Recent progress in the immobilization of catalysts for selective oxidation in the liquid phase

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Reliable strategies are presented for the immobilization of molecular catalysts for selective oxidation in the liquid phase. Besides classical strategies such as ion exchange or covalent anchoring, new approaches are emerging, *e.g.* based on supported ionic-liquid phases or on incorporation of the active centre in a coordination polymer or a metal–organic framework.

1 Introduction

Oxidation reactions remain challenging in the practical preparation of both intermediate and fine chemicals. In many cases, the low volatility or thermal instability of the reactants impose that the reactions are conducted in the liquid rather than in the gas phase. Effective molecular catalysts are available for the major reaction types such as epoxidation, alcohol oxidation or oxidation of heteroatoms, but recuperation of these dissolved catalysts from the reaction mixture is often still the bottleneck in designing cost-efficient and generic oxidation procedures.[1] The present feature article highlights recent progress in the immobilization of homogeneous oxidation catalysts.

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2 Covalently bound catalysts

Generally, covalently bound catalysts have a broad scope, since the link with the support is stable towards most solvents and additives such as salts or acids and bases. On the other hand, this method requires substantial chemical modification of the ligand and/or the support. The catalysts are more complex than their homogeneous counterparts, and many additional parameters such as the spacer length and flexibility, and the degree of surface coverage have to be optimized to obtain good catalytic performance. Ligands or metal complexes functionalized with reactive groups can be reacted with a preformed support (*e.g.*, polystyrene or silica) or alternatively, functionalized ligands may be co-polymerized with a suitable monomer.

Epoxidation

Site-isolated Fe^{II}-bis(1,10-phenanthroline) complexes were prepared on a SBA-15 mesoporous silica *via* a metal-template/

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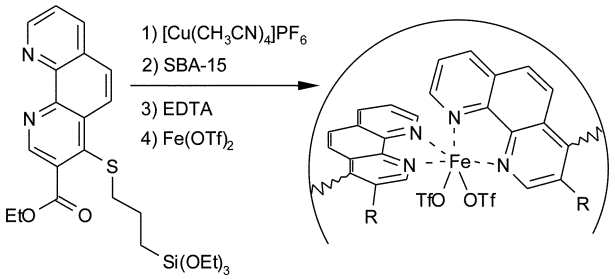
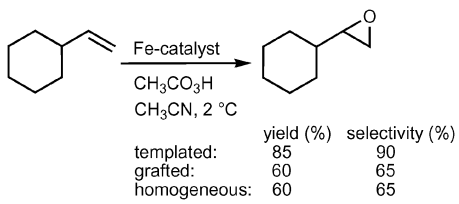


Scheme 1 Metal-template/metal-exchange synthesis route.

metal-exchange procedure.[2] This strategy allows the immobilization of Fe^{II}-bisphen species which are only transiently stable in solution; mixing of phen (2 equiv.) with Fe^{II} in solution results in the rapid formation of $[Fe^{II}(phen)_3]^{2+}$ and free Fe^{II}. As shown in Scheme 1, the synthesis route involves the initial formation of the thermodynamically stable $[Cu^{I}(phen)_2]^{+}$ complex, covalent attachment of this species to the silica surface, removal of the Cu^{I} template with EDTA, and finally metalation of the immobilized ligand with $Fe(OTf)_2$ (OTf = $CF_3SO_3^-$).

The catalytic activity of the resulting material was tested in the epoxidation of terminal olefins such as vinylcyclohexane with peracetic acid as the oxidant (eqn (1)). The catalyst with the templated ferrous bisphen sites showed higher activity and selectivity than the analogous homogeneous catalyst or an immobilized Fe^{II} catalyst prepared by random grafting of the ligand on SBA-15 in the absence of a metal template.

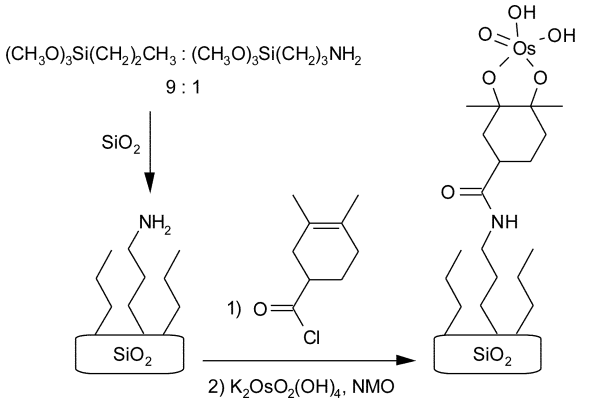


(1)

Whereas the homogeneous catalyst showed an induction period, both immobilized catalysts displayed constant initial reaction rates. The templated material also catalyzed the epoxidation of other α-olefins such as 1-octene, but more electron-deficient olefins such as 2-cyclohexen-1-one or allyl acetate reacted slowly. The recyclability of the immobilized Fe^{II} catalyst was not discussed.

Dihydroxylation

We previously reported a heterogeneous *cis*-dihydroxylation catalyst with Os covalently anchored onto a modified silica support.[3] The immobilization concept is based on two particular properties of the Os–diolate species involved in the *cis*-dihydroxylation reaction. First, it is well known that the hydrolytic release of a diol from an Os–diolate complex becomes increasingly difficult with increasing substitution. If the hydrolytic conditions are not too drastic, *cis*-diols are not formed out of tetrasubstituted olefins. A second important element for the design of the immobilized catalyst is the possibility of reoxidation of an Os(VI) monodiolate complex to *cis*-dioxo Os(VIII), without release of the diol. Under these well-defined conditions, *e.g.*, with *N*-methylmorpholine *N*-oxide (NMO) as the oxidant in *t*-BuOH–CH_2Cl_2, it is possible to immobilize Os by the addition of OsO_4 to a

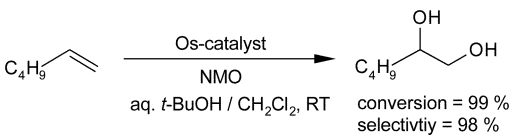


Scheme 2 Immobilization of Os in a stable diolate complex.

tetrasubstituted olefin that is covalently linked to a silica support (Scheme 2).

The tetrasubstituted Os–diolate ester that is formed is stable and keeps the catalyst fixed to the support. The *cis*-dihydroxylation reaction can take place at the remaining free binding sites of the Os centre. The first step is the reaction of an olefin, *e.g.*, 1-hexene, with Os(VIII) trioxomonodiolate, resulting in a bisdiolate complex (Scheme 3).

