Plug-and-Play Heterogeneous Catalysis Enabled by Metal–Organic Cage-Crosslinked Polymers

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Abstract: The immobilization of homogeneous catalysts onto solid supports to improve recyclability while maintaining catalytic efficiency is often a trial-and-error process limited by poor control of the local catalyst environment and a lack of modular strategies to append catalysts to support materials. Here, we introduce a “plug-and-play” heterogenous catalysis platform that overcomes these challenges. Our approach leverages the well-defined interiors of self-assembled Pd12L24 metal–organic cages/polyhedra (MOCs): through a simple combination of catalyst-ligands, polymeric ligands, and spacer ligands, we demonstrate facile self-assembly of a diverse range of polymer gels featuring endohedrally-catalyst-functionalized junctions. Through decoupling catalyst incorporation and environment from the physical properties of the support (polymer matrix), this simple strategy is shown to enhance the recyclability of various catalyst systems (e.g., TEMPO-catalyzed oxidation and Au(I)-catalyzed cyclization) and enable catalysis in environments where homogeneous catalyst analogs are not viable.

The development of reusable, effective, and selective catalysts is imperative for the implementation of green chemical practices and continues to drive innovation in the chemical sciences.1,2 Heterogenous catalysts have long been at the forefront of this endeavor due to their recyclability and ease
of isolation from reactants and product mixtures. Despite these advantages, developing heterogeneous catalysts *de novo* is challenging as mechanistic features of a catalytic process are much more difficult to study in the solid state. By contrast, homogeneous catalytic process are easier to study and optimize based on mechanistic insights but are inherently less amenable to facile catalyst recovery and reuse. Ideally, one could transfer well-defined homogeneous catalytic systems directly to solid supports in a modular and robust way without diminishing catalyst activity and/or selectivity.

Fig. 1. **a**, Previous methods to immobilize traditionally homogeneous catalysts have involved the use of polymer networks, or metal-organic frameworks (MOFs). However, these approaches typical result in a trade-off between catalytic activity, and desirable materials properties. **b**, The polyMOC catalyst-containing network (polyCAT) uses the templated assembly of metal organic cages (MOCs) to allow tunable and predictable catalyst environments regardless of catalyst identity. The polymer strands linking the MOCs dictate the physical and mechanical properties of the material, and can be changed without altering the catalyst environment.

Toward this end, the immobilization of homogenous catalysts onto amorphous crosslinked polymers is a common strategy that benefits from the compositional diversity, synthetic flexibility, and tunable physical properties of polymers, (Fig. 1a). When such catalyst-functionalized polymer
networks are in a swollen state (i.e., gels), reagent mobility can approach that within solution, facilitating reasonable reaction rates. Nevertheless, the amorphous nature of such materials makes it nearly impossible to control the local catalyst environment, giving rise to unpredictable outcomes and potential batch-to-batch variation. Crystalline polymer networks, including coordination polymers such as metal organic frameworks (MOFs), can overcome this challenge by enabling exquisite local tuning of catalyst environments; however, such materials are often glassy and brittle, they may require harsh and extended annealing conditions for their formation, and they can suffer reagent flux issues to and from their crystalline pores, leading to lowered catalytic efficiency compared to homogeneous processes.

An ideal heterogeneous catalysis platform would (1) enable modular conjugation of structurally distinct homogeneous catalysts to facilitate a wide range of catalytic transformations; (2) provide a tunable and predictable local catalyst environment that is distinct from the support; (3) allow for changing of the support composition to facilitate use in different solvents/conditions; and (4) would maintain, or even improve, catalyst efficiency and selectivity compared to the analogous homogeneous reaction conditions. Here, we demonstrate proof-of-concept of such a system. Our approach leverages metal–organic cage/polyhedra (MOC)-crosslinked polymer gels, where the MOCs serve as nanoscale porous junctions that provide tunable and predictable local catalyst environments; the polymer strands that link MOCs control the physical and mechanical properties of the materials (Fig. 1b). These “polyCATs” are readily prepared from simple mixing of 3–4 components, depending on the need: (i) endohedral catalyst-functionalized ligands (CLs), (ii) exohedral polymer-functionalized ligands (PLs), (iii) spacer ligands (SLs) where necessary to accommodate larger catalysts, and (iv) metal ions (e.g., Pd(II)), offering a “plug-and-play” approach to heterogenous catalysis, as demonstrated through the realization of two mechanistically distinct traditionally homogeneous catalytic transformations (a TEMPO-catalyzed oxidation and a Au(I)-mediated cyclization), facile catalyst recycling and correspondingly improved catalyst turnover numbers (TONs), and, in one case, catalyst reactivity that is impossible for the analogous homogeneous system.

