The Role of Outer-Sphere Surface Acidity in Alkene Epoxidation Catalyzed by Calixarene–Ti(IV) Complexes

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Abstract: Cooperativity between Bronsted acidic defect sites on oxide surfaces and Lewis acid catalyst sites consisting of grafted calixarene–Ti(IV) complexes is investigated for controlling epoxidation catalysis. Materials are synthesized that, regardless of the surface or calixarene substituent, demonstrate nearly identical UV–visible ligand-to-metal charge-transfer bands and Ti K-edge X-ray absorption near edge spectral features consistent with site-isolated, coordinatively unsaturated Ti(IV) atoms. Despite similar Ti frontier orbital energies demonstrated by these spectra, replacing a homogeneous triphenylsilanol ligand with a silanol on a SiO2 surface increases cyclohexene epoxidation rates with tert-butyl hydroperoxide 20-fold per Ti site. Supporting calixarene–Ti active sites on fully hydroxylated Al2O3 or TiO2, which possess lower average surface hydroxyl pKa than that of SiO2, reduces catalytic rates 50-fold relative to SiO2. These effects are consistent with SiO2 surfaces balancing two competing factors that control epoxidation rates—equilibrated hydroperoxide binding at Ti, disfavored by stronger surface Bronsted acidity, and rate-limiting oxygen transfer from this intermediate to alkenes, favored by strongly H-bonding intermediates. These observations also imply that Ti–OSi rather than Ti–OCalix bonds are broken upon hydroperoxide binding to Ti in kinetically relevant steps, which is verified by the lack of a calixarene upper-rim substituent effect on epoxidation rate. The pronounced sensitivity of observed epoxidation rates to the support oxide, in the absence of changes to the Ti coordination environment, provides experimental evidence for the importance of outer-sphere H-bonding interactions for the exceptional epoxidation reactivity of titanium silicalite and related catalysts.

Introduction

The design and characterization of solid catalysts at the atomic level is challenging, at least in part because of the difficulty in deconvoluting inner- and outer-sphere effects on their catalytic function.1,2 Inner-sphere effects arise from ligands coordinated directly to active atoms and consequent changes to the ground-state electronic structure of these atoms. The outer-sphere is less well-defined for inorganic solid catalysts and consists of noncoordinated moieties, such as vicinal Bronsted acid sites, coadsorbed species, and the fluid phase.

Titanosilicates, such as TS-1, represent a class of materials for which atomic-level details are only gradually emerging, despite their broad application as epoxidation catalysts.3 The accepted mechanism for epoxidation of unfunctionalized alkenes on all Ti–SiO2 materials involves concerted oxygen transfer from an electrophilic oxygen on Ti-bound hydroperoxides to the alkene substrate.4–7 In other epoxidation systems, reaction rates have been shown to increase with increasing electrophilicity of stoichiometric oxidants8 and homogeneous catalysts.9 Therefore, the superior alkene epoxidation properties of Ti–SiO2 relative to other molecular and supported metal oxides,10 have been primarily attributed to an inner-sphere effect of coordinately unsaturated tetrahedral Ti atoms stabilized within an electronegative SiO2 framework. This assignment of the active structure is consistent with theoretical calculations.11–17

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UV–visible spectroscopy studies,18,19 and X-ray absorption spectroscopy studies.20,21 The basis for the marked differences in epoxidation rates, optimal conditions, and preferred oxidants between TS-1 and other titanosilicates,22 Ti–SiO2 materials,23 and homogeneous complexes,24 however, remains controversial,25,26 particularly because all effective catalysts show similar Ti inner-sphere environments by the aforementioned electronic spectroscopies.

H-bonding assemblies of outer-sphere Brønsted acids have been proposed as intermediates in epoxidation catalysis on TS-1 to explain the strong effects of protic solvents on rates.27 These rate increases could not be explained solely on the basis of adsorption and partitioning.26,28 The presence of Brønsted acidic silanol nests15 or silanols generated by hydroperoxide binding,11 alone or in combination with protic solvents, has been suggested to explain differences between the reactivity of TS-1 and other Ti catalysts. However, experimental proof of an outer-sphere effect in TS-1 catalysis has remained elusive, at least in part, because of the difficulty in identifying which bond-breaking processes form Brønsted acids in the kinetically relevant steps,29,30 and because systematic and proven variations of the inner- and outer-sphere environments are difficult to achieve in heterogeneous catalysts without unintended changes in structural features of uncertain importance to catalytic function.31

Here, electron-donating and electron-withdrawing calixarenes (macrocyclic phenols 1a–4a) are synthesized and molecular calixarene–Ti complexes are crafted covalently to oxide surfaces (Scheme 1: SiO2, TiO2, Al2O3, and triphenylsilanol as a model) to address the kinetic relevance of outer-sphere Brønsted acidity on Ti-catalyzed cyclohexene epoxidation with tert-butylhydroperoxide. The Ti inner-sphere environment remains constant, as probed by ligand-to-metal charge transfers (LMCT) in the UV–visible spectrum and by Ti 1s–3d electronic transitions that give rise to near-edge features in the Ti K-edge absorption spectrum. In contrast, calixarene phenols and oxide support OH defects are chosen to span a broad pKa range. Therefore, the sensitivity of the observed epoxidation rate to ligand or support variations probes the kinetic relevance of Brønsted acids formed from Ti–O–support or Ti–O–calixarene bond cleavage.

