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Mn-salen@MIL101(Al): a heterogeneous, enantioselective catalyst synthesized using a 'bottle around the ship' approach†

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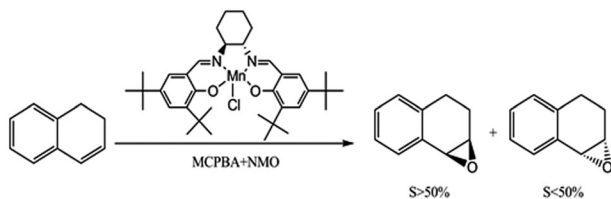
An enantioselective catalyst, consisting of a chiral Mn(III)salen complex entrapped in the MIL-101 metal organic framework, is reported. For the first time, we assemble a robust MOF-cage around a chiral complex. The heterogeneous catalyst shows the same selectivity as the homogeneous complex and is fully recyclable. Theoretical calculations provide insight into this retention of selectivity.

Chiral epoxides are valuable intermediates in the chemical industry. The high ring strain makes them very reactive and their enantioselectivity can be transferred to the products. Various methods have been proposed to enantioselectively synthesize these epoxides.¹ One of these methods is the use of the Jacobsen salen catalyst.² Such manganese complexes enable the epoxidation of unfunctionalized olefins (shown in Scheme 1) with selectivities one would expect from enzymes. In order for this system to be sustainable, an efficient recovery of this catalyst is required. Moreover deactivation of the manganese salen complex, that occurs readily *via* the formation of dimeric species,³ must be prevented. All these issues can be solved by immobilizing the complex on a solid material. Various processes for anchoring

chiral complexes to a support have already been proposed.⁴ We propose a simple immobilization procedure where the salen complex is encapsulated in a metal organic framework without any covalent bonds.

Metal organic frameworks (MOFs) are porous crystalline materials consisting of metal (-oxide) building blocks connected with organic linkers. Using various metals, linkers and synthesis procedures, a wide array of structures are available. In this study NH₂-MIL101(Al) is used as the carrier material. This MOF was first reported by Kapteijn *et al.*⁵ The use of MOFs as catalyst supports has been investigated previously.⁶ MIL-101 type MOFs (MIL stands for Materials Institute Lavoisier) are known for the highly porous structure consisting of large cages (2.9–3.4 nm) connected by windows of 1.2 and 1.6 nm⁷ diameter. The goal is to form the MOF around the complex, building a so-called 'bottle around the ship'. The dimensions of the Jacobsen salen complex (approximately 1.7 × 1.2 × 0.5 nm) allow it to reside in the cages without being able to pass through the windows, thus effectively immobilizing the complex. In contrast to using salen-type ligands as struts for the MOF⁸ the proposed method only makes use of easily available chemicals. "Ship in a bottle" methodologies for producing salen-type complexes have been proposed⁹ however they do not involve MOFs and require several reaction steps. In this communication we propose another approach, denoted as "bottle around a ship", in which the encapsulation procedure consists of a one-pot single-step synthesis. The linker and the commercially available salen complex were simultaneously dissolved in DMF after which AlCl₃ was added stepwise. While crystals are formed, the color of the solution changes from deep-red to a paler red-brownish color. This points to the decrease in concentration of the salen complex in the solution, meaning a fraction gets trapped in the pores.

Comparing the powder XRD pattern of pure NH₂-MIL101(Al) with the encapsulated catalyst shows minimal differences as shown in Fig. 1. This shows that the addition of the salen complex to the synthesis mixture has no effect on the formed structure. The Langmuir surface area, measured by N₂-sorption, was 2603 m² g⁻¹ and 2413 m² g⁻¹ for the empty and loaded structure respectively. The pore volume decreased from 0.984 cm³ g⁻¹ to 0.953 cm³ g⁻¹.



Scheme 1 The enantioselective epoxidation of dihydronaphthalene with the salen complex used in this study.

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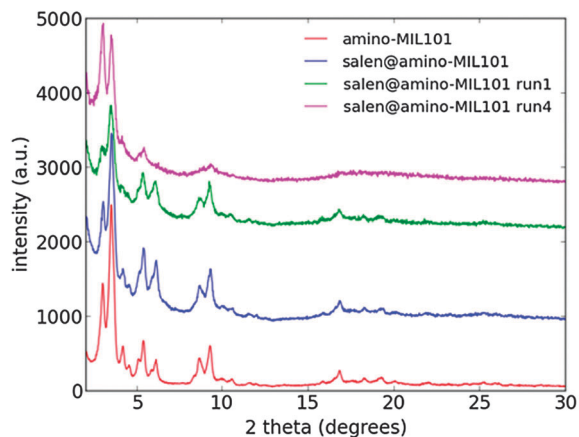


Fig. 1 Powder XRD patterns for the pure $\text{NH}_2\text{-MIL101}(\text{Al})$, $\text{salen@NH}_2\text{-MIL101}(\text{Al})$ and $\text{salen@NH}_2\text{-MIL101}(\text{Al})$ after one and four catalytic runs. The encapsulation of the complex does not significantly change the crystal structure. The retained crystallinity after various catalytic runs shows the stability of the catalyst.

