Catalytic asymmetric heterogeneous aziridination of alkenes using zeolite CuHY with [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane as nitrene donor

Christopher Langham,[a] Sophia Taylor,[a] Donald Bethell,[b] Paul McMorn,[a] Philip C. Bulman Page,[c] David J. Willock,[a] Chris Sly,[d] Frederick E. Hancock,[e] Frank King[e] and Graham J. Hutchings*[a]

[a] *Department of Chemistry, University of Wales Cardiff, PO Box 912, Cardiff, UK CF1 3TB*
[b] *Leverhulme Centre for Innovative Catalysis, Department of Chemistry, University of Liverpool, Liverpool, UK L69 3BX*
[c] *Department of Chemistry, Loughborough University, Loughborough, Leicestershire, UK LE11 3TU*
[d] *Robinson Brothers Ltd., Phoenix Street, West Bromwich, West Midlands, UK B70 OAH*
[e] *ICI Katalco, R&T Division, PO Box 1, Billingham, Teesside, UK TS23 1LB*

Received (in Cambridge) 13th August 1998, Accepted 16th March 1999

Copper-exchanged zeolite Y (CuHY) is found to be a highly effective heterogeneous catalyst for the aziridination of alkenes using [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) as the nitrogen source. Exchange of zeolite Y with other cations (Ag^{+}, Co^{2+}, Fe^{3+}, Mg^{2+}, Ni^{2+}, Zn^{2+}) was found to be ineffective. This is considered to be due to the ability of these metals to catalyse the breakdown of the PhI=NTs reagent into iodobenzene and toluene sulfonamide. Modification of the CuHY catalyst with bis(oxazolines) leads to preparation of the first heterogeneous enantioselective aziridination catalyst and the results showing the effect of temperature and modifier concentration are described and discussed. A pyridine-bridged bis(oxazoline) was observed to give the highest enantioselectivity of 61% ee for the aziridination of styrene using acetonitrile as solvent and at −10 °C.

Introduction

The identification of new commercial catalysts for the synthesis of the building blocks for pharmaceuticals and agrochemicals continues to attract public interest. In this respect, there is a need for catalysts to be designed that are stable, give high yields of the desired products, whether achiral or enantiomerically enriched, and can be readily re-used. Most attention has focused on the use of transition metal complexes in homogeneous solution processes, and much progress has been made with these systems. The identification, however, of a general approach to the design of suitable heterogeneous catalysts, has until now proved elusive since most examples tend to be substrate specific. Herein we report an approach based on zeolites that can in principle be generalized to the design of heterogeneous catalysts that have a potential to become commercially viable. We illustrate it by the asymmetric aziridination of alkenes, the first example of a heterogeneous catalyst reported for this reaction.

The requirement for new routes to racemic or enantiomerically pure intermediates for fine chemicals synthesis has bought a resurgence in interest in homogeneous catalysis in recent years.[1] The reason for this is that metal complexes that are used as catalysts can be located in well defined geometries that are necessary for the achievement of high specificity for the formation of the desired product. This approach to catalyst design has been thoroughly studied for a range of cations and reaction types; for example, titanium tartrate complexes for the enantioselective epoxidation of allylic alcohols (the Sharpless epoxidation reaction),[2] Cu^{2+} complexes for the cyclopropanation of alkenes[3] and aziridination of alkenes,[4] manganese salen complexes for the epoxidation of alkenes,[5] and ruthenium BINAP complexes for the hydrogenation of alkenes,[6] are all well established, and indeed the Sharpless epoxidation has been commercialized. A central problem with all these homogeneous systems relates to the separation and reuse of the catalyst which is often very difficult and expensive. To overcome this disadvantage considerable effort has been devoted to the heterogenization of these catalysts. To date there have been a number of approaches to heterogenization of homogeneous catalysts[7] but two have predominated. The first involves the use of a thin layer of a suitable solvent containing the homogeneous catalyst that is supported on the surface of a high area solid, an approach which can retain the performance of the homogeneous catalyst.[6] The second approach involves encapsulation of the homogeneous catalyst in the pores of a solid, typically a zeolite, and this is often designated as a 'ship in a bottle' method since the catalyst is constructed within the pores.[8] Both these approaches are general, but suffer the disadvantage that the active catalyst usually degrades with time and often is removed into the reaction medium through solubilization. In contrast to these approaches we have used the observations that zeolites are well known for their cation exchange properties and that the cations are in many cases known to be located in precise sites with the zeolite acting as a ligand.[9] We believe that such metal-exchanged zeolites could, with suitable modification, be useful heterogeneous catalysts for the reactions listed above. Zeolites have been used as catalysts for fine chemicals synthesis for many years[10] but the main emphasis has been on their Brønsted acidity/basicity and their well known shape selective properties. As an initial demonstration of our approach we focus on the aziridination of alkenes, since this was known to be homogeneously catalysed by a number of relatively simple copper compounds,[4] and no heterogeneous counterparts had yet been identified. Preliminary accounts of this and related work using the same catalyst design principles have already appeared.[11,12]

Table 1 CuHY-catalysed aziridination of representative alkenes

Entry	Alkene[a]	[Cu] (mol%)	Yield[b] (%)		
			$TsNH_2$	PhI	Aziridine
1	Styrene	25	10	100	90 (92)
2	Styrene[c]	25	13	100	87 (35)
3	Styrene	5	38	100	62
4	α-Methylstyrene	25	77	100	33
5	*p*-Chlorostyrene	25	24	100	76
6	*p*-Methylstyrene	25	34	100	66
7	Cyclohexane	25	50	100	50 (60)
8	Methyl (*E*)-cinnamate	25	16	100	84 (73)
9	(*E*)-Stilbene	25	100	100	0[d] (52)
10	(*E*)-Hex-2-ene	25	56	100	44

[a] Unless otherwise specified reaction conditions were: solvent MeCN, 25 °C, styrene : PhI=NTs = 5 : 1 molar ratio. [b] Isolated yield of aziridine based on PhI=NTs. [c] Styrene : PhI=NTs = 1 : 1 molar ratio. [d] No product observed by TLC. Values in parentheses indicate yields obtained from comparable homogeneous reactions.