We have previously demonstrated that calixarene–Ti complexes grafted covalently on SiO2 are single-site heterogeneous catalysts for epoxidation of alkenes with organic hydroperoxides.32 The single-site nature of these catalysts eliminates the confounding effects of ensemble-averaging in structural and functional characterization, in contrast with the nonuniform active sites that can arise from post-synthesis modifications of Ti centers33 or doping of support oxides.34 Grafted calixarene–Ti catalysts are also more active than samples prepared by removing their organic ligands by thermal treatment in air (material 1-SiO2-c) or Ti–SiO2 samples prepared by alkoxide grafting at similar Ti surface densities.34 The multidentate and bulky calixarene–Ti precursors enforce site isolation during synthesis and during reaction and organize phenolate ligands to create Ti Lewis centers stronger than those formed.

![Scheme 1. Overview of Surface-Grafted and Homogeneous Calixarene–Ti Complexes](image)

| 1a | X = OPr |
| 1b | X = OPh |
| 1c | X = OSiPh3 |
| 1d | X = Cl |

(31) We do not discuss here the role of surface Brønsted acidity in leading to undesired epoxide ring opening in the presence of water or other primary alcohols. This side reaction is eliminated here by strictly anhydrous process conditions and does not arise from cooperative interactions between the Ti active site and surface OH defects.


(35) See Supporting Information for further discussion.
from alkoxy precursors. We have recently shown that the calixarene macrocycle controls the oxygen coordination at the grafted Ti atom without perturbing the isolated nature of active Ti atoms.

Experimental Methods

General Analytical. The mass loss of all grafted calixarene materials was determined by thermogravimetry (TGA; TA Instruments 2950) in a flow of dry synthetic air (2.0 cm$^3$ s$^{-1}$ 3:1 N$_2$O$_2$ from vaporized liquid O$_2$ and N$_2$ at a heating rate of 0.083 K s$^{-1}$) after correction for hydroxyl condensation losses (determined from mass losses in unmodified supports). Calixarene contents were estimated by assuming that mass losses reflect combustion of a molecular weight of 612 g/mol site (C$_{45}$H$_{55}$O) in material I and were adjusted accordingly for other upper rim substituted grafted calixarenes. Ti inductively coupled plasma emission mass spectrometry (ICP/MS) was performed by Quantitative Technologies, Inc.

UV-visible spectra were measured at ambient conditions using a Cary 400 Bio UV-visible spectrophotometer (Varian) equipped with a Harrick Praying Mantis diffuse reflectance accessory. Pressed poly-(tetrafluoroethylene) powders were used as perfect reflector standard in calculating Kubelka-Munk pseudoabsorbances. The edge energies were calculated by assuming the lowest energy transitions (calixarenes-Ti LMCT) were indirect. Tangent lines as shown in Figure 2 were calculated from the first derivatives of the transformed sample spectra. Solid-state 1H magic angle spinning (MAS) and 13C cross-polarized magic angle spinning (CP/MAS) NMR spectra were collected using a Bruker DRX500 spectrometer operating at 500 MHz at the Caltech Solid-State NMR facility. Solution NMR spectra were measured using a Bruker AMX-400 spectrometer operating at 400 MHz at the UC-Berkeley NMR facility.

The A1 pre-peak arises from a t$_{2g}$ bandlike state, whereas A2 and A3 features reflect eg bandlike states. The t$_{2g}$ and e$_{g}$ states represent the environment surrounding the Ti center. In the particular case of anatase (Scheme 1a)-TiCl$_4$, as reported previously, Complexes 1b and 2a were synthesized from iodomethane and tert-butylcalix[4]arene 1 and calix[4]arene 2, respectively. Calix[4]arene 2 was synthesized from 1 via reaction with phenol in the presence of AlCl$_3$ in toluene. New compounds 3a and 4a were synthesized from 2a via modified Friedel-Crafts procedures described in the Supporting Information. These procedures led to selective substitution at the para position of free phenols and isolation of the desired "cone" conformation shown in Scheme 2. This "cone" conformation was confirmed from its methylene 13C NMR resonances at ~31.5 ppm.

Ti Complex and Grafted Materials Synthesis. Complex 1d (Scheme 1) was synthesized from calixarene ligands 1a and (bis(tert-butyldimethyldichloro)-TiCl$_4$ as reported previously. Complexes 1b, 2b, 3b, and 4b (Scheme 2) were synthesized by adding 1 equiv Ti(OPr$_i$)$_4$ (Aldrich 99.999%) to a 0.1 M solution of 1a-4a in toluene and then stirring under a N$_2$ atmosphere for 48 h at ambient temperature. Complexes 1b and 2b were isolated by evaporating solvents to form red glassy and dull orange solids, respectively. Complexes 3b and 4b could not be isolated successfully as analytically pure species because of their low solubility. Complexes 1e and 2e were prepared by adding 0.1 M solutions of 1b or 2b in toluene to 1 equiv triphenylsilanol and refluxing 24 h in N$_2$ flow. The evaporation of volatile species at ambient temperature produced analytically pure 1e as an orange solid. Analytically pure yellow powders of 2e were obtained after evaporation of the synthesis solution and washing with anhydrous hexane. Detailed characterization data for these complexes are provided in the Supporting Information.

