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Tailoring Distinct Reactive Environments in Lewis Acid Zeolites for Liquid Phase Catalysis

Blake A. Johnson, John R. Di Iorio, and Yuriy Román-Leshkov*

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CONSPECTUS: Lewis acidic zeolites are microporous crystalline materials that offer promise as catalysts for the activation and conversion of biomassderived precursors in the liquid phase due to their unique water tolerance and synthetic versatility. The active site environment in zeolite catalysts is multifaceted in nature and is composed of a primary catalytic binding site, the secondary pore structure that confines such binding sites, and occluded solvent and reactant molecules that interact with adsorbed species. Moreover, Lewis acidic heteroatoms can adopt structurally diverse coordination that selectively catalyze different classes of chemical transformations and can be difficult to control synthetically or characterize spectroscopically. Thus, precise mechanistic interpretation of liquid-phase zeolite catalysis necessitates the



development of synthetic, spectroscopic, and kinetic methods that can decouple such complex active site structures and probe the interactions that occur between confined active sites, solvent and reactant molecules, and adsorbed intermediates and transition states.

In this Account, we describe the development and application of synthetic, spectroscopic, and kinetic methods to investigate chemically distinct Lewis acid zeolite environments in siliceous zeolites for liquid-phase catalysis. Identification of unique Lewis acidic active site structures relied on the development of direct and indirect solid-state nuclear magnetic resonance (NMR) methods that probe the number and connectivity of framework Lewis acid sites for a diverse range of metal heteroatoms. Such methods enabled the quantitative comparison of catalytic turnover rates, on a per active site basis, measured on different catalysts in order to establish structure-function relationships between active site structure and reactivity. Rigorous normalization of turnover rate further permits comparison of catalytic turnover rates across materials of varying topology, metal heteroatom identity, solvent, and framework polarity to extract salient thermodynamic descriptors of catalysis through kinetic probes. Ex situ interrogation of alcohols adsorbed within hydrophobic and hydrophilic Sn-containing zeolites revealed that hydrophobic voids induce structural order on confined alcohol hydrogen-bonding networks, which give rise to enhanced turnover rates of liquid-phase transfer hydrogenation catalysis. This acceleration of turnover rates arises because ordered alcohol networks occluded within the pores of hydrophobic zeolites stabilize adsorbed transfer hydrogenation intermediates and transition states to a greater extent than liquidlike solvent networks observed in hydrophilic zeolites. The effects of confined solvent molecules can also influence catalysis, independent of framework polarity, due to differences in solvent polarity and substituent effects, which alter turnover rates via changes in how different solvent molecules interact with adsorbed intermediates and transition states. These observations underscore new opportunities to leverage specific interactions between active sites and solvent molecules to influence solvent organization and transition state stability at confined solid-liquid interfaces.

This work illustrates the importance of quantitative methods that count distinct active site structures in order to compare catalytic materials on a per active site basis. This information can be used to develop new synthetic procedures that predictably manipulate the functionalization of both the primary binding site and the secondary reaction environment to tailor catalytic function for a desired chemistry. Collectively, these advances highlight strategies to engineer and characterize microporous catalysts with unique reaction environments in order to capture salient mechanistic features and navigate the complex free energy landscape of catalysis in condensed solvent systems.

1. INTRODUCTION

Heterogeneous catalytic reactions performed in condensed media occur at solid–liquid interfaces where complex interactions among interfacial solvent molecules, solid surfaces, and adsorbed intermediates complicate the nature of the catalytic active site and modify reaction free energy landscapes.¹

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Solid catalytic surfaces often interact strongly with solvent molecules via interfacial adsorption or unwanted side reactions and, as a result, can undergo profound and sometimes irreversible changes in their structure and catalytic performance.¹ Thus, the design of catalysts capable of performing selective chemical transformations in the liquid phase requires a deep understanding of the interactions that occur between solvent molecules, active sites, and reactive moieties during catalysis.^{2,3} Biological catalysts navigate such complex free energy landscapes by manipulating solvent molecules to facilitate catalytic transformations via specific arrangements of hydrophobic and hydrophilic amino acid residues that comprise microporous reaction environments (<2 nm in diameter). These precise architectures regulate the structure of occluded solvent and substrate molecules along the reaction coordinate, granting enthalpy-entropy compromises that alter reaction free energy landscapes and enhance turnover rates.⁴ The ability of enzymatic active sites to modulate reactivity by manipulating the function of confined active sites has spurred interest in the design of active site environments within zeolite catalysts as inorganic alternatives.

Zeolites are a diverse class of crystalline, microporous (<2 nm pore diameter) frameworks constructed from oxygen-bridged SiO₄ tetrahedra. Catalytic active sites in zeolites generally arise from the isomorphous substitution of framework Si⁴⁺ atoms by different heteroatoms.⁵ For example, anionic lattice charges can be formed via the incorporation of trivalent framework metal atoms (e.g., Al³⁺) that can be charge balanced by a wide variety of extraframework cations, including Brønsted acidic protons or redox active transition metals (e.g., Cu²⁺). Zeolites can also be synthesized with stable, water-tolerant, isolated Lewis acid sites embedded within their siliceous lattice via isomorphous substitution of Si⁴⁺ by various tetravalent metal atoms (e.g., Sn⁴⁺, Zr⁴⁺, Hf⁴⁺, Ti⁴⁺) with empty coordination sites (Figure 1).^{2,6} Interest in Lewis acidic zeolites as versatile catalysts for the



Figure 1. M^{4+} -substituted (M^{4+} = Sn, Zr, Ti, Hf, etc.) zeolite Beta viewed down the *a*-axis and inset showing the TO₄ tetrahedra. Atom color codes: M^{4+} , blue; Si, silver; O, red.

selective transformation of biomass-derived oxygenates has surged in recent years. Indeed, zeolites have been shown to catalyze a wide range of reactions involved in the valorization of lignocellulosic biomass to sustainable fuel and platform chemicals, including transfer hydrogenations, isomerizations, etherifications, dehydrations, aldol condensations, and Diels– Alder reactions.^{2,7,8}

The properties of zeolite catalysts extend beyond isolated framework active sites. Their microporous voids introduce steric constraints that inhibit diffusion and catalysis of molecules larger than their pore diameters via size exclusion phenomena.⁹ Moreover, zeolite pores mirror biological catalysts in their ability to solvate reactive intermediates and transition states via dispersive interactions that can alter rates and selectivities of catalytic reactions.¹⁰ The solvating properties of the zeolite pore are critical for reactions run in condensed media where the number and arrangement of intraporous solvent and reactant molecules depend on the structure and composition of both the catalytic active site and secondary confining environment. Functional groups in the secondary reaction environment can be introduced through various synthetic methods, which determine the polarity of these confining voids and influence structures of occluded reactant, product, and solvent molecules. These effects are analogous to the role of different solvents in molecular catalysis¹¹ and of confined water networks in metalloenzymes,^{4,12,13} whose microporous reaction pockets can expel or rearrange occluded molecules to steer catalysis along a desired pathway while avoiding energetic penalties due to solvent reorganization.¹⁴ As such, the formation and arrangement of molecular clusters and solvent networks within confined catalytic binding sites depend on the functionality of both the primary and secondary reaction environments.

