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Reviews

Heterogeneous Catalysis in Liquid Phase Transformations of Importance in the Industrial Preparation of Fine Chemicals

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Abstract:

This review focuses on the use of heterogeneous catalysts in the production of fine and speciality chemicals. The major emphasis is on those systems which have been commercialised already and those which are close to commercialisation. These include the use of TS-1 for oxidation reactions including the production of hydroquinone, caprolactam, and alkene oxides, and clay-supported catalysts such as clayzic, which are commercially available for acid-catalysed reactions, in particular Friedel−Crafts reactions. Base catalysis and acid-catalysed halogenation and nitration are also covered.

1. Introduction

The use of solid heterogeneous catalysts in the chemical industry is a theme of exceptional importance. For decades, the use of such catalysts in reactions such as isomerisation and cracking has been practised on an enormous scale.[1] The use of heterogeneous catalysts in liquid phase applications has in comparison been limited, almost exclusively, to the field of hydrogenation. It is only in the last decade or so that solid catalysts have become important in liquid phase applications.

One of the driving forces behind the rapid expansion of such systems has been the development of the field of *supported reagents*. Supported reagents were first alluded to in the 1930s, but the main body of work has been carried out in the last 15 years.[2,3] The earlier supported reagents consisted mainly of stoichiometric reagents adsorbed onto a high surface area solid such as alumina, silica, or a clay, the rationale being that the dispersion of the reagent over the large surface areas typical of these supports would allow more rapid reaction through greater accessibility of the reagents to the substrates. While this is undoubtedly often a significant factor, one theme which will be developed in this review is the importance of other, more fundamental effects, some of which can have a dramatic influence on the system, often leading to entirely new structures. These original reagents are easily prepared and handled and allow a more rapid reaction and, crucially, an easier workup than the unsupported equivalent as the inorganic supported reagent and spent reagent can be easily filtered or centrifuged from the reaction system. Often, superior selectivity is also achieved. The one main drawback of the stoichiometric supported reagents remains the large amount of solid required in the reaction mixture.

It soon became apparent that one could also prepare supported reagents which were catalytically active. Such materials retain all the advantages of the stoichiometric supported reagents, without the disadvantage of requiring excessive quantities of solid. In particular, the current and increasing emphasis on *clean technology* has provided an additional driving force for the use of heterogeneous catalysts in an ever increasing range of chemical transformations. As is the case with the stoichiometric materials, not only are the catalytic supported reagents easy to separate and recycle, but, in addition, it has often been shown that supported reagent catalysts display enhanced selectivity compared to their solution phase counterparts.

Zeolites represent the second group of materials which have contributed to the boom in solid catalysts. While zeolites have been used for many years in gas phase reactions, their utility in liquid phase systems has only recently been exploited. This is largely due to the microporous nature of the original zeolites, which limits their utility to small molecules, and their suitability for high-temperature applications. More recently, the field of zeolites has expanded with a remarkable variety of structures and types of zeolitic materials becoming accessible. These include the redox zeolites, which are capable of catalytic oxidation,[4,5] and the large-pore zeolites such as the MCMs[6] (a class of *mesoporous* inorganic materials prepared in a similar way to zeolites, but possessing pores with tightly defined dimen-

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(1) See, for example: Malonowski, S.; Marczewski, M. In *Catalysis*; Bond, G. C., Ed.; RSC: Cambridge, 1989; Vol. 8, Chapter 4.

(2) Clark, J. H. *Catalysis of Organic Reactions by Supported Inorganic Reagents*; VCH: New York, 1994.

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sions, which can be varied, in a controlled fashion, from ca. 1.8 to 10 nm; the acronym MCM stands for Mobil composite materials), which make accessible materials of well-defined and tunable porosity. Particularly important is the fact that the porosity lies in the mesoporous range, which is exactly that required for the manipulation of fine chemicals. For the first time it is becoming possible to design solid catalysts whose physical characteristics can be "made to measure" for the intended application.

This review will discuss a few selected examples of such novel catalysts and their uses, without attempting to be comprehensive. Rather, those materials which are in commercial use, or are close to commercial exploitation, will be concentrated on and discussed in some depth.

2. Solid Acids

The theme of solid acids has long been actively researched. The majority of the older applications concern gas−solid heterogeneous catalysis, particularly high-temperature reactions of petrochemical feedstocks. Clays were used for this purpose as early as the 1930s. They were replaced firstly by synthetic silica−aluminas, which led to improved reproducibility, and then by the X and Y zeolites. Zeolites are better suited to such high-energy reactions, having greater resistance to tar formation and improved thermal stability compared to the natural clays. These advantages lead to longer lifetimes on-stream and easier regeneration of deactivated catalyst. The zeolites can also be more acidic than clays. Exchanging the naturally occurring exchangeable Na^+ ions of a clay for H^+ can boost the Bronsted acidity of a clay from ca. $H_0 = -1.5$ to ca. $H_0 = -8$. This significant increase in acidity leaves the clays still several orders of magnitude less acidic than high-Si zeolites, for which acidity as high as $H_0 = -12.8$ has been reported.[7] This level of acidity is approaching the superacid range, and these materials are capable of *n*-alkane isomerisation, albeit at $T > 500$ K.

A variety of solid acids are used industrially, predominantly in large-scale processes such as cracking (X and Y zeolites), alkylation (zeolites, SiO_2−phosphoric acid), and the formation of alcohols from olefins (SiO_2−phosphoric acid). Products accessed this way include styrene (via reaction of benzene with ethene) and *p*-xylene, which is then oxidised to the diacid for use in polyester manufacture. Such gas phase processes fall outside the scope of this article, but are well documented and reviewed.[1,8−11]

The choice of solid acid catalyst for liquid phase application is restricted on two general fronts: firstly, the harsh conditions required for many of the target reactions effectively preclude the use of acids based on organic polymers; and secondly, the low costs of existing processes further restrict the range of solid acid systems. These constraints have focused the research in this area onto those catalysts which can be readily prepared from inexpensive, stable materials. The clays, zeolites, and related oxides such as silica and alumina appear therefore to be suitable candidates for the development of appropriate catalysts.

Whereas zeolites find many applications within the field of bulk chemical manufacture because of their high acidity and stability, their impact in the field of speciality and fine chemicals has been much less dramatic. The reason for this is their restricted pore size. The zeolites mentioned above typically have pore sizes of <0.6 nm, denying access to medium-size and large molecules, and reducing diffusion rates of most small molecules sufficiently to render them ineffective as catalysts. While much effort is currently being expended on larger pore zeolitic materials (for example, the MCM materials) with significant success, research has not yet reached the point where large-scale applications are imminent. Nevertheless, the impact of such solid catalysts will almost certainly be significant in the near future.

This restriction has led to renewed interest in the clays, and particularly in modified clays, as acid catalysts. Three general approaches have been taken, based on the ability of the clays to act as ion exchangers, as supports, and as a base framework for pillaring, a technique which can be used to hold the layers of clays apart, allowing access to the interlamellar active sites. In addition to the exchange of Na^+ for H^+ mentioned earlier, the sodium ions can be exchanged for a variety of metal ions, leading to modification of acidity. These ion-exchanged clays have been investigated and evaluated in industrially important reaction types. Similarly, clays have been used as support materials for many Lewis acids in attempts to produce solid replacements for Lewis acids such as BF_3 and $AlCl_3$. The major target of this research has been the development of novel Friedel−Crafts catalysts.

Indeed, some industrial processes already use such materials for the Friedel−Crafts reaction.[12] For example, phenol can be alkylated using alkyl halides and a montmorillonite catalyst.[13] The activity of the catalyst is, however, too low to be generally applicable, and thus the search for highly active, selective, and easily handled solid acids has recently been intensive.

2.1. Friedel−Crafts Reactions. The Friedel−Crafts reaction is one of the most important reactions carried out industrially. Products from almost every sector of the chemical industry are prepared using this methodology. At one extreme lies the million tonne plus per year reaction of benzene with ethene, producing ethylbenzene, which is then dehydrogenated to styrene. Similar technology is used to produce surfactants *via* the reaction of benzene with longer chain alkenes, typically dodecene, followed by sulphonylation. At the other end of the scale is the production of pharmaceuticals such as ibuprofen, which involves, as an early step, the acetylation of isobutylbenzene.

The above reactions all require acid catalysts, typically $AlCl_3$, BF_3, or liquid HF, all of which are difficult to handle. Problems are also associated with toxicity, corrosivity, reaction selectivity, and effluent disposal. Furthermore, in the case of acylations carried out using Lewis acids, the reaction is complicated by the complexation of the product

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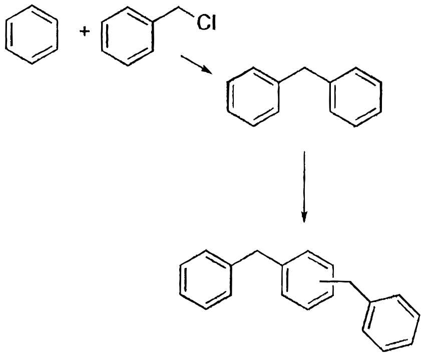
Scheme 1. **Friedel−Crafts reaction of benzene with benzyl chloride**



to the catalyst, requiring the use of greater than stoichiometric amounts of the "catalyst", a situation which exacerbates the drawbacks described above.

