

Catalytic asymmetric heterogeneous aziridination of styrene using CuHY: effect of nitrene donor on enantioselectivity

2 PERKIN

Sophia Taylor,^a John Gullick,^a Paul McMorn,^a Donald Bethell,^b Philip C. Bulman Page,^c Frederick E. Hancock,^d Frank King^d and Graham J. Hutchings^{*a}

^a Department of Chemistry, Cardiff University, PO Box 912, Cardiff, UK CF10 3TB.

E-mail: hutch@cardiff.ac.uk

^b Leverhulme Centre for Innovative Catalysis, Department of Chemistry, University of Liverpool, Liverpool, UK L69 3BX

^c Department of Chemistry, Loughborough University, Loughborough, Leics., UK LE11 3TU

^d Syntex, PO Box 1, Billingham, Teesside, UK TS23 1LB

Received (in Cambridge, UK) 22nd May 2001, Accepted 4th July 2001

First published as an Advance Article on the web 9th August 2001

The copper-catalysed aziridination of styrene with copper-exchanged zeolite Y (CuHY) and copper(II) triflate (trifluoromethanesulfonate) (Cu(OTf)₂) as catalysts is described in detail. Two nitrene donors, [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) and [*N*-(*p*-nitrophenylsulfonyl)imino]phenyliodinane (PhI=NNs) are compared. Modification of the catalyst with bis(oxazolines) affords enantioselective catalysts and a range of chiral bis(oxazolines) has been studied. The ratio of nitrene donor to styrene is shown to be an important factor controlling both the yield and ee of aziridine formed. The best results are obtained with PhI=NNs; ee, ≥ 90%, together with high yields (≥ 85%), can readily be achieved with this nitrene donor using acetonitrile as solvent. Addition of the nitrene donor over a period of time, rather than all at the start of the reaction, is shown to enhance the yield of the aziridine but the ee is significantly decreased for both the homogeneous and the heterogeneous catalysts. Experiments in which the breakdown products of the nitrene donor, iodobenzene and the corresponding sulfonamide, are added at the start of the reaction show that a complex interplay exists at the copper active site between the reactants, products, chiral modifier and the solvent. However, the heterogeneous catalyst, CuHY, is found to give enhanced enantioselection for a range of bis(oxazolines) compared to the homogeneous catalyst, and the effect is considered to be due to the confinement of the catalyst within the micropores of the zeolite.

Introduction

The synthesis of pure enantiomers using catalytic processes continues to receive very considerable attention. The identification of new catalysts has implications for future synthetic methodology for the production of pharmaceuticals and agrochemicals. Initially, most success was obtained with homogeneous catalysts, particularly for hydrogenation¹ and epoxidation² reactions. More recently, considerable attention has been given to immobilisation of these catalysts so that they can be readily re-used. This is particularly important for some catalysts which involve expensive chiral ligands and/or have low turnover numbers, e.g. Mn–salen catalysed epoxidation of alkenes.³

We have previously demonstrated that cations ion-exchanged into the intra-crystalline pores of zeolites and mesoporous materials can act as effective immobilised catalysts.^{4–10} In particular, we showed that Cu²⁺ ion-exchanged into zeolite H–Y, and modified by a chiral bis(oxazoline)[†] could act as the heterogeneous counterpart of the homogeneous copper triflate (trifluoromethane sulfonate) catalysed aziridination of alkenes recently reviewed by Jacobsen¹¹ and previously reported by Evans *et al.*^{12–15} This was the first reported heterogeneous aziridination catalyst and, furthermore, we demonstrated that the reaction was wholly heterogeneously catalysed.^{6,7} Using EPR spectroscopy,¹⁶ we have shown that Cu²⁺–bis(oxazoline) complexes form inside the zeolite Y pores in the presence of acetonitrile solvent. These complexes possess square pyramidal and square planar symmetries with spin Hamiltonian parameter analogues to those of the equivalent homogeneous catalysts.

The bis(oxazoline) modified at least 40% of all available Cu²⁺ and we ascertained that each supercage of the zeolite contained one Cu²⁺–bis(oxazoline) complex. Recently, Glos and Reiser¹⁷ and Burgeute *et al.*¹⁸ have investigated alternative methodologies for the immobilisation of copper bis(oxazoline) complexes using polymeric supports, and this approach has been shown to give high ee for cyclopropanation of alkenes. In our earlier papers^{6,7} we showed that, using [*N*-(*p*-tolylsulfonyl)imino]phenyliodinane ‡(PhI=NTs) as the nitrene donor, and 2,2-bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]propane **1** as the chiral ligand, we could obtain high yields of aziridines, but the enantioselectivities were limited to *ca.* 40% ee for styrene and *ca.* 60% for methyl (*E*)-cinnamate. In this paper, we present the results of a detailed study using alternative nitrene donors and show that, using [*N*-(*p*-nitrophenylsulfonyl)imino]phenyliodinane (PhI=NNs) as the nitrene donor, both high yields and high enantioselection can be achieved.

Results and discussion

Investigation of the nitrene donor

In our previous studies^{6,7} and the studies of Evans *et al.*,^{12–15} the nitrene donor used was PhI=NTs. However, other studies¹⁹ of the aziridination of alkenes using homogeneous transition metal catalysts have shown that PhI=NNs can also be used as a nitrene donor. In addition, Södergren *et al.*^{20,21} have investigated a range of nitrene donors based on an adaptation of PhI=NTs using a variation of the preparation methods of Yamada *et al.*²² A range of nitrene donors, PhI=NSO₂R (R = Me, 4-Me-

[†] The IUPAC name for 1,3-oxazoline is 4,5-dihydro-1,3-oxazole.

[‡] The IUPAC name for iodine is I³-iodane.

Table 1 Metal exchanged zeolite Y as catalyst for the aziridination of styrene^a

Cation-exchanged zeolite HY	PhI=NTs yield (%)			PhI=NNs yield (%)		
	Time ^b /h	Aziridine	Benzaldehyde	Time ^b /h	Aziridine	Benzaldehyde
None ^c	66	6	10	332	34	25
Zn ²⁺	66	3	10	332	56	6
Ni ²⁺	66	17	18	332	7	6
Fe ³⁺	66	12	24	332	45	25
Mn ²⁺	5	10	26	332	3	14
Co ²⁺	6	15	36	332	45	32
Cu ²⁺	3	86	12	5	93	5

^a CH₃CN, 25 °C, nitrene donor : styrene = 1.5 : 1 mol ratio. ^b Reaction time, followed by dissolution of the nitrene donor. ^c No catalyst added.

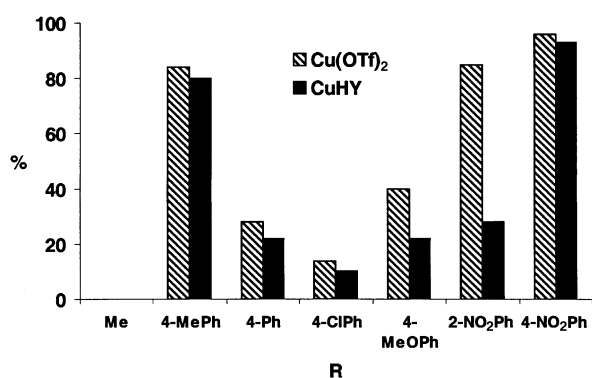
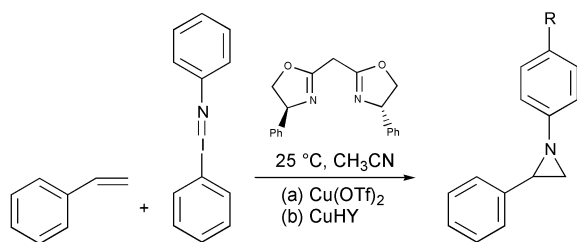


Fig. 1 Aziridination of styrene using PhI=NSO₂R as nitrene donor. Effect of R-group on the yield of aziridine (nitrene donor : styrene = 1.5 : 1 mol ratio, CH₃CN, 25 °C).

