New approaches to rate enhancement in heterogeneous catalysis

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Rate enhancement, or promotion, of heterogeneous catalysts has long been viewed as an empirical subject, and many catalysts have been designed on the basis of large catalyst screening programmes. This paper addresses recent advances in this topic and indicates that much progress is being made on the basis of a molecular approach, in contrast to the previous empirical methodology, and in particular highly effective enantioselective heterogeneous catalysts can be designed. Two catalyst systems are selected for detailed discussion, namely enantioselective hydrogenation using cinchona-modified platinum catalysts and the modification of zeolites with chiral molecules.

Introduction

The design of high activity heterogeneous catalysis is considered crucial for the successful operation of the chemical industry. Most bulk chemical and petrochemical processes could not be operated commercially without a heterogeneous catalyst. Recently, there has been an increased awareness that heterogeneous catalysts could significantly improve a large number of fine chemical processes. Historically, most people would consider that current commercial heterogeneous catalysts are designed mainly by empirical large scale testing programmes. While this is not strictly true, there remains one area that has received very limited attention and this concerns the effect of rate enhancement, or promotion, of heterogeneous catalysts caused by additional catalyst components that are often inactive for the reaction if used alone. This is a subject that has been almost exclusively studied in industrial laboratories and the results are typically only disclosed in the patent literature. Most commercially operated catalysts involve promoters; for example, the effect of the addition of K^+ to the Fe Fischer Tropsch synthesis or ammonia synthesis catalysts is well known.[1] The dichotomy between academic and industrial research is well exemplified in the research concerning oxides and phosphates as catalysts for heterogeneous hydrocarbon oxidation. Most academic studies are concerned with the reaction mechanism on non-promoted systems whereas most industrial studies are concerned with promoted catalysts.[2,3] The origin of the rate enhancement effects observed in these complex systems remains obscure[2] mainly because the precise structure of the active site is unknown. This problem is best exemplified by vanadium phosphate catalysts for the oxidation of butane to maleic anhydride, since even though they have been the subject of over a thousand research papers and patents[2,4] the structure of the active site remains a matter of debate. However, recent detailed electron microscopy[5] and *in situ* laser Raman spectroscopy studies[6] are starting to make progress in this area. This lack of detailed knowledge concerning the structure of the active site in heterogeneous catalysts makes it almost impossible to adopt a molecular approach to this subject which is essential if progress is to be made. This is not a disadvantage that is shared by related subject areas of surface science, homogeneous catalysis and theoretical studies, since all of these use a molecular approach. If significant progress is to be made in heterogeneous catalysis then a similar molecular approach has to be adopted. In this paper it is shown that the latest research approaches in the design of heterogeneous catalysts are using a molecular approach and that progress is being made in the understanding of rate enhancement in heterogeneous catalysts. Two systems have been selected as examples of recent work, namely enantioselective hydrogenation using cinchona-modified platinum catalysts and the modification of zeolites with chiral molecules. Both of these examples have been selected since they demonstrate the advantages of rate enhancement in enantioselective catalysis since, in the absence of rate enhancement, the unmodified active sites are not less active than modified sites, and in some cases are more active, and hence the attainment of high enantioselectivities requires the absence of unmodified sites. However, when rate enhancement is observed, then unmodified sites are not a significant source of reaction and do not interfere with enantioselective reactions.

Enantioselective hydrogenation using cinchona-modified platinum

The hydrogenation of α-ketoesters using modified heterogeneous catalysts has been extensively studied, particularly for the reaction of ethyl pyruvate using modified Pt catalysts,[7–9] although recent studies have begun to generalise this system to a broader range of substrates and metals.[10] The reaction was originally described by Orito *et al.*,[11–14] and has been become the most intensively studied heterogeneous enantioselective catalytic reaction. The reason for this interest is that it is viewed by many workers as a model reaction on which to base other enantioselective studies. The approach adopted, *i.e.* the creation of a chiral active site by the adsorption of pure enantiomers onto a metal surface, has also proved successful in the related studies by Izumi[15] for the hydrogenation of β-ketoesters with tartrate-modified nickel catalysts. The early work on this reaction has been extensively reviewed,[7–9,16,17] and consequently only the important features of the reaction will be described here.