Despite the ubiquitous use of Lewis acidic zeolites as catalysts for liquid-phase reactions, $^{2,7,15-17}$ there is still a great need to develop methods to control the formation of different active site structures and further understand how solvents organize within and alter confined catalytic reaction environments. Here, we summarize our recent advances in developing solid-state nuclear magnetic resonance (NMR) methods to probe chemically distinct Lewis acid sites in zeolites through both direct excitation (e.g., ¹¹⁹Sn) and indirect methods utilizing adsorbed probe molecules (e.g., ¹⁵N, ³¹P). These methods enable unique Lewis acid site coordination environments to be quantified and correlated with catalytic turnover rates in order to identify specific active site requirements of various liquid phase reactions. We then utilize spectroscopic site counting methods to normalize reaction kinetics measured on Sn-containing zeolites with different densities of hydrophilic binding sites (e.g., silanols) to demonstrate that hydrophobic voids order confined, nonaqueous solvent networks, which accelerate turnover rates to a greater extent compared with hydrophilic zeolites. Based on these advances, we outline future strategies to predict, engineer, and interrogate microporous catalysts with tailored active site structures and secondary reaction environments to promote liquid-phase catalysis.

2. SPECTROSCOPIC METHODS TO PROBE LEWIS ACIDIC ACTIVE SITES

The active centers in porous solid catalysts are multifaceted in structure. They comprise (i) primary sites that bind adsorbates, (ii) secondary environments that confine intermediates and transition states, and (iii) coadsorbed molecules, clusters, and solvent networks that interact with species along the reaction coordinate.¹⁷ Identifying the true nature of these active sites is challenging because of the wide variation in metal site speciation. Lewis acidic heteroatoms can be incorporated into the framework as fully connected tetrahedra ("closed" site) or at highly strained T-sites that only allow for 3-fold coordination to lattice O atoms where a hydroxyl ligand completes the tetrahedral site ("open" site).¹⁸ Recent work within our group has focused on the development of direct and indirect spectroscopic techniques that probe the number and connectivity of framework Lewis acid sites for a diverse range of metal heteroatoms.

2.1. Direct Investigation of Framework Heteroatoms Reveals Local Coordination

Direct detection techniques, namely, ¹¹⁹Sn magic angle spinning nuclear magnetic resonance (MAS NMR) spectroscopy, are used to determine the local coordination of framework heteroatoms and qualitatively assess the extent of extraframework metal oxide species (MO_x) present on a given sample. Although framework Sn incorporation can be quantitatively verified with ¹¹⁹Sn MAS NMR spectroscopy, the coupled effects of low natural abundance of the ¹¹⁹Sn isotope (natural abundance = 8.6%) and low Sn loadings in zeolitic samples (often <1 mol %) make such NMR analyses impractical without costly isotopic enrichment.¹⁹ To address these limitations, dynamic nuclear polarization (DNP) MAS NMR methods have been developed for zeolites containing ~2 wt % natural abundance ¹¹⁹Sn (Figure 2).^{20,21} In this approach, high-powered



Figure 2. Hyperpolarization of Sn-Beta zeolite using dynamic nuclear polarization. Reproduced with permission from ref 20. Copyright 2014 American Chemical Society.

microwaves irradiate a zeolite sample treated with an exogenous biradical polarizing agent and a glassing agent (e.g., 1,1,2,2-tetrachloroethane). The resulting electron polarization is transferred from the radical to protons in the system through electron–nuclear dipolar couplings, while cryogenic analysis temperatures (100 K) enable efficient ${}^{1}\text{H}{-}{}^{1}\text{H}$ spin diffusion to relay polarization to framework Sn atoms via intraporous protons using ${}^{1}\text{H}{-}{}^{119}\text{Sn}$ cross-polarization (CP).

¹¹⁹Sn DNP MAS NMR spectra measured on Sn-Beta zeolites under both hydrated and dehydrated conditions²⁰ were consistent with reports from Davis and co-workers who measured ¹¹⁹Sn MAS NMR spectra on isotopically enriched ¹¹⁹Sn-Beta zeolites.²² Spectra of dehydrated Sn-Beta showed two resonances for δ_{iso} (¹¹⁹Sn) at -420 and -440 ppm, corresponding to open Sn sites with 3-fold coordination to lattice O atoms and a hydroxide ligand ((SiO)₃SnOH) and

closed Sn sites with 4-fold coordination to lattice O atoms ((SiO)₄Sn), respectively,⁸ as only the resonance at δ_{iso} (¹¹⁹Sn) = -420 ppm was observed in ^{1}H - ^{119}Sn CP MAS NMR spectra.²² Remarkably, DNP enhancements led to spectra with high signalto-noise ratios in <24 h while conventional natural abundance ¹¹⁹Sn MAS NMR measurements showed no evidence of ¹¹⁹Sn resonances even after 246 h of continuous analysis.²⁰ Thus, these results demonstrated that DNP NMR methods are able to significantly reduce acquisition times without the need for costly isotopic enrichment. While DNP NMR techniques qualitatively corroborated evidence of multiple site types in Sn-containing zeolites, method optimization and appropriate selection of a biradical polarizing agent and glassing solvent are necessary to resolve precise local environments of framework sites in the bulk of the zeolite. Additionally, alternative methods are necessary to handle other heteroatoms of interest with low natural abundance, large quadrupolar moments, or low gyromagnetic ratios (e.g., $^{47/49}\mathrm{Ti},~^{177/179}\mathrm{Hf},$ and $^{91}\mathrm{Zr}).$ In spite of this, DNP NMR remains a powerful tool for characterizing the chemical structure of framework heteroatoms in challenging systems.

2.2. Combining Probe Molecule Adsorption and NMR Spectroscopy

In contrast to direct spectroscopic methods, indirect methods using probe molecules may be used to assess the local environment of metal centers regardless of heteroatom identity. The magnetic shielding observed in NMR spectroscopy is highly sensitive to the local electronic environment about the observed nucleus and may also be used to assess Lewis acidic character of target metal centers. This unique sensitivity provides a convenient tool to probe both heteroatom speciation and number. By choosing the appropriate titrant, this method can be used regardless of whether a heteroatom is NMR active. Recent work within our group has focused extensively on the development and refinement of ¹⁵N and ³¹P MAS NMR methods to interrogate and quantitate various Lewis acid sites present in metal-substituted zeolites.

