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Relevance of Protons in Heterolytic Activation of H₂O₂ over Nb(V). Insights from Model Studies on Nb-substituted Polyoxometalates

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ABSTRACT: Nb-monosubstituted Lindqvist-type polyoxometalates (POM), $(Bu_4N)_4[(NbW_5O_{18})_2O]$ (1)and $(Bu_4N)_3[Nb(O)W_5O_{18}]$ (2), catalyze epoxidation of alkenes with hydrogen peroxide and mimic the catalytic performance of heterogeneous Nb-silicate catalysts. Dimer 1 is more active than monomer 2, but the catalytic activity of the latter increases in the presence of acid. Kinetic and spectroscopic studies suggest a mechanism that involves generation of monomer (Bu₄N)₂[Nb(OH)W₅O₁₈] (3), interaction of 3 with H_2O_2 leading to a protonated peroxo niobium species, $(Bu_4N)_2[HNb(O_2)W_5O_{18}]$ (4), followed by oxygen transfer to a C=C bond in alkene. The previously unknown peroxo complex 4 has been isolated and characterized by elemental analysis, UV-vis, FT-IR, Raman, ⁹³Nb, ¹⁷O and ¹⁸³W NMR spectroscopy, cyclic voltammetry, and potentiometric titration. The physicochemical techniques support a monomeric Lindqvist structure of 4 bearing one peroxo ligand attached to Nb(V) in a η^2 coordination mode. While the unprotonated peroxo complex $(Bu_4N)_3[Nb(O_2)W_5O_{18}]$ (5) is inert toward alkenes under stoichiometric conditions, 4 readily reacts with cyclohexene to afford epoxide and 1,2-trans-cyclohexane diol, which proves the key role of protons for heterolytic activation of H_2O_2 over Nb(V). The IR, Raman, UV-vis, and ¹⁷O NMR spectroscopic studies along with DFT calculations showed that the activating proton in 4 is predominantly located at a Nb-O-W bridging oxygen. However, DFT calculations revealed that the protonated peroxo species 'HNb(O_2)' is present in equilibrium with a hydroperoxo species 'Nb(η^2 -OOH)', which has a lower activation barrier for the oxygen transfer to cyclohexene and is, therefore, the main epoxidizing species. The calculations indicate that protonation is crucial to generate the active species and to increase POM electrophilicity. KEYWORDS: epoxidation, hydrogen peroxide, niobium, peroxo complex, polyoxometalate, Lindqvist structure, DFT

INTRODUCTION

On the way to sustainable production of valuable chemicals, a challenging goal is the development of economic and ecologically sound oxidation processes which employ green, cheap and readily available oxidizing agents.¹⁻⁴ Along with molecular oxygen, hydrogen peroxide is the most environmentally friendly oxidant since it is atom-efficient, easy to handle and safe (<60 wt% in water and <20% wt% in organic solvent) and produces water as the sole byproduct.⁵⁻⁷ Likewise dioxygen, H₂O₂ itself is inert toward most organic substrates and its use in selective oxidation processes requires employment of catalysts. Redox transition metals readily perform homolytic activation of H_2O_2 , leading to the formation of radical species and Fenton-type chemistry.^{8,9} However, in this case, unproductive decomposition of H₂O₂ with evolution of molecular oxygen competes with the target oxygenation reaction, leading to very low oxidant utilization efficiency. Moreover, the formation of radicals (HO \cdot , HO₂ \cdot) is detrimental for selectivity of oxidation processes.

The selective catalytic epoxidation of alkenes with hydrogen peroxide is of both academic and industrial interest.¹⁰⁻¹³ To accomplish oxygen atom transfer from H₂O₂ to alkenes and to avoid the formation of intermediate radical species, heterolytic activation of the oxidant is required. Several highly effective homogeneous catalysts, including specific complexes of

W(VI),^{11,14-17} Re(VII),¹⁸⁻²⁰ Ti(IV),²¹⁻²³ Mn(II),^{12,24-26} and Fe(II/III)^{12,20,27,28}, have been reported for epoxidation of a wide range of alkenes. Among heterogeneous catalysts, the microporous titanium–silicalite TS–1 developed by the ENI group at the beginning of the 1980s remains a unique material that enables efficient transformations of linear olefins into epoxides using dilute H_2O_2 .^{29,30} The development of mesoporous Ti-silicates in the 2000s was targeted at oxidative transformations of large organic molecules; however, the hydrophilic nature of these materials favors adsorption and unproductive decomposition of hydrogen peroxide, which deteriorates selectivity of epoxidation, with the exception of some specific cases.^{31,32}

In recent years, niobium-containing materials have attracted growing interest as selective oxidation catalysts. In particular, mesoporous Nb-silicates turned out to be active and recyclable catalysts for alkene epoxidation using dilute H_2O_2 .³³⁻⁴² Several research groups noticed that Nb,Si-catalysts reveal superior selectivity in H_2O_2 -based epoxidation relative to their Ti counterparts.^{37,38,41,42} The reasons for this are not completely clear. While high levels of understanding mechanisms of alkene epoxidation have been reached for W, Re and Ti,^{30,43-45} as well as biomimetic Fe and Mn catalysts,^{24-27,43,46,47} epoxidation catalyzed by Nb is still poorly understood. A few attempts at rationalizing the catalytic behavior of Nb(V) have been reported.^{42,48-51} Nevertheless, the nature of the active epoxidizing

species still remains under debate. Our recent kinetic and spectroscopic studies on mesoporous Nb-silicates implicated a protonated, presumably hydroperoxo niobium species Nb– OOH as the active form responsible for epoxidation of electron-rich C=C double bonds in alkenes.^{42,52} On the other hand, Bregante et al. proposed that a superoxo Nb species is responsible for alkene epoxidation over Nb-substituted Betazeolite.^{50,51} More recently, they discarded superoxo Nb and suggested that, in sharp contrast to Ti single-site catalysts for which hydroperoxo species TiOOH has become a widely accepted concept,^{30,53,54} simply Nb(η^2 –O₂) surface intermediates epoxidize alkenes on Nb-based catalysts.⁵⁵ To shed more light on the nature of active Nb peroxo species, detailed experimental and theoretical model studies using soluble molecular compounds are needed.

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Anionic metal-oxygen clusters or polyoxometalates (POMs), owing to their metal oxide like structure, thermodynamic stability to oxidation and hydrolysis as well as tunable acidity and redox properties, have found applications in a wide range of research areas, covering catalysis, molecular magnetism, electronics and medicine.⁵⁶⁻⁶⁶ The evident structural analogy between POMs and metal oxide surfaces makes possible considering POMs as discrete, soluble fragments of extended metal oxide lattices, which can be characterized and investigated at the atomic/molecular level.^{67–72} Since lacunary polyanion frameworks can function as totally inorganic, hydrolytically and oxidation-resistant multidentate ligands toward a heterometal M, transition-metal mono-substituted POMs (M-POMs) meet the criteria of an important class of single-site catalysts⁷³ and can serve as tractable molecular models for studying mechanisms of oxidation catalysis.74-80 Earlier, some of us demonstrated that Ti-substituted POMs mimic well the catalytic performance of mesoporous titanium-silicate catalysts in a range of selective oxidations with H₂O₂.⁷⁶⁻⁷⁸ Alkene epoxidation mediated by two different POMs, the Timonosubstituted Keggin type POM [PTi(OH)W11O39]4- and the sandwich type POM [Ti₂(OH)₂As₂W₁₉O₆₇(H₂O)]⁸⁻, containing well-defined 6- and 5-coordinated titanium atoms, respectively, have been studied in detail using experimental and computational techniques.^{45,78,81} The higher selectivity of the sandwich anion was attributed to the larger energy cost of homolytic O-O bond breaking in the hydroperoxo intermediate 'TiOOH'.45 It was also demonstrated that electrophilicity and reactivity of the peroxo titanium derivative of the Keggin Ti-POM can be increased through polyanion protonation.⁸

Although a large number of Nb-containing POMs have been reported in the literature,⁸⁴ in particular in relation to their antitumor and antiviral activity,^{84,85} potential of Nb-POMs in catalysis is much less explored compared to Ti-POMs. Among them, very few works were devoted to oxidation catalysis.⁸⁶⁻ Nb-trisubstituted POMs, (Bu₄N)₅H₂[(NbO₂)₃ SiW₉O₃₇]⁸⁶ and (Bu₄N)₄H₂[(NbO₂)₃PW₉O₃₇],⁸⁷ could accomplish epoxidation of unsaturated allylic alcohols to the corresponding diols with aqueous H₂O₂, but they were inert toward unfunctionalized alkenes.⁸⁶ On the basis of kinetic and NMR data, the authors concluded that the Nb-POMs function primarily as catalyst precursors that produce active W, Nb or polyoxoanion fragments.^{86,87} More recently, Mizuno and coworkers reported synthesis and catalytic properties of a di-Nb-substituted silicodecatungstate, $(Bu_4N)_5[\gamma$ -HSiW₁₀O₃₈Nb₂(η^2 -O₂)₂].⁸⁸ This POM was able to catalyze oxidation of some organic substrates (cyclooctene, thioanisole, 1-phenylethanol, and allyl

alcohol) with H_2O_2 in the presence of 2 equiv. of protons source.



Figure 1. 3D representation for several monosubstituted Nbtungtates of the Lindqvist structure.

In the present work, we first explored the catalytic performance of Nb-monosubstituted Lindqvist tungstates, i.e. μ -oxo dimer $(Bu_4N)_4[(NbW_5O_{18})_2O]$ ((NbW_5)₂O, 1) and monomer $(Bu_4N)_3[Nb(O)W_5O_{18}]$ (Nb(O)W₅, 2) in alkene epoxidation with hydrogen peroxide. Hydrolysis of dimer 1 was anticipated to produce a monomer, $(Bu_4N)_2[Nb(OH)W_5O_{18}]$ (Nb(OH)W₅, **3**) with terminal Nb–OH bond. Figure 1 shows the 3D molecular structures of anions 1, 2 and 3. Given that both Nb=O and Nb-OH surface groups are present in Nbsilicates and zeolites⁸⁹⁻⁹¹ and both may potentially lead to an active peroxo niobium species,^{42,49,52,92,93} it was interesting to compare their reactivity towards H₂O₂ using well-defined molecular compounds. To elucidate the role of protons in the activation of the peroxo niobium group, we first synthesized a niobium complex, protonated peroxo $(Bu_4N)_2[HNb(O_2)W_5O_{18}]$ (HNb(O₂)W₅, 4), and fully characterized it by elemental analysis, potentiometric titration, cyclic voltammetry, UV-vis, FT-IR, Raman, and ¹⁸³W, ⁹³Nb, and ¹⁷O NMR spectroscopy. The structure and reactivity of 4 have been investigated by experimental and computational techniques in comparison with the unprotonated peroxo complex $(Bu_4N)_3[Nb(O_2)W_5O_{18}]$ (Nb(O₂)W₅, 5).

EXPERIMENTAL

Materials. Acetonitrile (Panreac, HPLC grade) was dried and stored over activated 3Å molecular sieves. Cyclohexene and cyclooctene were purchased from Sigma-Aldrich and purified prior to use by passing through a column filled with neutral alumina to remove traces of possible oxidation products. All the other compounds were the best available reagent grade and used without further purification. A solution of 77% H₂O₂ was obtained by concentration of a commercial 30% aqueous solution in vacuum. The concentration of hydrogen peroxide was determined iodometrically prior to use. Semiquantitative Quantofix peroxide test sticks were used for estimation of the amount of H₂O₂ at the end of catalytic reactions. Tetra-n-butylammonium hydroxide (TBAOH) (0.39 M in water) was titrated with HCl (0.1 M) prior to use. All the other compounds were the best available reagent grade and were used without further purification.

Synthesis and Characterization of POMs

 $Na_7HNb_6O_{19}\cdot xH_2O$ was prepared according to the known procedure.⁹⁴ Nb₂O₅ (25.5 g) was fused with 31 g of NaOH

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(1:8 molar ratio) in a nickel crucible at 600 °C for 5 h. The reaction product was dissolved in water (1.5 L) under heating (90 °C). The resulting solution was slowly evaporated to 200 mL at ambient temperature and the precipitate was washed with ethanol and recrystallized from water. The white product was washed with ethanol and air-dried overnight. The recrystallization yielded an analytical sample with 90% yield. FTIR (KBr, 1200–400 cm⁻¹): 860, 772, 677, 534.

 $(Bu_4N)_3[Nb(O_2)W_5O_{18}]$ (Nb(O₂)W₅, 5). The synthesis of ref.95 peroxo complex 5 was adapted from Na7HNb6O19.15H2O (3.55 g, 2.7 mmol) was dissolved in 140 mL of water (20 °C) and 5 mL of 30% aqueous H₂O₂. The resulting turbid solution was stirred overnight, then heated to 50 °C followed by the addition of 20 g (60.6 mmol) of Na₂WO₄·2H₂O in 50 mL H₂O and 15% HNO₃ (slowly) to adjust the pH at 2.3. After 1 h of stirring at 100 °C, a turbid yellow solution was centrifuged to remove precipitate of unreacted peroxoniobate. Then 12 g (37 mmol) of TBABr was added to the clear solution to afford a yellow precipitate which was collected by suction filtration, washed with 100 mL of water, dried at 100 °C, and purified by reprecipitation with water from CH₃CN. The resulting yellow solid (13.3 g) was dissolved in 100 mL of dichloroethane, centrifugated to remove insoluble impurities, evaporated in air, and then reprecipitated with the aqueous solution of H₂O₂ (2 mL of 30% H₂O₂ in 160 mL H₂O) from CH₃CN (80 mL). The resulting yellowish solid (11.2 g, yield 44% on W) was dried in air at 30 °C overnight and at 90 °C for 1 h. The presence of one peroxo group per molecule of 5 was confirmed by titration with triphenylphosphine (PPh₃) followed by monitoring with ³¹P NMR.⁸⁷ Anal. calcd (%) for C₄₈H₁₀₈N₃NbW₅O₂₀: C, 27.99; H, 5.29; N, 2.04; O, 15.54; Nb, 4.51; W, 44.63. Found: C, 27.71; H, 5.40; N, 1.96; O, 14.34; Nb, 4.16; W, 44.60. IR (KBr 1000–400 cm⁻¹): 980 (w, sh), 960 (s,W–Ot), 885 (w, TBA), 857 (sh), 806 (vs), 735 (sh, TBA), 639 (m), 602 (m), 586 (w), 567 (w), 546 (w), 442 (w), 428 (s). ¹⁸³W NMR (ppm, in CH₃CN): 62 $(4W_{eq})$, 101 $(1W_{ax})$. ⁹³Nb NMR (ppm, in CH₃CN): -1045. ¹⁷O NMR (ppm, in CH₃CN): 734 (W=O), 725 (NbO₂), 460 (NbOW), 396 (WOW), 390 (WOW), -72 (µO).

