Enantiospecificity in achiral zeolites for asymmetric catalysis†

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This article highlights the recent fundamental study in using achiral and chiral porous materials for the potential applications in asymmetric catalysis. Thanks to the new-generation synchrotron X-ray powder diffraction (SXRD) facilities, we reveal the presence of the unique ‘chiral region’ in achiral zeolites with the MFI topology. Both the inherent site-isolation effect of the active sites and internal confinement restraints in zeolites are critical for creating ‘chiral regions’ that can aid the design of more enantioselective catalytic reactions. We also offer an outlook on the challenges and opportunities of this research area.

1. Introduction

The use of chiral catalysts has been a promising solution to many enantioselective chemical and pharmaceutical synthesis processes. The homogeneous Sharpless and Jacobsen catalysts are excellent examples for asymmetric alkene epoxidation. It is achieved through directing functional groups, such as the hydroxyl group in the Sharpless catalyst, or through rational tailoring of the ligands of metal complexes, such as by using chiral salen-Mn(III) centre in the Jacobsen catalyst (salen: \(\text{trans-} (\text{R},\text{R})-1,2\text{-bis(salicylideneamino)cyclohexane}\)). This has accordingly inspired the heterogeneous community to design chiral catalysts for enantioselective reactions by the formation of ion-pair or adsorption,\(^1\) by the incorporation of chiral metal centres within a microporous support material,\(^2,3\) and so forth. By heterogenising homogeneous catalysts, product-catalyst separation can be more readily achieved by simple filtration or centrifugation.\(^4\) Due to site-isolation, the catalytic properties of the heterogenised catalysts (e.g., thermal stability and product selectivity) are often found comparable to the homogeneous analogues.\(^4,5\) Various strategies to heterogenise homogeneous catalysts have been discussed and reviewed by McMorn and Hutchings.\(^6\)

In general, to achieve diastereoselective or even enantioselective catalysis over porous materials, there are two commonly accepted strategies. The first strategy is to engineer ‘homochiral framework’\(^7\) such as the first chiral mesoporous ITQ-37 germanosilicate zeolite with one single gyroidal channel reported by Sun \textit{et al.}\(^8\) Dryzun \textit{et al.} revealed the existence of 20 chiral silicate zeolites which have not been recognised as chiral in their original publications, as revealed by comparative adsorption calorimetric experiments with D-/L-histidine.\(^9\) The use of chiral organic structure-directing agents can transfer the chiral functionality into the zeolite-type frameworks as discussed extensively by Gómez-Hortigüela and Bernardo-Maestro,\(^10,11\) and by Davis.\(^11,12\) The chirality induction effect can be often observed by templating with an enantiopure organic linker.\(^13\) Calero \textit{et al.} have investigated the potential for enantiomeric separation of chiral zeolites based on molecular simulations.\(^14\) Adsorption with different geometries and enthalpies have been shown, as seen in the illustration in Fig. 1.

Metal–organic frameworks (MOFs) are another class of microporous materials that can possess frameworks with chirality.

