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ARTICLE

Unprecedented HAT Rate Acceleration in Water by a Non-heme Manganese Oxo Complex

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Nature employs water as the reaction medium for enzymatic redox transformations, taking advantage of its unique physicochemical properties to precisely regulate reaction kinetics, selectivity, and proton-coupled electron transfer. In a biomimetic endeavour, using a newly developed non-heme (Et₄N)[Mn^{IV}(O)(Ph,Me-bTAML)] complex, we report a water-induced, enzyme-like rate acceleration in hydrogen atom transfer (HAT) reactivity with various substrates possessing BDEs of 67–78 kcal/mol. In acetonitrile, the reactivity is sluggish, but switching to water – particularly beyond 85% content – results in a dramatic rate enhancement, peaking in pure water with up to a 20,000-fold increase. This effect occurs without any structural changes or addition of external additives. Mechanistic insights suggest that water stabilises the minimum energy crossing point (MECP) more effectively than acetonitrile through enhanced electrostatics and hydrogen bonding in transition-state energetics. This is the first demonstration of a non-heme Mn(V)-oxo complex mimicking enzymatic rate enhancement solely via solvent modulation. The work highlights water's active role in driving selective, efficient, and green oxidation chemistry, unlocking new potential in bioinspired catalysis.

Introduction

Water acts as a safe, non-toxic, inexpensive, and environmentally benign alternative reaction medium for a broad range of organic transformations.¹ Green chemistry emphasises the use of water as an environmentally benign, non-toxic, and renewable solvent to replace hazardous organic solvents, thereby reducing pollution and enhancing sustainability in chemical processes.² In addition, seminal work by Breslow et al. in the 1980s has shown that water can enhance reaction rates and greater selectivity compared to classical organic solvents.^{3, 4} Nature harnesses the distinctive physical and chemical properties of water to control the rate, selectivity, and mass-transfer dynamics of enzymatic reactions by stabilising reactive intermediates through hydrogen bonding and enabling efficient proton-transfer pathways.^{5–8} Although these reactions take place in an aqueous environment, they are primarily influenced not by the bulk properties of water but by the hydrophobic pocket of the globular protein surrounding the active site.^{9–12} However, in certain enzymatic systems, such as in the oxidation of chromopyrrolic acid (CPA) by cytochrome

P450 StaP, a structured, confined water network forms within the hydrophobic pocket near the redox-active centre, playing a crucial role in modulating electron and proton transfer processes.¹³

Beyond biology, water has become a sustainable solvent that replaces toxic organics while reducing pollution and improving reaction efficiency.¹⁴ Previously, it was found that many pericyclic reactions, such as Diels-Alder cycloadditions and Claisen rearrangements of organic compounds, were accelerated in an aqueous medium.¹⁵ In 2005 K. Barry Sharpless reported the cycloaddition reaction between the DMAD and quadricyclane at 'On Water' conditions, which shows a high-rate acceleration at ambient conditions than in different polar and non-polar organic media (even under neat conditions).¹⁶ The accelerated rates of organic reactions in aqueous environments, particularly in "on-water" mechanisms, arise from several key factors such as the hydrophobic effect and solvophobicity, stabilisation of transition states through hydrogen bonding, and high cohesive energy density.^{17, 18} The partial polarisation at the solvent-solute interface due to sudden exchange of protons via grotthius mechanism, would lay the reactants and catalysts in definite orientations, forming highly oriented transition states, which also favour the high rate acceleration.^{3, 19} These characteristics underline water's pivotal role as an environmentally friendly solvent, enhancing the reactivity of organic and inorganic compounds in aqueous suspension.

Sen Gupta and co-workers have developed novel catalysts with biuret tetra-amido macrocyclic ligand (bTAML), capable of performing challenging oxidative organic transformations and catalytic water oxidation in organic solvents (CH₃CN) by

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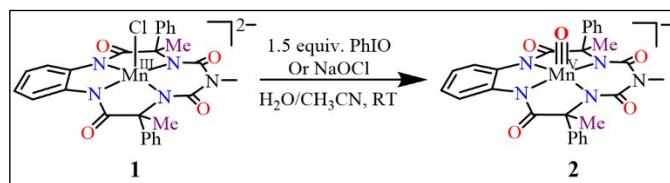
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