 $(Bu_4N)_3[Nb(O)W_5O_{18}]$ (Nb(O)W₅, **2**). Monomeric Nbsubstituted tungstate 2 was synthesized by reduction of Nb(O₂)W₅ with PPh₃. To a solution of 5 (3.8 g, 1.8 mmol) in 20 mL CH₃CN, PPh₃ (0.56 g, 2.1 mmol) dissolved in 10 mL of CH₃CN was added, and the reaction mixture was stored for 1 h. A white solid was precipitated by a two-fold excess of water, isolated by filtration, washed with ethanol and dried in air at 30 °C. Yield 83%. Anal. calcd (%) for C₄₈H₁₀₈N₃NbW₅O₁₉: C, 28.21; H, 5.33; N, 2.06; O, 14.88; Nb, 4.55; W, 44.98. Found: C, 28.06; H, 6.06; N, 2.12; O, 14.98; Nb, 4.34; W, 45.0. IR (KBr 1000–400 cm⁻¹): 977(w, sh), 957 (s, W-Ot), 915 (m, Nb-Ot), 883 (w, TBA), 804 (vs), 735 (sh, TBA), 589 (m), 572 (m). ¹⁸³W NMR (ppm, in CH₃CN): 71 $(4W_{eq})$, 27 $(1W_{ax})$. ⁹³Nb NMR (ppm, in CH₃CN): -899. ¹⁷O NMR (ppm, in CH₃CN): 732 (W=O), 730 (sh, W=O), 455 (NbOW), 392 (WOW), 390 (sh, WOW), -68 (µO).

 $(Bu_4N)_4[(NbW_5O_{18})_2O]$ ((NbW_5)₂O), **1**). The synthesis of dimer **1** was adapted from ref.⁹⁶ Acetylchloride (0.11 mL, 1.5 mmol) was added to a solution of Nb(O)W₅ (3.0 g, 1.5 mmol) in 20 mL CH₃CN. The reaction mixture was stirred for 15 min at room temperature (20 °C), and the resulting white precipitate was isolated by filtration and washed with 50 mL of ether

to give 1.8 g of product in 70% yield. Anal. calcd (%) for $C_{64}H_{144}N_4Nb_2W_{10}O_{37}$: C, 21.44; H, 4.05; N, 1.56; O, 16.51; Nb, 5.18; W, 51.26. Found: C, 21.64; H, 4.07; N, 1.69; O, 16.37; Nb, 5.13; W, 50.2. IR (KBr, 1000-400 cm⁻¹): 994 (w, sh), 974 (s), 877 (m), 835 (w, sh), 812 (s), 733 (w, sh), 720 (m, sh), 695 (s, NbONb), 588 (m), 547 (m), 447 (s). ⁹³Nb NMR (ppm, in CH₃CN): –950 (broad).

(Bu₄N)₂[HNb(O₂)W₅O₁₈] (HNb(O₂)W₅, **4**). Protonated peroxo complex **4** was synthesized by the addition of 30% H₂O₂ (0.2 mL, 2.3 mmol) to a suspension of (NbW₅)₂O (2.8 g, 0.7 mmol) in 20 mL CH₃CN. The yellow solution was stored for 30 min at room temperature and diluted with 120 mL of ether. The resulting yellowish solid (2.7 g, ca. 95% yield) was isolated by decantation and dried in air at room temperature. Anal. calcd (%) for C₃₂H₇₃N₂NbW₅O₂₀: C, 21.14; H, 4.05; N, 1.54; O, 17.60; Nb, 5.11; W, 50.57. Found: C, 21.22; H, 3.51; N, 1.68; O, 17.37; Nb, 4.96; W, 48.4. IR (KBr, 1000–400 cm⁻¹): 984 (w, sh), 973 (vs), 883 (w, TBA), 870 (w), 848 (m), 816 (m), 770 (m), 739 (w, TBA), 621 (w), 595 (m), 567 (w), 541 (w), 455 (m). ⁹³Nb NMR (ppm, in CH₃CN): -1015. ¹⁷O NMR (ppm, in CH₃CN): 754 (W=O), 742 (NbO₂), 414 (NbOW), 409 (WOW), 402 (WOW), and -63 (µO).

 $(Bu_4N)_2[W_6O_{19}]$ (W₆O₁₉) was prepared and characterized as described elsewhere.⁹⁷

 $(Bu_4N)_4PW_{11}NbO_{40}$ (PW₁₁Nb). H₃PW₁₂O₄₀·6H₂O (9 g, 3 mmol) was dissolved in 20 mL of water. Then 0.9 mL of 0.325 M H₃PO₄, 50 mL of hot aqueous solution of Na₇HNb₆O₁₉·15H₂O (0.702 g, 0.5 mmol), and 1 mL of 30% H₂O₂ (11 mmol) were subsequently added and the reaction mixture was stirred upon heating during 1 h. The resulting yellow solution of the peroxo species (Bu₄N)₄PW₁₁Nb(O₂)O₂₉ (³¹P NMR: -13.7 ppm) was evaporated until dryness and then dried in air at 140 °C for 2 h. The white residue was dissolved in water (20 mL), an insoluble precipitate was separated by centrifugation, and TBA salt was precipitated by the addition of TBABr (4.5 g). The resulting white solid was isolated by filtration, washed with water, dried at 100 °C and then recrystallized from CH₃CN. Large colorless crystals were dried in air at room temperature and then at 90 °C. Yield ca. 50%. The number of TBA cations (4) was determined by ignition. IR (KBr, 1100–400 cm⁻¹): 1082, 1070, 965, 890, 805, 600, 510. ³¹P NMR (ppm, in CH₃CN): -13.2. ¹⁸³W NMR (ppm, in CH₃CN): -67, -88, -93, -99, -106.

Interaction with H₂O₂. Interaction of Nb-POMs with 30% H_2O_2 was performed by the addition of H_2O_2 (0.1–50 equiv., taken as 30% solution in water) to a 0.01 M (⁹³Nb NMR monitoring) or 0.0005 M (UV-vis monitoring) solution of POM in dry CH₃CN at 20 °C.

Catalytic reactions. Catalytic oxidations were performed under vigorous stirring (500 rpm) in thermostated glass vessels. Typical reaction conditions were as follows: alkene 0.2 mmol, H₂O₂ 0.2 mmol, POM 0.004 mmol (0.002 mmol for (NbW₅)₂O), CH₃CN 1 mL, 50 °C. Reactions were started by the addition of 30% H₂O₂ to the reaction mixture containing acetonitrile solvent, alkene, POM and, in some cases, 1 equiv. (0.004 mmol) of HClO₄. Samples of the reaction mixture (0.5 μ L) were withdrawn periodically during the reaction course by a syringe. The oxidation products were identified by gas chromatography–mass spectrometry (GS–MS). The product yields and substrate conversions were quantified by gas chromatography (GC) using an internal standard, biphenyl. For GC analysis, the method described by Shul'pin⁹⁸ was used, which involves treatment of the reaction mixture with PPh₃ in order to reduce unreacted H_2O_2 and possible organic peroxides formed and comparison of chromatograms of the reaction mixture before and after the reduction of peroxides with PPh₃. Each experiment was reproduced at least 2 times.

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Kinetic experiments. Kinetic experiments were performed in temperature-controlled glass vessels under vigorous stirring (600 rpm). Reactions were initiated by the addition of 30 or 77% H₂O₂ to a CH₃CN solution containing CyOct substrate, catalyst (NbW₅)₂O, and internal standard for GC (biphenyl). The total volume of the reaction mixture was 1 mL. The reaction temperature was kept at 50 °C. Samples (0.5 μ L) of the reaction mixture were withdrawn periodically during the reaction with a syringe and analyzed by GC. Each experiment was reproduced at least 2–3 times. To rule out the possibility of evaporative losses of the substrate, blank experiments without catalyst and oxidant were carried out at the reaction temperature using the internal standard.

Reaction order in catalyst. The catalyst (NbW₅)₂O concentration was varied in the range 0.0006–0.004 M. Concentrations of other reactants were held constant: [CyOct] = 0.1 M, $[H_2O_2] = 0.1$ M.

Reaction order in substrate. The initial substrate concentration was varied between 0.02 and 0.3 M while maintaining constant concentrations of H_2O_2 (0.1 M) and catalyst (0.002 M).

Reaction order in H_2O_2 . The initial oxidant concentration was varied in the range of 0.1–0.9 M. The concentration of water in these experiments was kept constant by the addition of corresponding amounts of H_2O . To reduce the amount of water in the reaction mixture, 77% H_2O_2 was employed. The concentrations of other reactants were as follows: [CyOct] = 0.1 M, [(NbW₅)₂O] = 0.002 M.

Reaction order in H_2O . The initial concentration of water was varied from 0.08 to 1.8 M. Other parameters were held constant: [CyOct] = 0.1 M, [H₂O₂] = 0.1 M, and [(NbW₅)₂O] = 0.001 M.

Determination of activation energy. Temperature dependence of the reaction rate was studied in the range of 30-80 °C in CH₃CN using the following reaction conditions: [CyOct] = 0.1 M, [H₂O₂] = 0.1 M, and [(NbW₅)₂O] = 0.002 M.

Stoichiometric interaction with CyH. Stoichiometric reactions between CyH and peroxo complexes $Nb(O_2)W_5$ and $HNb(O_2)W_5$ were performed under Ar in thermostated glass vessels equipped with a magnetic stirrer at [POM] = 0.016 M, [CyH] = 0.08 M, and [HCIO₄] = 0.016 M (if any) in dry CH₃CN (1 mL) at 50 °C. The reaction course was monitored by UV-vis and GC. The oxidation products were identified by GC–MS and quantified by GC using internal standard.

Instrumentation and Methods. GC analyses were performed using a gas chromatograph Tsvet-500 equipped with a flame ionization detector and a quartz capillary column (30 $m \times 0.25$ mm) filled with Agilent DB–5MS. GC–MS analyses were carried out using an Agilent 7000B system with a triple– quadrupole mass–selective detector Agilent 7000 and a GC Agilent 7890B apparatus (quartz capillary column 30m×0.25mm/HP–5ms). ⁹³Nb, ¹⁷O, and ¹⁸³W NMR spectra were recorded at 97.94, 54.24, and 16.67 MHz, respectively, on an Avance-400 Brüker spectrometer using a high resolution multinuclear probe head with 10 mm o.d. (3 mL solution volume) sample tubes. ¹⁷O NMR spectra were measured at natural ¹⁷O abundance (0.037 %). Chemical shifts, δ , were referenced to NbCl₅, H₂O, and Na₂WO₄ for ⁹³Nb, ¹⁷O, and ¹⁸³W NMR spectra, respectively. For convenience, secondary external standards were used: 0.4 M H₄SiW₁₂O₄₀ for ¹⁸³W NMR (-103.6 ppm) and 0.05 M H₅SiW₁₁NbO₄₀ (-975 ppm) for ⁹³Nb NMR. Infrared spectra were recorded as 0.5–2.0 wt % samples in KBr pellets on an Agilent Cary 600 FTIR spectrometer. Electronic absorption spectra were run on a Carv-50 spectrophotometer using a 0.2 cm quartz cells. FT-Raman spectra (3600–100 cm⁻¹, 300 scans, resolution 4 cm⁻¹, 180° geometry) were recorded using a RFS 100/S spectrometer (Brüker). Excitation (1064 nm) was provided by a Nd-YAG laser (100 mW power output). Cyclic voltammetric measurements were performed under Ar using a P-8nano voltammetric analyzer (Elins Electrochemical Instruments), a threeelectrode cell, a Pt working electrode, a Pt auxiliary electrode, and an Ag/AgCl reference electrode (BAS). TBAClO₄ (0.1 M) was used as a supporting electrolyte. The analysis of W and Nb content was done by ICP-OES using a Perkin Elmer Optima-430 DV instrument. The concentrations of C, H, N and O in the samples were determined with a CHNSO analyzer Vario EL Cube (Elementar Analysensysteme GmbH).

Computational details. The DFT analysis of the reaction pathway was carried out with Gaussian09 rev. C01 software.⁵ Geometry optimization of reagents, intermediates, transition states and products was made using B3LYP density functional. $^{100-102}$ LANL2DZ pseudopotential 103 was used for W and Nb atoms and 6-31g(d,p) basis set $^{104-106}$ was used for other atoms. The geometry optimization was full and without any symmetry constrains, and solvent effects of acetonitrile were included using the IEF-PCM implicit solvation model as implemented in Gaussian09. This level of theory has been proved to be accurate and reliable enough to study the reactivity concerning POMs and their transition metal-substituted analogues, always showing a high degree of consistency with experimental outcomes and kinetic studies.¹⁰⁷⁻¹⁰⁹ Timedependent DFT (TD-DFT) calculations were performed with the long-range corrected CAM-B3LYP functional¹¹⁰ as implemented in Gaussian 09 using the same basis set. In order to compute protonation energies (ΔG_{H+}), we took the experimental standard free energy of a proton in aqueous solution 272.2 kcal·mol^{-1,111} NMR calculations were performed with ADF2107 package using a TZVP Slater type all-electron basis set and the OPBE functional¹¹² with spin-orbit (SO) corrections.113

RESULTS AND DISCUSSION

Catalytic performance of Nb-POMs in alkene oxidation. The catalytic properties of the well-known Lindqvist type dimer $(NbW_5)_2O$ and monomer Nb(O)W₅ were first assessed in the oxidation of cyclohexene (CyH) with hydrogen peroxide using equimolar amount of the oxidant (Table 1). CyH possesses highly reactive H atoms in the allylic position, which can be easily abstracted by radical species. Hence, the formation of allylic oxidation products, viz. cyclohexenyl hydroperoxide (HP), 2-cyclohexene-1-ol (enol) and 2-cyclohexene-1-one (enone), is a clear indication of a homolytic oxidation mechanism. Contrary, the selective formation of epoxide along with the ring opening product transcyclohexane-1,2-diol (diol) and its overoxidation product 2-hydroxycyclohexanone (ketol) points to heterolytic oxidation mechanism.