Results and discussion

Heterogeneous aziridination of alkenes with CuHY

Evans *et al.*[4] have shown that copper triflate is a homogeneous catalyst for the aziridination of a range of alkenes. Based on this previous study we investigated copper-exchanged zeolites as catalysts for this reaction and we have found that CuHY zeolite is successful in catalysing the aziridination of a range of alkenes employing [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) as the nitrogen source. Reactions were carried out at 25 °C in stirred flasks containing a mixture of PhI=NTs (typically 0.52 g), the CuHY (0.071 g, the amount being adjusted for the copper content of the zeolite so that the total amount of copper in the reaction mixture was 0.25 equivalents per mol of PhI=NTs), and an acetonitrile solution of the alkene, usually in five-fold excess over PhI=NTs. Analysis of the reaction mixtures for aziridine, toluenesulfonamide and iodobenzene was by HPLC. Reactions were followed until all the PhINTs (which is only sparingly soluble in acetonitrile) had disappeared and the yield of PhI by HPLC was constant (typically after 3 to 6 hours). The results are shown in Table 1. CuHY was initially screened in the aziridination of styrene (Table 1, entries 1–3), since this alkene affords good yields of aziridine when copper triflate is used as a homogeneous catalyst.[4] Using a five-fold molar excess of styrene, *i.e.* similar conditions to the homogeneous process, the desired *N*-tosylaziridine was obtained in 90% yield (entry 1). These initial results confirmed our contention that cations within zeolites could be used as heterogeneous counterparts of known homogeneous catalysts, and, to our knowledge, this is the first example of an aziridination reaction catalysed heterogeneously.

In order to confirm that this process was wholly heterogeneous, following reaction the zeolite catalyst was recovered by filtration, and another aliquot of reactants (styrene : PhI=NTs = 5 : 1 molar ratio) was added to the recovered filtrate; no further product was observed. Further, the removed catalyst was reused with fresh reagents and solvent, and the zeolite demonstrated similar activity to when it was used initially.

It was noted in earlier studies that, in the homogeneously catalysed reaction,[4] the yield of aziridine decreased to 37% when a 1 : 1 molar ratio of styrene : PhI=NTs was employed, presumably due to the competing breakdown of the PhI=NTs reagent to yield toluene-*p*-sulfonamide. This decrease was found to be dramatically less significant using our heterogeneous catalyst, where an 87% yield of aziridine was obtained when a styrene : PhI=NTs molar ratio of 1 : 1 was used (Table 1, entry 2), as compared to a yield of 90% when a styrene : PhI=NTs molar ratio of 5 : 1 was used (Table 1, entry 1). This is a particularly important observation since the procedure can be applied to the aziridination of expensive alkenes. Moreover it indicates that the environment of the catalytic sites is very different from that found in homogeneous copper(II)-containing acetonitrile solutions (see below).

CuHY was found to be successful in catalysing the aziridination of a range of alkenes (Table 1) in addition to styrene. It is observed that the catalyst gives best results with phenyl-substituted alkenes, lower yields being observed with cyclohexene and (*E*)-hex-2-ene. Interestingly, for the aziridination of (*E*)-stilbene no product was observed, although in this case the analysis was carried out by TLC.

Stirring PhINTs in an acetonitrile solution of a five-fold excess of styrene at 25 °C slowly leads to the formation of aziridine (22%) and toluene-*p*-sulfonamide (78%) over a period of 72 hours. We believe, however, that our results indicate that the aziridination of alkenes by PhI=NTs in the presence of zeolite CuHY is almost wholly heterogeneous and takes place within the pores of the zeolite. Our reasons are as follows.

1. The catalysed reaction is much faster; at the time when it reaches completion, the uncatalysed pathway would have contributed less than 5% of the consumption of PhI=NTs.

2. The failure of (*E*)-stilbene to undergo aziridination in the presence of the zeolite although reaction occurs with the rather similarly sized methyl (*E*)-cinnamate (84% yield), and for stilbene in the homogeneous copper catalysed process (52% yield) indicates that the active catalytic sites are within the zeolite pores. Catalysis of aziridination by the external surface of the zeolite is clearly insignificant for (*E*)-stilbene. Molecular modelling studies, based on a systematic evaluation of free volume available to each molecule, indicate that the aziridine formed from the ester can adopt a conformation that fits within the zeolite pores and is free to diffuse through the pore structure, whereas the aziridine from (*E*)-stilbene, although it can be constructed within the supercages of the zeolite, is too bulky to diffuse through the interconnecting channels in the structure.

3. For the zeolite Y crystallites used in this study only 0.5% of the available acid sites are present on the external crystallite surface[13] and hence any reaction resulting from these non-microporous sites can be expected to be negligible. The effect of the external sites was investigated in more detail by examining the yield of aziridine formed by zeolites containing different exchange levels of Cu^{2+}. A series of CuHY zeolites, containing 2.4, 3.1, 4.2 and 4.7% Cu, were prepared using $Cu(OAc)_2$ solutions with different concentrations (0.025–0.2 mol l^{-1}). These zeolites were then used in the aziridination of styrene and the amount of catalyst was adjusted so that in each reaction the same mass of Cu was utilized. The same yield of aziridine and rate of formation was observed in all four cases although the ratio of external to internal sites is significantly different for these catalysts. These results indicate that the sites on the external crystallite surface are not playing a disproportionately significant role in the reaction.

