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# Demonstrating the critical role of solvation in supported Ti and Nb epoxidation catalysts via vapor-phase kinetics

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## ■ ABSTRACT

Catalytic oxidation of hydrocarbons with hydrogen peroxide  $(H_2O_2)$  has been of the utmost importance for several decades. The vast majority of studies have been performed in the condensed phase, even though condensed phases introduce complex solvent effects and can promote the leaching of active sites. In response, we have built a custom reactor system to understand  $H_2O_2$  activation and selective oxidation in the vapor-phase. In this report, we study the epoxidation of cyclohexene with H<sub>2</sub>O<sub>2</sub> over four Lewis-acidic metal oxide catalysts: Ti and Nb grafted on SiO<sub>2</sub> and on the Zr based metal–organic framework, NU-1000. The M-SiO<sub>2</sub> materials are highly selective to the formation of epoxides and diols, as they can be in the condensed phase, while the NU-1000 based materials are far more prone to overoxidation to CO<sub>2</sub>, which appears to be connected to their strong reactant adsorption. Apparent activation energies are calculated for all materials when operating in the same kinetic regime, and the heats of cyclohexene adsorption into their pores are then used to directly compare intrinsic enthalpies of activation in the vapor vs. condensed phase for the M-SiO<sub>2</sub> catalysts. Nb-SiO<sub>2</sub> catalysts exhibit similar intrinsic enthalpies of activation in the vapor and condensed phases, whereas the condensed phase transition state in Ti-SiO<sub>2</sub> is 24 kJ/mol lower in energy than that of the same material in the vapor phase. These experiments establish another methodology for understanding the various roles of solvent in selective oxidation reactions and studying these reactions under conditions that differ significantly from the thousands of prior studies in the condensed phase.

KEYWORDS: epoxidation, hydrogen peroxide, selective oxidation, supported catalyst, metal oxide catalyst, metal–organic framework

## ■ INTRODUCTION

Hydrogen peroxide ( $H_2O_2$ ) is considered an attractive oxidant because its reaction byproducts are water and oxygen, and because its oxygen atom efficiency is higher than that of organic peroxides.<sup>1</sup>  $H_2O_2$  plays an important role as the terminal oxidant of innumerable oxidation reactions such as alkene epoxidation, alcohol oxidation, sulfoxidation, and so on.<sup>2</sup> Alkene epoxidation is of particular interest because epoxides serve as building blocks for many resins and fine chemicals.<sup>3</sup> Among them, epoxidation of cyclohexene is a frequent probe reaction because it provides extensive information about the mechanism of  $H_2O_2$  activation. In particular, its many reaction products (epoxide, diol, cyclohexenol,  $CO_2$ , etc.) can help distinguish between direct and radical reaction pathways that occur during the activation of  $H_2O_2$ .<sup>4-6</sup>

The vast majority of previous studies have focused on condensed phase reactions when using aqueous H<sub>2</sub>O<sub>2</sub> or organic peroxide, despite the following limitations. First and foremost, reaction solvents can significantly affect reactivity and/or selectivity due to competitive adsorption among solvents and reactants, effects of solvent acidity, variability solubility of reactants and products, and so on.<sup>7-9</sup> Second, it has been known for decades that some active sites, particularly those based on V or Mo ions, can leach into reaction solvent.<sup>10-11</sup> Conversely, materials like a UiO-66-supported VO<sub>x</sub> catalyst showed good time-on-stream stability under gas-phase oxidative dehydrogenation of cyclohexene without metal ion leaching.<sup>12</sup> Despite the promise of circumventing these issues and of better understanding solvent effects, practical issues have restricted the study of selective oxidation with vaporized H<sub>2</sub>O<sub>2</sub> under flow conditions. These issues largely arise from the competition between vaporization and decomposition of H<sub>2</sub>O<sub>2</sub> at elevated temperature. To the best of our knowledge, there are only two reported examples of heterolytic activation of vaporized H<sub>2</sub>O<sub>2</sub> in flow reactors.<sup>13-14</sup> Motivated by the previous two studies, we present a new vapor-phase peroxide reactor (scheme 1) which is robust and optimized for the purpose of studying  $H_2O_2$  activation in the vaporphase. With this reactor, we compare the kinetics of vapor-phase cyclohexene epoxidation over Ti and Nb grafted on a conventional support  $(SiO_2)$  and on a less conventional support consisting of the Zr based metal-organic framework, NU-1000. We then compare the kinetics of the reaction and the thermodynamics of reactant binding to those previously collected during high fidelity kinetics experiments of alkene epoxidation in the condensed phase.<sup>15-17</sup>

