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A heterogeneous, selective oxidation catalyst based on Mn triazacyclononane grafted under reaction conditions†

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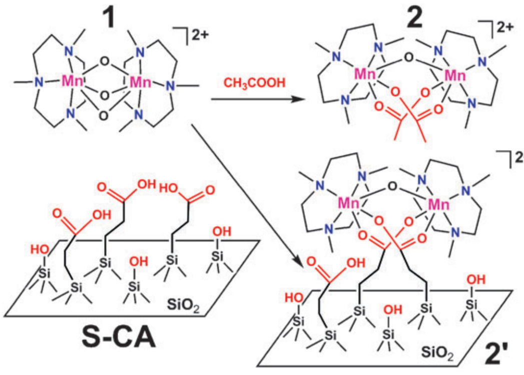
A unique method has been developed to synthesize an active heterogeneous oxidation catalyst by the *in situ* grafting of a 1,4,7-trimethyl-1,4,7-triazacyclononane manganese complex on carboxylic acid-functionalized supports serving dual roles as surface tether and necessary co-catalyst, massively increasing total turnovers as compared to the homogeneous analog.

The selective oxidation of olefins to *cis*-diols or epoxides remains of great industrial importance.[1] Manganese 1,4,7-trimethyl-1,4,7-triazacyclononane (tmtacn) complexes, *e.g.* **1**, were first reported in the late 1980's and were quickly realized to be powerful low temperature oxidation catalysts.[2] Mn(IV,IV) complex **1** efficiently catalyzes alkene oxidation with H_2O_2 in the presence of carboxylic acid (CA) co-catalysts that suppress the inherent catalase activity of **1** and enable tuning of the catalyst selectivity towards epoxide or *cis*-diol.[3] The exact role of the co-catalyst and the precise nuclearity of the active species in homogeneous systems remain under investigation, but it has been suggested that the system **1**–H_2O_2–CA forms a reduced bis(μ-carboxylato)–Mn_2^{III} complex **2** that is the resting state for alkene oxidation.[3b,c] Although explored less than for other molecular oxidation catalysts, a route to heterogenized Mn triazacyclononane catalysts supported on SiO_2 has been developed *via* modification of the ligand,[4] but its mechanism of reaction also remains incompletely understood.

Seizing on the requirement of CA co-catalysts for efficient H_2O_2 utilization in many homogeneous systems, we have developed a novel protocol for immobilization. Catalysts 'heterogenized' on solid supports often rely on covalent attachment of P, N, or S ligands, or strong electrostatic adsorption of an otherwise proficient homogeneous catalyst, and often results in a diminishment of reactivity or selectivity.[5] Also, immobilizing active homogeneous catalysts can create 'Trojan horse' effects where the solid is a reservoir for active soluble species.[6] Our approach instead combines complex **1** with co-catalytic CA-functionalized SiO_2 gel (S–CA), fumed SiO_2 (FS–CA) or Al_2O_3 gel (A–CA). Under reaction conditions, **1** grafts itself to the surface creating a solid catalyst (**2′**) that is more efficient for cyclooctene oxidation with aqueous H_2O_2 when in the grafted form.



Complex **1** was synthesized from tmtacn, $MnCl_2{\cdot}4H_2O$, and KPF_6.[7] Complex **2** was synthesized from tmtacn, $Mn(OAc)_3{\cdot}2H_2O$, CH_3COONa and KPF_6.[7c] CA-functionalized supports, S–CA, FS–CA and A–CA, were synthesized by grafting and subsequent deprotection of 2-(carbomethoxy)-ethyl-trimethoxysilane.[8] The silane precursor concentration was varied to synthesize supports with molar loadings ranging from 0.06–0.66 $\mathrm{mmol_{CA}(g_{SiO_2})^{-1}}$ or 0.07–0.80 $\mathrm{CA(nm_{surface})^{-2}}$. Supported structures and their loadings were verified by ^{13}C CP/MAS NMR spectroscopy and thermogravimetric analysis. Alkene oxidation was performed in sealed batch or semi-batch reactors in acetonitrile (MeCN) at 0 °C with controlled amounts of S–CA, FS–CA, A–CA, or valeric acid, *o*-dichlorobenzene internal GC standard, and 30% aqueous H_2O_2. Air was not excluded. Full synthesis, characterization, and catalysis details are found in the ESI†.