XRF analysis resulted in a loading of 0.02 mmol g^{-1} or one out of six cages containing a salen complex. This small loading is in good agreement with the limited decrease in internal volume. Given the high activity of the manganese–salen catalyst, a low loading is preferred to minimize pore blocking and diffusion limitations which lower the catalytic activity. To assess the behaviour of this encapsulated catalyst it was tested in a typical epoxidation of dihydronaphthalene with *meta*-chloroperoxybenzoic acid (MCPBA) and *N*-methylmorpholine *N*-oxide (NMO) as an axial ligand for the salen complex and adding toluene as an internal standard. This combination has been proven to be an effective oxidant to use in combination with the $\text{Mn}(\text{III})$ salen complex, both homogeneous as immobilized.^{10,11} The product distribution was analyzed by chiral HPLC. In a homogeneous medium the salen catalyst yielded a conversion of 82% with a %ee of 70. The heterogeneous catalyst showed a lower conversion of 69% when approximately the same amount of manganese was used (Table 1). However the enantioselectivity remained unchanged at a %ee of 70. This shows that the proposed encapsulation procedure has a minimal impact on the catalytic behaviour of the complex. After the catalytic run the solid catalyst is filtered off, and investigation of the crystallinity with XRD showed that the structure remained unchanged. The manganese content in the filtrate was analysed by XRF and was found to be below the detection limit of the device, showing none of the complex was leached out. This indicates that the catalyst is truly heterogeneous and stable in the reaction medium. To test the reusability of the catalyst, the powder was washed with dichloromethane and reused for another run, this was repeated three times. During the four runs the turn over number (TON) remained constant (see Fig. 2), proving this catalyst can be reused without significant loss in activity.

Table 1 Details on the amount of added catalyst in the experimental procedure

Catalyst	Weight (mg)	Mn (mmol)	Mn/substrate
Salen homogeneous	4	0.0062	1/1261
Salen@ $\text{NH}_2\text{-MIL101}(\text{Al})$	330	0.0066	1/1216

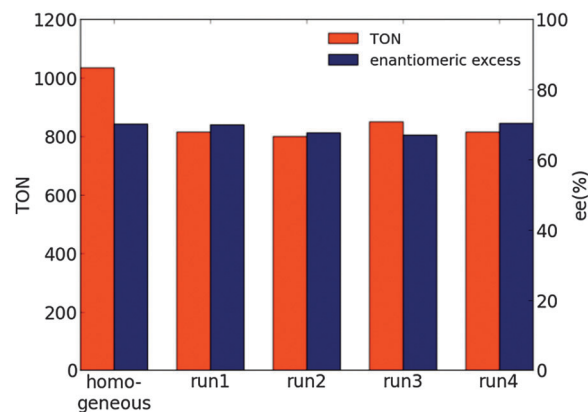


Fig. 2 TON and enantioselectivity for the $\text{salen@NH}_2\text{-MIL101}(\text{Al})$ compared to homogeneous catalysis with the salen complex for the same conditions. It appears the encapsulation procedure has no effect on the selectivity of the catalyst.

Moreover the selectivity remains constant showing the catalyst is very stable and possesses excellent reusability. Blank reactions using the pristine MOF and the mixture without any catalyst yielded only marginal conversion after two hours. In order to obtain more insight into the bottle around the ship approach, *ab initio* calculations were performed. They allow us to make a realistic prediction of the dimensions of the Mn salen complex and its transition state, which can be compared with the cage size of a MIL101 structure. Here we will use a full DFT level of theory instead of using force fields in order to get a more detailed picture. The DFT method used is the OPBE functional, which has shown to yield accurate energies when comparing spin states of organometallic complexes,¹² which is important since the Mn–salen complex has a small energy separation between the different spin states.¹³ All optimizations were done with a 6-31+G(d) basis set for H,C,O,N and a 6-311++G(2df,2p) basis set for Cl and Mn. Computations were done using the gaussian09 suite of programs.¹⁴ Calculations were done on the (*S,S*)-variant of the salen complex, the axial ligand was omitted for computational feasibility. Starting from an oxidized manganese complex, which is an experimentally proven intermediate,³ the proposed methodology showed that a system with a spin multiplicity of three is most favourable and this will be used further. For the first transition state (Scheme S1 of the ESI[†]), two

