Mechanism of selective benzene hydroxylation catalyzed by iron-containing zeolites


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A direct, catalytic conversion of benzene to phenol would have wide-reaching economic impacts. Fe zeolites exhibit a remarkable combination of high activity and selectivity in this conversion, leading to their past implementation at the pilot plant level. There were, however, issues related to catalyst deactivation for this process. Mechanistic insight could resolve these issues, and also provide a blueprint for achieving high performance in selective oxidation catalysis. Recently, we demonstrated that the active site of selective hydrocarbon oxidation in Fe zeolites, denoted α-O, is an unusually reactive Fe(IV)=O species. Here, we apply advanced spectroscopic techniques to determine that the reaction of this Fe(IV)=O intermediate with benzene in fact regenerates the reduced Fe(II) active site, enabling catalytic turnover. At the same time, a small fraction of Fe(III)-phenolate poisoned active sites form, defining a mechanism for catalyst deactivation. Density-functional theory calculations provide further insight into the experimentally defined mechanism. The extreme reactivity of α-O significantly tunes down (eliminates) the rate-limiting barrier for aromatic hydroxylation, leading to a diffusion-limited reaction coordinate. This favors hydroxylation of the rapidly diffusing benzene substrate over the slowly diffusing (but more reactive) oxygenated product, thereby enhancing selectivity. This defines a mechanism to simultaneously attain high activity (conversion) and selectivity, enabling the efficient oxidative upgrading of inert hydrocarbon substrates.

Significance

Fe zeolites are heterogeneous catalysts that show potential in a number of important industrial applications, including the selective partial oxidation of methane to methanol at room temperature, and the selective conversion of benzene to phenol. There are practical limitations associated with Fe-zeolite catalysts that may be resolved with mechanistic insight; however, reliable experimental data on Fe zeolites are limited. This study defines the mechanism of selective benzene hydroxylation catalyzed by Fe zeolites, clarifying the relationship between active site structure and catalytic performance (activity, selectivity). Mechanistic insight from this study represents an important step toward synthetic control over function in selective hydrocarbon oxidation catalysis.


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To define the ligation of $\alpha$-C$_6$H$_6$, we employed a combination of Fe K-edge X-ray absorption spectroscopy (XAS) coupled to $^{57}$Fe nuclear resonance vibrational spectroscopy (NRVS). NRVS is a synchrotron-based technique that selectively probes vibrations of Fe sites in metalloenzymes and zeolites (11, 12). Importantly, NRVS and XAS are sensitive to $S = 2$ Fe(II) centers, which can be difficult (or impossible) to resolve in optical absorption, resonance Raman (rR), and electron paramagnetic resonance spectroscopy. As shown in the X-ray absorption near-edge region in Fig. 1B, the reaction of $\alpha$-O (gray trace) with C$_6$H$_6$ (red trace) results in loss of the intense $\alpha$-O preedge features at 7,110–7,115 eV (Inset), as well as a downshift in the rising edge energy by $\sim$3 eV. These changes are consistent with reduction of $\alpha$-O to an Fe(II) species distinct from $\alpha$-Fe(II) (blue trace, with a low-energy $1s$–$4p$ transition at 7,120 eV that is characteristic of square planar geometry) (11). In the extended X-ray absorption fine structure (EXAFS) region in Fig. 1C, the Fourier transform (FT) shows a loss of first-shell intensity moving from $\alpha$-O (gray) to $\alpha$-C$_6$H$_6$ (red). Comparing the first-shell EXAFS fits of $\alpha$-C$_6$H$_6$ in Fig. 1C and of $\alpha$-O from Snyder et al. (11) shows this is due to the presence of the short 1.63-Å scattering path from the reactive terminal oxo ligand (see SI Appendix, Fig. S2 for full EXAFS fits). The first coordination sphere of $\alpha$-C$_6$H$_6$ was fit with $\pm 1$ oxygen ligands at 2.10 Å. However, the EXAFS fit does not clarify the nature of the axial ligand. (See SI Appendix, Fig. S2; this ligand could contribute to the 2.10-Å shell or, alternatively, be weakly bound and not significantly contribute to the experimental data.)