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Table 1. CyH oxidation with H_2O_2 in the presence of Nb-POMs^{*a*}

Entry	РОМ	Time,	CyH conv.,%	H ₂ O ₂ eff., ^b %	Product selectivity, ^c %					
Ē		h			epoxide	diol	ketol	HP	enol	enone
1	Nb(O)W ₅	5	55	64	53	25	14	2	3	3
2	$W_{6}O_{19}$	5	2	n.d. ^d	traces	-	-	n.d. ^d	traces	traces
3	PW ₁₁ Nb	5	20	n.d. ^d	8	20	5	50	10	5
4	$Nb(O)W_5 + 1 eq. H^+$	2	74	98	3	43	37	4	7	1
5	$(NbW_5)_2O^e$	1.5	76	97	3	51	33	3	3	1
6	$Nb(O)W_5 + 0.1 eq. H^+$	3	74	92	20	40	27	4	4	1
7	No catalyst	5	5	n.d. ^d	21	traces	-	33	33	11
8	1 eq. H ⁺	5	8	n.d. ^d	25	44	-	-	25	traces

^{*a*} Reaction conditions: 0.2 M CyH, 0.2 M H₂O₂ (30%), 0.004 M POM, 0.004 M HClO₄ (if any), 50 °C, 1 mL CH₃CN. ^{*b*} H₂O₂ utilization efficiency = total yield of products based on the oxidant consumed. ^{*c*} Based on substrate consumed. ^{*d*} Not determined. ^{*e*} Concentration of dimer (NbW₅)₂O was 0.002 M.

In the presence of Nb(O) W_5 , CyH conversion attained 55% after 5 h at 50 °C. Total selectivity toward heterolytic oxidation products (epoxide, diol, and ketol) and efficiency of hydrogen peroxide utilization were 92% and 64%, respectively (Table 1, entry 1). Epoxide prevailed among the oxidation products. Importantly, the Nb-free tungstate $(Bu_4N)_2[W_6O_{19}]$ was almost inactive in this reaction, indicating that the substitution of W(VI) for Nb(V) is indispensable for the observed activity (Table 1, entry 2). It is noteworthy that the Nbsubstituted Keggin phosphotungstate (Bu₄N)₄[PW₁₁NbO₄₀] revealed very poor activity and selectivity, producing HP as the main oxidation product and thereby indicating predomination of a homolytic oxidation pathway (Table 1, entry 3), which was also confirmed by reduction of the reaction rate in the presence of the conventional radical scavenger ionol. The reaction in the presence of Nb(O)W₅ was greatly accelerated with the addition of 1 equiv. of acid (Figure S1). Moreover, H₂O₂ utilization efficiency increased reaching 98% (Table 1, entry 4). A similar result was observed with dimer (NbW₅)₂O (Table 1, entry 5; Figure S1). In contrast to the reaction with $Nb(O)W_5$, the epoxide ring-opening product, diol, predominated among the oxidation products and the yield of the overoxidation product, ketol, also increased. Even minor (0.1 equiv.) additives of acid produced a significant effect on CyH oxidation rate and selectivity in the presence of Nb(O)W₅ (Table 1, entry 6). If 1 equiv. of acid was used as the sole catalyst, the selectivity toward heterolytic oxidation products (epoxide and diol) increased in the blank experiment either (Table 1, compare entries 7 and 8), but the reaction rate was insignificant relative to the Nb-POM-catalyzed reaction.

Importantly, the stability of the Lindqvist structure under the turnover conditions of CyH oxidation was confirmed. The IR spectra of the catalysts recovered by precipitation with ether revealed all the main vibrations of the Lindqvist tungstate and were very close to those of peroxo complex Nb(O₂)W₅ (Figure S2, compare spectra E and F with C). This is indicative that peroxo species participates in the reaction mechanism. The ⁹³Nb NMR spectrum of the reaction mixture after 24 h of the CyH oxidation revealed a sole resonance with δ –900 ppm, which is very close to that of Nb(O)W₅ (Figure S3, A and B), as one could expect after complete consumption of the oxidant. In turn, the ⁹³Nb NMR spectrum of the reaction mixture after the CyH oxidation in the presence of 1 equiv. of HClO₄ showed a resonance slightly shifted upfield (Figure S3, C),

which is, most likely, a manifestation of a partial protonation of $Nb(O)W_5$ (see Figure S4).

The catalytic properties of Nb(O)W₅ and (NbW₅)₂O were also tested in epoxidation of various alkenes with aqueous H₂O₂ (Table S1). For cyclic alkenes, such as cyclooctene (CyOct) and caryophillene, selectivity toward corresponding epoxides reached >99%. In the oxidation of methyl oleate and cis-stilbene, only cis-epoxides were formed, indicating a concerted mechanism of oxygen atom transfer that involves no radical or ionic intermediate capable of rotation around C-C bond. Note that stereospecificity in epoxidation of cis-alkenes is typical of mesoposous niobium-silicates.^{42,114,115} Styrene and stilbene produced, along with epoxides, a significant amount of benzaldehyde, the product of the oxidative C=C bond cleavage, which is also characteristic of heterogeneous Nbcatalysts.^{40,42} Therefore, the catalytic performance of the Lindqvist Nb-substituted tungstates is very similar to that of mesoporous niobium-silicates, which justifies use of the Nb-POMs as soluble molecular models for studying activation of H₂O₂ over Nb(V) sites.

Since unproductive decomposition of hydrogen peroxide is the main side reaction that competes for H_2O_2 with the target selective oxidation, activity of $(NbW_5)_2O$ and $Nb(O)W_5$ was also evaluated in decomposition of H_2O_2 in the absence of any organic substrate. While monomer $Nb(O)W_5$ revealed rather low activity, the addition of acid strongly enhanced the H_2O_2 degradation rate (Figure S5). Dimer $(NbW_5)_2O$ exhibited activity similar to that of monomer $Nb(O)W_5$ in the presence of 1 equiv. of acid. Therefore, protons accelerate both the target (epoxidation) and side $(H_2O_2$ degradation) reactions. However, given that a significant improvement of the oxidant utilization efficiency was observed in the presence of acid (Table 1, compare entries 1 and 4), we conclude that the effect of acid on epoxidation is more pronounced.

Kinetic Studies. To shed more light on the epoxidation mechanism over Nb-POM, the kinetics of CyOct oxidation with H_2O_2 in the presence of dimer $(NbW_5)_2O$ was studied. CyOct was chosen as a model substrate because it is less volatile than CyH and its epoxide is more stable toward ring opening and overoxidation (compare data in Table 1 and Table S1). Typical kinetic curves of CyOct consumption and epoxide product accumulation showed no induction period, autocatalysis or inhibition behavior. The absence of effect of light, oxygen or conventional chain radical scavengers, e.g., ionol, on

the reaction rate discarded radical chain oxidation mechanism, which is consistent with the minor amount of allylic oxidation products formed in the oxidation of CyH (*vide supra*).

The rate of CyOct oxidation in the presence of $(NbW_5)_2O$ exhibited a typical Arrhenius dependence (Figure 2), which implies that there was no change in the rate-limiting step over the evaluated temperature range. The value of the apparent activation energy (11.7 kcal mol⁻¹) turned out close to that previously found for CyOct epoxidation over mesoporous Nb-catalysts (11–12 kcal mol⁻¹).⁴² It is also noteworthy that the E_a for epoxidation is significantly lower than the E_a established for decomposition of H₂O₂ in the absence of organic substrate: 11.7 vs 16.3 kcal mol⁻¹ (Figure 2). The same trend was recently observed for mesoporous niobium-silicates.⁴²



Figure 2. Arrhenius plots for $(NbW_5)_2O$ -catalyzed CyOct epoxidation and H_2O_2 decomposition in CH₃CN. Reaction conditions: CyOct 0.1 M, H_2O_2 0.1 M, and $(NbW_5)_2O$ 0.002 M (for CyOct epoxidation) and H_2O_2 0.2 M, $(NbW_5)_2O$ 0.004 M (for H_2O_2 decomposition).

The CyOct epoxidation reaction showed a first-order dependence on alkene substrate (Figure S6a). The reaction order in oxidant and catalyst depended on the concentration of H₂O. With 30% H₂O₂ ([H₂O] was adjusted to 1.4 M in all experiments), the reaction was first order in oxidant (Figure S6b). While using 77% H₂O₂ ([H₂O] = 0.35 M), the reaction was slower and its rate exhibited a saturation behavior, indicating the formation of an active peroxo niobium intermediate (Figure S7a). In turn, the reaction was first order in catalyst with 30% H₂O₂ (Figure S6c) while the order changed to the fractional value (close to 0.5) when concentrated H₂O₂ was employed (Figure S7b). Finally, the rate of CyOct oxidation revealed a complicated, bell-shaped dependence on the concentration of water (Figure S8).

The observed kinetic trends allowed us to suggest a reaction mechanism that involves hydrolysis of $(NbW_5)_2O$ to form monomeric species $Nb(OH)W_5$ (Eq. 1), interaction of $Nb(OH)W_5$ with H_2O_2 generating a peroxo species $HNb(O_2)W_5$ (Eq. 2), followed by oxygen transfer from $HNb(O_2)W_5$ to alkene, producing epoxide (Eq. 3).

Interconversions between $(NbW_5)_2O$, $Nb(O)W_5$ and $Nb(OH)W_5$ in CH₃CN solution can be followed by ⁹³Nb NMR spectroscopy. The addition of water to a solution of $(NbW_5)_2O$ causes the narrowing of the ⁹³NMR resonance indicating the formation of Nb(OH)W₅ (Figure S9, spectrum B). After the addition of 1 equiv of acid to Nb(O)W₅, an upfield shift is initially observed (Figure S9, spectrum D) followed by broad-

ening of the ⁹³Nb NMR signal (Figure S9, spectrum E), which reflects the process of condensation of Nb(O)W₅ in the presence of acid. The formation of HNb(O₂)W₅ in the presence of H₂O₂ is discussed in more detail in the next section.

$$[(NbW_5O_{18})_2O]^{4_*} + H_2O \xrightarrow{\longrightarrow} 2[Nb(OH)W_5O_{18}]^{2_*}$$
(1)
(1) (3)

$$[Nb(OH)W_5O_{18}]^{2^{-}} + H_2O_2 \xrightarrow{(HNb(O_2)W_5O_{18}]^{2^{-}}} + H_2O \qquad (2)$$
(3)
(4)

 $[HNb(O_2)W_5O_{18}]^2 + alkene \longleftrightarrow [Nb(OH)W_5O_{18}]^2 + epoxide$ (3) (4) (3)

The first reaction order in (NbW₅)₂O found for 30% H₂O₂ implies that, at high concentration of water, dissociation of the dimer is not involved in the rate-limiting step of the oxidation process otherwise one would anticipate ca. 0.5 reaction order in (NbW₅)₂O, as it was observed earlier for thioether oxidation catalyzed by a Ti-monosubstituted µ-hydroxo Keggin dimer.116 Indeed, the reaction order in catalyst became close to 0.5 when the amount of water in the system was reduced (see Figure S7b). In turn, at low concentration of water, the overall reaction rate is proportional to H₂O concentration since water accelerates of the formation of Nb(OH)W₅ via Eq. 1. However, when water concentration becomes significant and all the Nb-POM is present in the form of monomer, the oxidation rate tends to decrease, most likely, because equilibrium (Eq. 2) shifts left, thereby decreasing the concentration of the active peroxo Nb species. The linear dependence of the reaction rate on the concentration of H₂O₂ at high concentration of water and saturation dependence at low water concentration are also consistent with the proposed mechanism. Note that stages similar to those described by Eq. 2 and Eq. 3 were recently suggested for epoxidation of electron-rich alkenes over mesoporous niobium-silicates on the basis of product, kinetic and spectroscopic data.42

Interaction of dimer 1 and monomer 2 with H_2O_2 . To confirm and understand the formation of the active peroxo niobium species, we studied the interaction of dimer $(NbW_5)_2O$ and monomer $Nb(O)W_5$ with hydrogen peroxide by using UV-vis and ⁹³Nb and ¹⁸³W NMR spectroscopy. Scheme 1 summarizes possible equilibriums between various Nb-POM species in the presence of aqueous hydrogen peroxide.



Scheme 1. Possible Nb-POM species and interconversion in the presence of aqueous H_2O_2 .

First, after the addition of H_2O_2 to Nb(O)W₅, the solution slowly turned pale yellow and a shoulder at 309 nm appeared

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in the UV-vis spectrum (Figure 3a). Note that yellow or light yellow color is characteristic of several Nb(V) peroxo complexes for which bidentate (η^2) coordination of the peroxo ligand has been proved by X-ray analysis.^{87,117,118} Hence, the shoulder at 309 nm can be assigned to peroxo ligand-to-metal charge transfer.



Figure 3. UV-vis spectra of Nb(O)W₅ (0.0005 M) after addition of (a) 5 equiv. of H_2O_2 and (b) 1 equiv. of $HClO_4$ and 5 equiv. of H_2O_2 . CH₃CN, 20°C.