Combining S–CA or FS–CA with **1** yielded substantially more total turnover numbers (TON = $\mathrm{mol_{product}\ mol_{1}^{-1}}$) to *cis*-cyclooctanediol and *cis*-cyclooctane epoxide products than **1** alone or **1** with un-functionalized SiO_2 or Al_2O_3 (Table 1). In the absence of effective CA co-catalysts, Mn tmtacn complexes are known to rapidly decompose H_2O_2.[2a,3a,9] Thus, total TON are a function of the initial concentrations and the relative rate constants for oxidation *vs.* H_2O_2 decomposition, assuming the catalytic cycles progress through the same intermediate (see ESI†). S–CA co-catalysts led to ~10× higher total TON and relative oxidation rate constants than its closest homogeneous analog, valeric acid, when similar amounts of co-catalyst were present, either alone or with unmodified SiO_2. Formation of the catalyst *in situ* creates a much more active catalyst than deliberate grafting and isolation of the air-stable catalyst (see ESI†) suggesting that the surface species is a true catalyst intermediate rather than another isolable pre-catalyst form. Slow addition of H_2O_2 in semi-batch reactions, which is typically employed for this class of catalyst, yields 450 total TON towards *cis*-diol and epoxide with only 2 eq. S–CA. Slightly higher catalyst loadings enable ~100% cyclooctene conversion at the expense of TON (see ESI†). In the absence of alkenes, S–CA

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† Electronic supplementary information (ESI) available: Synthesis, catalysis, and characterization procedures; solution and diffuse reflectance UV-visible spectra, NMR spectra, and thermogravimetric analyses of solid materials. See DOI: 10.1039/b920391e

Table 1 Alkene oxidation with **1** and various co-catalysts under equivalent conditions[a]

Co-catalyst	R/mol$_{CA}$ mol$_{Mn}^{-1}$	Reactant	Total TON	% Epoxide : % *cis*-diol : % other[c]
None	0	*cis*-Cyclooctene	<5	87 : 13 : 0
SiO_2	0	*cis*-Cyclooctene	24	76 : 24 : 0
Al_2O_3	0	*cis*-Cyclooctene	<5	75 : 25 : 0
S–CA	1	*cis*-Cyclooctene	147	66 : 34 : 0
S–CA	10	*cis*-Cyclooctene	465	61 : 39 : 0
S–CA[b]	2	*cis*-Cyclooctene	455	55 : 45 : 0
FS–CA	1	*cis*-Cyclooctene	198	58 : 42 : 0
A–CA	10	*cis*-Cyclooctene	<5	57 : 43 : 0
Valeric acid	1	*cis*-Cyclooctene	17	89 : 11 : 0
Valeric acid/SiO_2	10	*cis*-Cyclooctene	13	86 : 14 : 0
Valeric acid	10	*cis*-Cyclooctene	53	51 : 49 : 0
Valeric acid	500	*cis*-Cyclooctene	644	39 : 61 : 0
S–CA	10	Cyclohexene	835	63 : 6 : 31[c]
S–CA	10	Norbornene	585	91 : 3 : 6
S–CA	10	Cyclohexenone	238	75 : 15 : 10
S–CA	10	1-Octene	609	90 : 3 : 7
S–CA	10	Styrene	544	92 : 3 : 5
S–CA	10	α-Methylstyrene	824	83 : 16 : 1
S–CA	10	*trans*-β-Methylstyrene	248	79 : 11[d] : 10
S–CA	10	*cis*-Stilbene	213	41 : 55[d] : 4

[a] Unless noted, all reactions were performed in a batch reactor at 0 °C with 3 h reaction time, 2.0 mL MeCN, 0.13 mM **1**, 0.17 M *cis*-cyclooctene, and 130 μL 30 wt% H_2O_2. [b] Semi-batch. See ESI† for conditions. [c] Allylic oxidation products: 9% cyclohexenol, 9% radical-derived epoxide, 3% *trans*-diol, 4% cyclohexenone, 7% other. [d] Mixture of *cis*- and *trans*-diol.

