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Chiral porous organic frameworks for asymmetric heterogeneous catalysis and gas chromatographic separation†

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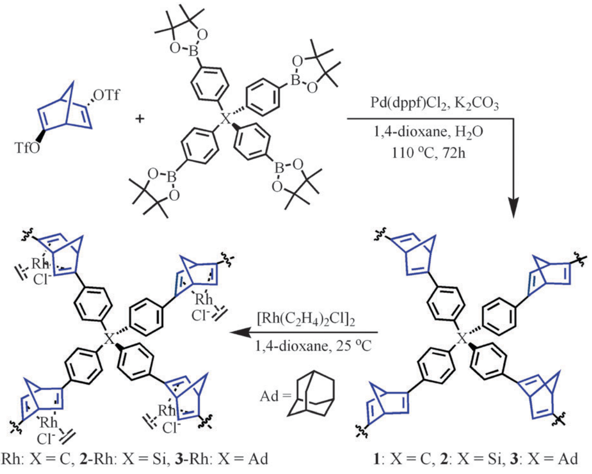
Three chiral robust diene-based porous organic frameworks (POFs) are prepared. POF-1 is shown to be an efficient heterogeneous catalyst after metallation for asymmetric conjugation addition with up to 93% ee, and it can also function as a new chiral stationary phase for gas chromatographic separation of racemates.

Porous organic frameworks (POFs), including covalent organic frameworks (COFs), are constructed from well-designed organic precursors through coupling or condensation reactions,[1,2] and have emerged as a new class of porous materials for diverse applications.[3–5] In particular, just like their metal–organic framework (MOF) counterparts,[6] POFs may serve as a solid platform for incorporating molecular catalytic modules into heterogeneous catalyst systems by taking advantage of their permanent porosity and the ability to tune their compositions at the molecular level.[1d,e,5] POFs, despite the amorphous nature for most of them, are unique because of their high thermal and chemical stability in comparison with MOFs. Although lots of POFs have been reported, only a small fraction of them are chiral species and versions featuring accessible functional sites that induced enantioselectivity remain scarce.[1,7] In fact, only several asymmetric POF catalysts have been generated either *via* a post-synthesis modification strategy or by direct incorporation of catalytically competent bridging units into the frameworks.[7]

As a recently emerging ligand class, chiral olefins have been widely utilized as steering ligands for transition-metal-catalyzed asymmetric reactions.[8] In particular, C_2-symmetric chiral diene ligands bearing internal olefins and rigidly bicyclic frameworks confer higher activities and enantioselectivities than phosphorus ligands in rhodium- and iridium-catalyzed asymmetric addition reactions.[9] We report here the synthesis of three robust chiral porous POFs based on enantiopure diene ligands and show that the solids could be utilized as recyclable heterogeneous catalysts, after being post-modified with Rh(I) ions, for asymmetric 1,4-addition reactions with up to 93% ee and as a new chiral stationary phase (CSP) for gas chromatographic separation of racemic molecules.

As shown in Scheme 1, POFs **1–3** were synthesized by the Suzuki–Miyaura cross coupling polycondensation of bis-triflate (1*R*,4*R*)-bicyclo[2.2.1]hepta-2,5-diene and three connectors in the presence of a Pd catalyst under alkaline conditions. Such polycondensation reactions lead to three inherent porous polymers with built-in chiral diene platforms. We examined the cross-coupling polycondensation reaction using different conditions, including solvent, base and Pd catalyst, with the aim of achieving maximal surface areas for the resulting materials. As optimal conditions, polycondensation in 1,4-dioxane/H_2O (4 : 1 v/v) in the presence of K_2CO_3 as base and Pd(dppf)Cl_2 as catalyst for 72 h allows for the preparation of the polymers with good surface areas. After repeated rinsing with water, THF, EtOH, CH_2Cl_2 and acetone, POFs **1–3** were rigorously washed by



Scheme 1 Synthesis of chiral POFs **1–3**.