Results

TEMPO-polyCAT design, synthesis, and application to alcohol oxidation reactions. To test the viability of the polyCAT concept, we first targeted a TEMPO-catalyzed oxidation reaction that had previously been reported to proceed under homogeneous conditions and within the pores of mesoporous silica using Pd$_{12}$L$_{24}$ MOCs. Here, the same TEMPO-conjugated bis-para-pyridine ligand TEMPO-CL was used along with a novel four-arm polyethylene glycol (PEG) star polymer terminated with bis-
para-pyridine ligands **PEG-PL** (Fig. 2a, see Supporting Information section “Materials and Methods” for gel formation conditions). We define the “C:P” ratio as the average number of bis-pyridyl units in each Pd$_{12}$L$_{24}$ cage that derive from the catalyst ligand (e.g., **TEMPO-CL**) and the polymer ligand (e.g., **PEG-PL**), respectively. Three C:P ratios were screened—9:1, 21:3, and 20:4—to balance a high catalyst loading (higher C:P) with minimal catalyst leaching into solution (lower C:P). Each mixture was combined with [Pd(MeCN)$_4$][BF$_4$]$_2$ in DMSO (65 mM Pd(II) in a 5 wt/wt % PEG-PL solution) and annealed for 4 h at 60 °C. The resulting gels were soaked 4 times for 4 h each in excess CDCl$_3$ and the supernatants of each wash were collected and analyzed via quantitative electron paramagnetic resonance (EPR) spectroscopy (Figs. S1–S2, see Supporting Information section “EPR Studies” for details). In each case, the catalyst incorporation was quite high, with only 5.3%, 4.5% and 2.6% of the TEMPO-CL not incorporated into the materials prepared from 9:1, 21:3 and 20:4 C:P ratios, respectively (Table S1). We note that these gels represent the first materials, to our knowledge, to be crosslinked with acetylene-linked, ~4.6 nm diameter Pd$_{12}$L$_{24}$ MOCs.$^{30}$

Based on these results, materials prepared using a 20:4 C:P ratio, referred to as “**TEMPO-polyCAT,**” were used for subsequent studies. In addition to limiting catalyst leaching and simultaneously providing a high average catalyst loading, this C:P ratio features an average of 4 polymer strands per MOC junction, thus matching the branch functionality of the PL and providing for a robust “A$_4$ + B$_4$”-like network topology.$^{24}$ Cross polarization-magic angle spinning (CP-MAS) $^1$H NMR (Fig. S3) and small-angle X-ray scattering (SAXS, Fig. S4) were used to characterize the structure of **TEMPO-polyCAT.** The former shows characteristic peak broadening and shifting associated with pyridine–Pd coordination-driven assembly while the latter displayed peaks associated with the average inter-MOC spacing and MOC form factor.$^{22-25}$ **TEMPO-polyCAT** had a storage modulus, $G'$, of 28 kPa at 10 rad/s as determined by linear shear rheology frequency sweep experiments (Fig. 2b). Notably, an analogous gel (**control gel 20:4**) prepared from PEG-PL but using a non-catalyst-functionalized methoxy spacer ligand (SL) with the same C:P ratio displayed nearly identical frequency sweep behavior, suggesting that catalyst incorporation is decoupled from the overall network mechanics and that the overall network structures are similar in the presence or absence of TEMPO.

Electron paramagnetic resonance (EPR) spectroscopy was used to gain a deeper understanding of the local nitroxide environment in **TEMPO-polyCAT.** Compared to **TEMPO-CL,** the EPR spectrum of **TEMPO-polyCAT** was significantly broadened as expected for immobilized free radicals (Fig. 2c).$^{31-33}$ Fitting the spectra revealed clear signs of reduced nitroxide mobility and strong spin-spin exchange interactions, indicative of the nitroxides being crowded within the MOC junctions (see Supporting
Information section “EPR Studies” for details). Moreover, the fitting indicated that 94% of the nitroxides existed within a similar chemical environment, which is expected given the symmetry of the MOC junctions. Remarkably, the spectrum for TEMPO-polyCAT was nearly identical to that of a soluble MOC composed of 20:4 TEMPO-CL and a methoxy-functionalized spacer ligand SL (Fig. 2c). In other words, introduction of polymer linkers to the exterior of the MOCs does not significantly perturb the catalyst environment, which should facilitate predictable and direct translation of these formerly homogeneous catalysts to polyCATs. Additionally, this result provides strong evidence for the existence of well-formed MOC junctions within TEMPO-polyCAT, as the EPR spectrum for an unannealed material with ill-defined metal–organic crosslinks clearly showed a larger distribution of distinct nitroxide environments (see Supporting Information section “EPR Studies” for details).