Extensive studies have revealed that hydrogenation of α-ketoesters in the presence of cinchona alkaloids as modifiers is best carried out using Pt catalysts (Fig. 1).[9,11–14,18] The Pt can be supported on a diverse range of materials, Al_2O_3, SiO_2, TiO_2, C, and the best results have been obtained using 5%Pt/Al_2O_3.[19]

The author has 23 years experience in the study and design of heterogeneous catalysts, particularly oxides and zeolites. His early career involved nine years in ICI in both research and production. In 1984 he left industry for an academic position at the University of Witwatersrand in Johannesburg prior to returning to the UK in 1987 to help establish the Leverhulme Centre for Innovative Catalysis at the University of Liverpool. In 1997 he was appointed as Head of Department and Professor of Physical Chemistry at Cardiff University.

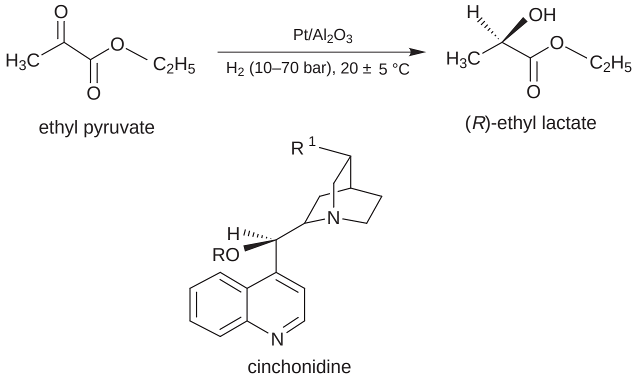


Fig. 1 Hydrogenation of ethyl pyruvate using Pt/Al$_2$O$_3$ catalysts modified with cinchonidine.

Interestingly, zeolites have also been successfully used as supports,[20–22] but no advantages for the specific use of microporous materials are apparent when compared with Al$_2$O$_3$ or other non-microporous supports. The optimum Pt particle size is considered to be > 2 nm, and catalysts with smaller Pt particle sizes have been shown to be less selective. It is generally agreed that the reason for the structure sensitivity remains a matter for debate. Some researchers[9] consider that the relatively flat low index planes are more suitable for adsorption of the cinchona modifier; however, Augustine *et al.*[23] dispute this and argue that the corner and ad-atoms are the active centres. Evidence in favour of the former viewpoint comes from heat pretreatment of the catalyst, which can be expected to stabilise low index planes, which shows an increase in enantioselectivity.

Most research effort for this reaction has concentrated on the optimisation of the enantioselection, and, specifically, on the design of the chiral modifier for the supported Pt catalyst with ethyl pyruvate as the substrate, and a selection of the results is summarised in Table 1. Early work focused on the method of modification by cinchona alkaloids and it was recognised that the choice of solvent was important for the attainment of high ee. The highest ee is obtained when acetic acid is used as solvent and the ee was found to increase in the order: ethanol < toluene < acetic acid when either 10,11-dihydrocinchonidine or 10,11-dihydro-*O*-methylcinchonidine were used as modifiers, and ethyl pyruvate or ethyl 4-phenyl-2-oxobutyrate were used as substrates. From this early work it was concluded[16] that the minimal requirements for an efficient modifier for the hydrogenation of α-ketoesters is the presence of a basic nitrogen centre in close proximity to one or more chiral centres and an aromatic ring system, with best results being obtained with planar ring systems, *e.g.* quinolyl or naphthyl. To date it is generally agreed that 10,11-dihydrocinchonidine is the most effective modifier for high pressure hydrogenation of ethyl pyruvate. However, recent extensive studies by Baiker[24] have indicated the efficacy of mechanistic studies for the design of new chiral modifiers in enantioselective hydrogenation that can be used to replace the cinchona alkaloids.

Table 1 Hydrogenation of ethyl pyruvate with Pt/Al$_2$O$_3$ using chinchona related modifiers[a]

Modifier[b]			
R	R[1]	Solvent	ee (%)[c]
H	Et	Acetic acid	90
Me	Et	Acetic acid	95
H	CH$_2$OH	Acetic acid	91
(*R*)-Lactate	Et	Acetic acid	44
(*S*)-Lactate	Et	Acetic acid	46
(*R*)-Benzyllactate	Et	Ethanol	20
(*S*)-Benzyllactate	Et	Ethanol	25

[a] Source ref. 16, *reaction conditions*: 50–100 mg Pt/Al$_2$O$_3$, 10 ml ethyl pyruvate, 20 ml solvent, ambient temperature, 100 bar. [b] R and R[1] as in Fig. 1. [c] Best ee reported for (*R*)-enantiomer.