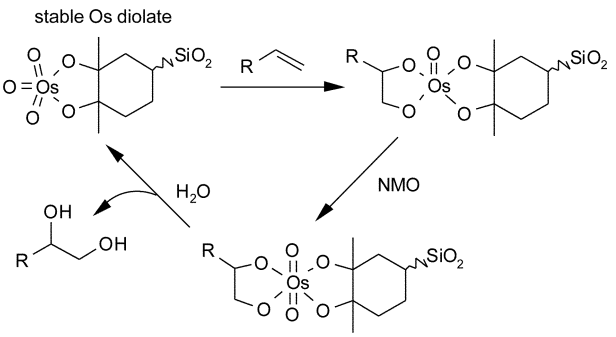
In the following reoxidation and hydrolysis steps, the diol originating from 1-hexene is released, and the immobilized Os(VIII) monodiolate complex is regenerated. The heterogeneity of the catalyst essentially relies on the different hydrolysis rates of the two diolates in the bisdiolate complex. When performing heterogeneity tests, it has been clearly shown that no catalytic activity is found in the filtrate of the reaction. This proves that under reaction conditions, no catalytically active Os species leach from the support. In the *cis*-dihydroxylation of a series of olefins with NMO as the oxidant, the catalyst showed good activity and very high selectivity (eqn (2)).



(2)

The same approach was later adopted to construct soluble dendrimer-bound,[4a] fluorous,[4b] and silsesquioxane-linked[4c] osmium catalysts which could be recovered by phase separation or precipitation.

Since the stoichiometric production of *N*-methylmorpholine (NMM) is a serious drawback of these systems, a coupled



Scheme 3 Catalytic cycle for *cis*-dihydroxylation.

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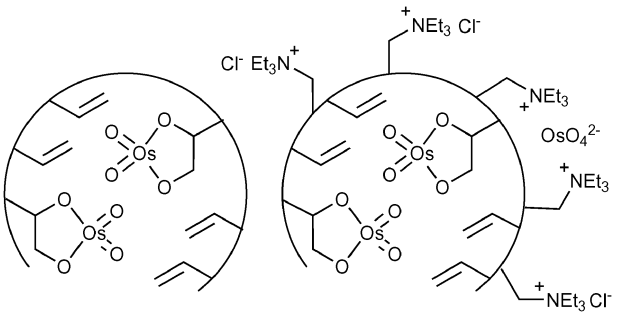
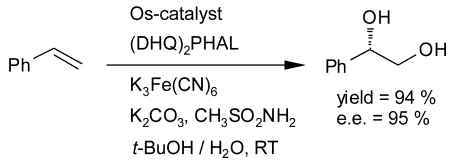


Scheme 4 Immobilization of Os on functionalized resins.

catalytic system was devised in which the NMM produced by the immobilized Os catalyst is regenerated using H_2O_2 as the terminal oxidant and Ti-MCM-41 or tungstate-exchanged layered double hydroxide as a heterogeneous catalyst.[5]

Following a similar approach, the high reactivity of OsO_4 towards C=C double bonds was exploited to immobilize Os on polymeric materials bearing residual vinyl groups.[6] Macroporous resins such as polystyrene-based Amberlite XAD-4 were treated with OsO_4, and XPS analysis demonstrated that the osmium is anchored as Os(VI) and Os(IV) diolate species (Scheme 4). In the presence of a chiral cinchona alkaloid ligand (0.1–1 mol% $(DHQ)_2PHAL$), the catalyst (0.1–1 mol% Os) showed high activity in the asymmetric *cis*-dihydroxylation of olefins using $K_3Fe(CN)_6$ as the oxidant (eqn (3)).[6a]

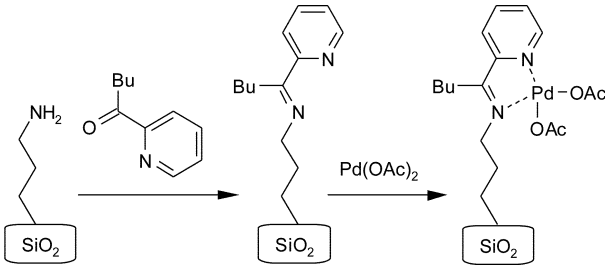


(3)

It was proposed that under reaction conditions, the resin releases Os into solution. This can be expected since contrary to the previously mentioned tetrasubstituted Os–diolate, the Os(VI) complex formed upon addition of OsO_4 to the supported vinyl groups is rapidly hydrolyzed. At the end of the reaction, OsO_4 binds to residual vinyl groups on the solid support. Although the resin-bound OsO_4 could be recycled five times with only a small loss of activity and with constant enantioselectivity, partial leaching of Os into solution necessitated longer reaction times upon reuse. Since part of the supported vinyl groups is consumed in each run, this approach might be inefficient for multiple runs with the same catalyst. Moreover, additional acid/base extraction is needed for ligand recovery. The problem of Os leaching was partially alleviated by the use of macroporous resins containing both vinyl groups and quaternary ammonium moieties.[6b] The bifunctional resin might catch OsO_4 as well as OsO_4^{2-} and this improved the recyclability of the catalyst (Scheme 4).

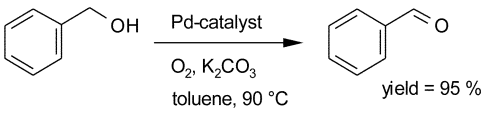
Alcohol oxidation

Palladium was covalently anchored onto the surface of a silica gel which was modified with N–N, N–S or N–O chelating ligands.[7] For instance, activated silica was treated with 3-aminopropyltrimethoxysilane, followed by the addition of *n*-butyl 2-pyridyl ketone to yield the corresponding silica-supported Schiff base. Complexation of $Pd(OAc)_2$ afforded an immobilized Pd catalyst (Scheme 5).



Scheme 5 Synthesis of a covalently anchored Pd catalyst.

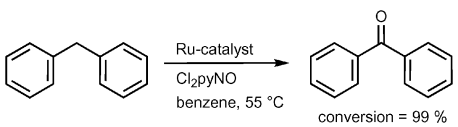
The resulting material showed high activity in the oxidation of benzyl alcohol to benzaldehyde with molecular oxygen as the oxidant (eqn (4)). Primary and secondary aliphatic alcohols were reactive as well. On the other hand, the oxidation of cinnamyl alcohol proceeded very slowly. A filtration test indicated that the observed catalysis is purely heterogeneous. Recycling experiments showed a constant activity during the first three runs, after which the catalyst slowly deactivated.



