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Cooperative activating effects of metal ion and Brønsted acid on a metal oxo species†

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Metal oxo (M=O) complexes are common oxidants in chemical and biological systems. The use of Lewis acids to activate metal oxo species has attracted great interest in recent years, especially after the discovery of the $CaMn_4O_5$ cluster in the oxygen-evolving centre of photosystem II. Strong Lewis acids such as Sc^{3+} and Sc^{3+}

Introduction

High-valent metal oxo (M=O) complexes are common oxidants in the chemical laboratory and in biological systems. Brønsted acids have long been used to increase the oxidizing power of M=O via protonation of the oxo ligand (M=O+HX \rightarrow M-OH⁺+X⁻). However, in recent years, the use of Lewis acids (LA) such as metal ions and boranes to activate M=O has received tremendous attention (M=O+LA \rightarrow M=O-LA).¹⁻³ In particular, the interest in understanding the interaction of Lewis acids with metal oxos is stimulated by the discovery that the oxygen-evolving center (OEC) of photosystem II (PSII) is composed of a CaMn₃O₄ cubane and a dangling Mn linked via two μ -oxos.⁴⁻¹⁰ A possible role of Ca²⁺ is to function as a Lewis acid to modulate the redox reactivity of the manganese oxo complexes.

Strong Lewis acids such as BF₃ and Sc³⁺ are usually used to activate metal oxo species. For example, we have reported that the oxidation of alkanes by MnO₄⁻ is accelerated by over seven orders of magnitude in the presence of BF₃.¹¹ The strong Lewis acid Sc³⁺ and the strong Brønsted acid CF₃SO₃H have been used

There is also much interest in the use of the relatively weak Lewis acid, Ca^{2+} , to activate M=O because of its relevance to the CaMn₄O₅ cluster in Photosystem II; although as expected, its effect is usually much smaller than those of Sc³⁺ or BF₃. For example, Agapie et al. reported that Ca2+ and other metal ions can increase the reduction potentials (E^0) of manganese oxo clusters, and there is a linear correlation between E^0 and pK_a of the metal ions. 16,17 Ca2+ can also enhance the catalytic water oxidation activity of manganese oxides18,19 and induce the oxidative release of O2 from a non-heme iron peroxo complex.20 We have also recently reported that Ca²⁺ can increase the rate of oxidation of alcohols by MnO₄ (ref. 21) and induce intermolecular O-O coupling of FeO₄²⁻ to give O₂.²² So far, significant activating effects of Ca2+ are only reported on metal oxo complexes that are thermodynamically strong oxidants. On the other hand, there has been little or no report on the activation of metal oxo species by weak Brønsted acids such as alkanoic acids.

We have been investigating the effects of Lewis acids on the reactivity of simple metal oxo species bearing two or more oxos without bulky ancillary ligands. 11,21-25 In this type of systems, more than one oxo sites are available for binding to two or more metal ions or Brønsted acids. We report herein the activation of a stable metal oxo complex, RuO₄⁻, by weak Lewis acids such as Ca²⁺ and other group II ions, as well as by weak Brønsted acids such as CH₃CO₂H. Although iron oxo complexes are common oxidants in chemical and biological systems, they are usually relatively unstable. Hence, we choose to investigate a very stable ruthenium oxo species. Although in a high oxidation state of

to activate Fe(IV) and Mn(IV) oxo complexes, 12,13 as well as metal superoxo species. 14,15

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+VII, RuO_4^- is a mild oxidant that readily oxidizes alcohols but is inactive towards alkanes. However, in the presence of a few equiv. of group 2 metal ions or acetic acid, it readily oxidizes cyclohexane at ambient conditions. Notably, the use of Ca^{2+} and CH_3CO_2H together produces a remarkable cooperative effect on RuO_4^- , resulting in a much more efficient oxidant than the use of a strong Lewis acid in the presence or absence of a Brønsted acid

Results and discussion

Effects of Lewis acids on oxidation of cyclohexane by $Ru^{VIII}O_4$ and $Ru^{VII}O_4^-$