C₆H₄, Ph, 4-Cl-C₆H₄, 4-MeO-C₆H₄, 2-NO₂-C₆H₄, 4-NO₂-C₆H₄) were investigated for the aziridination of styrene using Cu(OTf)₂ and CuHY zeolite as catalysts (Scheme 1) and the



Scheme 1

results are shown in Fig. 1 for the reaction at 25 °C in acetonitrile. The reactions were followed by the dissolution of the nitrene donor. It is clear that, when R = Me, no yield of the aziridine is observed with either the homogeneous or the heterogeneous catalyst. For the homogeneous Cu(OTf)₂ catalyst, high yields of the aziridine (>80%) were observed with R = 4-Me-C₆H₄ (PhI=NTs), 4-NO₂-C₆H₄ (Ph=NNs) and 2-NO₂-C₆H₄. In contrast, high yields of the aziridine for the heterogeneous catalyst, CuHY, were observed only with PhI=NTs and PhI=NNs as nitrene donors. For the nitrene donor with R = 2NO₂-C₆H₄, it is considered that the nitro-substituent in the 2-position may sterically hinder the function of the nitrene donor in the micropores of the zeolite. Based on these results, a comparative study of PhI=NTs and PhI=NNs as nitrene donors was carried out for the transition metal catalysed aziridination of styrene.

Aziridination of styrene using transition metal catalysts

Although the literature concerning the homogeneously catalysed aziridination of alkenes is dominated by copper catalysts, based on the studies of Evans *et al.*^{12–15} and Jacobsen and co-workers,^{11,23,24} earlier studies have shown that other metal catalysts can also be effective, including manganese,^{25–27}

ruthenium²⁸ and rhodium.²⁹ Evans *et al.*¹³ contrasted a number of soluble triflates (Cu, Mn, Fe, Co, Ni) as homogeneous catalysts with PhI=NTs as the nitrene donor and, although Cu²⁺ was found to be the most effective, non-negligible yields of aziridine were observed with the other cations. Consequently, we investigated a range of metal-exchanged zeolite Y catalysts using both PhI=NTs and PhI=NNs as nitrene donors. The results for the aziridination of styrene (acetonitrile as solvent, 25 °C, styrene : nitrene donor = 5 : 1 mol ratio) are shown in Table 1. It is apparent that, in the absence of a zeolite catalyst, some aziridine was formed and this was more pronounced with PhI=NNs as nitrene donor. In general, the reactions were slower for PhI=NNs than for PhI=NTs, but this is mainly attributed to the different solubilities of the nitrene donor. With PhI=NTs as nitrene donor, only CuHY gave significant yields of the aziridine whereas, with PhI=NNs, quite high yields of aziridine, above those expected for the blank reaction, were observed with ZnHY, FeHY and CuHY. However, for PhI=NNs, CuHY was by far the superior catalyst, and gave a higher yield of the aziridine than that observed with PhI=NTs.

Benzaldehyde was observed as a by-product in these aziridination reactions (Table 1) although, with the CuHY catalyst, only relatively low levels were apparent. There are several possibilities for the formation of benzaldehyde from styrene^{30–35} or from styrene oxide,³⁶ but it barely seems feasible that benzaldehyde could be formed from the aziridine, and indeed in a standard experiment, where styrene was replaced by the aziridine, no benzaldehyde was formed and, hence, this pathway is discounted here. The formation of benzaldehyde from styrene oxide was also considered to be unlikely since styrene oxide is stable under the reaction conditions used in this study. Benzaldehyde can be formed by oxidative cleavage of styrene, and this has been observed using molecular oxygen as oxidant with Cu²⁺ in acetonitrile.³⁵ In this earlier work, higher reaction temperatures were used but it is possible that this may be a pathway for by-product formation. However, it has been observed^{31–34} that benzaldehyde can be formed by the reaction of styrene with iodobenzene in the presence of a transition metal catalyst and this is enhanced when oxygen is bubbled through the reaction mixture. In our experiments, residual water in the reaction mixtures, added with the solvent or with the zeolite catalyst, could hydrolyse the nitrene donor to iodobenzene and this is most likely to provide the pathway for the benzaldehyde by-product formation. Indeed, separate experiments in which styrene was reacted with iodobenzene with CuHY as catalyst demonstrated that benzaldehyde could be formed in significant amounts. In addition, the addition of water has been found to increase the yield of the benzaldehyde product under the standard aziridination reaction conditions.³⁷

Effect of styrene : nitrene donor molar ratio on the aziridination of styrene

In the initial studies of the aziridination of alkenes by Evans *et al.*^{12–15} using homogeneous Cu²⁺ catalysts, high molar ratios

Table 2 Effect of the amount of nitrene donor on the aziridination of styrene^a

Styrene : nitrene donor mol ratio	PhI=NTs		PhI=NNs	
	Reaction time ^b /h	Yield ^c (%)	Reaction time ^b /h	Yield ^c (%)
5 : 1	0.3 (0.5)	85 (87)	0.75 (0.75)	87 (88)
3 : 1	0.75 (0.5)	70 (73)	1.5 (1)	73 (76)
1 : 1	0.75 (1)	57 (60)	1.5 (1.5)	57 (59)
1 : 1.5	1 (2)	85 (89)	1.5 (2)	85 (93)

^a CH₃CN, 25 °C, CuHY (0.3 g); data in parentheses are for the homogeneously catalysed reaction with Cu(OTf)₂ (0.015 mmol) under identical conditions. ^b Reaction time followed by the dissolution of the nitrene donor. ^c Yield based on limiting reagent.

Table 3 Effect of the amount of nitrene donor on the asymmetric aziridination of styrene at 25 °C^a

Styrene : nitrene donor mol ratio	PhI=NTs			PhI=NNs		
	Reaction time ^b /h	Yield ^c (%)	Ee (%)	Reaction time ^b /h	Yield ^c (%)	Ee (%)
5 : 1	0.75 (0.25)	86 (93)	29 (74)	1 (0.5)	83 (92)	78 (61)
3 : 1	2 (0.3)	67 (78)	32 (74)	3 (1.5)	67 (80)	45 (48)
1 : 1	1.5 (0.5)	55 (73)	76 (53)	2.5 (1)	53 (64)	36 (40)
1 : 1.5	3 (1)	78 (91)	76 (73)	5 (1.5)	78 (96)	85 (81)
1 : 3	8 (4)	45 (76)	79 (84)	10 (5)	61 (71)	68 (72)
1 : 5	12 (6.5)	22 (15)	81 (84)	16 (8.5)	53 (63)	46 (57)

^a CH₃CN, 25 °C, 2,2-bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]propane as chiral modifier, CuHY (0.3 g). Data in parentheses are for the homogeneous catalyst Cu(OTf)₂ (0.015 mmol) under identical conditions. ^b Reaction time followed by dissolution of the nitrene donor. ^c Yield based on limiting reagent.