(4)

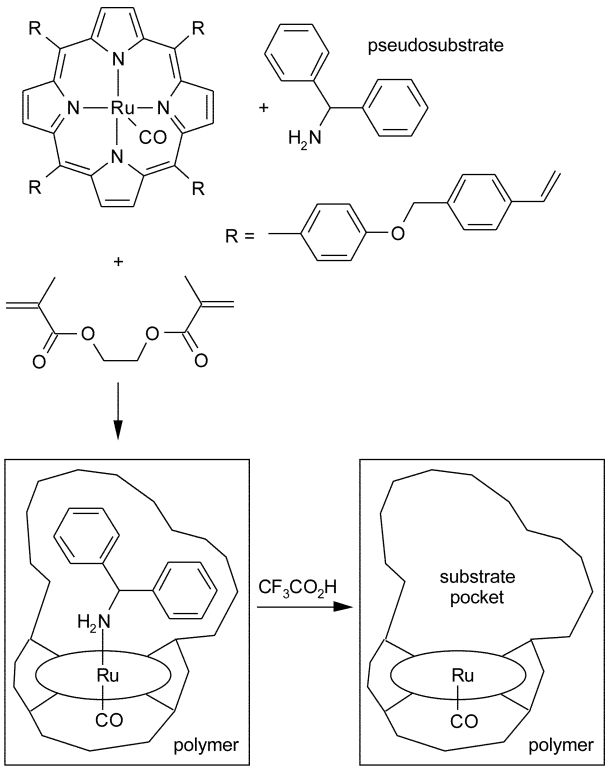
Alkane oxidation

Following earlier reports on the immobilization of ruthenium porphyrins on Merrifield's peptide resin[8a] or on a cross-linked polymer,[8b] a *meso*-tetraaryl Ru–porphyrin complex having four polymerizable 4-vinylbenzoxy groups was recently immobilized by co-polymerization with an excess of ethylene glycol dimethacrylate.[8c] By using diphenylaminomethane or 1-aminoadamantane as coordinatively bound templates during the polymerization step, molecularly imprinted polymers were obtained (Scheme 6). In the oxidation of alkanes and secondary alcohols with 2,6-dichloropyridine *N*-oxide (Cl_2pyNO) as the oxidant, the polymeric catalysts were found to be superior to their homogeneous counterpart (eqn (5)). Presumably, this is due to a site-isolation effect.



(5)

Compared to the conventional polymer, the imprinted catalysts displayed increased activity with rate enhancements of up to a factor of 16 in the oxidation of anthracene. The rate enhancement due to molecular imprinting was found to depend strongly on the reaction temperature and the nature of the substrate. The recyclability of the immobilized Ru–porphyrin catalysts was not reported. In this context, the stability of the polymeric backbone under the conditions for alkane oxidation might be an important issue. The oxidation reactions catalyzed by the immobilized Ru porphyrin were accelerated when perfluoromethylcyclohexane was used as a co-solvent.[8d] In addition, the fluorous solvent was found to

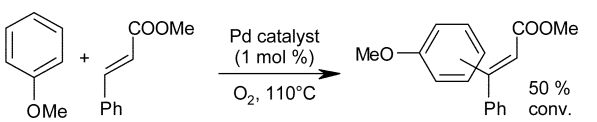


Scheme 6 Preparation of a polymeric Ru–porphyrin catalyst.

alter the substrate selectivity. Both effects could be explained by a solvent-induced partitioning of substrates and oxidant into the polymeric, catalyst-containing matrix.

Oxidative alkenylation of aromatics

Oxidative alkenylation offers the attractive potential of coupling a vinyl group to an aromatic ring without the need for any pre-functionalization of this ring.[9] For instance, acrylate esters can be arylated with electron-rich rings such as toluene or anisole to yield cinnamate esters. The overall process is a two-electron oxidation. We recently discovered that oxygen can be used as a terminal oxidant in combination with Pd as the catalyst and aromatic carboxylic acids, *e.g.* benzoic acid as the co-catalyst.[9a] An immobilized version of this catalyst was designed by incorporating 4-vinylbenzoic acid as a co-monomer in a methacrylate polymer.[9c] The Pd^{2+} is firmly immobilized because of its coordination to the covalently incorporated benzoic acid. However, the maximum Pd turnover numbers were significantly lower for the heterogenized catalyst ($\sim$100) than for the free, homogeneous catalyst ($\sim$800) (eqn (6)). Heterogeneity tests demonstrated the absence of catalytic activity in the filtrate of the reaction, while AAS measurements showed negligible leaching of



(6)

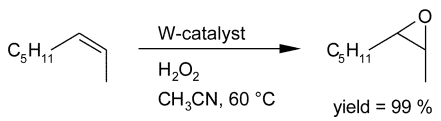
3 Supported ionic liquid-phase catalysts

Recently, ionic liquids (ILs) have been introduced as an alternative medium for the immobilization of homogeneous catalysts in supported liquid-phase systems.[10] In analogy to well-established supported aqueous phase catalysis,[11] this approach has been coined supported ionic liquid-phase (SILP) catalysis. In a SILP system, a film of the ionic liquid is supported on the surface of a solid material (*e.g.*, silica) *via* covalent anchoring or adsorption. Alternatively, additional ionic liquid is impregnated on a support that already contains a monolayer of covalently anchored ionic liquid. The homogeneous catalyst is dissolved in the ionic liquid film, with the advantage that the surface area of the ionic liquid is greatly enhanced relative to its volume and the substrate can readily diffuse to the catalyst. SILP catalysis is ideally suited for gas-phase reactions and has the potential for continuous-flow operation. Liquid phase reactions require careful tuning of the polarities of all reaction constituents in order to prevent leaching of the catalyst and/or the ionic liquid.

Epoxidation

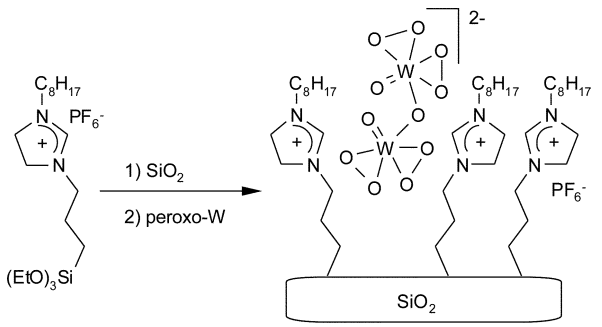
The ion liquid fragment [1-octyl-3-(3-triethoxysilylpropyl)-4,5-dihydroimidazolium][PF_6] was covalently anchored to the surface of silica.[12a] Anion exchange of the ionic liquid-modified silica with the dinuclear $K_2[W(=O)(O_2)_2(H_2O)_2(\mu\text{-}O)]$ resulted in the immobilization of the peroxotungstate catalyst (Scheme 7).

This material was used for the epoxidation of olefins with H_2O_2 as the oxidant and CH_3CN as the solvent (eqn (7)). The reaction rates observed for the epoxidation of various olefins were comparable to those obtained for a homogeneous catalyst analogue. ICP-AES analysis showed no W species in the filtrate (W detection limit $<$16 ppb) and the catalyst was reused three times for the epoxidation of cyclooctene without loss of catalytic activity.



(7)

A very similar silica-supported ionic liquid was used for the immobilization of the $[\gamma\text{-}1,2\text{-}H_2SiV_2W_{10}O_{40}]^{4-}$ anion.[12b] The resulting catalyst was used for the epoxidation of alkenes and the oxidation of sulfides to sulfoxides with H_2O_2 as the



Scheme 7 Immobilization of peroxotungstate on ionic liquid-modified silica.