⁹³Nb NMR spectroscopy is very useful to characterize the Nb(V) compounds both in solids¹¹⁹ and solution. ⁹³Nb has the high NMR sensitivity, high spin (9/2) and the large electric quadrupolar moment which, coupling to the local electric field gradients in typical for Nb(V) distorted environments, accelerates the nuclear magnetic relaxation, significantly broadening the signal. In solution, the signal widths increase also with the complex dimension and concentration. The Lindqvist-type Nb-substituted tungstates are appropriate for studying by ⁹³Nb NMR.^{96,120} The width of the ⁹³Nb NMR signal of anion Nb(O)W₅ in its 0.008M CH₃CN solution (δ -898 ppm) is about 1000 Hz, and it is the sharpest signal among those of the derivative anions studied in this work. Niobium in the composition of this anion has a distorted C_{4v} -like octahedral oxygen environment with one terminal unshared oxygen atom. A significant signal broadening observed for dimer (NbW₅)₂O (Figure S9, A) can be explained by almost two-fold increase of the anion dimensions which results in a larger correlation time of molecular rotation,96 although the symmetry of the ⁹³Nb environment in the dimer is similar to that in monomers Nb(O)W₅ and Nb(OH)W₅.

Upon addition of H_2O_2 to Nb(O)W₅, a new broad signal (δ – 1048 ppm) appeared in the ⁹³Nb NMR spectrum (Figure 4a). A

similar high field shift was recently observed for peroxoniobate (Bu₄N)[NbO(O₂)(OH)₂] as compared to the spectrum of $(Bu_4N)[NbO(OH)_2R]$.¹²¹ The intensity of this resonance increased with increasing concentration of H₂O₂ and, after the addition of 2 equiv., the initial signal of Nb(O)W₅ (δ -898 ppm) disappeared completely (Figure 4, spectrum D). Evidently, the resonance at -1048 ppm belongs to peroxo complex $Nb(O_2)W_5$ formed via reaction of $Nb(O)W_5$ with H_2O_2 . The correctness of this process was confirmed by experiments with additives of water. Indeed, the resonance of initial Nb(O)W₅ (δ -898 ppm) appeared if 10 vol% of H₂O was added to the equilibrated mixture of Nb(O)W5 and H2O2 (Figure 4a, spectrum E). The approximately five-fold broadening of the signal of Nb(O)W₅ indicates that the ⁹³Nb quadrupolar relaxation rate in it is five times faster,¹²⁰ which is due to the increase of the Nb coordination number from six to seven and consequently to the increase of the electric field gradients, produced by more distorted oxygen environment. The Lindquist structure of the peroxo Nb-POM (Nb(O₂)W₅) proved to be stable toward excess of hydrogen peroxide. No signs of the structure degradation were detected by ⁹³Nb NMR even after exposure to a 50-fold excess of H₂O₂ during one week. DFT calculations on Nb(O)W₅ and Nb(O₂)W₅ also showed an upfield shift of the ⁹³Nb NMR signal when the oxo ligand in the Lindqvist structure was replaced by peroxo group with η^2 coordination, although the computed upfield shift of 106 ppm was somewhat lower than the observed one of 150 ppm.



Figure 4. (a) ⁹³Nb NMR spectra of Nb(O)W₅ (A); Nb(O)W₅ in the presence of 0.5, 1 and 2 equiv. of H_2O_2 (B, C and D, respectively) and spectrum D after addition of 10 vol% H_2O (E). (b) ⁹³Nb NMR spectra of Nb(O)W₅ in the presence of 1 equiv. of H_2O_2 and 1 equiv. of HClO₄ (A), (NbW₅)₂O in the presence of 1 equiv. of H_2O_2 (B), Nb(O₂)W₅ (C), Nb(O₂)W₅ in the presence of 1 equiv. of HClO₄ (D), and HNb(O₂)W₅ (E). Nb-POM 0.01 M, CH₃CN, 20 °C.

In the presence of 1 equiv. of acid, the shoulder in the UV spectrum of H₂O₂-treated Nb(O)W₅ displayed a substantial red shift (Figure 3b). The TD-DFT simulated spectra for Nb-peroxo species Nb(O₂)W₅ shows one peak centered around 305 nm, as shown in Figure S10. The absorption arises from the HOMO to LUMO excitation, which has a $\pi^*_{O-O} \rightarrow d(M)$ nature. The protonation of Nb(O₂)W₅ at the bridging Nb–O–W

oxygen to give HNb(O₂)W₅ shifts the peak for $\pi^*_{O-O} \rightarrow d(M)$ excitation to 315 nm, reproducing nicely the experimental red shift. The analysis of molecular orbitals revealed that upon protonation at the POM framework the d-type orbitals of W suffer a larger stabilization than the π^*_{O-O} -type orbital of peroxo moiety reducing the energy gap. Moreover, the addition of protons greatly accelerated generation of the peroxo species, which completed within few minutes (compare Figures 3a and 3b). Dimer (NbW₅)₂O reacted with H₂O₂ very fast and the UV-vis spectrum of (NbW₅)₂O after interaction with H_2O_2 was similar to the spectrum of Nb(O_2)W₅ in the presence of acid (Figure S11). A pronounced bathochromic shift was earlier observed in the UV-vis spectra of the H₂O₂-Nb₂O₅-H₂SO₄ system as the concentration of sulfuric acid was increased.¹²² It is noteworthy that a blue shift of the DR UV-vis band, which was preliminary assigned to a 'NbOOH' species (307 nm), was detected upon addition of base to an H₂O₂treated mesoporous Nb-silicate.42 Hence, we may conclude that the UV-vis absorption associated with the peroxo Nb species generated in mesoporous Nb-silicate and homogeneous Nb-POM reveal a similar response to acid/base additives.

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The protonation of the Nb-POM peroxo species was also manifested in the ⁹³Nb NMR spectra (Figure 4b). In the presence of 1 equiv. of acid, the resonance of H₂O₂-treated Nb(O)W₅ shifted downfield relative to the proton-free system (δ –1015 versus –1048 ppm). A resonance with the same chemical shift (δ –1015 ppm) was observed in the ⁹³Nb NMR spectrum of dimer (NbW₅)₂O upon interaction with hydrogen peroxide (Figure 4b, spectrum B). In turn, the broad ⁹⁵Nb NMR resonance of peroxo complex Nb(O₂)W₅ (δ –1048 ppm) narrowed significantly in the presence of protons and moved to –1015 ppm (Figure 4b, spectrum D). Thus, the observed changes in the UV-vis and ⁹³Nb NMR spectra allowed us to suggest that the same protonated niobium peroxo species could be generated via interaction of H₂O₂ with either (NbW₅)₂O or Nb(O)W₅ in the presence of H⁺ (see Scheme 1).

Importantly, the ¹⁸³W NMR spectrum of $(NbW_5)_2O$ in the presence of 3 equiv. of H_2O_2 (Figure S12, spectrum D) showed two resonances with the intensity ratio of 4:1 typical of monosubstituted Lindqvist tungstates.

Characterization and reactivity of Nb-peroxo species. While our attempts to isolate a protonated peroxo niobium complex from a solution of Nb(O)W₅ in the presence of acid and an excess of H_2O_2 failed, we managed to synthesize it starting from dimer (NbW₅)₂O and H_2O_2 (Scheme 1).

The presence of one peroxo group per Nb atom was confirmed by titration with PPh₃ monitored by ³¹P NMR according to the procedure described in the literature.⁸⁷ The elemental analysis data agreed with the formulation of (Bu₄N)₂[HNb(O₂)W₅O₁₈]. Although attempts to grow X-ray quality crystals of HNb(O₂)W₅ failed, this compound could be comprehensively characterized using various analytic and spectroscopic techniques. Potentiometric titration of HNb(O₂)W₅ in CH₃CN with aqueous Bu₄NOH showed a sharp breakpoint at 0.73 equiv. of OH⁻ (Figure S13), indicating that the exact [H⁺]/[Nb] ratio is a little less than 1. Cyclic voltammetry indicated a significant increase in the oxidation potential of HNb(O₂)W₅ relative to Nb(O₂)W₅ (Figure S14). The UVvis spectrum of $HNb(O_2)W_5$ differed from that of $Nb(O_2)W_5$, but it practically coincided with the spectrum of $Nb(O_2)W_5$ in

the presence of 1 equiv. of acid (Figure S11), corroborating the presence of proton in $HNb(O_2)W_5$.

The purity of HNb(O₂)W₅ was verified by using ⁹³Nb NMR spectroscopy. The only peak detected in the ⁹³Nb NMR spectrum was located at δ –1015 ppm (Figure 4b, spectrum E). The same chemical shift was observed for the peroxo species generated *in situ* upon addition of 1 equiv. of H⁺ to Nb(O₂)W₅ (Figure 4b, spectrum D). ⁹³Nb NMR monitoring of the stepwise addition of HClO₄ to Nb(O₂)W₅ (Figure S15a) and Bu₄NOH to HNb(O₂)W₅ (Figure S15b) clearly indicated that species HNb(O₂)W₅ and Nb(O₂)W₅ are in fast exchange on the ⁹³Nb NMR time scale, which implies that both peroxo complexes have a similar structure and differ only in their protonation state. As one can judge from Figure S15, the interconversion between HNb(O₂)W₅ and Nb(O₂)W₅ is reversible and the Lindqvist structure of the NbW₅ peroxo complexes is stable toward, at least, 3 equiv. of acid and 1.5 equiv. of base.

The structure of HNb(O₂)W₅, in particular a possible site of the proton localization, was probed by vibrational spectroscopic techniques. No IR bands were observed for solid HNb(O₂)W₅ in the characteristic 1800–1600 cm⁻¹ region (Figure S16), indicating that no H_3O^+ was present and that the proton is directly attached to the POM surface.^{123,124} The FT-IR spectra of $HNb(O_2)W_5$ and $Nb(O_2)W_5$ confirm the retention of the Lindqvist structure (see Figure S2). The absence of the vibration stretches of Nb=O and Nb-O-Nb at 915 and 695 cm^{-1} present in the parent compounds Nb(O)W₅ and (NbW₅)₂O, respectively, clearly indicates changes at the terminal position of the Nb atom. The FT-IR spectrum of Nb(O₂)W₅ revealed new bands at 857, 638 and 602 cm⁻¹. On the basis of the literature data reported for various peroxo niobium complexes, $^{86,95,125-131}$ the band at 857 cm⁻¹ can be assigned to the stretching fundamental of the O-O bond while the couple at 638 and 602 cm⁻¹ is associated with symmetric and asymmetric Nb-peroxide stretches. The IR spectrum of HNb(O₂)W₅ revealed some important distinctive features relative to that of Nb(O₂)W₅. First, the frequencies of v(W=O) and v(O-O) are shifted to higher energy: 973 vs 960 cm^{-1} and 870 vs 857 cm^{-1} , respectively, which reflects a decrease in the corresponding bond lengths due to the contraction of the structure via reduction of the negative charge. This indicates that protonation of the peroxo derivative occurs at Nb-O-W bridging oxygen rather than at the peroxo group, because, in the latter case, one would expect a lower-energy shift due to lengthening of the O–O bond. A higher energy shift of v(W=O) was observed earlier upon protonation of the di-Nb-substituted Lindqvist tungstate $[Nb_2W_4O_{19}]^{4-.132}$

The assignment of the IR bands in the peroxo Nb species and the hypothesis about protonation of the Nb–O–W bridging oxygen were further supported by Raman spectroscopy. In comparison with the spectra of peroxo-free compounds (NbW₅)₂O and Nb(O)W₅, new bands appeared in the Raman spectra of the peroxo derivatives at 860–863 and 603–623 cm⁻¹ (Figure S17) and can be assigned to v(O–O) and v(NbO₂) vibrations, respectively.^{118,125,126,133–135} Similarly to the IR spectra, a higher-energy shift of the stretching vibrations of terminal W=O groups was clearly observed in the Raman spectrum of solid HNb(O₂)W₅ as compared to the spectra of Nb(O₂)W₅ generated *in situ* from Nb(O₂)W₅ and 1 equiv. of H⁺ in CH₃CN solution (Figure 5) showed shearing of v(W=O) and v(NbO₂) to higher energies (*ca.* 13 and 7 cm⁻¹, respective-

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ly). Thus, both IR and Raman spectroscopy provided evidence in favor of the side-on (η^2) bonding mode of the peroxo ligand in HNb(O₂)W₅ and Nb(O₂)W₅, with proton located at Nb–O– W oxygen site in the former. In agreement with this interpretation, the DFT-simulated Raman spectra of Nb(O₂)W₅ and HNb(O₂)W₅ (Figure S18) revealed a shift to higher energies for v(W=O) and v(NbO₂) bands of complex HNb(O₂)W₅ by 14 and 5 cm⁻¹, respectively, which is close to what was observed experimentally. Moreover, DFT calculations (*vide infra*) showed that in HNb(O₂)W₅ protonation at Nb–O–W is thermodynamically favored relative to protonation at the W–O–W bridging oxygen and at the peroxo moiety by 3.0 and 8.7 kcal·mol⁻¹, respectively.



Figure 5. Raman spectra of CH_3CN (A) and CH_3CN solutions of $Nb(O)W_5$ (B), $Nb(O_2)W_5$ (C), and $Nb(O_2)W_5$ in the presence of 1 equiv. of $HClO_4$ (D). POM 0.1 M, CH_3CN , 20 °C.



Figure 6. ¹⁷O NMR spectra of Nb(O)W₅ (A), Nb(O₂)W₅ (B), and HNb(O₂)W₅ (C). 0.1 M POM, CH₃CN, 20 °C. The spectrum of HNb(O₂)W₅ was accumulated in the presence of a 10-fold excess of 30% H₂O₂. Peaks corresponding to H₂O₂ and H₂O are marked with asterisks * and **, respectively.