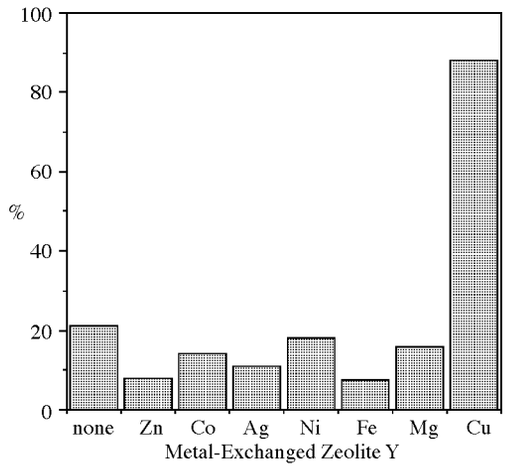


Fig. 1 Effect of metal-exchanged zeolite Y on the aziridination of styrene. Reaction conditions: PhI=NTs : styrene molar ratio = 1 : 5, metal-exchanged zeolite Y in CH_3CN at 25 °C, 'none' indicates the yield obtained when no catalyst is added. Reaction time for CuHY catalysed reaction was five hours. All other reactions were left for five days without complete dissolution of PhI=NTs reagent.

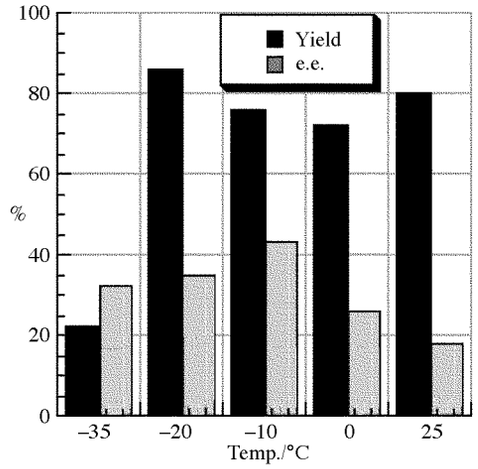


Fig. 2 Effect of temperature on aziridination of styrene. Isolated yields based on PhI=NTs, ee determined by chiral HPLC. Reaction conditions: solvent CH_3CN, styrene : PhI=NTs : bis(oxazoline) = 5 : 1 : 0.05 molar ratio.

It should be noted that, given that the reaction takes place in the intracrystalline space of the zeolite, the almost identical aziridine yields in reactions with styrene : PhI=NTs ratios of 1 and 5 suggest that the alkene is preferentially bound within the zeolite pores compared with solvent molecules (which are weak ligands for copper). Thus the reaction of PhI=NTs at the catalytic site, which we presume to give rise to a copper–tosylnitrenoid intermediate (which we represent as TsN=CuHY), occurs in an environment in which trapping to form aziridine is favoured by the presence of the alkene in close proximity and at an effective concentration substantially higher than in the bulk liquid phase. Alkenes, particularly ones capable of chelation, are known to form copper complexes. While this might be thought to be an explanation of the better aziridine yields from phenyl-bearing alkenes, such complexation takes place only to copper in its +1 oxidation state. It should be borne in mind, however, that Evans has offered no compelling evidence for the actual oxidation state of copper in the homogeneously catalysed reaction, although he expressed the belief that it was Cu(II).

Several other metal exchanged zeolites were also screened, but CuHY was found to be the most active. The results are shown in Fig. 1. In most cases when zeolite Y was exchanged with other metals, *e.g.* Ag^+, Co^{2+}, Fe^{3+}, Mg^{2+}, Ni^{2+}, Zn^{2+}, the yield of the aziridine was lower than that obtained when compared with the uncatalysed and the CuHY catalysed reactions. We consider that this is due to the ability of these metals to catalyse the breakdown of the PhI=NTs reagent into iodobenzene and toluene-*p*-sulfonamide. This catalysed breakdown has also been noted by Burrows *et al.*[14] and was confirmed in our experiments by the observation of high yields of iodobenzene.

Heterogeneous asymmetric aziridination of alkenes with CuHY

Evans *et al.*[4] have shown that modification of the copper homogeneous catalysts using chiral bis(oxazoline) ligands induces enantioselectivity in the aziridination reaction. We have examined modification of the CuHY catalyst with a range of oxazolines and have observed *N*-tosylaziridine products with up to 61% enantiomeric excess. The racemic heterogeneous aziridination of alkene, in the absence of bis(oxazoline), gave yields of 80% in the temperature range −20 to +25 °C using acetonitrile as solvent. However, the higher temperatures gave shorter reaction times (*e.g.* 2 h at +25 °C) and hence 25 °C was considered optimal from a practical viewpoint for non-enantioselective aziridination. For the enantioselective reaction, the use of lower reaction temperatures was found to give the highest enantioselectivities. The temperature variation of yield and ee requires comment. The yield of the aziridine is determined by competing processes for the tosylnitrenoid active species within the zeolite, whereas the ee will determined by competing processes *via* the diastereoisomeric transition states. In both situations, competing reactions will in general have different activation parameters and so a temperature variation is to be expected. That both yield an ee showing a maximum is not unique and a number of possible reasons could account for our observations. One is the possibility that there is reaction of copper uncomplexed by the bis(oxazoline) giving racemic aziridine that is slow at higher temperatures but becomes important at low temperatures because of a lower enthalpy of activation than the reaction catalysed by the copper–bis(oxazoline) complex; such a situation would then oppose the increase in ee that is expected as the temperature falls leading to a maximum being observed in the ee *versus* temperature plot. We have found that a temperature of −10 °C provides the highest enantioselectivity of 42% ee without compromising yield when using acetonitrile solvent and 2,2-bis[((4*R*)-4-phenyl-1,3-oxazolin-2-yl)]propane (**1**) as the chiral modifier simply added to the reaction mixture (Fig. 2). Evans *et al.*[4] observed that benzene was the preferred solvent for the homogeneous copper catalyst. In contrast, we do not observe improved enantioselection or activity when benzene is used as the solvent with the heterogeneous CuHY catalyst (Fig. 3).