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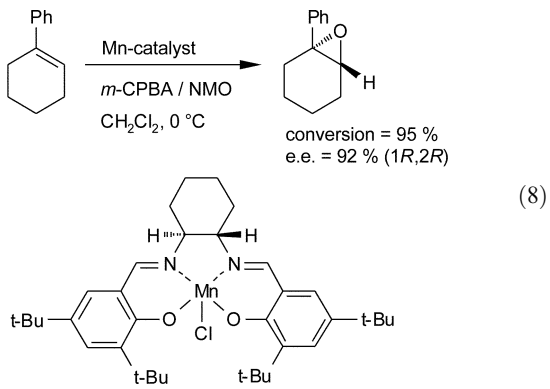
oxidant. Filtrate tests and elemental analysis confirmed the heterogeneous nature of the observed catalysis.

Asymmetric epoxidation

The IL fragment [1-methyl-3-(3-trimethoxysilylpropyl)imidazolium][PF_6] was covalently anchored to MCM-48 and the IL-modified material was impregnated with additional [bmim][PF_6] and the chiral (*S*,*S*)-Mn(III) salen complex.[13] The immobilized catalyst was used in the asymmetric epoxidation of unfunctionalized olefins in CH_2Cl_2 as the solvent using a mixture of *m*-chloroperbenzoic acid and NMO as the oxidant (eqn (8)). For some olefins such as 1-phenyl-1-cyclohexene, the SILP catalyst showed higher ee values at the same conversion level compared to the corresponding homogeneous catalyst. The immobilized catalyst could be reused three times without loss of activity or enantioselectivity. NMR and ICP-AES measurements showed no leaching of ionic liquid or Mn–salen complex.



(8)

Alcohol oxidation

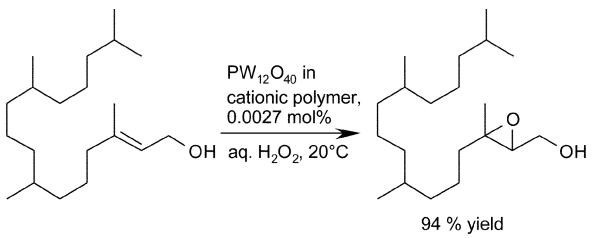
A silica-entrapped ionic liquid was prepared by co-polycondensation of TEOS and [1-methyl-3-(triethoxysilylpropyl)imidazolium][Cl] in the presence of hexadecyl pyridinium chloride as a structure-directing agent.[14] The resulting material was anion-exchanged with $KRuO_4$. The immobilized Ru catalyst was applied in the aerobic oxidation of alcohols using supercritical CO_2 as the reaction medium. Compared to supported Pt-group metals, the Ru catalyst showed moderate activity in the oxidation of benzyl alcohol to benzaldehyde (TOF = 1.72 h^{-1}). However, no overoxidation of the aldehyde to the carboxylic acid was observed. Other alcohols such as 1-phenylethanol and 1- and 2-octanol showed lower reactivities. The catalyst could be reused for three runs with minor loss ($<3\%$) of activity. Ru leaching to the $scCO_2$ phase was not observed (Ru detection limit <1 ppb).

4 Electrostatically withheld catalysts

Electrostatic interactions can be extremely effective in withholding an active compound within the solid material, at the condition that one makes a proper choice of support material, catalytic species and operating conditions. In particular, the active compound should retain a sufficient charge through all steps of the catalytic cycle. Suitable active compounds are oxoanions of Mo or W, heteropolyanions of various structures and composition, and a large number of cationic first row transition metal compounds. Especially when the catalysts are employed in partially organic media with a relatively low dielectric constant, the retention of the metal on the support is excellent, and the material survives intact after many re-use cycles.

Epoxidation

Oxotungsten-based catalysts for epoxidation with H_2O_2 are readily immobilized on anion exchangers, as was demonstrated in the seminal work of Venturello and co-workers.[15] The theme remains particularly popular; recently employed supports include hybrid silica materials functionalized with quaternary ammonium groups (see above),[12,16] inorganic materials such as layered double hydroxides, or organic supports. For instance, a solid W catalyst was obtained by quaternization of *N*-(3-dimethylaminopropyl)acrylamide, followed by polymerization and addition of the $PW_{12}O_{40}^{3-}$ anion.[17] While the polymer as such is water-soluble, it becomes insoluble in the presence of the phosphoperoxotungstate anion, proving that the latter acts as a true cross-linker. The material is porous, with pore diameters between 10 μm and <100 nm. Remarkably, this material catalyzes the solvent-free epoxidation of even hydrophobic allylic alcohols with aqueous H_2O_2. Thus, the total turnover number in the epoxidation of phytol amounted to 35 000 (eqn (9)).

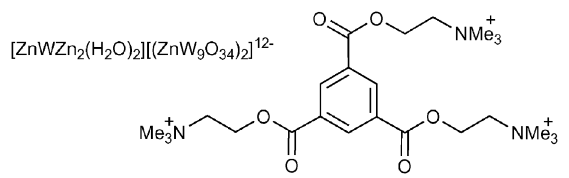


(9)

Isolated yields in three successive runs with the recycled catalyst amounted to 96, 93 and 97%. Other successful applications of the same catalyst include the oxidation of secondary amines to nitrones, and of thioethers to sulfones.

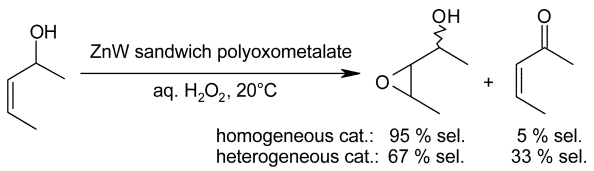
A similar cross-linking approach was adopted by Neumann and co-workers to prepare polyoxometalate based mesoporous catalysts.[18] Co-crystallization of the 'sandwich' polyoxometalate $[ZnWZn_2(ZnW_9O_{34})_2(H_2O)_2]^{12-}$ with tripodal polyammonium cations resulted in insoluble, coral-shaped amorphous particles with BET areas between 25 and 50 m^2 g^{-1}, and a broad size distribution of mesopores (Scheme 8).

The catalyst was effective not only for allylic alcohol epoxidation, but also for the oxidation of aliphatic and



Scheme 8 Cationic and anionic building blocks of a mesoporous tungsten catalyst.

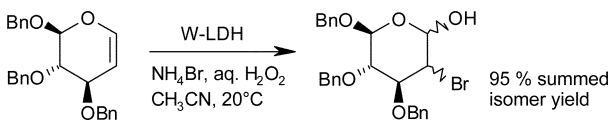
alicyclic secondary alcohols to the corresponding ketones. Comparison of the heterogenized catalysts to the sandwich compound dissolved in dichloroethane showed that the chemoselectivity for epoxidation of *e.g.* (*Z*)-3-penten-2-ol was lower with the heterogeneous catalyst than with the homogeneous compound (eqn (10)). In the proposed rationalization, coordination of the 3-penten-2-ol *via* its alcohol group on the W centre requires more space than oxidation of the alcohol, proving that steric constraints are more pronounced in the solid porous catalyst.