stabilising an Fe(V)-oxo intermediate at room temperature.²⁰⁻²⁶ In 2023, they introduced a modified complex, $(\text{Et}_4\text{N})_2[\text{Fe}(\text{Cl})(\text{Ph},\text{Me-bTAML})]$, which enables regio and stereoretentive oxidation of unactivated C–H bonds in 100% water using H_2O_2 effectively mimicking the cytochrome P450 enzymes.²⁵ The proposed Fe(V)-oxo intermediate for this reaction was successfully trapped in water using *m*CPBA, exhibiting a half-life ($t_{1/2}$) of approximately 6 seconds at 298 K. Interestingly, in pure water, the intermediate demonstrated nearly 300 times higher reactivity toward the 6-methylheptan-2-yl isonicotinate substrate compared to its behaviour in acetonitrile.²⁵ The remarkable rate enhancement observed for the high-valent Fe(V)-oxo complexes naturally sparks a strong sense of curiosity to explore the role of water in driving such extraordinary reactivity. However, despite these advancements, the instability of the Fe(V)-oxo intermediate in pure water posed significant challenges, limiting a comprehensive investigation of its thermodynamic and kinetic properties. This limitation redirected attention toward manganese-based complexes, which offer a more stable Mn(V)-oxo intermediate,²⁷ paving the way for further exploration and breakthroughs. By treating $[\text{Et}_4\text{N}]_2[\text{Mn}^{\text{III}}(\text{Cl})(\text{Ph},\text{Me-bTAML})]$ with iodosyl benzene or NaOCl, a high-valent Mn(V)-oxo complex was generated, demonstrating a dramatic change in kinetic properties in changing the solvent from acetonitrile to water. The Mn(V)-oxo complex showed an astonishing up to twenty-thousand-fold rate increase in hydrogen atom transfer (HAT) reactions in water compared to organic solvent, CH_3CN . This dramatic rate enhancement was attributed to favourable activation enthalpy and a structured transition state enabled by water's hydrogen-bonding network. Our results highlight the unique potential of Mn-oxo complexes for efficient C–H bond oxidation in aqueous media. To the best of our knowledge, this work represents the first demonstration of such a remarkable HAT rate enhancement in pure water using a non-heme metal-oxo complex. Importantly, this acceleration was achieved without any structural modification of the complex or the involvement of redox-active/inactive metal ions, Lewis acids, or Brønsted acids — arising solely from solvent modulation.²⁸⁻³⁷ This finding underscores a greener and more sustainable approach for tuning reactivity in bioinspired oxidation chemistry.

Results and Discussion

Generation and characterisation of $(\text{Et}_4\text{N})[\text{Mn}^{\text{V}}(\text{O})(\text{Ph},\text{Me-bTAML})]$, **2**



Scheme 1: Schematic diagram for the synthesis of complex $(\text{Et}_4\text{N})[\text{Mn}^{\text{V}}(\text{O})(\text{Ph},\text{Me-bTAML})]$, **2** from **1**.

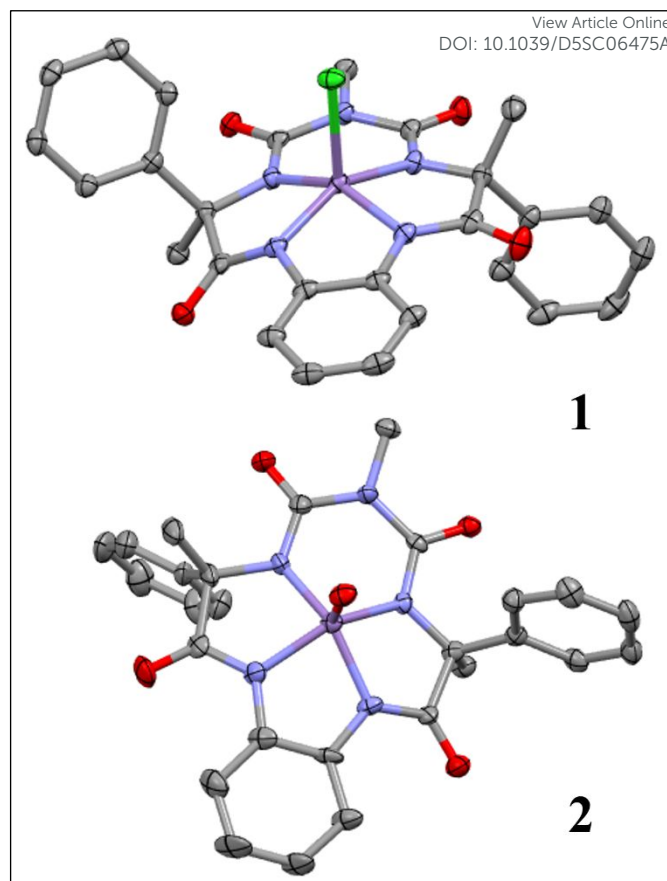


Figure 1. X-ray crystal structures of both **1** and **2** with ellipsoid probability 50% and 40% respectively (hydrogens, solvent molecules, tetraethyl ammonium molecules are omitted for clarity).

The (Ph,Me-bTAML) ligand was synthesised by following the previously reported procedure.²⁵ A new Mn-bTAML complex $[\text{Et}_4\text{N}]_2[\text{Mn}^{\text{III}}(\text{Cl})(\text{Ph},\text{Me-bTAML})]$, **1**, was synthesised by mixing an excess amount of anhydrous MnCl_2 to the solution of ligand (Ph,Me-bTAML) and *n*-BuLi in THF at 0 °C (Detailed procedure is described in the SI, Experimental results section 4A). The resulting complex was purified and subsequently characterised by UV-vis, ESI-MS (Figure 2A, Figure S1) and X-ray crystallography (Figure 1). Treatment of **1** with 1.5 equiv. of iodosylbenzene (PhIO) or NaOCl, either in 100% CH_3CN or water (or mixtures of CH_3CN -water) under ambient conditions (d^2 system, diamagnetic confirmed by EPR and NMR, Figures S7-8) generated a nonheme Mn(V)-oxo complex, **2**, which was highly stable at room temperature in both solvents. High stability of the complex allowed us to characterise this using single crystal X-ray crystallography (Figure 1, see SI, Experimental results section 4B) and various other spectroscopic techniques. The UV-vis absorption spectrum of this Mn(V)-oxo complex displayed λ_{max} of 442 nm ($\epsilon = 4500 \text{ M}^{-1} \text{ cm}^{-1}$) in 100% CH_3CN and 432 nm in 100% water (Figure 2A). HRMS of **2** at negative mode, in both CH_3CN and water medium, exhibited a major peak at $m/z = 552.1038$ corresponding to the formation of