Fig. 1 Snapshots of pure L (left), and pure R (right) CHBrClF isomers adsorbed in STW at 298 K and a total fugacity of 100 kPa. The central carbon atom of the molecule is coloured red for the L-isomer and light blue for the R-isomer. The different atoms of the molecule are also coloured: Br = grey; Cl = yellow; F = green; H = white. Reprinted (adapted) with permission from ref. 14. Copyright (2010) American Chemical Society.
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organic linkers play a pivotal role in governing the dimension
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chirality of the MOF framework. Readers can find more infor-
dichroism (CD) spectroscopy is a handy tool to reveal the
addition to the typical characterisation techniques for solid-
instance, Li
chiral metal complexes to achieve asymmetric catalysis. For
works (MOFs) have gained increasing attention as they can host
limiting their potential in broader commercial applications.
Another example is the aziridination of styrene over Cu–Y
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supercage, meanwhile, can prevent the Cu-salen from leaching
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zeolite; the confinement effect exerted by the rigid
framework of zeolites. The highly ordered hierarchical structures of
zeolites can isolate the metal complexes through electrostatic
interaction. These two effects (i.e. active site isolation and zeolitic
confinement) can work in synergy to offer steric specificity to
enhance the catalytic properties in asymmetric catalysis. For
instance, the supercage of Y zeolite can only accommodate a
Cu-salen species with quasi-planar tetragonal coordinate.23 The
supercage, meanwhile, can prevent the Cu-salen from leaching
during catalysis. Even after six catalytic cycles, high catalytic
performance (activity and selectivity) can be maintained. Another example is the aziridination of styrene over Cu–Y
zeolite; the confinement effect exerted by the micropores of Y
zeolite introduces notable diffusion limitations for the reactants
and products. The active site in the Cu–Y catalyst is proposed to be
more constrained than the homogeneous counterparts. It is also
found that water has a slightly deleterious effect over enantio-
metric excess (e.e.) during the aziridination of styrene.25,28

In some cases, the zeolitic framework can exert additional
confinement effect onto the substrate, rendering various reac-
tions with higher enantioselectivity than the homogeneous
counterparts.29 It should be noted that for most immobilised
catalysts in zeolites, the enantioselectivity (in terms of e.e.)
typically remains or declines with the extent of reaction. There
are extensive reports over the use of encapsulated chiral metal-
salen complexes for asymmetric catalysis.2,10–36 Besides zeolitic
Duan et al. reported an enantiomorph pair of Ce-based MOFs
resulted using opposite enantiomeric organic linkers.15 Similar
to the syntheses of achiral MOFs, the inherent structures of the
organic linkers play a pivotal role in governing the dimension of
the channels/pores.16,17 Wu, Lin and co-workers reported a
Cd-based homochiral MOF (1) which is constructed by linking
infinite one-dimensional [Cd(μ-Cl)]₄ zigzag chains with axially
chiral bipyridine bridging ligands ((R)-6,6'-dichloro-2,2'-dihydroxy-
1,1'-binaphthyl-4,4'-bipyridine) containing orthogonal secondary
dihydroxy groups18,19 (see Fig. 2). The secondary dihydroxy groups
were utilised as the asymmetric catalytic active sites for highly
selective conversion of aromatic aldehydes to secondary alcohols.
Lin and co-workers also employed a similar strategy to prepare a
Cu-based (using 4,4',6,6'-tetramethoxybenzilidene) and Ni-based (using
(R,R)-2,2'-dihydroxy-1,1'-binaphthyl as the organic linker)17 and a Ru-based (using (R,R)-1,2,cyclo-
hexanediimino-N,N'-bis(3-tert-butyl-salicylidene) as the organic
linker) homochiral MOFs20 for asymmetric catalysis. Cui et al.
reported a series of Cd-based homochiral MOFs by employing
Co- and Ni-based salen complexes as the precursors.21 In
addition to the typical characterisation techniques for solid-
state materials (such as X-ray diffraction), solid-state circular
dichroism (CD) spectroscopy is a handy tool to reveal the
chirality of the MOF framework. Readers can find more infor-
mation in the detailed review covering various spectroscopic
techniques by Castiglioni et al.22 However, the synthesis of
chiral zeolite-type materials remains a significant challenge,
limiting their potential in broader commercial applications.

The second strategy is to incorporate external chirality into
the pores/channels; achiral zeolites and metal–organic frame-
works (MOFs) have gained increasing attention as they can host
chiral metal complexes to achieve asymmetric catalysis. For
instance, Li et al. reported the encapsulation of Cu-salen complex
into zeolite Y (see Fig. 3) for the selective oxidation of benzyl alcohol.23 Hutchings and co-workers have employed a similar
approach to design asymmetric heterogeneous catalysts for alcohol
dehydration,24 aziridination and epoxidation of alkene,25,26 and
carbonyl-ene and imino-ene reactions.27 These catalysts possess
high activity associated with homogeneous catalysts and facile
recyclability adherent to heterogeneous catalysts. In these studies,
the structure–activity relationship of asymmetric catalysts has been
more constrained than the homogeneous counterparts. It is also
found that water has a slightly deleterious effect over enantio-
metric excess (e.e.) during the aziridination of styrene.25,28