Several papers have addressed the Friedel−Crafts reaction, focusing predominantly on the less demanding alkylation reaction. For the majority of substrates, the base clay does not display significant reactivity and must be modified. Initial work was devoted to ion-exchanged clays, many of which showed significant improvements over the untreated clay. Many types of clay have been investigated, including bentonites, vermiculites, halloysites, and kaolinites.[14−16] The first significant study appeared in 1987. Lazslo and Mathy[17] reported the synthesis and reactivity of a series of ion-exchanged montmorillonites in a variety of alkylations. The commonly employed montmorillonite K10 was used as the base clay for these catalysts. As K10 is an acid-treated clay, it already has some inherent acidity. Three reactions were attempted, representing the alkylation of aromatics (benzene and toluene were generally the substrate and solvent) with the three major classes of alkylating agents, namely, alkyl halides, alcohols, and alkenes. The relative activities displayed by each of the catalysts varied from case to case. In the case of alkyl halides, the test reaction was that of benzene and benzyl chloride (Scheme 1).

Laszlo and Mathy found that, of nine metals exchanged, four were particularly active, the other five being roughly comparable to the untreated clay. The order of reactivity was Fe(III) > Zn(II) > Cu(II) > Zr(IV) ≫ Ti(IV) > Ta(V) > Al(III) > Co(II) > K10 > Nb(V). Interestingly, the relative activities of the various exchanged cations are significantly different from those of the corresponding Lewis acidic chloride derivatives. In particular, the activity of Zn is quite high, while that of Al is remarkably low, whereas the opposite is true of homogeneous systems, where $AlCl_3$ is one of the most powerful Lewis acids, and $ZnCl_2$, one of the weakest. Obviously, in the case of ion-exchanged clays, the environment around the metal centre is significantly different from that of e.g., $AlCl_3$ in a typical Friedel−Crafts reaction system, and therefore the acidity displayed is due to other factors. K10 has both Lewis and Bronsted sites. The activity of ion-exchanged clays is considered to be due, at least in part, to the effect of the "new" ion on the water molecules in the vicinity, the water being more or less strongly coordinated by the Lewis acid centre, generating H-bonded protons in a highly polarising environment.

The activity shown by the best ion-exchanged catalyst in this series (in the reaction benzene−benzyl chloride) is approximately 20 times greater (measured by time to 50% conversion) than that of the untreated clay. Reaction at reflux in excess benzene (benzene:benzyl chloride ratio ca. 12:1, 10 g of catalyst/mol of benzyl chloride) gave a 100% conversion of benzyl chloride after 0.25 h. Selectivity to monoalkylated product was, however, only 2.1:1, leading to an isolated yield of 57%, along with 27% of dibenzylbenzenes. The rate of reaction is much higher than that of K10 itself, but the isolated yield and selectivity were not greatly improved upon. The best compromise between selectivity and conversion was displayed by the Ti(IV)-exchanged catalyst which effected a 90% conversion of benzyl chloride after 5 h, producing a 66% isolated yield of product, along with 20% dialkylated material.

Alkylations using cyclohexene and benzyl alcohol as alkylating agents proved somewhat more resistant, requiring 25 and 50 g of catalyst/mol, respectively. The relative effectiveness of the catalysts is different in each case, but Ti(IV) is generally one of the better variants. The requirement of larger amounts of catalyst is unfortunate, but the catalysts do appear to be reusable, at least a few times, as evidenced by the reuse of K10−Fe(III) in the benzylation of toluene with benzyl chloride. Five reuses were possible without decrease in activity, although further reuse led to longer reaction times. The authors do not speculate on the reasons for the deactivation, but it is likely that the lamellar structure of the catalysts is gradually broken down by dealumination caused by the HCl generated during the reaction. Such processes are well-known to destroy the lamellar structure of clays. If this is the primary cause of the progressive reduction in activity, then the alkylations with alkenes and alcohols, despite requiring more catalyst, may in fact allow longer catalyst lifetimes, a factor which might well prove significant economically. Alkenes and alcohols have the added benefit of being inherently more environmentally friendly with respect to side products, alkenes adding to the substrate, alcohols generating water, whereas HX is formed with alkyl halides. Unfortunately, the yields obtained with these more attractive substrates are modest. Conventional homogeneous catalysts do not appear to give significantly better yields, and with alcohols the catalysts (e.g., $AlCl_3$) are prone to decomposition.

A real breakthrough in this field of catalysis came two years later with the discovery of "clayzic".[18] Whereas prior work had concentrated on traditional clay modification techniques such as ion exchange and acid treatment, clayzic was formed by supporting $ZnCl_2$ on K10. In this way a highly active heterogeneous Friedel−Crafts catalyst is formed. It displays activity several orders of magnitude higher than the ion-exchanged materials, the conversion of benzyl chloride to diphenylmethane in the above test reaction being complete within 15 min at 20 °C with selectivity towards

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monoalkylation at 100% conversion being >80%. The isolated yield of 80% is also much higher than that obtained for the ion-exchanged catalysts and conventional systems. The authors screened a range of salts and found that the order of activity was again dramatically different from that found with the unsupported species. Thus, Zn salts are all highly active, with the exception of the fluoride. $ZnCl_2$ is the most active, despite the fact that $ZnCl_2$ itself is an extremely poor catalyst for such reactions. Again, supported $AlCl_3$ is surprisingly inactive, being one of a group of supported catalysts less active than the untreated support, K10.

2.1.1. Structure/Activity Relationships of Clayzic. The exceptional activity of supported $ZnCl_2$ and the remarkable synergy shown between the components of this material have been the focus of a great deal of research, in an attempt to rationalise the findings.

Montmorillonite K10 is a member of the bentonite family of clays. It is formed from the parent bentonite, Tonsil 13, by acid treatment. The original structure is typical of clays, being a sheet structure, the sheets consisting of, in this case, three layers, the outer layers being SiO_4 tetrahedra, the inner, AlO_6 octahedra. Acid treatment increases the overall acidity of the material, but causes loss of the sheet structure due to progressive exchange of Al ions for protons, with eventual collapse of the layer structure. This delamination can be monitored using XRD and is quite extensive for K10. During structure/activity studies, it was found that the remaining regular crystalline structure of K10 disappears during thermal activation. Likewise, thermally activated clayzic shows virtually no long-range order, appearing to be essentially amorphous.

The fact that the activity of the catalyst is orders of magnitude higher than that of either of its constituent parts suggests that considerable structural change may have taken place. This supposition was backed up by Rhodes and Brown in a series of papers dealing with the optimisation of this and other similar materials.[19−21] The clay support used in the preparation of clayzic, montmorillonite K10, is an acid-treated bentonite and has therefore lost much of the lamellar structure of the parent clay. However, the exact details of the acid treatment are not readily available. Rhodes and Brown approached the problem by using the related clay carmargo white, a bentonite which has not undergone acid treatment.[19] By preparing supported $ZnCl_2$ catalysts based on this clay, and on carmargo white which had been acid treated for various periods of time, they were able to determine the effect of a variety of structural parameters on the activity of the supported catalyst. The best of their catalysts was comparable in activity to clayzic, justifying their use of a slightly different support material.

Their analysis of these results indicated several important features. Firstly, as the length of acid treatment increases, the lamellar structure of the clay breaks down, while the activity of the supported catalysts prepared from the acid-treated clays increases, with an optimum activity being found after 1000 min of acid treatment. Untreated clay has essentially no activity. What is interesting is that acid treatment removes all the aluminium from the framework after only 15 min, at which time all resolved structure is lost in the XRD pattern. ^{29}Si CPMAS NMR indicates that some lamellar structure is still present at this time, but is completely absent after 1000 min. Surface area, often considered to be one of the determining factors in heterogeneous catalysis, reaches a maximum after 15 min and then declines. The surface density of acid sites, which one might also expect to be important, peaks at ca. 15 min and returns to low levels in the optimum clays. Cation exchange capacity decreases steadily on acid treatment. Thus, none of these parameters correlate with the activity of the catalysts, which remains very low with 15 min treated clay, implying that they are not *per se* particularly important in determining the activity of the supported catalysts. In their second paper, Rhodes and Brown show that the acid treatment has a profound effect on the porosity and, in particular, on the pore size distribution of the clay.[20] The initial pore size distribution of the untreated clay displays a large, sharp peak at ca. 4 nm, with a tail reaching ca. 100−200 nm. Acid treatment causes a gradual loss in intensity of the 4 nm peak and the appearance of a second peak in the distribution centred at 10−12 nm. After 15 min, this second peak is still small, and no real change in pore size distribution has taken place. After 10 h, the original distribution has totally disappeared, being replaced with a large, broader peak at 10−12 nm.