To resolve this ambiguity, we directly synthesized candidates for $\alpha$-C$_6$H$_6$ by binding either phenol (product) or C$_6$H$_6$ (substrate, present in excess under reaction conditions) to $\alpha$-Fe(II). As shown in SI Appendix, Fig. S1, in each case this leads to quantitative conversion of $\alpha$-Fe(II) to a new $S = 2$ Fe(II) species with Mössbauer parameters that are highly similar to $\alpha$-C$_6$H$_6$. However, XAS and NRVS data presented in Fig. 2 show significant differences for benzene- and phenol-ligated $\alpha$-Fe(II). FT EXAFS data in Fig. 2A show excess first-shell intensity for the phenol-bound site (black trace; see 1–2-Å region) relative to $\alpha$-C$_6$H$_6$ (red trace). The EXAFS fit given in the inset indicates this is due to the presence of a fifth oxygen ligand at 2.09 Å. The X-ray absorption near edge structure (XANES) region presented in SI Appendix, Fig. S2 shows the phenol-bound site also does not reproduce the $\alpha$-C$_6$H$_6$ preedge or rising edge. Finally, as shown in Fig. 2B, the phenol-bound site (black trace) does not reproduce the distribution of NRVS intensity for $\alpha$-C$_6$H$_6$ (red trace) in the 0–250-cm$^{-1}$ region, which contains FeL$_2$ core modes that are highly sensitive to coordination geometry (11). In this region, $\alpha$-C$_6$H$_6$ shows a distinct peak at 165 cm$^{-1}$, while the phenol-bound site has a plateau from 165 to 210 cm$^{-1}$. The experimental Mössbauer, EXAFS, and NRVS data of the phenol-bound site are reproduced by the $S = 2$ Fe(II) DFT model presented in SI Appendix, Fig. S3. Alternatively, EXAFS data in Fig. 2C, NRVS data in Fig. 2D, and XANES data in SI Appendix, Fig. S2 demonstrate the spectroscopic features of C$_6$H$_6$-ligated $\alpha$-Fe(II). (b) K-edge XANES of $\alpha$-C$_6$H$_6$ (red trace) and benzene-bound $\alpha$-Fe(II) (blue trace). (Inset) The phenol-bound $k^2$-weighted EXAFS is shown (solid gray, fit in dashed black), with the first shell fit parameters given below. (d) Comparison of NRVS spectra of $\alpha$-C$_6$H$_6$ (red trace) and benzene-bound $\alpha$-Fe(II) (blue trace). A structural model of the benzene-bound site is illustrated at the right of the figure, based on correlation of spectroscopy to DFT (SI Appendix, SI Methods). (C) Comparison of FT EXAFS of $\alpha$-C$_6$H$_6$ (red trace) and benzene-bound $\alpha$-Fe(II) (blue trace). (Inset) The benzene-bound $k^2$-weighted EXAFS is shown (solid red, fit in dashed black), with the first shell fit parameters given below. (d) Comparison of NRVS spectra of $\alpha$-C$_6$H$_6$ (red trace) and benzene-bound $\alpha$-Fe(II) (blue trace). A structural model of the benzene-bound site, based on correlation of spectroscopy to DFT (SI Appendix, SI Methods), is illustrated at the right of the figure.
α-Fe(II) (blue traces) overlay with the features of α-C6H6 (red traces). The experimental Mössbauer, EXAFS, and NRVS spectroscopy of α-C6H6 are reproduced by an S = 2 DFT model of α-Fe(II) with a weakly bound π-π*-C6H6 ligand (see SI Appendix, Fig. S3 for detail). As shown in SI Appendix, Fig. S4, the C6H6 ligand desorbs from α-C6H6 at room temperature, consistent with a weak bonding interaction.

The quantitative conversion of α-O to the substrate-bound reduced active site at room temperature has significant mechanistic implications. α-C6H6 is not a reaction intermediate, and its formation requires α-Fe(II) to first release the phenol product before binding the excess C6H6 in the reactant stream. These results contradict earlier studies suggesting product desorption from the active site is rate limiting (13, 14), and/or driven by subsequent activation of N2O (2, 14). High temperatures are therefore not required to regenerate the active site, but do assist in the subsequent desorption of phenol from the zeolite lattice [see temperature-programmed desorption (TPD) data in SI Appendix, Fig. S5]. The absence of overoxidized products (2, 3) indicates the released phenol does not go on to react with α-O. Interestingly, α-O does react directly with phenol vapor at room temperature to form diphenols—see SI Appendix, Fig. S6 and ref. 15. This suggests the benzene substrate is able to outcompete the phenol product, despite its lower activation toward electrophilic aromatic substitution reactions. The reactivity of α-Fe(II) toward a different from other mononuclear Fe(IV)=O intermediates: α-O achieves high levels of selectivity (95%+) at high levels of conversion (40%+) (6), while other Fe(IV)=O intermediates attain lower levels of selectivity (0–70%) at lower levels of conversion (<10%) (16–18). The clean regeneration of the α-Fe(II) active site following aromatic hydroxylation also raises an important contrast to methane hydroxylation in Fe zeolites, which is not catalytic (9), and where past Mössbauer studies show single-turnover results in a heterogeneous distribution of Fe species (SI Appendix, Fig. S7) (10). DFT studies presented below clarify the unique features of α-O leading to its unusually high reactivity and selectivity in aromatic hydroxylation.