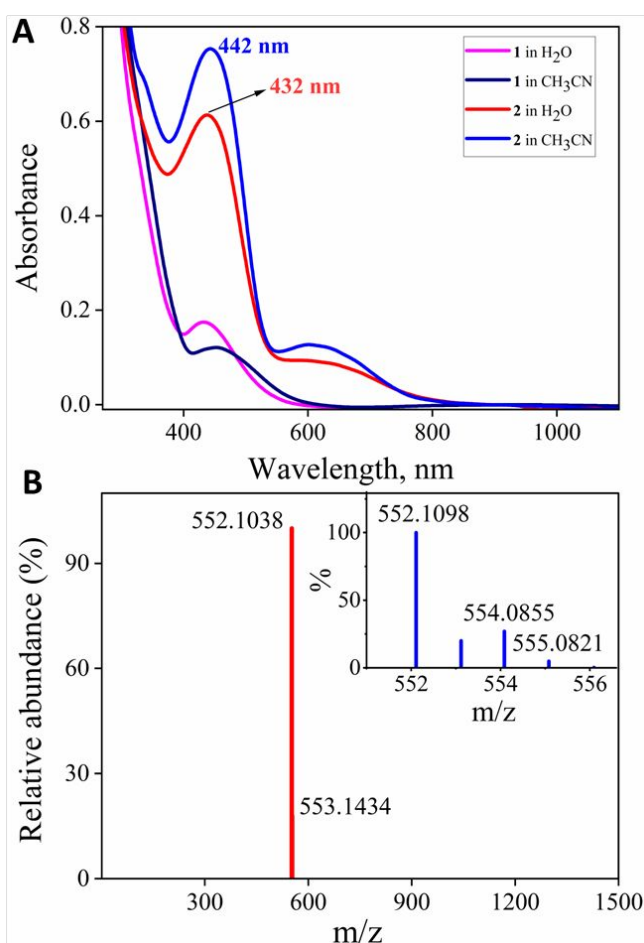
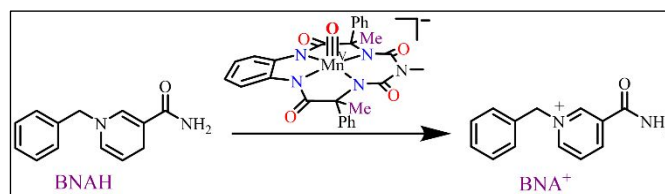


Figure 2. A. UV-vis spectra of **2**, both in 100% CH₃CN and water from **1** at RT. B. Negative mode HRMS spectrum of **2** (0.05 mM) in water and mass spectrum of **2** in H₂O¹⁸ (inset).

[Mn^V(O)(Ph,Me-bTAML)]⁻ [Calculated m/z = 552.11] (Figure 2B). When **2** was stirred in H₂O¹⁸, a mass peak corresponding to [Mn^V(¹⁸O)(Ph,Me-bTAML)]⁻ (~27%) appeared at m/z = 554.0855 [Calculated m/z = 554.11], along with the mass peak of [Mn^V(O)(Ph,Me-bTAML)]⁻ (Figure 2B). The short Mn–O bond length of 1.556(7) Å in the X-ray crystal structure of **2** (Figure 1; see SI Tables S7 and S8) is consistent with the Mn–O triple bond character. The rRaman spectrum of complex **2** performed upon excitation at 413 nm at 78 K, revealed a single isotopically sensitive band for Mn–O stretch at 979 cm⁻¹ in water, which shifted to 939 cm⁻¹ upon using H₂O¹⁸ (Figure S5). The observed isotopic shift of 40 cm⁻¹ upon ¹⁸O labelling was consistent with the predicted shift of the Mn–O stretch using Hooke's law, confirming the presence of a triple Mn–O bond character.²⁷ Single crystal X-ray studies indicate Mn in a slightly distorted square-pyramidal geometry, which arises from the axial oxo ligand and the four amido–N ligands (Mn–N average distance of 1.8645 Å). Taken together, **2** is a low-spin (*S* = 0) Mn(V)-oxo complex with Mn–O triple bond character.

Reactivity studies of **2** towards C–H bonds and Mechanistic investigation

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Scheme 2: Schematic diagram for the reaction of **2** (0.05 mM) with BNAH.