Porous silicas having larger pore diameters than this value do not show any further increase in activity, and it appears that this feature may be crucial to the catalytic efficiency of the materials.

Studies on the thermal activation of clayzic have revealed several features of this material.[22] Surface area was measured using the BET isotherm with dinitrogen as adsorbate. The surface area of unactivated clayzic is ca. 130 m^2/g, significantly less than that of K10. A graph of thermal activation temperature vs surface area is striking in that the surface area of clayzic, after thermal activation at a range of temperatures between 25 and 300 °C, rises linearly to a final value of ca. 180 m^2/g, whereas that of K10 drops steadily from ca. 230 m^2/g to ca. 200 m^2/g at 250 °C and then rapidly to reach 180 m^2/g at 300 °C. This indicates that the presence of zinc chloride has a clear effect on the structural properties of the material. The fact that a graph of activation temperature vs catalytic activity shows a distinctly different trend, with an optimum activation temperature of 275 °C,[23] confirms that the increase in catalytic activity is not caused by changes in surface area. The linear increase in surface area with increasing activation temperature is indicative of structural change within the catalyst. Porosimetry studies on activated clayzic and K10 provide evidence that the activity is caused by changes in the pore size distribution of the material. The pore size distributions for both materials are shown in Figure 1.

It is immediately apparent that the pore size distribution of K10 indicates a large number of mesopores in the range

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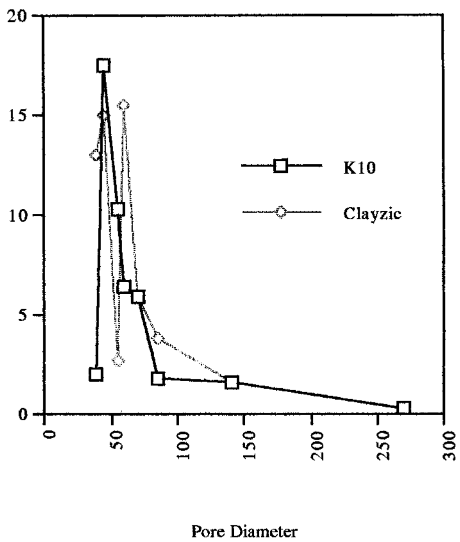


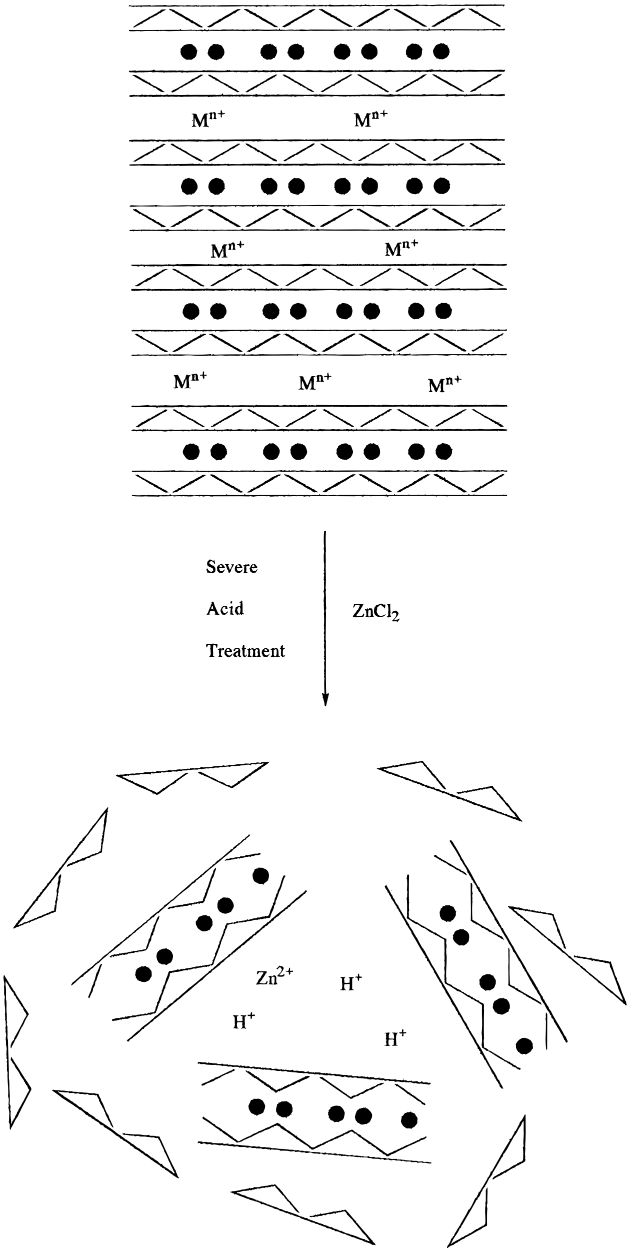
Figure 1. **Pore size distribution of clayzic and K10 (pore diameter, Å).**

5–10 nm. The sudden dip in the graph at 5–6 nm is due to the presence of very polar pores. It is known that dinitrogen cannot enter such pores.[24] A comparison of the pore size distribution of clayzic indicates that the pores are partially filled with zinc chloride. Thus the catalyst can be seen as a material consisting of essentially amorphous, mesoporous silica containing zinc chloride in a very polar environment.

2.1.2. Vibrational Spectroscopic Studies on the Acidity of Clayzic. Whereas the direct detection of the active centres in solid acids can be extremely difficult (although see below), the use of probe molecules such as pyridine and benzonitrile has shed considerable light on the nature of the acidic centres. Pyridine is the more commonly employed of the two,[25] as it displays a number of IR bands which arise from interaction of pyridine with the solid acid. These bands can be assigned specifically to Lewis acid coordinated pyridine, H-bonded pyridine, and pyridinium ion, allowing differentiation between Lewis and Bronsted sites. The relative intensities of these bands relate to the amounts of each type of acid site present, and thus a detailed picture can be built up.

From pyridine adsorption studies on K10 and clayzic, it is clear that K10 has more Bronsted sites than clayzic, implying a loss of some Bronsted sites during the preparation of clayzic, and countering the proposition that the role of $ZnCl_2$ is to provide a cation capable of polarising solvated water molecules. It was also demonstrated that K10 has essentially no Lewis acidity, whereas characteristic pyridine–Lewis acid bands are apparent in the spectrum of clayzic. This indicates that the zinc ions are behaving as Lewis acid centres, although the position of the IR bands suggests that they are relatively weakly Lewis acidic. Thermal activation of both K10 and clayzic effectively removes the bands associated with the pyridinium ion, which is indicative of Bronsted acidity. K10 still shows bands due to H-bonded pyridine, and clayzic displays bands characteristic of Lewis acidity. The fact that the positions of these bands are not significantly different from those in the unactivated catalyst tends to suggest that these Lewis acid centres are no more intrinsically active as a consequence of activation procedure, despite the experimental evidence that thermal activation leads to substantial rate increases.

Scheme 2. **Structure of clayzic**



Benzonitrile is another probe molecule which can provide information regarding solid acids. Benzonitrile coordinates with Lewis acid centres, leading to an increase in the s character of the N atom and thus to an increase in absorption frequency. The propensity of benzonitrile to form H bonds with, e.g., Bronsted centres is minimal, and thus no change in absorption frequency is expected. The results obtained using this probe parallel those obtained from pyridine adsorption, in that no shift in wavelength is seen with K10, i.e., no Lewis centres, but a shift of $+37$ cm^{-1} is seen for clayzic.

Recently Brown and co-workers have provided direct evidence for the existence of $ZnCl_2$ in clayzic and the related silizic (zinc chloride on silica). They used Raman spectroscopy to detect the Zn–Cl stretch and compared the wavelength with bulk and $SOCl_2$-dried zinc chloride. They drew the conclusion that the active site of clayzic contains zinc

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(25) Patty, G. P. *J. Catal.* **1963**, *2*, 371.

chloride units and that at least part of the synergy between the support and the salt is due to the fact that zinc chloride can be effectively thermally dehydrated in the presence of the support, whereas such drying techniques are not effective with the bulk material, and lead to partial decomposition of the salt. Thus zinc chloride can be more efficiently activated towards Lewis acidic behaviour in combination with an appropriate support material such as a clay than in its absence. Scheme 2 illustrates the major changes in structure on forming clayzic.

2.1.3. Reactivity of Clayzic. Clayzic is a highly active Friedel−Crafts catalyst and catalyses the reaction of alkyl halides, aldehydes, and alcohols with aromatics.

Of particular interest are the seemingly unusual trends seen in some of the reactions studied. These peculiarities can be explained using the information gained during studies on the structure of clayzic. These unusual effects seen in competitive experiments, studies of structure/activity relationships, and reaction kinetics are discussed in terms of the catalyst structure below.