**Fig. 2.** Analysis of the structure and reactivity of the TEMPO-polyCAT gel. a, Scheme and image showing the synthesis of the polyCAT gel. b, Comparison of a control gel (black) with an unfunctionalized ligand to the TEMPO-polyCAT (red) using a frequency sweep in a
sheer rheometer. c, EPR spectra showing TEMPO-CL (CHCl₃), TEMPO-CL assembled as MOCs (TEMPO-MOC, CHCl₃) and TEMPO-polyCAT. TEMPO-polyCAT shows significantly broadened peaks compared to TEMPO-CL, indicative of strong spin-spin interactions resulting from spatially localized TEMPO molecules. d, The oxidation of 3-phenyl-1-propanol (1) to its corresponding aldehyde (2) using TEMPO-polyCAT. e, Comparison of the rate of oxidation of TEMPO-CL free in solution (black) and TEMPO-polyCAT gel (red). f, Cycling of the oxidation using TEMPO-polyCAT. Conversions are calculated based on ¹H NMR integration vs. an internal standard. g, Deswelling, storage, and swelling of the material does not diminish the catalytic activity.

To investigate the activity of TEMPO-polyCAT as a heterogeneous catalyst for alcohol oxidation, a solution of 3-phenyl-1-propanol (1, 1.0 equiv) and diacetoxyiodobenzene (1.2 equiv) in CDCl₃ (0.1 M) with tetrakis(trimethylsilyl)silane as an internal standard was added to a 1 mL reaction solution containing a 200 mg TEMPO-polyCAT gel (0.02 mmol TEMPO-CL, 10 mol % relative to 3-phenyl-1-propanol) (Fig. 2d). >95% conversion of 1 to the corresponding aldehyde 2 was observed within 12 h. Moreover, the extent of conversion as a function of time was nearly identical to a homogeneous reaction using the same loading of TEMPO-CL as the catalyst. To ensure catalyst leaching was not responsible for the observed catalytic activity of TEMPO-polyCAT, the same reaction was run using the supernatant collected after washing a freshly prepared TEMPO-polyCAT sample four times with chloroform; conversion was <3% after 24 h. Additionally, the activity of the supernatant at the end of the catalytic reaction was tested: TEMPO-polyCAT was removed from the mixture and an additional portion of 1 and oxidant were introduced to the solution. After 10 h, less than 5% of the new substrate was converted to 2. These results strongly suggest that the catalytic behavior of TEMPO-polyCAT is not due to leached catalyst but is instead driven by the endohedrally-bound catalysts within the polymer network junctions.

Highlighting the utility of TEMPO-polyCAT as a heterogeneous system, the material was cycled through 9 rounds of the above reaction with 3 × 30 min washes between each cycle. ¹H NMR conversion of 1 to 2 was >95% for the first 5 cycles and decreased during cycles 6–9 (Fig. 2d). While TEMPO-polyCAT maintained its gel form throughout this process, it became grey in color after 9 reaction cycles, perhaps indicating decomposition of TEMPO. Nevertheless, this performance over 9 cycles amounts to nearly an order-of-magnitude increase in the catalyst turnover number (TON). Finally, to demonstrate the long-term storability of TEMPO-polyCAT, a sample was fabricated, dried under a stream of nitrogen for 30 min, and stored at −20°C for 3 weeks. After this time, the material was swelled in CDCl₃ and used to catalyze the oxidation of 1; no loss in activity was observed (>95% NMR conversion, Fig. 2e).
Au-PolyCATs for Au(I)-catalyzed cyclization reactions. Reek and coworkers have reported fascinating homogeneous bis-pyridyl-based Au(I) phosphine complexes (e.g., Au-CL, Fig. 3a) that are poor catalysts themselves but, due to local concentration effects, function as highly active catalysts when assembled into MOCs through Pd(II) coordination.\textsuperscript{34-36} Successful translation of these systems to polyCATs would not only further the polyCAT concept but would provide further evidence for the presence of assembled catalytic MOC junctions within polyCAT networks. Thus, a new polyCAT—Au-polyCAT—was prepared following the same procedure used for TEMPO-polyCAT but by simply exchanging TEMPO-CL for Au-CL (here a modified C:P ratio of 16:8 instead of 20:4 was necessary due to the solubility of Au-CL).\textsuperscript{34} The SAXS curve for Au-polyCAT was very similar to that of TEMPO-polyCAT (Figure S4), showing equivalent MOC diameters but a small decrease in the inter-MOC spacing of Au-polyCAT as expected from the modified C:P ratio, and shear rheology suggested a nearly identical frequency response compared to an analogous gel (control gel 16:8) prepared from methoxy-functionalized SL with the same
C:P ratio (Fig. 3b). These results are remarkable, showing that by simply choosing the CL of interest, TEMPO-CL or Au-CL, it is possible to generate robust polyCATs from the same PL and Pd(II) salt through simple mixing, offering modularity to heterogeneous catalyst design.