Mesoporous SiO$_2$ (Selecto Scientific) consists of 250–500 nm diameter aggregates with ~6.0 nm average diameter pores, possesses a N$_2$ BET surface area of 498 m$^2$/g, and produces pH 7 as a 5% suspension in H$_2$. Hombikat UV100 TiO$_2$ (Solablenbe) consists of 12 nm anatase crystallites embedded within 50 nm primary particles, which further form ~15 nm agglomerates possessing only macropores and a N$_2$ BET surface area of 343 m$^2$/g. Al$_2$O$_3$ (Brockman I; CAMAG)
Scientific) is a pseudo-boehmite phase material treated to 773 K during manufacture to remove 30% of its constitutional water resulting in a material with a N2 BET surface area of 155 m$^2$ g$^{-1}$ and pH 4.5 in a 5% suspension in H$_2$O. SiO$_2$ was treated in dynamic vacuum at 773 K for 24 h before grafting calixarene–Ti complexes. TiO$_2$ and Al$_2$O$_3$ were treated in dynamic vacuum at 393 K for 4 h before grafting calixarene–Ti species. Surface-grafted complexes were synthesized by treating 0.1 M solutions or suspensions of 1b–4b in toluene with the corresponding oxide support (0.25 mmol 1b–4b per gram oxide) in sufficient additional toluene to fully suspend particles during magnetic stirring. Complexes 1b–4b were used as synthesized without intervening purification steps. After adding 1b–4b, suspensions were refluxed for 24 h, and the reactor was held at 388 K as N$_2$ was bubbled through the suspension until all volatiles were removed. The dry solids were washed with boiling toluene until calixarenes were no longer visible in the effluent and treated in dynamic vacuum for 4 h at ambient temperature.

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Catalysis. Cyclohexene epoxidation rates and selectivities were measured by combining ~30 mg of catalyst and ~200 mg 4A molecular sieves (previously dehydrated at 573 K under dynamic vacuum, 12 h) in a 25 mL sidearm flask and heating under dynamic vacuum for 1 h to the prescribed temperature indicated in the text (393–523 K). The flask was then backfilled with Ar and 20 mL of anhydrous n-octane (Aldrich, 99.8%, passed over SiO$_2$ and Al$_2$O$_3$ columns, freshly distilled off CaH$_2$) and 0.3 mL of cyclohexene (Aldrich, 99%, passed over Al$_2$O$_3$ column, freshly distilled off CaH$_2$) were added, and the reactor was sealed, magnetically stirred, and heated to 333 K. A solution of tert-butyl hydroperoxide (TBHP) in nonane (0.125 mL, 4.8 M solution in nonane with added 4A sieves, Aldrich) was added, and liquid aliquots were periodically removed and analyzed for reactants and products by gas chromatography (Agilent 6890, HP-1 methylsilicone capillary column) to measure catalytic reaction rates and selectivities. Solvents and reagents were kept rigorously dry to eliminate ring opening of epoxides catalyzed by Bronsted or Lewis acids. Neither diols nor other cyclohexene oxidation products were detected on SiO$_2$– and TiO$_2$–supported catalysts; less than one turnover to cyclohexane diol after 24 h was detected in reactions catalyzed by 1-Al$_2$O$_3$. TBHP was used as the oxidant instead of the more reactive cumene hydroperoxide so as to minimize hydroperoxide decomposition (to acetone and phenol) in the presence of Bronsted acids.\(^{50}\) Homogeneous catalysts were used at a concentration of ~0.2 mM, which led to the same total Ti atom

concentration in the reactor as for the heterogeneous reactions. Homogeneous catalysts were removed from the reaction solution before injecting liquid aliquots into a gas chromatograph by passing over a dimethylaminopropyl-modified SiO$_2$ column (~0.5 g, Aldrich), which adsorbed alkyl hydroperoxides and calixarene–Ti species without altering epoxide concentrations. As discussed elsewhere, epoxidation rates on calixarene–Ti materials depend on reactant and catalyst concentrations as described by

$$ \text{rate} = \frac{[\text{epoxide}]}{\text{Ti}} = k[\text{alkene}][\text{TBHP}] $$

in which [Ti] is the total Ti concentration in the reactor, and all concentrations are in moles L$^{-1}$, resulting in a rate constant $k$ with units of M$^{-2}$ s$^{-1}$. This rate expression was previously shown to accurately describe reaction rates in the range of reactant concentrations used here. The rate equation and the rate constants were independent of the surface density of Ti on SiO$_2$, consistent with uniform single-site catalytic structures.  