The HAT reactivity of **2** was investigated with a range of C–H bond substrates in both CH₃CN and water. To compare second-order reaction rates, a common substrate soluble in both solvents was selected. 1-Benzyl-1,4-dihydronicotinamide (BNAH) was chosen as the primary substrate for these comparative studies in aqueous media owing to its solubility. This property enabled the investigation of pseudo-first-order kinetics under homogeneous conditions. The addition of BNAH to a solution containing **2** in CH₃CN led to a very slow decay of

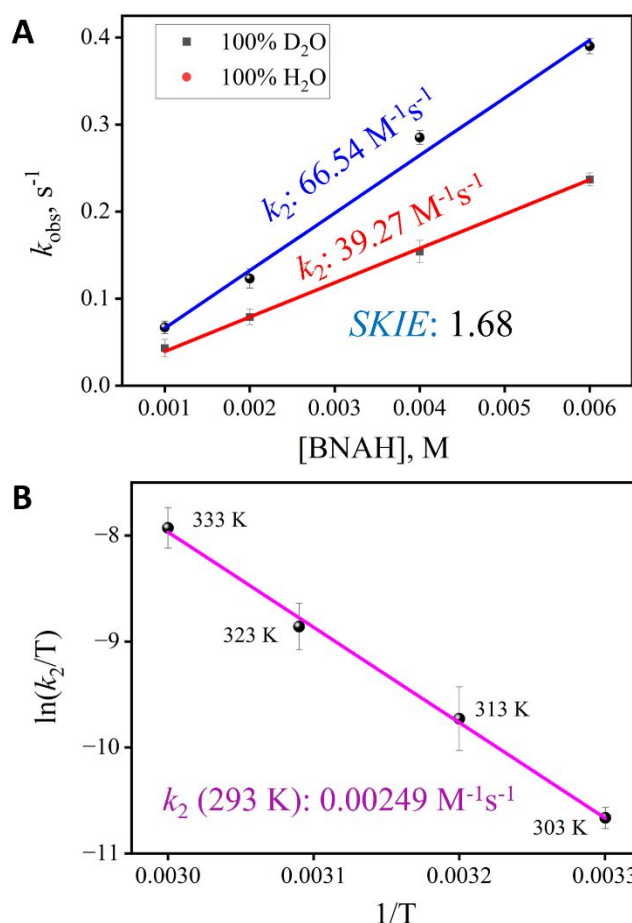


Figure 3. A. Plot of *k*₂ value for the reaction of **2** (0.05 mM) with varying [BNAH] at 293 K, in H₂O and D₂O, to determine the solvent kinetic isotope effect. B. Determination of *k*₂ at 293 K for reaction **2** (0.05 mM) with BNAH in pure acetonitrile solvent from the Eyring plot.



the characteristic UV-vis peak at 442 nm, which enabled us to obtain the pseudo-first-order rate constants over the temperature range 333–303 K (Figure S11, S14). At 293 K, the kinetics of this reaction was very slow to reliably determine pseudo-first-order rate constants. Notably, the Mn(V)-oxo species remained stable even at these elevated temperatures, ensuring the absence of any background rates (Figure S4). In contrast, a much rapid decay of the characteristic UV-vis peak at 432 nm was observed when the same reaction was carried out in 100% water at 293 K (Figure S11). The second-order rate constants (k_2) were subsequently determined by plotting the pseudo-first-order rate constants (k_{obs}) as a function of the relative increase of the substrate concentration at 293 K (Figure 3A, Figure S17). In both H_2O and CH_3CN , the reaction of complex **2** with BNAH formed BNA^+ with the concomitant

exponentially from 80% water, and saturates at 95%, giving a sigmoidal curve (Figure 4). This indicates that a particular water concentration ($\geq 90\%$) was required for such a large rate acceleration.

In addition to BNAH (67 kcal/mol), the comparison of HAT reactivity in both media towards different C–H bond substrates, including 9,10-dihydroacridine (AcrH₂) (72 kcal/mol), xanthene (75.5 kcal/mol), and 9,10-dihydroanthracene (DHA) (78 kcal/mol), was also studied at room temperature.^{39–41} Product formation was detected by GC-MS under single turnover

k' ($k_{\text{H}_2\text{O}} / k_{\text{CH}_3\text{CN}}$)	Substrates			
	^a BNAH	^b 9,10 AcrH ₂	^b Xanthene	^b 9,10 DHA
	26,700	3500	4700	5000

Table 1. Determination of the rate enhancement factor (k') for complex **2** (0.4 mM) with different C–H bond substrates in both solvents at RT. Relative rates (k') were determined either from second-order rate constants (a) or from initial rate constant values (b).

condition (Table S9). These substrates span a narrow range of C–H bond dissociation energies ($\text{BDE}_{\text{C-H}}$) from 70 to 78 kcal mol^{−1} and hence should elucidate the thermodynamics behind the HAT reaction rates by **2**. Next, we plotted the natural logarithm of the initial rate constants (Figure S21) [Initial rates are calculated by checking the formation of product concentration using GC-MS at different time intervals] for HAT by **2** versus the $\text{BDE}_{\text{C-H}}$ of the substrates (Figures S20, S22–25, Table 1). The linearity and the nonzero slope value of the Bell-Evans-Polanyi plot ($\log k_2$ versus $\text{BDE}_{\text{C-H}}$) gives evidence of a rate-determining step involving hydrogen atom abstraction reaction (Figure S21). Again, in water, the reaction rates of **2** with 9,10-dihydroacridine, xanthene, and 9,10-dihydroanthracene increased remarkably, reaching values 3500, 4700, and 5000 times higher, respectively, than those observed in the acetonitrile medium (Table 1, SI Table S11).