## EXPERIMENTAL METHODS

**Synthesis of Catalysts.** For the synthesis of M-SiO<sub>2</sub>, 5 g of Selecto SiO<sub>2</sub> (Fisher Chemical, 6 nm pore size, 550 m<sup>2</sup>/g, 63-200  $\mu$ m particle size) was dried for 30 min at 120 °C in a glass oven. Then, the SiO<sub>2</sub> was added to an oven dried 250 mL round bottom flask along with 50 mL of freshly distilled anhydrous toluene (Sigma-Aldrich, ACS Reagent, > 99.5%) and stirred at 200 rpm with an oven dried teflon stir bar at ambient temperature. Metal precursors, 227 mg of titanocene dichloride (Cp<sub>2</sub>Ti(IV)Cl<sub>2</sub>, Strem Chemicals, > 99%) or 269 mg of niobocene dichloride (Cp<sub>2</sub>Nb(IV)Cl<sub>2</sub>, Strem Chemicals, > 99%), were added to the mixture. A high dispersion (0.2 metal/nm<sup>2</sup>) was targeted for Ti-SiO<sub>2</sub> and Nb-SiO<sub>2</sub>. The mixtures were stirred for 1 h at ambient temperature, then the mixtures were vacuum filtered, washed with 200 mL of toluene and hexanes (Fisher Chemical, Certified ACS, > 98.5%), and dried in air for 5 min. The as-made Cp<sub>2</sub>Ti-SiO<sub>2</sub> and Cp<sub>2</sub>Nb-SiO<sub>2</sub> were loaded into a muffle furnace and calcined at 550 °C for 6 h with a 10 °C/min ramp rate to yield Ti-SiO<sub>2</sub> and Nb-SiO<sub>2</sub>.

The catalyst support, NU-1000, was prepared and activated following methods previously established.<sup>18</sup> For the synthesis of M-NU-1000, 200 mg of NU-1000 (185.1 µmol of the  $Zr_6$  node) and 449.3 µL of titanium(IV) isopropoxide (Sterm, min. 98%) or 555.1 µL of (tertbutylimido)tris(diethylamino)niobium(V) (Strem, min. 98%) were mixed in 10 mL heptane (Sigma Aldrich, 99%, anhydrous) for Ti-NU-1000 and Nb-NU-1000, respectively. These loadings correspond to 8 metal equivalents per  $Zr_6$  node. The reaction mixtures were stored in a glove box overnight with occasional swirling. The mixtures were decanted, and 10 mL of fresh heptane were added. The heptane washing cycle was repeated for four times to remove unreacted metal precursors. After these heptane washing steps, the materials were transferred from the glove box, and then washed in acetone four times. Any ligands remaining on the grafted Ti and Nb precursors were removed when exposed to moist air to yield TiO<sub>x</sub> and NbO<sub>x</sub> on the nodes of NU-1000.

**Characterization of Catalysts.** M-SiO<sub>2</sub> catalysts (ca. 2mg) were digested in a mixture of 1 mL of hydrofluoric acid (Macron, 48 wt.%) [CAUTION: handle HF with extreme care] and 9 mL of nitric acid (Fisher Chemicals, 67-70% w/w, trace metal grade) with mixing on a shaker plate. M-NU-1000 catalysts (ca. 2 mg) were microwave digested in 2 mL of nitric acid at 150 °C for 15 min. Titanium (323.452, 334.941, 336.121, and 337.280 nm), niobium (309.418, 316.340, 319.498, and 322.548 nm), and zirconium (327.305, 339.198, 343.823, and 349.621

nm) loadings were analyzed using inductively coupled plasma atomic emission spectroscopy (ICP-AES, iCAP 7600, Thermo Scientific) by comparing calibrated standard solutions.

Prior to N<sub>2</sub> physisorption, catalysts were degassed at 120 °C under dynamic vacuum for 18 h using a Smart VacPrep (Micromeritics). N<sub>2</sub> adsorption/desorption isotherms were collected at 77 K using a Tristar II (Micromeritics). Cyclohexene vapor adsorption isotherms on bare supports (NU-1000 and SiO<sub>2</sub>) were collected at 313 K, 353 K, and 383 K using a 3 Flex (Micromeritics). The isosteric heat of adsorption of cyclohexene on SiO<sub>2</sub> was calculated using a linear portion of the isotherm between 0.5-2 cm<sup>3</sup> (STP)/g<sub>SiO2</sub>, using equation (1).

$$\frac{d}{dT}(\ln(\mathbf{P}_{c6}))\Big|_{\mathbf{n}_{ads}} = \frac{\Delta H_{ads}}{RT^2}\Big|_{\mathbf{n}_{ads}}$$
(1)

Catalysis. A reactor system was built by our team based on a design shown in Scheme 1. The system is equipped with a syringe pump (KDS) to inject liquid-phase H<sub>2</sub>O<sub>2</sub> from to a plastic syringe (Norm-Ject, 10 mL) through a FEP (fluorinated ethylene propylene) capillary tube (Valco Instruments, 1/16 inch OD, 0.03 inch ID). This tube material minimizes decomposition of H<sub>2</sub>O<sub>2</sub>, unlike stainless-steel. The reactant vapor (cyclohexene in this study) was introduced through a quartz bubbler (Wilmad Labglass, 1/4 inch connection with extra coarse frit). The reactor furnace (Northwestern University Instrument Shop) consists of three aluminum heating blocks separated by a ceramic insulator to minimize heat conduction between adjacent blocks. The temperatures of all three aluminum heating blocks were individually controlled by a Quad-K temperature controller (J-KEM scientific) with K-type thermocouples (Omega) and stainless-steel sheath cartridge heaters (Omega, 150 Watts). During kinetic measurements, the temperature of the inlet block was fixed at 110 °C to minimize H<sub>2</sub>O<sub>2</sub> thermal decomposition, as well as to ensure complete vaporization of H<sub>2</sub>O<sub>2</sub> liquid. Figure S1 (150°C vaporization temperature) shows massive fluctuations in product concentration with time-on-stream (TOS), while Figure S2 shows discontinuities in the product concentrations with TOS that result from a low vaporization temperature of 80 °C. The temperature of the outlet block was fixed at 115 °C to minimize thermal decomposition of the products. A counter example (150 °C outlet) is shown in Figure S3.