### Results and Discussion

#### Spectroscopic Consequences of Support

Calixarene surface densities (from TGA) and Ti surface densities (from ICP/MS) are given in Table 1 for all materials. A ∼1:1 Ti:calixarene molar ratio was measured for all grafted calixarenes and oxide supports, except 1-TiO$_2$, for which Ti content cannot confirm the concentration of grafted complexes. These surface densities were achieved upon contacting supports with excess calixarene–Ti complexes; similar surface densities on SiO$_2$, TiO$_2$, and Al$_2$O$_3$ indicate that surface concentrations are predominantly limited by the calixarene footprint and not by the number or type of surface defect sites. Surface densities were measured after extensive extraction in hot toluene and therefore represent covalent grafting on SiO$_2$, TiO$_2$, and Al$_2$O$_3$.

Solid-state $^{13}$C CP/MAS NMR spectra of grafted materials 1-SiO$_2$, 1-Al$_2$O$_3$, and 1-TiO$_2$ (Figure 1) exhibit sharp resonances at 23 ppm and 63–70 ppm, consistent with surface Si$^{51}$, Ti$^{51}$, and Al alkoxides$^{52}$ formed from the titanium isopropoxide precursor. Resonances at 30–35 ppm and 120–145 ppm are consistent with the spectrum of calixarene 1a in solution. Homogeneous complex 1c, 1-SiO$_2$, 1-TiO$_2$, and 1-Al$_2$O$_3$ all possess a resonance at ∼161 ppm due to the calixarene ipso carbon (adjacent to the phenol oxygen), which is shifted significantly from the corresponding resonance in the free calixarene ligand 1a (152 ppm), indicative of calixarene–Ti coordination in all samples. In complexes with additional electron-withdrawing ligands, this resonance is shifted further downfield, as in tert-butylphenol-TiCl$_3$ (169 ppm$^{36}$) and calixarene–TiCl$_3$ 1d (163 ppm$^{29}$). The calixarene–Ti LMCT edge energies of 1-SiO$_2$, 1-Al$_2$O$_3$, and 1-TiO$_2$, obtained from diffuse-reflectance UV-vis spectroscopy (Figure 2) are all at ∼2.20 eV, irrespective of the identity of the support. Calixarene–TiOPr$_2$ 1b and homogeneous calixarene–TiOSiPh$_3$ 1c also give similar LMCT energies (2.34 and 2.37 eV, respectively, Figure S1). These latter complexes have slightly higher energies because charge separation in the excited state is less favorable in low dielectric solvents (e.g., chloroform) than in high dielectric environments typical of hydroxylated oxide surfaces. $^{53}$ The edge energy of calixarene–TiCl$_3$ 1d is lower at 1.9 eV$^{32}$.

The position of the pre-edge maximum and relative areas of the pre-peaks in the pre-edge region of Ti K-edge (Figure 3, Table 1) for 1c and 1-SiO$_2$ are the same within the accuracy of the spectra and their analysis. The A2 + A3 area (see Figure 3) in 1-Al$_2$O$_3$ is

### Table 1. Physicochemical and Spectroscopic Data for Synthesized Materials and Complexes

<table>
<thead>
<tr>
<th>material $^a$</th>
<th>X</th>
<th>Ti calix</th>
<th>LMCT edge $^b$</th>
<th>Ti K-edge XANES pre-edge $^c$</th>
</tr>
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<tbody>
<tr>
<td>Ib</td>
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<td>-OPr</td>
<td>2.34$^d$</td>
<td>4968.8 0.77</td>
</tr>
<tr>
<td>1c</td>
<td>Bu</td>
<td>OSiPh$_2$</td>
<td>2.37$^e$</td>
<td>4968.7 0.83</td>
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<td>2.26</td>
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<td>4968.9 0.75</td>
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</tbody>
</table>

$^a$ Labeled as per Scheme 1. $^b$ Determined by Ti ICP/MS or by TGA. $^c$ ± 0.02 eV. $^d$ Energy of pre-edge maximum ± 0.2 eV, component peak area ± 0.07.

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Figure 1. Solid-state $^{13}$C CP/MAS NMR spectra of 1-SiO$_2$, 1-TiO$_2$, and 1-Al$_2$O$_3$ collected at a spinning rate of 14 kHz. Inset shows 10× magnification of region around ipso carbon resonance at ∼161 ppm. Curves shown result from 20-point finite Fourier transform smoothing of the experimental data to remove high frequency noise.
smaller than in 1c and 1-SiO₂ by ~0.1 units and appears at higher energies (0.4 eV), but this difference is significantly smaller than would indicate an increase in average coordination number from 4 to 5.4,8 Ti K-edge XANES data were not specific to grafted species in 1-TiO₂ because of the overlapping features and strong contributions from ubiquitous Ti in the support.

