coworkers, we have capitalised upon this fact. In particular, we have inserted[55] cluster carbonylate salts such as [Ru$_6$C(CO)$_{16}$CuCl]$_2$[PPN]$_2$, where PPN stands for bis-(triphenylphosphino)iminium, into MCM-41 silica. These salts can be shown by *ex situ* HREM studies[55] to be encapsulated in a spatially uniform manner along the inner surfaces of the

mesopores. (The Si–OH groups undergo hydrogen-bonding with the O–C–M bond of the carbonyls). *In situ* XAFS and FTIR studies are used to chart the progressive conversion, by gentle thermolysis, of the carbonylate salts into the denuded, bimetallic (carbided) nanoparticle catalysts. Separate Cu and Ru K-edge XAFS studies, for example, yield[55] a good picture of the active nanoparticle catalyst (*ca.* 15 Å diameter), which has a composition Cu$_4$Ru$_{12}$C$_2$. (They exhibit high turnover frequencies for hex-1-ene, diphenylacetylene, stilbene, *cis*-cycloctene, D-limonene and 1,5,9-cyclododecatriene.)

In a further collaboration with Johnson and his group, a number of solvent-free selective hydrogenations of polyenes using a bimetallic Ru$_6$Sn nanoparticle catalyst have been highlighted[56] (see Fig. 15 and 16). The selective hydrogenation
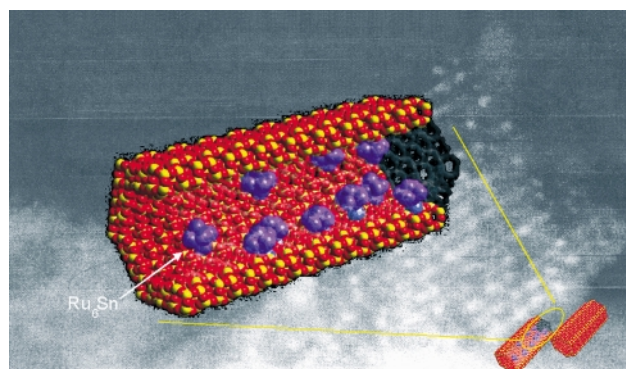

Fig. 15 Clusters of Ru$_6$Sn, anchored at the inner surfaces of mesoporous silica (MCM-41) function as powerful catalysts in the solvent-free selective hydrogenation of a variety of polyenes. In the background electron micrograph the linearly arranged white spots demarcate the anchored bimetallic clusters (diameter *ca.* 10 Å).[15]
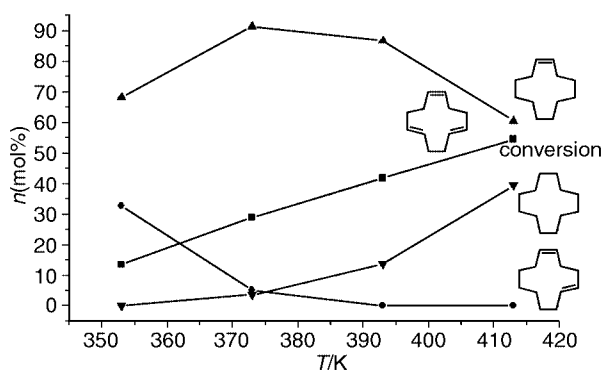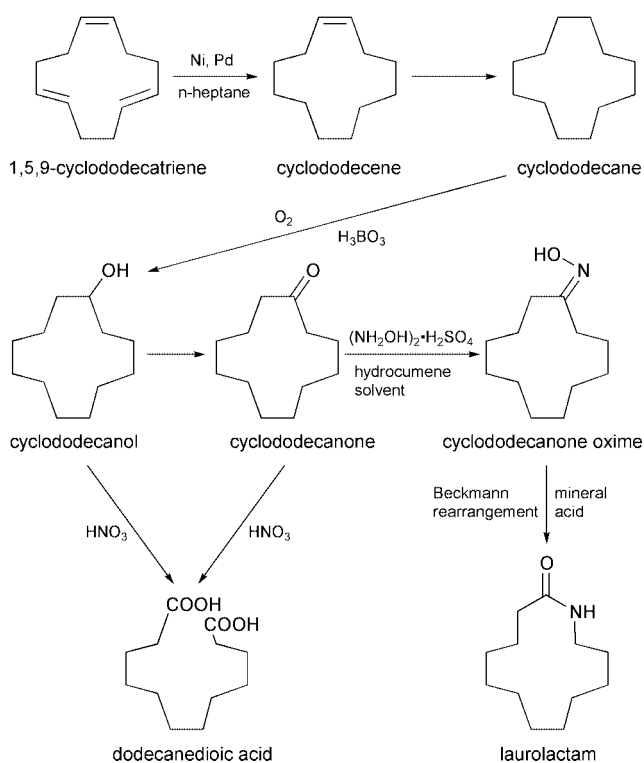

