

Heterogeneous aziridination of styrene using [N-(p-nitrophenylsulfonyl)imino]phenyliodinane as nitrene donor: influence of the reaction parameters on yield and enantioselectivity

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

^a Department of Chemistry, Cardiff University, P.O. Box 912, Cardiff CF10 3TB, Wales, UK

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

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

^d Syntex, P.O. Box 1, Billingham, Teeside TS23 1LB, UK

Received 4 July 2001; accepted 31 October 2001

Abstract

The copper-catalysed aziridination of styrene with copper-exchanged zeolite Y (CuHY) and copper(II) triflate (Cu(OTf)₂) as catalysts is described and discussed. In particular, the effects of reaction conditions on the yield and enantiomeric excess of the aziridine product are described using [N-(p-nitrophenylsulfonyl)imino]phenyliodinane (PhI=NNs) as nitrene donor. By careful control of the styrene:nitrene donor molar ratio and the solvent, an ee of 95% can be obtained for the heterogeneously catalysed bis(oxazoline)-modified zeolite CuHY. The ee achieved with the zeolite immobilised catalyst is significantly higher than that achieved for the non-immobilised homogeneous catalyst under comparable reaction conditions. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Styrene aziridination; Bis(oxazoline)-modified CuHY zeolite; Nitrene donors

1. Introduction

The immobilisation of homogeneous catalysts continues to be a research topic that attracts considerable attention. The design of asymmetric heterogeneous catalysts is of particular importance, and the immobilisation of known homogeneous asymmetric catalysts provides a viable pathway. Previous studies [1–5] have shown that copper-bis(oxazoline) complexes can

act as effective asymmetric homogeneous catalysts for the aziridination of alkenes. We subsequently demonstrated that cations ion-exchanged into the intra-crystalline pores of zeolites and mesoporous materials can act as heterogeneous asymmetric catalysts [6–12]. We used this approach to show that Cu²⁺ ion-exchanged in zeolite H-Y, when modified by bis(oxazolines), was active for the aziridination of alkenes but, in our early studies [8,9], the ee was relatively low, ca. 35–40%. In these initial studies, we used [N-(p-tolylsulfonyl)imino]phenyliodinane (PhI=NTs) as the nitrene donor. Recently, we have found that using an alternative nitrene do-

* Corresponding author. Tel.: +44-29-20874805;
fax: +44-29-20874075.
E-mail address: hutch@cardiff.ac.uk (G.J. Hutchings).

nor, [*N*-(*p*-nitrophenylsulfonyl)imino]phenyliodinane (PhI=NNs), the ee for styrene aziridination can be increased to ca. 80% [13]. In this paper, we demonstrate that even higher ee's can be achieved by careful optimisation of the reaction conditions.

2. Experimental

2.1. Materials

Ultrastabilised NH_4^+ Y zeolite (Union Carbide, 5.0 g) was stirred with a solution of copper(II) acetate (0.5 mol l^{-1} , 100 ml) for 24 h at 25 °C. The material was then centrifuged, washed with distilled water. The copper-exchanged zeolite Y (CuHY, 3.2 wt.% Cu) so obtained was then dried (110 °C, 24 h), calcined (550 °C, 5 h) and stored in a desiccator prior to use. Styrene and the bis(oxazoline) were obtained from Aldrich. The PhI=NNs nitrene donor was prepared according to the following procedure. 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 methanol (40 ml), keeping the temperature at 0 °C during the addition. The solution was stirred at room temperature and the precipitate, formed over a 4 h period, was recovered by filtration, washed with distilled water and dried at 25 °C in a vacuum desiccator. The material was confirmed to be PhI=NNs by NMR spectroscopy and the yield was 3.23 g (80.6%).