The mechanism by which enantioselection occurs has been a matter of some speculation in recent years, and most recently has become a matter of intense debate.[25,26] Most researchers agree that the cinchona modifier interacts with the metal catalyst surface to form a new enantioselective catalytic site. Augustine *et al.*[23] proposed that the cinchona molecule is adsorbed through the quinoline N atom adjacent to a Pt ad-atom, where the substrate and H coadsorb with the N interacting with a CO group of the substrate. Baiker and coworkers[27–30] have utilised molecular simulations of the interaction between the substrate and the modifier and have suggested that protonated cinchonidine interacts with the oxygen atom of the CO bond that is subsequently hydrogenated, and that this interaction activates the substrate and thereby leads to the observed rate enhancement. An alternative proposal concerning the origin of the enantioselection, the shielding effect model, has been proposed by Margitfalvi and coworkers.[31,32] This model also uses molecular simulations as an integral part of the study. It is proposed that the modifier and the substrate preferentially form a 1 : 1 complex in solution, and this activated complex is subsequently hydrogenated by adsorbed hydrogen on the metal surface. Recently, we have considered these approaches using molecular simulations,[33] and it is clear that molecular simulation studies are playing a valuable role in aiding the design of new chiral modifiers, but there remains a central problem with this approach, namely that the platinum metal surface is not included in these simulations. Since the interaction between the cinchona and the platinum surface is considered to be crucial, this represents a major flaw. The alternative approach involving a more rigorous quantum mechanics calculation would prove to be too costly in computing time at present, and only relatively simple systems have been studied to date.

One of the most important observations for the Pt/cinchona catalyst system is the observation that the rate of hydrogenation of the α-diketone is significantly enhanced on the addition of the cinchona modifier (Table 2). A rate enhancement is observed with cinchonidine and 10,11-dihydrocinchonidine. The same effect is observed when Pt colloids are used as catalysts (Table 3), and this indicates that the nature of the support may not be of great significance for this effect. To date, the origin of the rate enhancement has not been determined, partly due to the fact that most studies have concentrated on the

Table 2 Effect of cinchona modifier on the rate of hydrogenation of ethyl pyruvate with Pt/Al$_2$O$_3$ catalysts[a]

Modifier[b]	Modification time/h	Solvent	Rate/mmol^{-1} g^{-1}
None	—	None	50
None	—	Ethanol	35
C	1	Ethanol	1100–1300
DHC	1	Ethanol	1100–1300
DHC	18	Ethanol	1490

[a] Data taken from ref. 10, H$_2$ pressure 10 bar, 20 °C. [b] C = cinchonidine, DHC = 10,11-dihydrocinhonidine.

Table 3 Enantioselective hydrogenation of ethyl pyruvate with Pt colloids using 10,11-dihydrocinchonidine as modifier[a]

Solvent	ee (%)	Relative rate[b]
Ethanol[c]	0	1
Ethanol	45	6
Toluene	15	2
Isopropanol	50	4

[a] Data taken from ref. 16. [b] Rates relative to hydrogenation rate in absence of modifier. [c] No modifier present.

optimisation of enantioselection. It is tempting to link the observation of the rate enhancement effect with the enantioselection that is achieved with this catalyst system. However, the rate enhancement is observed for racemic hydrogenation. For example Blaser *et al.*[19] have shown that aniline, triethylamine and quinuclidine all enhanced the rate of racemic hydrogenation of ethyl pyruvate when added to the Pt/Al_2O_3 catalyst and that there was a relationship between the pK_a of the nitrogen base and the degree of rate enhancement. The rate enhancement observed with cinchonidine is much higher than that predicted by pK_a considerations alone, indicating that other factors are important. Interestingly, Rylander[34] had previously noted that racemic amines could enhance the rate of hydrogenation of ketones. It is possible that the rate enhancement observed in the Pt/cinchona system is similar in origin to that observed in a number of homogeneously catalysed reactions (*e.g.* the enantioselective oxidation catalysts based on Mn–salen complexes[35]). It can be considered that the Pt/cinchona system will be a catalyst where the nature of the active site will be identified at the molecular level in the near future using a combination of experimental and theoretical studies.