It would be reasonable to assume that one chiral modifier would be required per zeolite supercage to obtain maximum enantioselectivity. We have, however, found that very low levels of the expensive modifier can be used without resulting in decreases in yield or enantioselectivity (Fig. 4). An excess of bis(oxazoline) significantly reduces the yield of aziridine, due to pore-blocking, but both yield and enantioselectivity were maximized with only a molar ratio of PhI=NTs : bis(oxazoline) = 1 : 0.05. This corresponds to a molar ratio of Cu^{2+} : bis(oxazoline) of 2 : 1, indicating, remarkably, that not all the Cu^{2+} cations are modified in our experiments. In a subsequent experiment, an excess of bis(oxazoline) **1** was stirred with CuHY [molar ratio Cu^{2+} : bis(oxazoline) = 1 : 5] in acetonitrile. The zeolite was filtered and washed with acetonitrile, then used as the catalyst in fresh solvent and reactants. Both yield and enantioselectivity observed were identical to those obtained when the bis(oxazoline) was added directly to the reaction mixture (molar ratio of PhI=NTs: bis(oxazoline) = 1 : 0.05). It is clear that very low levels of the modifier are required to obtain the enantioselectivities reported. It is possible that different copper sites are present within the zeolite

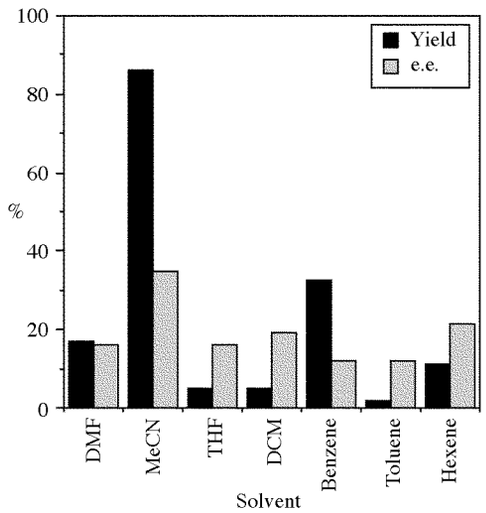


Fig. 3 Effect of solvent on the aziridination of styrene. Isolated yields based on PhI=NTs, ee determined by chiral HPLC. Reaction conditions: 25 °C, styrene : PhI=NTs : bis(oxazoline) = 5 : 1 : 0.05 molar ratio.

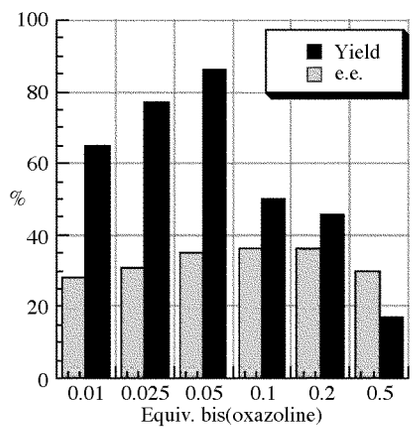


Fig. 4 Dependence of the aziridination of styrene on the amount of bis(oxazoline) measured as molar equivalents based on PhI=NTs. Isolated yields based on PhI=NTs, ee determined by chiral HPLC. Reaction conditions: solvent CH_3CN, −20 °C, styrene : PhI=NTs = 5 : 1 molar ratio.

and that only a fraction of the total are active in the activation of PhI=NTs,[15] or that the bulky oxazoline molecules diffuse slowly into the zeolite pore structure and only sites close to the surface are modified. Further detailed spectroscopy will be needed to clarify this point.

With the optimum conditions established for the enantioselective aziridination of styrene, other bis(oxazolines) and alkenes were screened with CuHY as the catalyst (Table 2). (*E*)-β-Methylstyrene was found to show similar degrees of enantioselectivity to styrene. However, methyl (*E*)-cinnamate gave a much superior result of 61% ee, albeit in poorer yield. The *tert*-butyl substituted bis(oxazoline) **2**, when used in acetonitrile solvent, gave racemic aziridine. We suggest that this is because acetonitrile, a ligand for Cu^{2+}, competes more effectively with this bis(oxazoline) for the active sites. Support for this interpretation comes from our observation that, by carrying out the reaction using styrene as the solvent, enantioselectivity was restored, although both yield and enantiomeric excess were then lower than for the homogeneous reaction. To provide further evidence that the reaction is proceeding within the supercages of the zeolite, reactions were carried out using a simple phenyl substituted bis(oxazoline) **3**, which is known to fit inside the zeolite, and using a diphenyl substituted analogue **4**, which was considered as the result of molecular simulations to be too bulky to fit inside the zeolite pores. At 25 °C the smaller bis(oxazoline) **3** gave 10% ee for both the heterogeneous and homogeneous reactions. However, for the heterogeneously catalysed reaction, using CuHY as catalyst, the bulky diphenyl bis(oxazoline) **4** gave racemic product, despite inducing 15% ee for the equivalent homogeneously catalysed reaction. This is again evidence that the reaction is truly heterogeneous and is occurring within the pores of the zeolite. Further modification of the bis(oxazoline) has shown that the pyridine-bridged bis(oxazoline) **5** gives the highest enantioselectivity of 61% ee for the aziridination of styrene (Table 2). We consider these initial results to be encouraging and that careful optimization of choice and concentration of the chiral ligand might result in further improvements in ee and yield.

The major advantage of the use of CuHY as a catalyst for this reaction is the ease with which it can be recovered from the reaction mixture by simple filtration if used in a batch reactor (alternatively it could be used in a continuous flow fixed bed reactor). We have carried out the heterogeneous asymmetric aziridination of styrene until completion, filtered and washed the zeolite then added fresh styrene, PhI=NTs and solvent, without further addition of bis(oxazoline) **1**, for several consecutive experiments; the results are shown in Fig. 5. After each consecutive experiment a portion of CuHY was retained to determine the concentration of copper still present in the zeolite. For each experiment we found that only traces of the copper were removed from the catalyst (<0.5% of the total Cu^{2+} is lost from the catalyst). The filtrate containing the trace concentration of Cu^{2+} has been used in a reaction and was not found to catalyse aziridination. The yield and the enantioselectivity decline on reuse; we have found that adsorbed water can build up within the pores of the zeolite on continued use and we believe that this is the cause of loss of activity and enantioselection. However, full enantioselectivity and yield can be recovered if the catalyst is simply dried in air prior to reuse (Fig. 5) or alternatively the catalyst can be recalcined and fresh oxazoline ligand added. We are therefore confident that this catalyst system can form the basis of a commercial heterogeneous catalyst for the aziridination of alkenes.