(3 eq.) reduced the catalase activity of **1** by 20% at 0 °C or 45% at 25 °C (see ESI†). Thus, the supported CA was more effective both at decreasing catalase activity and increasing oxidation activity.

The enhanced reactivity with solid co-catalysts is likely due to the high local surface densities of CA, equivalent to an average CA separation of 0.85 nm, which is more than adequate to multiply-coordinate Mn even at low total CA due to the surface chelate effect.[10,11] Weak Brønsted acidity of SiO_2 may also assist in activating the H_2O_2, as for Ti–SiO_2.[12]

Strong support effects on catalyst productivity and selectivity were observed, demonstrating a role for the oxide support beyond that of inert spectator. Co-catalyst A–CA did not increase total TON above that of **1** alone, in contrast to the large increases in productivity for functionalized SiO_2. Functionalized, non-porous fumed SiO_2 (FS–CA) exhibited slightly higher productivity than S–CA at low co-catalyst ratios. FS–CA and A–CA have 0.45 and >0.8 CA(nm$_{surface}$)$^{-2}$, respectively, comparable to S–CA, so TON are not likely influenced by geometric ability to form the active structure **2′**. Differences in TON and selectivity among supports are hypothesized to be due to the density and pK_a of residual surface hydroxyls, which is under investigation.

For no co-catalyst, low levels of valeric acid, or unfunctionalized SiO_2 or Al_2O_3, none of which interact strongly with **1**, intrinsically low selectivity to *cis*-cyclooctanediol was observed. All functionalized supports gave relatively constant *cis*-diol selectivities near 40% for the co-catalyst ratios R = mol$_{CA}$ mol$_{Mn}^{-1}$ investigated, suggesting similar active species for all SiO_2-supported catalysts.

High oxidation productivity was observed for diverse alkenes. Total TON to epoxide and diol, that is, the relative rate of oxidation *vs.* H_2O_2 decomposition, increases with increasing electron density at the double bond and with decreasing steric congestion. Cyclohexenone has a low yield of oxidation products, as expected from the electron-withdrawing ketone. The dependence on sterics is demonstrated by higher yields with α-methylstyrene than with β-methylstyrene, increasing yields with decreasing ring size, and the higher yields with styrene and *n*-octene than one might expect for monosubstituted alkenes. *cis*-Stilbene, which is both bulky and relatively electron deficient, has a low yield. Multiply substituted alkenes generally give lower selectivity to epoxide. Only 3% selectivity to *trans*-cyclohexanediol was observed, indicating low epoxide hydrolysis activity.

The effects of CA surface loading and co-catalyst ratio R on catalyst productivity are given in Fig. 1. For constant amounts of Mn, total TON increased sharply up to $R \approx$ 1–1.5 mol$_{CA}$ mol$_{Mn}^{-1}$, and rose more slowly at greater ratios. For constant CA, H_2O_2 utilization E was maximized near equimolar CA and Mn (inset, F = 0.5). Low Mn loadings are kinetically limited, and H_2O_2 decomposition dominates with excess Mn. For S–CA, changing CA surface loading did not have a significant effect on total TON, suggesting that the CA groups may cluster more than is implied by their average surface density. The effects of surface density remain under investigation. Elemental analysis indicates that $>75\%$ of the Mn is complexed with R = 2.0, UV-visible spectra indicate loss of $>95\%$ of **1** from solution with R = 1.5, and even at R = 1.0, the solution above the S–CA solids displayed no oxidation productivity after being removed from the solids, even with additional H_2O_2 or S–CA added to the decanted solution (see ESI†). These results indicate that the curve shape in Fig. 1 is due to an increasing fraction of productive surface Mn complexes with increasing S–CA content, rather than simple trapping of an active complex. This ability to assign two-electron oxidation activity primarily to the surface species is in contrast with the free-radical, metal-initiated oxidations observed for the limited prior examples of metals combined with CA-functionalized supports.[13]

The structure of the Mn species in the catalyst cycle remains a subject of debate,[3] however the stoichiometry at maximum TON is consistent with either a dimeric surface structure with two to three bridging and surface-linking CA groups (*e.g.* **2′**) or a monomeric surface structure with one surface-linking CA group per monomer. However, electronic spectra of the