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**Fig. 2** Crystal structure of the Cd-based homochiral MOF reported by Wu et al.16 (A) The 2D square grid in 1. (B) The 1D zigzag polymeric chain in 1. (C) Schematic representation of the 3D framework of 1. (D) Schematic representation of the twofold interpenetration of 1. (E) Space-filling model of 1 as viewed down the c axis showing the chiral 1D channels of 13.5 × 13.5 Å² in dimensions. Colour scheme for (A), (B), and (E): cyan: Cd, green: Cl, red: O, blue: N, grey: C, and light grey: H. Reprinted (adapted) with permission from ref. 18. Copyright (2007) John Wiley and Sons.

**Fig. 3** Schematic of zeolite encapsulated metal-salen complexes. Reprinted (adapted) with permission from ref. 23. Copyright (2018) Elsevier.
materials, siloxane is another class of support material. Ogunwumi and Bein have immobilised Mn-salen complex into a siloxane elastomer network. However, the reported enantioselectivities for many cases without the use of a rigid chiral ligand, like salen, are quite short-lived.

Asymmetric catalysis reactions have been documented over achiral zeolites,[37–44] particularly for β zeolites as summarised in the early review by Davis.[45] Renz et al. reported the catalytic epoxidation of chiral allylic alcohols by the Ti-β and TS-1 zeolites.[46] Akin to enzymatic catalysis, zeolites can stabilise one transition state of a stereoisomer over another due to the restriction and confinement of the pores. The location of the active sites with respect to the porous frameworks is pivotal. The intrinsic reactivity of the metal active site is another important factor for catalysis.[16,47,48] For example, the reactivity (in terms of conversion and yields) of Rh-BINAP-MOF is higher than the Ru analogue.[48] The reaction activity of heterogeneous Rh-BINAP-MOF catalyst was compared with a homogeneous control; the reactivity of Rh-BINAP-MOF was found three times better than the homogeneous analogue, which has been ascribed to the site isolation effect within solid-state materials. It prevents the catalysts from intermolecular deactivation. However, it is still challenging to achieve highly selective chiral reactions (high e.e.) because of the high framework rigidity of these types of solid-state materials.

Based on the density functional theory (DFT) calculations, specific ‘chiral cells’ can be tailored by doping Ca+ into Al-rich zeolites with the MFI topology to create an enantiospecific environment for 4-ethyl-4-methylpentane.[49] Das and Marek have employed R- and S-4-ethyl-4-methylpentane (the simplest chiral saturated hydrocarbon with a quaternary stereogenic centre) as a chiral probe molecule to demonstrate the enantiospecific adsorption preference on MFI zeolites.[49] For non-bulky and flexible polar organic molecules, there is a high degree of rotational freedom with respect to the zeolitic channels/pores, leading to the absence of enantioselective adsorption. But for bulky and rigid adsorbates, like ibuprofen, the comparable size between the adsorbate molecule and the pore/channel (in achiral MIL-47 and MIL-53)[49,51–53] creates notable confinement effect, promoting the formation of intermolecular hydrogen bonds. Even with the aid of computation modelling, it is challenging to predict a very detailed molecular knowledge of the system. Neither a chiral MOF can necessarily separate small isomers nor is an achiral MOF unselective towards some mixtures of enantiomers, as summarised by the prediction computations by van Erp and co-workers.[49,51]

The key factors to incorporate chiral functionality into porous materials are (a) the site-isolation effect and (b) the confinement restraints exerted by the rigid frameworks. Given the low-cost and high abundance of achiral zeolites and MOFs, it is valuable to study how to design specific ‘chiral regions’ that can offer extensive possibilities and potential for asymmetric catalysis. We have recently discussed the differential adsorption properties of lysine (Lys) by achiral MFI zeolites.[54] It has been ascribed to the difference in the local adsorption geometries of L- and D-Lys on the zeolitic Bronsted acid sites (BASs), as revealed by combined thermogravimetric analyses (TGA) and the Rietveld refinements of the high-quality synchrotron X-ray powder diffraction (SXRD) data.