(10)

Oxidative halogenation

Tungstate catalysts immobilized on layered double hydroxides (LDH) have been valorized in the oxidative halogenation of anhydrosugars and related dihydropyrans.[19] Glycals are extremely versatile synthons for incorporation of sugar residues in fine chemicals, and transformation of the glycal to a halohydrin can be the starting point for further modification. In view of replacing hazardous or polluting reagents such as elemental halogens or hypervalent iodine(III) and (V) reagents, it is of interest to oxidize halides *in situ* with a green oxidant such as H_2O_2. Starting from NH_4Br or NH_4I and adding gradually the peroxide, the LDH-immobilized tungstate continuously delivers OBr^- or OI^-, which in their protonated form react spontaneously with the enol ether substrates. The main effects of the LDH are not only to immobilize the peroxotungstate, but also to compensate the charge repulsion between the halides and the negatively charged peroxotungstate. As an example, the benzylated glucal is converted to a 95% yield of halohydrin isomers (eqn (11)).

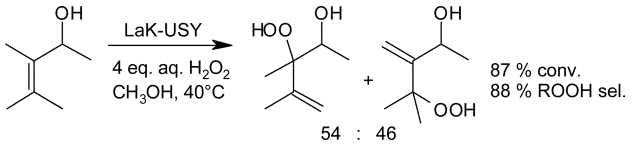


(11)

No active tungsten species were found in filtration tests. After reuse, similar results were obtained as with a fresh catalyst. Tungstate is hence retained on the LDH, even in the presence of I^- or Br^- which potentially compete for ion exchange capacity.

Singlet oxygenation

Finally, La^{3+} cations offer new perspectives for use as immobilized catalysts in oxygenation by singlet oxygen ($^1O_2$).[20] In these reactions, the metal catalyzes the selective decomposition of H_2O_2 to $^1O_2$, which then spontaneously reacts with electron-rich olefins, *e.g.* in a hydroperoxidation. While modified molybdate-exchanged LDHs are the best heterogeneous catalysts in terms of efficiency of H_2O_2 use, La-exchanged zeolites have a complementary potential as they are more selective for hydroperoxidation of allylic alcohols than the Mo catalysts, which often catalyze a competitive epoxidation (eqn (12)).



(12)

The effect of zeolite structure and porosity on the catalyst performance was studied in detail; the highest hydroperoxide yields are achieved with zeolites with a small crystal size or possessing large intersecting pores, such as zeolites Beta or US-Y. This allows a facile diffusion of the $^1O_2$ generated towards the unsaturated substrate, before $^1O_2$ decays to the ground state.

5 Coordination polymers and metal–organic frameworks

A recently emerging group of materials with potential catalytic activity are coordination polymers (CPs). These materials are composed of mostly transition metal ions connected by organic polyfunctional ligands. These coordinatively bound assemblies may extend in one, two or three dimensions, while other and weaker interactions such as hydrogen bonds may keep together chains or layers to form solids. Due to the high degree of flexibility of many CPs, determination of the specific metal coordination environment may be difficult. Nevertheless, some CPs have a considerable porosity.[21] More recently, a subgroup of very rigid and crystalline CPs has been developed, which are often denoted as *metal–organic frameworks* (MOFs).[22] Their pores always remain accessible, even after solvent removal. Rigidity is imparted due to the presence of a three-dimensional coordinatively bound lattice formed by specific combinations of ligands and metal cations.[23] The most stable MOFs contain for instance ligands with resonance-stabilized aromatic rings and their metal cations are grouped in clusters often connecting four or more organic ligands, or even in chains.[24] Therefore, among CPs, MOFs generally have a higher thermal stability and their pore structure and coordination environment are more strictly defined.

As many transition metal coordination compounds are selective homogeneous oxidation catalysts, the incorporation of such complexes in a solid CP or MOF may generate self-supporting catalysts. However, as each CP or MOF is a unique combination of cations and linkers, the chemical stability has to be investigated for each material, particularly against moisture.[25] Especially in the case of MOFs, the metal ions are coordinatively saturated to enhance rigidity and are hence usually unaccessible.[22b] Nevertheless, a few strategies have already been developed for the production of catalytically active structures, as illustrated by following examples.

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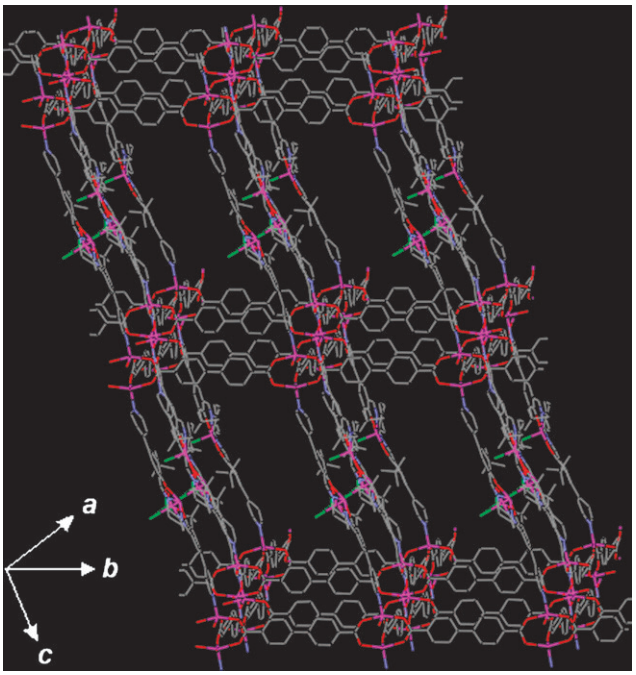
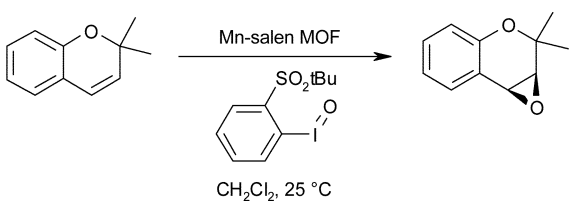


Fig. 1 An enantioselective MOF epoxidation catalyst. Zn-(1,4′-biphenyldicarboxylate) sheets in the *ab* direction are connected by functionalized Mn–salen ligands to form a doubly interpenetrated porous structure (Zn = purple; Cl = green; C = gray; O = red; N = blue; Mn = pink; hydrogen atoms have been omitted for clarity).