Tetraoxo complexes of ruthenium in oxidation states +VIII and +VII are known, with RuVIIIO4 being a much stronger oxidant than Ru^{VII}O₄-. As a comparison, we have initially chosen to study the effects of Brønsted and Lewis acids (metal ions and BF₃) on the oxidation of alkanes by RuO₄. RuO₄ is a strong oxidant that is known to oxidize alkanes slowly at room temperature.26 In our hands, when RuO4 (0.01 M) was treated with an excess of cyclohexane (1.0 M) in CH₃CN, 0.2 mol of cyclohexanone/mol of RuO₄ (20 mol%) was produced after 5 h at 23 °C, as analysed by GC and GC/MS (Fig. 1a and Table S1†). No cyclohexanol could be detected. Since we previously reported that the oxidation of alkanes by MnO₄⁻ is greatly enhanced by just a few equiv. of BF3,11 we attempted to do the same with RuO₄. However, when BF₃ was added to RuO₄, no enhancement in the rate of cyclohexane oxidation was observed; on the contrary, a lower yield of cyclohexanone (11 mol%) was obtained (Fig. 1a and Table S1†). We then examined if Ca²⁺ can activate RuO4, but virtually no effect on cyclohexane oxidation was observed when a few equiv. of Ca(OTf)₂ (OTf is CF₃SO₃⁻) was added. We also tried to activate RuO₄ with Brønsted acids such as CF₃SO₃H and CH₃CO₂H (AcOH), but again there were no effects. These results indicate that the oxo ligands in the highly electrophilic RuO₄ have little or no affinity for CH₃CO₂H and various Lewis acids.

On the other hand, RuO_4^- is a much weaker oxidant than RuO_4 ; it is known to oxidize alcohols but not alkanes.²⁷ When we treated [nPr_4N][RuO_4] with cyclohexane in CH₃CN, no product could be detected after 5 days at 23 °C. Electrospray ionization mass spectrometry (ESI/MS) of the solution after 5 days shows that RuO_4^- and $^nPr_4N^+$ are the only species present.

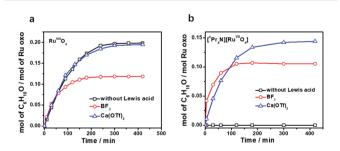


Fig. 1 Time traces for cyclohexane oxidation by (a) $RuO_4/Lewis$ acid and (b) $RuO_4^-/Lewis$ acid in CH_3CN . Conditions: RuO_4 or $[^{7}Pr_4N]$ $[RuO_4]$ (0.01 M), Lewis acid (0.04 M), cyclohexane (1.0 M) at 23 °C.

The UV/Vis spectrum of the solution also remained unchanged after 5 days. However, upon adding 4 equiv. of BF₃ to [ⁿPr₄N] [RuO₄] in CH₃CN, 10 mol% of cyclohexanone was produced within 3 h at 23 °C (Fig. 1b and Table S2†). Again, no cyclohexanol product could be detected. More significantly, Ca(OTf)₂ is also able to activate RuO₄⁻, and a higher yield of 14 mol% of cyclohexanone was attained (Fig. 1b, S1 and Table S2†). As will be described below, the RuO₄⁻/Ca²⁺ system functions as oneelectron oxidant, and since the oxidation of cyclohexane to cyclohexanone is a four-electron process, the actual yield is 56%. Other group II metal ions were also found to activate RuO₄-, with cyclohexanone production ranging from 11 to 15 mol% (Fig. 2, Table S2†). The relatively strong Lewis acid Sc(OTf)3 was also used and it gave the highest amount of 23 mol% of cyclohexanone. The rate and yield decrease in the order of Sc^{3+} (p $K_a = 4.3$) > Mg^{2+} (11.2) > Ca^{2+} (12.7) > Sr^{2+} (13.2) $>> Ba^{2+}$ (13.4); this trend correlates with their p K_a values in H₂O, which is a measure of their Lewis acidity.28 These results indicate that the oxo ligands in RuO₄ are much more basic than those in RuO4, so they readily bind to Lewis acids. Electronwithdrawing by the Lewis acids via the oxo ligand enhances the oxidizing power of RuO₄⁻.