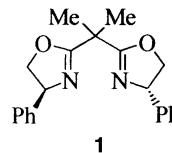
2.2. Aziridination of styrene

Styrene (1.0 mmol), nitrene donor (0.2–5.0 mmol) and catalyst (heterogeneous catalyst CuHY = 0.3 g; homogeneous catalyst $\text{Cu}(\text{OTf})_2 = 1.5 \times 10^{-4} \text{ mmol}$) were stirred together in dry solvent (2.5 cm^3) at 25 °C. If a chiral bis(oxazoline) (0.07 mmol) was added, this was stirred with the catalyst in the dry solvent prior to the addition of the styrene and the nitrene donor. The reaction mixture was stirred at 25 °C until complete dissolution of the nitrene donor. The product was then filtered through a plug of silica gel with acetonitrile (50 ml) together with biphenyl as an internal standard as eluent. Flash chromatography gave the aziridine as a colourless solid.

3. Results and discussion

3.1. Effect of solvent on the aziridination of styrene

In our previous studies using PhI=NTs as nitrene donor, we found that acetonitrile was the preferred solvent for the heterogeneously catalysed process using CuHY. A series of experiments was, therefore, carried out with PhI=NNs as nitrene donor with CuHY as catalyst using a range of coordinating (acetonitrile, nitromethane, methanol, anisole, acetone) and non-coordinating (toluene) solvents. The results are shown in Fig. 1. In the absence of the bis(oxazoline), high yields of the aziridine are obtained with nitromethane and acetonitrile, and intermediate yields are obtained with methanol, acetone and toluene. Anisole appears to give a poor yield of the aziridine. However, when the bis(oxazoline), 2,2-bis[(4*R*)-4-phenyl-1,3-oxazolin-2-yl] propane (**1**) was added, acetonitrile and nitromethane retained high yields of aziridine. However, only acetonitrile gave the aziridine with a high ee (85%). Hence, these experiments confirm that acetonitrile is the preferred solvent for PhI=NNs as nitrene donor for the heterogeneous catalyst CuHY.



A similar set of experiments was carried out using the homogeneous catalyst $\text{Cu}(\text{OTf})_2$ and the results are also shown in Fig. 1. In the absence of the bis(oxazoline), the yield obtained for the homogeneous catalyst is significantly lower than that obtained with CuHY for all the solvents investigated. However, when the chiral ligand is present, the yields are significantly higher for the homogeneous catalyst. This may indicate that the heterogeneous CuHY catalyst may become diffusion limited when the chiral ligand is present, and this leads to the decrease in the yield observed. Alternatively, it is possible that the relative concentrations of the reagents within the pore of the zeolite may be significantly different from the solution concentration, and this effect is exacerbated by the presence of the chiral ligand. This differential