Table 4 Effect of styrene : PhI=NNs molar ratio on the asymmetric aziridination of styrene at 25 °C^a

Styrene : PhI=NNs mol ratio	Yield (%) ^b		
	Aziridine	Benzaldehyde	Aziridine ee (%)
1 : 1	68.3 (27.3)	7.2	49.4 (65.2)
1 : 1.1	84.7 (82.8)	11.3	81.2 (76.6)
1 : 1.2	87.8 (72.2)	11.2	89.4 (87.6)
1 : 1.3	82.0 (99.5)	17.9	91.0 (79.8)
1 : 1.4	76.6 (99.4)	20.1	95.2 (78.8)
1 : 1.5	67.2 (83.1)	21.2	87.8 (86.8)

^a CH₃CN, 25 °C, 2,2-bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]propane as chiral modifier, reaction time 16 h. Data in parentheses are for the homogeneous catalyst Cu(OTf)₂ (0.015 mmol) under identical conditions. ^b Yield based on styrene.

of the substrate relative to the nitrene donor were used, typically styrene : PhI=NTs = 5 : 1, to drive the reaction rapidly to completion. However, in our earlier work,^{6,7} we showed that high yields of aziridine could be formed for the CuHY catalysed reaction at lower styrene : PhI=NTs molar ratios. In addition, Södergren *et al.*²⁰ reported that high yields of the aziridine could be obtained when an excess of the nitrene donor was used (nitrene donor : substrate = 1.5 : 1 mol ratio) for the homogeneously catalysed reaction. Hence, the effect of the amount of the nitrene donor on the aziridination of styrene was investigated for the homogeneous catalyst Cu(OTf)₂ and the heterogeneous catalyst CuHY, containing equivalent amounts of Cu²⁺, and the results are shown in Tables 2 and 3. As noted previously, the reaction times for PhI=NNs were slightly longer than with PhI=NTs, and this was observed with both catalysts whether the bis(oxazoline) was present (Table 3) or absent (Table 2). In general, the yield of aziridine decreased with decreasing molar ratio of the styrene to nitrene donor. However, in agreement with the observation of Södergren *et al.*,²⁰ the yield, when a slight excess of the nitrene donor is used (nitrene donor : styrene = 1.5 : 1), is significantly higher. This molar ratio was used in the subsequent studies reported in this paper.

With PhI=NTs as nitrene donor, the enantioselectivity increased markedly for the heterogeneous CuHY catalyst with decreasing styrene : nitrene donor molar ratio and the heterogeneous catalysts only give high ee at high nitrene

donor : styrene ratios (styrene : PhI=NTs ≥ 1 : 3). This was not so apparent with the homogeneous Cu(OTf)₂ catalyst and, generally, the homogeneous catalyst gave higher ee. This is probably due to competitive effects within the micropores of the zeolite. The current study indicates that much of the previous work for the heterogeneous system^{6,7} was carried out under non-optimal conditions. In contrast, with PhI=NNs, the heterogeneous catalyst often gave higher or comparable enantioselectivity than the homogeneous catalyst, and this is discussed below. This effect is observed even at high styrene : nitrene donor molar ratios and indicates that PhI=NNs may preferentially partition into the zeolite pores and hence, by virtue of this enhanced concentration within the zeolite, PhI=NNs may have enhanced access to the active sites in the micropores when compared with PhI=NTs.

A further set of experiments were carried out using PhI=NNs as the nitrene donor to investigate the effect of a small molar excess of the nitrene donor. The results, shown in Table 4, show that for the heterogeneously catalysed reaction both the yield and ee show maxima in the region between styrene : PhI=NNs molar ratios of 1 : 1 and 1 : 1.5. Most importantly, ee for the homogeneously catalysed reactions are consistently lower than those obtained in the heterogeneously catalysed reaction. It is clear that the loss in yield of the aziridine, as the concentration of the nitrene donor is increased, is due to increased formation of the benzaldehyde by-product.

Table 5 Effect of solvent on the aziridination of styrene^a

Solvent	PhI=NTs		Ee (%)	PhI=NNs		
	Yield (%)			Yield (%)		
	Unmodified ^b	Modified ^c		Unmodified ^b	Modified ^c	Ee (%)
Toluene	38 (41)	17 (64)	32 (4)	46 (27)	28 (57)	64 (28)
Acetone	28 (32)	13 (56)	19 (11)	44 (20)	25 (48)	30 (25)
Anisole	0 (0)	0 (0)	0 (0)	27 (18)	21 (40)	23 (27)
Methanol	54 (33)	20 (56)	41 (70)	64 (25)	55 (54)	48 (81)
Nitromethane	90 (85)	82 (96)	36 (25)	85 (79)	76 (85)	43 (73)
Acrylonitrile	85 (87)	78 (91)	76 (73)	92 (81)	78 (96)	85 (81)

^a 25 °C, nitrene donor : styrene = 1.5 : 1 mol ratio, CuHY (0.3 g); figures in parentheses are for the homogeneous catalyst Cu(OTf)₂ (0.015 mmol) under identical conditions. All reactions followed by dissolution of the nitrene donor. ^b Reactions in the absence of chiral modifier. ^c 2,2-Bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]propane added as chiral modifier.

Effect of solvent on the aziridination of styrene

The aziridination of styrene using PhI=NTs and PhI=NNs with Cu(OTf)₂ and CuHY as catalysts was investigated with a range of coordinating (acetonitrile, nitromethane, methanol), partially-coordinating (anisole, acetone) and non-coordinating (toluene) solvents. The results for reactions in the presence and absence of a chiral bis(oxazoline) are shown in Table 5. In the absence of the bis(oxazoline), both nitrene donors gave high aziridine yields only with nitromethane and acetonitrile. Interestingly, even after 96 h reaction, no aziridine was observed with anisole when PhI=NTs was used, although a low yield was observed with PhI=NNs. In addition, with PhI=NNs, higher yields of the aziridine were observed for CuHY than for Cu(OTf)₂, although both reaction systems contained the same amount of copper. This may be caused by a combination of the electrostatic field within the micropores of copper-exchanged zeolite Y and the confinement of the reactant enhancing the activation of the nitrene donor in this case.

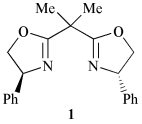
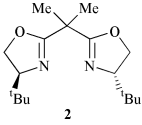
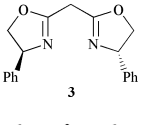
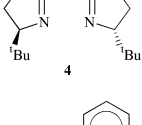
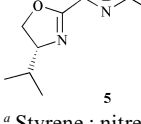
In the presence of the bis(oxazoline), 2,2-bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]propane **1**, the homogeneous Cu(OTf)₂ catalyst was now observed to give much higher yields of the aziridine for both nitrene donors. High ee's (>70%) were observed only with methanol and acetonitrile, both of which are coordinating solvents. Yields and enantioselection with acetone and toluene were significantly lower than those observed with acetonitrile, and the reaction times were significantly longer with acetone and toluene, 72 and 168 h respectively. Nitromethane gives high yields of aziridine but the enantioselectivity in this solvent is much lower than with acetonitrile when using PhI=NTs. This may indicate that nitromethane competes more effectively for coordination at the Cu²⁺ cation than does the chiral bis(oxazoline). However, with PhI=NNs as nitrene donor, the homogeneous catalyst Cu(OTf)₂ gives 73% ee with nitromethane as solvent. The heterogeneous catalyst gives a lower ee, indicating that nitromethane probably competes for coordination more effectively than the bis(oxazoline) in the micropores of the zeolite.

The highest yields and enantioselection are observed using PhI=NNs with acetonitrile as solvent. Interestingly, as noted previously for both PhI=NTs and PhI=NNs, the heterogeneous CuHY catalyst gives slightly higher ee than does Cu(OTf)₂ with acetonitrile as solvent.