Two examples of competitive reaction have been published where reversed reactivities have been observed.[26a,b,27] These are as follows:

In the competitive reaction of toluene with two electrophiles, benzyl chloride and benzyl alcohol, the product (benzyltoluene) is formed exclusively from the alcohol while the alcohol is present. When the alcohol has completely reacted, the chloride reacts rapidly, giving the same products. In separate reactions, the chloride reacts orders of magnitude faster than the alcohol.

Similarly, Laszlo et al. claim that, in a competitive reaction with two nucleophilic partners (toluene and mesitylene) and benzyl chloride, mesitylene, despite being intrinsically less active under noncompetitive conditions, reacted preferentially in a mixed system.

These results can be explained if one considers one prerequisite for reaction: the accessibility of the active site. As has been previously noted in porosimetry measurements, the pores containing the active sites, while being too large to restrict movement due to steric constraints, are extremely polar and do not allow ingress of dinitrogen. Thus, it is reasonable to expect that accessibility of reactants will be influenced by their polarity. Thus benzyl alcohol reaches, and is activated by, the active sites to the exclusion of benzyl chloride, and thus the alcohol reacts first. Only when no more alcohol is present to block the chloride does the chloride reach the active sites and react. A more recent paper[26b] has indicated that small amounts of benzyl ether are also formed during the reaction. These ether molecules complex the active site less strongly than the alcohol, but more strongly than the chloride, adding some complexity to the detailed kinetic understanding of the reaction. The inverted reactivity of toluene is likely to be due to such a rate-controlling partition of the two reactants between the active sites and the bulk.

Such an explanation is backed up by other pieces of independent evidence. The relative reactivity of halobenzenes is opposite to that expected in a homogeneous reaction system.[23,28] Thus, the order of reactivity, using unactivated clayzic, is PhBr > PhI > PhCl > PhF, PhH. This parallels the polarisability of the halobenzenes, a factor which is likely to determine their ability to enter the highly polar pores. Similar effects have been observed in the reaction of various alkyl aromatics with benzyl chloride.

A commercial version of clayzic, Envirocat EPZ10, is available. (Envirocats is a trade name of Contract Chemicals, Knowsley Industrial Park, Prescot, Merseyside, UK.) Applications of this catalyst include alkylations. These reactions are typically carried out in a stirred batch mode, with the catalyst being removed by centrifugation or filtration.

2.1.4. Supported $AlCl_3$. Attempts to prepare stable, supported forms of aluminium chloride have been numerous. Early attempts relied on the sublimation of $AlCl_3$ vapour through a bed of support. Numerous examples exist in the literature of such work.[29,30] The catalysts prepared by such routes proved to be highly acidic, being capable of the isomerisation of alkanes in the gas phase at $T < 450$ K. However, attempts to use these materials in liquid phase applications have not been successful.

In 1988, Drago and Getty[31] published an account of their preparation of a related group of substances, accessed by refluxing aluminium chloride in the presence of a solid support, using carbon tetrachloride as the solvent. Silica, alumina, a high-silica zeolite, and boron oxide all gave active catalysts, as measured by gas phase cracking of hydrocarbons. Interestingly, the catalysts had to be prepared in carbon tetrachloride, other halogenated hydrocarbons and hydrocarbons themselves yielding materials of markedly poorer activity. Unfortunately, the activity of these materials in liquid phase Friedel−Crafts processes was found to be disappointingly low, and much lower than that of aluminium chloride itself.[32]

More recently still, Clark et al.[33] have succeeded in preparing an immobilised form of $AlCl_3$, which displays high activity in such liquid phase applications, the activity being comparable to that of $AlCl_3$ itself. Silica, K10, and acidic alumina were all suitable as supports, with pore size playing an important role in selectivity. Thus, the reaction between oct-1-ene and benzene at room temperature, catalysed by the supported $AlCl_3$ materials, gives 100% conversion at room temperature with a 3:1 ratio of monooctylated:dioctylated products, using a 2:1 benzene:octene ratio. A 20:1 ratio gives 92% selectivity towards the monosubstituted product. No other products are formed.

The activity of some of these materials is superior to that of $AlCl_3$. The mesoporous silica-derived materials show the best activity, with 70A silica giving the optimum catalyst, in terms of both conversion and selectivity. Similar behaviour was found with clayzic, as noted above. With this

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(29) Krzywicki, A.; Marczewski, M. *J. Chem. Soc., Faraday Trans. 1* **1980**, *76***,** 1311 and references therein.

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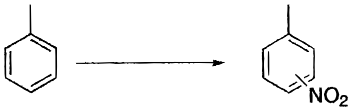
Scheme 3. **Mononitration of toluene**



material, reaction is complete after only 1.25 h at 20 °C, with a 78.3:21.2 selectivity in favour of monoalkylation. This catalyst could be reused up to eight times without loss of activity or selectivity.

In the related dodecene−benzene reaction, of interest in the detergency industry, selectivity towards position of alkylation is important. The 2-alkyl isomer is reported to possess the best emulsibility characteristics.[34] Selectivity towards this isomer is much higher (47%) with the heterogeneous catalysts described here than with $AlCl_3$ itself (32%) or with HF (13−20%). Most zeolites are similarly less selective, with the exception of lower acidity zeolites, with which incomplete reaction is generally seen.

Alkyl halides also are reactive, and it is possible to alkylate aromatics easily using SiO_2-AlCl_3. In this respect, the supported $AlCl_3$ catalysts are much more active than clayzic, which displays poor activity towards alkyl halides (with the exception of benzylic species). For example, benzene and dichloromethane are converted to diphenylmethane in a yield of 62% after 2.5 h of reaction at 40 °C.

2.2. Nitration. The nitration of aromatics is a longstanding reaction of great industrial significance. A major environmental problem associated with this area of chemistry is the traditional method of nitration, which involves the use of nitric acid−sulphuric acid mixtures and is responsible for the generation of large amounts of waste acid. A further drawback is the often poor selectivity of the reactions. Indeed, in some cases, production costs have been kept down by the use of the undesired isomeric product(s) as fuel to heat the plant!

Several workers have thus investigated the area, and some significant advances have been made, in terms of both the waste acid generated and the selectivity achievable. Solid acids have been used in place of sulphuric acid, eliminating the generation of spent sulphuric acid waste, and modified nitrating reagents have been employed which have improved the selectivity of the transformation. The more significant of these procedures will be discussed briefly.

The use of NO_2 and benzene in the gas phase over solid catalysts such as $SiO_2-Al_2O_3$, supported sulphates, supported benzenesulphonic acid, and a zeolite (ZSM-5)[35] led successfully to nitrobenzene. The yields were generally modest, with only the benzenesulphonic acid achieving over 50% (maximum yield achieved was 77% and was very dependent on the exact operating temperature).

Liquid phase applications have mainly centred around the use of acyl nitrates as the nitrating agent. These can conveniently be prepared *in situ* from nitric acid, and their bulkiness can lead to improvements in selectivity. A particularly thorny problem is the selective para nitration of toluene (Scheme 3).

Traditional methods lead to mixtures of ortho:para ratio ca. 2:1. Whilst many attempts were made to effect high regioselectivity, these were generally accompanied by problems such as modest improvements in selectivity (large-port mordenites gave 60% selectivity using benzoyl nitrate),[36] very high para selectivity but extremely low yield (ZSM-11 pretreated with tributylamine gave 98% selectivity but in a yield of only a few percent[37]), or lack of catalytic ability (copper nitrate on montmorillonite gives quantitative nitration, but high selectivity is achieved only under inconvenient conditions of long reaction times at high dilution[38]). Recently, Smith et al. have shown that the use of the H^+ form of zeolite β and acetyl nitrate is an excellent method for highly regioselective para nitration.[39] With this combination, quantitative yields of mononitrated products were obtained under mild conditions (30 min at room temperature). The best selectivity was 79% in the case of toluene, and selectivities up to 92% were seen for other substrates. Recovery and reuse of the catalyst was possible. The major drawback of this method is the large amount of catalyst required for the reaction.

2.3. Halogenation of Aromatics. As with the nitration of aromatics, the production of haloaromatics has long been a major industry. Similar concerns exist regarding selectivity and waste acid generation, although the dangers of generating hazardous materials through overreaction are less. While definite progress has been made towards the goals of cleaner methodology coupled with higher selectivity, we are still some way from industrially applicable systems. The following section illustrates briefly the main advances made.

2.3.1. Chlorination. One of the most important targets is again the para functionalisation of toluene. *p*-Chlorotoluene is used as an intermediate in a variety of industrial sectors such as the pesticide, dyestuff, and pharmaceutical industries. The traditional route for its manufacture requires the use of ferric chloride as catalyst and leads to low selectivity: the monochloro products contain less than 30% of the desired isomer. Other catalyst systems have been developed which use the sulphides of various metals. These do increase the proportion of para isomer in the monochlorinated fraction to ca. 50%, but are also responsible for an increase in the level of di- and trichlorination.