Work we have carried out[36] on a related reaction, the hydrogenation of α,β-unsaturated aldehydes, has also shown a rate enhancement effect. We modified the surface of a Cu/Al_2O_3 catalyst with thiophene and this enhanced the rate of formation of the unsaturated alcohol, this being the first example of the catalytic activity of copper being promoted by sulfur. In this case, the thiophene modifier dissociates and the active site is considered to involve the interaction between a sulfur atom and the copper surface, based on detailed spectroscopic study.

Zeozymes: catalysts of the future

In recent years, the use of zeolites as high activity/high selectivity catalysts has received significant interest. The one clear driving force for these studies is that the three dimensional structure of the zeolite and, in particular, the structure of the active site are well known from detailed spectroscopic and diffraction studies. In zeolites all the atoms are on the surface and hence this class of materials enable a link to be formed with the elegant and detailed surface spectroscopic studies on single crystal surfaces, since both approaches allow heterogeneous catalysis to be studied at the molecular level with well-defined systems that can be probed with surface sensitive techniques. For zeolites, since all atoms are on the surface, normal bulk techniques (NMR, FTIR and X-ray diffraction) become surface sensitive techniques. Three distinct approaches are apparent in the recent literature, and these involve (a) using zeolites as supports for homogeneous catalysts or grafting active complexes onto mesoporous materials, (b) encapsulating large homogeneous complexes using a *ship-in-a-bottle* technique, and (c) chiral modification of zeolite surfaces.

(a) The first approach was exemplified by Corma *et al.*[37] for the hydrogenation of prochiral alkenes using Rh and Ni complexes supported on zeolite Y. Enantioselective hydrogenation using homogeneous Rh complexes is well documented,[38] and the rationale for this work was the requirement to find a less expensive heterogeneous route to pharmaceutical chemicals. Corma *et al.*[37] utilised Rh and Ni complexes with a range of ligands derived from proline. The complexes were anchored through silanol groups onto either silica or zeolite Y. The zeolite was prepared by steam calcination at 1027 °C of an 80% exchanged NH_4^+ zeolite Y, followed by treatment with citric acid. The zeolite is described as having a 'supermicropore' system (pore size 1.2–3.0 nm). These catalysts were found to be highly active for the hydrogenation of *N*-acyldehydrophenylalanine derivatives. They observed that the rate of hydrogenation was enhanced when the catalyst was supported on the zeolite compared to the rate observed for the non-supported complex or for the silica supported material, and they suggest that the confinement within the pores of the zeolite may play a role in the observed rate enhancement. However, in other cases, the same group have shown that reactions promoted by zeolite-supported catalysts are slower than those promoted by silica-supported complexes.[39] Hence, this approach cannot be considered to be a general method of securing rate enhancement.

A similar approach has been exemplified in the study of Ti-containing silicates, although in this case the Ti atoms are components of the active site and do not act as a promoter. On the basis of the developments in wider pore zeolites and related materials[40,41] Thomas *et al.*[42–44] have shown that titanium metallocenes grafted onto MCM-41 can act as effective oxidation catalysts with higher activity than Ti-MCM-41 catalysts when the Ti is incorporated into the silicate framework. Thomas *et al.*[42] have based their catalyst design on the concepts of interfacial coordination chemistry, surface organometallic chemistry and shape selective catalysis. However, other researchers[45] have shown that Ti-MCM-41 catalysts can be synthesised with very high activities.

(b) Encapsulation of large complexes within the micropores of zeolites has been pioneered by the studies of Jacobs *et al.*[46,47] The initial examples of this approach[46] involved the encapsulation in zeolites Y and X of iron phthalocyanine complexes, and these were shown to be active for the oxidation of alkanes with H_2O_2 as a mimic for cytochrome 450, the biological oxidation catalyst. Subsequently, complexes of manganese(II) with bipyridene (bpy) have been examined in detail.[47] In solution, the catalytic efficacy of these materials is limited by their catalase activity, *i.e.* their tendency to decompose hydrogen peroxide catalytically. When *cis*-$[Mn(bpy)_2]^{2+}$ complexes are encapsulated within the micopores of zeolite Y and X, however, they can act as effective alkene epoxidation catalysts without complications of competing processes such as self-oxidation or catalase activity. The catalysts are able to epoxidise a broad range of alkenes, and high epoxide selectivities ($>60\%$) are observed with hex-1-ene, cyclohexene, dodec-1-ene and cyclododecene. Owing to the acidic nature of the zeolites used, the products of the acid catalysed ring opening reactions were observed at extended reaction times. These catalysts are, therefore, further examples of a bifunctional catalyst combining oxidation and acid catalytic functions. The encapsulated *cis*-$[Mn(bpy)_2]^{2+}$ catalysts are remarkably stable, and are found to remain active for up to 1000 cycles for the oxidation of cyclohexene with H_2O_2. The catalyst can also be reused following drying at 47 °C and it is reported that repeated catalyst regeneration is possible, indicating that encapsulation of the *cis*-$[Mn(bpy)_2]^{2+}$ complex reduces the rate of oxidative destruction. The authors report that after repeated regeneration no changes in catalytic activity or spectroscopic properties of the complex could be observed. Electronic, rather than steric, factors were considered to control the reaction of the encapsulated catalysts and the hydrogen peroxide is considered to be activated by the formation of a high-valent manganese species [for example Mn(IV)=O], and it is the oxygen associated with this species that is inserted into the alkene C=C double bond.