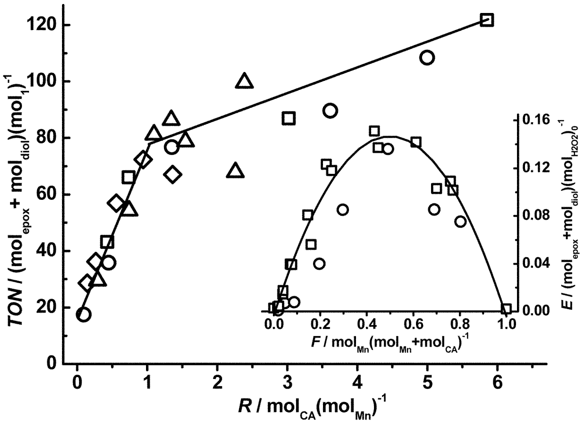

Fig. 1 Effect of CA to Mn molar ratio and CA surface density of S–CA on total TON to epoxide and *cis*-diol at a constant 2.7 ± 0.3 × 10^{-3} mmol **1** under batch reactor conditions. (Inset) Effect of mole fraction Mn *vs.* CA on H_2O_2 utilization at constant 2.9 ± 0.4 × 10^{-3} mmol surface CA under batch reactor conditions. Lines are included as a guide to the eye. Δ 0.06, ◇ 0.14, ○ 0.25, and □ 0.51 $\text{mmol}_{\text{CA}}(\text{g}_{\text{SiO}_2})^{-1}$.

surface species formed under reaction conditions are more consistent with the former. In the absence of oxidant, solution and diffuse reflectance UV-visible spectra show **1** disappearing from MeCN–H_2O solution (see ESI†) and adsorbing without change onto S–CA (Fig. 2c and d). In contrast, with H_2O_2 present, **1** disappears more rapidly from solution and the solid-supported species shows a characteristic shoulder at ~320 nm, virtually identical to **2** in solution (Fig. 2a and b). Diffuse reflectance UV-visible spectra of A–CA with adsorbed **1** are structureless indicating the absence of a well-defined Mn complex (see ESI†), in line with the lack of catalyst activity.

In conclusion, carboxylic acids grafted onto SiO_2 (*e.g.* S–CA) are an especially effective co-catalyst for selective oxidation with tmtacn manganese(IV) dimer **1**. The oxidant-dependant reaction between **1** and the supported CA synthesizes a heterogeneous catalyst (**2′**) under reaction conditions, and this heterogeneous catalyst has >10× productivity for cyclooctene oxidation *vs.* H_2O_2 decomposition than for the same ratios of analogous homogeneous co-catalyst valeric acid. Many non-heme oxidation catalysts require carboxylic acid co-catalysts or additives for selective oxidation of various substrates,[14] and this communication demonstrates a generalizable route to the synthesis of molecularly well-defined, solid-supported versions of this type of catalyst that avoids synthetic modification of the ligand, which can complicate catalyst development and understanding. Finally, the analogy can be made between the active sites in this work and those of many oxidation enzymes, in which a 'metal cofactor' (*e.g.* **1**) is embedded in a coordinating scaffold (*e.g.* S–CA) to create a new, more productive catalyst (*e.g.* **2′**) whose reactivity is sensitive to subtle changes to the scaffold structure.

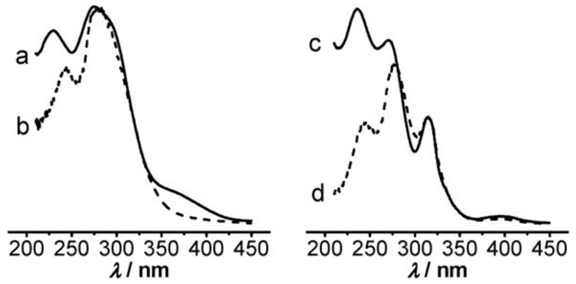

Fig. 2 Normalized UV-visible spectra of (a) **2** in MeCN, (b) **2′** *via* self-catalyzed grafting of **1** on S–CA from MeCN–H_2O_2, (c) **1** in MeCN, and (d) **1** adsorbed on S–CA from MeCN–H_2O.

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