As in the case of nitration, the use of zeolites has allowed enhanced selectivity to be achieved. Singh and Kumar[40] used a series of zeolites as catalysts in place of the traditional Lewis acids in the chlorination of toluene with elemental chlorine. They compared their results with amorphous silica, a material of some similarity to zeolites in terms of acidity, but markedly different in porosity. Their results showed a number of things: the selectivity towards para chlorination varied as a function of type of zeolite from 22.4% to 74.5%, with zeolite L being the most selective; $FeCl_3$ gave 26.5% para, and silica, 34.8% (Scheme 4).

It was found that the presence of chloroacetic acid was beneficial and led to significant improvements in the para:

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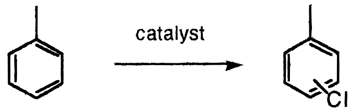
Scheme 4. **Chlorination of toluene with different catalysts**



catalyst	conversion	para selectivity
$FeCl_3$	44.1%	26.5%
silica	39.7%	34,8%
zeolite KL	45.3%	59.8%
zeolite KL / $ClCH_2CO_2H$	58%	93.2%

ortho ratio. The reason for this is not clear, but similar behaviour in the chlorination of biphenyl using the same zeolite had been noted previously.[41] Minor amounts of benzyl chloride were put down to small amounts of photoinitiated radical chlorination, although the homolysis of alumina-containing zeolites[42] may initiate this reaction too. Such a mechanism is most pronounced for high-Al zeolites, of which zeolite KL is an example. Furthermore, the results from the silica led the authors to the conclusion that reaction on the external surface of the zeolite is unselective with respect to the ring chlorination, and that the main selectivity is, as is to be expected, achieved in the pores. The origins of this selectivity may not be due solely to shape selectivity, but may also involve electrostatic effects within the highly polar interior of the material. Studies on the effect of reaction solvent concluded that 1,2-dichloroethane was optimum, and the best temperature for high selectivity was 353 K. Overall, with a fully optimised set of conditions the para:ortho ratio achieved was 6.66, corresponding to 83.2% selectivity to *p*-chlorotoluene at a 58% conversion. Unfortunately, the catalyst is deactivated by the HCl produced, and reuse leads to a deterioration in performance.

Smith has shown that alkylbenzenes can be chlorinated exclusively in the ring positions with a combination of *tert*-butyl hypochlorite and silica. *N*-Chloroamines such as dichloramine-T and *N,N*-dichlorourethane[43] can also be used as the chlorinating agent. Other substrates include anisole and halobenzenes. Nitrobenzene is not active under these conditions. Such reagents are based on large-pore materials and do not display any significant degree of regioselectivity, the results being essentially those found in the liquid phase. Polychlorination does seem to be less prevalent, however. In a second paper, the same group[44] showed that the use of a zeolite rather than a silica can increase the amount of para isomer in the chlorination of toluene and chlorobenzene. Optimisation of a number of variables led to the discovery of the best system for these reactions. The best zeolite was found to be a partially proton exchanged faujasite, denoted as H^+,Na^+ faujasite X. This material is a weak acid, having a low Si:Al ratio of 1.2. The Si:Al ratio was found to be important, as higher proportions of Si gave impurities derived from Friedel–Crafts reactions. With this solid, and acetonitrile as solvent, the para:ortho ratio in the chlorination of toluene was 82:18 (use of dichloromethane/ether gave even higher selectivity, 91:9, but was less suitable due to possible side reactions with the ether). Chlorobenzene gave 97% para chlorination.

2.3.2. Bromination. Similar strategies have been followed in the bromination of aromatics. Silica has been used as a catalyst for the bromination of various aromatics with NBS[45,46] and with polymer-bound tribromide.[47] Initial work on bromination using bromine and zeolites was carried out by van Bekkum et al.[48] This work did not lead to particularly high para selectivities, which was attributed to the role of the HBr formed during the reaction. Neutralisation of this acid with bicarbonate did not lead to significant improvements in selectivity. Sasson et al.[49] improved the situation by using a system consisting of bromine, toluene, Na-Y zeolite, and propylene oxide as an HBr scavenger. Thus they acheived a 98:2 selectivity in favour of the para isomer in the bromination of toluene. Unfortunately, the conversion of toluene could not be increased beyond 13%. A further development has been very recently published. In this work[50] the same zeolite is again used to impart selectivity. The authors concentrated on the amount of the zeolite and found that the reaction consists of two separate components. Firstly, the Na-Y zeolite catalyses a very selective bromination of the substrate, and subsequently, the H-Y zeolite formed acts as a less selective catalyst. Thus by adjustment of the amount of zeolite such that there is a stoichiometric amount of Na^+ cations, *p*-bromotoluene can be obtained in 95% conversion with a selectivity of 93:1. This paper demonstrates the exceptionally high selectivities achievable with zeolites under the correct conditions, but the major drawback is obviously the noncatalytic nature of the reaction.

3. Oxidation

Oxidation plays a crucial role in the transformation of organic molecules, from the introduction of functionality via oxygenation of primary hydrocarbon feedstocks and the high-temperature formation of short-chain unsaturated species to the selective transformation of functional groups within complex molecules. In general, the former processes are carried out at high temperature, the gaseous reactants being passed over or through solid catalyst beds in a continuous mode. The latter, dealing with larger, typically more elaborate molecules, which are less volatile and possess lower thermal stability, are usually carried out in the liquid phase. Many of these systems pose real environmental problems, requiring stoichiometric amount of oxidants such as chromates which are difficult to recycle, and whose disposal causes many problems. Thus, the last few years have seen much effort expended in the search for newer, more efficient and acceptable oxidation catalysts. The catalysts are generally based on inexpensive oxides such as silica, alumina, and clays, modified in a variety of ways to introduce catalytic

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Table 1. **Reactions catalysed by TS-1**

reaction	refs
hydroxylation of aromatics	51−55
epoxidation of olefins	56−60
ammoximation	63, 64
alkane oxidation	56, 57, 61, 62
amine oxidation	65
oxidation of alcohols	65
oxidation of thioethers	65

centres. Modified zeolites incorporating redox-active framework sites have proved an exciting source of new materials. These catalysts are normally designed to be capable of catalysing the oxidation of substrate with inexpensive, inoffensive oxidants such as air or hydrogen peroxide. While the majority of the work has centred on new catalytic replacements for stoichiometric liquid phase oxidations, some of the novel catalysts also have applications in gas−solid catalyst reactions.

One of the major current areas of activity is the field of Ti-containing materials, which are showing real promise in the area of selective oxidation. Preeminent amongst these is the novel zeolite TS-1.

3.1. TS-1. The synthesis, by chemists at Enichem, of a family of titanium silicate zeolites in the 1980s was without doubt one of the major breakthroughs in catalysis in the last 15 years. The most important member of the family, TS-1, has been the subject of many articles and forms the basis of a route to hydroquinone which is carried out on a 10 000 tonne/year scale in Ravenna. Two other processes, the epoxidation of propene and the ammoximation of cyclohexanone, are currently nearing the production stage.

3.1.1. Preparation and Structure. TS-1 is synthesized hydrothermally from, e.g., tetraethyl orthotitanate, tetraethyl orthosilicate (Si:Ti ratio is typically 30−50), tetrapropylammonium hydroxide, and water.[51,52] The reaction is carried out at 160−180 °C, followed by calcination at 550 °C. Keeping the Si:Ti ratio high ensures that the Ti atoms occupy lattice sites with no near neighbour Ti atoms. As will be seen later, this is a prerequisite for an active catalyst. The typical pore size is of the order of 0.55 nm, thus endowing the catalyst with shape selectivity, but thereby restricting its use to small substrates.

3.1.2. Reactivity. TS-1 is active in a variety of oxidations using H_2O_2 as oxidant. The main types of reaction are summarised in Table 1. Of the reaction types listed in Table 1, examples of the first three have been commercialised, or are close to commercialisation. These will now be discussed in more detail.

3.1.3. Hydroxylation of Aromatics. The introduction of an oxygen function into an aromatic nucleus represents an important challenge. Phenols are used widely in industry as antioxidants, and hydroquinone, which is easily oxidised to quinone, finds use in the photographic industry.

The hydroxylation of aromatics using TS-1 is carried out at temperatures between 80 and 120 °C, using excess aromatic and, optionally, a polar solvent such as *tert*-butyl alcohol. The role of the solvent is to render the liquid phase homogeneous. Hydrogen peroxide is used as oxidant, and it is not necessary to run the reaction with highly concentrated oxidant, thus minimising potential handling problems. Yields based on hydrogen peroxide are in the range 20−53% and vary depending on the substrate and, to some extent, on the solvent used; methanol is slightly poorer than other alcohols in this respect. Oxidation of benzene to phenol proceeds chemoselectively only at low conversions, phenol being readily oxidised further to dihydroxybenzenes. Interestingly, the hydroxylation of other aromatics such as toluene is much more selective to monooxygenation, giving substituted phenols as the major product. Products derived from the oxidation of side chains are detectable but are formed only in trace amounts. This can be contrasted to the results obtained using materials substituted with vanadium rather than titanium. In this case side chain oxidation is the main reaction pathway, indicating a difference in mechanism between the two systems, the Ti case involving electrophilic attack on the substrate, the V-doped catalysts behaving more like radical sources.[65] Exceptions to ring hydroxylation with TS-1 are found only with aromatics bearing reactive side chains, such as alcohols or unsaturated groups, in which case the oxidation of these groups to the expected products predominates (see below). As would be expected for such an electrophilic species, the reactivity of aromatics bearing electron-withdrawing substituents is low.