Fig. 16 The influence of temperature on the activity and selectivity of an anchored Ru$_6$Sn nanoparticle catalyst in the selective hydrogenation of 1,5,9-cyclododecatriene.[56]

of polyenes such as 1,5,9-cyclododecatriene is quite an important procedure in the synthesis of organic and polymeric intermediates such as laurolactam, 12-aminododecanoic acid and dodecanedioic acid, which are important monomers for nylon 12, nylon 612, copolyamides, polyesters and for various materials used as coatings (see Scheme 6). Hitherto, Raney nickel, Pd, Pt, Co, and mixed transition metal complexes have been used for these hydrogenations, and all the reactions entail the use of organic solvents (such as n-heptane or benzonitrile) and often in the presence of efficient hydrogen donors (such as 9,10-dihydroanthracene). Our procedures emphasize that there are solvent-free routes available for such processes.

## C Constrained chiral catalysts for enantioselective hydrogenation

The large diameters of mesoporous silica permit the direct grafting of complete chiral metal complexes on to the inner walls by functionalizing the pendant surface silanols with organic groups such as alkyl halides, amines, carboxylates and

Scheme 6 (left column top)

1,5,9-cyclododecatriene → cyclododecene → cyclododecane

Ni, Pd
n-heptane

O₂ / H₃BO₃

cyclododecanol   cyclododecanone   cyclododecanone oxime

(NH₂OH)₂·H₂SO₄
hydrocumene solvent

HNO₃   HNO₃

Beckmann rearrangement | mineral acid

dodecanedioic acid   laurolactam

Scheme 6

phosphanes. As pointed out by our colleague Maschmeyer,[57] this opens routes to the preparation of novel catalysts consisting of quite large concentrations of accessible, well-spaced and structurally well-defined active centres. As detailed elsewhere,[8,57,58] chiral chelate ligands based on 1,1′-bis(diphenylphosphino)ferrocene (dppf) are particularly attractive for tethering on to mesoporous silica; and the superior performance of the chiral, heterogenized catalyst compared with the unconfined homogeneous analogue in the allylic amination (Tsuji–Trost) reaction between cinnamyl acetate and benzylamine has been described.[58]

We have recently demonstrated[59] that this kind of confined dppf catalyst displays remarkable increases in both enantioselectivity and activity in the one-step hydrogenation of ethyl nicotinate to ethyl nipecotinate (see Scheme 7) when compared to an analogous homogeneous compound. Some of the key points to note here are as follows:

ethyl nicotinate → 1,4,5,6-tetrahydronicotinate → ethyl nipecotinate

(i) 2H₂ Pd/C   (ii) H₂ Pd/C chiral modifier
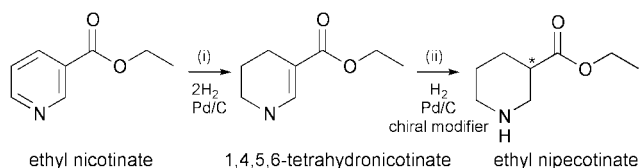
Scheme 7

- the previously available[60] procedure for producing the biologically relevant nipecotinate entailed a two-step process (Scheme 7) and the use of a chiral modifier, such as dihydrocinchonidine, in one of the steps;
- confinement is a crucial step in producing the enantioselective, anchored ferrocenyl precursor that is prepared as outlined in Scheme 8;
- when exactly the same ferrocenyl precursor is attached in a spatially unconstrained fashion to a silsesquioxane, thereby producing a homogeneous catalytic analogue of the chiral catalyst confined within mesoporous silica, no enantioselectivity results (Fig. 17);
- to maximize the efficiency of such confined chiral catalysts the exterior surfaces of the mesoporous silica are first reacted with dichlorodiphenylsilane, so as to ensure that anchoring of