Ogunmumi and Bein[48] and Sabater *et al.*[49] have extended the use of encapsulation to prepare heterogeneous catalysts for enantioselective epoxidation. The catalysts are based on the recently developed Jacobson homogeneous oxidation catalyst. Ogunmumi and Bein[48] and Sabater *et al.*[49] have also reported the successful encapsulation of Mn(III) salen complexes into zeolite Y using a *ship-in-a-bottle* approach previously used in the work of Jacobs and coworkers. Assembly of the reagents within the zeolite supercages leads to entrapped complexes that are too large to diffuse out of the zeolite host. The encapsulated complexes were characterised using vibrational and electronic spectroscopies together with ESR spectroscopy to confirm that the Mn(III) salen complex had been formed. The epoxidation of prochiral alkenes was studied using sodium hypochlorite as oxidant. Bein has reported high ee for the epoxidation of *cis*-β-methylstyrene and there are indications that the encapsulated complex does not leach from the host zeolite. Turnover numbers based on Mn are not high, and the regeneration and reuse of catalysts is an issue that has yet to be confirmed. This approach essentially uses the advances made in homogeneous catalyst systems and it is not anticipated that the encapsulation process can be expected to lead to further enhancement in catalytic performance.

(c) Modification of zeolites by pure enantiomers is the most recent of the approaches to be developed, although clearly it has its basis in the well-studied catalysts for enantioselective hydrogenation based on Pt/cinchona and Ni/tartrate. An initial report on the use of a zeolite as host for chiral induction was by Sundarababu *et al.*[50] In this study two zeolites NaY and NaX were modified by (−)-ephedrine and modest ee (< 10%) in the photolysis of ketones capable of undergoing the Norrish–Yang reaction. The most important observation related to the nature of the enantiomer that is enhanced in reactions using the two selected zeolites. In NaY, (−)-ephedrine showed enantioselectivity in favour of the (+) isomer of the product; however, the same chiral modifier favoured the (−)-isomer in NaX, although to a lesser extent. This remarkable effect was attributed to differences in the supercage free volume, as this was found to be different for the two modified zeolites.

The concept of modification of zeolite supercages to create the chiral environment required to favour the formation of one of a pair of diastereoisomeric transition states, a necessary condition for enantioselection, has been pioneered in our recent research. We selected chiral dithiane oxides since these were readily available to us with high optical purity, and as they provide a number of heteroatoms to ensure that the modifier is firmly anchored within the zeolite. A surprising early result we obtained is that the dithiane oxides are remarkably stable within the zeolite: they were only decomposed thermally at temperatures > 400 °C, and they were not racemised by adsorption in the zeolite. We selected the dehydration of butan-2-ol as an example of a simple acid catalysed reaction that can in principle demonstrate both enantioselectivity [differentiation between (*R*)- and (*S*)-butan-2-ol] and product selectivity (formation of but-1-ene, *cis*- and *trans*-but-2-ene).