The oxidation of toluene to cresols serves to illustrate another important feature of the reactivity of TS-1. As might be expected of small-pore zeolitic materials, TS-1 exhibits shape selectivity. Typical homogeneous hydroxylation of toluene proceeds with a selectivity of ortho:meta:para = 78.2:2.3:19.5.[66] In contrast, the proportion of *p*-cresol is significantly increased to as high as 82%[53] (Scheme 5).

The most significant reaction in this area has undoubtedly been the hydroxylation of phenol, giving mixtures of hydroquinone and catechol. This represents an extremely attractive and clean option, allowing excellent conversion to product, with very little waste material being generated. Three different commercial routes to hydroquinone exist and are summarised in Scheme 6.

In total there are five processes for the production of hydroquinone. The Eastman oxidation of aniline is a two-step process, neither of which is catalytic. The production

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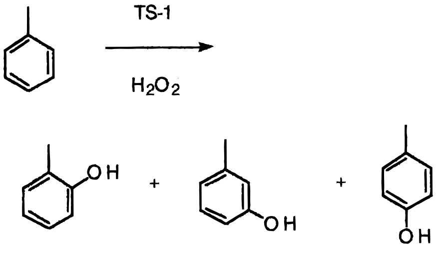
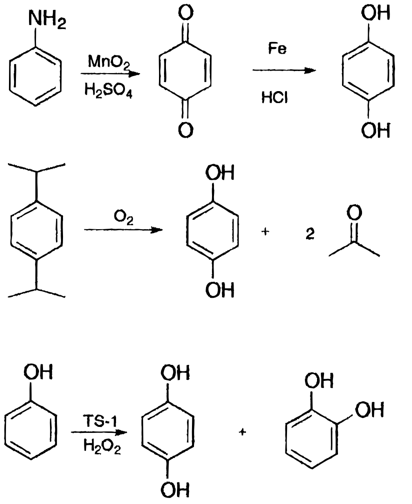
Scheme 5. **Hydroxylation of toluene**



TS-1	12%	7.5%	81.5%
Homogeneous	78.2%	2.3%	19.5%

Scheme 6. **Processes for the preparation of hydroquinone**



of large amounts of effluent (($(NH_4)_2SO_4$, Mn, and Fe wastes), and the use of mineral acids will make this old process redundant in the near future. The second process is a variant on the cumene to phenol process, which is carried out by Signal and Goodman in the USA. It relies on *p*-diisopropylbenzene as raw material and generates acetone as a byproduct. Three processes exist based on the use of hydrogen peroxide as oxidant. All three are run in Europe by Rhone-Poulenc, Brichima, and Enichem; 50% of the total world production of hydroquinone (i.e., 25 000 tonnes per year) is accounted for by these three processes. All of these reactions produce catechol as a byproduct. As can be seen from the summary shown in Table 2, the TS-1 process not only is cleaner, avoiding the use of strong acids or soluble transition metal catalysts, but also outperforms the other two processes, particularly in terms of conversion, an important factor in the economics of the process.

The reason for the higher conversion is that the formation of tars, resulting from side reactions and overoxidation, is significantly less in the case of TS-1. Selectivity to hydroquinone is also higher and can be varied by modification of the catalyst.

3.1.4. Epoxidation of Olefins. The epoxidation of olefins has been the subject of intense activity in recent years, not least due to the spectacular work of Sharpless and Jacobsen in enantioselective catalysis. The activity of titanium silicates in epoxidation represents another major area of progress. As with hydroxylation, TS-1 catalyses the epoxidation of olefins using dilute hydrogen peroxide as oxidant.[56−58] Conventional systems require the use of >95% hydrogen peroxide to ensure high selectivity to epoxide, avoiding the formation of diols by attack from water. Even with dilute hydrogen peroxide, the selectivity to epoxide can be very high using TS-1. Hydrogen peroxide is also utilised very efficiently, with drastic reductions in the amount of homolytic decomposition normally associated with traditional, transition metal based systems. This lack of homolytic decomposition makes an important contribution to the selectivity of the oxidation, with oxidations due to competing oxidants being negligible. Typical epoxidations of small, linear olefins are rapid, being essentially complete at room temperature or slightly above within 1−2 h. Shape selectivity is evident, and larger linear olefins are oxidised more slowly than their shorter counterparts, Similarly, branched olefins react much more sluggishly than linear, 1-hexene being epoxidised ca. 100 times faster than cyclohexene.[58] Styrene gives good yields of phenylacetaldehyde, via isomerisation of the intermediate epoxide.[59,60]

The epoxidation of propylene has been intensively studied and is nearing commercialisation. Propylene oxide is an important monomer in the production of polyethers, which find use as nonionic surfactants, and is produced to the extent of ca. 3 000 000 tonnes/year. Approximately 60% of this amount is produced via the chlorohydrin route, the remainder via hydroperoxide oxidation. The reaction schemes are represented in Scheme 7. Process 1 is noncatalytic and generates large quantities of calcium chloride waste. The second group of processes can be catalysed heterogeneously, but require the use of expensive alkyl hydroperoxides. Indeed, Shell developed a catalyst using the reaction of $TiCl_4$ with silica, followed by hydrolysis of the remaining Ti−Cl bonds, which is active in this process.[67] The structure of the catalyst has been proposed to be as depicted in Scheme 8.

The TS-1-catalysed process is extraordinarily efficient, both in terms of conversion of propylene to the oxide and in terms of hydrogen peroxide utilisation. The reaction is run in aqueous methanol as solvent, at a temperature <60 °C and a propylene pressure of ca. 4 bar. Selectivity to product is >90% and can be as high as 97%, based on hydrogen peroxide. Byproducts such as glycols and ethers are formed only in small quantities, even in the presence of substantial amounts of water. The amounts of these products can be further reduced by silylation of the surface. This also holds true for the Shell catalyst and can be rationalised by the fact that both catalysts are weakly acidic (due to Si−OH groups) and the blocking of these groups suppresses acid-catalysed solvolysis of the product. Treatment with weak base has been shown to be an effective posttreatment for the catalyst, reducing product losses due to ring opening. The catalyst deactivates slowly under the reaction conditions, but can be regenerated by simply calcining at 550 °C or by washing with hot solvent. It is thought that these processes remove organic impurities, most likely (poly)ethers, which are formed within the catalyst and diffuse only very slowly away from the active sites. Larger crystals of TS-1 deactivate more rapidly than small crystals, this being caused by more rapid occlusion of the pores.

A variety of structures have been proposed for the active site, and for the mechanism of epoxidation. These models

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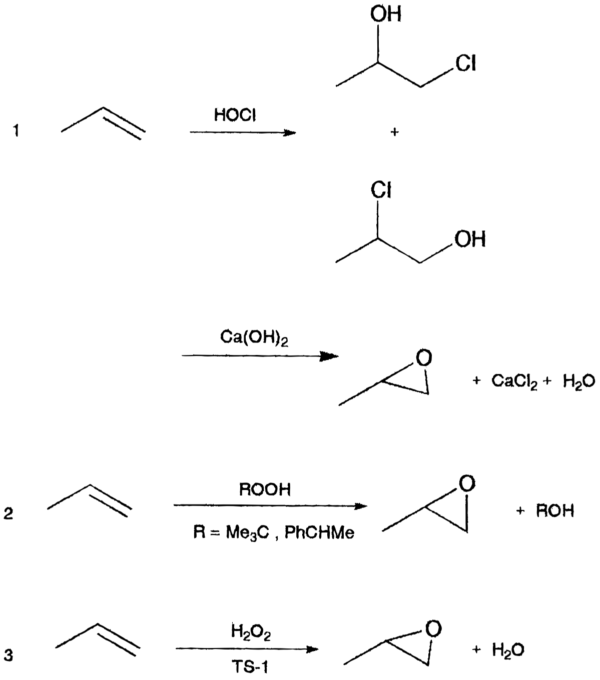
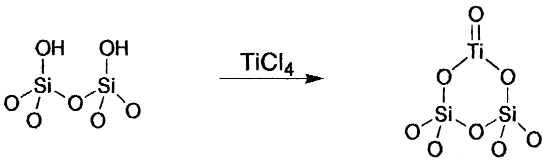
Table 2. **Relative efficiencies of routes to hydroquinone**

process	PhOH conversion (%)	yield (H_2O_2) (%)	PhOH selectivity (%)	1,2:1,4	tar/dihydroxy products (%)
$HClO_4/H_3PO_4$	5	70	80	2.3	10
Fe(II)/Co(II)	10	50	90	1.4	20
TS-1	25	70	90	1	12