Scheme 1. Vapor-phase hydrogen peroxide reactor scheme

Kinetic tests were performed at reaction block temperatures of 110, 120, 130, 140, and 150 °C to test apparent activation barriers of catalysts. M-SiO<sub>2</sub> (20 mg) and M-NU-1000 (10 mg) were both diluted in 200 mg of quartz sand, and these catalysts beds were supported on quartz wool in a quartz tube reactor (Wilmad Labglass, 18 inch long, 3/4 inch diameter). In a typical reaction test, the reactor bed was brought to temperature and cyclohexene (Sigma-Aldrich,  $\geq$  99.0%) was introduced by flowing He (5 mL/min, 99.999%, Airgas) through the bubbler at nominal atmospheric pressure at 25 °C (11.9 kPa). Additional He (20 mL/min) was added through a second mass flow controller (Brooks Instruments). The cyclohexene partial pressure was varied between 0.6 to 3 kPa by varying the rates of the two He flows while maintain a constant total He flow of 25 mL/min. Aqueous H<sub>2</sub>O<sub>2</sub> (30 wt. %) was diluted in acetonitrile (10 mL H<sub>2</sub>O<sub>2</sub> and 20 mL acetonitrile), and then 7 g of anhydrous magnesium sulfate was added to remove water, followed by decanting to yield a 4 M H<sub>2</sub>O<sub>2</sub> in acetonitrile solution.<sup>19</sup> This solution was loaded into a plastic syringe, bubbles were removed, and this solution was injected directly into the quartz tube reactor with a rate of 0.2 mL/h. The solution was diluted further with acetonitrile to vary its partial pressure (0.8 to 3 kPa), while maintain a constant injection rate 0.2 mL/h. Here, it was important that the tip of the FEP capillary tube was inside the inlet heating block zone, otherwise droplets would form and lead to system

instability (e.g. Figure S4) Concentration profiles of cyclohexene and products were collected up to 1000 mins time-on-stream (TOS). C6 products were separated by GC-FID (Agilent 7890, He carrier) with a HP-INNOWAX (50 m length, 0.2 mm diameter, 0.4  $\mu$ m film) column. Products detected and quantified were cyclohexene oxide (epoxide), trans-1,2-cyclohexane diol (diol), 2-cyclohexen-1-one (cyclohexenone), 2-cyclohexen-1-ol (cyclohexenol), and cyclohexanone (cyclohexanone). H<sub>2</sub>O, O<sub>2</sub>, and CO<sub>2</sub> were separated by a combination of HP-PLOT/Q (30 m length, 0.53 mm diameter, 40  $\mu$ m film) and HP-MOLESIEVE (15 m length, 0.53 mm diameter, 50  $\mu$ m film) and detected with a TCD in the same GC.

Product yields were normalized with respect to the cyclohexene feed, as per equation (2). Some experiments were carried out at high cyclohexene conversion to verify good carbon balance (> 90%) using CO<sub>2</sub> and the C<sub>6</sub> products listed above, but otherwise, kinetic studies were carried out in the differential conversion regime (< 10%) and thus it is more accurate to discuss product yields rather than reactant conversion. Product yields at near steady state (typically > 400 min TOS) were extrapolated linearly to t = 0 min to calculate turnover frequencies (TOF). The conclusions of this paper are not significantly changed if average rates at long TOS are used instead. H<sub>2</sub>O<sub>2</sub> conversions in the reactor cannot be directly measured; GC-TCD confirms that all H<sub>2</sub>O<sub>2</sub> fed is converted to H<sub>2</sub>O under all conditions, presumably due in part to decomposition in the stainless-steel transfer lines downstream of the reactor.

Product yield

$$=\frac{\sum mol_{product}}{mol_{reactant} + \sum mol_{product}}$$
(2)

Where the sum of products is given in equation (3).

$$\sum_{\text{mol}_{\text{product}}} = \text{mol}_{\text{epoxide}} + \text{mol}_{\text{diol}} + \text{mol}_{\text{enone}} + \text{mol}_{\text{anone}} + \frac{\text{mol}_{\text{CO}_2}}{6}$$
(3)

## RESULTS AND DISCUSSION

#### **Catalysts Synthesis.**

Table 1 summarizes the bulk properties of the catalysts synthesized in this study. All catalysts were synthesized to possess low surface density (i.e. a high dispersion of  $MO_x$ ), which leads to a high fraction of active Lewis acid sites for heterolytic  $H_2O_2$  activation, as shown in our

previous works.<sup>19-21</sup> In the case of M-NU-1000, we were able to achieve low surface density with high metal loading because of the spatial isolation of the grafting sites (the  $Zr_6$  nodes) afforded by the ~1 nm linkers. M-SiO<sub>2</sub> were calcined at 550 °C after grafting of metal precursors to generate MO<sub>x</sub> sites, while the grafting ligands used to prepare M-NU-1000 were hydrolyzed by ambient moisture because the organic linkers of NU-1000 do not permit high temperature calcination.