Our initial experiments were carried out using zeolite Y modified with racemic 1,3-dithiane 1-oxide. We found that the dithiane oxide-modified zeolite Y is considerably more active than unmodified zeolite Y by several orders of magnitude, and that this activity was maintained without significant loss over several days. Under our reaction conditions, unmodified zeolite Y only became active at temperatures above 150 °C and required a reaction temperature of 225 °C to achieve 90% conversion, whereas the modified zeolite gave 90% conversion at 115 °C. We have now observed this effect with a number of other dithiane oxides (Fig. 2).[50,51] These early results show that modification of zeolite Y with the dithiane oxide creates a new high activity acid site. As noted previously, it is this observation of rate enhancement that we consider of crucial importance in the design of novel enantioselective catalysts. Since the active sites in the modified zeolite are considerably more active than those of the unmodified zeolite, we believed that the modified zeolite could form the basis of a new enantioselective catalyst. Our initial experiments confirm that this can indeed be observed, and the results are given in Table 4.[50] In these experiments, we reacted racemic butan-2-ol over zeolite Y which had been modified with an enantiomerically enriched dithiane 1-oxide. The chiral acid catalyst is selective for the reaction of one of the enantiomers preferentially, even though both enantiomers are present in equal concentration at the inlet to the reactor.

Modification of zeolite H-Y with dithiane oxide (**I**) leads to the creation of a catalyst that has enhanced activity for the acid catalysed dehydration of butan-2-ol when compared with the unmodified zeolite or when modified with the corresponding dithiane (**II**). This effect is observed both for samples prepared by addition of the modifier to the synthesis gel and for the post synthesis modification of two different commercial samples of zeolite Y (Crossfield and Union Carbide). When the modifier is added to the synthesis gel, the resulting zeolite contains only a small quantity of the modifier, but the effect is still apparent.[52]

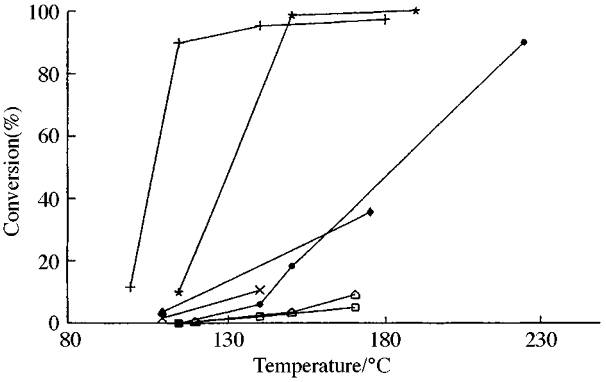
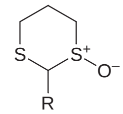


Fig. 2 Effect of temperature on the conversion of butan-2-ol over zeolite Y, key: (●) Zeolite H-Y (LZY 82, Union Carbide), (+) Zeolite H-Y (LZY 82) after modification with 1,3-dithiane 1-oxide, (★) Zeolite H-Y (LZY 82) after modification with 2-methyl-1,3-dithiane 1-oxide, (□) Zeolite H-Y (Crossfield), (X) Zeolite H-Y (Crossfield) with 1,3-dithiane 1-oxide, (⌂) Zeolite H-Y (Crossfield) after modification with 2-phenyl-1,3-dithiane 1-oxide and (◆) H-Y (LZY 82) after modification with 1,3-dithiane, reaction conditions: catalyst (0.3 g) reacted with butan-2-ol (3.2×10^{-3} mol h^{-1}) prevaporised in nitrogen (4.3×10^{-2} mol h^{-1}).



I

II

The interaction of alcohols with the acid forms of zeolites has been well studied in recent years, and for butanols it is generally considered that the adsorbed species that is formed initially is a butoxide species adsorbed at the active site that is formed from the dehydration of butan-2-ol. *In situ* FTIR spectroscopy confirmed that, in the present study, a butoxide species is formed on reaction of the butan-2-ol with both the unmodified zeolite and the dithiane oxide modified zeolite.[48] Consistent with the enhanced reactivity observed with the flow reactor studies, the *in situ* FTIR spectroscopy experiments reveal that the alkoxide species is formed at a significantly lower temperature for the dithiane oxide modified zeolite than for the unmodified zeolite.

All these data indicate that when the dithiane oxide is added to the zeolite, a new high activity site is formed, and it was concluded that the degree of rate enhancement observed can be related to the presence of extra-framework aluminium. This must, however, act in combination with the Brønsted acid site of the bridging hydroxy group associated with the zeolite framework aluminium, since the dehydration reaction investigated is catalysed by Brønsted acidity. A number of studies have indicated that a combination of extra-framework (Lewis acid sites) and framework (Brønsted acid sites) aluminium can give enhanced acidity in zeolite catalysts. Haag and Lago[53] showed that steaming zeolites at 500 °C with low levels of water vapour can lead to an increase in the activity of the zeolite for acid catalysed reactions. Mirodatos and Bartemeuf[54] showed that superacid sites could be created in mordenite by a steaming procedure. These effects were subsequently explained by Fritz and Lunsford[55] in terms of the initial dealumination of the zeolite to form non-framework aluminium that imparts, presumably through an electrostatic effect, strong acidity of the

