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An achiral manganese salen catalyst encapsulated in a peptidic phosphonate homochiral solid for the enantioselective formation of diols by consecutive epoxidation and hydration reactions†

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An insoluble, porous, amorphous, homochiral material based on a polypeptide titanium–phosphonate scaffold with an encapsulated *achiral* Mn^{III}–salen was prepared and characterized. Consecutive epoxidation and hydration of styrene and its derivatives by aqueous hypochlorite in THF showed the highly enantioselective (> 99%) formation of styrene diol derivatives.

High atom and chiral economy[1] towards waste-free processes is an important goal in asymmetric catalysis.[2] High enantioselection has been achieved with homogeneous catalysts, yet separation, recovery, and reuse remain arduous.[3,4] A number of approaches have been developed for the design of immobilized homogeneous chiral catalysts or heterogeneous chiral catalysts.[3–6] Heterogeneous chiral catalysts can be divided into the following types: (i) insoluble chiral catalysts, which either contain an organic (*e.g.* cross-linked polymers) or inorganic (*e.g.* zeolites) stationary support or are formed from homochiral organic–inorganic coordination polymers; the latter are also called self-supported catalysts. (ii) Soluble chiral catalysts with polymer or dendritic supports. (iii) Chiral catalysts coupled with a nonconventional reaction medium such as aqueous, fluorous, ionic liquid or $scCO_2$ media.[7] Organic–inorganic hybrid materials can be used to create porous structures by constructing extended solids from molecular building blocks.[8] In this way chiral porous coordination networks have been synthesized by choosing appropriate ligands and metals as building blocks.[8,9] Such metal–phosphonate based materials are advantageous since they (i) can be prepared using mild polymerization conditions, (ii) can form relatively stable materials and (iii) can incorporate a variety of functional groups.[10] Recently, we prepared a porous, homochiral and insoluble titanium–phosphonate using short L-leucine polypeptide chains as building blocks. This material catalyzed the enantioselective ring opening hydrolysis of styrene oxides to the corresponding chiral vicinal diols by a mechanism that differs from kinetic resolution.[11]

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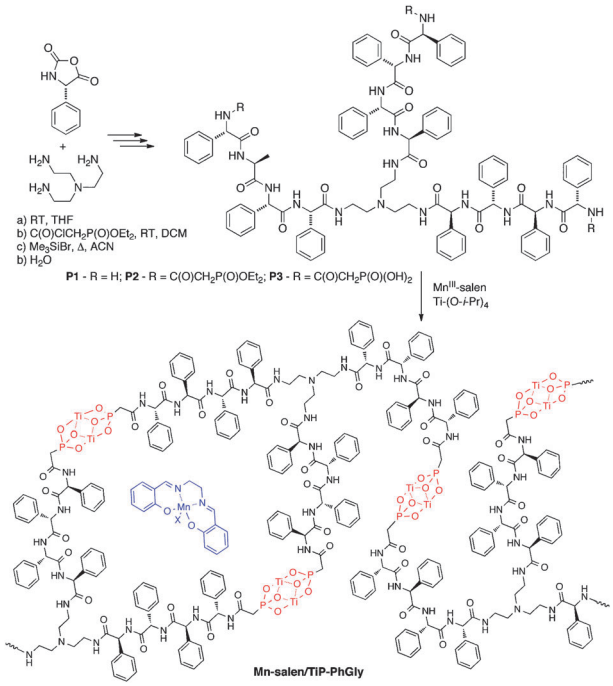
† Electronic supplementary information (ESI) available: Full experimental details of synthesis and characterization including elemental analysis, NMR, IR, UV-vis, and MALDI-TOF Mass spectroscopy, powder XRD, N_2-sorption, thermogravimetric analysis, and scanning and transmission electron microscopy. See DOI: 10.1039/c0cc04205f