Heterogeneous asymmetric aziridination of alkenes with Cu-MCM41

To demonstrate that alternative types of silicate framework can be used for this reaction, experiments were carried out using Cu^{2+}-exchanged MCM-41, a mesoporous material with pores of 3.5 nm in diameter.[15] Yields of up to 87% of the aziridine and ee of 37% were obtained. Using this mesoporous material greatly increases the versatility of heterogeneous aziridination since larger alkenes and chiral modifiers can be used, while retaining all the advantages of the heterogeneous catalyst system.

Conclusions

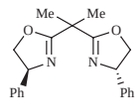
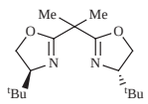
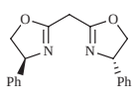
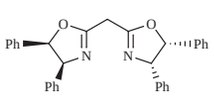
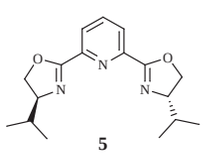
In this paper we have presented results for the first heterogeneously catalysed aziridination reaction. Furthermore we have shown that this catalyst can be modified to induce enantioselectivity. The design ideas upon which this catalyst discovery is based are the detailed understanding that cations can be located at defined locations in zeolite pores and that the zeolite acts as part of the coordination sphere, and that the remaining coordination sites on the metal can be filled by the addition of further ligands that can be chiral and hence (or in other ways) control the reactivity. We consider that this approach can have general applicability and will be of value in the design of improved asymmetric catalysts.

Experimental

Apparatus

a) ^1H and ^{13}C NMR spectra were recorded on Bruker AC300 and AMX 400 spectrometers, equipped with an X32 computer.

Table 2 Representative bis(oxazolines) for the enantioselective aziridination of alkenes

Oxazoline	Alkene[a]	Temp./ °C	Yield (%)	ee (%)[b]
 **1**[c]	Methyl (*E*)-cinnamate	−10	8 (21)	61 (70)
	(*E*)-β-Methylstyrene	−10	74	36
	Styrene	−10	82	44
	Styrene	25	87	29
 **2**	Styrene	−20	64	0
	Styrene[d]	−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 CH_3CN, alkene : PhI=NTs = 5 : 1 molar ratio. [b] Enantioselectivity determined by chiral HPLC. Absolute configurations of major products, determined by optical rotation, are (*S*) for (*E*)-β-methylstyrene and methyl (*E*)-cinnamate, (*R*) for styrene. Values in parentheses indicate yields obtained from homogeneous reactions. [c] The absolute configuration shown in ref. 11 as the *S*-enantiomer is incorrect, the *R*-enantiomer of I was used in all the reported studies. [d] Styrene was used as solvent.

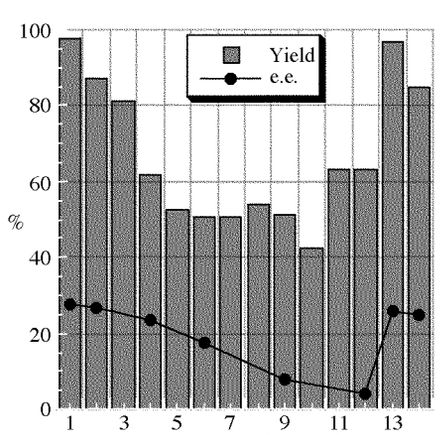


Fig. 5 Reusability of CuHY as a catalyst for the aziridination of styrene. Following experiment 12 the catalyst was recovered by filtration, recalcined and fresh oxazoline was added. Reaction time increased from 1 h for initial use to 35 h for run 12; reaction times for runs 13 and 14 were 1 h.

Unless otherwise stated deuteriochloroform was used as the solvent. Spectra were recorded on the d scale and signals quoted in the form: chemical shift measured in ppm (no. of protons, multiplicity, assignment).

b) Infrared spectra were recorded in the range 4000–600 cm^{-1}, using Perkin-Elmer 1320 and 883 infrared spectrometers with a polystyrene reference. Spectra of the liquids were taken as films, or as solutions in chloroform, using sodium chloride cells. Spectra of solids were taken as nujol mulls.

c) Mass spectra were obtained on VG analytical 7070E and Fisons TRIO1000 double focusing magnetic sector spectrometers, using electron impact (E.I.) or chemical ionisation (C.I.) techniques with ammonia as the carrier gas.

d) Microanalyses were performed by the University of Liverpool, Department of Chemistry, Microanalytical Laboratory.

e) Flash column chromatography was performed on Merck Kieselgel 60 (230–400 mesh) and analytical TLC on silica gel 60 F-254 plates.

f) HPLC analysis was recorded on a Varian 5000 liquid chromatograph, using C18 Apex Octadecyl 5μ reverse-phase columns for analytical work. The eluent system was water–acetonitrile (50 : 50), 235 nm, flow rate 0.6 ml min^{-1}. Baseline separation was achieved for all reagents and products. For chiral HPLC analysis a 25 cm chiralcel OJ column was used. The eluent system was hexane–isopropan-2-ol (95 : 5), 235 nm, flow rate 1.0 ml min^{-1}. Baseline separation was achieved for both enantiomers. Absolute configuration was confirmed by optical polarimetry and comparison with the literature.[3]

Materials

(*E*)-Stilbene and bis-oxazolines were obtained from Aldrich. Synthesis of [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) was carried out following the method of Yamada *et al.*[16]

Cu-MCM-41

AlMCM-41 was prepared according to the method of Beck *et al.*[17] Calcined AlMCM-41 (3.0 g) was stirred in copper(II) acetate solution (100 ml, 0.2 M) for 24 h. The material was then filtered, washed, dried and then stirred again in fresh manganese(II) acetate solution (100 ml) for another 24 h. This process was repeated a further two times. Finally the exchanged zeolite was calcined (550 °C) for eight hours prior to use; Cu content 5.0% by weight.