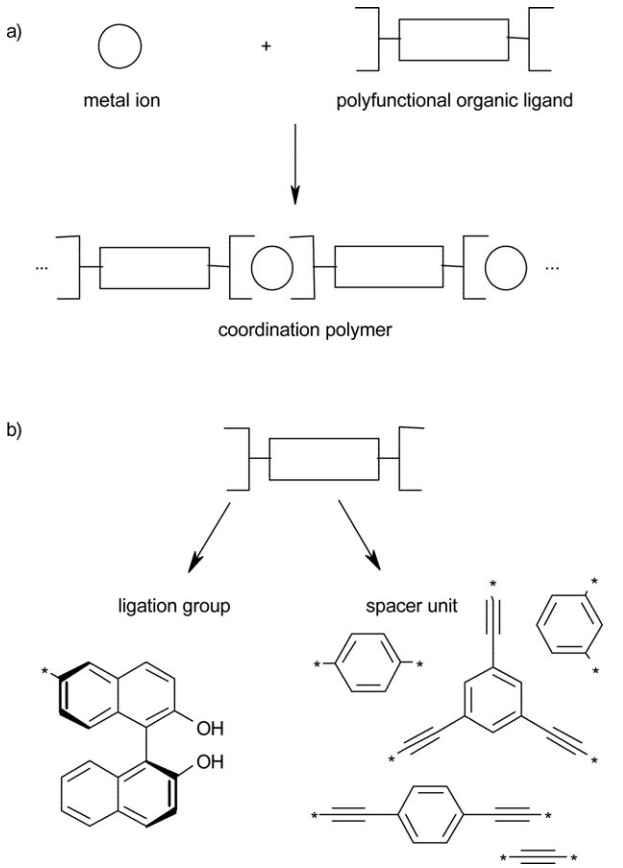
Structural incorporation of catalytically active metal complexes in a metal–organic framework

This first approach for the heterogenization of transition metal complexes is encountered in the preparation of a Zn-based MOF with Mn(salen) ligands.[26] These ligands are provided with extra peripheral pyridine functional groups, in order to anchor them to sheets composed of Zn paddlewheels connected by 1,4′-biphenyldicarboxylate ligands. These sheets have only a structural role and are not involved in catalysis. The resulting crystalline structure is doubly interpenetrated with channels with dimensions of 6.2 × 15.7 Å and 6.2 × 6.2 Å with all Mn^{3+} sites accessible *via* the channels (Fig. 1). This material was applied in the asymmetric epoxidation of 2,2-dimethyl-2*H*-chromene with 2-(*tert*-butylsulfonyl)iodosylbenzene as oxidant (eqn (13)). The reaction was shown to occur within the pores by reactant shape selectivity studies with a large porphyrinic substrate.



(13)

A comparison with the activity of free Mn(salen) ligands shows that the activity of the MOF catalyst is lower, but more stable over time, as the immobilization of the Mn(salen) complexes prohibits reactive encounters between different complexes. The enantioselectivity of the MOF was only slightly lower than that of the homogeneous Schiff base complex (ee of 82 and 88%, respectively), possibly due to the higher rigidity of the ligands as a consequence of their immobilization. Upon reuse of the MOF, a small loss (4–7%) of catalytically inactive manganese was noticed after each reaction run, while enantioselectivity remained constant.

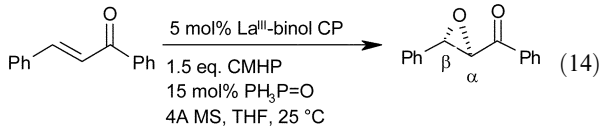


Scheme 9 Construction of La^{3+}- or Ti^{4+}-binol coordination polymer (a); the organic ligand contains binol ligation groups and a spacer unit of varying structure (b).

A similar example is provided by the CP containing the bis(triesterified) hexavanadate units $[V_6O_{13}(OCH_2)_3CNHCH_2(4\text{-}C_6H_4COOH)_2]^{2-}$. These units are inserted *via* the carboxylic groups into a lattice containing Co^{2+} and 4,4′-bipyridine.[27] The resulting material was used for the aerobic oxidation of 1-propanethiol to the disulfide. The reaction proceeds rather slowly: in dichloroethane, 3 turnovers are obtained after 7 days at 45 °C.

Another strategy uses the common ligation groups of transition metal catalysis, and connects these groups by spacer units to form polyfunctional organic ligands. These bridging spacers should be rigid to avoid the intramolecular interaction of two ligation groups with the same metal centre. An example is provided by a series of self-supporting Shibasaki La^{3+} catalysts synthesized from reaction of $La(OiPr)_3$ with ligands consisting of a spacer unit and two or more chiral 2,2′-dihydroxy-1,1′-binaphthyl (binol) groups (Scheme 9).[28] These CPs were used for enantioselective epoxidations of α,β-unsaturated ketones with cumene hydroperoxide (CMHP). A La-binol catalyst with 1,4-diethynylphenyl linkers was able to epoxidize the aromatic unsaturated ketone shown in eqn

(14) in 0.5 h with a yield of 99% and an enantioselectivity of 97.6% (TOF = 40 h^{-1}).



(14)

Activity and enantioselectivity of La-CPs were strongly dependent on their bridging spacer units, demonstrating the importance of the supramolecular structures of the catalysts. As these CPs are non-ordered materials, it is difficult to explain how the surroundings of the active sites influence their behavior, or to find out whether reactions take place inside the CP or at the surface.

The same authors reported similarly constructed, non-ordered Ti binol CPs (Scheme 9) for sulfoxidation of aromatic thioethers with cumene hydroperoxide.[29] The enantioselectivity attained with these catalysts was often higher than 99% ee, but the product yields were only low to moderate (30–45%). Possibly, kinetic resolution in the further oxidation of sulfoxide to sulfone may increase the enantiopurity of the primary oxidation product but simultaneously decrease sulfoxide yields. In particular, the Ti binol CP with binol ligands constructed from 1,3-phenylene units demonstrated a significant improvement in enantioselectivity for the oxidation of *p*-nitrothioanisole in comparison with a homogeneous binol/Ti/H_2O catalyst under otherwise identical conditions (89 *vs.* 25% ee). An increase in steric bulk of the alkyl group in the substrate resulted in a reduction of enantioselectivity, providing evidence for an intraporous reaction. The catalysts could be reused for more than one month without significant loss of metal or enantioselectivity, but may however disintegrate when excess water is present in the reaction mixture, for instance by the use of aqueous H_2O_2 solutions.

Inherent catalytic activity of metal centres in MOFs and CPs

Although the metal concentration in CPs and MOFs is generally very high, only in a rather limited number of structures can metal ions with a structural role also take part in catalytic conversions, for instance *via* open metal sites obtained by substituting or thermally removing a labile ligand.[30] Even if TONs may be rather limited, the productivities can still be considerable when expressed based on catalyst weight instead of on metal loading.