2. Enantiospecificity in achiral zeolites

This work will further investigate the enantiospecificity in achiral zeolites with MFI and MOR topologies. Circular dichroism (CD) spectroscopy, TGA and the Rietveld refinements of the high-resolution SXRD data will be employed to understand the adsorption chemistry. The inherent site-isolation effect and the confinement restraints will shed light on the future design of asymmetric catalysis reactions over achiral materials.

As presented in Fig. 4, the difference in the Bragg’s peak intensities of the SXRD patterns of L- and D-Lys in MFI (‘MFI-L-Lys’ and ‘MFI-D-Lys’) can be noticeably observed. However, as seen in the normalised intensity of L- and D-Lys in MOR (‘MOR-L-Lys’ and ‘MOR-D-Lys’), no significant difference is observed, inferring that the adsorbate structures are similar. The structural parameters as determined by the Rietveld refinements of the SXRD patterns are summarised in Table S1 (ESI†). The unit cell volume expands by 0.47% and 0.42% upon the adsorption of L- and D-Lys on MFI. It expands to a similar extent upon L-Lys (0.16%) and D-Lys (0.06%) adsorption on MOR. The marginal change in the unit cell volumes can be ascribed to the high rigidity of the zeolitic frameworks that can host Lys without affecting the original T–O–T (where T = Al or Si) covalent arrangements.

The derived crystal structures from the Rietveld refinements of the high-resolution SXRD data of MFI-L-Lys and MFI-D-Lys are presented in Fig. 5. The MFI structures have two independent sites, I and II (both Wyckoff letters of 4c, Fig. 5(a) and (b)), whereas MOR-L-Lys and MOR-D-Lys only reveal a binding site, I (Wyckoff letter of 16h, Fig. 5(c) and (d)). The O\textsubscript{Lys}·O\textsubscript{Framework} and N\textsubscript{Lys}·O\textsubscript{Framework} interatomic distances in both zeolites are in the range between 2.4–3.2 Å, which falls in the typical range of molecular adsorption in zeolites. As reported, both L- and D-Lys exhibit an end-on interaction to the protons BASs (δ+) via an oxygen of the α-carboxylate group (δ−).[54] In MOR, Site I resides along the major [0 0 1] 12-membered ring (12-MR) straight channel (channel diameter of 6.5 × 7.0 Å), which agrees with the adsorption findings by Arletti et al.[55,56] Note that MOR is often represented by isolated cylindrical columns, which also contains [0 0 1] 8-MR straight channels but its dimension of 2.6 × 5.7 Å is too small to host Lys molecules. Due to the isolated-cylindrical-column system of MOR, the L- and D-Lys adsorbate structures in MOR are highly comparable. On the other hand, the adsorbate structures of L- and D-Lys on MFI are noticeably dissimilar, where the lysyl side chains are directed to different channel exits. It can be ascribed to the unique framework structure, with the interconnected straight-sinusoidal channel along the [1 0 0] axis. The much more stable conformation of the L-Lys adsorption within MFI has been verified by the DFT calculations.[54] In the cases of MOR-L-Lys and MOR-D-Lys, the adsorbate geometries of L- and D-Lys can hardly be affected by the MOR framework. The combination of site-isolation effect
(inherent BASs) and confinement restraints (by the zeolitic framework) gives us a much more extensive perspective in understanding why MOR does not offer differential adsorption on Lys.