CuHY ion-exchange

Ultrastabilised NH_4^+Y zeolite (5.0 g), obtained from Union Carbide, was calcined (550 °C) for five hours, then stirred in 0.5

molar solution of copper(II) acetate solution (100 ml) for 24 hours at room temperature. The mixture was then centrifuged and washed with distilled water. This was repeated until all unexchanged copper was removed. The zeolite was then dried at 100 °C for 24 hours then recalcined (550 °C) for five hours; Cu content 4.0% by weight.

N-(*p*-Tolylsulfonyl)-2-phenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and styrene (0.69 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.33 g (90%) of the aziridine as a crystalline solid. (for asymmetric aziridination of styrene $[\alpha]_D^{20} = -29.2$ (25 °C, chloroform)). mp 89–90 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3015, 1325, 1215, 1160, 915, 785, 770, 715, 695, 665; δ_H (300 MHz, $CDCl_3$) 7.86 (d, 2H, J = 8.1 Hz, Ar-*H*), 7.32 (d, 2H, J = 8.1 Hz, Ar-*H*), 7.10 (s, 5H, Ar-*H*), 3.74 (dd, 1H, J_{cis} = 7.0, J_{trans} = 4.8 Hz, C*H*Ph), 2.96 (d, 1H, 7.0 Hz, *cis*-C*H*-aziridine), 2.42 (s, 3H, Ar-CH_3), 2.37 (d, 1H, J = 4.8 Hz, *trans*-C*H*-aziridine); δ_C (75 MHz, $CDCl_3$) 144.7, 135.2, 129.8, 128.6, 128.4, 128.0, 126.6, 41.1, 35.9, 21.6; HRMS (FAB,MNBA) exact mass calcd. for $C_{15}H_{15}NO_2S$ $(M + Na)^+$ 273.08234, found 273.08251. Anal. calcd. for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.31; H, 5.59; N, 4.93%.

N-(*p*-Tolylsulfonyl)-2-methyl-3-*n*-propylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and (*E*)-hex-2-ene (0.56 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1.5 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.17 g (44%) of the aziridine as a colourless oil: ν_{max}/cm^{-1} (thin film) 2959, 2932, 1456, 1325, 1306, 1291, 1233, 1163, 1092, 957, 943, 924, 866, 816, 716, 694, 662; δ_H (300 MHz, $CDCl_3$) 7.80 (d, 2H, J = 8.3 Hz, Ar-*H*), 7.27 (d, 2H, J = 8.3 Hz, Ar-*H*), 2.67 (m, 1H, C*H*-aziridine), 2.61 (d, 1H, J = 7.0 Hz, *cis*-C*H*-aziridine), 2.38 (s, 3H, Ar-C*H*3), 1.54 (m, 1H, aliphatic), 1.31–1.22 (m, 6H, aliphatic), 0.83 (t, 3H, J = 7.1 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 143.8, 138.3, 129.5, 127.3, 49.5, 45.7, 32.3, 21.5, 20.4, 14.7, 13.6; HRMS (FAB,MNBA) exact mass calcd. for $C_{16}H_{17}NO_2S$ $(M + Na)^+$ 287.09799, found 287.09799. Anal. calcd. for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 65.26; H, 5.61; N, 4.31%.

N-(*p*-Tolylsulfonyl)-2-(*p*-methylphenyl)aziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and *p*-methylstyrene (0.79 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.25 g (67%) of the aziridine as a crystalline solid: mp 137–138 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3034, 1600, 1516, 1380, 1322, 1158, 1092, 1018, 978, 911, 814, 716, 708, 692, 660; δ_H (300 MHz, $CDCl_3$) 7.86 (d, 2H, J = 8.2 Hz, Ar-*H*), 7.31 (d, 2H, J = 7.9 Hz, Ar-*H*), 7.09 (s, 4H, Ar-*H*), 3.73 (dd, 1H, J_{cis} = 7.2 Hz, J_{trans} = 4.5 Hz, C*H*Ph-aziridine), 2.96 (d, 1H, Ar-*H*, J = 7.2 Hz, *cis*-C*H*-aziridine), 2.42 (s, 3H, Ar-CH_3), 2.36 (d, 1H, J = 4.5 Hz, *trans*-C*H*-aziridine), 2.32 (s, 3H, Ar-CH_3); δ_C (75 MHz, $CDCl_3$) 144.3, 138.1, 135.1, 132.0, 129.8, 129.3, 128.0, 126.5, 41.8, 35.8, 21.5, 21.0; HRMS (FAB,MNBA) exact mass calcd. for $C_{16}H_{17}NO_2S$ $(M + Na)^+$ 287.09799, found 287.09799. Anal. calcd. for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 65.26; H, 5.61; N, 4.31%.

N-(*p*-Tolylsulfonyl)-2-(*p*-chlorophenyl)aziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and *p*-chlorostyrene (0.92 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.31 g (76%) of the aziridine as a crystalline solid: mp 115–116 °C; ν_{max}/cm^{-1} (CH_2Cl_2) 3055, 1600, 1494, 1462, 1376, 1325, 1185, 1160, 1190, 1014, 980, 908, 812, 688, 667; δ_H (300 MHz, $CDCl_3$) 7.85 (d, 2H, J = 8.3 Hz, Ar-*H*), 7.33 (d, 2H, J = 7.8 Hz, Ar-*H*), 7.25 (d, 2H, J = 8.5 Hz, Ar-*H*), 7.15 (d, 2H, J = 8.5 Hz, Ar-*H*), 3.72 (dd, 1H, J_{cis} = 7.3 Hz, J_{trans} = 4.3 Hz, C*H*Ph-aziridine), 2.29 (d, 1H, J = 7.3 Hz, *trans*-C*H*-aziridine), 2.42 (s, 3H, Ar-CH_3), 2.35 (d, 1H, J = 4.3 Hz, C*H*-aziridine); δ_C (75 MHz, $CDCl_3$) 144.8, 134.8, 134.1, 133.6, 129.8, 128.8, 128.0, 40.2, 36.1, 21.1; HRMS (FAB,MNBA) exact mass calcd. for $C_{15}H_{14}ClNO_2S$ $(M + Na)^+$ 307.04337, found 307.04348. Anal. calcd. for $C_{15}H_{14}ClNO_2S$: C, 58.62; H, 4.60; N, 4.56. Found: C, 59.29; H, 5.07; N, 4.21%.