Effect of bis(oxazoline) structure

In our previous study⁷ we showed that variation in the structure of the bis(oxazoline) could affect the enantioselection with the CuHY catalyst. However, as noted above, these experiments were carried out under non-optimal conditions (high styrene : nitrene donor ratio) when only low enantioselection was observed. We have now extended this earlier study to reaction conditions using an excess of the nitrene donor, and the results

Table 6 Effect of bis(oxazoline) on the aziridination of styrene^a

Bis(oxazoline)	PhI=NTs		PhI=NNs	
	Yield (%)	Ee (%)	Yield (%)	Ee (%)
	78 (91)	76 (73)	78 (96)	85 (81)
	58 (78)	24 (35)	68 (79)	82 (43)
	70 (74)	77 (28)	80 (85)	82 (54)
	80 (85)	28 (8)	72 (42)	77 (31)
	55 (70)	5 (11)	29 (42)	6 (15)

^a Styrene : nitrene donor ratio = 1 : 1.5, 25 °C, CuHY (0.3 g); figures in parentheses are for the homogeneous catalyst Cu(OTf)₂ (0.015 mmol) under identical conditions. All reactions followed by dissolution of the nitrene donor, reaction times for all oxazolines similar for Cu(OTf)₂: 1 and 1.5 h for PhI=NTs and PhI=NNs respectively; for CuHY: 3 and 5 h for PhI=NTs and PhI=NNs respectively.

for a range of bis(oxazolines) with PhI=NTs and PhI=NNs are shown in Table 6.

With CuHY as catalyst, with both PhI=NTs and PhI=NNs, the (*S*)-aziridine was formed when the (*S,S*)-bis(oxazoline) was used. When the (*R,R*)-bis(oxazoline) was used the (*R*)-aziridine was formed. In the homogeneously catalysed reaction, (*S*)-aziridine was also observed with the (*S,S*)-bis(oxazoline)s, except when the ^tBu substituted bis(oxazolines) **2** and **4** were used. This difference between the immobilised and non-immobilised catalysts indicates that the zeolite pores significantly affect the interaction of the substrate and catalyst. In this case, the (*R*)-aziridine was observed, and it is apparent that, with these modifiers, the heterogeneous catalyst gives significantly higher ee. There are significant differences that can be observed between the heterogeneously and homogeneously

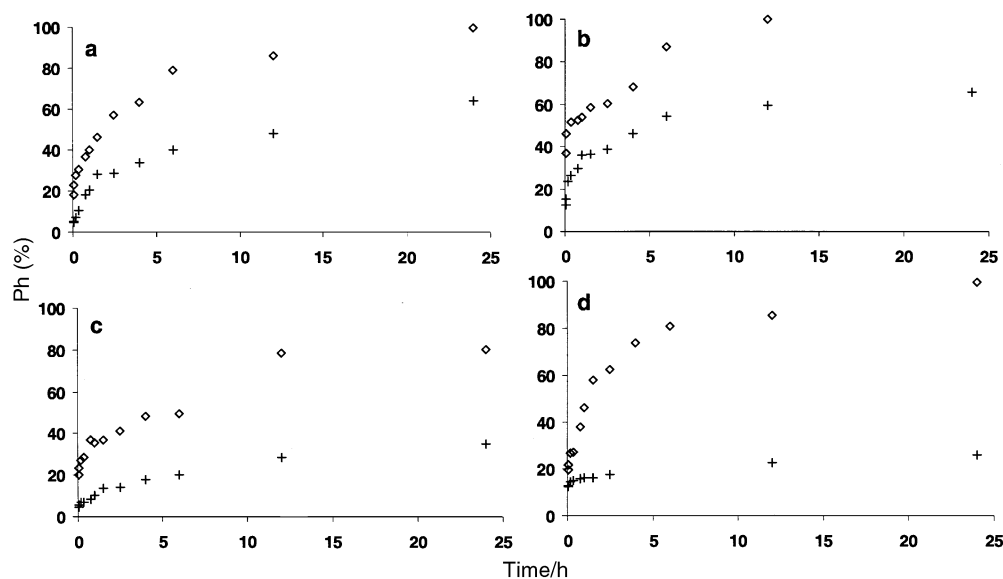


Fig. 2 Effect of chiral modifier {2,2-bis[(4*R*)-1,3-oxazolin-2-yl]propane} on the decomposition of the nitrene donor in the absence of styrene, 25 °C, CH₃CN, catalyst: CuHY (0.3 g) or Cu(OTf)₂ (0.015 g), nitrene donor 1.5 equivalents. (a) PhI=NTs with CuHY, (b) PhI=NTs with Cu(OTf)₂, (c) PhI=NNs with CuHY, (d) PhI=NNs with Cu(OTf)₂. Key: + non-modified, ◇ modified with chiral ligand.

catalysed reactions. Modification of modifier **1** by removal of the bridging methyl groups (**3**), or replacement of the phenyl substituents by *tert*-butyl groups (**2**), leads to a significant decrease in the enantioselection for the homogeneously catalysed reaction, but this is not observed for the CuHY heterogeneous catalyst. This is particularly apparent when **1** is modified by simultaneous removal of the bridging methyl groups and replacement of the phenyl substituents with *tert*-butyl groups (**4**). This leads to almost total loss of enantioselection for the homogeneously catalysed reaction but, with PhI=NNs, 77% ee is obtained with CuHY. It is interesting that, for PhI=NTs and PhI=NNs, similar trends are observed when the bridging methyl groups are removed. When comparing the ee obtained with bis(oxazoline) **1** and **3** or **2** and **4**, for the homogeneously catalysed reaction the ee is significantly reduced, whereas for the heterogeneously catalysed reaction the ee is maintained.

These results indicate that, with the immobilised CuHY catalyst, the chiral modifier need not be as bulky as that required by the non-immobilised Cu²⁺ homogeneous catalyst. This is thought to be due to the zeolite framework occupying part of the coordination sphere of Cu²⁺ in the CuHY catalyst and this confinement affects the conformation of the bis(oxazoline) which in turn modifies the requirements of the chiral modifier for the immobilised catalyst. This reaction, therefore, represents a further example of an asymmetric reaction for which the heterogeneously catalysed reaction affords higher enantioselection than the corresponding homogeneous reaction, as noted recently by Raynor *et al.*³⁸ for an asymmetric amination reaction.

Using a chiral bis(oxazoline) with a bridging pyridine **5** led to a low ee being observed with both CuHY and Cu(OTf)₂ catalysts under these conditions. This is in contrast to our earlier study⁷ where this modifier gave 61% ee for the aziridination of styrene with CuHY at -10 °C. It may indicate that careful optimisation of the reaction conditions with the heterogeneous CuHY catalysts for a particular chiral modifier may lead to further improvements in ee being observed. Indeed, we have recently observed ee of ≥90% at high yields with bis(oxazoline) **1** as shown in Table 4 for experiments where we carefully controlled the substrate : nitrene donor molar ratio.

Ligand accelerating effects

It is well known that ligands can influence the rate of metal-

catalysed reactions and often significant promotion in the rate of reaction is observed. Such fast reactions have been described, for example, by Berrisford *et al.*³⁹ as 'ligand accelerated reactions'. Furthermore, it has been shown that this approach can be extended to heterogeneous catalysts.⁴⁰ To investigate this effect for the aziridination of styrene, a number of experiments were carried out in the presence and absence of styrene to investigate the effect of the addition of the bis(oxazoline) modifier **1**. The results are shown in Figs. 2 and 3.

In the absence of styrene (Fig. 2), the catalytic breakdown of PhI=NTs and PhI=NNs to iodobenzene and sulfonamide was followed with reaction time. The homogeneous and heterogeneous catalysts both show similar effects for the decomposition of the nitrene donor with time, indicating that the immobilisation of Cu²⁺ within the micropores of the zeolite Y is not substantially affecting the rate of this reaction. In addition, both catalysts show a rate enhancement for nitrene-donor decomposition when the bis(oxazoline) **1** is added. In general, PhI=NTs decomposition is more rapid than that of PhI=NNs under comparable conditions.