Alcohol oxidation. A common coordination complex with open metal sites is the Cu paddlewheel structure, which serves as a building unit in a series of CPs and MOFs.[24a,31] This structural motif can be used as an oxidation catalyst, for instance after incorporation into the two-dimensional dinuclear Cu^{2+} *trans*-1,4-cyclohexanedicarboxylate CP. This material consists of sheets kept together by Cu–O bonds between adjacent Cu paddlewheels (Fig. 2). This catalyst was used for the oxidation of various aliphatic and aromatic alcohols to aldehydes or ketones with H_2O_2 with selectivities above 99% (eqn (15)).[21c]

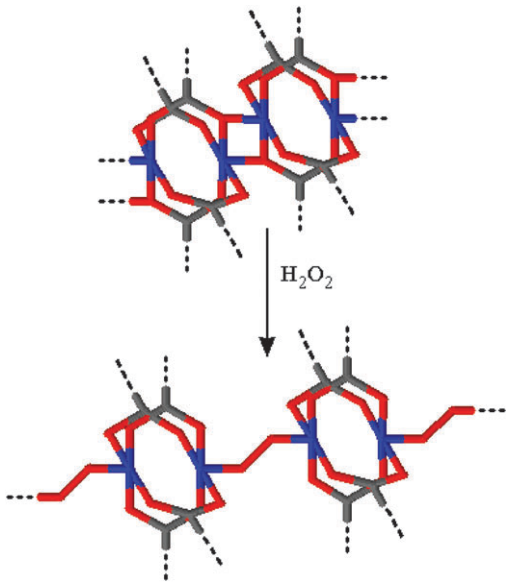
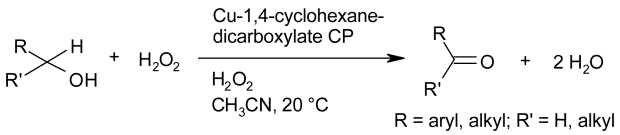


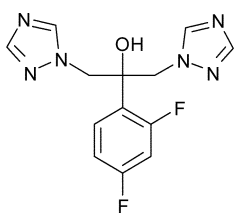
Fig. 2 A MOF oxidation catalyst based on Cu paddlewheels connected by 1,4-cyclohexanedicarboxylate ligands (only carboxylate groups are explicitly shown). During oxidation by H_2O_2, paddlewheels become linked by peroxo bridges.



(15)

The reaction proceeds fully heterogeneously *via* a proposed peroxo intermediate on the Cu cations, as shown by DRS and resonance Raman spectroscopy. Upon oxidation, the Cu paddlewheels are disconnected, rotated and again linked to each other by peroxo bridges (Fig. 2). The BET surface areas of the non-oxidized and the oxidized catalysts are 390 and 330 $m^2\ g^{-1}$, respectively, while the effective pore size is 4.9 Å for both compounds, which might be too small for the larger substrate molecules.

A series of nonporous CPs containing Fe or Cu, $\{[FeL_2Cl_2]\cdot 2CH_3OH\}_n$, $\{[CuL_2(H_2O)]\cdot SO_4\cdot DMF\cdot 2CH_3OH\cdot 2H_2O\}_n$, and $\{[CuL_2Cl_2]\cdot 2CH_3OH\}_n$ (L = 1-(2,4-difluorophenyl)-1,1-bis[(1-*H*-1,2,4-triazol-l-yl)methyl]methanol; see Scheme 10), were used for the oxidation of benzyl alcohol.[32] In all three components, the metal coordination spheres consist of four N atoms from different ligands and two axial ligands. Reactions are performed with H_2O_2 in aqueous medium at 140 °C. All CPs suffered however from considerable leaching, as the



Scheme 10 1-(2,4-Difluorophenyl)-1,1-bis[(1*H*-1,2,4-triazol-l-yl)methyl]-methanol ligand.

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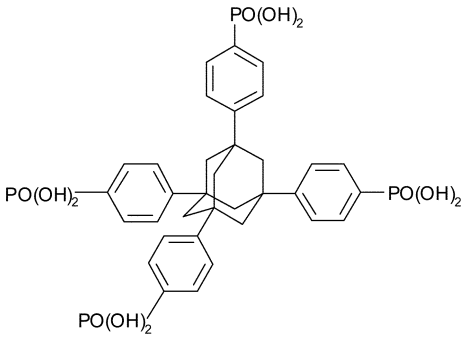


Scheme 11 Tetrakis-1,3,5,7-(4-phosphonatophenyl)adamantane ligand.

filtrated supernatant showed a conversion of 10–15% of the original value.

Benzylic alcohols can also be oxidized using a vanadyl CP containing an extended phosphonate ligand with rigid tetrahedral conformation (Scheme 11).[33] Although the periodicity of this material is rather limited, a specific surface of 118 $m^2 g^{-1}$ and pore diameters of 38–39 Å were obtained from nitrogen sorption. Oxidation reactions were performed at 100 °C in toluene with oxygen. Benzylic alcohols were produced at high conversion and selectivity (both mostly >96%). The lower conversion for oxidation of 2,4,6-trimethylbenzyl alcohol points to shape selective behavior of this vanadylphosphonate CP.

CO oxidation. The intrinsic potential of Cu paddlewheel clusters for catalytic oxidation is also illustrated by a MOF constructed from Cu^{2+} and 5-methylisophthalate ligands used for gas-phase CO oxidation.[34] Activities are similar to or higher than those of CuO and CuO/Al_2O_3, with full conversion at 200 °C. The porous lattice has a stable activity and remains intact after catalytic reaction; no CuO is formed. A microporous Ni-MOF, constructed from the cubic building block $[Ni_8L'_{12}]^{20-}$ (H_3L' = 4,5-imidazoledicarboxylic acid) with Na^+ counterions (Fig. 3), is also active for this reaction.[35] Its activity was between those of NiO and Ni-Y zeolite, but far lower than the activity of the Cu-methylisophthalate MOF.

Thioether oxidation. A series of three-dimensional CPs constructed from succinic acid and Sc, Y or La, and one MOF constructed from terephthalic acid and Sc were used as catalysts for the oxidation of sulfides with H_2O_2 at 40 °C (eqn (16)).[36] The Sc terephthalate contains infinite chains of Sc-octahedra connected in six directions by terephthalate ligands, forming small one-dimensional triangular channels with diameters of 3 Å. Two thioethers, methylphenyl sulfide and (2-ethylbutyl)phenyl sulfide, were used as model substrates; these molecules are too large to penetrate into the pores of the Sc-terephthalate MOF. Differences in yield between the succinate-based CPs could be due to their different ability to increase their coordination number to allow the proposed formation of a peroxo derivative: Y and La more easily assume a high coordination number than Sc, while for the Sc-succinate CP the accommodation of an extra oxygen in the coordination polyhedron seems to be more difficult. Interestingly, the Sc-terephthalate MOF is faster and more selective as compared to the Sc-succinate CP. All catalysts are fully heterogeneous and can be reused without loss of selectivity. In comparison with their corresponding metal oxides, all four catalysts present a similar selectivity, but a higher activity. However, it should be mentioned that the materials were used in large, almost stoichiometric amounts.