**A Mechanism Leading to Catalyst Deactivation.** The regeneration of α-Fe(II) following aromatic hydroxylation in Fe-BEA contrasts with studies of Fe-ZSM-5, where phenolate-ligated products are proposed (19–22). A C6H6/α-O formed spectroscopic product with a broad absorption (Abs) band at 13,900 cm⁻¹ has been identified in Fe-ZSM-5, assigned as a binuclear Fe(III)-phenolate species based on rR data (20). This is proposed to be either a catalytic intermediate, a poisoned state of the active site, and/or a precursor to coke formation (19–23). We used a range of spectroscopies to clarify the nature of this putative Fe(III) phenolate and its relation to the α-O active site. Mössbauer spectra in SI Appendix, Fig. S8 show the reaction of C6H6 with Fe-ZSM-5 parallels the Fe-BEA reaction, resulting in near-quantitative formation of a single Fe(II) product, with <5% Fe(III) present. However, as shown in Fig. 3, this also results in the 13,900-cm⁻¹ Abs band assigned to an Fe(II)=C phenolate by Xia et al. (20) (Fig. S4).

Tuning a laser into the 13,900-cm⁻¹ Abs feature enhances a number of Raman vibrations shown in Fig. 3B, with frequencies and intensities consistent with those in ref. 20. Reacting 18O-labeled α-O (see ref. 24 and Materials and Methods) with C6H6 results in the rR isotope shifts given in parentheses in Fig. 3B, which are diagnostic of a bound phenolate ligand. (An analogous 15,200-cm⁻¹ Abs feature forms in Fe-BEA—see SI Appendix, Fig. 8S. Issues with fluorescence precluded rR studies of this system.) Incorporation of the 18O label indicates the phenolate ligand is correlated with the active site (i.e., unrelated to spectator sites).

We used variable-temperature variable-field magnetic circular dichroism (VTVH-MCD) (9, 25) to define the electronic structure of this phenolate-bound species. As shown in Fig. 3C, the 13,900-cm⁻¹ room-temperature (RT) Abs band resolves into two components at 11,600 cm⁻¹ and 13,300 cm⁻¹ in 3K MCD spectroscopy. VTVH-MCD isomserhs collected from these bands overlay within error, suggesting they derive from the same species. The 11,600-cm⁻¹ VTVH-MCD isosmehs in Fig. 3D require a spin-Hamiltonian fit with an S = 5/2 ground state, consistent with a high-spin mononuclear Fe(III) phenolate [but not an oxo-hydroxo-bridged 2Fe(III) site, which would have an integer-spin, likely singlet ground state (26)]. Compared with other mononuclear S = 5/2 Fe(III) phenolates, the 647-cm⁻¹ Fe-O-H stretching frequency from rR is high [typically 570–620 cm⁻¹ for S = 5/2 Fe(III) phenolates] (27, 28), indicating a strong bonding interaction. Finally, the reaction of α-O with phenol results in >95% regeneration of Fe(II) (SI Appendix, Fig. S6), and the formation of diphenols (15). The small amount of Fe(III) phenolate that forms during the benzene reaction is therefore unrelated to small contributions from overoxidation. Site-selective spectroscopy therefore characterizes the geometric and electronic structure of this S = 5/2 Fe(III) phenolate, and shows this is a poisoned state of the α-Fe(II) active site generated during productive turnover. The absence of an Fe(III) signal in Mössbauer indicates <5% of sites are poisoned following single turnover, while analysis of diffuse reflectance UV-vis (DR-UV-vis) band intensities indicates ~0.2% poisoning (see Materials and Methods for detail). This would lead to 20–100% deactivation after 100 turnovers. DFT calculations presented below suggest phenolate poisoning occurs via H-atom loss from a bound catalytic intermediate.