Scheme 8 (right column top)

silane-functionalized ferrocenyl ligand → metal-containing ferrocenyl precursor
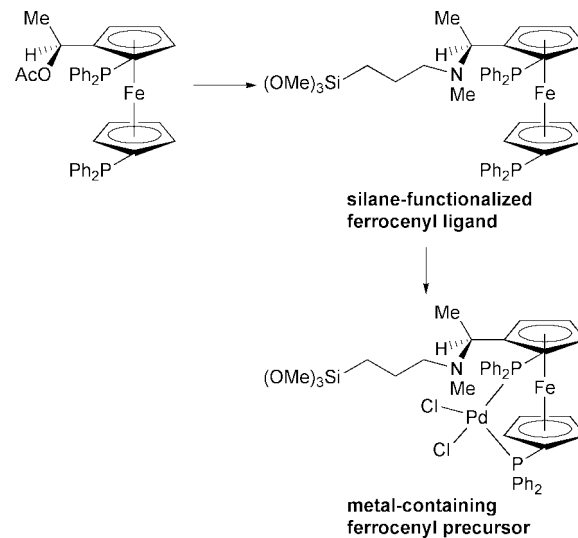
Scheme 8

the dppf precursor occurs only at the interior faces of the siliceous support.[58]

It is to be emphasized that the enantioselectivity that we achieve in this approach (with constrained chiral catalysts) is somewhat different from that which was introduced by Corma[61] but quite distinct from that used by Hutchings.[62]

D Selective oxidations and oxidative dehydrogenations

Here we illustrate briefly the merits of engineering well-defined active centres at mesoporous silica surfaces for the purposes of (i) oxidatively dehydrogenating methanol at Mo^{VI}-centred sites; and (ii) selectively oxidizing hydrocarbons grafted at vanadyl centres and an anchored oxo-centred Co^{III} acetate oligomer.

Just as $Ti(\eta^5\text{-}C_5H_5)_2Cl_2$ serves as an excellent means of introducing isolated Ti^{IV}-centred, catalytically active sites on a silica support (for epoxidation and other conversions[50]), so also does[63] $Mo(\eta^5\text{-}C_5H_5)_2Cl_2$ function as a similar precursor for the creation of Mo^{VI}-centred sites for the oxidative dehydrogenation of methanol to produce formaldehyde. Mo K-edge XAFS shows that, at low loadings, isolated, tetrahedrally-bound MoO_4 species are generated on the surface; however, these bipodally attached oxo–molybdenum species are held less strongly to the silica support than the tripodal Ti^{IV} centres described earlier.

Designed vanadium-centred active sites situated at the inner surface of mesoporous siliceous hosts (as well as at amorphous, microporous mixed-metal oxides of the types described by Maier et al.[64]) are catalysts, under mild conditions, for both the epoxidation of alkenes (typified by cyclohexene) and the selective oxidation of alkanes (typified by cyclohexane). XAFS studies proved invaluable in determining the nature of these active sites (see Fig. 18), the performance of which could be boosted[65] by juxtaposing methyl groups (to enhance the hydrophobicity) in the immediate vicinity of the vanadyl active centre.