The protonation site in HNb(O₂)W₅ was also confirmed by ¹⁷O NMR spectroscopy. As shown in Figure 6 and Table S2, the ¹⁷O NMR spectrum of HNb(O₂)W₅ revealed a pronounced upfield shift of the Nb–O–W signal (δ 414 ppm) relative to its position in the ¹⁷O NMR spectra of Nb(O)W₅ (δ 456 ppm)^{97,120} and Nb(O₂)W₅ (460 ppm). This shift in combination with downfield shifts for the rest of signals is, according to the literature, ^{132,136} an unambiguous prove for the protonation of Nb–O–W bond in solution.¹³⁷ Hence, IR, Raman, and ¹⁷O NMR spectroscopic techniques along with DFT calculations (see below) all support the conclusion that in HNb(O₂)W₅ the proton is preferably located at the Nb–O–W bridging oxygen site rather than at the peroxo ligand.

Finally, we investigated the stoichiometric interaction of $Nb(O_2)W_5$ and $HNb(O_2)W_5$ with CyH as model alkene substrate. The results on the substrate conversion and product selectivity are shown in Table 2. Peroxo complex Nb(O₂)W₅ was found to be completely inert toward CyH. However, it became reactive and produced heterolytic oxidation products, epoxide and diol, if 1 equiv. of protons was added. In turn, protonated peroxo complex HNb(O₂)W₅ was also able to oxidize CyH under stoichiometric conditions, leading to epoxide and diol. The amount of the oxygenated products corresponded to the amount of active oxygen (i.e., peroxo oxygen activated by proton) in HNb(O2)W5. These experiments unambiguously prove that protons play a crucial role in the activation of the peroxo niobium moiety and that namely protonated Nb peroxo species is responsible for heterolytic oxidation of C=C bond in alkene.

Table 2. Interaction of HNb(O₂)W₅ and Nb(O₂)W₅ with CyH^a

Entry	POM	СуН	Product yield, ^b %		
		conv. %	epoxide	diol	
1	$Nb(O_2)W_5$	0	0	0	
2	$Nb(O_2)W_5 + 1 eq. H^+$	19.5	13.5	6	
3	HNb(O ₂)W ₅	16	10	6	

^{*a*} Reaction conditions: 0.016 M POM, 0.016 M HClO₄ (entry 2), 0.08 M CyH, CH₃CN, 50 °C, 2 h. ^{*b*} Based on substrate.

The stoichiometric reaction can be easily followed by UVvis. The decrease in the characteristic absorption region due to the ligand-to-metal charge transfer (310-350 nm) in the UVvis spectra of HNb(O₂)W₅ (Figure 7) or HNb(O₂)W₅ generated in situ from $Nb(O_2)W_5$ and H⁺ (Figure S19) is much slower than in the presence of CyH. This implies that thermal decomposition of HNb(O₂)W₅ is rather slow and that the observed decay of the absorption is due to the reaction with CyH. ⁹³Nb NMR monitoring of the reaction between HNb(O₂)W₅ and CyH revealed transformation of the sharp resonance at δ – 1015 ppm into the broad resonance at ca. -950 ppm attributed to $(NbW_5)_2O_5^{96}$ which appeared at the end of the reaction as a result of dimerization of Nb(OH)W₅. Importantly, interaction of HNb(O₂)W₅ with cis-stilbene produced exclusively cisepoxide along with the C-C cleavage product benzaldehyde, corroborating a concerted oxygen transfer mechanism.





We have analyzed the heterolytic oxygen transfer to CyH from both side-on Nb-hydroperoxo (4b) and -peroxo (4) species. Figure 9 collects the geometries of the reactants and the transition states, as well as, the corresponding free energy barriers. The less stable hydroperoxo anion 4b shows a lower free energy barrier than the peroxo anion 4 (17.6 vs 27.1 $kcal \cdot mol^{-1}$). In Nb-hydroperoxo species 4b, the alkene attack occurs preferably at the proximal, non-protonated α -oxygen because the σ^*O-O orbital is polarized toward $O\alpha$, favoring the donation from the nucleophilic double bond.⁴⁵ In this case, the transition state for β -oxygen transfer (see Figure S20) is 2.3 kcal·mol⁻¹ higher than the corresponding transition state for a-oxygen transfer TS_{4b-P} . Nevertheless, the β -oxygen transfer could be favored in complexes with metal ions in sterically hindered or strongly embedded in non-flexible environment that make the $O\beta$ more accessible to the substrate.¹³⁹



Figure 8. Calculated Gibbs free energy profile $(\text{kcal} \cdot \text{mol}^{-1})$ for the epoxidation of cyclohexene (CyH) with H₂O₂ catalyzed by Nb(OH)W₅ (**3**).

Another important feature of the potential free-energy profile (Figure 8) is the relative rates between the hydrogen and the oxygen transfer from 4b to form the peroxo species 4 (TS_{4b-4}) and the epoxide (TS_{4b-P}) , respectively. The hydrogen transfer is computed to be faster, its free energy barrier being 2.5 kcal·mol⁻¹ lower in energy. Thus, it is reasonable to assume that a large proportion of the reacting species, reaching the Nb-hydroperoxo 4b intermediate, evolve to the Nb-peroxo complex 4, which becomes the resting-state of the catalytic process. From Nb-peroxo species 4, the reaction can proceed directly to oxygen transfer to the alkene through TS_{4-P} structure, overcoming a computed free-energy barrier of 27.1 kcal·mol⁻¹, or it can come back to the less stable but more reactive Nb-hydroperoxo species 4b, overcoming an overall free-energy barrier (4 \rightarrow TS_{4b-P}) of 26.3 kcal·mol⁻¹. In summary, our calculations indicate that most of the reaction proceeds via heterolytic oxygen transfer from Nb- η^2 -hydroperoxo species 4b, involving a previous formation of protonated Nbperoxo species 4, which acts as the resting-state of the catalyst. However, other two energetically accessible paths can contribute to the formation of epoxides: (i) the direct oxygen transfer from 4b without the formation of peroxo species 4, and (ii) the heterolytic oxygen transfer from the Nb-peroxo



Figure 7. UV-vis spectra of $HNb(O_2)W_5$ (a) in time and (b) in time in the presence of 5 equiv. of CyH. Reaction conditions: 0.0005 M HNb(O₂)W₅, 0.0025 M CyH, CH₃CN, 50 °C.

DFT study of reaction mechanism. To understand the reaction mechanism at atomistic level and identify the active species of the oxygen transfer process, we have performed DFT calculations on Nb-substituted Lindqvist anions using CyH as substrate. Our previous study on the effect of the metal nature on the oxygen transfer mechanism showed that when we move from Ti to Nb (down in the periodic table), both peroxo and hydroperoxo energy barriers decrease, but the latter does it more appreciably.⁴⁵ However, in order to obtain a complete picture of the reaction, one should also evaluate the effect of the larger radius of Nb(V) ion on the stabilization of 7coordinated species such as η^2 -peroxo and η^2 -hydroperoxo ones.¹³⁸ Figure 8 depicts the calculated free energy profile for the epoxidation of CyH with H2O2 catalyzed by $[Nb(OH)W_5O_{18}]^{2-}$ (3) anion. In the first step, the interaction of H₂O₂ with the Nb-hydroxo moiety of **3** results in the hydroperoxo species 4a, in which the OOH group is η^{1} -coordinated, and the release of a water molecule. The H2O2 activation proceeds through transition state TS_{3-4a} (see Figure S20), and the computed free-energy barrier is moderate, 15.3 kcal mol⁻¹. The generated η^1 -OOH species (4a) can evolve to the more stable η^2 -OOH species **4b** because the size of the second-row Nb(V) ion allows to accommodate 7-fold coordination. The η^2 -hydroperoxo species **4b** is lower in energy (-3.5 kcal·mol⁻ ¹) than the corresponding η^1 -hydroperoxo **4a**, but higher in energy (+8.7 kcal·mol⁻¹) than the corresponding η^2 -peroxo complex 4 in agreement with experimental data. Nb-peroxo complex 4 can be formed from 4b via hydrogen transfer from the hydroperoxo moiety to a bridging W-O-Nb oxygen overcoming a moderate free energy barrier of 15.1 kcal·mol⁻¹ (see transition state structure TS_{4b-4} in Figure S20). As commented

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species 4. According to the computed values, at 50° C, the contribution of the two latter paths is approximately 2 and 21%, respectively.



Figure 9. Combined balls-and-sticks and polyhedral representation of some of the most relevant intermediates (**4b** and **4**) and transition states (TS_{4b-P} and TS_{4-P}) in reaction mechanism. Main distances are shown in Å. Free energy barriers for the electrophilic O-transfer step occurring from **4b** and **4** are shown in kcal mol⁻¹.

To further validate our proposed mechanism, we analyzed the zero-point corrected energy profile (Figure S21) for CyOct epoxidation by dimer (NbW₅)₂O and compared it with the experimental E_a (11.7 ± 0.8 kcal·mol⁻¹) in Figure 2. In the absence of entropic effects, the computed overall energy barrier for direct oxygen transfer from hydroperoxo species **4b** is 8 kcal·mol⁻¹ (too low) while those involving the formation of peroxo species **4** are about 16 kcal·mol⁻¹ (too high). However, assuming that several paths contribute to the reaction, the weighted average of the computed energy barriers should be close to experimental E_a value.

Next, to understand the role of protons on the reactivity, we evaluated feasibility of the epoxidation process using the nonprotonated peroxo species $[Nb(O_2)W_5O_{18}]^{3-}$ (5). The free energy barrier for the oxygen transfer from 5 to CyH was computed to be 31.6 kcal mol⁻¹, which is larger than that for the epoxidation by protonated peroxo species 4, 26.3 kcal·mol⁻¹ (from 4 to **TS**_{4b-P}). This is consistent with lack of reactivity observed over species 5. Moreover, the free-energy barrier for H_2O_2 activation by the non-protonated species 2 is ~4 kcal mol⁻¹ higher than that from the protonated species **3** (see Figure 8) in full agreement with the accelerated generation of peroxo species observed upon addition of protons (Figure 3). Thus, protonation has two important consequences in the catalytic performance of Nb-substituted anions: (i) it allows forming the more reactive Nb-hydroperoxo species, and (ii) it reduces the overall negative charge of the POM favoring the electrophilic oxygen transfer to the alkene as observed also for Ti-substituted POMs.83

Table 3. Calculated protonation free-energies (ΔG_{H^+}) and freeenergy barriers for oxygen transfer ($\Delta G^{\ddagger}_{Otrans}$) from Lindqvist (Nb(O₂)W₅ **5** and HNb(O₂)W₅ **4**) and Keggin (**5k** and **4k**) anions in kcal·mol⁻¹.

Catalyst	$\Delta G_{\rm H^+}$	Active species	q/M	$\Delta G^{\ddagger}_{Otrans}$
5	-	5	0.50	31.6
5k	-	5k	0.33	29.6
$5 + 1 \mathrm{H}^+$	-3.7	4	0.33	26.3 ^{<i>a</i>}
$5\mathbf{k} + 1\mathbf{H}^+$	+2.7	4k	0.25	23.8 ^{<i>a</i>}

^{*a*} Free-energy barriers through hydroperoxo path.

Finally, we analyzed computationally the reactivity of Nbsubstituted Keggin anions $[PW_{11}O_{39}Nb(O_2)]^{4-}$ (5k) and $[HPW_{11}O_{39}Nb(O_2)]^{3-}$ (4k), which also display a poor performance in alkene epoxidation (Table 1). Two main trends are observed in Table 3, which collects the computed protonation energies (ΔG_{H+}) and the free-energy barriers for oxygen transfer ($\Delta G_{\text{Otrans}})$ through peroxo (5/5k \rightarrow TS_{5-P}/TS_{5k-P}) and hydroperoxo $(4/4k \rightarrow TS_{4b-P}/TS_{4bk-P})$ paths. First, ongoing from Lindqvist to Keggin anion the charge density decreases as reflected in the total charge per metal ratio (q/M).^{107,140–142} Consequently, the POM becomes better electrophile favoring the oxygen transfer to the nucleophilic alkene by $\sim 2 \text{ kcal} \cdot \text{mol}^-$ ^{1.83} Second, the less basic Keggin anion is more difficult to protonate resulting in an endergonic process according to our calculations (+2.7 kcal·mol⁻¹ for $5\mathbf{k} + 1\mathbf{H}^+ \rightarrow 4\mathbf{k}$). The computed atomic charge from electrostatic potential at the bridging Nb-O-W oxygen for 5k (-.74 au) is less negative than that of the corresponding oxygen for Lindqvist species 5 (-.86 au). Thus, although Keggin structures are more reactive as oxygen transfer agents than Lindqvist ones, they are more difficult to be activated via protonation. Overall, these opposite trends might result in a loose of reactivity for Keggin structures. In summary, for the alkene epoxidation by Nb-substituted POMs the art consists of tuning the charge density of the anion. The POM should have low electron density in order to favor the electrophilic oxygen transfer to alkenes, but basic enough to be protonated and enable the hydroperoxo path.

CONCLUSIONS

Nb-substituted tungstates of the Lindqvist structure are highly active and selective catalysts for H2O2-based oxidation of alkenes via heterolytic pathway. In this work, we demonstrated that the Lindqvist Nb-POMs mimic well the catalytic performance of heterogeneous Nb-silicate catalysts and can be successfully employed as soluble molecular models for studying mechanism of H₂O₂ activation on Nb(V). Product, spectroscopic and computational studies revealed that protons play a crucial role in the catalytic activity of niobium sites. While a suitable source of protons is required to accelerate interaction of the terminal Nb=O bond in monomer Nb(O)W₅ with H₂O₂, μ -oxo dimer (NbW₅)₂O is highly active without any additives. Interaction of $(NbW_5)_2O$ (alternatively Nb(O)W₅ + H⁺) with H₂O₂ affords protonated Nb peroxo derivative HNb(O₂)W₅ which, in contrast to proton-free peroxo complex $Nb(O_2)W_5$, is able to epoxidize alkenes under stoichiometric conditions. Therefore, protons are important not only for the generation of peroxo niobium species but also for its reactivity. Spectroscopic (UV-vis, IR, Raman, and ¹⁷O NMR) and computational techniques strongly support a monomeric Lindqvist structure of HNb(O₂)W₅ with one peroxo ligand attached to Nb(V) in a η^2 -coordination mode and proton located at a Nb–O–W bridging oxygen. DFT calculations also revealed that η^2 -hydroperoxo niobium species, which is present in equilibrium with the protonated peroxo species HNb(O₂)W₅ in CH₃CN solution, is the main epoxidizing species since it drives the reaction by a less energy-demanding reaction path. The protonation of the Nb-POMs plays a crucial role in activating the oxidant by allowing the formation of the more reactive hydroperoxo intermediate and increasing its electrophilicity that favors the oxygen transfer to nucleophiles. Future catalyst designs should fine-tune its electrostatic properties reducing electron density but allowing protonation in order to enable the hydroperoxo path.