**A Mechanism Enabling High Reactivity and Selectivity.** To define features of α-O contributing to its high reactivity and selectivity in aromatic hydroxylation, we constructed a DFT reaction coordinate that cleanly regenerates the reduced α-Fe(II) active
The associated free-energy changes (ΔΔG at 300 K) are reported in parentheses. In the first step of this reaction coordinate, α-O (1) oxidizes C₆H₆ by one electron to form an Fe(III)-α-complex (2). The evolution of the α-LUMO during this electron transfer is shown in the blue inset. The α-complex undergoes an NH shift (formal 1,2-hydride shift) to form an Fe(III)-dienone product (3). The evolution of the highest occupied molecular orbital (HOMO) during this second electron transfer is shown in the red inset. The dienone rearranges to phenol (4, 5), and then desorbs regenerating α-Fe(III) (6), which binds benzene to form α-C₆H₆ (7).

While reduction to Fe(II) is facile, our experiments show a small amount of Fe(III) phenolate is also formed during productive turnover. DFT calculations support a strong Fe-O-C₆H₆ bond in this poisoned active site (δdFe-O = 1.79 Å), consistent with rR. This species can be generated by homolyzing the ipso C–H bond of the σ-complex (intermediate 2), which is very weak (bond dissociation enthalpy = 15.6 kcal/mol), suggesting H-atom loss from the bound substrate as a potential poisoning mechanism. We reacted α-O with deuterated substrate to evaluate this mechanism, which predicts an H/D KIE of 1.44–2.89 (see SI Appendix, SI Methods for detail). As shown in SI Appendix, Fig. S9, the reaction of α-O with C₆D₆ results in a 30 ± 5% decrease in the Fe(III)-phenolate DR-UV-vis feature, reflecting an H/D KIE of α = 1.33–1.54 in agreement with the predicted value.

Proceeding from intermediate 3 in Fig. 4, the zeolite lattice can catalyze the tautomerization of the dienone to phenol. A potential mechanism would involve transfer of a proton from the dienone to one of the two adjacent Al T sites (intermediate 4), as required by experiment. Reactivity occurs entirely on the S = 2 surface (SI Appendix, Fig. S10), and starts with electrophilic attack of α-O (intermediate 1 in Fig. 4) on C₆H₆. As shown in the blue inset, an electron is transferred from C₆H₆ into the Fe 3dₓ²₋ᵧ²-derived lowest unoccupied molecular orbital (α-LUMO) of α-O in this step, forming a new C–O bond. The resulting σ-complex (intermediate 2) contains an S = 5/2 Fe(III) antiferromagnetically coupled to an S = 1/2 substrate radical. A significant and unique reactivity feature of α-O is the absence of a barrier for CO bond formation. In contrast, this is the rate-limiting step for electrophilic aromatic hydroxylation in Fe metalloenzymes (29–31) and homogeneous catalysts (32). From the analysis presented in SI Appendix, SI Methods, two factors contribute to the elimination of this barrier in the reaction of α-O with C₆H₆. First, the reduction potential of α-O is unusually high (11), contributing a ∼20-kcal/mol driving force for C–O bond formation relative to other Fe(IV)=O intermediates. Second, the Fe≡O bond of α-O is unusually covalent (10, 11), leading to a frontier molecular orbital that is intrinsically activated for electrophilic chemistry (9–11). Both factors derive from the “entatic state” (33) of α-O defined in previous studies, where rigid constraints from the zeolite lattice enforce an otherwise unstable square pyramidal coordination geometry for this S = 2 Fe(IV)=O site with no axial ligand (9–11).