The 13C CP/MAS NMR, UV-visible, and XANES Ti K-edge spectra for all materials discussed thus far are similar and quite distinct from those for complexes with deliberate modifications to the Ti inner-sphere. These spectra are therefore consistent with our assertion that 1-Al₂O₃, 1-TiO₂, and 1-SiO₂ all consist of single-site, isolated Ti centers with inner-sphere coordination environments similar to those in soluble compound 1c. In the absence of outer-sphere effects, which are largely undetectable by these techniques, these four Ti species should give similar epoxidation turnover rates on the basis of previously established quantitative correlations between catalytic reactivity and Ti electronic structure.38

Catalytic Consequences of Altering the Support. Alkene epoxidation with hydroperoxides involves equilibrated coordination of hydroperoxides to Ti centers, electrophilic attack by alkenes at O₁ oxygens in bound hydroperoxides, and desorption of alcohol coproducts (steps 2, 3, and 4 in Scheme 3).6,7 The higher rates measured for electron-rich alkenes 4,7,32 and the theoretical estimates of activation barriers for cluster models 14,15 indicate that epoxidation events occur either as the rate-determining step or before it. Thus, the rate constant k, (eq 1) used here to report epoxidation reactivity, is given by k = k₃K₂. These steps have been proposed as a common mechanism on Ti sites in titanosilicates (e.g., TS-1), surface grafted Ti species, and homogeneous silsesquioxanes, which share in common the required isolated Ti centers with 4-fold coordination (discussed above).

The [Ti] nomenclature used here is intended to represent the Ti atom and all ligands that remain connected to Ti during kinetically relevant steps; these “static” ligands can be the oxide framework, as in TS-1, an organic ligand, or both. The intermediates are drawn to reflect the expansion of the Ti coordination sphere required for epoxidation.21 The structure for A used in Scheme 3 was proposed by Sinclair and Catlow12 on the basis of a comparison of density functional theory estimates and measured epoxidation rates for different solvents and additives. The identity of ligand X participating in k₃, and therefore the source of the acidic protons involved in stabilizing intermediate A, remains unclear.11-16 Moreover, the group to which the proton is transferred from the hydroperoxide in K₂ is often written as distinct from the species providing the proton-stabilizing intermediate A. Scheme 3 allows, but does not require, that these groups be indistinguishable. In this section,
epoxidation rates in soluble calixarene–TiOPr 1b and calixarene–TiOSiPh 3 1c complexes are compared to those on grafted 1-SiO 2, 1-Al 2 O 3, and 1-TiO 2 to probe the catalytic consequences of hydroxylated supports acting as the source of outer-sphere Bronsted acidity for Ti centers that are otherwise electronically similar.

Figure 4a shows that epoxide turnover rates on homogeneous species 1b and 1c are similar to each other but ∼20 times lower than on 1-SiO 2 treated at 393 K. 54 Complexes 1b and 1c also deactivate with time, while 1-SiO 2 is stable (Figure S3). As previously reported for incompletely condensed Ti-silsesquioxanes,29 these data indicate that Ti–OSi connectivity is, by itself, insufficient for epoxidation catalysis, even though triphenylsilanil ligands can provide steric bulk and electron-withdrawing properties comparable to those for monodentate silesquioxane ligands or isolated silanols on SiO 2 55 and have been previously used as ligands in Ti epoxidation catalysts. 29,56 Figure 4b shows that initial epoxide turnover rates on 1-TiO 2 and 1-Al 2 O 3 are ∼50 times lower than on 1-SiO 2 samples treated similarly. The integrated hydroperoxide selectivity (mol epoxide produced per mol hydroperoxide consumed) is ∼35% at ∼25% hydroperoxide conversion on 1-TiO 2, which is similar to selectivities measured on 1-SiO 2 for nonactivated alkenes (e.g., n-octene). 32 At high conversions, selectivities on 1-SiO 2 are near 100%, indicating that the low apparent selectivities on other samples reflect competing noncatalytic pathways that become apparent for catalysts with low epoxidation reactivity. This noncatalytic hydroperoxide consumption is not significant during the initial stages of reaction, where the reported epoxidation rate constants are measured. Products of other cyclohexane oxidation pathways (cyclohexenol and cyclohexenone) were not detected in any of the experiments.

Figure 5 extends our previously reported rate constants for alkene epoxidation as a function of the area of XANES pre-edge component peaks relative area (A A 2+ A A 3)/A T (treated before analysis at 383 K at 10⁻⁶ Torr, 1 h), for materials 1c (X), 1-SiO 2 (O), 1-SiO 2-c (●), 1-Al 2 O 3 (□), 3-SiO 2 (△), and 4-SiO 2 (○). The dashed line marks a correlation developed previously 38 that spans all tested 4- and 5-coordinate Ti–SiO 2 materials between the two extremes shown (●). This correlation fails to account for the low reactivity of soluble 1c and 1-Al 2 O 3, consistent with outer-sphere effects.
catalysts in Figure 5. Thus, we conclude that the low turnover rates measured on 1-TiO2 and 1-Al2O3 do not reflect inner-
sphere effects on Ti centers caused by these supports acting as 
monodentate ligands, but instead arise from outer-sphere effects 
that do not cause detectable changes in the electronic state of 
Ti centers.