Adsorption of ¹⁵N-enriched pyridine onto Beta zeolites with different Lewis (e.g., Sn, Ta, Nb, Zr, Hf, and Ti) and Brønsted (e.g., B, Ga, and Al) acid centers was used to assess the solid acid character of zeolite samples by ¹⁵N CP MAS NMR spectroscopy.²³ We rationalized that interactions of pyridine with different metal sites would lead to commensurate changes in the shielding of the ¹⁵N nucleus due to different extents of delocalization of the N lone pair electrons upon coordination at various binding sites. ¹⁵N CP MAS NMR spectra revealed distinct chemical shifts of ¹⁵N-pyridine adsorbed at Lewis acid sites (δ_{iso} (¹⁵N) = 260–280 ppm), while silanol defect sites featured a broad band near δ_{iso} (¹⁵N) = 290 ppm and extraframework MO_x sites gave sharp resonances near δ_{iso} $(^{15}N) = 320 \text{ ppm}$ (Figure 3A). Similar to IR spectra of pyridine adsorbed on Lewis acidic zeolites,²⁴ ¹⁵N MAS NMR spectra provided quantitative information about the number of framework Lewis acid sites in Sn- and Zr-Beta zeolites containing different total metal contents (Figure 3B). Resonances associated with Lewis acid centers appear as a convolution of multiple components, potentially indicating the presence of multiple framework Lewis acid sites with different coordination (e.g., open and closed Sn sites), but were unable to distinguish individual contributions from distinct site architectures. Interestingly, in agreement with theoretical investigations,^{6,25} chemical shifts of ¹⁵N-pyridine scaled linearly with Mulliken electronegativities (Figure 3C), indicating that the



Figure 3. (A) ¹⁵N CP MAS NMR spectra of ¹⁵N-pyridine adsorbed on metal-substituted zeolites. Dashed data correspond to spectra of hydrated samples; vertical gray lines correspond to nonbound pyridine (left) and pyridinium (right). Al-Beta-F had Si/Al \sim 50, Al-Beta-OH had Si/Al \sim 19, and all other materials had Si/M \sim 100. (B) Quantification of adsorbed pyridine using ¹⁵N MAS NMR relative to the framework Sn content calculated from ¹¹⁹Sn MAS NMR data and ICP-MS analyses. The dotted line represents a parity line, while error bars reflect standard errors among triplicate experiments. (C) Experimental Mulliken electronegativity vs pyridine ¹⁵N MAS NMR chemical shift. The dashed line and gray envelope show a regression with standard errors. Reproduced with permission from ref 23. Copyright 2016 American Chemical Society.



Figure 4. (A) ¹¹⁹Sn MAS NMR spectra of a ¹¹⁹Sn-Beta sample: (i) Pristine sample. (ii and v) Dosed with TMPO/Sn = 0.52. (iii and vi) Dosed with TMPO/Sn = 1.17. Spinning sidebands in the ¹¹⁹Sn spectra are marked with asterisks. Experimental NMR spectra are shown in black (lower traces), while the simulated spectra are shown in gray (upper traces). Shaded regions in the ¹¹⁹Sn spectra correspond to regions of tetrahedral Sn ([4]Sn; green), pentacoordinated Sn ([5]Sn; violet/blue), and six-coordinate Sn ([6]Sn; pink). (iv) Peak assignments. (B) ³¹P MAS NMR spectra of TMPO dosed on Lewis acid zeolites with different heteroatoms at a TMPO/M ratio of approximately 1.0. The dashed lines mark the resonance positions in Sn-Beta at δ_{iso} = 58.6 ppm (blue) and 54.9 ppm (violet). Reproduced with permission from ref 27. Copyright 2018 American Chemical Society.

chemical shift of adsorbed ¹⁵N-pyridine can serve as a proxy for Lewis acid site strength in metal-substituted zeolites. Despite the ability of adsorbed pyridine to quantify the total number of Lewis acidic sites from both IR and NMR methods, even in the presence of MO_x species, alternative methods appear to be necessary in order to distinguish framework heteroatoms with different local coordination.

To address these limitations, we turned to ³¹P MAS NMR using trimethylphosphine oxide (TMPO) as a molecular probe.²⁶ This procedure utilizes the 100% natural abundance and favorable nuclear properties of the ³¹P nucleus (nuclear spin

= 1/2 and high gyromagnetic ratio) to shorten acquisition times, avoid costly isotopically enriched precursors, and increase signal-to-noise despite the low concentrations of metal atoms present in Lewis acidic zeolites (typically Si/M > 100). ³¹P MAS NMR spectra of Sn-Beta samples dosed with different loadings of TMPO (TMPO/Sn = 0-1.17) displayed resonances at $\delta_{iso}(^{31}P) = 55.8$ and 54.9 ppm that increased in intensity at low TMPO coverages (TMPO/Sn < 0.52), while the $\delta_{iso}(^{119}Sn) =$ -420 ppm resonance in ¹¹⁹Sn MAS NMR spectra, previously assigned to open Sn sites with no adsorbates,⁸ decreased (Figure 4A). ³¹P resonances at δ_{iso} (³¹P) = 58.6 and 57.2 ppm were also observed at elevated coverages (TMPO/Sn > 0.52),²⁷ suggesting that TMPO can distinguish between different types of framework Lewis acidic Sn sites (e.g., open and closed), similar to what has been seen from IR spectra of acetonitrile- d_3 (CD₃CN) adsorbed on Sn-Beta.^{24,28} The general applicability of the ³¹P MAS NMR technique was demonstrated by probing a range of Lewis acidic heteroatoms (i.e., Sn, Zr, Ti, Hf) in Beta zeolites (Figure 4B).²⁷ Notably, TMPO adsorption on Ti-, Zr-, and Hf-Beta featured signals with similar widths and chemical shifts to those of TMPO bound to framework sites in Sn-Beta and this method resolves at least two distinct metal sites in the range of 50-60 ppm for all framework heteroatoms studied. These results provide strong evidence that TPMO can distinguish different coordination environments of framework Lewis acid heteroatoms and open exciting opportunities to probe distributions of distinct active sites in different Lewis acidic zeolites for reliable normalization of catalytic turnover rates.

3. CATALYTIC TURNOVER RATES DEPEND ON LEWIS ACIDIC ACTIVE SITE IDENTITY

The catalytic consequences of distinct reaction environments manifest as differences in the activation and adsorption enthalpies and entropies that comprise free energy landscapes. Precise molecular-level descriptions of adsorbate and transition state solvation require that catalytic turnover rates be measured as functions of reactant thermodynamic activities and rigorously normalized by the number of active sites that facilitate such chemical transformations.^{3,29} This allows for kinetic data to be interpreted in terms of equilibrium adsorption constants and apparent (or intrinsic) rate constants in order to extract free energy differences between final and initial states for a sequence of elementary catalytic steps and establish structure–function relationships that describe catalysis at solid–liquid interfaces.²