We now demonstrate that the inclusion of a Mn^{III}–salen achiral catalyst into a porous, homochiral and insoluble titanium–phosphonate, thus confining the catalyst in a homochiral space, can be used for consecutive epoxidation and hydration reactions where styrene derivatives yield the corresponding vicinal diols with very high enantioselectivity. To our knowledge such a cascade of epoxidation–hydration has not been preformed consecutively in a one-pot reaction. Compounds with tethers containing amide groups tend to self organize through formation of hydrogen bonds between adjoining tethers.[12] We utilized this self organization by incorporating tripodal scaffolds into a titanium–phosphonate material. The synthetic strategy is outlined in Scheme 1. Polymerization of an amino acid, L-phenylglycine (L-PhGly), using its *N*-carboxy anhydride[13] on a tris(2-aminoethyl)amine initiator yielded the tripodal polypeptide with primary amine termini (P1). The terminal amines were then capped by



Scheme 1 Synthesis and idealized pictorial representation of the Mn–salen/TiP–PhGly material.

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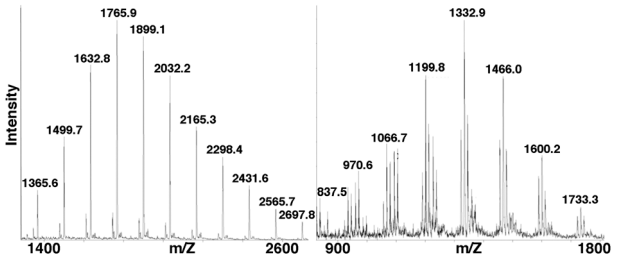

Fig. 1 MALDI MS of P1 (left) and P3 (right). For P1 there are M and M + Na (major) peaks. For P3 there are peaks for M, M + Na, M + 2Na, M + 3Na, M + Na + K and M + 2Na + K with $Z = 2$, and M, M + Na, M + K with $Z = 1$.

phosphonate functionalities (P2 and P3) with mild hydrolysis carried out by Me_3SiBr. Finally in the presence of Mn^{III}–salen, Ti–iso-propoxide was used for the non-hydrolytic condensation with the phosphonate P3 to yield the desired tripodal polypeptide scaffolds which were then immobilized by the titanium phosphonate network (TiP–PhGly) with encapsulated Mn^{III}–salen.

The degree of polymerization of L-PhGly was determined by MALDI mass spectrometry and showed a distribution of peaks attributable to 9–19 L-PhGly moieties in P1, Fig. 1, with a maximum at $m/z = 1766$ assigned to the molecular cation with 12 L-PhGly units plus Na. The MS of P3 reveals a distribution of peaks with a repeating unit of 66 indicating a range of doubly charged cation adducts for longer polymers. These are overlapped by peaks with a repeating unit of 132 for the shorter polymers.

Mn–salen/TiP–PhGly is not soluble in any solvent due to the cross-linked nature of metal–phosphonate structures. BET measurements showed a moderately high specific surface area of 77 $m^2\ g^{-1}$ with a wide distribution of nanometric pore sizes, notably micropores with an average diameter of 18 Å and mesopores of 35 and 123 Å, Fig. 2; see ESI† for details.

Mn–salen/TiP–PhGly was analyzed by elemental analysis and thermogravimetrically, see ESI.† The EDS measurement showed a Mn : P ratio of 1 : 9 indicating on average one Mn–salen complex per 3 tripodal polypeptides. The Ti : P ratio was 5 : 1. This ratio suggests that a cross-linked polymer may contain tripod arms linked *via* ten titanium groups between each two phosphorus atoms, and organized in a

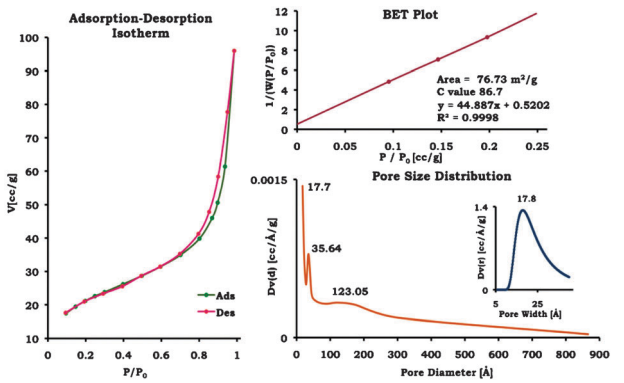

Fig. 2 N_2 adsorption isotherm (left), BET surface area (top right) and Barrett Joyner Halenda and Dubinin–Astakhov (inset) plots for mesopores and micropores, respectively (right bottom).