trans-*N*-(*p*-Tolylsulfonyl)-2,3-diphenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and (*E*)-stilbene (1.21 g, 6.7 mmol) was stirred in dichloromethane (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.25 g (52%) of the aziridine as a crystalline solid: mp 139–140 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3031, 3019, 1327, 1306, 1215, 1161, 1088, 930, 910, 814, 745, 741, 708, 698, 691; δ_H (300 MHz, $CDCl_3$) 7.61 (d, 2H, J = 8.4 Hz, Ar-*H*), 7.45–7.36 (m, 10H, Ar-*H*), 7.32 (d, 2H, J = 8.4 Hz, Ar-*H*), 4.26 (s, 2H, C*H*-aziridine), 2.41 (s, 3H, Ar-CH_3); δ_C (75 MHz, $CDCl_3$) 170.2, 144.1, 134.9, 132.2, 131.4, 129.6, 129.2, 128.2, 50.3, 21.6; HRMS (FAB,MNBA) exact mass calcd. for $C_{21}H_{19}NO_2S$ $(M + Na)^+$ 350.1215, found 350.1227. Anal. calcd. for: C, 72.18; H, 5.48; N, 4.01. Found: C, 72.19; H, 5.46; N, 4.05%.

cis-*N*-(*p*-Tolylsulfonyl)-2,3-diphenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and (*Z*)-stilbene (1.2 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.21 g (45%) of the aziridine as a crystalline solid: mp 154-155 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3034, 1599, 1495, 1329, 1306, 1186, 1161, 1092, 1026, 909, 814, 801, 698, 675; δ_H (300 MHz, $CDCl_3$) 7.97 (d, 2H, J = Ar-*H*), 7.36 (d, 2H, J = 8.2 Hz, Ar-*H*), 7.12-7.03 (m, 10H, Ar-*H*), 4.21 (s, 2H, C*H*-aziridine), 2.43 (s, 3H, Ar-CH_3); δ_C (75 MHz, $CDCl_3$) 144.6, 134.8, 132.1, 129.8, 128.0, 127.8, 127.7, 127.6, 47.4, 21.6; HRMS (FAB,MNBA) exact mass calcd. for $C_{21}H_{19}NO_2S$ $(M + Na)^+$ 350.1215, found 350.1219. Anal. calcd. for $C_{21}H_{19}NO_2S$: C, 72.18; H, 5.48; N, 4.01. Found: C, 71.83; H, 5.49; N, 3.95%.

N-(*p*-Tolylsulfonyl)-2-methyl-2-phenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and α-methylstyrene (0.79 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.14 g (33%) of the aziridine as a crystalline solid: mp 84–85 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3060, 3028, 2992, 2930, 1600, 1449, 1330, 1267, 1160, 1128, 1089, 1027, 939, 870, 715, 694, 680, 650; δ_H (300 MHz, $CDCl_3$) 7.65 (d, 2H, J = 8.3 Hz, Ar-*H*), 7.38–7.11 (m, 5H, Ar-*H*), 7.08 (d, 2H, J = 8.3 Hz, Ar-*H*), 3.91 (s, 1H, C*H*-aziridine), 2.40 (s, 3H, CH_3), 2.02 (s, 1H, C*H*-aziridine), 1.58 (s, 3H, CH_3); δ_C (75 MHz, $CDCl_3$) 145.0, 143.5, 136.8, 129.8, 128.5, 127.3, 127.1, 124.9, 73.7, 53.8, 27.5, 21.5; HRMS (FAB,MNBA) exact mass calcd. for $C_{16}H_{17}NO_2S$ $(M + Na)^+$ 310.0878, found 310.0897. Anal. calcd. for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.94; H, 5.93; N, 4.87%.

trans-*N*-(*p*-Tolylsulfonyl)-2-methyl-3-phenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and (*E*)-β-methylstyrene (0.79 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.31 g (74%) of the aziridine as a crystalline solid: mp 73–74 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3031, 1458, 1321, 1306, 1291, 1217, 1159, 1090, 1038, 974, 891, 814, 772, 743, 710, 698, 687, 667; δ_H (300 MHz, $CDCl_3$) 7.85 (d, 2H, J = 8.3 Hz, Ar-*H*), 7.28–7.19 (m, 5H, Ar-*H*), 7.19 (d, 2H, J = 8.0 Hz, Ar-*H*), 3.79 (d, 1H, J = 4.3 Hz, C*H*Ph), 2.91 (dq, 1H, J = 6.1, 4.5 Hz, C*H*CH_3), 2.38 (s, 3H, Ar-CH_3), 1.83 (d, 3H, J = 6.1 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 143.9, 137.9, 135.5, 129.5, 128.4, 128.0, 127.1, 126.2, 49.1, 21.5, 14.1; HRMS (FAB,MNBA) exact mass calcd. for $C_{16}H_{17}NO_2S$ $(M + Na)^+$ 310.0878, found 310.0889. Anal. calcd. for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87. Found: C, 66.89; H, 5.98; N, 4.85%.