The catalytic efficacy of Lewis acidic zeolites strongly depends on the electron affinity (i.e., the Lewis acid strength) of the active site. Our group has examined this in the context of methyl levulinate (ML) reduction to 4-hydroxypentanoate (4HP) and subsequent lactonization to γ -valerolactone (GVL) using Beta zeolites with different framework heteroatoms (e.g., Sn, Hf, Zr, Ti; Figure 5A).³⁰ We observed that Hf-Beta zeolites convert ML to GVL in a 2-butanol solvent with an apparent first-order rate constant (per metal site, 423 K) that is twice as large than that of Zr-Beta and seven times larger than that of Sn-Beta in spite of similar apparent activation energies $(52 \pm 2 \text{ kJ mol}^{-1}, \text{ Figure})$ 5B). These results suggest either that first-order activation energies, which consist of the sum of the intrinsic activation enthalpy to form the hydride-shift transition state and the enthalpy of ML adsorption, are independent of heteroatom identity or that any differences in the intrinsic activation and adsorption enthalpies for each metal site fortuitously offset to give similar apparent activation enthalpies. Ti-Beta zeolites,



Figure 5. (A) Arrhenius plot for the MPV reduction of 0.02 mol dm⁻³ ML in 2-butanol solvent with various zeolite-Beta catalysts: Hf-Beta (black circle), Zr-Beta (blue square), Sn-Beta (red triangle), and Ti-Beta (green diamond). Rates are measured in moles of GVL produced per second normalized per total mole metal center in the catalyst. (B) Values of apparent activation energies and pre-exponential factors determined from experimental kinetics measured on different M-Beta catalysts with a 0.02 mol dm⁻³ ML feed in 2-butanol. Units of E_a are kJ mol⁻¹, and units of A are 10⁵ (mol dm³)(mol metal s mol ML)⁻¹. Reproduced with permission from ref 30. Copyright 2014 Elsevier.

however, displayed significantly lower turnover rates of ML transfer hydrogenation (per total Ti) at all temperatures, and apparent activation energies that were $\sim 17 \text{ kJ mol}^{-1}$ more positive than that on Hf-, Zr-, or Sn-Beta (69 \pm 2 kJ mol⁻¹, Figure 5B). Moreover, pre-exponential factors, which depend on both the change in entropy between final and initial states and the total number of active sites, are different on each zeolite but do not appear to correlate with the chemical shift of ¹⁵N pyridine from MAS NMR spectra (Figure 3C), a proxy for Lewis acid strength. The difference in ML transfer hydrogenation turnover rates between Ti and other Lewis acidic heteroatoms could potentially be explained by differences in the propensity of Tisites to form closed sites,³¹ whereas Sn, Zr, and Hf sites form mixtures of both open and closed sites,^{28,32,33} with the former being the active site for transfer hydrogenations over metallosilicates. Notably, all catalysts likely host a similar intraporous solvent environment, assuming a similar defect density for Beta zeolites synthesized in fluoride media with similar metal loadings $(Si/M^{4+} = 108-121)$. This indicates that differences in transfer hydrogenation free energy barriers may reflect changes in how the hydride-shift transition state and adsorbed precursors are stabilized at each Lewis acidic heteroatom. Precise interpretation of these results, however, requires the development of spectroscopic and/or titrimetric techniques (e.g., TMPO adsorption) that are able to probe distributions of distinct active sites in Lewis acidic zeolites with different heteroatoms.

As described in section 2.2, ³¹P MAS NMR spectra of TMPO adsorbed on Lewis acidic Sn sites in Beta zeolites are able to resolve distinct NMR features corresponding to TMPO adsorbed at different Lewis acidic Sn sites (Figure 4A). These TMPO adsorption experiments were coupled with catalytic probe reactions of glucose isomerization in water and aldol condensation of benzaldehyde with acetone in toluene to correlate specific sites identified by ³¹P MAS NMR to catalytic activity toward different probe reactions. Glucose isomerization and aldol condensation proceed via distinct reaction mechanisms: the former involves a ring-opening step followed by an intramolecular hydride transfer that is facilitated by open Sn sites in Sn-Beta zeolites,^{24,34} while the latter is proposed to proceed via the formation of an enolate at the metal site after cleavage of a framework M-O bond.³⁵ Thus, we hypothesized that different tetrahedral Sn geometries could serve as distinct active sites for each reaction. Site-time yields (STY, per total Sn) of glucose isomerization (358 K) and aldol condensation (383 K) plotted against the integrated peak area (normalized by total Sn content) revealed that rates of glucose isomerization correlated with the total area of the peaks at $\delta_{iso}(^{31}P) = 55.8$ and 54.9 ppm while rates of aldol condensation correlated with the peaks at 58.6 and 57.2 ppm. From these data, we concluded that the active site for glucose isomerization corresponded to the site(s) titrated by TMPO at $\delta_{iso}(^{31}P) = 55.8$ and 54.9 ppm (Figure 6A)



Figure 6. Site time yield for (A) glucose isomerization in water and (B) aldol condensation of benzaldehyde and acetone in toluene catalyzed by different Sn-Beta catalysts plotted against the percent integrated ³¹P peak area normalized by P and Sn content at (A) $\delta_{iso} = 55.8$ and 54.9 ppm and (B) $\delta_{iso} = 58.6$ and 57.2 ppm. The red lines are linear fits of the data. Reproduced with permission from ref 27. Copyright 2018 American Chemical Society.

while the active site for aldol condensation reactions corresponded to the site(s) titrated by TMPO at $\delta_{iso}(^{31}P) = 58.6$ and 57.2 ppm (Figure 6B). These results were particularly insightful because prior literature had hypothesized that the same site, a hydrolyzed open site, was the catalytic site for both types of reactions.²⁸ To reconcile these positions, we ascribed the rate correlation of these different resonances to differing T-site locations within the Beta framework where the signals correlating with glucose isomerization STYs ($\delta_{iso}(^{31}P) = 55.8$ and 54.9 ppm) represent TMPO bound to Sn atoms at T-sites that preferentially form open sites,¹⁸ the reported active site for glucose isomerization.²⁴

Reactions that occur within the microporous voids of zeolite catalysts are also sensitive to changes in the size and shape of the confining void that surround active metal centers. Differences in the pore architecture alter how zeolites solvate reactive intermediates and transition states confined within their pores due to changes in the number and strength of dispersive interactions between adsorbates and the zeolite framework.¹⁰ Such interactions can alter selectivities and turnover rates of catalytic reactions if the size and shape of the confining pore match the structure of reactive intermediates and transition states, even when active sites are otherwise identical.³⁶ We have explored the effects of confinement on liquid-phase catalysis by performing kinetic studies of the intermolecular Meerwein-Ponndorf-Verley-Oppenauer (MPVO) transfer hydrogenation reaction between cyclohexanone and 2-butanol using different Sn-containing zeolites.³⁷ Specifically, transfer hydrogenation reactions on Sn-zeolites are selectively catalyzed by open Sn sites (i.e., (SiO)₃SnOH),^{22,28,30} which can be quantified independent of closed Sn sites (i.e., (SiO)₄Sn) using spectroscopic methods that distinguish between different Lewis acid site coordination.^{24,27} Initial transfer hydrogenation turnover rates were measured on Sn-BEC and Sn-Beta zeolites as a function of cyclohexanone concentration and revealed that zero-order rate constants (per open Sn site, 373 K) were similar on both Sn-BEC and Sn-Beta zeolites when rates were normalized by the total number of open Sn sites on each catalyst. In contrast, first-order rate constants (per open Sn site, 373 K) were 3-4× larger on Sn-BEC zeolites than on Sn-Beta, despite similar apparent zero-order rate constants and normalization by the total number of active sites (Figure 7). This