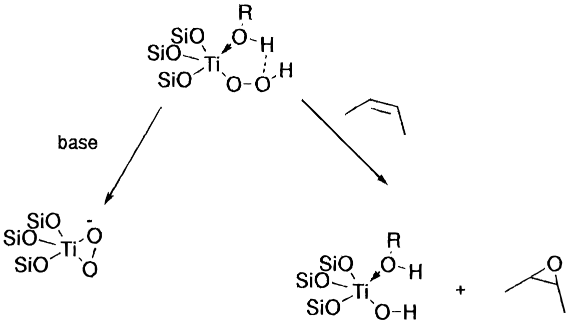
Scheme 7. **Routes to propylene oxide**



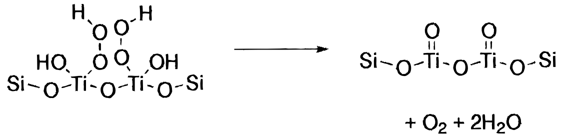
Scheme 8. **Proposed structure of the Shell TiO_2-SiO_2 catalyst**



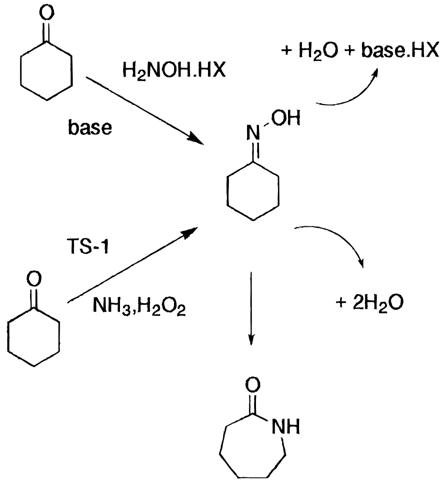
Scheme 9. **Postulated mechanism of epoxidation**



Scheme 10. **Homolysis of H_2O_2 at adjacent Ti centres**



Scheme 11. **Production of caprolactam**



must account for many observations, including solvent effects, the importance of having isolated Ti sites, structural selectivity, and the effect of acids and bases. A plausible scheme has been put forward by Clerici and Ingallina.[58] This involves a Ti-centred complex containing both a peroxy group and a solvent molecule forming a five-membered ring (Scheme 9). Thus, the role of solvent is rationalised by the necessity of having a molecule of solvent at the active site, bulkier alcohols being less able to efficiently form such a structure within the narrow pores, the restrictions of which preclude bulk solvent effects in the vicinity of the active centres. Water is also active, but significantly less so, being less well suited as a donor. The structure of the proposed active species bears similarities to those proposed in a variety of other epoxidising species.[69−71] The role of base is 2-fold; on the positive side the acidity is regulated, avoiding acid-catalysed decomposition of the epoxide, while too much base converts the active species to the inactive peroxide species.

The presence of adjacent Ti centres leads to homolysis (Scheme 10).

3.1.5. Ammoximation. Caprolactam is produced on an enormous scale and is used in the manufacture of Nylon. Its production is carried out classically by the reaction of cyclohexanone with hydroxylamine, which is produced as a salt by the reaction of ammonia and oxygen to nitric acid, with subsequent reduction. This stage of the process generates substantial quantities of salt. The second step requires the use of a strong mineral acid to effect the rearrangement to caprolactam, again producing large quantities of inorganics (Scheme 11).

The TS-1-catalysed process uses cyclohexanone, ammonia, and hydrogen peroxide (which is formed catalytically from hydrogen and oxygen) and avoids the need to preform hydroxylamine. The amount of salt formed in the production of cyclohexanone oxime, and thus in caprolactam, is therefore significantly reduced. Again, this process is nearing

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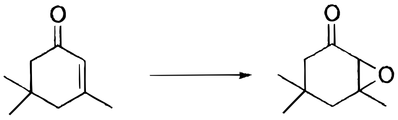
full-scale production.[72] A continuous process is planned, which will circumvent the potential danger of having significant concentrations of ammonium peroxides and hydroxylamine present together. The second step, the Beckmann rearrangement of the oxime, still requires stoichiometric amounts of mineral acid.

3.2. Other Ti−Si-Based Oxidation Catalysts. The remarkable properties of the TS materials have led to a great deal of interest in the scientific community. One area of importance is the application of such materials to the oxidation of larger molecules. As described above, the small pores of TS-1 endow the catalysts with shape selectivity. While this is a definite advantage in some cases, it is a severe drawback inasmuch as the catalysts are of no utility in the oxidation of molecules larger than simple mononuclear aromatics, or linear aliphatics. Initial results have been published relating to the development of catalysts capable of the selective oxidation of larger substrates. This work is described below.

Corma et al.[73] prepared a Ti-substituted zeolite β in which the Ti atoms occupied lattice sites. Again a low Ti:Si ratio was found to be advantageous. The characteristic IR vibration at 960 cm^{-1} correlated with oxidation activity in the oxidation of saturated hydrocarbons. The hydroxylation of cyclododecane was carried out using hydrogen peroxide at 100 °C, using a 3-fold excess of oxidant and 3.6 wt % catalyst. After 10 h, the major product was cyclododecanone (15.2%) with significant amounts of the corresponding alcohol (6.1%) and smaller amounts of olefin and diol. TS-1 gave a similar product distribution, but the reaction was only ca. 50% as rapid. Cyclohexane gave only the alcohol and ketone, in a ratio of ca. 6:1 with the Ti-zeolite β, and ca. 2.5:1 with TS-1. Again TS-1 was less active, although the difference was less marked in this case. Interestingly, a catalyst prepared by treatment of silica with $TiCl_4$, which had been purported to have framework Ti centres,[74] proved to be a poor catalyst for these reactions.

The same group[75] has prepared an analogous MCM-41 titanium silicate which is isomorphous with zeolite β, and which has 2 nm diameter pores. The Ti atoms occupy lattice sites, as evidenced by IR. The Si:Ti ratio is 60, which, as in TS-1, limits the likelihood of near neighbour Ti atoms, and hence minimises homolytic cleavage of the peroxide. Two substrates were investigated: 1-hexene, which poses no significant steric problems, and norbornene, which is much too bulky for TS-1. Epoxidation of 1-hexene proceeded with good selectivity with respect to H_2O_2 (75%) and towards epoxide (>90% without end-capping of acidic Si−OH groups). The epoxidation of norbornene was also successful, with 30% conversion after 5 h, giving 90% selectivity towards epoxide using *tert*-butyl hydroperoxide as oxidant. While the efficiency with respect to the peroxide was not quoted, Ti-zeolite β gave a lower conversion and Ti-ZSM-5 failed to catalyse the reaction.

Scheme 12. **Epoxidation of isophorone**



Peroxide	selectivity (olefin)	selectivity (peroxide)
CHP*	98%	85%
TBHP**	99%	83%

* CHP = cumene hydroperoxide
**TBHP = *tert*-butyl hydroperoxide

A third catalyst has been prepared by Baiker et al.[76,77] This catalyst is prepared by a sol−gel technique, followed by extraction with supercritical CO_2. This drying method is claimed to be vital to the activity as it stops agglomeration of TiO_2 which would reduce activity. The aerogels thus prepared contain up to 20% Ti. The catalysts prepared are mesoporous, allowing the epoxidation of bulky substrates such as cyclohexene and isophorone. The authors showed that the epoxidation rate correlates with Ti−O−Si connectivity, again demonstrating that isolated Ti sites are the active centres. The best of these catalysts proved more efficient than TiO_2/SiO_2, TS-1, and titania−silica aerogels in the reactions studied. Unfortunately, the catalysts require relatively expensive alkyl hydroperoxides to function, no epoxide formation being detected with hydrogen peroxide. Highest reaction rates were achieved in low-polarity solvents, in contrast to the results from TS-1, where highly polar solvents were preferred. Isophorone, a sterically hindered and electronically deactivated substrate, was epoxidised with high efficiency with this catalyst, the selectivities with respect to olefin and peroxide being shown in Scheme 12.

While these materials show obvious promise, one drawback is evident in that leaching of catalysts was detected. However, the materials described display significant activity in the epoxidation of relatively large, deactivated olefins, and continued work in this direction will certainly lead to further advances.

4. Solid Bases

In contrast to the areas of acid catalysis and oxidation catalysis, the theme of solid bases has not yielded the major advances associated with the former areas. This is despite a great deal of effort aimed at producing basic solid surfaces, which are of significance industrially, although lacking perhaps the variety and volume of applications associated with the other two groups of materials.