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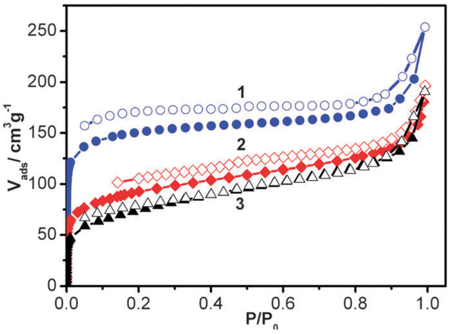


Fig. 1 N_2 adsorption isotherms (filled symbols) and desorption isotherms (open symbols) of **1–3** at 77 K.

Soxhlet extraction for 24 h with THF, EtOH, CH_2Cl_2 and acetone as solvents, respectively, to remove any entrapped molecules and impurities and then dried under vacuum overnight.

The permanent porosity of **1–3** was demonstrated by N_2 adsorption measurements at 77 K (Fig. 1). All of them exhibit a type I sorption behavior with Brunauer–Emmett–Teller (BET) surface areas of 471, 312 and 252 $m^2 g^{-1}$, respectively, with total pore volumes of 0.393, 0.304 and 0.295 $cm^3 g^{-1}$. The pore size distribution calculated using nonlocal density functional theory reveals three pore size distributions at around 7.1, 6.9 and 6.8 Å. The ^{13}C CP/MS NMR spectrum of **1** displayed four peaks at 125.31, 121.98, 46.17, 30.36 ppm assignable to chiral diene linkages and signals at 64.63, 145.50, 130.56, 128.92 and 128.08 ppm owing to the tetraphenylmethane units (Fig. 2). ^{13}C CP/MS NMR spectra of **2** and **3** also suggested the successful incorporation of diene units in their polymers (Fig. S6, ESI†).

These POFs are insoluble in water, hydrochloric acid (6 M), sodium hydroxide (8 M) and common organic solvents that were tested, consistent with their cross-linked networks. TGA show that the decomposition of these framework starts at ~550 °C. The PXRD patterns indicated that these POFs are amorphous in nature. Field emission scanning electron microscopy (FE-SEM) revealed that they consist of spherical particles and display rough surfaces and appear to be aggregates of much smaller particles (Fig. 3). The average particle sizes of **1–3** were about 40, 400 and 550 nm, respectively. Interestingly, the microporous structure of **1** can even be directly visualized by high resolution tunneling electron microscopy (HR-TEM), as shown in Fig. 3b. One clear feature of the porous texture is that the micropores are present homogenously and are similar in size.

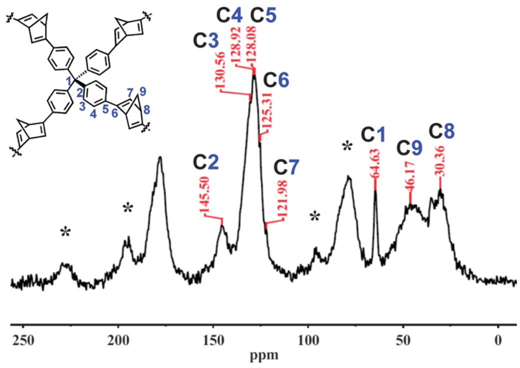


Fig. 2 The solid-state ^{13}C CP/MS NMR spectrum of **1** (signals with * are sidebands).