To reveal the enantiospecific desorption behaviours of Lys from MFI, in situ SXRD measurements as a function of temperature were conducted. The change in the atomic parameters of L- and D-Lys in MFI at temperature-resolved conditions can provide a more thorough understanding of the adsorption chemistry. The in situ synchrotron data were collected on Beamline BL02B2 at SPring-8 (Japan) with the X-ray energy optimised at 18 keV. The wavelength of the synchrotron X-ray was calibrated as $\lambda = 0.689556(2)$ Å and 2θ-zero-point = $-0.000015(1)$° using SRM674b CeO$_2$ standard (space group: Fm$\overline{3}$m, $a = 5.41153(30)$ Å). The temperature-programmed desorption conditions were applied on the capillary samples using an N$_2$ gas flow device. From 25 to 500 °C (Fig. 6), in situ SXRD profiles with different shapes can be noted. Taking the first peak at around 3.5° (merged Bragg (101) and (011) reflections) as an example, the profile dips at around 225–250 °C. An upward trend is typical due to the removal of adsorbate species from the microporous frameworks. Notably, the merging of (200) and (020) at elevated temperatures were observed in the in situ SXRD profile of MFI-D-Lys. The variations in the crystallographic parameters are presented in Fig. S2(a)–(d) (ESI†). The unit cell volume decreases gradually at elevated temperatures, signifying the removal of L-/D-Lys adsorbate from the host. For MFI-L-Lys, the unit cell shrinks by 0.23% (from 5403.29 Å$^3$ to 5391.27 Å$^3$) from 25 to 500 °C; for MFI-D-Lys, the unit cell shrinks by 0.21%.

The Rietveld refinements of the in situ synchrotron data were applied to study the change in the site occupancy factors (SOFs) of Sites I and II with respect to the sample temperature. Rigid body Z-matrices were employed to describe L- and D-Lys species within the zeolite hosts. The variations in the atomic parameters from the Rietveld refinements are presented in Fig. S2(e) and (f) (ESI†).
decreasing trends with two apparent regions of desorption behaviours. In both SOF curves, the slopes change consistently at ca. 225–250 °C. This agrees with our TGA findings that the sharpest differential peak of each sample lies at ca. 235 °C (discussed later). Interestingly, the SOF of Site I in MFI-v-Lys decreases at a much slower rate beyond 250 °C than that observed in MFI-I-Lys; we can also observe a similar pattern in the variation in the unit cell volume.

We also employed CD spectroscopy and TGA to verify our crystallographic findings. CD, the most common technique to study the chirality of different species, can directly measure the extent of polarised light passing through a sample. As seen in Fig. S3 (ESI†), upon sequential additions of MFI zeolites, the changes in the normalised CD intensities of the v- and n-Lys differ by 18% (cf. k = −0.0648 (for v-Lys) vs. k = −0.0794 (for n-Lys)). In contrast, the corresponding changes upon the addition of MOR zeolites are alike (cf. k = −0.0997 vs. k = −0.0951). Our TGA data also reveal a similar extent of differential adsorption of Lys by MFI and MOR (Fig. S4, ESI†). From the TGA of Lys from MFI, the first desorption behaviour peaks at around 160 °C, followed by a sharp desorption peak at around 235 °C. The peak desorption temperature of v-Lys is 11.3 °C higher than that of n-Lys from MFI. For the adsorption of Lys by MOR, the TGA results are consistent with the CD findings, with comparable peak desorption temperature (cf. 206.8 °C vs. 207.7 °C). Based on the TGA results as presented in Fig. S4 (ESI†), the n/v-Lys ratio of adsorption by MFI was determined to be 1:1.12 (cf. 73 mgg−1Lys per gMFI and 82 mgg−1Lys per gMFI). The n/v-Lys ratio of adsorption by MOR was determined to be 1:1 (cf. 69 mgg−1Lys per gMOR and 69 mgg−1Lys per gMOR). The difference in the quantity adsorbed suggests that an obvious differential adsorption behaviour of n/v-Lys only over MFI. It should be noted that these calculations were based on the weight difference from 100 °C as measured in TGA, where the weight loss below 100 °C was disregarded that can be primarily caused by physisorption.