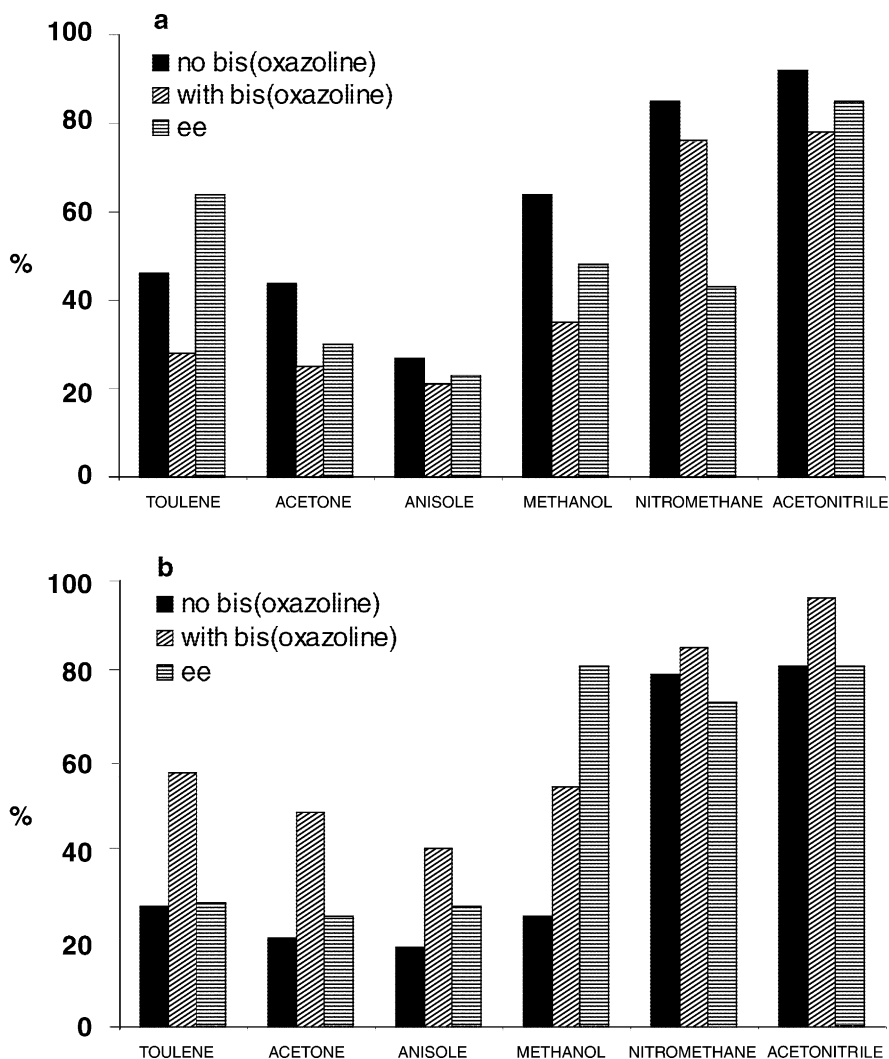


Fig. 1. Effect of the solvent on the yield and ee for the CuHY and Cu(OTf)₂ catalysts with and without the addition of bis(oxazoline): (a) CuHY; (b) Cu(OTf)₂.

distribution effect has recently been demonstrated in aromatic acetylations using zeolite catalysts in a detailed study by Derouane et al. [14,15].

The bis(oxazoline)/Cu(OTf)₂ catalyst gives the aziridine high ee in methanol and nitromethane, in addition to acetonitrile. This is in contrast to the bis(oxazoline)-modified CuHY catalyst, which gives relatively poor ee in methanol and nitromethane. In addition, the heterogeneous catalyst gives a significantly higher ee in toluene, when compared with the

homogeneous catalyst. These differences demonstrate that the immobilised catalyst behaves differently from its non-immobilised counterpart, as we have previously noted with PhI=NTs as the nitrene donor [8,9].

3.2. Effect of nitrene donor:styrene molar ratio on aziridination

In the initial studies concerning the aziridination of alkenes using homogeneous Cu²⁺ catalysts,

Table 1

Effect of amount of nitrene donor on the aziridination of styrene in the absence of bis(oxazoline) ligand

Styrene:nitrene donor molar ratio	CuHY		Cu(OTf) ₂	
	Reaction time ^a (h)	Yield (%)	Reaction time ^a (h)	Yield (%)
5:1	0.75	87	0.75	88
3:1	1.5	73	1.0	76
1:1	1.5	57	1.5	59
1:1.5	1.5	85	2.0	93

^a Reaction time followed by dissolution of the nitrene donor.

by Evans and co-workers [2–5], high molar ratios of the substrate relative to the nitrene donor were used. Typically, ratios of substrate:nitrene donor of 5:1 were used to drive the reaction rapidly to completion and to obtain optimal yield. In our earlier work [8,9,13], we have shown that high yields of the aziridine can be obtained with the heterogeneous CuHY catalyst with much lower substrate:nitrene donor molar ratios. Södergren et al. [16] have also reported that high yields of the aziridine can be achieved when an excess of the nitrene donor is used (nitrene donor:substrate = 1.5:1 molar ratio) with the homogeneous catalyst. Hence, the effect of the nitrene donor:styrene molar ratio was investigated for the unmodified and bis(oxazoline)-modified catalysts.