Four possible types of basic sites can be envisaged. Hydroxyls on the surface of, e.g., alumina or silica can be at best only very weakly basic, with low maximum charge density; values of ca. −0.35 have been obtained from quantum mechanical calculations.[78,79] These hydroxyls can

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be deprotonated using basic hydroxides or alkoxides, yielding materials which are more basic than the untreated supports, and can have a charge of at least −0.5 on the surface oxygens. Many parameters are important here, such as the nature of the support and the type and concentration of the metal counterion; posttreatment, such as calcination, is also an important factor. Metal oxides, such as MgO, are basic due to both surface hydroxyls and oxide anions, their basicity being modified by the adsorption of salts such as alkali metal hydroxides, nitrates, carbonates, and carboxylates and subsequent calcination. In the case of MgO, the nitrate, oxalate, and acetate yield much more basic materials than, e.g., the sulphate, chloride, or carbonate.[80] Metal fluorides and alkoxides are also known to generate basic solids. One step further is the treatment of alumina with sodium methoxide and subsequently, with metallic sodium, producing a blue (due to the formation of 1e colour centres), superbasic material.[81] Such drastic treatment of support materials is likely to produce quite profound changes in the nature of the support itself, and thus the nature of the product may well be quite different from the simple picture of a base dispersed on the surface of the support. A final consideration, of particular importance with highly basic materials, must be their reaction with acidic materials in the environment. Just as powerful bases can be generated by the thermal decomposition of supported carbonates, it is also possible that powerful bases can react, in some cases very rapidly, with, e.g., CO_2 to give a weakly basic material.

A further variety of supported base is represented by surface-bound amines. An example of such a material is “aminopropyl silica”, prepared by functionalisation of silica with (aminopropyl)trialkoxysilane. Such materials suffer from the drawback of surface heterogeneity, and, by analogy with chromatographic materials, a variety of structures can be formed.[82] These materials display basicity typical of a simple amine.

4.1. KF/Alumina. Of the above materials, few have been studied in great detail in relation to liquid phase reactivity, and most have not attracted much attention. One exception to this is KF/alumina, which has been the subject of a great deal of work both as a catalyst[83−88] and in terms of its structure,[89] the complexities of which clearly illustrate the profundity of change associated with such materials. KF/alumina is commercially available.

Whereas most basic fluoride ion sources (e.g., KF, Bu_4NF, KF/CaF_2) are also active nucleophiles, one of the most striking features of KF/alumina is its complete lack of nucleophilic activity. It has never been reported to deliver fluoride in even the most trivial nucleophilic substitutions, despite its efficiency as a moderately strong base. There are conflicting reports of its base strength in the literature: while most authors consider it to be weakly or moderately basic, there are reports which mention high basicity (or even super-basicity). The conditions of activation and the loading seem to be critical to its properties. A crucial early observation was that the loading of the most efficient variants of KF/Al_2O_3 is significantly higher than that required for monolayer coverage. Of all supported reagents studied, KF/alumina has perhaps been the most extensively analysed, with the possible exception of clayzic. The major details are given below and serve to illustrate the significant changes which take place upon preparation and activation: (a) At low loadings of KF, no crystallinity is detectable by X-ray diffraction. At higher loadings, one can observe the presence of both KF and K_3AlF_6. (b) IR studies indicate the presence of AlF_6^{3-}, and possibly also AlF_4^-. After exposure to the atmosphere (for a matter of seconds) the buildup of carbonate is evident. (c) Only a small proportion of the titratable basicity is soluble in water, the majority of the basic sites remaining on the solid surface. (d) No nucleophilic F^- is observed.

These results can be rationalised by the occurrence of an essentially complete reaction between KF and alumina which can be represented by the following scheme:

$$12KF + Al_2O_3 \rightarrow 3K_2O + 2K_3AlF_6$$

Such a scheme explains the detection of hexafluoroaluminate in the IR and X-ray studies, as well as explaining the lack of fluoride nucleophilicity. The presence of K_2O must be inferred, but is consistent with the observed rapid reaction with atmospheric CO_2, leading to a less active material. This reaction is obviously dependent on the handling and exposure of the activated catalyst, and it has been reported that preparation of KF/alumina under strictly anaerobic conditions does indeed give an unusually active catalyst.

The presence of a complex and variable mixture of F^-, AlF_6^{3-}, CO_3^{2-}, OH^-, and O^{2-} is likely in most samples of KF/alumina, and it is thus no wonder that a wide range of basicities and catalytic activities have been reported.

4.1.1. Reactions Catalysed by KF/Alumina. A variety of reactions have been investigated using KF/alumina as catalyst. These include the Michael addition, the Knoevenagel and related reactions, aldol condensations, hydration of amides, enolisations, and the Darzens reaction. Outstanding results have been obtained in the Michael reaction, where KF/alumina is often the catalyst of choice. A comparative study of several fluoride base systems revealed that KF/alumina was an extremely effective catalyst for the reaction of nitroethane with 3-butene-2-one (Scheme 13). With the most active KF/alumina, the reaction was complete within 3 min. After this time, KF itself and KF−18-crown-6 have effected around 1% conversion.[90]

The reactions are generally rapid and give high isolated yields with extremely small amounts of catalyst. KF/alumina has been shown to be more active than sodium methoxide

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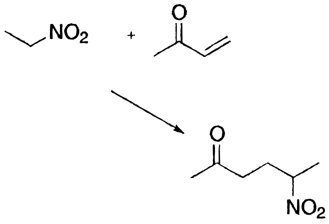
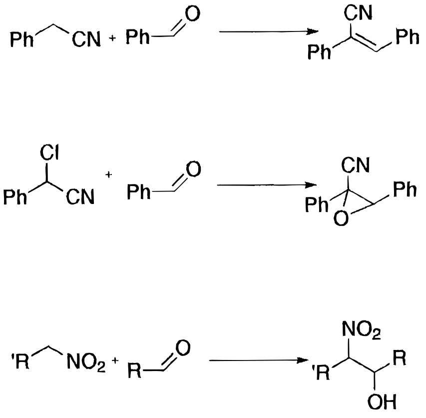
Scheme 13. **Addition of nitroethane to methyl vinyl ketone**



Scheme 14. **Selected reactions catalysed by KF/alumina**



in some cases.[91] It has a further advantage over this base in that it is much less sensitive to water than methoxide, and no special precautions need be taken in this respect. Its only drawback is its loss of activity on reuse. This is surprising considering that it is capable of many turnovers during one batch. Activity can be restored by treatment with aqueous KF and recalcination.

The Knoevenagel reaction is a valuable C−C bond forming reaction and can be very efficiently catalysed by KF/alumina. Yields are high, and the catalyst can in this case be successfully reused after thermal activation. The tolerance of water by the catalyst is an especially attractive feature in such reactions. Reactions have also been carried out in columns, which allow for extremely simple procedures. The related Darzens and Wittig−Horner condensations, as well as the Henry reaction are also amenable to catalysis by KF/alumina[86,92,93] (Scheme 14).

5. Conclusions and Future Directions

As can be seen from the above text, the scope of solid catalysts in liquid phase reactions is expanding on many fronts. Already, the first examples of commercial processes are being run on full-scale plants and solid acid and oxidation catalysts are commercially available.

The chemistry of these materials is often very complex and rarely corresponds to simple mixtures of the two (or more) components. Changes which can occur during preparation of the catalyst include structural modification of the support, be it minor, or significant alteration to the porosity characteristics, or even complete reaction with the second component to generate entirely different species. More subtle effects such as site isolation, which plays so vital a role in the activity of the TS-1 catalyst, may also be at play. Differences in catalytic activity can be due to site isolation, leading to different chemistry (e.g., heterolytic activation of hydrogen peroxide versus its homolytic decomposition), changes in diffusional characteristics due to pore size restrictions and/or electrostatic effects, or the presence of new species on the surface. The selectivity of the catalyst is often due, in great part, to such parameters, in particular pore size distribution. The importance of such factors and the choice of method of preparation and activation of the catalyst is becoming clear.

Prospects for future advances in this field must surely be great given the recent strides made in the understanding of such systems. For years, the zeolites displayed astonishing shape selectivity by dint of their highly regular and narrow pores. However, the small pore diameters of even the most open of the zeolites precluded all but the smallest molecules, and thus almost completely eliminated the zeolites from fine chemical manufacture. The possibility of preparing larger pore zeolitic materials in a simple and reproducible fashion has now been demonstrated with the discovery of the MCM materials.[6] For the first time chemists can synthesise zeolitic structures with pore sizes large enough for more complex molecules. Additionally, the pore size can be tailored to suit the system under investigation. Few results have been published on the use of such materials as catalysts, but many such applications will surely be known in the next few years.

A second area of growing importance is chemical surface modification. Here, surfaces are modified by covalent binding of organic molecules onto the surface of, e.g., silica. The concept has been known for several years (and is applied in the field of chromatography) but has always been hampered by the relative instability of the bonded phase under reaction conditions. More recently, newer methods have been developed which are capable of yielding more stable (and often better defined) materials. One area of potential is the chlorination of silica (which can be carried out easily in a fluidised bed reactor), followed by reaction with an organometallic reagent (e.g., RMgX or RLi).[94] The use of sol−gel coprecipitation techniques[95] is a related area where organic groups can easily and robustly be attached to a surface and used in catalysis.[96−98] Application of these technologies will also lead to novel catalytic systems in the future.

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