Except in the patent literature,10 there have been few 
 systematic studies of isolated Ti sites supported on oxides other 
than SiO2,72 such as Al2O328 or TiO2, which would provide 
evidence for outer-sphere effects caused by support surfaces. 
Sol-gel mixed oxides containing TiO2,26,40 are not well-suited 
to explore support effects because of their complex and poorly 
defined Ti environments. Strong Bronsted acids34,60 open 
epoxide rings rapidly in the presence of traces of water and 
lead to low epoxide yields and to deactivation via chelation of 
Lewis acid active sites by thealkane diols.61 Cluster density 
functional theory studies of titanosilicate structures suggest that 
Ti Lewis centers with vicinal weakly acidic protons form 
hydrogen-bonded structures such as intermediate A (Scheme 3), 
which decrease the activation barrier for the kinetically 
relevant step 3 in the catalytic cycle (Scheme 3).11-15 This 
decrease in activation barriers is accompanied by a concomitant 
increase in [Ti]=OR bond lengths and by a decrease in the 
energy level of the σ* orbital involved in the O-O bond.13,15

These outer-sphere effects caused by protons have been 
difficult to detect unambiguously in solid oxidation catalysts, 
but have been more clearly established in homogeneous systems. 
H-bonding has been implicated in hydroperoxide activation by 
homogeneous Ti(OSiMe3)4 catalysts in high alkyl hydroperoxide 
concentrations,17 by protonated analogues of Ti-salen salts.62

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surfaces more acidic than SiO$_2$. These compensating thermodynamic and kinetic factors lead to optimal rates for outer spheres with protons of intermediate acid strengths. These effects are consistent with intermediates resembling Ti complexes, $^{13}$C NMR spectra (Figure 6) were used to probe the degree of ligand electron delocalization. However, this behavior has not, to our knowledge, been previously considered in Ti-based epoxidation catalysis.

Spectroscopic and Catalytic Consequences of Altering Calixarene Ligands. We next test whether the phenolic groups on the calixarene ligand can create an outer-sphere Brønsted acid effect on epoxidation rates similar to those we have described here for oxide supports. The upper rim groups in calixarene–Ti complexes can be used to cover a broad range of Hammett constants, from electron-donating (tBu) to electron-withdrawing (NO$_2$); these systematic modifications are expected to lead in turn to large changes in the $pK_a$ of the calixarene ligand. The tabulated $pK_a$ values for monomeric phenol (Table 2) can be used to provide an upper bound for the respective free calixarenes, because macrocycles stabilize the conjugate base more effectively than phenol monomers. $^{76}$

In lieu of a direct measure of the acidity of the protonated form of the grafted calixarene–Ti complexes, $^{13}$C NMR spectra (Figure 6) were used to probe the degree of ligand electron delocalization. In particular, the position of the ipso carbon resonance is sensitive to reactions of free phenols to form Ti-phenolate complexes. $^{36}$ In all SiO$_2$-grafted materials, this resonance is shifted downfield by $\sim$10 ppm (Table 2) from the corresponding free calixarene in solution, $^{32,49}$ consistent with calixarene–Ti connectivity in these materials. The resonances for the free ligand and the SiO$_2$-grafted complexes shift further downfield as the macrocycle aromatic $\pi$ system becomes more electron-deficient (Table 2), as expected from the changes in

Table 2. Tabulated Values of the Upper Rim (R$_2$) Group Hammett Inductive Parameter ($\sigma^*$), $^{77}$ and Monomeric Phenol $pK_a$.$^{78}$

<table>
<thead>
<tr>
<th>calixarene</th>
<th>ipso $^{13}$C NMR shift (ppm)$^a$</th>
<th>$R_2\sigma^*$</th>
<th>phenol $pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>tBu</td>
<td>151.6</td>
<td>-0.3</td>
<td>10.31</td>
</tr>
<tr>
<td>H</td>
<td>150.6</td>
<td>+0.5</td>
<td>9.99</td>
</tr>
<tr>
<td>(CO)Ph</td>
<td>155.5</td>
<td>+2.2</td>
<td>-9.0</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>161.2</td>
<td>+4.0</td>
<td>7.18</td>
</tr>
</tbody>
</table>

$^a$ Data for the monomeric phenols are provided in the absence of data on the calixarenes themselves. Data for calixarene 3 are estimated from correlations of $pK_a$ to Hammett constants presented in the cited references. $^b$ Labeled as per Scheme 1. $^c$ Considered to be the resonance at lowest field.

Figure 6. Solid-state $^{13}$C CP/MAS NMR spectra of upper-rim modified graftedspecies collected at a spinning rate of 14 kHz and a contact time of 1.0 ms. A resonance at $\sim$196 ppm corresponding to carbonyl species in 3-SiO$_2$ was observed using a contact time of 2.5 ms. Signals are normalized per g of material. Inset shows 10$^3$ (20$^3$ for 3-SiO$_2$) magnification of region near ipso carbon resonance and fit with a 20-point finite Fourier transform to remove high frequency noise.

Figure 7. Correlation between observed ipso carbon $^{13}$C CP/MAS NMR shifts and tabulated values of the Hammett constant and individual phenol $pK_a$.