To gain further insight into the reaction mechanism, the HAT of BNAH-4,4'-d₂ with **2** was studied, and KIE of 11 was obtained (Figure S28). The process of hydrogen atom abstraction generally involves the simultaneous transfer of a proton and electron. The 10⁴-fold acceleration in reactivity, compared to other C–H bond substrates (10³-fold), can be attributed to the redox potential of BNAH being less than 1 V.⁴² This value closely aligns with the redox potential of complex **2**, facilitating a reaction primarily driven by asynchronous electron transfer-proton transfer (ET-PT).⁴³ However, a significant KIE implies that the proton transfer plays a significant role in determining the rate of oxidation of C–H bonds by **2** which is consistent with the earlier report.⁴⁴ The reaction of BNAH with **2** accelerates by a factor of 1.64 when lithium chloride is added to the aqueous solvent, while it decelerates by a factor of 4.59 upon the addition of guanidinium chloride (Figure S19, S29). This observation highlights the role of the Breslow hydrophobic

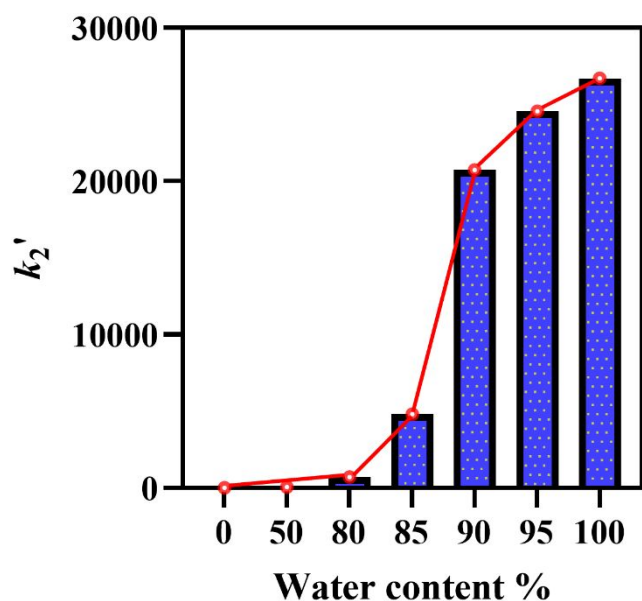


Figure 4. Graphical representation of relative second-order rate constant values (k_2') for the reaction of **2** (0.05 mM) with BNAH at 293 K at different water ratios where $k_2' = k_{2, \text{H}_2\text{O}} / k_{2, \text{CH}_3\text{CN}}$.

regeneration of complex **1** (detected via water HRMS, Figure S31–32). To compare the reactivity of complex **2** with BNAH in both CH_3CN and H_2O , we chose 293 K as the temperature, since at temperatures of 303 K and above, the reactivity in 100% water was too fast for reliable determination of k_2 . The k_2 value for the reaction in 100% CH_3CN at 293 K was therefore obtained by extrapolating the linear Eyring plot to 293 K (Figure 3B). Remarkably, the reaction of compound **2** with BNAH was 26,700 times faster in water than in CH_3CN at 293 K. The kinetic investigation using BNAH was also carried out in deuterated water to determine the SKIE value. The SKIE value of 1.68 (Figure 3A), which was corrected by taking into account both the concentrations of water and deuterated water,³⁸ indicates the stabilisation of the transition state with the hydrogen bonding network. Kinetic studies of **2** with BNAH were also carried out in different CH_3CN -water mixtures to understand the impact of increasing water concentration at 293 K (Figure S12–13). Remarkably, the rate enhancement occurs



effect as a contributing factor to the rate enhancement observed when transitioning to water from organic solvent.¹⁸

Determination of thermodynamic parameters for BNAH oxidation with **2**

For a better understanding of the transition state, variable-temperature kinetic measurements were carried out for BNAH oxidation to determine the activation parameters (Figure 3B, Figure S16) on the basis of Eyring plots for the rate constants. According to the activation parameters for BNAH oxidation with **2** in CH₃CN ($\Delta H^\ddagger = 17.81 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -2.80 \text{ kcal mol}^{-1}$; 293 K) and 100% H₂O ($\Delta H^\ddagger = 7.53 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -7.26 \text{ kcal mol}^{-1}$; 293 K), the twenty-thousand-fold increase in the reaction rate is mainly governed by the favourable activation enthalpy terms (a gain of $10.27 \text{ kcal mol}^{-1}$ in ΔH^\ddagger). In contrast, the contribution of the activation entropy (as loss of $4.46 \text{ kcal mol}^{-1}$ in ΔS^\ddagger) to the transition state is negative in water. Because the enthalpy gain is 2.30 times greater than the entropic loss, a favourable Gibbs energy of activation, ΔG^\ddagger , leads to rate acceleration in water. The gain in enthalpy with a concomitant loss in entropy indicates the formation of an ordered transition state involving water molecules.