Catalyst	M loading [wt. %]	Surface density [M/nm²]	BET Surface area [m <sup>2</sup> /g <sub>catalyst</sub> ]
Ti-SiO <sub>2</sub> <sup>a</sup>	0.87	0.2	380
Nb-SiO <sub>2</sub> <sup>a</sup>	1.66	0.2	300
Ti-NU-1000 <sup>b</sup>	5.16	0.3	1930
Nb-NU-1000 <sup>b</sup>	9.55	0.3	1330

Table 1. Summary of catalyst properties

<sup>a</sup> Bare SiO<sub>2</sub> surface area 550 m<sup>2</sup>/g.

<sup>b</sup> Bare NU-1000 surface area 2160 m<sup>2</sup>/g.

#### Catalysis.

Vapor-phase cyclohexene epoxidation with  $H_2O_2$  was examined to study trends in reactivity and selectivity over M-SiO<sub>2</sub> and M-NU-1000. After addressing experimental complexities in delivering stable amounts of vaporized cyclohexene and  $H_2O_2$ , such as optimizing the temperature of the  $H_2O_2$  vaporization region and placement of the  $H_2O_2$  feed tube (discussed in experimental section), we can achieve stable yields (Figure 1) and cyclohexene concentration (Figure S5) profiles over long times-on-stream. All kinetic tests were performed in the differential conversion regime for cyclohexene, and the reaction was run in the absence of external transport limits (Figure S6). Blank reactor tests indicate that all oxidation reactions – the formation of  $C_6$  products and  $CO_2$  – require both  $H_2O_2$  and catalyst. We observe some epoxide hydrolysis to diol in the stainless-steel transfer lines downstream of the reactor, so we do not include rate laws for diol formation in the kinetic model.



**Figure 1**. Representative time-on-stream yield and C<sub>6</sub> product selectivity profiles of cyclohexene epoxidation with  $H_2O_2$  at 120 °C, cyclohexene 3 kPa,  $H_2O_2$  3 kPa over (a) Ti-SiO<sub>2</sub> and (b) Ti-NU-1000. ( $\circ$  total product yield, (green) epoxide, (orange) diol, (yellow) cyclohexanone, (blue) cyclohexenol, (gray) cyclohexenone) Dashed lines show how data are extrapolated back to t=0 min. Only selectivity to C<sub>6</sub> products are shown in (b) for clarity. See Figure 2 for representative selectivities including CO<sub>2</sub>.

Yield profiles of both types of catalysts follow the same general trend in that they decrease sharply over the first  $\sim 200$  min, then reach a relatively steady rate with constant selectivity among  $C_6$  species. After the initial period, the activity over Ti-SiO<sub>2</sub> or Nb-SiO<sub>2</sub> (Figure 1(a) and Figure S7(a)) is very stable, while the activity over Ti-NU-1000 or Nb-NU-1000 continues to decrease with time on stream without a change in selectivity, indicating a loss of accessibility to the active sites due to framework restructuring. In the following, rates are extrapolated back to zero time, but similar conclusions are reached using rates after a given time on stream. Cyclohexene conversion turnover frequencies vary by 20-fold, with Ti-SiO<sub>2</sub> ( $1.1 \times 10^{-1} \text{ mol}_{C6}$  $mol_{Ti}^{-1} min^{-1}$ ) being ten times faster than Ti-NU-1000 (1.1 × 10<sup>-2</sup> mol<sub>C6</sub> mol<sub>Ti</sub><sup>-1</sup> min<sup>-1</sup>), and Nb- $SiO_2$  (5.1 × 10<sup>-2</sup> mol<sub>C6</sub> mol<sub>Nb</sub><sup>-1</sup> min<sup>-1</sup>) being an order of magnitude faster than Nb-NU-1000 (5.9  $\times 10^{-3}$  mol<sub>C6</sub> mol<sub>Nb</sub><sup>-1</sup> min<sup>-1</sup>) at 120 °C with 3 kPa of both reactant and oxidant. In addition, there are significant differences in product selectivity between the two catalyst supports. The silica supported Ti and Nb catalysts (Figure 1(a) and Figure S7(a)) cleanly yield only epoxide and trans-cyclohexanediol, each at ~50% selectivity under all reaction conditions studied. Neither allylic oxidation C<sub>6</sub> products (e.g. cyclohexenol) nor CO<sub>2</sub> were detected at any temperature or reactant partial pressure studied with the M-SiO<sub>2</sub> catalysts. No cis-cyclohexanediol was

 detected, indicating that all diol was derived from hydrolysis of epoxide, rather than direct *cis*dihydroxylation.<sup>22</sup> Separately, oxidizing *cis*-3-hexene with vaporized H<sub>2</sub>O<sub>2</sub> over M-SiO<sub>2</sub> catalysts results in only *cis*-3,4-epoxyhexane, and the absence of isomerization products is consistent with epoxide formation by a concerted mechanism. In contrast, NU-1000 supported Ti and Nb (Figure 1(b) and Figure S7(b)) catalysts produce a variety of C<sub>6</sub> products including cyclohexenone, cyclohexenol, and cyclohexanone, in addition to epoxide and diol. Co-feeding experiments (Table S1) suggest that *trans*-cyclohexanediol is dehydrated to cyclohexanone over M-NU-1000 catalysts. Increasing either P<sub>H2O2</sub> or time on stream results in a decrease in cyclohexanone selectivity that is coupled with increasing CO<sub>2</sub> selectivity. It appears that there is a species on M-NU-1000 that begins as a dehydration site and evolves into a combustion site after extended exposure to H<sub>2</sub>O<sub>2</sub>. Zirconia-based mixed oxides frequently show this type of behavior.<sup>23-25</sup> With the exception of the transient formation of cyclohexanone, the selectivity to other C<sub>6</sub> products remains constant with time on stream for all catalysts.