The catalytic activity of Au-polyCAT was examined in the context of the intramolecular ring closing of alleneol 3 to form furan 4 (Fig. 3c). A solution of 3 in CDCl\textsubscript{3} (0.05 M) containing tetrakis(trimethylsilyl)silane as an internal standard was added to a 2 mL reaction solution containing a 400 mg Au-polyCAT gel (0.016 mmol Au-CL, 20 mol% relative to alleneol 3). After 48 h, ~90% conversion of 3 to 4 was observed by \textsuperscript{1}H NMR spectroscopy (Fig. 3d). Moreover, the Au-polyCAT was cycled through 7 rounds of the same reaction without loss of activity and achieved 60% conversion after 10 cycles giving a TON of 41. By contrast, and as expected based on the work of Reek and colleagues,\textsuperscript{34} the reaction reached only 20% conversion when Au-CL was used as the catalyst (Fig. S5), supporting the presence of well-assembled MOC junctions within Au-polyCAT.\textsuperscript{34}

A key potential advantage of the polyCAT system is that through decoupling of the catalyst environment from the polymer support, it could enable catalytic transformations in solvents or conditions where the catalysts are not otherwise compatible. For example, Au-CL and Au-MOC are not soluble in water; however, due to the polar nature of PEG-PL, Au-polyCAT swells extensively (swelling ratio of 4.4 in D\textsubscript{2}O). As a result, Au-polyCAT outperformed Au-CL and Au-MOC in the cyclization of 5 to 6 in D\textsubscript{2}O (Fig. 3e), achieving 96% conversion in 8 h compared to 1% for Au-CL and 21% for Au-MOC (Fig. 3f). While water-soluble gold(I) N-heterocyclic carbene\textsuperscript{37-39} and triphenylphosphine complexes\textsuperscript{40} have been reported for analogous cyclization reactions, catalyst recovery is challenging and has not been demonstrated for these homogeneous systems. By contrast, Au-polyCAT could be cycled at least 12 times, maintaining >94% (Fig. 3g) conversion and achieving a TON of 115. An increase in swelling and a 3-fold decrease in \textit{G}' was observed after these 12 cycles, suggesting some mechanical wearing of the material (Fig. S6). To rule out catalyst leeching from the network due to gel degradation over these 12 cycles, substrate 4 was added to the supernatant of an Au-polyCAT-catalyzed reaction; after 8 h, <5% of 4 had cyclized to the lactone product (<15% after 24 h), indicating that the catalytic activity of gel degradation products is negligible. Altogether, these results highlight the potential to use polyCATs under conditions that are not compatible with homogeneous catalyst analogues (e.g., aqueous conditions wherein the catalysts are not soluble) and for facile catalyst recycling.

Finally, to further demonstrate the modularity of this system using different polymer supports, two new polyCATs were prepared from Au-CL by exchanging PEG-PL with bis-pyridyl-functionalized linear polystyrene (PS-PL, \(M_n = 31,000, D = 1.08\) and star poly(\textit{tert}-butyl acrylate) (PBA-PL, \(M_n =\)
22,000, $D = 1.09$) ligands (Fig. S7, see Supporting Information “Materials and Methods” for full details). The conversion of 5 to 6 in toluene-$d_8$ solvent was >88% after 8 h for all three of these polyCATs, showing that the same catalyst (Au-CL) can be modularly swapped with different polymers even of different architecture (linear versus star) to produce active polyCATs (Fig. S8).

Conclusions

Herein, we have demonstrated a novel polymer network strategy—polyCATs—that allows us to combine the control of homogeneous catalysis with the benefits of heterogeneous catalysts through decoupling catalyst incorporation and environment (within the pores of MOC junctions) from the physical properties of the support (polymer strands). Two different CLs (TEMPO-CL and Au-CL) and three different PLs (PEG-PL, PS-PL, PBA-PL) were used to demonstrate the versatility and modularity of this approach using mechanistically distinct reactions. PolyCATs provided high reaction conversions in each test case, and they could be easily recycled and reused over subsequent reaction cycles, requiring only simple washing between reactions. Additionally, due to the distinct nature of polyCAT junctions versus strands, polyCATs allow recyclable catalysis in solvents where the traditional homogeneous catalyst is insoluble (e.g., H₂O). In the future, the polyCAT strategy will leverage the diversity of MOCs of varied shape and composition available today, along with numerous polymer compositions, to facilitate the creation of catalytic materials for a range of synthetic endeavors, potentially simplifying organic synthesis, enabling novel cascade processes and greener manufacturing strategies, and ultimately achieving multifunctional materials that combine the robust mechanical properties of polymer networks with catalytic functions.

Associated Content

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