trans-*N*-(*p*-Tolylsulfonyl)-2-(methoxycarboyl)-3-phenylaziridine

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and (*E*)-β-methyl cinnamate (1.09 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.37 g (84%) of the aziridine as a crystalline solid: mp 45–46 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3068, 3021, 2960, 1750, 1600, 1498, 1456, 1440, 1412, 1338, 1306, 1292, 1161, 1086, 1081, 1004, 938, 906, 834, 812, 709, 692, 646; δ_H (300 MHz, $CDCl_3$) 7.78 (d, 2H, J = 8.4 Hz, Ar-H), 7.32–7.22 (m, 7H, Ar-H), 4.42 (d, 1H, J = 4.0 Hz, CH-aziridine), 3.85 (s, 3H, OCH_3), 3.53 (d, 1H, J = CH-aziridine), 2.41 (s, 3H, Ar-CH_3); δ_C (75 MHz, $CDCl_3$) 166.1, 144.2, 136.5, 132.3, 129.6, 128.7, 128.6, 127.6, 127.1, 53.1, 47.7, 21.6; HRMS (FAB,MNBA) exact mass calcd. for $C_{17}H_{17}NO_4S$ $(M + Na)^+$ 331.08783, found 331.08735. Anal. calcd. for $C_{17}H_{17}NO_4S$: C, 61.62; H, 5.17; N, 4.23. Found: C, 61.06; H, 5.08; N, 3.99%.

N-(*p*-Tolylsulfonyl)-7-azabicyclo[4.1.0]heptane

A solution of PhI=NTs (0.52 g, 1.34 mmol), CuHY (71 mg, 25 mol%) and cyclohexene (0.55 g, 6.7 mmol) was stirred in acetonitrile (15 cm^3). Reaction time: 1 h at room temperature. Flash column chromatography (1.5 × 20 cm silica, 10:1.5 petroleum ether (40/60)–ethyl acetate) afforded 0.18 g (50%) of the aziridine as a crystalline solid: mp 55–56 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3020, 2950, 2860, 1600, 1440, 1395, 1315, 1305, 1155, 1090, 965, 920; δ_H (300 MHz, $CDCl_3$) 7.81 (d, 2H, J = 8.2 Hz, Ar-*H*), 7.34 (d, 2H, J = 8.5 Hz, Ar-*H*), 2.99 (t, 2H, J = 1.4 Hz, C*H*-aziridine), 2.44 (s, 3H, Ar-CH_3), 1.80 (m, 4H, ring-C*H*), 1.44–1.36 (m, 4H, ring-C*H*), 1.26–1.19 (m, 2H, ring-C*H*); δ_C (75 MHz, $CDCl_3$) 144.0, 136.0, 129.6, 127.7, 39.8, 22.8, 21.6, 19.4; HRMS (FAB,MNBA) exact mass calcd. for $C_{17}H_{17}NO_4S$ $(M + Na)^+$ 274.0878, found 274.0872. Anal. calcd. for $C_{13}H_{12}INO_2S$: C, 41.84; H, 3.24; N, 3.75. Found: C, 41.68; H, 3.21; N, 3.71%.

Homogeneous aziridination reactions catalysed by $Cu(OTf)_2$

The synthesis was carried out following the method of Evans *et al.*[4]

To anhydrous copper(II) triflate (0.024 g, 0.067 mmol, 5.0 mol%) and 15 cm^3 of HPLC grade acetonitrile, in a 25 cm^3 round bottom flask equipped with a stirrer bar, were added alkene (6.7 mmol, 5.0 equiv.) and [*N*-(*p*-tolylsulfonyl)imino]-phenyliodinane, PhI=NTs (0.52 g, 1.34 mmol). The reaction was stirred in air at room temperature until complete dissolution of PhI=NTs. When all the PhI=NTs had been drawn into solution, the reaction was filtered through a plug of silica with ethyl acetate (50 cm^3) as eluent. The solvent was removed *in vacuo* to give an oil that was purified by flash column chromatography.

Acknowledgements

We thank ICI Katalco, Robinson Brothers, the EPSRC and the DTI LINK programme on asymmetric synthesis for funding.

References

1 R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994.
2 T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974.
3 D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul, *J. Am. Chem. Soc.*, 1991, **113**, 726.
4 D. A. Evans, M. M. Faul and M. T. Bilodeau, *J. Am. Chem. Soc.*, 1994, **116**, 2742.
5 (*a*) K. Srinivasan, P. Michaud and J. K. Kochi, *J. Am. Chem. Soc.*, 1986, **108**, 2309; (*b*) W. Zhang, J. L. Loebach, S. R. W. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801.
6 K. T. Wan and M. E. Davis, *Nature*, 1994, **370**, 449.
7 H. U. Blasser, *Tetrahedron: Asymmetry*, 1997, **8**, 1693.
8 P. P. Knops-Gerrits, D. De Vos, F. Thibault-Starzyk and P. A. Jacobs, *Nature*, 1994, **369**, 543.
9 K. Klier, *Langmuir*, 1998, **4**, 13.
10 C. B. Dartt and M. E. Davis, *Catal. Today*, 1994, **19**, 151.
11 C. Langham, P. Piaggio, D. Bethell, D. F. Lee, P. McMorn, P. C. B. Page, D. J. Willock, C. Sly, F. E. Hancock, F. King and G. J. Hutchings, *Chem. Commun.*, 1998, 1601.
12 P. Piaggio, P. McMorn, C. Langham, D. Bethell, P. C. B. Page, F. E. Hancock and G. J. Hutchings, *New J. Chem.*, 1998, 1167.
13 D. A. Whan, *Chem. Br.*, 1981, **17**, 532.
14 C. J. Burrows, K. J. O'Conner and S.-J. Wey, *Tetrahedron Lett.*, 1992, **33**, 1001.
15 T. Maschmeyer, F. Rey, G. Sankar and J. M. Thomas, *Nature*, 1995, **378**, 159.
16 Y. Yamada, *Chem. Lett.*, 1975, 361.
17 J. S. Beck, J. C. Vartuli, W. J. Roth, M. E. Leonowicz, C. T. Kresge, K. D. Schmitt, C. T.-W. Chu, D. H. Olson, E. W. Shepherd, S. B. McCullen, J. B. Higgins and J. L. Schlenker, *J. Am. Chem. Soc.*, 1992, **114**, 10834.

Paper 8/06409A