Superior performance of a chiral catalyst confined within mesoporous silica

Brian F. G. Johnson,*[a] Stuart A. Raynor,[a] Douglas S. Shephard,[a] Thomas Mashmeyer,[ab] John Meurig Thomas,*[b] Gopinthar Sankar,[b] Stefen Bromley,[b] Richard Oldroyd,[b] Lynn Gladden[c] and Mike D. Mantle[c]

[a] *Department of Chemistry, The University of Cambridge, Lensfield Road, Cambridge, UK CB2 1EW. E-mail: bfgj1@cam.ac.uk*

[b] *Davy-Faraday Research Laboratories, The Royal Institution of Great Britain, 21 Albemarle Street, London, UK W1X 4BS*

[c] *Department of Chemical Engineering, The University of Cambridge, New Museum Site, Cambridge, UK CB2 3QZ*

Received (in Cambridge, UK) 26th March 1999, Accepted 12th May 1999

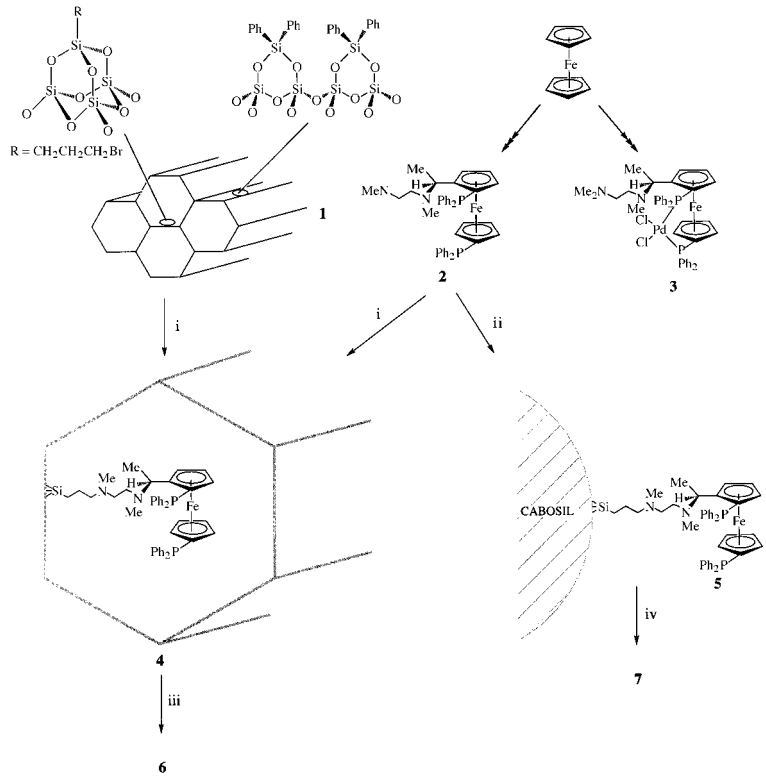
A chiral catalyst from the ligand 1,1′-bis(diphenylphosphino)ferrocene (dppf) anchored to the inner walls of the mesoporous support MCM-41 and co-ordinated to Pd^{II} has been shown to exhibit a degree of regioselectivity and enantiomeric excess, in the allylic amination of cinnamyl acetate, which is far superior to that of its homogeneous counterpart or that of a surface-bound analogue attached to a non-porous silica.

Stereo- and regio-selective catalysis lies at the heart of current developments in pharmaceutical, agrochemical and cognate industries.[1–3] The recognition that a small amount of a chiral catalyst may yield large quantites of a targeted chiral product has already led to the development of several ingenious methods for the design of such catalysts. These include modified metals,[4] metal oxides[5] and zeolites,[6,7] and the so-called 'ship-in-bottle' or 'tea-bag' systems.[8–10] In this work we have been able to demonstrate that a chiral ligand derived from 1,1′-bis(diphenylphosphino)ferrocene (dppf) bonded to an active metal centre (in this case Pd^{II})† and tethered, *via* a molecular link of appropriate length, to the inner walls of a mesoporous silica support (MCM-41, *ca*. 30 Å diameter) yields a degree of catalytic regioselectivity as well as an enantiomeric excess that is far superior to either the homogeneous counterpart or the cabosil-bound catalyst (Cabosil is a non-porous, high-area silica).