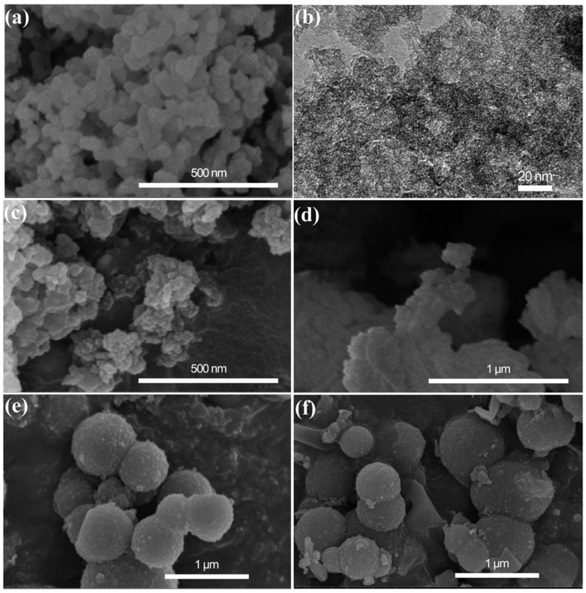


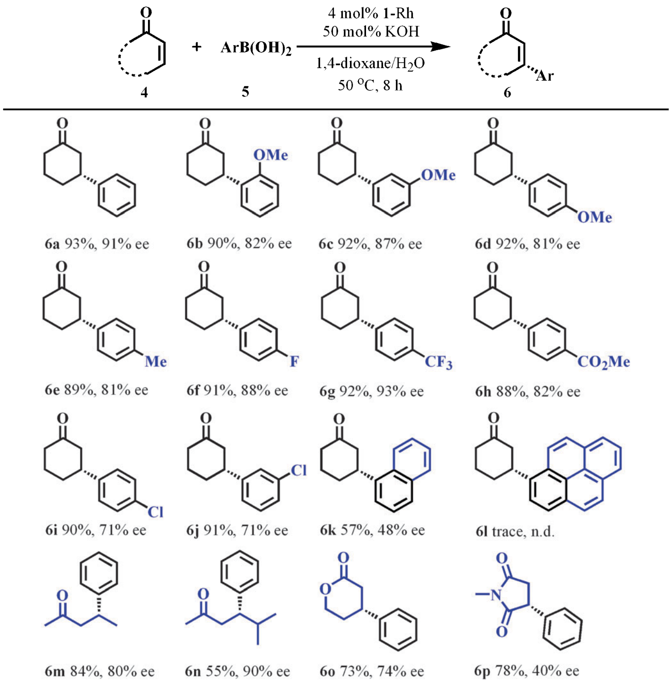
Fig. 3 (a) SEM and (b) TEM images of **1**, SEM images of (c) **1**-Rh and (d) **1**-Rh after five cycles and SEM images of (e) **2** and (f) **3**.

We have utilized **1–3** for heterogeneous asymmetric catalysis by taking advantage of the accessible chiral diene groups. $[Rh(C_2H_4)_2Cl]_2$ can react with the dienes in the polymers or its analogues to afford Lewis acidic $[(diene)Rh(C_2H_4)]^+$ species,[9] which are active catalysts for the addition of carbon-based nucleophiles to α,β-unsaturated ketones and esters. Post-synthetic metalation of the POFs was performed by treating with 0.5 equiv. of $[Rh(C_2H_4)_2Cl]_2$ (relative to the diene equivalents in polymers) in 1,4-dioxane at room temperature to afford **1**-, **2**- and **3**-Rh. Inductively coupled plasma optical emission spectrometer (ICP-OES) analyses of the digested metalated polymer gave the Rh loading of 20.5, 19.0 and 16.5 wt% for **1**-, **2**- and **3**-Rh, respectively. **1**-Rh gave a decreased BET surface area (186.0 $m^2 g^{-1}$) compared with **1**, whereas **2**-Rh and **3**-Rh only gave surface sorption. After optimization of reaction conditions, **1**-Rh was found to be an active catalyst for the 1,4-addition of arylboronic acid to 2-cyclohexenone in 1,4-dioxane/H_2O (10 : 1 v/v) in the presence of KOH at 50 °C. Specifically, 4 mol% loading of **1**-Rh catalyzes the addition of phenylboronic acid to 2-cyclohexenone to give the 1,4-addition product (**6a**) in nearly quantitative conversion with 93% isolated yield and 91% ee in 8 h. Under similar conditions, the yield and ee observed for **1**-Rh are comparable with those obtained using the homogeneous analogue (94% yield and 96% ee), although the heterogeneous reaction required longer time because of slow-mass diffusion (8 h *vs.* 1 h).[9] Notably, relatively few heterogeneous catalysts are active in asymmetric conjugate 1,4-addition reactions.[6e,10] Very recently, Lin *et al.* reported the use of a Rh-BINAP MOF for the catalytic addition of phenylboronic acid to 2-cyclohexenone, affording the product in 99% ee but with moderate activity (80% yield in 20 h).[10]