Figure 7. Cyclohexanol formation rates (373 K, per open Sn site) measured on Sn-BEC (solid squares) and Sn-Beta (open squares). Error bars represent propagated experimental uncertainty. Reproduced with permission from ref 37. Copyright 2020 Royal Society of Chemistry.

difference in first-order rate constant is likely due to the more favorable adsorption of cyclohexanone reactants within the smaller diameter pores of the BEC framework (~0.7 nm in diameter)³⁷ compared to larger stacking faults present in Sn-Beta (~1–1.5 nm) where open Sn sites, the active sites for transfer hydrogenation catalysis, are located.^{18,38} These data further emphasize the complex nature of reactions catalyzed at confined solid–liquid interfaces, where free energies of reaction are sensitive to differences in both the primary (e.g., metal site identity and coordination) and secondary (e.g., pore architecture, solvent structure) reaction environments.¹⁷



Figure 8. (A) Proposed MPVO reaction mechanism between 2-butanol and cyclohexanone over an open Sn site in a 2-butanol solvent. (B) Cyclohexanol formation rates (per open Sn site) measured on (a) Sn-Beta-F and (b) Sn-Beta-OH as a function of cyclohexanone activity (0.01-1 M cyclohexanone) in 2-butanol at 333 K (triangle), 353 K (diamond), 373 K (square), and 393 K (circle). Reproduced with permission from ref 46. Copyright 2020 American Chemical Society.



Figure 9. (A) Cyclohexanone adsorption equilibrium constants (a) and apparent zero-order rate constants (b) per open Sn site determined by regression to initial MPVO turnover rates (per open Sn site) measured on Sn-Beta-F (filled) and Sn-Beta-OH (open) in a 2-butanol solvent as a function of temperature (333–393 K). Dashed lines are exponential fits to the data. (B) Fractional cyclohexanone coverage (per open Sn site) as a function of temperature (333–393 K light to dark) and cyclohexanone activity (0.01–1 M cyclohexanone) in a 2-butanol solvent on (a) Sn-Beta-F and (b) Sn-Beta-OH. (C) Values of ΔH_{ads} , ΔS_{ads} , ΔH_{app} , and ΔS_{app} determined from experimental kinetics measured on Sn-Beta-F and Sn-Beta-OH in a 2-butanol solvent. Units of ΔH are kJ mol⁻¹, and units of ΔS are J mol⁻¹ K⁻¹. Reproduced with permission from ref 46. Copyright 2020 American Chemical Society.

4. ORDERED SOLVENT STRUCTURES ACCELERATE TRANSFER HYDROGENATION CATALYSIS

Turnover rates of catalytic reactions measured in the liquid phase are influenced by the presence of hydrophilic silanol defect sites within zeolitic pores that alter the structure and stability of confined solvent clusters and extended networks.¹⁷ The hydrophobicity of such microporous voids can directly affect reaction kinetics by altering free energy barriers for reactions in aqueous media,³⁹ by altering the structure and dielectric properties of confined water relative to the bulk,⁴⁰ or by enabling selective adsorption of molecules from solution based on polarity.⁴¹ Zeolites containing defect-free micropores are hydrophobic and stabilize chainlike, weakly bound water molecules, while water preferentially forms small clusters at hydrophilic binding sites (e.g., silanol defects or a Lewis acidic heteroatom) that persist even when extended solvent networks form.⁴⁰ Similar to the characterization of metal heteroatom speciation, silanol defects can be quantified through vibrational spectra upon adsorption of probe molecules (e.g., CD₃CN) as perturbations of vibrational modes in probe molecules are sensitive to the properties of the hydrophilic binding site.^{24,42} Differences in the polarity of the zeolite pore have been recognized to have profound consequences on turnover rates of various catalytic reactions when water is present in the reaction medium.^{24,31,43–45} Despite tremendous progress toward understanding how water influences reactions in condensed media,

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Figure 10. IR difference spectra (relative to the parent spectrum) of (A) Sn-Beta-F and (B) Sn-Beta-OH with increasing equilibrium pressure of 2butanol (light to dark) measured at 303 K. Insets show the region from 2200 to 1300 cm⁻¹. (C) Adsorption of cyclohexanone within 2-butanol filled pores of hydrophobic Sn-Beta-F and hydrophilic Sn-Beta-OH catalyst. Reproduced with permission from ref 46. Copyright 2020 American Chemical Society.

the impact of nonaqueous solvents on liquid-phase catalysis in confined spaces is still not fully understood. We have recently shown that the structure of confined alcohols (e.g., 2-butanol) can be modulated by framework polarity in hydrophobic (Sn-Beta-F) and hydrophilic (Sn-Beta-OH) Sn-Beta zeolites and alters free energies of adsorption and catalysis.⁴⁶

Turnover rates (normalized per open Sn site) of the MPVO transfer hydrogenation of cyclohexanone by 2-butanol (Figure 8A) were measured on hydrophobic Sn-Beta-F and hydrophilic Sn-Beta-OH in a 2-butanol solvent as a function of temperature (333-393 K) and cyclohexanone thermodynamic activity (a_c) . Here, we use the thermodynamic activity, instead of liquid phase concentration, to describe the chemical potential of solution phase species in order to account for changes in activity coefficients that arise due to nonideal interactions at different reactant concentrations.⁴⁷ MPVO turnover rates increased linearly on both Sn-Beta-F and Sn-Beta-OH zeolites at low cyclohexanone activities $(a_c < 0.02)$ and approached a zeroorder regime with increasing cyclohexanone activity ($a_c > 0.1$), reflecting a change in the most abundant reactive intermediate (MARI) from a 2-butanol-covered site to a coadsorbed 2butanol-cyclohexanone adduct (Figure 8B). Apparent zeroorder rate constants (per open Sn) were ~10× larger on Sn-Beta-F than on Sn-Beta-OH at all temperatures (333-393 K), reflecting the preferential stabilization of the hydride-shift transition state within hydrophobic Sn-Beta-F zeolites. Moreover, cyclohexanone adsorption equilibrium constants increased with increasing temperature on both Sn-Beta zeolites but were more sensitive to changes in temperature on Sn-Beta-F ($\sim 10 \times$ larger at 393 K than at 333 K) than on Sn-Beta-OH (~2.5× larger at 393 K than at 333 K) (Figure 9A). This manifests as cyclohexanone coverages that are strongly dependent on temperature, at a given cyclohexanone activity, on hydrophobic Sn-Beta-F, a phenomenon not observed on Sn-Beta-OH (Figure 9B), suggesting that the intraporous 2-butanol solvent environment in Sn-Beta-OH changes more similarly to that of 2-butanol in the bulk solution than that confined within hydrophobic Sn-Beta-F.