Figure 2. Selectivity dependence on reaction temperatures over Ti-NU-1000 (cyclohexene 3 kPa, and H<sub>2</sub>O<sub>2</sub> 3 kPa) at 400 min TOS. (shaded) CO<sub>2</sub>/6, (blue) cyclohexenol, (gray) cyclohexenone, (green) epoxide, (orange) diol.

In addition to C<sub>6</sub> products, we observe CO<sub>2</sub> only over the M-NU-1000 catalysts. Figure 2 shows selectivity trends (Figure S8 for Nb-NU-1000) with respect to reaction temperature (110 – 130 °C). Data were not collected above 130 °C for M-NU-1000 due to instability in the reaction rate. Selectivity to CO<sub>2</sub> and the radical-derived products cyclohexenol and cyclohexenone increases from ~40 % to ~60 % with increasing temperatures. However, selectivity among the other C<sub>6</sub> products is largely independent of reaction temperatures over

the temperature range studied. The ratio between cyclohexenol and cyclohexenone is 1:1 regardless of reaction temperatures, consistent with a common origin through the decomposition of cyclohexenyl hydroperoxide.<sup>4-5, 26</sup> As in the case of M-SiO<sub>2</sub>, all detected diol is *trans*-cyclohexanediol, indicating that it is produced from epoxide hydrolysis.

We have previously investigated the same reaction over Nb-NU-1000 (indicated as Nb-SIM in the previous study), but in condensed phase batch reactors operating at 1M cyclohexene in acetonitrile and 65 °C.<sup>19</sup> In the previous study, the product selectivity over Nb-NU-1000 was consistent with 57-72 % pathway selectivity for heterolytic activation of  $H_2O_2$  leading directly to epoxide + diol. Over Nb-NU-1000 in the vapor phase, if we include cyclohexanone and the diol both as epoxide-derived products, the pathway selectivity is 53-63%, depending on TOS, and remarkably similar to the results in the condensed phase. Individual selectivities to the various C<sub>6</sub> products are also similar in the liquid and vapor phases, indicating that the higher temperature and the presence or absence of solvent does not change the *relative* barriers to formation of the various C<sub>6</sub> products, and that the barriers to heterolytic vs homolytic pathways must be similar to one another over Nb-NU-1000. The similarity between liquid and gas-phase operation for Nb-NU-1000 is also consistent with the strong adsorption of cyclohexene in this framework, corresponding to a relatively liquid-like 0.8 cyclohexene molecules/nm<sup>2</sup> at 3 kPa (Figure 3).



**Figure 3**. Cyclohexene vapor adsorption isotherms at 110 °C on bare supports: number of cyclohexene molecule per area of supports basis ( $\circ$ : SiO<sub>2</sub>,  $\bullet$ : NU-1000).

Gas phase reaction of  $H_2O_2$  and cyclohexene over M-SiO<sub>2</sub> produces only epoxide and diol. The absence of any detectable radical-derived products (cyclohexenol and cyclohexenone)

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contrasts with the results in 1M cyclohexene in acetonitrile at 65 °C, where radical pathways account for 48 and 16% of the products for Ti-SiO<sub>2</sub> and Nb-SiO<sub>2</sub>, respectively,<sup>20</sup> but are comparable to selectivities observed by other studies at more dilute conditions over M-beta (< 50 mM cyclohexene in acetonitrile) where epoxide is the only product.<sup>15</sup> Higher selectivity toward direct pathways (to epoxide and diol) can be attributed to the (1) low reactant partial pressures and attendant low C<sub>6</sub> surface concentrations over SiO<sub>2</sub> (Figure 3), making it less likely that homolytic decomposition of the M-OOH will react with a C<sub>6</sub> species and (2) intrinsically more favorable direct vs. radical pathways at the higher reaction temperatures of the vapor-phase experiments. In condensed phase experiments, homolytic decomposition of H<sub>2</sub>O<sub>2</sub> has been seen to have a lower or comparable barrier to epoxidation over Ti-SiO<sub>2</sub> catalysts,<sup>17</sup> from which one would expect selectivity to improve with temperature.



Figure 4. Reaction orders at 120 °C with respect to (a) cyclohexene (partial pressure: 0.6 to 3 kPa) with fixed H<sub>2</sub>O<sub>2</sub> partial pressure at 3 kPa, and (b) H<sub>2</sub>O<sub>2</sub> (partial pressure: 0.8 to 3 kPa) with fixed cyclohexene partial pressure at 3 kPa (○: Ti-SiO<sub>2</sub>, Δ: Nb-SiO<sub>2</sub>, •: Ti-NU-1000, ▲: Nb-NU-1000). All C<sub>6</sub> products and CO<sub>2</sub> are considered when calculating TOF.