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Author Contributions

The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript.

Notes

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The authors declare no competing financial interests.

ASSOCIATED CONTENT

Supporting Information. Data on product yields for various alkenes, ¹⁸³W and ⁹³Nb NMR, IR, Raman, and UV-vis spectra, ¹⁷O NMR data, potentiometric titration, cyclic voltammograms, kinetic data on CyOct epoxidation, structures of transition state, energy profile.

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REFERENCES

(1) Sheldon, R.; Arends, I. W. C. E.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, 2007.

(2) Sustainable Industrial Processes. Cavani, F., Centi, G., Perathoner, S., Trifiro, F., Eds; Wiley-VCH: Weinheim, 2009.

(3) Handbook of Advanced Methods and Processes in Oxidation Catalysis; Duprez, D., Cavani, F., Eds.; Imperial College Press: London, 2014.

(4) Cavani, F.; Teles, J. H. Sustainability in Catalytic Oxidation: An Alternative Approach or a Structural Evolution? *ChemSusChem* **2009**, *2*, 508–534.

(5) Jones, C. W. Application of Hydrogen Peroxide and Derivatives; Royal Society of Chemistry: Cambridge, 1999.

(6) Strukul, G.; Scarso, A. In: *Liquid Phase Oxidation via Heterogeneous Catalysis: Organic Synthesis and Industrial Applications*; Clerici, M. G., Kholdeeva, O. A., Eds.; Wiley: Hoboken, 2013; p. 1.

(7) Campos-Martin, J. M.; Blanco-Brieva, G.; Fierro, J. L. G. Hydrogen Peroxide Synthesis: An Outlook beyond the Anthraquinone Process. *Angew. Chem. Int. Ed.* **2006**, *45*, 6962–6984.

(8) Walling, C. Fenton's Reagent Revisited. Acc. Chem. Res. 1975, 8, 125–131.

(9) Masarwa, A.; Rachmilovich-Calis, S.; Meyerstein, N.; Meyerstein, D. Oxidation of Organic Substrates in Aerated Aqueous Solutions by the Fenton Reagent. *Coord. Chem. Rev.* **2005**, *249*, 1937–1943.

(10) Lane, B. S.; Burgess, K. Metal–Catalyzed Epoxidations of Alkenes with Hydrogen Peroxide. *Chem. Rev.* **2003**, *103*, 2457–2474.

(11) Grigoropoulou, G.; Clark, J. H.; Elings, J. A. Recent Developments on the Epoxidation of Alkenes Using Hydrogen Peroxide as an Oxidant. *Green Chem.* **2003**, *5*, 1–7.

(12) Bryliakov, K. P.; Talsi, E. P. Chemo– and Stereoselective C– H Oxidations and Epoxidations/cis–Dihydroxylations with H_2O_2 , Catalyzed by Non–Heme Iron and Manganese Complexes. *Coord. Chem. Rev.* **2012**, *256*, 1418–1434.

(13) Hauser, S. A.; Cokoja, M.; Kühn, F. E. Epoxidation of Olefins with Homogeneous Catalysts – Quo Vadis? *Catal. Sci. Technol.* **2013**, *3*, 552–561.

(14) Venturello, C.; D'Aloisio, R. Quaternary Ammonium Tetrakis(diperoxotungsto)phosphates(3–) as a New Class of Catalysts for Efficient Alkene Epoxidation with Hydrogen Peroxide. *J. Org. Chem.* **1988**, *53*, 1553–1557.

(15) Bregeault, J.-M. Transition–Metal Complexes for Liquid– Phase Catalytic Oxidation: Some Aspects of Industrial Reactions and of Emerging Technologies. *Dalton Trans.* **2003**, 3289–3302.

(16) Mizuno, N.; Yamaguchi, K.; Kamata, K. Epoxidation of Olefins with Hydrogen Peroxide Catalyzed by Polyoxometalates. *Coord. Chem. Rev.* **2005**, *249*, 1944–1956.

(17) Amini, M.; Haghdoost, M. M.; Bagherzadeh, M. Monomeric and Dimeric Oxido–Peroxido Tungsten(VI) Complexes in Catalytic and Stoichiometric Epoxidation. *Coord. Chem. Rev.* **2014**, *268*, 83–100.

(18) Herrmann, W. A.; Fischer, R. W.; Scherer, W.; Rauch, M. U. Methyltrioxorhenium(VII) as Catalyst for Epoxidations: Structure of the Active Species and Mechanism of Catalysis. *Angew. Chem. Int. Ed.* **1993**, *32*, 1157–1160.

(19) Crucianelli, M.; Saladino, R.; De Angelis, F. Methyltrioxorhenium Catalysis in Nonconventional Solvents: A Great Catalyst in a Safe Reaction Medium. *ChemSusChem* **2010**, *3*, 524–540.

(20) Kück, J. W.; Reich, R. M.; Kühn, F. E. Molecular Epoxidation Reactions Catalyzed by Rhenium, Molybdenum, and Iron Complexes. *Chem. Rec.* **2016**, *16*, 349-364.

(21) Goto, Y.; Kamata, K.; Yamaguchi, K.; Uehara, K.; Hikichi, S.; Mizuno, N. Synthesis, Structural Characterization, and Catalytic Performance of Dititanium–Substituted γ –Keggin Silicotungstate. *Inorg. Chem.* **2006**, *45*, 2347–2356.

(22) Hussain, F.; Bassil, B. S.; Kortz, U.; Kholdeeva, O. A.; Timofeeva, M. N.; de Oliveira, P.; Keita B.; Nadjo, L. Dititanium– Containing 19–Tungstodiarsenate(III) [Ti₂(OH)₂As₂W₁₉O₆₇(H₂O)]⁸⁻: Synthesis, Structure, Electrochemistry, and Oxidation Catalysis. *Chem.–Eur. J.* **2007**, *13*, 4733–4742.

(23) Kholdeeva, O. A.; Donoeva, B. G.; Trubitsina, T. A.; Al-Kadamany, G.; Kortz, U. Unique Catalytic Performance of the Polyoxometalate $[Ti_2(OH)_2As_2W_{19}O_{67}(H_2O)]^{8-}$: The Role of 5–

Coordinated Titanium in H₂O₂ Activation. *Eur. J. Inorg. Chem.* **2009**, 5134–5141.

(24) Miao, C.; Wang, B.; Wang, Y.; Xia, C.; Lee, Y.-M.; Nam, W.
W.; Sun, W. Proton–Promoted and Anion–Enhanced Epoxidation of Olefins by Hydrogen Peroxide in the Presence of Nonheme Manganese Catalysts. *J. Am. Chem. Soc.* 2016, *138*, 936-943.

(25) Ottenbacher, R. V.; Samsonenko, D. G.; Talsi, E. P.; Bryliakov, K. P. Enantioselective Epoxidations of Olefins with Various Oxidants on Bioinspired Mn Complexes: Evidence for Different Mechanisms and Chiral Additive Amplification. *ACS Catal.* **2016**, *6*, 979-988.

(26) Saisaha, P.; de Boer, J. W.; Browne, W. R. Mechanisms in Manganese Catalysed Oxidation of Alkenes with H_2O_2 . *Chem. Soc. Rev.* **2013**, *42*, 2059-2074.

(27) Mas-Ballesté, R.; Que, L. Iron–Catalyzed Olefin Epoxidation in the Presence of Aacetic Acid: Insights into the Nature of the Metal–Based Oxidant. J. Am. Chem. Soc. 2007, 129, 15964-15972.

(28) Cusso, O.; Ribas, X.; Costas, M. Biologically Inspired Non– Heme Iron–Catalysts for Asymmetric Epoxidation; Design Principles and Perspectives. *Chem. Commun.* **2015**, *51*, 14285–14298.

(29) Notari, B. In: *Advances in Catalysis*; Eley, D. D., Haag, W. O., Gates, B. C. Eds.; Academic Press: San Diego, 1996; Vol. 41, p. 253.

(30) For recent review see: Clerici, M. G.; Domine, M. E. In: *Liquid Phase Oxidation via Heterogeneous Catalysis: Organic Synthesis and Industrial Applications*; Clerici, M. G., Kholdeeva O. A. Eds.; Wiley: Hoboken, 2013; p. 21.

(31) Kholdeeva, O. A. In: *Liquid Phase Oxidation via Heterogeneous Catalysis: Organic Synthesis and Industrial Applications*; Clerici, M. G., Kholdeeva O. A. Eds.; Wiley: Hoboken, 2013; p. 127.

(32) Kholdeeva, O. A. Recent Developments in Liquid–Phase Selective Oxidation Using Environmentally Benign Oxidants and Mesoporous Metal Silicates. *Catal. Sci. Technol.* **2014**, *4*, 1869–1889.

(33) Nowak, I.; Kilos, B.; Ziolek, M.; Lewandowska, A. Epoxidation of Cyclohexene on Nb–Containing Meso- and Macroporous Materials. *Catal. Today* **2003**, *78*, 487–498.

(34) Nowak, I.; Ziolek, M. Effect of Texture and Structure on the Catalytic Activity of Mesoporous Niobosilicates for the Oxidation of Cyclohexene. *Micropor. Mesopor. Mater.* **2005**, *78*, 281–288.

(35) Somma, F.; Strukul, G. Niobium Containing Micro-, Mesoand Macroporous Silica Materials as Catalysts for the Epoxidation of Olefins with Hydrogen Peroxide. *Catal. Lett.* **2006**, *107*, 73–81.

(36) Feliczak-Guzik, A.; Nowak, I. Mesoporous Niobosilicates Serving as Catalysts for Synthesis of Fragrances. *Catal. Today* **2009**, *142*, 288–292.

(37) Gallo, A.; Tiozzo, C.; Psaro, R.; Carniato, F.; Guidotti, M. Niobium Metallocenes Deposited onto Mesoporous Silica via Dry Impregnation as Catalysts for Selective Epoxidation of Alkenes. *J. Catal.* **2013**, *298*, 77–83.

(38) Tiozzo, C.; Bisio, C.; Carniato, F.; Guidotti, M. Grafted Non-Ordered Niobium-Silica Materials: Versatile Catalysts for the Selective Epoxidation of Various Unsaturated Fine Chemicals. *Catal. Today* **2014**, *235*, 49–57.

(39) Ramanathan, A.; Zhu, H.; Maheswari, R.; Thapa, P. S.; Subramaniam, B. Comparative Study of Nb–Incorporated Cubic Mesoporous Silicates as Epoxidation Catalysts. *Ind. Eng. Chem. Res.* **2015**, *54*, 4236–4242.

(40) Ivanchikova, I. D.; Maksimchuk, N. V.; Skobelev, I. Y.; Kaichev, V. V.; Kholdeeva, O. A. Mesoporous Niobium–Silicates Prepared by Evaporation–Induced Self–Assembly as Catalysts for Selective Oxidations with Aqueous H₂O₂. *J. Catal.* **2015**, *332*, 138– 148.

(41) Thornburg, N. E.; Thompson, A. B.; Notestein, J. M. Periodic Trends in Highly Dispersed Groups IV and V Supported Metal Oxide Catalysts for Alkene Epoxidation with H₂O₂. *ACS Catal.* **2015**, *5*, 5077–5088.

(42) Ivanchikova, I. D.; Skobelev, I. Y.; Maksimchuk, N. V.; Paukshtis, E. A.; Shashkov, M. V.; Kholdeeva, O. A. . Toward Understanding the Unusual Reactivity of Mesoporous Niobium Silicates in Epoxidation of C=C Bonds with Hydrogen Peroxide. *J. Catal.* **2017**, *356*, 85–99.

(43) Mechanisms in Homogeneous and Heterogeneous Epoxidation Catalysis, Oyama, S. T., Ed.; Elsevier: Amsterdam, 2008.

(44) Deubel, D. V.; Frenking, G.; Gisdakis, P.; Herrmann, W. A.; Rösch, N.; Sundermeyer, J. Olefin Epoxidation with Inorganic Peroxides. Solutions to Four Long–Standing Controversies on the Mechanism of Oxygen Transfer. *Acc. Chem. Res.* **2004**, *37*, 645-652.

(45) Antonova, N. S.; Carbó, J. J.; Kortz, U.; Kholdeeva, O. A.; Poblet, J. M. Mechanistic Insights into Alkene Epoxidation with H_2O_2 by Ti– and other TM–Containing Polyoxometalates: Role of the Metal Nature and Coordination Environment. *J. Am. Chem. Soc.* **2010**, *132*, 7488–7497.

(46) Que Jr., L.; Tolman, W. B. Biologically Inspired Oxidation Catalysis. *Nature* **2008**, *455*, 333–340.

(47) Bryliakov, K. P.; Talsi, E. P. Active Sites and Mechanisms of Bioinspired Oxidation with H_2O_2 , Catalyzed by Non–Heme Fe and Related Mn Complexes. *Coord. Chem. Rev.* **2014**, *276*, 73–96.

(48) Ziolek, M.; Sobczak, I.; Decyk, P.; Sobanska, K.; Pietrzyk, P.; Sojka, Z. Search for Reactive Intermediates in Catalytic Oxidation with Hydrogen Peroxide over Amorphous Niobium (V) and Tantalum (V) Oxides. *Appl. Catal. B: Environ.* **2015**, *164*, 288–296.