Understanding the perturbation of redox potential and pKa with change in solvent

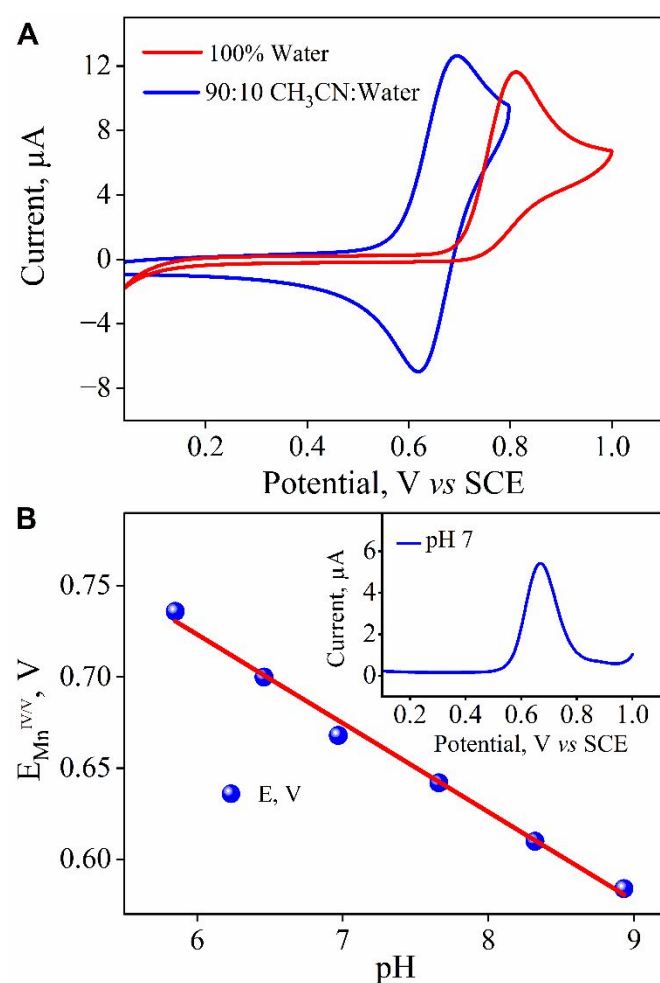
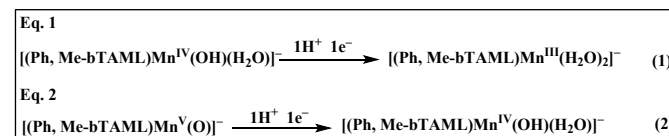


Figure 5. **A.** CV of **1** (0.5 mM) both in 9:1 CH₃CN:H₂O and 100% water using glassy carbon as working and Pt wire as counter electrode at RT (scan towards positive direction). **B.** Plot of Mn(IV)/Mn(V) redox potential vs. pH in water with slope of 49 mV/unit, indicating a $1\text{H}^+/1\text{e}^-$ PCET process; inset shows DPV data of **1**.

The dramatic change in reactivity upon switching the solvent from CH₃CN to water may stem from changes in the pKa of the “oxo” group in the Mn(V)-oxo or the shift in the Mn(IV)/Mn(V) redox potential. To probe this, rRaman spectroscopy was employed to monitor the Mn–O stretch, which can be a reflection of its pKa, in both solvents. Upon excitation at 413 nm at 78 K, **2** revealed a Mn–O stretching vibration at 972 cm^{-1} in CH₃CN, which shifted slightly to 979 cm^{-1} in water (Figure S5). This minor shift upon switching the solvent to water suggests that changes in pKa are unlikely to drive the observed increase in HAT reactivity in water.

Next, the redox behaviour of complex **1** was evaluated by cyclic voltammetry (CV) in both 9:1 CH₃CN:H₂O and 100% water, using a glassy carbon working electrode and a platinum wire counter electrode (Figure 5A). In H₂O, a quasi-reversible one-electron wave at $E_{1/2} = 0.76 \text{ V}$ vs SCE was observed by cyclic voltammetry. Controlled-potential electrolysis (CPE) performed at 0.8 V vs SCE led to the formation of the dark green Mn(V)-oxo that fully resembled **2** (Figure S9). Further, differential pulse voltammetry (DPV) in water revealed a pH-dependent shift in this redox couple with a slope of 49 mV per pH unit (Figure 5B), indicative of a proton-coupled electron transfer (PCET) process involving $1\text{H}^+/1\text{e}^-$.^{45–47} This led us to conclude that in 100% water, this feature in CV corresponds to Mn^V(O)/Mn^{IV}(OH) couple (see Eq. 2 below). Similarly, the Mn(III/IV) couple was detected using a gold working electrode⁴⁸ and exhibited the same pH dependence (49 mV/pH unit), further supporting the involvement of $1\text{H}^+/1\text{e}^-$ PCET process (Eq. 1 below, Figure S10). In 9:1 CH₃CN:H₂O, the Mn(IV/V) couple was observed at $E_{1/2} = 0.66 \text{ V}$ vs SCE and CPE at this potential also led to the formation of **2**. Overall, the formation of **2** from **1** is governed by sequential PCET events, as assigned based on the observed redox couples. It is important to note that in both solvents, the Mn(IV/V) redox couple appeared at a close redox potential ($\Delta E_{1/2} = 100 \text{ mV}$) (Figure 5A). The striking 10^4 order enhancement in reactivity upon moving from CH₃CN to water, despite minimal changes in redox potential, unequivocally rules out redox tuning as the predominant driving force.