Figure 4 shows rates used to determine reaction orders of  $M-SiO_2$  and M-NU-1000 with respect to cyclohexene and  $H_2O_2$ . Orders of reaction with respect to cyclohexene are close to unity over all catalysts (Ti-SiO<sub>2</sub> 1.1, Nb-SiO<sub>2</sub> 1.0, Ti-NU-1000 0.8, Nb-NU-1000 1.3), and orders with respect to  $H_2O_2$  are near zero for all catalysts. Reaction orders for individual products generally follow the same pattern (Figure 5). The zeroth order dependence on  $H_2O_2$  allows us to be confident of our conclusions about reaction kinetics even without necessarily





Figure 5. The dependence of product formation rates on reactant and oxidant partial pressures over Ti-NU-1000 at 120 °C and 400 min TOS. Dependence on (a) cyclohexene partial pressures with H<sub>2</sub>O<sub>2</sub> 3 kPa and (b) H<sub>2</sub>O<sub>2</sub> partial pressures with cyclohexene 3 kPa (+CO<sub>2</sub>/6, Δepoxide and diol, ×cyclohexanone, ♦cyclohexenol, □cyclohexenone).

Figure 5(a) indicates that the formation rate of all C<sub>6</sub> products and CO<sub>2</sub> linearly depend on partial pressure of cyclohexene. Note that only CO<sub>2</sub> has a non-zero intercept, presumably arising from a small contribution from oxidation of acetonitrile (the carrier of the H<sub>2</sub>O<sub>2</sub>). Varying H<sub>2</sub>O<sub>2</sub> partial pressure (Figure 5(b)), has a slightly more complex impact on the reaction orders of product formation. Within the uncertainties for these slow catalysts, the rates to epoxide + diol, cyclohexenol and cyclohexenone are relatively stable with P<sub>H2O2</sub>. In contrast, cyclohexanone rates decrease with P<sub>H2O2</sub> while CO<sub>2</sub> rates increase with P<sub>H2O2</sub> at a given TOS. Consulting Figures 1(b) or S7(b), we see that this behavior parallels the TOS behavior: cyclohexanone decreased with TOS and CO<sub>2</sub> rates increased with TOS for a given partial pressure, while the other species were stable. Nb-NU-1000 (Figure S9) has similar reaction orders to those of Ti-NU-1000, but even smaller selectivities to cyclohexenol and cyclohexenone. This is consistent with condensed phase trends for Ti-SiO<sub>2</sub> vs. Nb-SiO<sub>2</sub>.<sup>20</sup>



Figure 6. Arrhenius plot of all catalysts. Cyclohexene 3 kPa, H<sub>2</sub>O<sub>2</sub> 3 kPa, and 110-150 °C.
(○: Ti-SiO<sub>2</sub>, Δ: Nb-SiO<sub>2</sub>, •: Ti-NU-1000, ▲: Nb-NU-1000). All C<sub>6</sub> products and CO<sub>2</sub> are considered when calculating TOF.

Figure 6 gives an Arrhenius plot of all catalysts collected at 3 kPa partial pressure of both cyclohexene and  $H_2O_2$ , corresponding to the 1<sup>st</sup> order regime in cyclohexene and 0<sup>th</sup> order in  $H_2O_2$  for all catalysts. All four catalysts have similar slopes, corresponding to apparent activation barriers of 26 ± 4 kJ mol<sup>-1</sup> (Table 2), activation enthalpies (23 ± 4 kJ mol<sup>-1</sup>) and entropies (-130 ± 20 J mol<sup>-1</sup> K<sup>-1</sup>). Only the data between 110-130 °C were used for M-NU-1000, because reaction rates become unstable at higher temperatures. Overall, the significant differences in rates absent significant differences in activation enthalpy or entropy, suggests that these materials primarily differ in the fraction of each MO<sub>x</sub> that are kinetically relevant under vapor phase conditions.

Table 2. Apparent activation barriers, activation enthalpies and entropies of catalysts

Catalyst	E <sub>a</sub> [kJ mol <sup>-1</sup> ]	ΔH <sup>‡</sup> [kJ mol <sup>-1</sup> ] <sup>a</sup>	ΔS <sup>‡</sup> [J mol <sup>-1</sup> K <sup>-1</sup> ] <sup>a</sup>
Ti-SiO <sub>2</sub>	30	27	-110
Nb-SiO <sub>2</sub>	27	24	-130
Ti-NU-1000	22	19	-150
Nb-NU-1000	29	26	-140

<sup>a</sup> Reported values are calculated using Eyring equation (Figure S10) and steady TOF.

To describe the observed behavior, we propose an overall Ely-Rideal type reaction mechanism shown in Scheme 2 for Ti-SiO<sub>2</sub> (left) and Nb-SiO<sub>2</sub> (right), which follows the extensively supported mechanism of Bregante et. al.<sup>15, 17</sup>



Scheme 2. Proposed reaction networks of vapor-phase cyclohexene epoxidation in the steady conversion regime with H<sub>2</sub>O<sub>2</sub> over Ti-SiO<sub>2</sub> or Ti-NU-1000 (left) and Nb-SiO<sub>2</sub> or Nb-NU-1000 (right).