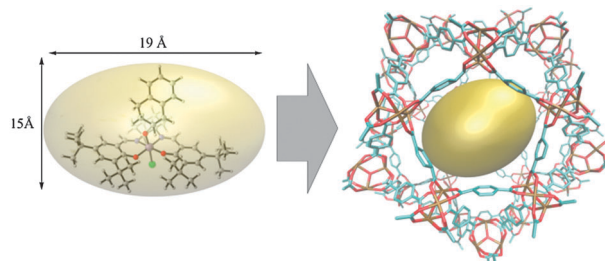


Fig. 3 Schematic representation of the transition state contained in the small (2.9 nm diameter) cage of MIL101. Hydrogens and amine-groups are omitted for clarity. The space needed for transition state to be contained in the cage is represented by an ellipsoid with radii of 19 and 15 Å. This fits readily in the MIL101 cage.

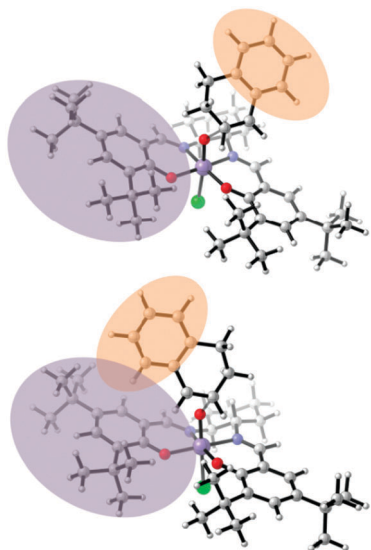


Fig. 4 Transition state for the two possible approaches of dihydronaphthalene leading to the (1*R*,2*S*)-enantiomer (left) and the (1*S*,2*R*)-enantiomer (right). The first approach suffers from more steric hindrance than the latter.

possible approaches leading to a different enantiomer were calculated. Both transition state dimensions were $1.7 \times 1.2 \times 1.0$ nm, taking NMO as an axial ligand into account this would increase to approximately $1.7 \times 1.5 \times 1.0$ nm. This means both transition states fit readily in the cages (Fig. 3).

Upon closely analyzing the mechanism of oxygen transfer, as presented in various theoretical contributions,¹⁵ it appears that the first transition state determines the resulting selectivity. Once the first C–O bond is formed the second one can only form on the same side. Since both transition states fit in the cages of the host without any interaction, the observed selectivity should be the same as the Jacobsen catalyst under homogeneous conditions, as can be observed from the experiments. Using the two approaches one can also rationalize reasons for the selectivity of the salen complex. The transition state leading to (1*R*,2*S*)-epoxydihydronaphthalene is clearly less favorable since the steric bulk of the substrate is directed towards the side of the complex facing upwards (Fig. 4). The (1*S*,2*R*)-approach does not suffer from this steric hindrance. This demonstrates that the folded structure of the salen complex is very important to induce selectivity of the substrate in the approaches. The free energy difference at 273 K between the transition states is 10 kJ mol^{-1} which can explain the preference for the formation of (1*S*,2*R*)-epoxydihydronaphthalene. To assess the influence of the cage we performed a single point calculation with a MIL-101 cage surrounding the transition states. The Jacobsen complex was modeled on the same level of theory as described before, the MOF cage was modeled with the universal force field (details in ESI†). The electronic energy difference between the transition states was 12 kJ mol^{-1} , which confirms the results described above.

In summary, we proposed a novel “bottle around the ship” encapsulation procedure for heterogenizing an enantioselective manganese complex in the pores of NH₂-MIL101(Al). The catalyst synthesis occurs in a single step using readily available chemicals which allows easy scale-up. The metal organic framework is used as a micro-reactor containing a single active complex, with limited influence of the walls. This results in a catalyst with good activity and a selectivity comparable to the homogeneous complex. The unchanged selectivity after heterogenization is due to the ‘soft’ encapsulation strategy. The trapping of the active complex without any covalent or coordinative bonds keeps the structure in the optimal shape needed for achieving the high selectivity. This catalyst was tested for up to four runs with a minimal decrease in activity and retention of the selectivity. This allows for the easy separation and the reuse of this catalyst without loss as was the case for the homogeneous variant. *Ab initio* calculations allow computing the dimensions of the important steps in the reaction, rationalizing the unchanged selectivity after encapsulation. The transition state which determines the selectivity fits the pores of the host unhindered, allowing the reaction to exhibit the same behaviour as with the homogeneous catalyst.

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