Theoretical Insight

The reaction pathway was further studied employing density functional theory (DFT) to gain additional insight into the dramatic increase in the reaction rate upon changing the solvent. The computational method is extensively benchmarked against experimental IR and Raman spectra (see SI Section 3 for



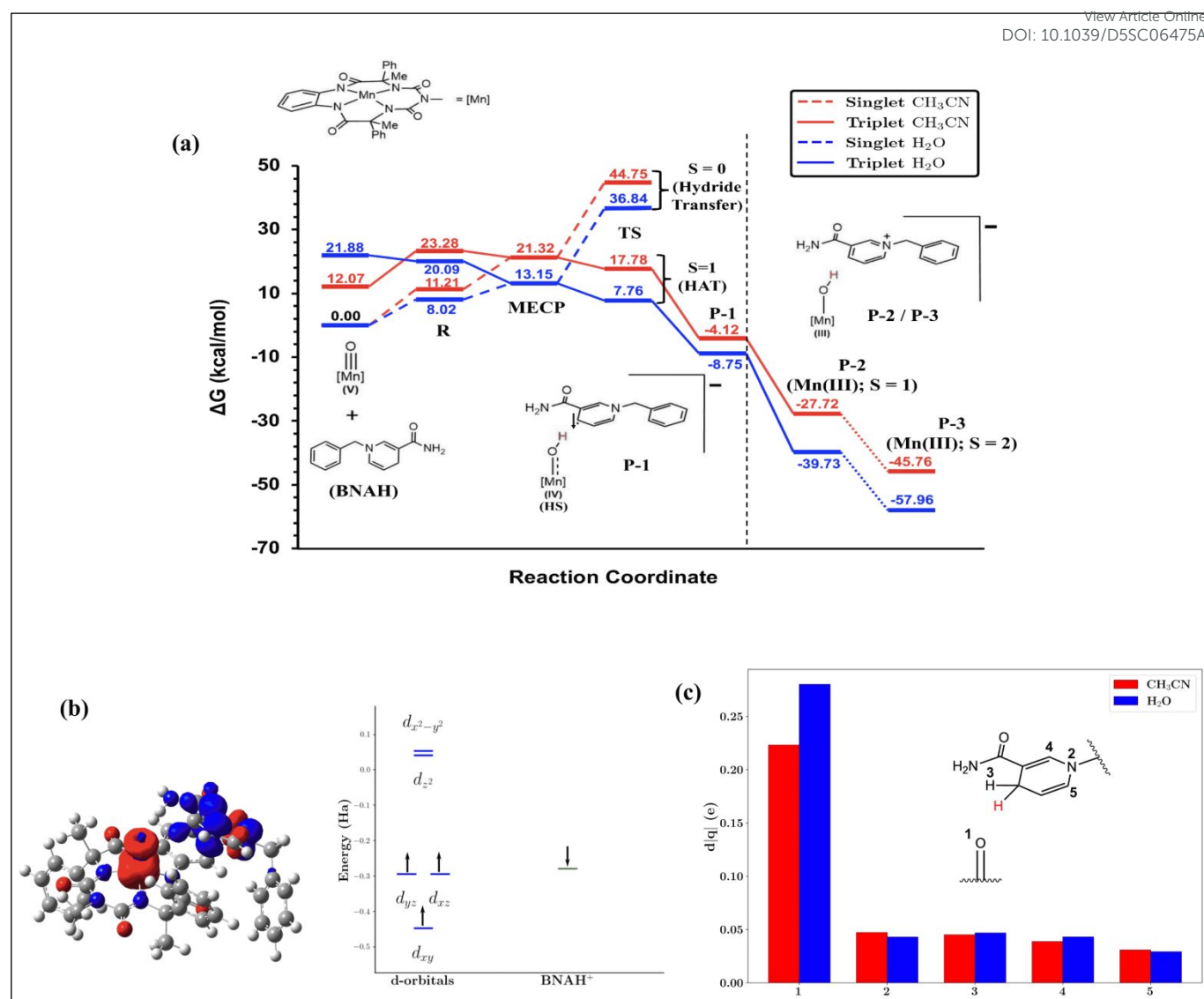


Figure 6. **(a)** Mechanism of the net hydride transfer that involves a H-atom transfer from BNAH to the Mn(V)O complex, **2** to generate the triplet P1 state. The system demonstrates a 2-state reactivity where the lowest energy spin configuration of the ground state is singlet but the transition state is more stable in the triplet configuration. **(b)** The spin density distribution at the MECP in water; Red = alpha, Blue = beta **(c)** The difference in partial charges on each atom (major contributors) between the MECP and the ground state in water (blue) and acetonitrile (red).

details). The ground state of the Mn(V)-oxo complex, **2**, is a singlet. The corresponding triplet state is significantly higher in energy, 12 kcalmol⁻¹ in CH₃CN and 22 kcalmol⁻¹ in water. As the reaction proceeds, however, the triplet state becomes lower in energy than the singlet state. We have captured the minimum energy crossing point (MECP) for the intersection of the two potential energy surfaces (Figure 6a). Analysis of the partial atomic (Hirshfeld) charges suggests that there is significant charge transfer from BNAH to the metal complex at the MECP (0.7e in ACN and 0.8e in water). Due to increased polarity, the MECP is more stable in the highly polar solvent water (by ~ 8 kcalmol⁻¹) with the O-atom bonded to the Mn centre, gaining majority of the excess charge (Figure 6c). We believe that the striking increase in rate in water as compared