Table 1 Epoxidation and hydration of styrene derivatives (4-$R^1PhCR^2{=}CH_2$) catalyzed by Mn–salen/TiP–PhGly

Substrate	Conversion (%)	Epoxide selectivity %ee	Diol selectivity %ee
R^1 = H, R^2 = H	17	25, 36	65, >99
R^1 = H, R^2 = Me	84	35, 7	20, >99
R^1 = Me, R^2 = H	20	15, 10	40, >99
R^1 = Me, R^2 = Me	86	25, 5	25, >99

Reaction conditions: 4-$R^1PhCR^2{=}CH_2$ (0.1 mmol), NaOCl (0.5 mL buffered solution, 0.2 mmol oxidant), THF (0.5 mL), Mn–salen/TiP–PhGly (10 mg), 3 °C, 48 h. Conversion and selectivity were determined by GC; mostly chlorohydrins and dichlorostyrene derivatives were the by-products in a non-catalytic reaction.§ The %ee was determined by HPLC. The *S* isomer was the major isomer in all cases.

titanium phosphonate octahedral coordination sphere. The solid-state absorption spectra of Mn–salen/TiP–PhGly and of TiP–PhGly alone, see ESI†, clearly showed the incorporation of Mn–salen in the material.

The Mn–salen/TiP–PhGly‡ material was tested for a consecutive reaction sequence where Mn–salen catalyzes the epoxidation of a styrene derivative with NaOCl[14] and the homochiral TiP–PhGly scaffold catalyzes the highly enantioselective ring opening of the intermediate epoxide to the corresponding diol.[11] The results are shown in Table 1.

There are several notable points concerning the catalytic results. (1) Although Mn–salen is achiral, its encapsulation within the homochiral TiP–PhGly led to the formation of the *S* epoxide with low to moderate enantioselectivity. This is a rather unusual case where the chirality of the reaction medium induces an enanatioselective transformation using an achiral catalyst.[15,16] (2) As previously described for TiP–Leu,[11] § the hydration of the epoxide to the diol proceeds with almost exclusive formation of the *S* diol. We have suggested that the epoxide is activated by the polypeptide scaffold, followed by an enantioselective attack of water at the benzylic position directed by the homochiral peptide to yield *S*-styrene glycol. This was supported by using $H_2{}^{18}O$ in the hydration reaction of racemic epoxides by a non-encapsulated polypeptide titanium–phosphonate scaffold.[11] (3) The catalytic system is stable towards deactivation and leaching; recovery-recycle was carried out 3 times using styrene as the substrate with negligible loss to conversion and selectivity, neither in the case when the catalyst was washed and dried between recycles nor in the case when it was reused as is. The later method was also used to see if the pores were "blocked" by the substrate or product.

This research presents a proof of principle that an achiral catalyst encapsulated within a homochiral, insoluble porous material can lead to heterogeneous reactions with very high enantioselectivity and effective catalyst recovery.

Notes and references

‡ Mn–salen/TiP–Leu was also active for epoxidation–hydration reaction cascade, but the epoxide enantioselectivities were slightly lower. One can hypothesize that this is due to a better interaction between Mn–salen and PhGly *versus* Leu.

§ In reactions without Mn–salen, that is with TiP–PhGly only, no epoxide or diols were obtained although the chlorohydrins and dichlorostyrene derivatives were obtained as may be expected for non-catalytic addition of HOCl and Cl_2 to the double bonds.

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