The initial experiments concerned the unmodified catalysts and the results are shown in Table 1. It is apparent that similar yields of the aziridine are obtained for both the Cu(OTf)₂ and CuHY catalysts. However, the reaction time increased significantly with the increasing amount of the nitrene donor but this probably merely reflects the solubility of PhI=NNs in the acetonitrile solvent. Interestingly, the yield of aziridine is

highest for conditions where there is either an excess of substrate or an excess of nitrene donor.

A set of experiments was then carried out in the presence of the bis(oxazoline) (**1**) and the results are shown in Table 2. These experiments were conducted until the dissolution of the PhI=NNs was complete, and this was taken as the completion of the reaction. For both CuHY and Cu(OTf)₂ in the presence of the bis(oxazoline), the reaction time increased significantly compared with the reaction in the absence of the ligand (compare Tables 1 and 2). The yield of aziridine follows the same trend with styrene:PhI=NNs molar ratios, as observed in the absence of the bis(oxazoline). In addition, the ee's are also observed to follow the same trend. In particular, the highest combination of yield and ee, in these experiments, for both Cu(OTf)₂ and CuHY, is observed for the styrene:PhI=NNs = 1:1.5 molar ratio. In view of this, a series of experiments was carried out to explore the styrene:PhI=NNs molar ratios between 1:1.0 and 1:1.5, in the presence of bis(oxazoline) (**1**), and these data are shown in Table 3. These experiments were carried out for a standard time of 16 h, in contrast to the previous experiments which were carried

Table 2

Effect of amount of nitrene donor on the asymmetric aziridination of styrene

Styrene:nitrene donor molar ratio	CuHY			Cu(OTf) ₂		
	Reaction time ^a (h)	Yield (%)	ee (%)	Reaction time ^a (h)	Yield (%)	ee (%)
5:1	1.0	83	78	0.5	92	61
3:1	3.0	67	45	1.5	80	48
1:1	2.5	53	36	1.0	64	40
1:1.5	5.0	78	85	1.5	96	81
1.3	10.0	61	68	5.0	71	72
1.5	16.0	53	46	8.5	63	57

^a Reaction time followed by dissolution of PhI=NNs.

Table 3
Effect of amount of nitrene donor on the asymmetric aziridination of styrene^a

Styrene:nitrene donor molar ratio	CuHY		Cu(OTf) ₂	
	Yield (%)	ee (%)	Yield (%)	ee (%)
1:1.0	68	49	27	65
1:1.1	85	81	83	77
1:1.2	88	89	72	88
1:1.3	82	91	99	80
1:1.4	77	95	99	79
1:1.5	67	88	83	87

^a Reaction time: 16h.

out for a range of times based on the dissolution of PhI=NNs. Both the heterogeneous CuHY and the homogeneous Cu(OTf)₂ catalysts show significant increases in both the yield and ee of the aziridine. The trends are, however, slightly different for the two catalysts. For the homogeneous catalyst, Cu(OTf)₂, the highest yields of the aziridine are formed with a styrene:PhI=NNs molar ratio of 1:1.3 and 1:1.4. For CuHY, the highest yields are obtained at a lower excess of the nitrene donor, and the highest yields are obtained with styrene:PhI=NNs molar ratios of 1:1.1 and 1:1.2. This is perhaps due to the molar ratio of the substrate and nitrene donor being different within the micropores of the zeolite immobilised catalyst when compared with the solution concentration. The ee's also show significant differences between the two catalysts under these experimental conditions. In particular, the ee with the CuHY catalyst is significantly higher than that observed with the homogeneous catalyst, Cu(OTf)₂. Using bis(oxazoline)-modified CuHY with styrene:PhI=NNs ratios of 1:1.3 and 1:1.4, it is possible to achieve an ee greater than 90%. These experiments were repeated three times with reproducible results being achieved. These experiments demonstrate that, by careful manipulation of the experimental conditions, in particular the substrate:nitrene ratio, high ee can be achieved with the heterogeneous catalyst. It is possible that different conditions will be required for different substrate/nitrene donor/bis(oxazoline) combinations. However, it can be concluded for the present study that the immobilisation of catalysts within the micropores of zeolite

represents a viable approach to achieving asymmetric catalysis capable of achieving an ee greater than 90%.