to CH₃CN is due to this differential stabilisation of the MECP, the highest energy point in the reaction path. The sigmoidal behaviour of the rate enhancement, however, is a more subtle issue that cannot be captured accurately by considering the solvent as a dielectric continuum. The nature of dielectric constant dependence of the Born solvation free energy indicates that the gradient of the change in the free energy difference between the MECP and the ground state should decrease with the increase in the dielectric constant of the medium. However, it does not account for the heterogeneity in the water structures at low mole fractions. Moreover, the absolute value of the stabilisation should be considered in a qualitative fashion rather than quantitatively while comparing with the experimental findings because of the approximate way



by which the MECP has been calculated. A more accurate calculation would require at least the energy difference between the two spin surfaces to be evaluated at a multi-reference level. Beyond the MECP, the reaction proceeds downhill towards the Mn(IV)O intermediate, P-1, by encompassing the transition state. While the proton is mostly on the reactant side at the MECP, it is almost in between the donor and the acceptor sites at the TS. Since there is no stable intermediate between the MECP and the TS on the triplet surface, the reaction is still supposed to exhibit KIE, which is characteristic of a PCET reaction.^{49, 50}

At P-1, a fast electron transfer to the Mn(III)O species gives rise to the P-2 species, which then undergoes a spin-state transformation to the stable high-spin state, P-3. The lowest energy spin-configuration of the intermediate state P-1 can be best described as a high spin Mn(IV) centre that is anti-ferromagnetically coupled to the BNA radical (Figure 6b). Note that the higher energy transition state on the singlet surface involves a hydride transfer where the Mn(V) centre in the reactant is directly reduced by two electrons to the low-spin Mn(III) state as shown by dashed line in Figure 6a.

OAT reactivity studies of **2** in both medium

Since **2** did not react with styrene, oxygen atom transfer (OAT) reactivity was also examined using **2**, which used thioanisole and triphenylphosphine as substrates. Owing to the substrates solubility problem in water, initial rate calculations under pseudo-first order circumstances were used to compare the kinetic studies in the two media (checking the product formation by GC-MS at different time intervals) at RT (Figures S26-27, S33). It was demonstrated that the oxygen atom transfer rate in water was 60 times higher than in acetonitrile medium using triphenylphosphine as a substrate. The increase in OAT rate was not as large as that of HAT.

Conclusions

Before concluding, it is essential to compare the water-assisted rate enhancement observed for Mn(V)-oxo bTAML complex with the analogous effects induced by redox inactive metal ions and Lewis or Brønsted acids on other Mn(IV) and Mn(V)-oxo complexes. For instance, coordination of one or two redox inactive metal ions to Mn(IV) or Mn(V)-oxo complexes supported by N₄Py, Bn-TPEN, or TAML ligand frameworks significantly enhances the rates of electron transfer (ET) and oxygen atom transfer (OAT) reactions by modulating redox potentials, while concurrently leading to a decrease in HAT rate.^{28-32, 33} In contrast, the addition of Lewis acids (LAs), such as Zn(OTf)₂, B(C₆F₅)₃, to high-valent corrole Mn(V)-oxo complex enhances their HAT reactivity due to their conversion into the Mn(IV)-oxo radical cation valence tautomer.³⁴ Likewise, treatment of Mn-oxo complexes with brønsted acids such as triflic acid markedly increases the rates of ET and OAT (up to 10⁵-fold) by tuning the redox potential, although the HAT rate for CHD decreases under such conditions.³⁵⁻³⁷ However, no previous report has shown HAT rate enhancement in any Mn-

oxo complex achieved solely through solvent modulation, or transition into an aqueous medium. DOI: 10.1039/D5SC06475A

In summary, we report a remarkable water-driven rate enhancement in hydrogen atom transfer (HAT) reactivity using a newly developed non-heme Mn(V)-oxo complex. This complex, thoroughly characterised in terms of structure and properties, is quite stable towards C–H bonds in organic solvents such as acetonitrile. However, its HAT rate towards C–H bonds (<80 kcal/mol) increases dramatically with rising water content, reaching a maximum in pure water (up to ~26,000-fold in comparison to CH₃CN). Previous studies reported a 60-fold increase in reaction rate at 70% water content compared to pure CH₃CN for the related [Fe^V(O)bTAML][–] complex,²² and a 300-fold increase in pure water compared to CH₃CN for the [Fe^V(O)(Ph,Me-bTAML)][–] complex.²⁵ For this Mn(V)-oxo complex, the >25,000-fold increase in reactivity in water occurs despite having nearly identical ground-state properties in both water and CH₃CN, such as pK_a and redox potential. This unexpected rate enhancement was attributed to the stabilisation of minimum-energy crossing points (MECPs) in water, facilitated by stronger electrostatic interactions via greater partial-charge stabilisation of all atoms in the transition state due to water's higher dielectric constant compared to CH₃CN. Notably, this represents the first example of a non-heme Mn(V)-oxo complex achieving unprecedented rate enhancement solely through solvent modulation, without structural alteration or external additives,^{29, 36, 37, 51-56} highlighting water's pivotal role in bioinspired catalysis.

Author contributions

The concept of the work was designed by S.S.G. and P.D. P.D. performed major experiments. K.M. assisted P.D. during CV measurements. S.S. carried out the rRaman experiment. S.A. and S.G. performed all DFT calculations. P.D. and S.S.G. analyzed the data and wrote the manuscript. S.S.G. and P.D. thank Prof. Abhishek Dey for his assistance with the rRaman measurements and his valuable scientific inputs on this project. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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