With the optimal reaction conditions in hand, the substrate scope of the reaction was examined. A range of arylboronic acids could react with 2-cyclohexenone to produce the corresponding products (**6a–6j**) in 88–93% yields with 71–93% ee. Arylboronic acids with an electron-donating methoxy group, regardless of its relative position (*ortho*, *meta* or *para*), gave the products **6b–d** in ∼90% yield with 81–87% ee. Whereas arylboronic acids with electron-withdrawing groups such as –F, –Cl and –CO_2Me and –CF_3 gave the products **6f–j** in ∼90% yield with 71–93% ee. The highest enantioselectivity of 93% ee was attained with the phenylboronic acid bearing a 4-trifluoromethyl group. Besides, **1**-Rh was also active in the addition of phenylboronic acid to linear enones, producing **6m** and **6n** in 84% yield with 80% ee and 55% yield with 90% ee, respectively. Heterocyclic enones were also converted into the addition products, producing **6o** and **6p** in 73% yield with 74% and 78% yield with 40% ee, respectively. We also examined the catalytic activities of **2**- and **3**-Rh, both of which exhibited lower activity and enantioselectivity than **1**-Rh under otherwise identical conditions. For example, 4 mol% loading of **2**-Rh and **3**-Rh catalyzed the conjugated addition of 3-methoxyphenylboronic acid to 2-cyclohexenone affording the product in 78% yield with 76% ee and 76% yield with 68% ee, respectively (Table 1).

To investigate whether the catalysis by **1**-Rh occurred predominantly within the pores of the solid or just on the surface, competitive size selectivity studies were carried out. The addition of 1-naphthylboronic acid to 2-cyclohexenone gave the product **6k** in 57% yield in 8 h. When a sterically more demanding substrate 1-pyrenylboronic acid was subjected to the reaction, almost no desired product **6l** was detected after 12 h, whereas the homogeneous diene catalyst could still give the product in 96% yield. This result may suggest that this bulky substrate cannot access the catalytic sites in the framework due to its large diameter. It is thus likely that the catalytic reactions are heterogeneous and may occur within the POF.

Table 1 Asymmetric conjugation addition of arylboronic acids to 2-cyclohexenone catalyzed by **1**-Rh[a,b,c]



6a 93%, 91% ee
6b 90%, 82% ee
6c 92%, 87% ee
6d 92%, 81% ee
6e 89%, 81% ee
6f 91%, 88% ee
6g 92%, 93% ee
6h 88%, 82% ee
6i 90%, 71% ee
6j 91%, 71% ee
6k 57%, 48% ee
6l trace, n.d.
6m 84%, 80% ee
6n 55%, 90% ee
6o 73%, 74% ee
6p 78%, 40% ee

[a] Reactions were carried out with enone (0.2 mmol), arylboronic acid (0.4 mmol), 4 mol% **1**-Rh, and 50 mol% KOH in 1,4-dioxane (1.0 mL, 10 : 1 v/v) for 8 h at 50 °C. [b] Isolated yield. [c] ee values were determined by HPLC.

All of the products obtained with (*R*,*R*)-**1**-Rh have the absolute *R* configuration, consistent with that observed in the homogenous control system. This suggests that the POF catalyst relies on the intrinsic chiral environments of the active diene sites to exert stereocontrol. The walls of the pores in the solid catalyst may provide preferential secondary interactions between the substrate and the framework, leading to shape- and size-selectivities that are not achievable in homogeneous systems.

The supernatant from the reaction of phenylboronic acid to 2-cyclohexenone after filtration through a regular filter did not afford any additional addition product, suggesting the heterogeneous nature of the reaction system. Upon completion of the reaction, polymer **1** could be readily recovered by centrifugation and, after washing with THF and heating under vacuum, reused for the next cycle by the addition of 0.004 mol $[Rh(C_2H_4)_2Cl]_2$ without significant loss of activity and enantioselectivity.[11] The yield/ee's for the five consecutive runs are 91/86%, 90/85%, 90/84%, 88/84% and 87/84%, respectively.