(49) Thornburg, N. E.; Nauert, S. L.; Thompson, A. B.; Notestein, J. M. Synthesis–Structure–Function Relationships of Silica–Supported Niobium(V) Catalysts for Alkene Epoxidation with H_2O_2 . *ACS Catal.* **2016**, *6*, 6124–6134.

(50) Bregante, D. T.; Priyadarshini, P.; Flaherty, D. W. Kinetic and Spectroscopic Evidence for Reaction Pathways and Intermediates for Olefin Epoxidation on Nb in *BEA. J. Catal. **2017**, *348*, 75–89.

(51) Bregante, D. T.; Flaherty, D. W. Periodic Trends in Olefin Epoxidation over Group IV and V Framework–Substituted Zeolite Catalysts: A Kinetic and Spectroscopic Study. *J. Am. Chem. Soc.* **2017**, *139*, 6888–6898.

(52) Kholdeeva, O. A.; Ivanchikova, I. D.; Maksimchuk, N. V.; Skobelev, I. Y. H_2O_2 -Based Selective Epoxidations: Nb–Silicates versus Ti–Silicates. *Catal. Today* [Online early access]. DOI: 10.1016/j.cattod.2018.04.002. Published Online: Apr 17, 2018. https://www.sciencedirect.com/science/article/pii/S092058611830375 4 (accessed Sept 7, 2018).

(53) Yoon, C. W.; Hirsekorn, K. F.; Neidig, M. L.; Yang, X.; Tilley, T. D. Mechanism of the Decomposition of Aqueous Hydrogen Peroxide over Heterogeneous TiSBA15 and TS–1 Selective Oxidation Catalysts: Insights from Spectroscopic and Density Functional Theory Studies. *ACS Catal.* **2011**, *1*, 1665–1678.

(54) Bordiga, S.; Groppo, E.; Agostini, G.; van Bokhoven, J. A.; Lamberti, C. Reactivity of Surface Species in Heterogeneous Catalysts Probed by In Situ X-ray Absorption Techniques. *Chem. Rev.* **2013**, *113*, 1736–1850.

(55) Bregante, D. T.; Thornburg, N. E.; Notestein, J. M.; Flaherty, D. W. Consequences of Confinement for Alkene Epoxidation with Hydrogen Peroxide on Highly Dispersed Group 4 and 5 Metal Oxide Catalysts. *ACS Catal.* **2018**, *8*, 2995–3010.

(56) Pope, M. T. *Heteropoly and Isopoly Oxometalates*; Springer-Verlag: Berlin, 1983.

(57) Thematic issue on polyoxometalates; Hill, C. L., Guest Ed.; Chem. Rev. 1998, 98, 1–390.

(58) Neumann, R. In: *Transition Metals for Organic Synthesis*, 2nd ed.; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p. 415.

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57 58 59

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(59) Hill, C. L. In: *Comprehensive Coordination Chemistry II*; Wedd, A. G., Ed.; Elsevier Science: New York, 2004; Vol. 4, p. 679.

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57

58 59

60

(60) Thematic issue *Polyoxometalates in Catalysis*; Hill, C. L., Guest Ed.; *J. Mol. Catal. A: Chem.* **2007**, *262*, 1–242.

(61) Mizuno, N.; Kamata, K.; Uchida, S.; Yamaguchi, K. In: *Modern Heterogeneous Oxidation Catalysis: Design, Reactions and Characterization*; Mizuno, N., Ed.; Wiley-VCH: Weinheim, 2009; p. 185.

(62) Thematic issue *Frontiers in Metal Oxide Cluster Science*; Weinstock, I. A., Guest Ed.; *Israel J. Chem.* **2011**, *51*, 169–302.

(63) Themed collection *Polyoxometalate Cluster Science*; Cronin, L., Müller, A., Guest Eds.; *Chem. Soc. Rev.* **2012**, *41*, 7325–7648.

(64) Hill, C. L.; Kholdeeva, O. A. In *Liquid Phase Oxidation via Heterogeneous Catalysis*; Clerici, M. G., Kholdeeva, O. A., Eds.; Wiley: Hoboken, 2013; p. 263.

(65) Sun, M.; Zhang, J.; Putaj, P.; Caps, V.; Lefebvre, F.; Pelletier, J.; Basset, J.-M. Catalytic Oxidation of Light Alkanes (C₁–C₄) by Heteropoly Compounds. *Chem. Rev.* **2014**, *114*, 981–1019.

(66) Wang, S.-S.; Yang, G.-Y. Recent Advances in Polyoxometalate-Catalyzed Reactions. *Chem. Rev.* 2015, *115*, 4893–4962.

(67) Day, V. W.; Klemperer, W. G. Metal Oxide Chemistry in Solution: The Early Transition Metal Polyoxoanions. *Science* **1985**, *228*, 533–541.

(68) Finke, R. G.; Droege, M. W. Trisubstituted Heteropolytungstates as Soluble Metal Oxide Analogues. 1. The Preparation, Characterization, and Reactions of Organic Solvent Soluble Forms of Si₂W₁₈Nb₆O₇₇⁸⁻, SiW₉Nb₃O₄₀⁷⁻, and the SiW₉Nb₃O₄₀⁷⁻ Supported Organometallic Complex [(C₅Me₅)Rh–SiW₉Nb₃O₄₀]⁵⁻. J. Am. Chem. Soc. **1984**, 106, 7274–7277.

(69) Fournier, M.; Louis, C.; Che, M.; Chaquin, P.; Masure, D. Polyoxometallates as Models for Oxide Catalysts: Part I. An UV– visible Reflectance Study of Polyoxomolybdates: Influence of Polyhedra Arrangement on the Electronic Transitions and Comparison with Supported Molybdenum Catalysts. *J. Catal.* **1989**, *119*, 400–414.

(70) Pope, M. T.; Müller, A. Polyoxometalate Chemistry: an Old Field with New Dimensions in Several Disciplines. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 34–48.

(71) Chen, Q.; Zubieta, J. Coordination Chemistry of Soluble Metal Oxides of Molybdenum and Vanadium. *Coord. Chem. Rev.* **1992**, *114*, 107–167.

(72) Baker, L. C. W.; Glick, D. C. Present General Status of Understanding of Heteropoly Electrolytes and a Tracing of Some Major Highlights in the History of Their Elucidation. *Chem. Rev.* **1998**, *98*, 3–50.

(73) Thomas, J. M. Design and Applications of Single-site Heterogeneous Catalysts: Contributions to Green Chemistry, Clean Technology and Sustainability; Imperial College Press: London, 2012.

(74) Kholdeeva, O. A.; Maksimov, G. M.; Maksimovskaya, R. I.;
Kovaleva, L. A.; Fedotov, M. A.; Grigoriev, V. A.; Hill, C. L. Dimeric Titanium–Containing Polyoxometalate. Synthesis, Characterization, and Catalysis of H₂O₂–Based Thioether Oxidation. *Inorg. Chem.* 2000, *39*, 3828–3837.

(75) Kholdeeva, O. A.; Trubitsina, T. A.; Maksimov, G. M.; Golovin, A. V.; Maksimovskaya, R. I. Synthesis, Characterization, and Reactivity of Ti (IV)–Monosubstituted Keggin Polyoxometalates. *Inorg. Chem.* **2005**, *44*, 1635–1642.

(76) Kholdeeva, O. A. Titanium–Monosubstituted Polyoxometalates: Relation Between Homogeneous and Heterogeneous Ti– Single–Site–Based Catalysis. *Top. Catal.* **2006**, *40*, 229–243.

(77) Kholdeeva, O. A.; Maksimovskaya, R. I. Titanium–and Zirconium–Monosubstituted Polyoxometalates as Molecular Models for Studying Mechanisms of Oxidation Catalysis. *J. Mol. Catal. A: Chem.* **2007**, *262*, 7–24. (78) Kholdeeva, O. A. Hydrogen Peroxide Activation over Ti^{IV}: What Have We Learned from Studies on Ti-Containing Polyoxometalates? *Eur. J. Inorg. Chem.* **2013**, 1595–1605.

(79) Guillemot, G.; Matricardi, E.; Chamoreau, L.-M.; Thouvenot, R.; Proust, A. Oxidovanadium (V) Anchored to Silanol–Functionalized Polyoxotungstates: Molecular Models for Single–Site Silica–Supported Vanadium Catalysts. *ACS Catal.* **2015**, *5*, 7415–7423.

(80) Zhang, T.; Mazaud, L.; Chamoreau, L.-M.; Paris, C.; Guillemot, G.; Proust, A. Unveiling the Active Surface Sites in Heterogeneous Titanium–Based Silicalite Epoxidation Catalysts: Input of Silanol–Functionalized Polyoxotungstates as Soluble Analogues. *ACS Catal.* **2018**, *8*, 2330–2342.

(81) Donoeva, B. G.; Trubitsina, T. A.; Antonova, N. S.; Carbó, J. J.; Poblet, J. M.; Al-Kadamany, G.; Kortz, U.; Kholdeeva, O. A. Epoxidation of Alkenes with H_2O_2 Catalyzed by Dititanium-Containing 19-Tungstodiarsenate(III): Experimental and Theoretical Studies. *Eur. J. Inorg. Chem.* **2010**, 5312–5317.

(82) Kholdeeva, O. A.; Trubitsina, T. A.; Timofeeva, M. N.; Maksimov, G. M.; Maksimovskaya, R. I.; Rogov. V. A. The Role of Protons in Cyclohexene Oxidation with H₂O₂ Catalysed by Ti(IV)–Monosubstituted Keggin Polyoxometalate. *J. Mol. Catal. A: Chem.* **2005**, *232*, 173-178.

(83) Jiménez-Lozano, P.; Ivanchikova, I. D.; Kholdeeva, O. A.; Poblet, J. M.; Carbó, J. J. Alkene Oxidation by Ti–Containing Polyoxometalates. Unambiguous Characterization of the Role of the Protonation State. *Chem. Commun.*, **2012**, *48*, 9266–9268.

(85) Rhule, J. T.; Hill, C. L.; Judd, D. A.; Schinazi, R. F. Polyoxometalates in Medicine. *Chem. Rev.* **1998**, *98*, 327–357.

(86) Droege, M. W.; Finke, R. G. A Novel Triperoxyniobium– Containing Polyoxoanion, $SiW_9(NbO_2)_3O_{37}^{7-}$: Synthesis, Characterization, Catalytic Allylic Epoxidations with H_2O_2 and Preliminary Kinetic Studies. *J. Mol. Catal.* **1991**, *69*, 323–338.

(87) Harrup, M. K.; Kim, G.-S.; Zeng, H.; Johnson, R. P.; VanDerveer, D.; Hill, C. L. Triniobium Polytungstophosphates. Syntheses, Structures, Clarification of Isomerism and Reactivity in the Presence of H_2O_2 . *Inorg. Chem.* **1998**, *37*, 5550–5556.

(88) Satake, N.; Hirano, T.; Kamata, K.; Suzuki, K.; Yamaguchi, K.; Mizuno, N. Synthesis, Structural Characterization, and Oxidation Catalysis of a Diniobium–Substituted Silicodecatungstate. *Chem. Lett.* **2015**, *44*, 899–901.

(89) Burcham, L. J.; Datka, J.; Wachs I. E. In Situ Vibrational Spectroscopy Studies of Supported Niobium Oxide Catalysts. *J. Phys. Chem. B* **1999**, *103*, 6015–6024.

(90) Tielens, F.; Shishido, T.; Dzwigaj, S. What Do the Niobium Framework Sites Look Like in Redox Zeolites? A Combined Theoretical and Experimental Investigation. J. Phys. Chem. C 2010, 114, 3140–3147.

(91) Wojtaszek, A.; Ziolek, M.; Tielens, F. Probing Acid–Base Properties in Group V Aluminum Containing Zeolites. *J. Phys. Chem. C* **2012**, *116*, 2462–2468.

(92) Somma, F.; Canton, P.; Strukul, G. Effect of the Matrix in Niobium–Based Aerogel Catalysts for the Selective Oxidation of Olefins with Hydrogen Peroxide. *J. Catal.* **2005**, *229*, 490–498.

(93) Aronne, A.; Turco, M.; Bagnasco, G.; Ramis, G.; Santacesaria, E.; Di Serio, M.; Marenna, E.; Bevilacqua, M.; Cammarano, C.; Fanelli, E. Gel Derived Niobium–Silicon Mixed Oxides: Characterization and Catalytic Activity for Cyclooctene Epoxidation. *Appl. Catal. A Gen.* **2008**, *347*, 179–185.

(94) Flynn, C. M.; Stucky. G. D. Heteropolyniobate Complexes of Manganese(IV) and Nickel(IV). *Inorg. Chem.*, **1969**, *8*, 332–334.

(95) Bannani, F.; Driss, H.; Thouvenot, R.; Debbabi, M. Structural Determination by X–Ray Diffraction and ¹⁸³W NMR Spectroscopy of Mono Substituted Hexatungstates $[(n-C_4H_9)_4N]_3MW_5O_{19}$ (M = Nb,

V). J. Chem. Cryst. 2007, 37, 37-48.
(96) Lu, Y. J.; Lalancette, R.; Beer, R. H. Deoxygenation of Polynuclear Metal–Oxo Anions: Synthesis, Structure, and Reactivity of the Condensed Polyoxoanion [(C₄H₉)₄N]₄(NbW₅O₁₈)₂O. *Inorg. Chem.*, 1996, 35, 2524–2529.

(97) Clegg, W.; Elsegood, M. R. J.; Errington, R. J.; Havelock, J. Alkoxide Hydrolysis as a Route to Early Transition–Metal Polyoxometalates: Synthesis and Crystal Structures of Heteronuclear Hexametalate Derivatives. J. Chem. Soc. Dalton Trans. **1996**, 681–690.

(98) Shul'pin, G. B. Metal–Catalyzed Hydrocarbon Oxygenations in Solutions: The Dramatic Role of Additives: A Review. *J. Mol. Catal. A: Chem.* **2002**, *189*, 39–66.