Table 4 Reaction of racemic butan-2-ol over zeolite Y modified by enantiomerically enriched dithiane oxides

Catalyst[a]				Product composition[c]/× 10^{-3} mol h^{-1}				Butan-2-ol conversion (%)		
Zeolite	Modifier	*T*/°C	Conversion (%)[b]	But-1-ene	But-2-ene	(*R*)-Butan-2-ol	(*S*)-Butan-2-ol	*R*	*S*	Relative rate
Y[d]	(*R*)-**I**, R = H	110	0.5	—	0.037	3.673	3.640	0.002	0.035	1 : 17.5
Y[d]	(*R*)-**I**, R = H	120	1.3	0.015	0.085	3.669	3.581	0.006	0.094	1 : 15.7
Y[d]	(*R*)-**I**, R = H	150	9.9	0.105	0.620	3.657	2.968	0.018	0.707	1 : 39.3
Y[e]	(*S*)-**I**, R = Ph	110	4.2	0.020	0.271	3.399	3.660	0.276	0.015	18.4 : 1
Y[e]	(*S*)-**I**, R = Ph	120	7.5	0.044	0.507	3.260	3.594	0.415	0.081	5.1 : 1

[a] **I** = Dithiane 1-oxide (see text). [b] Total conversion of (*R*) and (*S*)-butan-2-ol. [c] Flow rate: 10^{-3} mol h^{-1}. [d] Zeolite Y (Crossfield NaY, ion exchanged with NH_4NO_3 and calcined at 550 °C), modified with (*R*)-1,3-dithiane 1-oxide, 1 molecule per supercage (0.1 g), tested in a convential glass microreactor with racemic butan-2-ol (7.35×10^{-3} mol h^{-1}), prevaporized in a nitrogen diluent (6.7×10^{-3} mol h^{-1}). [e] Zeolite Y (ultrastabilized LZY 82, Union Carbide) modified with (*S*)-2-phenyl-1,3-dithiane,1 molecule per supercage (0.1 g), tested in a convential glass microreactor with racemic butan-2-ol (7.35×10^{-3} mol h^{-1}), prevaporized in a nitrogen diluent (6.2×10^{-3} mol h^{-1}).

remaining framework Brønsted acid sites. This leads to an increase in acidity of the zeolite, and, for simple acid catalysed reactions such as cracking, an enhanced activity is observed. In the present work, the high activity site is considered to be formed by the specific interaction of the dithiane oxide with both the extra-framework aluminium and the Brønsted acid site associated with the framework aluminium (Fig. 3). Supporting evidence for this proposed model comes from detailed ^{27}Al MAS NMR spectroscopy studies and molecular simulations[56,57] that have shown that the dithiane oxide interacts strongly with the extra-framework aluminium atoms.

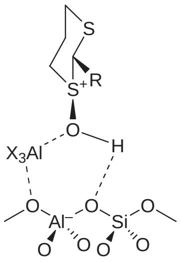


Fig. 3 Schematic representation of the structure of the high activity site formed on addition of 1,3-dithiane 1-oxide to zeolite H-Y (AlX_3 denotes extra-framework aluminium species).

The formation of high activity acid sites enables these modified zeolites to be used as enantioselective catalysts, since, although only one active site per supercage is modified, it is many orders of magnitude more active than the remaining unmodified sites. When the dithiane oxide is used in the enantiomerically enriched form, the active sites are able to discriminate between the enantiomers of butan-2-ol. This important effect is achieved by enantioselective rate enhancement, *i.e.* both enantiomers react faster in the chiral environment than in the absence of the chiral modifier, but one reacts faster than the other.