In homogeneous mixtures of Co^{III} acetates rich in acetic acid, such as those used commercially in the selective oxidation of cyclohexane, many oligomers of the cobalt salt are present. By isolating and testing the catalytic activity of each separate oligomer it was found that the trimer displayed exceptional selectivity in oxidizing the CH groups of adamantane.[66] Specimens of the trimer were accordingly tethered to the inner walls of mesoporous silica, and the resulting uniform heterogeneous catalyst exhibited high activity in the solvent-free oxidation of cyclohexane to cyclohexanol and cyclohexanone using the sacrificial oxidant TBHP.[17] Moreover, in situ XAFS measurements showed that significant structural changes occurred in the tethered trimer during the initial period of induction prior to the onset of catalysis. There is reason to
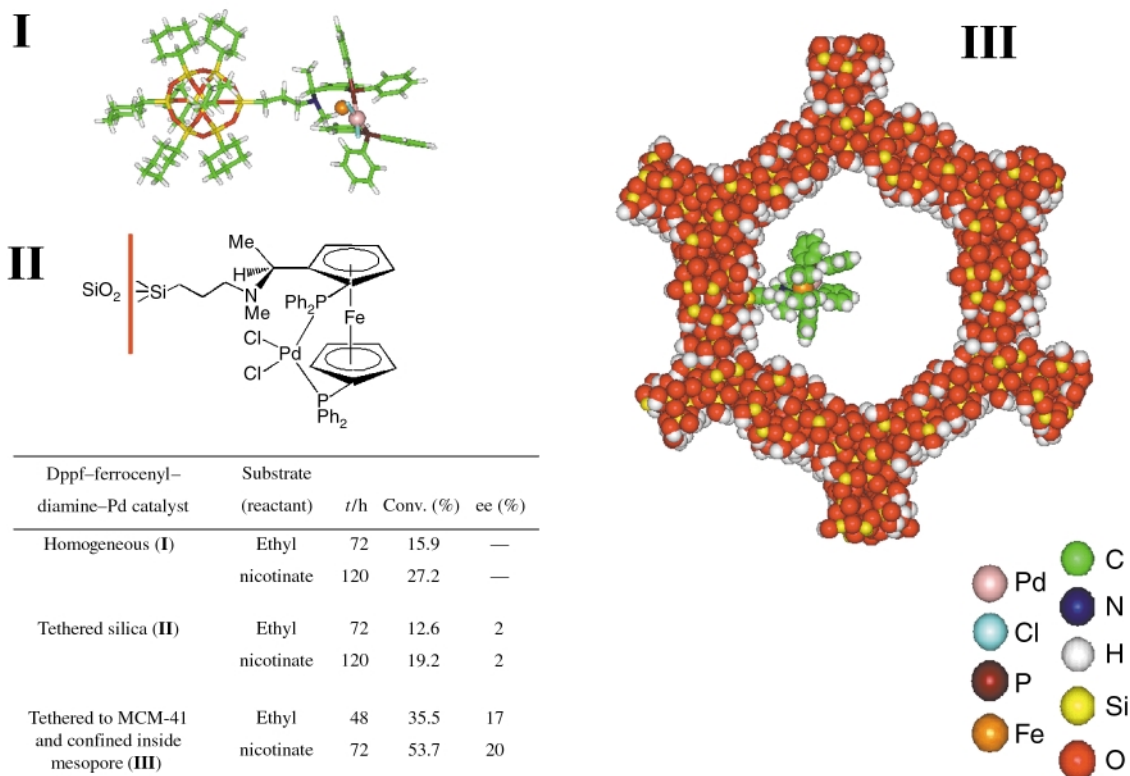
Fig. 17 Depiction of the catalytically active centre attached to a soluble silsesquioxane moiety **I** (top left) to a non-porous silica particle **II**, and bound in a constrained manner inside mesoporous silica **III** (right). The table (bottom left) shows that a significant measure of enantiomeric excess (ee) and substantial conversions are obtained only when the dppf–ferrocenyl–Pd-catalyst is in a constrained environment within the mesopore.

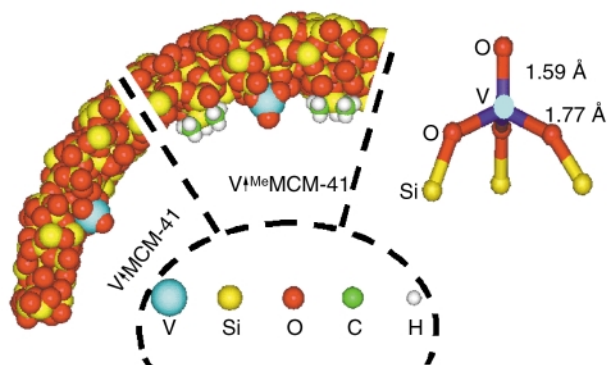| Dppf–ferrocenyl–diamine–Pd catalyst	Substrate (reactant)	t/h	Conv. (%)	ee (%)
Homogeneous (**I**)	Ethyl	72	15.9	—
	nicotinate	120	27.2	—
Tethered silica (**II**)	Ethyl	72	12.6	2
	nicotinate	120	19.2	2
Tethered to MCM-41 and confined inside mesopore (**III**)	Ethyl	48	35.5	17
	nicotinate	72	53.7	20

Fig. 18 A vanadyl active centre: (left) grafted onto a mesoporous silica; (centre) surrounded by nearby surface methyl groups to boost hydrophobicity; and (right) model, with bond distances derived from XAFS spectra (not shown), of the four-coordinated vanadium ion.[65]

believe[67] that certain metal complexes anchored to the inner walls of mesoporous silica may function as effective oxidation catalysts.