Differences in the structure of confined 2-butanol solvent networks were further investigated by measuring IR spectra of Sn-Beta-F and Sn-Beta-OH zeolites in equilibrium with various gas-phase partial pressures of 2-butanol (303 K, $PP_0^{-1} = 0.001 -$ 0.8). Adsorption of 2-butanol within hydrophilic Sn-Beta-OH occurs via hydrogen bonding to SiOH groups as evidenced by the decrease in intensity of various SiOH groups (~3740-3650 cm⁻¹; nests and isolated SiOH) and coincident formation of a broad peak centered near 3300 cm⁻¹ (Figure 10B). The peak attributed to perturbed SiOH groups (\sim 3300 cm⁻¹) increases in intensity and red-shifts with increasing adsorption of 2-butanol, suggesting increasing extents of hydrogen-bonding at higher 2butanol coverages. At intermediate 2-butanol coverages, the formation of 2-butanol dimers (3480 cm⁻¹) appears to precede the formation of confined oligomeric 2-butanol clusters, which give rise to a new feature centered near 3393 cm⁻¹ at high partial pressures and resemble bulk liquidlike 2-butanol networks. Contrasting hydrophilic Sn-Beta-OH, adsorption of 2-butanol within hydrophobic Sn-Beta-F is characterized by the formation of 2-butanol monomers at low equilibrium pressures of 2butanol as evidenced by the appearance of an O-H stretching feature centered at 3605 cm⁻¹ (Figure 10A). Increasing the partial pressure of 2-butanol results in an increase in intensity of the 2-butanol monomer peak and is accompanied by a blue-shift $(\sim 3620 \text{ cm}^{-1})$ and sharpening of this feature, which likely reflects the adsorption of 2-butanol within a less polar solvating environment at higher coverages. At intermediate partial pressures, a new feature centered at \sim 3510 cm⁻¹ appears and grows with increasing 2-butanol pressure that is reminiscent of the formation of H-bonded alcohol dimers observed from IR spectra of light alcohols $(C_1 - C_4)$ adsorbed in nonpolar solvents (3540-3500 cm⁻¹).⁴⁸ Thus, the hydrophobic pores of Sn-Beta-



Figure 11. (A) Proposed catalytic cycle for the MPV reduction of methyl levulinate to 4-hydroxypentanoate with 2-butanol over a partially hydrolyzed framework metal site. (B) Arrhenius plot for the MPV reduction of ML (0.02 mol dm⁻³) with Hf-Beta using different hydrogen donors: 2-BuOH (blue square), 1-BuOH (red square), 2-PrOH (cyan square), 1-PrOH (orange circle), EtOH (pink triangle), and Cy-PeOH (purple diamond). Rates are measured in moles of GVL produced per second normalized per total mole metal center in the catalyst. (C) Values of apparent activation energies and pre-exponential factors determined from experimental kinetics measured on Hf-Beta with a 0.02 mol dm⁻³ ML feed in different alcohol solvents. Units of E_a are kJ mol⁻¹, and units of A are 10⁵ (mol dm³)(mol metal s mol ML)⁻¹. Reproduced with permission from ref 30. Copyright 2014 Elsevier.

F appear to impede the formation of liquidlike 2-butanol oligomers observed within hydrophilic Sn-Beta-OH and instead give rise to primarily dimeric 2-butanol species near pore-filling that we speculate adopt a one-dimensional structure during catalysis similar to that observed for water confined within subnanometer (pore diameter <1 nm) hydrophobic pores (Figure 10C).^{31,40,49}

The different 2-butanol solvent structures observed in hydrophobic and hydrophilic Sn-Beta zeolites (Figure 10) manifest as differences in the enthalpies and entropies of adsorption and activation that comprise the MPVO free energy landscape. Adsorption enthalpies (ΔH_{ads}) and entropies (ΔS_{ads}) reflect differences between the final adsorbed 2-butanolcyclohexanone adduct and 2-butanol in solution and the 2butanol-covered open Sn site and cyclohexanone in solution (K_1 in Figure 8A). Apparent activation enthalpies (ΔH_{app}) and entropies (ΔS_{app}) reflect differences between the MPVO transition state and the coadsorbed adduct $(K_2K_3^{\ddagger})$ in Figure 8A). Adsorption and activation enthalpies and entropies were extracted from kinetic data measured as functions of cyclohexanone activity and temperature (Figure 9C), and not from single-point rate measurements, in order to capture differences in the transition between first- and zero-order kinetic regimes which vary strongly with temperature in Sn-Beta-F (Figure 8B). Values of ΔH_{app} are 7 kJ mol⁻¹ smaller on Sn-Beta-F than on Sn-Beta-OH, while ΔS_{app} is similar on both zeolites, suggesting that the more tightly ordered 2-butanol solvent structure present in the pores of Sn-Beta-F enthalpically stabilizes the MPVO transition state, relative to the coadsorbed adduct, leading to 10× larger zero-order rate constants on Sn-Beta-F than on Sn-Beta-OH at all temperatures (333-393 K; Figure 9A).

Adsorption of cyclohexanone within both Sn-Beta-F and Sn-Beta-OH from the solution phase results in positive values of both $\Delta H_{\rm ads}$ and $\Delta S_{\rm ads}$ (Figure 9C) despite confinement and adsorption of cyclohexanone within the micropores of Beta zeolites from the solution phase. This behavior contrasts classical gas-phase adsorption, which is typically characterized by negative values of $\Delta H_{\rm ads}$ and $\Delta S_{\rm ads}$ due to favorable

coordination of adsorbates at the adsorption site. Furthermore, the adsorption of cyclohexanone within the 2-butanol-filled pores of hydrophilic Sn-Beta-OH is more enthalpically favorable than that in Sn-Beta-F ($\Delta\Delta H_{ads}$ (F-OH): 29 kJ mol⁻¹) but results in a smaller gain in entropy ($\Delta\Delta S_{ads}(F-OH)$: 70 J mol⁻¹ K⁻¹). This likely arises because adsorption within an ordered hydrogen bonding network, like that which occurs in confined hydrophobic pores (Figure 10), is dominated by the breakup of solvent-solvent interactions that result in an increase in solvent disorder.⁴⁶ Consequently, the Gibbs free energy of cyclohexanone adsorption within Sn-Beta-F becomes more negative with increasing temperature, which results in cyclohexanone coverages that increase with temperature (Figure 9B) and shift the onset of the zero-order kinetic regime to higher values of cyclohexanone activity at elevated temperature (Figure 8B). Collectively, these results emphasize how the number and arrangement of intraporous solvent and reactant molecules are intimately connected to the structure and composition of both the catalytic active site and secondary confining environment. These effects are analogous to the effects of solvent molecules in molecular catalysis¹¹ and of water networks in metalloenzymes,⁴ whose confining pockets can expel or rearrange solvent molecules to steer catalysis along a desired pathway while avoiding entropic penalties for solvent reorganization.