In the presence of styrene (Fig. 3), the reaction could now be monitored by the formation of aziridine, which was always far more rapid than the competing decomposition reaction observed in the absence of styrene. For the homogeneous catalyst, Cu(OTf)₂, different effects are observed with PhI=NTs and with PhI=NNs. With PhI=NTs, an acceleration in the rate of formation of the aziridine is observed whereas, for PhI=NNs, the opposite effect is observed. With the heterogeneous catalyst CuHY, the addition of the bis(oxazoline) leads to a significant decrease in the rate of formation of the aziridine in the later stages of the reaction. However, with PhI=NNs, there is an initial acceleration effect which is lost on subsequent reactions. These results indicate that there is a complex interaction at the active site of the zeolite catalysts for the solvent, modifier, reactants and products and this is explored in the subsequent experiments.

Staged addition of nitrene donor

In a further attempt to optimise the conditions for the selective aziridination of styrene, a set of experiments was carried out in which the nitrene donor was added, either all at once at the start of the reaction, or in four equal aliquots over a 3 h period. The results are shown in Table 7 for two bis(oxazolines) **1** and **3**. As

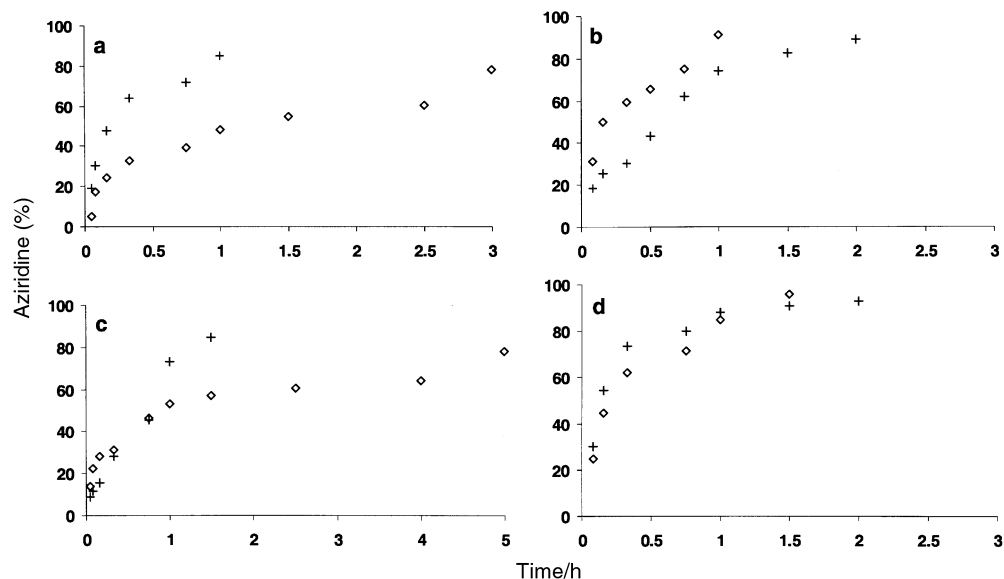


Fig. 3 Effect of chiral modifier {2,2-bis[(4*R*)-1-phenyl-1,3-oxazolin-2-yl]propane} on the formation of aziridine, 25 °C, CH₃CN, nitrene donor : styrene mol ratio = 1.5 : 1, catalyst: CuHY (0.3 g) or Cu(OTf)₂ (0.015 g). (a) PhI=NTs with CuHY, (b) PhI=NTs with Cu(OTf)₂, (c) PhI=NNs with CuHY, (d) PhI=NNs with Cu(OTf)₂. Key: + non-modified, ◇ modified with chiral ligand.

Table 7 Effect of staged addition of the nitrene donor on the aziridination of styrene^a

Nitrene donor ^b	Bis(oxazoline)	Reaction time/h	Yield (%)	Ee (%)
PhI=NTs, 0	1	3 (1)	78 (91)	76 (73)
PhI=NTs, 3	1	5 (3)	83 (90)	64 (69)
PhI=NTs, 0	3	3 (1)	58 (78)	24 (35) ^c
PhI=NTs, 3	3	6 (3)	67 (87)	15 (13) ^c
PhI=NNs, 0	1	5 (1.5)	78 (96)	85 (81)
PhI=NNs, 3	1	6 (4)	81 (86)	52 (58)
PhI=NNs, 0	3	7 (1.5)	68 (79)	82 (43) ^c
PhI=NNs, 3	3	10.5 (3.5)	81 (88)	69 (38) ^c

^a Reaction conditions: CH₃CN, 25 °C, nitrene donor : styrene = 1.5 : 1 mol ratio, CuHY (0.3 g), figures in parentheses are for the homogeneously catalysed reaction with Cu(OTf)₂ (0.015 mmol) under identical conditions. Reactions followed by dissolution of the nitrene donor. ^b 0, denotes the nitrene donor was added at the start of the reaction. 3, denotes the nitrene donor was added in four equal portions over a 3 h reaction period so that the total nitrene donor : styrene = 1.5 : 1 mol ratio at 3 h. ^c Cu(OTf)₂ gives (*R*)-aziridine, CuHY gives (*S*)-aziridine.

expected, the reaction times for PhI=NNs were longer than those for PhI=NTs. Two trends were apparent in these data for both chiral modifiers and for both heterogeneous and homogeneous catalysts. First, the yield of aziridine is increased by the staged addition of the nitrene donor (Figs. 2, 3). Secondly, and most importantly, the ee is always markedly lower for the staged addition. Hence, to secure high enantioselection for either the homogeneously or the heterogeneously catalysed reaction, it is essential that the nitrene donor is added at the beginning of the reaction. These results may have implications concerning the use of a continuous flow reactor for this reaction, as compared to the batch reactor studies described here, since this would require continuous addition of the nitrene donor.

Effect of the addition of iodobenzene/sulfonamide on the aziridination of styrene

The reactions with the staged additions of the nitrene donor and the results obtained concerning the ligand accelerating effects indicate that there exists a complex interplay at the active site between reactants, products, chiral modifier and solvent. To explore this further, sets of experiments were carried out in which iodobenzene and the corresponding sulfonamide, a potential breakdown product of the nitrene donor, were either added separately or together at the start of the reaction. The results, simulating 10% and 100% degradation of the nitrene donor, are given in Figs. 4–6.

It is apparent that complex relationships exist between the components of the reaction mixture, *i.e.* reactants and products, and the addition of the products can cause a decrease in both the rate of reaction and the final yield of aziridine. In the homogeneously catalysed reaction, in the absence of bis(oxazoline) **1**, the addition of the products leads to a marked decrease in the rate of reaction and the final yield of aziridine (Figs. 4c, 5c, 6c). The effect is more marked for PhI=NNs than PhI=NTs. For the homogeneously catalysed reaction in the presence of bis(oxazoline) **1**, the decrease in rate is significantly reduced (Figs. 4d, 5d, 6d). These results suggest that the coordination of the bis(oxazoline) may suppress the product inhibition effects, and this may be an alternative explanation for the ligand accelerating effect observed with this catalysed reaction.

The addition of products to the heterogeneously catalysed reaction, in the absence of bis(oxazoline) **1**, shows significant differences when compared with the homogeneously catalysed reaction. The decrease in rate and final yield of aziridine is much more significant for the immobilised catalysts, probably due to pore diffusion limitations (Figs. 4a, 5a, 6a). The reaction with the immobilised catalyst can be expected to be affected by pore diffusion effects, and the addition of additional iodobenzene and sulfonamide can be expected to enhance this effect. In this case, the effects are less marked for PhI=NNs (Fig. 5a) when contrasted with PhI=NTs (Fig. 4a). As with the homogeneously catalysed reaction, addition of bis(oxazoline) **1** significantly reduces the inhibition effects (Figs. 4b, 5b, 6b).