The presence of ‘chiral regions’ can be ascribed to the site-isolation effect of the protonic BASs and the confinement restraints by the MFI framework. We further testify this postulation by incorporating an extra-framework adsorption site by ion-exchange with Cu(NO3)2. As presented in Fig. S5 (ESI†), the powder X-ray diffraction patterns of Cu2+-exchanged MFI-L-Lys and MFI-v-Lys show noticeable differences in the Bragg’s peak intensities, which is consistent with the synchrotron data on the undoped MFI collected in SPring-8. The structural parameters are summarised in Table S5 (ESI†). From the Rietveld refinement of the diffraction data, the content of Cu2+ per unit cell of H-ZSM-5 was determined as 1.89(3). It suggests that about a low concentration of BASs (about 0.2 per unit cell) were remaining after ion-exchange, by taking the structural formula of the pristine zeolite sample (H4Al6Si14O42) into account. The unit cell volume decreases marginally by 0.015% and 0.058% respectively. Interestingly, the first peak desorption temperature from the differential TGA of the two samples doped with Cu2+ become 204.0 °C and 204.2 °C (see Fig. S6, ESI†), suggesting almost identical sorption properties. It contrasts with the samples without Cu2+ doping, where the first peak desorption temperatures differ by 11.3 °C. Without high-temperature calcination treatment, the extra-framework hydrated metal ions typically locate about 3 Å away from the framework O atoms.5,57,58 This provides a much less confined environment for Lys adsorption on the Lewis acidic Cu2+ ions, where the lysyl side chains of both v- and n-Lys possess more spatial freedom. The ‘strain-free’ adsorption environments on the Lewis acidic Cu2+ sites have almost eliminated the strain as observed over the BASs in the pristine MFI samples. Based on previous computational findings, the asymmetric positioning of the extra-framework cationic sites (such as Cu2+) in unique framework structures can create chiral environments due to the difference in channel exits.49 Despite that we have reported a ‘strain-free’ environment for the adsorption of lysine molecules by the doping of Cu2+ in H-ZSM-5, this experimental result has inferred the realisation the rational tuning of the enantiospecific properties of microporous structures.

3. Conclusion and outlook

In summary, we have revealed the enantiospecific adsorbate structures of v- and n-Lys in zeolites with the MOR and MFI topologies. The difference is originated from the host zeolite structures. In particular, the adsorption sites at the interconnecting straight-sinusoidal channel framework of MFI render specific adsorption geometries with respect to the chirality of v- and n-Lys. Whereas, in the straight-channel-only MOR structure, the corresponding adsorption geometries are similar. Both the inherent site-isolation effect of the BASs and internal confinement restraints are critical for creating ‘chiral regions’ that leads to enantioselective adsorption behaviours (Scheme 1). While achieving highly enantioselective reactions over heterogeneous catalysts...
is challenging, the advantages of using solid-state materials for gas/liquid phase reactions should be recognised. This fundamental understanding and insights will help the rational design of enantiospecific sites in both achiral and chiral materials for more selective asymmetric catalysis reactions. For instance, it is promising to introduce the site-isolation effect in the channel of porous materials by utilising the metal-doping strategy with the intrinsic confinement effect by the channels.

In the near future, the application of porous material can be extended to asymmetric catalysis based on the rational design of ‘chiral region’ in achiral solid-state materials. We believe that the product selectivity (in terms of e.e.) in asymmetric catalysis can be enhanced by establishing active sites with well-fitted structural specificity for the adsorption and stabilisation of certain reaction substrates and intermediates (or transition states) over another stereoisomer. Elucidating the adsorbate structures of enantiomeric pairs on the cationic sites will thus be pivotal for the utilisation of the ‘chiral regions’. It will offer a rational guide towards where the cationic sites should be placed with respect to the microporous frameworks for the optimisation of adsorption geometries in asymmetric catalysis.

Conflicts of interest
There are no conflicts to declare.

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