Epoxide hydrolysis is not included in the mechanism, as it may occur in the reactor or downstream of it. The transient formation of cyclohexanone over M-NU-1000 is also not included. Olefin binding to the catalyst center is assumed to be weak and not along the reaction trajectory, and thus not shown. However, its concentration in the pore is expected to be strongly dependent on the support. Reaction in polar solvent may also include bound solvent in resting and transition states, which are also not shown. Finally, the nature of the H<sub>2</sub>O<sub>2</sub> activation in step  $k_3$  may vary depending on the reaction environment (solvent vs. vapor phase).

For M-SiO<sub>2</sub>, radical pathways lead only to the consumption of  $H_2O_2$ , since no CO<sub>2</sub>, cyclohexenol or cyclohexenone are observed. For M-NU-1000, the radical pathways lead to these three products. As shown in Scheme 3, the weak allylic C-H on cyclohexene is expected to be abstracted first, followed by reaction with O<sub>2</sub>. Once cyclohexenyl peroxy species form

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(radical or the neutral hydroperoxide), they can undergo bimolecular pathways to cyclohexenol and cyclohexenone. The  $CO_2$  observed also is presumably the result of serial radical reactions that begin with the formation of cyclohexenyl radicals.



Scheme 3. Proposed sequence of radical reactions

The remainder of this discussion uses only the catalytic cycle in Scheme 2 and M-SiO<sub>2</sub> catalysts. This mechanism presents quasi-equilibrated adsorption/desorption steps of H<sub>2</sub>O<sub>2</sub> (K<sub>1</sub>), epoxide (K<sub>4</sub>), and water (K<sub>6</sub>) on MOx sites. Following the work of Bregante et. al.,<sup>15, 17</sup> which observed the same reaction orders, we assume that the M-OOH intermediate is formed upon irreversible activation of H<sub>2</sub>O<sub>2</sub> ( $k_2$ ) and that it is the most abundant surface intermediate (MASI). For the purposes of this discussion, the exact structure of the M-OOH intermediate is not critical. This active intermediate can then form epoxides via reaction with cyclohexene ( $k_3$ ) or can undergo homolytic decomposition ( $k_5$ ), which contributes only to H<sub>2</sub>O<sub>2</sub> decomposition over M-SiO<sub>2</sub>. Here, the rate of epoxide and diol formation ( $r_{epox}$ ) is defined as per equation (4):

$$r_{epox} = k_3 [\text{M} - \text{OOH}] [C_6 \text{H}_{10}^{\#}]$$
 (4)

In the limit that [M-OOH] = [M], the turnover frequency (TOF =  $r_{epox}/M$ ) is simply

$$TOF = k_3 [C_6 H_{10}^{\#}]$$
(5)

The notation  $[C_6H_{10}^{\#}]$  denotes the intrapore concentration of  $C_6H_{10}$ . If we let  $[C_6H_{10}^{\#}] = K_{ads}[C_6H_{10}]$  for adsorption in the Henry's law regime, then overall TOF is defined by equation (6):

$$TOF = k_3 K_{ads} [C_6 H_{10}] = k_{app} [C_6 H_{10}]$$
(6)

This simple rate expression is in accordance with the observed dependences of  $H_2O_2$  and cyclohexene. Finally, we define the measured activation enthalpy as a combination of terms intrinsic to oxidant activation and O transfer, and a term for adsorption of the olefin:

$$\Delta H_{app}^{\vec{I}} = \Delta H_{int}^{\vec{I}} + \Delta H_{ads} \tag{7}$$

where  $\Delta H^{\ddagger}_{int}$  is the intrinsic reaction barrier for O transfer (step 3) and  $\Delta H_{ads}$  is enthalpy change associated with adsorption of cyclohexene into the pores near the active site.



Scheme 4. Proposed Born-Haber thermochemical cycle of cyclohexene epoxidation in condensed phase and vapor phase. The vertical heights are approximately to scale. (Unit of numbers in scheme is kJ/mol.)

In order to quantitatively compare the cyclohexene oxidation kinetics in the vapor and condensed phases, a Born-Harber thermochemcial cycle of cyclohexene epoxidation is constructed (Scheme 4). In both the liquid and gas phases, apparent activation energies are referenced to fluid-phase cyclohexene, and the influence of cyclohexene adsorption in the pores near the active site can be removed by calculating an intrinsic reaction enthalpy ( $\Delta H^{\ddagger}_{int}$ ) that is given by equation (7). Strong adsorption can make for an apparently smaller enthalpy of activation, and vice versa.  $\Delta H_{ads}$  is assumed to be dependent on the pore structure and reaction environment, but not the active site identity. The low-coverage  $\Delta H_{ads}$  of cyclohexene vapor on SiO<sub>2</sub> was determined to be -45 kJ/mol (Figure S11 and Table S2), giving a  $\Delta H^{\ddagger}_{int}$  in the vapor-phase for Ti-SiO<sub>2</sub> and Nb-SiO<sub>2</sub> of 72 kJ/mol and 69 kJ/mol. The  $\Delta H_{ads}$  of cyclohexene from acetonitrile solution into zeolite  $\beta$  is only -5 kJ/mol.<sup>27</sup> Combined with published apparent enthalpies of activation for cyclohexene epoxidation,<sup>15</sup> this results in a  $\Delta H^{\ddagger}_{int}$  for Ti- $\beta$  and Nb- $\beta$  of 48 kJ/mol and 77 kJ/mol, respectively, for cyclohexene oxidation in liquid acetonitrile.