Figure 8. Catalytic turnovers as a function of time for materials 1-SiO$_2$ ($k = 5.8 \text{ M}^{-1}\text{s}^{-1}$, ○), 2-SiO$_2$ ($k = 4.3 \text{ M}^{-1}\text{s}^{-1}$, □), 3-SiO$_2$ ($k = 3.5 \text{ M}^{-1}\text{s}^{-1}$, △), and 4-SiO$_2$ ($k = 3.7 \text{ M}^{-1}\text{s}^{-1}$, ◦), after pretreatment at 523 K and expressed as mol cyclohexene epoxide per mol Ti per s.

with previous theoretical studies, reported NMR spectra, and the position of the maximum intensity of their pre-edge features in X-ray absorption spectra (Table 1). These findings are consistent with previous theoretical studies, reported NMR spectra, and electrochemical data, which report electronic effects on Ti as a result of changes in phenolate geometry, but not phenol substituent. This property enables outer-sphere effects of calixarene substituents to be determined independently of concomitant changes in the electronic structure of Ti centers.

Figure 8 shows that epoxide formation turnover rates on -SiO2 are only weakly influenced by the calixarene upper rim. -SiO2 gave slightly higher rates than -SiO2, consistent with weak inner-sphere effects expected from XANES spectra and their correlation with reactivity (Figure 5). These small changes in epoxidation rates with >3 changes in calixarene phenol acid strength between -SiO2 and -SiO2 suggest that Ti-OCalix bonds are not cleaved in kinetically relevant steps required for epoxidation turnovers. The preferential cleavage of Ti-OCalix bonds over Ti-Osi bonds was previously proposed on the basis of thermodynamic arguments, such as the strained nature and greater number of Ti-Osi bonds, and of the relative acidity of isolated phenols and silanols. The stoichiometric replacement of alkyl hydroperoxides for alkoxides has been reported for Ti(OiPr)4 grafted onto SiO2. The stoichiometric replacement of alkyl hydroperoxides for alkoxides has been reported for Ti(OiPr)4 grafted onto SiO2. In this approach, macrocyclic multidentate calixarenes lead to Ti centers with similar inner-sphere environments, confirmed by UV-visible spectra and pre-edge features at the Ti K-edge. Grafting onto supports, however, places Ti centers in environments where vicinal OH groups differ markedly in acid strength as a result of the Brønsted acid properties of SiO2, TiO2, and Al2O3 supports. These latter outer-sphere effects lead to ~50-fold changes in epoxidation turnover rates. The absence of comparable catalytic consequences when altering the pKa of calixarene ligands via changes in their upper rim lead us to conclude that the single Ti-Osi bond (instead of any of the three Ti-Ocalix bonds) is cleaved in kinetically relevant epoxidation steps on Ti-Osi.

Epoxidation rates increased as homogeneous 1c was grafted onto SiO2 (1-SiO2), and rates were observed previously to increase for mild pretreatment temperatures that would retain the high local hydroxyl surface density on SiO2. We attribute both effects to an increase in the rate of O transfer from Ti-hydroperoxide complexes to alkenes (k3) via cooperative H-bonding assemblies (intermediate A) between Ti centers and vicinal weakly acidic protons. We note that because of the high densities of OH groups pre-existing on these SiO2 surfaces, the SiOH generated by Ti-Osi bond breaking is not required to be the same SiOH involved in increasing k5, but the two groups are thermodynamically indistinguishable. These H-bonded structures also lead to rapid and thermodynamically favored regrafting of Ti intermediates onto the SiO2 surface following O transfer to the alkene, consistent with the observed lack of

the Hammett constants of the upper rim groups and from the stronger acidity of the respective conjugate phenol (Figure 7). These systematic changes in NMR resonances for the calixarene aromatic π system were not accompanied by significant changes in the energy of ligand-to-metal charge-transfer bands in their UV-visible spectra (Table 1, Figure S4) or in the energy position of the maximum intensity of their pre-edge features in X-ray absorption spectra (Table 1). These findings are consistent with previous theoretical studies, reported NMR spectra, and electrochemical data, which report electronic effects on Ti as a result of changes in phenolate geometry, but not phenol substituent. This property enables outer-sphere effects of calixarene substituents to be determined independently of concomitant changes in the electronic structure of Ti centers.