E Other related reactions

The atomic engineering of active centres on silica surfaces described above is part of a widely-applicable approach used previously by us[17,38,66,68] and others, especially by Basset and his group in their pioneering work[69] on surface organometallic chemistry. Basset *et al*.[70–73] have, for example, shown how various kinds of C–C bond cleavage and formation (involving hydrogenolysis or metathesis of alkanes) may proceed smoothly at tantalum hydride centres that are either monopodally or bipodally anchored to silica surfaces.

Among the principles that we seek to emphasize in this review are the twin advantages in using (a) synchrotron radiation for the *in situ* and *ex situ* characterisation[47] of the precise nature of the engineered active centres, and (b) well-defined mesoporous silicas with their high internal surface areas and adjustable pore diameters.

4 The stability of our catalysts

When we began our studies of MeAlPO selective oxidation catalysts, many practitioners who had earlier studied such solids predicted that we would run into insurmountable obstacles largely because of the tendency for the framework ions that constitute the active sites to be leached out of the molecular sieves during reaction. It is undoubtedly true that such solids do tend to suffer leaching if aggressive solvents (such as acetic acid) are used. But, from the outset, our aim was to achieve desirable chemical conversions in a solvent-free manner. By simply using the reactants (such as n-alkanes and oxygen as oxidant) we found that our microporous, molecular sieve catalysts (Me^{III}AlPO-n with Me ≡ Fe^{III}, Co^{III} or Mn^{III}) remained intact even after repeated use, provided that the overall conversion in the oxidations was kept relatively low (*ca.* 10–12%). This level of conversion avoids leaching by the polar products of the reaction (such as the n-alkanoic acids).

One recommended experimental test designed to ascertain whether the catalysis is truly heterogeneous or merely apparently so entails filtering off the 'active' solid catalyst from the reaction mixture (when hot) and then determining whether the reactants are still catalytically converted (by leached out active entities) in the residual liquid. Whenever we have carried out such tests they have always been negative: no reaction ensues in the absence of the solid molecular sieve catalyst [a striking example is shown in Fig. 2b of ref. 10(a)].

There is another incontrovertible procedure[20] to test whether the catalysis is truly heterogeneous or only apparently so because leached out ions are retained within the liquid phase that closely adheres to the molecular sieve. This is the one which involves taking an equimolar mixture of n-hexane and cyclohexane and subjecting it to aerobic oxidation over a Co^{III}AlPO-18 (or Mn^{III}AlPO-18) catalyst. There is, unsurprisingly, no conversion whatsoever of the cyclohexane molecule

as it is too large to gain access into the interior of the MeAlPO-18 where the vast majority of the active sites are located. The conversion of the n-hexane, however, is, as expected, to be quite substantial (there being good selectivity for terminally oxy-functionalised products). However, when the same reactant mixture is dissolved in acetic acid, the $Co^{III}AlPO$-18 catalyst gives rise to considerable oxidation of both cyclohexane and n-hexane. Moreover, C_2 and C_3 alcohols and ketones are now the main products (not the C_1 alcohols or acids) from n-hexane. Clearly, acetic acid as a solvent results in homogeneous as well as heterogeneous catalysis.

Other work (as yet unpublished) using CrAlPO-5 as a molecular sieve catalyst has likewise been found to facilitate genuine heterogeneous conversions (such as the decomposition of cyclohexyl hydroperoxide) of organic chemical compounds.

Leaching has to be considered as a factor also in the epoxidation and other oxidative reactions catalyzed by mesoporous silica on to which Ti^{IV} or Mo^{VI} centres have been grafted. Whereas tripodally attached Ti^{IV} ions stand up well to continued use as epoxidation catalysts with reagents such as TBHP,[54] detailed investigations[52c,53a] with model silsesquioxanes show that bipodally or monopodally attached Ti^{IV} ions are less securely held and tend to be leached out during reaction. Moreover, in the case of dipodally attached Mo^{VI} ions, leaching is quite appreciable, making the molybdenocene-derived Mo/SiO_2 catalyst[63] analogue of Ti/SiO_2 less effective in oxidative dehydrogenation reactions.

Acknowledgements

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