5. TURNOVER RATES OF LIQUID PHASE REACTIONS DEPEND ON SOLVENT SUBSTITUTION

Mirroring the impact of zeolite pore polarity on adsorption and catalysis, solvent identity has also been shown to alter the partitioning of adsorbates between the solution and intraporous zeolite phases^{41,45} leading to differences in adsorption equilibrium constants that rationalize kinetic trends observed during liquid-phase alkylation⁵⁰ and epoxidation⁴⁴ catalysis. The promotional effects of solvent molecules on Brønsted acid catalysis in zeolites has been well-studied,^{3,51,52} where solvation within the pores leads to varied catalytic effects because protons become solvated within solvent and solvent—reactant clusters that are surrounded by extended solvent networks.⁵³ The

presence of cosolvents in aqueous systems (e.g., alcohols, CH₃CN) has also been shown to alter turnover rates on Lewis acidic zeolites where active sites are embedded within the siliceous lattice and are no longer solvated within extraframework solvent clusters.^{17,43} Such examples underscore new opportunities to leverage specific interactions between adsorption sites (e.g., framework heteroatoms, SiOH) and solvent molecules that influence solvent reorganization and transition state stability at confined solid–liquid interfaces.

We have investigated how substitution of the alcohol hydrogen donor leads to differences in MPVO transfer hydrogenation rates (per metal site) over Hf-Beta for the reduction of ML to 4HP and subsequent lactonization to GVL.³⁰ This serial reaction proceeds via adsorption and deprotonation of the alcohol over the Lewis acid center (step 1; Figure 11A) followed by adsorption of ML and then proceeds through the rate-controlling hydride shift transition state (step 3). First-order rate constants (per total Hf) were measured as a function of temperature (393-453 K) to extract activation energies and pre-exponential factors in the presence of different alcohol hydrogen donors (Figure 11B). Notably, first-order rate constants were $\sim 10 \times$ larger using secondary alcohols (e.g., 2butanol) compared with primary alcohols (e.g., 1-butanol) across the entire temperature range studied. Specifically, secondary alcohols (e.g., 2-butanol, 2-propanol, and cyclopentanol) gave first-order apparent activation energies around $52 \pm 5 \text{ kJ mol}^{-1}$, whereas primary alcohols (e.g., 1-butanol, 1propanol, and ethanol) gave activation energies of 71 ± 2 kJ mol⁻¹, respectively (Figure 11C). We hypothesized that the lower apparent activation barrier for secondary alcohols was primarily a result of stabilization of the hydride shift transition state by the electron-donating alpha methyl group and correlated with oxidation enthalpies of the respective alcohols, which segregate between primary and secondary alcohols.⁵⁴

Pre-exponential factors for reactions performed with primary alcohols were nearly 2 orders of magnitude greater than those for secondary alcohols, likely reflecting reduced steric hindrance of both the bound intermediates and the transition state due to the absence of a terminal methyl group in primary alcohols. The larger pre-exponential factors of primary alcohols, however, did not compensate for their unfavorable activation energies at the temperatures investigated, resulting in first-order rate constants that were an order of magnitude lower than those of their secondary counterparts (Figure 11C). Within each series of primary or secondary alcohols, reaction rates were found to increase with increasing length of linear alkyl chains. We attributed this to increases in pre-exponential factors, as activation energies only varied by 5-10 kJ mol⁻¹ within each class of alcohol. We hypothesized that more polar solvent molecules (i.e., alcohols with shorter alkyl chains) enthalpically stabilize MPVO transition states but lead to more negative entropies of activation due to a decrease in flexibility of the bound intermediate and transition state. Changing the alcohol identity may also result in differences in the structure of confined alcohol networks (see Section 4) which would produce distinct solvation environments that can alter the stability of kinetically relevant adsorbed intermediates and activated complexes.^{30,46} First-order rate constants, however, represent coupled adsorption and activation phenomena and preclude fundamental understanding of enthalpy-entropy compromises among different solvents without measurement of turnover rates in distinct first- and zero-order kinetic regimes or heats of adsorption from independent experiments.

6. OUTLOOK

Turnover rates of reactions catalyzed at confined solid-liquid interfaces reflect complex interactions between active sites, adsorbed reactive intermediates and transition states, and spectating solvent molecules that occupy the void space between active sites. Incorporation of metal heteroatoms within siliceous zeolitic frameworks gives rise to Lewis acidic active sites that can adopt different coordination environments depending on their identity and placement at different T-site locations. The diverse nature of such Lewis acid sites complicates the normalization of turnover rates and requires characterization methods that can independently interrogate both the primary binding site and the secondary solvating environment that comprise confined active sites. Dynamic nuclear polarization MAS NMR methods are able to directly probe the local coordination of NMR active nuclei anchored within zeolites without the need for isotopic enrichment or prohibitively long acquisition times.²⁰ MAS NMR techniques can also be used to identify NMR inactive nuclei through surrogate molecules containing NMR active nuclei (e.g., ¹⁵N or ³¹P) that selectively bind to Lewis acid sites. The chemical shifts of adsorbed probe molecules can provide information about both the Lewis acid strength (e.g., ¹⁵Npyridine)²³ and differences in the local coordination of framework heteroatoms (e.g., ³¹P-TPMO), which can be used to correlate the reactivity of various chemical transformations (e.g., transfer hydrogenation, aldol condensation) to different active site structures.^{27,55} These methods can enable the comparison of catalytic turnover rates measured on different catalysts on a per active site basis, but changes in the secondary solvating environment, and the structure of solvent molecules that occupy such voids during liquid phase catalysis, must also be considered as part of the active site.

Rigorous interpretation of catalytic turnover rates requires a fundamental understanding of how microporous voids of different size organize and shape confined solvent structures. Methods to control the formation of defect sites may enable precise placement of active sites at specific T-sites within a given zeolite framework via postsynthetic grafting,³⁷ but also provide an opportunity to modulate the density of hydrophilic binding sites that nucleate solvent clusters and facilitate the formation of extended solvent networks. The density of hydrophilic sites (e.g., Lewis acid sites, silanol defects) alters the polarity of the zeolite framework and has been well-recognized as a critical design parameter for zeolite catalysis in the presence of water for reactions performed at low temperatures (<473 K) in both the liquid phase and gas phase.^{17,39} Hydrophobic zeolites synthesized in the presence of F⁻ anions inhibit the formation of extended H-bonded water structures within their pores,³¹ but open questions still remain as to how the polarity of the zeolite framework influences catalysis in nonaqueous solvent systems. Similar to zeolite catalyzed reactions in the presence of water, alcohols (e.g., methanol, ethanol, 2-butanol) are also able to form hydrogen-bonded solvent clusters and extended H-bonded networks whose structures are dependent on both the thermodynamic activity of the alcohol in the bulk and the density of hydrophilic binding sites.^{3,46,56,57} These H-bonded alcohol networks alter the stability of adsorbed intermediates and transition states that can inhibit gas-phase alcohol dehydration at high alcohol activities when desorption of extraneous alcohol molecules is required prior to the formation of transition states. This organization of confined alcohol networks can also lead to enhanced turnover rates of liquid-