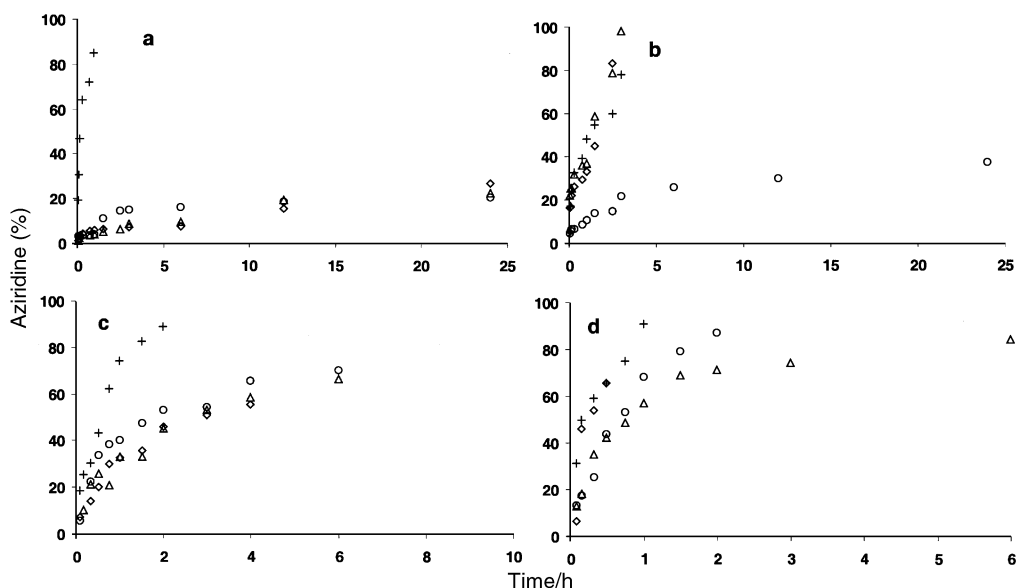


Fig. 4 Effect of addition of iodobenzene and toluenesulfonamide on the formation of aziridine in the presence and absence of the chiral modifier, **1**, 25 °C, CH₃CN, PhI=NTs : styrene mol ratio = 1.5 : 1, catalyst: CuHY (0.3 g) or Cu(OTf)₂ (0.015 g). (a) CuHY without chiral modifier, (b) CuHY with chiral modifier, (c) Cu(OTf)₂ without chiral modifier, (d) Cu(OTf)₂ with chiral modifier. Key: + standard reaction, ◇ 10% PhI added, Δ 10% TsNH₂ added, ○ 10% PhI + 10% TsNH₂ added.

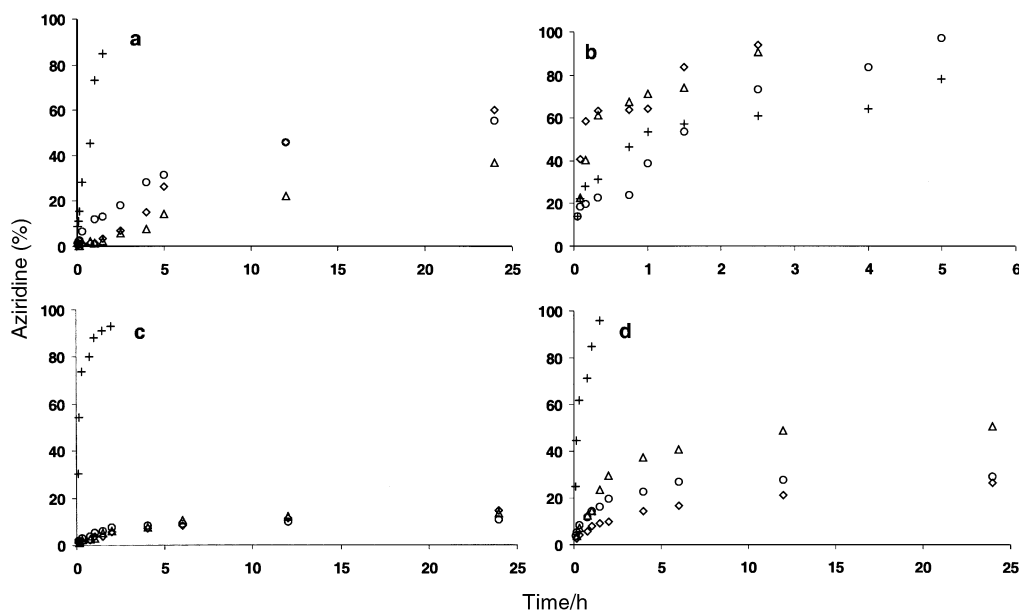


Fig. 5 Effect of addition of iodobenzene and toluenesulfonamide on the formation of aziridine in the presence and absence of the chiral modifier, **1**, 25 °C, PhI=NNs : styrene mol ratio = 1.5 : 1, catalyst: CuHY (0.3 g) or Cu(OTf)₂ (0.015 g). (a) CuHY without chiral modifier, (b) CuHY with chiral modifier, (c) Cu(OTf)₂ without chiral modifier, (d) Cu(OTf)₂ with chiral modifier. Key: + non-modified, ◇ 10% PhI added, Δ 10% NsNH₂ added, ○ 10% PhI + 10% NsNH₂ added.

Indeed, with both nitrene donors, addition of 10% iodobenzene or 10% sulfonamide alone can lead to an enhancement in the final yield of the aziridine. However, when the iodobenzene and sulfonamide are added together, the reduction in rate of reaction and final yield of aziridine is still observed for PhI=NTs, but the effect is less significant for PhI=NNs.

These results serve to show the complexity of this heterogeneously catalysed reaction, and that care has to be taken with respect to the optimisation of the reaction conditions for any particular combination of nitrene donor and chiral modifier, if high product yields are to be obtained. In addition, it is clear that there are significant differences between the homogeneously and heterogeneously catalysed reactions. In the homogeneous reaction, the addition of iodobenzene or sulfonamide always leads to a reduction in the rate of reaction and

final aziridine yield, but this is not the case for the heterogeneously catalysed reaction.

Conclusions

In this paper, we have presented a detailed study of the aziridination of styrene contrasting the use of PhI=NTs and PhI=NNs as nitrene donors with both the homogeneous catalyst, Cu(OTf)₂, and the heterogeneous catalyst, CuHY. The ratio of styrene : nitrene donor is found to affect significantly the yield of the aziridine formed and the enantioselection when a chiral bis(oxazoline) ligand is added to the reaction. In general, a slight excess of the nitrene donor is found to give the best results, and high ee's (≥85%) can be achieved with the heterogeneous catalyst, particularly when PhI=NNs is used as nitrene donor. Coordinating solvents (acetonitrile, nitromethane) are