We also examine the utility of the diene-based POF-**1** as a new chiral stationary phase (CSP) for gas chromatographic (GC) separation of racemic compounds. The **1**-coating open tubular column (15 m × 250 μm i.d.) for GC was prepared by a dynamic coating method.[12] The average of the McReynolds constants is calculated to be 135, indicative of the moderate polarity of the CSP.[12] SEM images showed that the fabricated column had an approximately 1 μm thick coating on the inner wall (Fig. S8, ESI†). The performance of the CSP was evaluated by GC separation of racemates of secondary alcohols and amines. After many attempts, racemic mixtures of 1-phenylethanol and 1-phenylethylamine were resolved at 150 °C, with separation factors (α) of 1.13 and 1.17 and retention factors (k_1) of 0.23 and 0.21, respectively (Fig. 4). There are the same elution orders for the two analytes, in which *S* enantiomers are eluted after *R*. All enantioseparations have short retention times, and it might be suitable to perform a quick analysis of the enantiomers. Notably, the **1**-coating GC column remained active for separation of 1-phenylethanol after 30 h working time. In addition, 1-phenylpropanol and 1-phenylpropylamine could also be partly

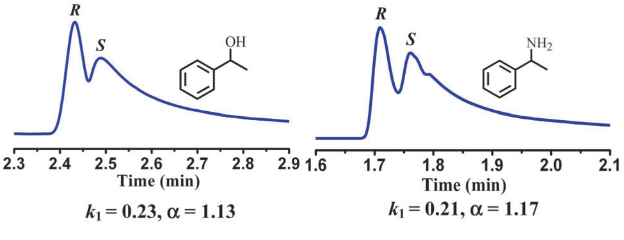


Fig. 4 GC separation of 1-phenylethanol (left) and 1-phenylethylamine (right) on the **1**-coating column at 150 °C.

resolved by this CSP (Fig. S9, ESI†). Despite the moderate stereoselectivity, **1** represent a new generation of robust porous materials that are capable of chiral separation of racemates. Chiral separation has been reported for MOFs[6d,13,14] and supramolecular metal–organic and organic assemblies.[15] Porous organic materials, however, might have specific advantages given their scalability and chemical stability and hold great potential for analytical chiral separations and even preparative separations. Further study on enantioseparation with chiral organic frameworks is in progress.

To better understand the GC column separation process, we obtained the Van't Hoff plot of 1-phenylethanol by changing the column separation temperature (Fig. S11, ESI†).[16,17] According to the Van't Hoff equation, we calculated the molar adsorption enthalpy and entropy changes ($\Delta_{\mathrm{ads}}H_{\mathrm{m}}$ and $\Delta_{\mathrm{ads}}S_{\mathrm{m}}$, respectively) of (*R*)- and (*S*)-1-phenylethanol binding with the column. The $\Delta_{\mathrm{ads}}H_{\mathrm{m}}$ of (*R*)- and (*S*)-1-phenylethanol are -34.0 and -35.4 kJ mol^{-1}, respectively. The isoenantioselective temperature (T_{iso}) of 336 °C was above the GC oven temperature of 150 °C, suggesting that the separation process is enthalpy controlled and strong interactions such as hydrogen bonding and CH$\cdots\pi$ interactions between the analyte and the CSP are the major driving forces.[15] In addition, the difference $\Delta(\Delta_{\mathrm{ads}}H_{\mathrm{m}})_{R-S}$ of 1.4 kJ mol^{-1} between (*R*)- and (*S*)-1-phenylethanol suggests that the (*S*)-enantiomer binding with the column is more stable than the (*R*)-one, consistent with that the (*S*)-enantiomer was eluted after the (*R*)-enantiomer.

In conclusion, we have prepared three chiral porous diene-based POFs *via* cross coupling polycondensation. The diene groups accessible *via* open pores of the frameworks could be metallated with rhodium ions to give an efficient heterogeneous catalyst for asymmetric 1,4-addition of arylboronic acids to enones with up to 93% ee. For the first time, we demonstrated the utility of a porous POF as a CSP in the chromatographic separation of racemates based on their different supramolecular interactions with the selector. The ready tunability of such a modular approach based on olefins promises to lead to a number of chiral organic solids with unique and practically useful enantioselective functions.

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