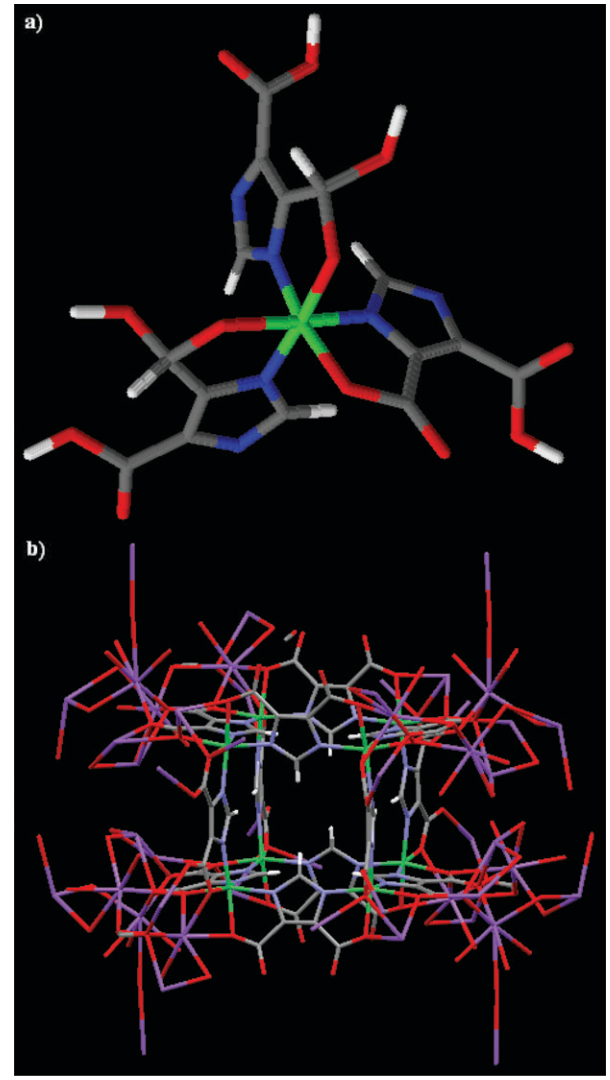
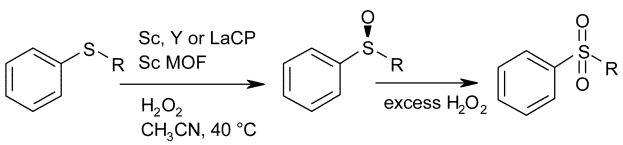
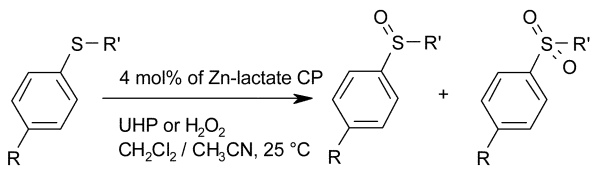


Fig. 3 Representation of the cubic building block $[Ni_8L'_{12}]^{20-}$: (a) coordination complex of Ni^{2+} and 4,5-imidazoledicarboxylate (L′); (b) eight Ni ions occupy the corner positions of an imaginary cube with six L′ molecules as the sides. Na^+ ions balance the negative charge of this Ni cube and provide the connections to neighboring cubes (not shown) (Ni = green; C = gray; O = red; Na = purple; H = white; N = blue).



(16)

Oxidation of sulfides to sulfoxides or sulfones can also be catalyzed by a CP consisting of chiral Zn-lactate clusters further interlinked by terephthalate (eqn (17)).[37] DMF can however not be totally removed from this framework without causing degradation of the structure. After partial evacuation, the Zn–lactate–terephthalate has a specific surface of 190 m^2 g^{-1} with pores of roughly 5 Å. Using H_2O_2 and varying the solvent composition (CH_2Cl_2–CH_3CN), conversion and selectivity reached a quantitative level, and at least 30 catalytic cycles could be performed without loss of oxidation selectivity. The reaction primarily occurs inside the uniform micropores of the framework as proven by reactant size selectivity (see eqn (17)). Despite the presence of chiral centres in the CP, no asymmetric induction was found.



	conversion (UHP)
R = H, R' = Me:	64%
R = Br, R' = Me:	58%
R = NO_2, R' = Me:	7%
R = H, R' = CH_2Ph:	3%

(17)

Olefin oxidation. A Cu-containing CP, $[Cu(Pht)(Im)_2]\cdot 1.5H_2O_n$ (Pht = dianion of *o*-phthalic acid; Im = imidazole), was used for oxidation of cyclohexene.[38] The nonporous structure consists of $[Cu(Im)_2]$ units linked by 1,2-phthalate ions to form infinite chains, connected by extended hydrogen bonds. Reactions were performed in acetone using 30% H_2O_2 at ambient temperature. The product distribution, with mainly the allylic oxidation products 2-cyclohexen-1-one and 2-cyclohexen-1-ol, reflects that some Cu can participate in the one-electron redox reactions that lead to decomposition of H_2O_2 into free radicals such as $HOO^{\bullet}$ or $HO^{\bullet}$. Substitution of the Cu^{2+} by Co^{2+} gives analogous results. A crystalline vanadium CP consisting of VO_4 tetrahedra linked by two-connected trimethyltin moieties, $[Me_3SnVO_3]$, was used for epoxidation of various olefins in liquid phase at 65 °C with *tert*-butyl hydroperoxide in decane.[39] Reaction takes only place at the external surface or at the entrances of pores or channels. The catalyst is not fully heterogeneous as a conversion of 10% of the original value was observed with the filtrate alone.

Impregnation with metals

CPs and MOFs can be converted into active catalysts by impregnation with metals or metal cations. For instance, the neutral framework of MOF-5 can be impregnated by crystallization of $AgNO_3$ inside the pores at 60 °C for 20 h using a diethylformamide/acetonitrile mixture.[40] This catalyst was used for the gas phase oxidation of propylene to propylene oxide with O_2 at 220 °C, with a selectivity of 10.3% at a propylene conversion of 4.3%. MOF-5 can also be loaded with metals by chemical vapor deposition.[41] Metal precursors such as $(\eta^5\text{-}C_5H_5)Pd(\eta^3\text{-}C_3H_3)$ are brought into the pores and next reduced with H_2 to form nanosized aggregates. A MOF-5 catalyst loaded in this manner with Au particles with diameters of 5–20 nm was however inactive in CO oxidation, apparently due to the lack of a strong metal–support interaction or promotion.

Ship-in-a-bottle catalysts

A number of MOFs have a particular pore system with windows and cages, providing a possibility for occlusion of large species. For instance, Mo/W-containing Keggin-type polyoxometalates can be placed inside the large pores of $[Cu_3(BTC)_2]$.[42] Keggin ions are formed during synthesis of $[Cu_3(BTC)_2]$ by addition of their starting reagents to the original synthesis mixture. Such a material may for instance find applications as an epoxidation or sulfoxidation catalyst.[43]

Conclusions

While traditional heterogeneous catalysts are often regarded as ill-defined materials, in which active sites are non-uniform, the approaches presented here show that immobilized molecular catalysts may allow to reach a better control of the active site's architecture and accessibility. The active sites seem most strictly defined in covalently anchored or MOF-type catalysts; in supported ionic liquids, the immediate solvent environment of the site can be tuned in a unique way. MOF-type catalysts and other porous supports allow to maximize the efficiency of the catalysts by ensuring optimal accessibility. In view of the merits of the respective approaches, they should be considered complementary rather than competitive. In all cases, evaluation of the catalysts' stability will be critical for further development.

Acknowledgements

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