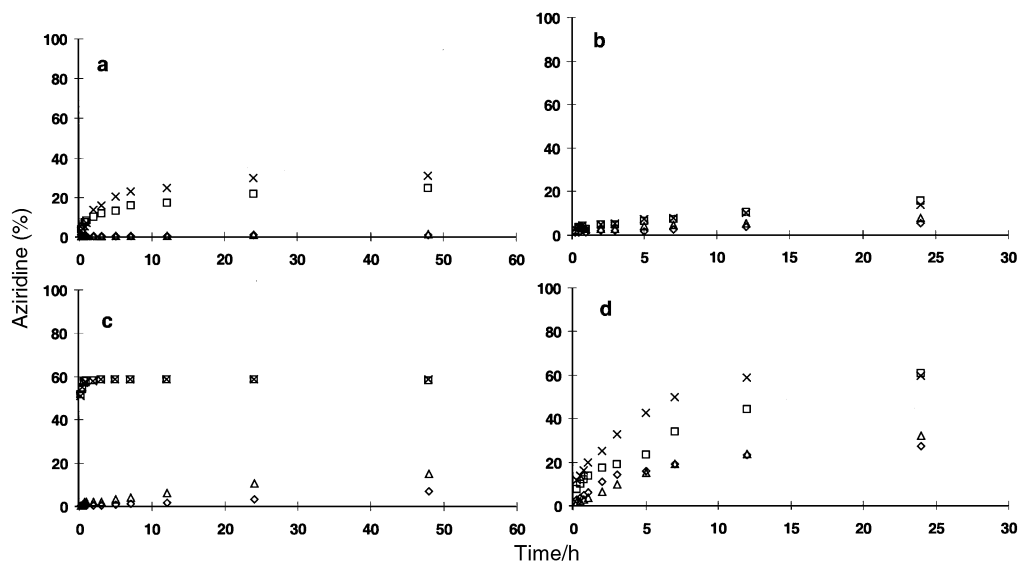


Fig. 6 Effect of addition of iodobenzene and toluenesulfonamide on the formation of aziridine in the presence and absence of chiral modifier, **1**, 10 °C, PhI=NTs : styrene mol ratio = 1.5 : 1, catalyst: CuHY (0.3 g) or Cu(OTf)₂ (0.015 g). (a) CuHY without chiral modifier, (b) CuHY with chiral modifier, (c) Cu(OTf)₂ without chiral modifier, (d) Cu(OTf)₂ with chiral modifier. Key: × standard reaction, ◇ 100% PhI added, □ 100% TsNH₂ added, Δ 100% PhI + 100% TsNH₂ added.

shown to give the highest yields of the aziridine but, with CuHY, high ee's are only obtained with acetonitrile. The heterogeneous catalyst is found to be significantly different from the homogeneous catalyst with respect to the requirements of the structure of the chiral modifier. In particular, the heterogeneous catalyst can give much higher enantioselectivity than the corresponding homogeneous catalyst for many ligands. This is considered to be due to the confinement of the catalyst within the micropores of the zeolite and, consequently, less bulky chiral ligands can retain their effectiveness. Furthermore, we have shown that competitive adsorption effects at the active site can complicate this reaction for both the homogeneous and heterogeneous catalyst. Consequently, each combination of nitrene donor and chiral modifier requires careful optimisation to obtain the best results, and we have shown that 90% ee can be achieved with the wholly heterogeneously catalysed reaction using PhI=NNs as nitrene donor.

Experimental

Apparatus

(a) ¹H NMR spectra were obtained using a Bruker 'Avance' 400 MHz DPX spectrometer, equipped with a Silicon Graphics workstation. The chemical shifts of ¹H NMR spectra are recorded in deuterated chloroform (CDCl₃) and deuterated dimethyl sulfoxide (d₆-DMSO). Spectra were recorded on the δ scale and signals quoted in the form: chemical shift measured in ppm (no. of protons, multiplicity, assignment).

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

(c) Microanalyses were performed by the Cardiff University, Department of Chemistry microanalysis service.

(d) Atomic absorption spectroscopy was performed using a Perkin-Elmer 373 Atomic Absorption spectrometer using an air-acetylene flame.

(e) HPLC analysis was recorded using a Dynamax SD200 pump equipped with Dynamax AI-3 autosampler, Dynamax injector and UV absorbance detector. An Apex ODS 5 μ column was used for analytical work. The eluent system was acetonitrile–water (85 : 15). 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–propan-2-ol (82 : 18). Baseline separation was achieved for both

enantiomers. Absolute configuration was confirmed by optical polarimetry and comparison with the literature.¹²

Materials

Styrene and the bis-oxazolines were obtained from Aldrich. Ultrastabilised NH₄⁺Y zeolite (Union Carbide, LZY84, 5.0 g) was calcined (550 °C) for 5 h, then stirred in 0.5 mol solution of copper(II) acetate solution (100 ml) for 24 h at room temperature. The mixture was then centrifuged and washed with distilled water. This was repeated a further two times. The CuHY zeolite was then dried at 100 °C for 24 h, then recalcined (550 °C) for 5 h. Cu content 3.2% by weight. ZnHY (4% by weight Zn), NiHY (3.6% by weight Ni), FeHY (3.4% by weight Fe), MnHY (4.0% by weight Mn) and CoHY (3.75% by weight Co) were prepared in a similar manner using solutions of the appropriate acetate.

Preparation of nitrene donors

[N-(*p*-Tolylsulfonyl)imino]phenyliodinane ‡ (PhI=NTs). Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and toluene-*p*-sulfonamide (1.71 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature below 10 °C during the addition. The resulting clear yellow solution was stirred for three hours at room temperature and then poured into distilled water (250 mL). Over a period of 12 hours a yellow precipitate formed and this was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (2.56 g, 68.8%). δ_H (d₆-DMSO, 400 MHz) 7–7.8 (m, 9H), 2.32 (s, 3H). Anal. calcd. C 41.82, H 3.18, N 3.75; Found C 41.79, H 3.29, N 3.74%.

[N-(*p*-Nitrophenylsulfonyl)imino]phenyliodinane (PhI=NNs). Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and *p*-nitrobenzenesulfonamide (2.02 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and over a 4 hour period a cream precipitate formed. The precipitate was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (3.23 g, 80.6%). δ_H (d₆-DMSO, 400 MHz) 8.2 (d, 2H), 7.95 (m, 4H), 7.56 (m, 1H), 7.4 (m, 2H). Anal. calcd. C 35.69, H 2.27, N 6.93; Found C 35.56, H 2.29, N 6.62%.

[N-(*o*-Nitrophenylsulfonyl)imino]phenyliodinane. Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and *o*-nitrobenzenesulfonamide (2.02 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and over a 4 hour period a cream precipitate formed. The precipitate was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (2.41 g, 59.6%). δ_{H} (d_6 -DMSO, 400 MHz) 7.6–7.9 (m), 7.5 (m, 1H), 7.4 (m, 2H). Anal. cald. C 35.69, H 2.27, N 6.93; Found C 35.61, H 2.24, N 6.75%.

[N-(*p*-Methoxyphenylsulfonyl)imino]phenyliodinane. Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and *p*-methoxybenzenesulfonamide (1.87 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and over a 4 hour period a cream precipitate formed. The precipitate was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (2.58 g, 66.3%). δ_{H} (d_6 -DMSO, 400 MHz) 7.7 (m, 2H), 7.35 (m, 4H), 6.7 (d, 2H), 3.7 (s, 3H). Anal. cald. C 40.1, H 3.08, N 3.59; Found C 40.15, H 3.18, N 3.55%.

[N-(Phenylsulfonyl)imino]phenyliodinane. Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and benzenesulfonamide (1.57 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature below 10 °C during the addition. The resulting clear yellow solution was stirred for three hours at room temperature and then poured into distilled water (250 mL). Over a period of 12 hours a yellow precipitate formed and this was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (2.14 g, 59.6%). δ_{H} (d_6 -DMSO, 400 MHz) 7–7.8 (m, 10H, aromatic protons). Anal. cald. C 40.11, H 2.78, N 3.59; Found C 40.25, H 2.64, N 3.58%.

[N-(*p*-Chlorophenylsulfonyl)imino]phenyliodinane. Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and *p*-chlorobenzenesulfonamide (1.93 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and over a 4 hour period a cream precipitate formed. The precipitate was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (1.45 g, 36.8%). δ_{H} (d_6 -DMSO, 400 MHz) 7.8 (d, 2H), 7.5 (m, 2H), 7.2 (m, 4H). Anal. cald. C 36.64, H 2.29, N 3.56; Found C 36.74, H 2.38, N 3.61%.

[N-(Methylsulfonyl)imino]phenyliodinane. Iodobenzene diacetate (3.22 g; 1.0 mmol) was added to a stirred mixture of potassium hydroxide (1.4 g; 0.025 mmol) and methanesulfonamide (1.58 g; 1.0 mmol) in HPLC grade methanol (40 mL), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and over a 4 hour period a cream precipitate formed. The precipitate was then filtered, washed with distilled water and dried at room temperature in a vacuum desiccator (0.94 g, 33.2%). δ_{H} (d_6 -DMSO, 400 MHz) 7–7.8 (m, 5H, aromatic protons), 2.6 (s, 3H). Anal. cald. C 28.28, H 2.63, N 4.71; Found C 28.48, H 2.76, N 4.73%.