Our conceptual methodology was to take a homogeneous system of known catalytic behaviour and, by performing suitable modifications, to tether this catalyst within the mesopore.[11] Care is taken to ensure that all activity is confined to the internal surface of the MCM-41 channels. This is achieved by selectively deactivating the external surface of the support. We have shown previously by electron microscopy, on functionalised mesopores stained with Ru_6-based clusters, that this is a reliable and satisfactory method.[12]

Our approach to the preparation of the catalytic system is shown in Scheme 1. The mesoporous framework was first treated with Ph_2SiCl_2 under *non-diffusive conditions* to deactivate the exterior walls of the material. The interior walls of this same material were then derivatised with 3-bromopropyltrichlorosilane to give the activated MCM-41 **1**.

The ferrocenyl-based ligand, (*S*)-1-[(*R*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethyl-*N*,*N*′-dimethylethylenediamine **2**, was prepared from ferrocene by literature methods.[13,14] On



Scheme 1 The synthetic routes used in the preparation of the homogeneous catalyst **3**, the mesopore-supported **6** and the carbosil-bound **7**. *Reagents and conditions*: formation of **1**(a) Ph_2SiCl_2–THF, 25 °C, (b) $Cl_3SiCH_2CH_2CH_2Br$–THF, −78 °C; i, THF, 25 °C; ii, THF, 25 °C; iii $PdCl_2$–MeCN–THF, 25 °C; iv $PdCl_2$–MeCN–THF, 25 °C.

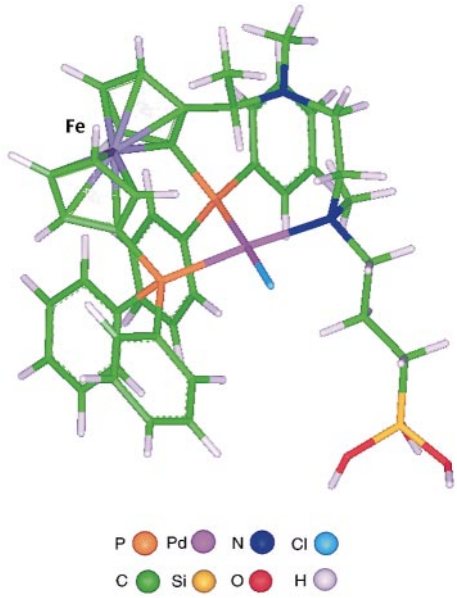
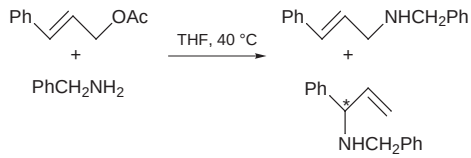


Fig. 1 Computer model of the catalytic centre inside MCM-41.

treatment of the activated MCM-41 **1** with an excess of **2** yields the chiral catalytic precursor **4** which, on reaction with $PdCl_2$–MeCN, gives the required catalyst **6**. In a separate experiment the closely related cabosil-supported catalyst **7** was prepared in a similar manner from surface-activated cabosil and **2** followed by addition of the required palladium(II) salt.

The catalyst **6** was fully characterised by a range of techniques. First, the structural integrity of the MCM-41 catalytic precursor **4** was established by MAS NMR and EXAFS spectroscopy. The presence of the tethered ferrocenyl catalysts was confirmed by comparison of the ^{13}C MAS NMR spectrum of **4** with that of the unattached precursor **2**. Apart from the additional signals arising from the propyl tethering unit the spectra were essentially the same. Examination of the ^{31}P MAS NMR of **2** and **4** showed identical chemical shift values. On incorporation of the Pd^{II} ion to yield the active catalyst **6**, significant changes in the aliphatic region of the ^{13}C MAS NMR and in the ^{31}P MAS NMR spectra were noted. Two ^{31}P resonances at δ 15.9 and 34.4 were recorded, clearly indicating two different phosphorous environments, these have been assigned as one being *trans* to a nitrogen and the other being *trans* to a chloride.[15] The change in the aliphatic region of the ^{13}C MAS NMR corresponds to changes in the methyl resonances of the amines, further corroborating the assignment of the ^{31}P spectrum. This entire arrangement was borne out by a detailed EXAFS analysis of **6**. The coordination environment of the cationic species within the mesopore is depicted in Fig. 1.