The activation energies for the dehydration of the separate enantiomers over the zeolites doped with the enantiomerically enriched dithiane oxides were found to be identical within experimental error (105 ± 5 kJ mol^{-1}). In addition, it was noted that the enantiomeric discrimination obtained from the reaction of racemic butan-2-ol is higher than that based on the conversions of the separate enantiomers. The apparent inconsistency can be resolved by regarding the modified zeolite as if it were an enzyme (a zeozyme) operating with its active sites saturated with substrate and, due to this saturation, the alcohol–catalyst complexation constant does not appear in the experimental kinetics. The conversions of the separate enantiomers then yield the relative reactivities in the catalytic step, whereas the results using the racemate reflect the enantioselection, not only of the catalytic step, but also of the competitive binding of the substrates. Present indications, supported by molecular modelling studies, are that the latter effect is the larger.[52,56,57]

It is important to note that the reactants and products in this reaction are gas phase. However, the reactant butan-2-ol is present at high partial pressures, and, at the lower temperature used in this study, which is only 12 °C above the boiling point of butan-2-ol, it is possible that condensation may occur in the micropores of the zeolite. This effect would not, however, be expected to contribute significantly to the results obtained at the higher temperatures, where enantioselection is still observed, albeit briefly. We consider that these results provide the first example of a gas-phase enantioselective reaction heterogeneously catalysed by a zeolite. Although the initial approach described here has concerned the design of a catalyst that consumes chiral molecules, the study should be viewed, in effect, as a proof of the concept that a zeolite can be modified so that it preferentially catalyses the reaction of one enantiomer of a chiral substrate in the presence of both. In view of the immense range of microporous zeolites available together with the large number of enantiomerically pure modifiers, we consider that this approach will provide the basis for the generic design of a new type of enantioselective catalysts. As further evidence for this viewpoint, we have recently shown[58] that Cu^{2+}-exchanged zeolites HY modified by chiral oxazolines are highly effective catalysts for the enantioselective aziridination of alkenes employing [*N*-(*p*-tolylsulfonyl)imino)]phenyliodinane (PhI=NTs) as the nitrogen source. (Fig. 4, Table 5) and that the Mn^{3+}-exchanged Al-MCM-41 modified by a chiral salen ligand is an enantioselective epoxidation catalyst using iodosyl benzene as oxidant.[59]

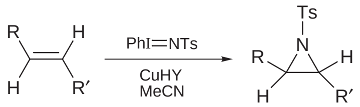


Fig. 4 Aziridination of alkenes using CuHY as catalyst.

These examples, it is hoped, demonstrate that a molecular approach can be taken to the design of novel high activity/selectivity heterogeneous catalysts. The approach proposed for the design of heterogeneous catalysts is similar in concept to that of the ‘ligand accelerated reaction’ described by Berrisford *et al.*[60] and exemplified in extensive homogeneous catalytic systems. In addition, it should be noted that the approach detailed in the present paper can also be useful in the design of chiral catalysts supported on different materials, *e.g.* amorphous oxides, organic polymers and dendrimers. In the future it is expected that the approaches outlined herein will become standard and that, in particular, the design of heterogeneous catalysts will involve an interplay between experimental and theoretical studies using catalysts with known structures. The recent work also demonstrates that rate enhancement in heterogeneous catalysis is now being studied at the molecular level, in contrast to the earlier approaches well exemplified in many patents published on this topic.

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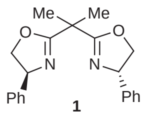
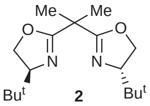
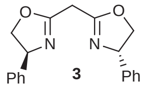
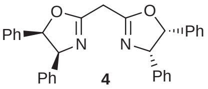
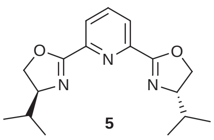
Table 5 Representative bis(oxazolines) for the enantioselective aziridination of alkenes

Oxazoline	Alkene[a]	T/°C	Yield(%)	e.e.(%)[c]
 1	*trans*-β-Methyl cinnamate	–10	8 (21)	61 (70)
	trans-β-Methylstyrene	–10	74	36
	Styrene	–10	82	44
	Styrene	25	87	29
 2	Styrene	–20	64	0
	Styrene[b]	–20	15 (89)	18 (63)
 3	Styrene	25	78 (75)	10 (10)
 4	Styrene	25	73 (74)	0 (15)
 5	Styrene	–10	4	61

[a] Unless otherwise specified reaction conditions were: solvent MeCN, alkene: PhI = NTs = 5 : 1 molar ratio. [b] Styrene was used as solvent. [c] Enantioselectivity determined by chiral HPLC. Absolute configurations of major products, determined by optical rotation, are (*S*) for *trans*-β-methylstyrene and *trans*-β-methylcinnamate, (*R*) for styrene values in parentheses indicate yields obtained from homogeneous reactions.

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