Acknowledgements

We thank the EPSRC and Syntex for financial support.

References

- [1] E.N. Jacobsen, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), *Comprehensive Asymmetric Catalysis*, Vol. 2, Springer, Berlin, 1999, p. 607.
- [2] D.A. Evans, M.M. Faul, M.T. Bilodeau, *J. Org. Chem.* 56 (1991) 6744.
- [3] D.A. Evans, M.M. Faul, M.T. Bilodeau, *J. Am. Chem. Soc.* 116 (1994) 2741.
- [4] D.A. Evans, K.A. Woerpel, M.M. Hinman, M.M. Faul, *J. Am. Chem. Soc.* 113 (1991) 726.
- [5] J.S. Johnson, D.A. Evans, *Acc. Chem. Res.* 33 (2000) 325.
- [6] S. Feast, D. Bethell, P.C. Bulman-Page, F. King, C.H. Rochester, M.R.H. Siddiqui, D.J. Willock, G.J. Hutchings, *J. Chem. Soc., Chem. Commun.* (1995) 2499.
- [7] S. Feast, M.R.H. Siddiqui, R.P.K. Wells, D.J. Willock, F. King, C.H. Rochester, D. Bethell, P.C. Bulman-Page, G.J. Hutchings, *J. Catal.* 167 (1997) 533.
- [8] C. Langham, P. Piaggio, D. Bethell, P. McMorn, P.C. Bulman-Page, D.J. Willock, C. Sly, F.E. Hancock, F. King, G.J. Hutchings, *Chem. Commun.* (1998) 1601.
- [9] C. Langham, S. Taylor, D. Bethell, P. McMorn, P.C. Bulman-Page, D.J. Willock, C. Sly, F.E. Hancock, G.J. Hutchings, *J. Chem. Soc., Perkin Trans. 2* (1999) 1043.
- [10] P. Piaggio, P. McMorn, C. Langham, D. Bethell, P.C. Bulman-Page, F.E. Hancock, G.J. Hutchings, *New J. Chem.* (1998) 1167.
- [11] P. Piaggio, P. McMorn, D.M. Murphy, D. Bethell, P.C. Bulman-Page, F.E. Hancock, C. Sly, G.J. Hutchings, *J. Chem. Soc., Perkin Trans. 2* (2000) 143.
- [12] P. Piaggio, P. McMorn, D.M. Murphy, D. Bethell, P.C. Bulman-Page, F.E. Hancock, C. Sly, O.J. Kerton, G.J. Hutchings, *J. Chem. Soc., Perkin Trans. 2* (2000) 2009.
- [13] G.J. Hutchings, C. Langham, P. Piaggio, S. Taylor, P. McMorn, D.J. Willock, D. Bethell, P.C. Bulman-Page, C. Sly, F.E. Hancock, F. King, *Stud. Surf. Sci. Catal.* 130 (2000) 521.
- [14] E.G. Derouane, C.J. Dillon, D. Bethell, S.B. Derouane-Abd Hamid, *J. Catal.* 187 (1999) 209.
- [15] E.G. Derouane, G. Crehan, C.J. Dillon, D. Bethell, H. He, S.B. Derouane-Abd Hamid, *J. Catal.* 194 (2000) 410.
- [16] M.J. Södergren, D.A. Alonso, P.G. Andersson, *Tetrahedron: Asymm.* 8 (1997) 3563.