(99). Gaussian 09, Revision C.01; Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., Scalmani, G., Barone, V., Mennucci, B., Petersson, G. A., Nakatsuji, H., Caricato, M., Li, X., Hratchian, H. P., Izmaylov, A. F., Bloino, J., Zheng, G., Sonnenberg, J. L., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Montgomery Jr., J. A., Peralta, J. E., Ogliaro, F., Bearpark, M., Heyd, J. J., Brothers, E., Kudin, K. N., Staroverov, V. N., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A., Burant, J. C., Iyengar, S. S., Tomasi, J., Cossi, M., Rega, N., Millam, J. M., Klene, M., Knox, J. E., Cross, J. B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R. E., Yazyev, O., Austin, A. J., Cammi, R., Pomelli, C., Ochterski, J. W., Martin, R. L., Morokuma, K., Zakrzewski, V. G., Voth, G. A., Salvador, P., Dannenberg, J. J., Dapprich, S., Daniels, A. D., Farkas, O., Foresman, J. B., Ortiz, J. V., Cioslowski, J., Fox, D. J., Eds.; Gaussian Inc.: Wallingford CT, 2010.

(100) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle– Salvetti Correlation–Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, *37*, 785–789.

(101) Becke, A. D. Density-Functional Thermochemistry. III. The Role of Exact Exchange. J. Chem. Phys. **1993**, *98*, 5648–5652.

 (102) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M.
 J. Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* 1994, *98*, 11623–11627.

(103) Hay, P. J.; Wadt, W. R. Ab Initio Effective Core Potentials for Molecular Calculations. Potentials for K to Au Including the Outermost Core Orbitals. *J. Chem. Phys.* **1985**, *82*, 299–310.

(104) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. Self-Consistent Molecular Orbital Methods. XXIII. A Polarization-Type Basis Set for Second-Row Elements. J. Chem. Phys. **1982**, *77*, 3654–3665.

(105) Hehre, W. J.; Ditchfield, R.; Pople, J. A. Self—Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian— Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. J. Chem. Phys. **1972**, *56*, 2257–2261.

(106) Hariharan, P. C.; Pople, J. A. The Influence of Polarization Functions on Molecular Orbital Hydrogenation Energies. *Theoret. Chim. Acta* **1973**, *28*, 213–222.

(107) López, X.; Carbó, J. J.; Bo, C.; Poblet, J. M. Structure, Properties and Reactivity of Polyoxometalates: a Theoretical Perspective. *Chem. Soc. Rev.* **2012**, *41*, 7537–7571.

(108) Skobelev, I. Y.; Zalomaeva, O. V.; Kholdeeva, O. A.; Poblet,
J. M.; Carbó, J. J. Mechanism of Thioether Oxidation over Di-and Tetrameric Ti Centres: Kinetic and DFT Studies Based on Model Ti– Containing Polyoxometalates. *Chem.-Eur. J.* 2015, *21*, 14496–14506.

(109) Skobelev, I. Y.; Evtushok, V. Y.; Kholdeeva, O. A.;
Maksimchuk, N. V.; Maksimovskaya, R. I.; Ricart, J. M.; Poblet, J. M.; Carbó, J. J. Understanding the Regioselectivity of Aromatic

Hydroxylation over Divanadium–Substituted γ–Keggin Polyoxotungstate. *ACS Catal.* **2017**, *7*, 8514–8523.

(110) Yanai, T.; Tew, D. P.; Handy, N. C. A New Hybrid Exchange–Correlation Functional Using the Coulomb–Attenuating Method (CAM–B3LYP). *Chem. Phys. Lett.* **2004**, 393, 51–57.

(111) Tissandier, M. D.; Cowen, K. A.; Feng, W. Y.; Gundlach, E.; Cohen, M. H.; Earhart, A. D.; Coe J. V. The Proton's Absolute Aqueous Enthalpy and Gibbs Free Energy of Solvation from Cluster–Ion Solvation Data *J. Phys. Chem. A*, **1998**, *102*, 7787-7794.

(112) Perdew, J. P.; Burke, K.; Ernzerhof, M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.*, **1996**, *77*, 3865–3868.

(113) ADF2017, SCM, Theoretical chemistry, Vrije Universiteit, Amsterdam, The Netherlands [Online]. https://www.scm.com (accessed Sept 7, 2018).

(114) Feliczak, A.; Walczak, K.; Wawrynczak, A.; Nowak, I. The Use of Mesoporous Molecular Sieves Containing Niobium for the Synthesis of Vegetable Oil–Based Products. *Catal. Today* **2009**, *140*, 23–29.

(115) Tiozzo, C.; Bisio, C.; Carniato, F.; Marchese, L.; Gallo, A.; Ravasio, N.; Psaro, R.; Guidotti, M. Epoxidation with Hydrogen Peroxide of Unsaturated Fatty Acid Methyl Esters over Nb (V)–Silica Catalysts. *Eur. J. Lipid Sci. Technol.* **2013**, *115*, 86–93.

(116) Kholdeeva, O. A.; Kovaleva, L. A.; Maksimovskaya, R. I.; Maksimov. G. M. Kinetics and Mechanism of Thioether Oxidation with H_2O_2 in the Presence of Ti(IV)–Substituted Heteropolytung-states. *J. Mol. Catal. A: Chem.* **2000**, *158*, 223–229.

(117) Bayot, D.; Tinant, B.; Mathieu, B.; Declercq, J.-P.; Devillers M. Spectroscopic and Structural Characterizations of Novel Water–Soluble Peroxo[polyaminocarboxylato bis(*N*-oxido)]niobate(V) Complexes. *Eur. J. Inorg. Chem.* **2003**, 737–743.

(118) Maniatakou, A.; Makedonas, C.; Mitsopoulou, C. A.; Raptopoulou, C.; Rizopoulou, I.; Terzis, A.; Karaliota A. Synthesis, Structural and DFT Studies of a Peroxo–Niobate Complex of the Biological Ligand 2–Quinaldic Acid. *Polyhedron* **2008**, *27*, 3398– 3408.

(119) Papulovskiy, E.; Shubin, A. A.; Terskikh, V. V.; Pickard, C. J.; Lapina, O. B. Theoretical and Experimental Insights into Applicability of Solid–State ⁹³Nb NMR in Catalysis. *Phys. Chem. Chem. Phys.* **2013**, *15*, 5115–5131.

(120) Besecker, C. J.; Klemperer, W. G.; Maltbie, D. J.; Wright, D. A. ¹⁷O Nuclear Magnetic Resonance Spectroscopy of Polyoxometalates. 2. Heteronuclear Decoupling of Quadrupolar Nuclei. *Inorg. Chem.* **1985**, *24*, 1027–1032.

(121) Ma, W.; Yuan, H.; Wang, H.; Zhou, Q.; Kong, K.; Li, D.; Yao, Y.; Hou, Z. Identifying Catalytically Active Mononuclear Peroxoniobate Anion of Ionic Liquids in the Epoxidation of Olefins. *ACS Catal.* **2018**, *8*, 4645–4659.

(122) Adler, N.; Hiskey, C. F. Spectra of the Peroxy Complexes of Niobium in Sulfuric Acid. J. Am. Chem. Soc. **1957**, *79*, 1827–1830.

(123) Finke, R. G.; Rapko, B.; Saxton, R. J.; Domaille, P. J. Trisubstituted Heteropolytungstates as Soluble Metal Oxide Analogs. III. Synthesis, Characterization, ³¹P, ²⁹Si, ⁵¹V, and 1– and 2–D ¹⁸³W NMR, Deprotonation, and Proton Mobility Studies of Organic Solvent Solute Forms of $H_xSiW_9V_3O_{40}^{x-7}$ and $H_xP_2W_{15}V_3O_{62}^{x-9}$. J. Am. Chem. Soc. **1986**, *108*, 2947–2960.

(124) Kholdeeva, O. A.; Trubitsina, T. A.; Maksimovskaya, R. I.; Golovin, A. V.; Neiwert, W. A.; Kolesov, B. A.; López, X.; Poblet, J. M. First Isolated Active Titanium Peroxo Complex: Characterization and Theoretical Study. *Inorg. Chem.* **2004**, *43*, 2284–2292.

(125) Bayot, D.; Devillers, M.; Peeters, D. Vibrational Spectra of Eight-Coordinate Niobium and Tantalum Complexes with Peroxo Ligands: A Theoretical Simulation. *Eur. J. Inorg. Chem.* **2005**, 4118–4123.

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54

55

56

57 58 59

60

ACS Catalysis

(126) Bayot, D.; Devillers, M. Peroxo Complexes of Niobium(V) and Tantalum(V). *Coord. Chem. Rev.* **2006**, *250*, 2610–2626.

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6

7

8

9

10

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54

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58 59

60

(127) Wang, H.; Liang, Z.; Wang, Y.; Zhang, D.; Ma, P.; Wang J. Niu, J. Insight into the Reactivity of In Situ Formed {(NbO₂)₃SiW₉}: Synthesis, Structure, and Solution Properties of a Trimeric Polytungstosilicate Trapping a {MnNb₉} Core. *Dalton Trans.*, **2016**, *45*, 15236–15241.

(128) Lachter, E. R.; San Gil, R. A. S.; Kaiser, C. R.; Leite, M A. B.; Nunes, A. S.; Fernandes, R. M.; Gelbard, G. Synthesis and Characterization of Niobium Complexes Employed as Homogeneous Oxidation Catalysts by ³¹P and ⁹³Nb Nuclear Magnetic Resonance. *Ann. Magn. Reson.* **2007**, *6*, 40–45.

(129) Geng, Q.; Liu, Q.; Ma, P.; Wang, J.; Niu, J. Synthesis, Crystal Structure and Photocatalytic Properties of an Unprecedented Arsenic–Disubstituted Lindqvist–Type Peroxopolyoxoniobate Ion: $\{As_2Nb_4(O_2)_4O_{14}H_{1.5}\}^{4.5-}$. *Dalton Trans.* **2014**, *43*, 9843–9846.

(130) Gogoi, S. R.; Boruah, J. J.; Sengupta, G.; Saikia, G.; Ahmed, K.; Bania K. K.; Islam, N. S. Peroxoniobium(V)–Catalyzed Selective Oxidation of Sulfides with Hydrogen Peroxide in Water: a Sustainable Approach. *Catal. Sci. Technol.* **2015**, *5*, 595–610.

(131) Chen, C.; Yuan, H.;Wang, H.; Yao, Y.; Ma, W.; Chen, J.; Hou Z. Highly Efficient Epoxidation of Allylic Alcohols with Hydrogen Peroxide Catalyzed by Peroxoniobate–Based Ionic Liquids. ACS Catal. 2016, 6, 3354–3364.

(132) Day, V. W.; Klemperer, W. C.; Schwartz, C. Synthesis, Characterization, and Interconversion of the Niobotungstic Acid Nb₂W₄O₁₉H³⁻ and Its Anhydride and Alkyl/Silyl Esters. *J. Am. Chem. Soc.* **1987**, *109*, 6030–6044.

(133) Narendar, Y.; Messing, G. L. Synthesis, Decomposition and Crystallization Characteristics of Peroxo–Citrato–Niobium: an Aqueous Niobium Precursor. *Chem. Mater.* **1997**, *9*, 580–587.

(134) Thomadaki, H.; Lymberopoulou-Karaliota, A.; Maniatakou, A.; Scorilas, A. Synthesis, Spectroscopic Study and Anticancer Activity of a Water–Soluble Nb(V) Peroxo Complex. J. Inorg. Biochem. 2011, 105, 155–163.

(135) Chen, C.; Zhao, X.; Chen, J.; Hua, L.; Zhang, R.; Guo, L.; Song, B.; Gan, H.; Hou, Z. Niobium Peroxide-Catalyzed Selective Epoxidation of Allylic Alcohols. *ChemCatChem* **2014**, *6*, 3231–3238.

(136) Errington, R. J. Nonaqueous Polyoxometalate Synthesis for Systematic Studies of Hydrolysis, Protonation, and Reduction. *Adv. Inorg. Chem.* **2017**, *69*, 287–336.

(137) Pascual-Borràs, M.; López, X.; Rodríguez-Fortea, A.; Errington, R. J.; Poblet, J. M. ¹⁷O NMR Chemical Shifts in Oxometalates: From the Simplest Monometallic Species to Mixed–Metal Polyoxometalates. *Chem. Sci.* **2014**, *5*, 2031–2042.

(138) Jiménez-Lozano, P.; Carbó, J. J.; Chaumont, A.; Poblet, J. M.; Rodríguez-Fortea, A.; Wipff. G. Nature of Zr–Monosubstituted Monomeric and Dimeric Polyoxometalates in Water Solution at Different pH Conditions: Static Density Functional Theory Calculations and Dynamic Simulations. *Inorg. Chem.* **2014**, *53*, 778–786.

(139) Jiménez-Lozano, P.; Skobelev, I. Y.; Kholdeeva, O. A.; Poblet, J. M.; Carbó, J. J. Alkene Epoxidation Catalyzed by Ti-Containing Polyoxometalates: Unprecedented β–Oxygen Transfer Mechanism. *Inorg. Chem.* **2016**, *55*, 6080–6084.

(140) López, X.; Miró, P.; Carbó, J. J.; Rodríguez-Fortea, A.; Bo C.; Poblet, J. M. Current Trends in the Computational Modelling of Polyoxometalates. *Theor. Chem. Acc.*, **2011**, *128*, 393–404.

(141) López, X.; Fernández, J. A.; Poblet, J. M. Redox Properties of Polyoxometalates: New Insights on the Anion Charge Effect. *Dalton Trans.* 2006, 1162–1167.

(142) Solé-Daura, A.; Goovaerts, V.; Stroobants, K.; Absillis, G.; Jiménez-Lozano, P.; Poblet, J. M.; Hirst, J. D.; Parac-Vogt, T. N.; Carbó, J. J. Probing Polyoxometalate–Protein Interactions Using Molecular Dynamics Simulations. *Chem.–Eur. J.* 2016, 22, 15280– 15289. SYNOPSIS TOC