Scheme 4 shows the measured  $\Delta H^{\ddagger}_{app}$  values and the values of  $\Delta H^{\ddagger}_{int}$  backed out from equation (7). All of the experiments in both the vapor- and condensed phases were carried out in the same kinetic regime of first-order olefin and zero-order H<sub>2</sub>O<sub>2</sub>, allowing the rate-limiting

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O-transfer step to be probed directly. Therefore, the intrinsic activation enthalpies can be compared between the vapor- and condensed-phase experiments. For Nb-SiO<sub>2</sub>, the intrinsic activation enthalpies are similar in the two phases, requiring that the precursor state and the transition state are stabilized similarly by solvent ( $\Delta H_{solv,cat} \sim \Delta H_{solv,TS}$  in Scheme 4). On the other hand, the Ti-SiO<sub>2</sub> transition state in the condensed phase ( $\Delta H_{int,solv}^{\ddagger} = 48$  kJ/mol) appears to be stabilized by 24 kJ/mol relative to the same transition state in the vapor phase ( $\Delta H_{int,vap}^{\ddagger} = 72$  kJ/mol), which results in larger  $\Delta H_{solv,TS}$  than  $\Delta H_{solv,cat}$ . No charge develops in the transition state, so significant stabilization by a mean field solvation effect is not expected.<sup>28</sup> Instead, we assign it to the role of liquid solvent in helping shuttle protons during the O transfer step and greatly decreasing the barrier. Equivalently, the transition state is more stabilized than the precursor state because of this direct involvement of the solvent.

In liquid phase reactions, the polar acetonitrile solvent and the water co-fed with  $H_2O_2$  provide ample opportunities to H-bond to the activated  $H_2O_2$  species. Prior calculations have shown that coordinated solvent, water, or silanol (for in-framework, microporous materials) substantially lower the barrier for epoxidation over Ti-based catalysts, via structures as shown in Figure 7(a).<sup>29-31</sup> At the low partial pressures of the vapor phase experiments, these structures presumably cannot form (Figure 7(b)), and the mechanism is forced through a higher barrier pathway. Engineering new catalysts to possess an adjacent H-bonding motif may help lower barriers in the vapor phase. In contrast, Nb-SiO<sub>2</sub> does not appear to be in need of an external H-shuttle, due to its additional Nb-OH bond (Figure 7(c)). Therefore, the liquid and gas-phase barriers are similar. Overall, the comparisons between the liquid- and gas-phase operation help support a decades-old computational prediction about the mechanism of epoxidation by Ti-SiO<sub>2</sub> and suggest new avenues of mechanistic investigation and materials design.



**Figure 7.** Proposed active sites and calculated  $\Delta H^{\ddagger}_{int}$  for (a) Ti-SiO<sub>2</sub> in solvent (S), (b) Ti-SiO<sub>2</sub> in the vapor phase, and (c) Nb-SiO<sub>2</sub> for either phase.

## CONCLUSIONS

A unique reactor has been built to study vapor phase  $H_2O_2$  activation reactions, such as cyclohexene epoxidation over solid Lewis acid catalysts. M-SiO<sub>2</sub> catalysts cleanly give only epoxide and diol products, in contrast to many reports of allylic oxidation in the condensed phase. In contrast, the M-NU-1000 catalysts show extensive allylic oxidation and  $CO_2$ formation in the vapor-phase. The strong adsorption of reactants into MOFs is frequently an advantage, but here, the strong adsorption of cyclohexene may be a liability.

The reactor design allows for high fidelity kinetics experiments to be carried out with vaporized  $H_2O_2$ . Running all catalysts under conditions where rates were first order with respect to cyclohexene and zeroth order with respect to  $H_2O_2$  allows us to directly compare activation energies for the rate-limiting O-transfer step. Activation energies did not differ significantly between the different catalysts in the vapor phase, even though apparent TOFs varied by more than 20 times, suggesting that the fraction of kinetically relevant  $MO_x$  active sites varies between the samples. Secondly, we compare intrinsic activation enthalpies between the condensed and vapor-phases over M-SiO<sub>2</sub>. Nb-SiO<sub>2</sub> behaves very similarly in the two phases, while Ti-SiO<sub>2</sub> has a much lower activation enthalpy in the condensed phase. These experimental findings provide evidence for a long postulated direct role for solvent in  $H_2O_2$  activation in the absence of a liquid solvent and residual species like water will be broadly useful in understanding the role of solvent in many heterogeneously-catalyzed reactions.

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given approval to the final version of the manuscript.

#### Notes

The authors declare no competing financial interest.

## ■ ASSOCIATED CONTENT

#### **Supporting Information**

Additional characterization data and kinetic data (PDF) are available in the Supporting Information, free of charge on the ACS Publications website at DOI: XXX.

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