Figure 8 shows that epoxide formation turnover rates on 1-, 2-, 3-, and 4-SiO2 are only weakly influenced by the calixarene upper rim. 1-SiO2 gave slightly higher rates than 2-, 3-, and 4-SiO2, consistent with weak inner-sphere effects expected from XANES spectra and their correlation with reactivity (Figure 5). These small changes in epoxidation rates with >3 changes in calixarene phenol acid strength between 1-SiO2 and 4-SiO2 suggest that Ti-OCalix bonds are not cleaved in kinetically relevant steps required for epoxidation turnovers. The preferential cleavage of Ti-OCalix bonds over Ti-Osi bonds was previously proposed on the basis of thermodynamic arguments, such as the strained nature and greater number of Ti-Osi bonds, and of the relative acidity of isolated phenols and silanols. The stoichiometric replacement of alkyl hydroperoxides for alkoxides has been reported for Ti(OPr)3 grafted onto SiO2. The data reported here indicate that phenols are either not generated during hydroperoxide binding (k5 ≪ k2, Scheme 4) or are generated only momentarily as minority species leading to a kinetic dead-end (k5[TBABP] ≪ 1 and k6 ≪ k3, Scheme 4). A large kinetic barrier to Ti-Oc cleavage is consistent with previously observed larger losses of Ti-Osi species compared with Ti-OC species during reaction of molecules containing both groups with SiO2. Scheme 4 summarizes our conclusions that the “static” [Ti] core in Scheme 3 represents an intact calixarene-Ti complex, in which Ti-Osi bonds are broken in kinetically relevant intermediates in Ti-catalyzed epoxidation reactions.

Mechanistic Conclusions

The synthesis and grafting of calixarene-Ti complexes onto oxide surfaces can be used to control independently the inner-sphere ligands at active Ti centers and the surrounding outer sphere. In this approach, macrocyclic multidentate calixarenes lead to Ti centers with similar inner-sphere environments, confirmed by UV-visible spectra and pre-edge features at the Ti K-edge. Grafting onto supports, however, places Ti centers in environments where vicinal OH groups differ markedly in acid strength as a result of the Brønsted acid properties of SiO2, TiO2, and Al2O3 supports. These latter outer-sphere effects lead to ~50-fold changes in epoxidation turnover rates. The absence of comparable catalytic consequences when altering the pKa of calixarene ligands via changes in their upper rim lead us to conclude that the single Ti-Osi bond (instead of any of the three Ti-Ocalix bonds) is cleaved in kinetically relevant epoxidation steps on Ti-Osi.

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leaching of active structures during epoxidation catalysis on
grafted calixarene–Ti complexes. In TS-1 and related materi-
als, silanols formed during synthesis or by hydroperoxide
binding can form the required H-bonded intermediate A (akin
to structures shown in Scheme 4); the low concentrations of
pre-existing OH defect sites and the restricted mobility of Ti
centers in these materials, however, decrease the likelihood
that these structures form. Then, protic solvents with increasing pK_a
can bridge silanols and Ti active sites and create the requisite
H-bonded intermediate A and, in this manner, increase epoxi-
dation turnover rates.15,26

Epoxidation rates decrease when stronger acid sites inhibit
the formation of H-bonded intermediates (K_2). The lower
epoxidation turnover rates on Al-containing Ti-silicalites may
reflect, in part, the presence of strong Brønsted acids,83 which
destabilize intermediate A (decrease K_2). Similarly, the unre-
active nature of I-TiO_2 catalysts indicates that the unreactive
nature of Ti centers in anatase TiO_2 and Ti–SiO_2 with high Ti
contents84 reflects the unfavorable equilibrium dictated by low
K_2 values, even though coordinatively unsaturated Ti centers
are present on surfaces of small anatase crystallites.85 We
conclude that a “volcano”-type relationship leads to optimal
epoxidation turnover rates at intermediate acid strengths of
vicinal protons, which maximize the values of the relevant
(k_1*K_2) product that determines epoxidation rates.

The grafting of catalytic entities with uniform structure onto
oxide supports extends the range of outer-sphere environments
accessible with protic cosolvents and represents a novel route
to tune and to probe the function of active Ti centers. The range
of acid strengths and their high density of surface species make
oxide surfaces well-suited to promote the cooperative behavior
between active sites and acidic protons2 observed for condensa-
tion11 and hydrogenation46 reactions. The data and conclusions
reported here illustrate how outer-sphere protons positioned by
supports also influence epoxidation rates on Ti centers with
otherwise identical electronic properties. As a result, an accurate
description of the structure and function of inorganic catalysts
such as TS-1 and Ti–SiO_2 requires that we include outer-sphere
effects that complement inner-sphere effects intrinsic to Ti
centers and their catalytic properties.

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Supporting Information Available: 1H, 13C, and 29Si NMR
resonances, FAB-MS, and elemental composition for 1c and
2c; UV–visible spectra of homogeneous calixarene–Ti com-
plexes 1b and 1c (Figure S1); a correlation between Ti surface
densities determined by Ti ICP/MS, calixarene surface densities
determined by TGA, and 13C CP/MAS NMR intensities for
resonance corresponding to calixarene methylene bridges (Figure
S2); linearized form of epoxide production vs. time for 1b, 1c,
1-SiO_2, and 1-Al_2O_3 showing stable rate constants for grafted
catalysts (Figure S3); UV–visible spectra of upper-rim modified
calixarene–Ti materials 1–4 on SiO_2 (Figure S4); extended
comparison of grafted calixarene–Ti catalyst 1-SiO_2 with
sequentially assembled calixarene and Ti materials and calcined
Ti–SiO_2 catalysts including synthesis (Scheme S1), UV–visible
spectroscopic comparison (Figure S5), and comparison of
catalytic turnovers to epoxide (Figure S6). This material is
available free of charge via the Internet at http://pubs.acs.org.

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