Figure 12. (A) Schematic representation of the multistep synthesis procedure to selectively place Sn in *d4r* of high-silica BEC zeolites. (B) ¹⁹F MAS NMR spectra of the as-prepared Ge-containing BEC materials after different crystallization times. The measured signal ratios are included for all Ge-BEC samples. (C) ³¹P MAS NMR spectra of TMPO dosed on deGe-BEC, Sn-BEC, and Sn-Beta at TMPO/Sn = 0.5 loading. Reproduced with permission from ref 37. Copyright 2020 Royal Society of Chemistry.

phase transfer hydrogenation catalysis because ordered alcohol networks occluded within hydrophobic zeolites stabilize adsorbed intermediates and transition states to a greater extent compared with liquidlike solvent networks observed in hydrophilic zeolites. The nature of these interactions between the zeolite pore and confined solvent molecules can be further tuned through judicious choice of solvent polarity or even the addition of cosolvents to the reaction medium, that alter the stability of adsorbed intermediates or promote the selective partitioning of reactant, solvent, and product molecules between the bulk and intrapore phases.

Fundamental understanding of the role that confined solvent structures play during catalysis in condensed media will require the development of quantitative relationships between synthesis methods that manipulate active site structure with characterization and kinetic probes that are sensitive to differences in the intraporous solvent environment. Previous NMR^{8,22,27} and IR^{24,28} spectroscopic studies have demonstrated that Lewis acid metal centers can adopt different configurations in Beta zeolites and feature different reactivity profiles. Although methods to control the precise structure of Lewis acidic metal centers has proven elusive with conventional hydrothermal synthesis methods, sacrificial heteroatoms (e.g., Ge) can be used to preferentially occupy specific crystallographic positions in the BEC framework,⁵⁸ thus enabling grafting of Lewis acid centers at high strain T-sites after gently removing the original heteroatoms.^{59,60} We have recently demonstrated that BEC

zeolites can be successfully synthesized with Sn atoms positionally biased into the double-four membered ring (d4r)of the BEC framework via postsynthetic grafting of Sn into degermanated BEC zeolites (deGe-BEC) containing low concentrations of Ge in the starting framework (Si/Ge = 155; Figure 12A).³⁷ ¹⁹F and ²⁹Si MAS NMR spectra (Figure 12B) revealed the preferential incorporation of Ge atoms into the d4rsecondary building unit of the BEC framework and showed that silanol defect sites, which serve as grafting sites for reactive Sn alkyl halide precursors, form upon degermanation. ³¹P MAS NMR spectra of adsorbed TMPO (TMPO/Sn = 0.5) gave rise to a single resonance ($\delta_{iso}(^{31}P) = 59.8 \text{ ppm}$), indicating a greater homogeneity of Sn sites than observed for Sn-Beta (Figure 12C). These observations were supported by density functional theory (DFT) calculated ³¹P chemical shifts of TMPO adsorbed at Sn atoms located at different T-sites within the BEC framework and suggested that Sn atoms are predominantly incorporated at the T1 site of the BEC d4r. IR spectra of adsorbed CD₃CN, a known titrant of open and closed Sn sites in Sn-zeolites,²⁴ revealed that Sn atoms grafted at the T1 site in degermanated BEC zeolites preferentially formed open Sn sites (open/closed = 1.4) in higher amounts compared with conventional hydrothermally synthesized Sn-Beta zeolites (open/closed = 0.4-0.7). We hypothesize that this reflects the inability of Sn to accommodate the same bond angles as Ge atoms in order to form four bonds to framework O atoms at the T1-site of the d4r, similar to recent data that suggests open Sn

sites preferentially form at stacking faults in Sn-Beta zeolites.¹⁸ These data underscore potential opportunities to utilize other sacrificial heteroatoms (e.g., Al, B) to selectively position catalytic active sites at specific T-sites for the design of Lewis acidic zeolites with tailored active site structures.

We further envision that zeolites synthesized with controlled defect densities will enable the preparation of catalysts with strategically placed active and defect sites to predictably alter the structure of confined solvent domains. Critical to this will be the development of spectroscopic (e.g., IR, NMR) and chemical titration methods that elucidate how the secondary solvating environment influences the structure and stability of confined intermediates as a function of the reaction coordinate. The dynamic nature of reactant and solvent molecules along the reaction coordinate can influence a range of solvated reaction systems involving carbocation intermediates⁶¹ and even during reactions when active sites become mobilized due to solvation by reactant molecules.⁶²⁻⁶⁴ Transient experiments under reaction conditions, ideally where spectroscopic techniques can be coupled to measure reaction rates under operando conditions, will be critical to infer changes in the active site structure during catalytic turnover. These kinetic and spectroscopic measurements create an opportunity to connect experimental observations to computational models to interpret nonideal thermodynamic behavior of adsorbates and transition states solvated by confined molecular ensembles. Interpretation of complex solvent-adsorbate interactions, particularly those that occur within microporous cavities at high pore occupancy, would certainly benefit from advanced computational methods that utilize time-dependent molecular simulations, such as ab initio molecular dynamics and metadynamics techniques, which accurately capture dynamic processes to map complex free energy landscapes.⁶⁵ These rigorous mechanistic interpretations can be coupled with emerging synthetic methods that utilize organic structure-directing agents, identified by machine learning algorithms, that best mimic the size and shape of catalytically relevant transition states.^{66–68} This selection in turn informs predictive guidance for the design of tailored reaction environments that manipulate confined solvent structures for selective catalytic transformations in the liquid phase.

AUTHOR INFORMATION

Corresponding Author

Yuriy Román-Leshkov – Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States; Occid.org/0000-0002-0025-4233; Email: yroman@mit.edu

Authors

- Blake A. Johnson Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States
- John R. Di Iorio Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, United States

Complete contact information is available at: https://pubs.acs.org/10.1021/accountsmr.1c00146

Notes

The authors declare no competing financial interest.

Biographies

Blake A. Johnson received his B.S. and B.Ch.E. degrees from the University of Minnesota—Twin Cities in 2019. He is currently a graduate student at MIT under the supervision of Professor Yuriy Román-Leshkov. His research interests explore the fundamentals of heterogeneous catalysis at solid–liquid interfaces in the area of renewable biomass conversion.

John R. Di Iorio received his B.S. in Chemical Engineering from the University of Washington in 2013 and his Ph.D. in Chemical Engineering from Purdue University in 2018. Since 2019, he has been a postdoctoral associate at the Massachusetts Institute of Technology under the guidance of Professor Yuriy Román-Leshkov.

Yuriy Román-Leshkov is the Robert T. Haslam (1911) Professor of Chemical Engineering at MIT. He received his Ph.D. from the University of Wisconsin—Madison in 2008 under the guidance of Professor Jim Dumesic and completed postdoctoral studies with Professor Mark Davis at Caltech. At MIT, the Román group specializes in elucidating the structure–activity relationships of heterogeneous catalysts and the design of novel catalytic materials.

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