In testing our catalysts we decided to use an allylic amination reaction between cinnamyl acetate and benzylamine (Scheme 2). This reaction has two possible products: a straight chained product (which is favoured due to the retention of the delocalised π system) and a chiral branched product. The aim of the reaction is to produce the greatest possible yield of the branched product with the highest possible enantiomeric excess



Scheme 2 The catalytic reaction between cinnamyl acetate and benzylamine.

Table 1 Catalytic results

Catalyst[a]	Conversion[b] (%)	Straight chain[c] (%)	Branched (%)	ee[d] (%)
3 (*S*)	76	99+	—	—
7 (*S*)	98	98	2	43
6 (*S*)	99+	49	51	99+
6 (*R*)	99+	50	50	93

[a] Symbols in parentheses denote chirality of the directing group. [b] % Conversion is stated relative to the use of benzylamine. [c] Regio- and enantio-selectivity determined by gas chromatography on a Chiraldex G-DA column (Alltech) with γ-cyclodextrin as the active phase (20 m). *Conditions*: He pressure 12.5 psi; temperature ramped 50–180 °C at 10 °C min^{-1} and then held for the duration of the run. [d] Major stereoisomer possesses the same chirality as the catalyst. Retention time *ca.* 38 min.

(ee). Three catalysts were examined: the homogeneous {(*S*)-1-[(*R*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethyl-*N*,*N*′-dimethylethylenediamine} palladium dichloride **3**, the cabosil-supported one **7** and that attached within the mesoporous material **6**. Preliminary results of the studies are listed in Table 1. With the homogeneous catalyst **3** the reaction is directed solely towards the straight chain product whilst catalyst **7** shows some of the desired regioselectivity by producing 2% of the branched product. Unfortunately the enantioselectivity of the reaction is relatively low with an ee of 43%. The use of the mesopore-confined catalyst **6** promotes a dramatic change in the regioselectivity of the reaction, producing 51% of the branched product. The enantioselectivity of the catalysis is also greatly improved relative to the cabosil-bound catalyst with the ee approaching 100%.

These results indicate that the control exercised by the MCM-41 on the activity of the ferrocenyl catalyst is considerable. The profound changes in the regio- and enantio-selectivity are clearly apparent from the data listed in Table 1. Other, related systems are currently under investigation.

This work was supported by the EPSRC, ICI (Wilton) and the Newton Trust (S. A. R.), a Royal Society Fellowship and Peterhouse (D. S. S).

Notes and references

† Other metal ions, *e.g.* Rh(I) may also be employed.

1 R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994.
2 J. M. Brown and S. G. Davies, *Nature*, 1994, **370**, 418.
3 *Advances in Catalytic Processes: Asymmetric Chemical Transformations*, ed. M. Boyle, JAI, Greenwich, CT, vol. 1.
4 A. Pfalz and T. Heinz, *Top. Catal.*, 1997, 4, 229.
5 A. Baiker, *Curr. Opin. Solid State Mater. Sci., 1998*, **3**, 86.
6 *Top Catal*., ed. D. G. Blackmond and W. Leitner, 1997, **4**, Part 1.
7 A. Corma, M. Iglesias, C. del Pino and F. Sanchez, *J. Chem. Soc., Chem. Commun.*, 1991, 1253.
8 J. M. Thomas, *Philos. Trans. R. Soc. London, Ser. A*, 1990, **333**, 173.
9 C. L. Hill, *Activation and Functionalisation of Alkanes*, Wiley, New York, 1989.
10 M. J. Sabater, A. Corma, A. Domenech, V. Fornes and H. Garcia, *Chem. Commun.*, 1997, 1285.
11 J. M. Thomas, T. Maschmeyer, B. F. G. Johnson and D. S. Shephard, *J. Mol. Catal.*, 1999, **141**, 139.
12 D. S. Shephard, W. Z. Zhou, T. Mashmeyer, J. M. Matters, C. L. Roper, S. Parsons, B. F. G. Johnson and M. J. Duer, *Angew. Chem., Int. Ed.*, 1998, **37**, 2719.
13 G. W. Gokel and I. K. Ugi, *J. Chem. Educ.*, 1972, **49**, 294.
14 T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Konishi, K. Yamamoto and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1138.
15 T. Suzuki, M. Kita, K. Kashiwabara and F. Fujita, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 3434; P. J. Stang, D. H. Cao, S. Siato and A. M. Arif, *J. Am. Chem. Soc.*, 1995, **117**, 6273.

Communication 9/02441G