Proceeding from the σ-complex, an NH shift (formal 1,2-hydride shift) (34) would occur with a low barrier (ΔH = 1.2 kcal/mol). This is a generally observed mechanism of aromatic hydroxylation by Fe(IV)=O intermediates (16, 29–31). This NH shift induces transfer of a second electron from the substrate (see Fig. 4, red inset), forming 2,4-cyclohexadienone bound to the reduced Fe(II) active site (intermediate 3). The NH-shift barrier is the highest on the reaction coordinate, leading to a predicted hydrogen/deuterium kinetic isotope effect (H/D KIE) of α = 1.00–1.16 (see Materials and Methods for detail). This is in agreement with the experimental intramolecular α=0.10–0.16 measured by Dubkov et al. (35), but different from the inverse KIEs of α = 0.8–0.9 typically observed with other Fe(IV)=O intermediates (32), where C–O bond formation is rate limiting. Alternative, disfavored mechanisms are evaluated and discussed in SI Appendix, SI Methods.
and then back to the substrate to yield the phenol-bound Fe(II) active site (intermediate 5). The stabilities of the dienone- and phenol-bound active sites are similar (ΔΔH = 2.2 kcal/mol), despite the 13.9-kcal/mol destabilization of the free dienone relative to phenol. The Fe(II) active site therefore binds the dienone more strongly (ΔHdes = 28.6 kcal/mol, versus 16.9 kcal/mol for phenol), potentially favoring the premature release of this more reactive species. Phenol then desorbs, regenerating α-Fe(II) (intermediate 6). Alternatively, the dienone may be released from the active site and tautomerize to phenol elsewhere, in a process catalyzed by a remote Bronsted site. Finally, excess benzene present in the reactant stream is calculated to bind weakly to α-Fe(II) (ΔH = −3.4 kcal/mol) to form α-C6H5—

the species observed experimentally after single turnover.

Conclusion

This study applies advanced spectroscopic techniques to define the mechanism of benzene hydroxylation and Fe(III)-phenolate poisoning in Fe zeolites. A key finding is that the RT reaction of benzene with the Fe(IV)=O intermediate α-Fe(III) in fact regenerates the reduced α-Fe(II) active site, explaining how catalysis is possible for this Fe-zeolite system. This requires that benzene is hydroxylated through an associative electrophilic mechanism. We find that the phenol product desorbs from the active site, but TPD experiments show it remains bound to the catalyst surface. This elucidates the mechanism of productive turnover. At the same time, a small fraction (0.2-5%) of partially oxidized, catalytically inactive Fe(III)-phenolate sites are formed, further defining a mechanism of active site poisoning.

Experimental data coupled to DFT calculations indicate Fe(III)–phenolate formation occurs through H-atom loss from a bound catalytic intermediate—likely the α-C6H5OH α-complex (intermediate 2 in Fig. 4), which has a very weak ipso C–H bond. This mechanism, which is entropically favored (over the NIH shift), would be favored at high temperatures. Our data show high temperatures are not required to desorb phenol from the active site, but do aid in desorption of product from the zeolite lattice. Moving from BEA or ZSM-5 to a different zeolite lattice that adsorbs phenol less strongly could enhance catalysis, enabling a lower-temperature process to minimize Fe(III)–phenolate and coke formation. DFT calculations provide further insight into the experimentally defined mechanism for productive turnover. Due to the extreme reactivity of α-Fe(III), there is no rate-limiting barrier for aromatic hydroxylation (Fig. 4). Reactivity data from Fe–ZSM-5 show the apparent rate of benzene hydroxylation is in fact 19× greater than that of phenol hydroxylation (2). Combined, these insights suggest benzene is hydroxylated selectively due to its more rapid diffusion through the zeolite lattice—even at high levels of conversion. This model is supported by studies that show the diffusivity of phenol through zeolite lattices is significantly diminished relative to benzene due to its greater polarity (36). Thus, by embedding a highly reactive active site in a matrix that selectively limits the diffusion of the product, it is possible to achieve high conversion and selectivity simultaneously. These mechanistic insights elucidate the remarkable performance of Fe-zeolite catalysts in selective hydrocarbon oxidation. It will be important to explore how these insights can be used to enhance the catalytic hydroxylation of inert hydrocarbons in microporous materials.

Materials and Methods

Zeolite samples were prepared as described in refs. 10 and 11. XAS data were collected at beam lines 7–3 and 9–3 at the Stanford Synchrotron Radiation Lightsource (SSRL) under ring operating conditions of 500 mA over an energy range of 6,785–7,876 eV (k = 14 Å−1). NRVS spectra were collected at the Advanced Photon Source (APS) in Argonne, IL, at beamline 3-ID-D. DFT calculations were performed using the Gaussian 09 software package (see SI Appendix for citation). Details on sample preparation and spectroscopic experiments (DR-UV-vis, rIR, MCD) are included in SI Appendix.

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