Homogeneous aziridination reactions catalysed by Cu(OTf)₂

Styrene (0.101 g, 1.0 mmol), nitrene donor (1.5 mmol) and copper(II) triflate (0.15 mmol) were stirred in acetonitrile (2.5 cm³) at 25 °C. If a chiral bis(oxazoline) (0.07 mmol, Aldrich, 98%) was added, this was added together with the copper(II)

triflate in dry acetonitrile prior to the addition of the styrene and nitrene donor. Reaction time varied according to the different nitrene precursor. The reaction was stirred in air at 25 °C until complete dissolution of the nitrene donor. The reaction mixture was then filtered through a plug of silica with ethyl acetate (50 cm³) as eluent. Flash chromatography gave the aziridine as a white solid. Experiments were carried out in triplicate and reproducible results are reported.

Heterogeneous aziridine reaction catalysed by CuHY

Styrene (0.101 g, 1.0 mmol), nitrene donor (1.5 mmol) and CuHY (0.3 g) were stirred together in dry acetonitrile (2.5 cm³) at 25 °C. If a chiral bis(oxazoline) (0.07 mmol, Aldrich, 98%) was added, this was stirred with the CuHY in the acetonitrile prior to the addition of the styrene and nitrene donor. Reaction times varied depending on the nitrene donor. The reaction mixture was stirred in air at 25 °C until complete dissolution of the nitrene donor. The reaction mixture was then filtered through a plug of silica with ethyl acetate (50 cm³) as eluent. Flash chromatography gave the aziridine as a white solid. Experiments were carried out in triplicate and reproducible results are reported.

Acknowledgements

We thank Syntex and the EPSRC 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 W. Zhang, J. L. Loebach, S. R. W. Wilson and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1990, **112**, 2801.
- 4 S. Feast, D. Bethell, P. C. B. Page, F. King, C. H. Rochester, M. R. H. Siddiqui, D. J. Willock and G. J. Hutchings, *J. Chem. Soc., Chem. Commun.*, 1995, 2499.
- 5 S. Feast, M. R. H. Siddiqui, R. P. K. Wells, D. J. Willock, F. King, C. H. Rochester, D. Bethell, P. C. B. Page and G. J. Hutchings, *J. Catal.*, 1997, **167**, 533.
- 6 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.
- 7 C. Langham, S. Taylor, D. Bethell, P. McMorn, P. C. B. Page, D. J. Willock, C. Sly, F. E. Hancock and G. J. Hutchings, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1043.
- 8 P. Piaggio, P. McMorn, C. Langham, D. Bethell, P. C. B. Page, F. E. Hancock and G. J. Hutchings, *New J. Chem.*, 1998, 1167.
- 9 P. Piaggio, C. Langham, P. McMorn, D. Bethell, P. C. B. Page, F. E. Hancock, C. Sly and G. J. Hutchings, *J. Chem. Soc., Perkin Trans. 2*, 2000, 143.
- 10 P. Piaggio, P. McMorn, D. M. Murphy, D. Bethell, P. C. B. Page, F. E. Hancock, C. Sly, O. J. Kerton and G. J. Hutchings, *J. Chem. Soc., Perkin Trans. 2*, 2000, 2009.
- 11 E. N. Jacobsen, in *Comprehensive Asymmetric Catalysis*, ed. E. N. Jacobsen, A. Pfaltz, H. Yamamoto, Springer Verlag, Berlin, 1999, vol. 2, p. 607.
- 12 D. A. Evans, M. M. Faul and M. T. J. Bilodeau, *J. Org. Chem.*, 1991, **56**, 6744.
- 13 D. A. Evans, M. M. Faul and M. T. J. Bilodeau, *J. Am. Chem. Soc.*, 1994, **116**, 2741.
- 14 D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul, *J. Am. Chem. Soc.*, 1991, **113**, 726.
- 15 J. S. Johnson and D. A. Evans, *Acc. Chem. Res.*, 2000, **33**, 325.
- 16 Y. Traa, D. M. Murphy, R. D. Farley and G. J. Hutchings, *Phys. Chem. Chem. Phys.*, 2001, **3**, 1073.
- 17 M. Glos and O. Reiser, *Org. Lett.*, 2000, **2**, 2045.
- 18 M. I. Burguete, J. M. Fraile, J. I. García, E. García-Verdugo, S. V. Luis and J. A. Mayoral, *Org. Lett.*, 2000, **2**, 3905.
- 19 P. Müller, *Adv. Catal. Processes*, 1997, **2**, 113.
- 20 M. J. Södergren, D. A. Alonso, A. V. Bedekar and P. G. Andersson, *Tetrahedron Lett.*, 1997, **38**, 6897.
- 21 M. J. Södergren, D. A. Alonso and P. G. Andersson, *Tetrahedron: Asymmetry*, 1997, **8**, 3563.
- 22 Y. Yamada, T. Yamamoto and M. Okawara, *Chem. Lett.*, 1975, 361.

- 23 Z. Li, K. R. Conser and E. J. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326.
- 24 Z. Li, R. W. Quan and E. J. Jacobsen, *J. Am. Chem. Soc.*, 1995, **117**, 5889.
- 25 K. Noda, N. Hosoya, R. Irie, Y. Ito and T. Katsuki, *Synlett*, 1993, 469.
- 26 H. Nishikori and T. Katsuki, *Tetrahedron Lett.*, 1996, **37**, 9245.
- 27 T.-S. Lai, H.-L. Kwang, C.-H. Che and S.-M. Peng, *Chem. Commun.*, 1997, 2373.
- 28 S.-M. Au, W.-H. Fung, M.-C. Chem, C.-M. Che and S.-M. Peng, *Chem. Commun.*, 1997, 1655.
- 29 P. Müller, C. Baud and Y. Jacquier, *Can. J. Chem.*, 1998, **76**, 738.
- 30 L. Hagiropoglou, A. Varvoglis, N. W. Alcock and G. A. Pike, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2839.
- 31 C. C. Franklin, R. B. Van Atta, A. F. Tai and J. S. Valentine, *J. Am. Chem. Soc.*, 1984, **106**, 814.
- 32 R. B. Van Atta, C. C. Franklin and J. S. Valentine, *Inorg. Chem.*, 1984, **23**, 4121.
- 33 J. F. Kinneary, J. S. Albert and C. J. Burrows, *J. Am. Chem. Soc.*, 1988, **110**, 6124.
- 34 S. Ozaki, H. Mumura, N. Yasuhara, M. Masui, Y. Yamagata and K. Tomita, *J. Chem. Soc., Perkin Trans. 2*, 1990, 395.
- 35 T. Koyama, A. Kitani, S. Ito and K. Sasaki, *Chem. Lett.*, 1993, 395.
- 36 Z. H. Fu, D. L. Yin, D. H. Yin, L. X. Zhang and Y. Y. Zhang, *J. Chem. Res. (S)*, 1998, **12**, 764.
- 37 C. Langham, P. Piaggio, D. Bethell, D. F. Lee, P. C. B. Page, D. J. Willock, C. Sly, F. E. Hancock, F. King and G. J. Hutchings, *Catalysis of Organic Reactions*, ed. F. E. Herkes, Marcel Dekker, 1998, vol. 3, p. 25.
- 38 S. A. Raynor, J. M. Thomas, R. Raja, B. F. G. Johnson, R. G. Bell and M. D. Mantle, *Chem. Commun.*, 2000, 1925.
- 39 D. J. Berrisford, C. Bolm and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1059.
- 40 G. J. Hutchings, *Chem. Commun.*, 1999, 301.