Kinetics of the oxidation of cyclohexane by RuO₄⁻/Ca²⁺

The initial rate for cyclohexanone production by $[^nPr_4N][RuO_4]$ increases with $[Ca^{2+}]$ but eventually levels off at $[Ca^{2+}] > 5$ mM (Fig. 3a). A plot of 1/(initial rate) *versus* 1/ $[Ca(OTf)_2]$ is linear (Fig. 3b). In addition, when the concentration of RuO_4^- was doubled, the initial rate was also doubled. Such a kinetic behavior can be represented by eqn (1) and (2). The reacting calcium species is proposed to be $Ca(OTf)^+$, as supported by results of DFT calculations described below. The initial rate of the reaction is shown in eqn (3).

$$Ca(OTf)^{+} + RuO_{4}^{-} \stackrel{K}{\rightleftharpoons} [Ca(OTf)^{+} \cdot RuO_{4}^{-}]$$
 (1)

$$\left[\text{Ca}(\text{OTf})^+ \cdot \text{RuO}_4^- \right] + c - C_6 H_{12} \xrightarrow{k} \text{products}$$
 (2)

$$\label{eq:initial_rate} Initial\ rate = \frac{\textit{kK}\big[\text{Ca}(\text{OTf})_2\big]}{1 + \textit{K}\big[\text{Ca}(\text{OTf})_2\big]}\big[\text{RuO_4}^-\big][c - C_6H_{12}] \hspace{0.5cm} (3)$$

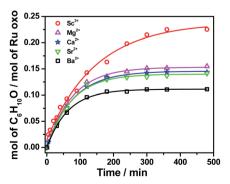


Fig. 2 Effects of various Lewis acids on cyclohexane oxidation by RuO_4^- in CH_3CN . Conditions: $[^nPr_4N][RuO_4]$ (0.01 M), Lewis acid (0.04 M), cyclohexane (1.0 M) at 23 °C.

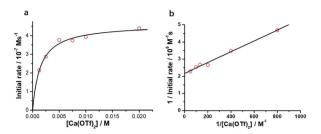


Fig. 3 Effects of [Ca(OTf)₂] on cyclohexane oxidation by RuO₄ $^-$ in CH₃CN. Conditions: [^nPr₄N][RuO₄] (0.01 M), cyclohexane (1.0 M) in CH₃CN at 23 °C. (a) Plot of initial rate vs. [Ca(OTf)₂]. (b) Plot of 1/initial rate vs. 1/[Ca(OTf)₂] (slope = (3.16 \pm 0.15) $\times 10^3$, y-intercept = (2.16 \pm 0.06) \times 10⁶, r= 0.988).

From Fig. 3b, $k=1/(\text{intercept}\left[\text{RuO}_4^{-}\right])=(4.63\pm0.13)\times10^{-5}$ M⁻¹ s⁻¹ and $K=\text{intercept/slope}=(6.83\pm0.18)\times10^2$ M⁻¹ at 23 °C. The observed equilibrium constant K indicates relatively strong binding of Ca(OTf)⁺ to RuO₄⁻, in accordance with the observed rate saturation behaviour.

Activation of RuO₄ by Brønsted acids

The effects of Brønsted acids on cyclohexane oxidation by RuO_4^- were also investigated. Addition of 1 equiv. of the strong acid CF_3SO_3H ($pK_a=0.23$ in H_2O) to $[^nPr_4N][RuO_4]$ (0.01 M) in CH_3CN containing excess cyclohexane led to the formation of 15 mol% of cyclohexanone after 3 h at 23 °C. However, addition of ≥ 4 equiv. of CF_3SO_3H to $[^nPr_4N][RuO_4]$ resulted to rapid formation of a black precipitate with only a trace amount of cyclohexanone. Such a phenomenon is due to disproportionation of RuO_4^- , as represented by eqn (4):²⁹

$$4RuO_4^- + 4H^+ \rightarrow 3RuO_4 + RuO_2 + 2H_2O E^0 = 0.46 V$$
 (4)

Interestingly, ["Pr₄N][RuO₄] is also readily activated by the relatively weak acid CH_3CO_2H (p $K_a = 4.76$) to oxidize cyclohexane to cyclohexanone, with no evidence of disproportionation even in the presence of high concentrations of AcOH (>1 M). Upon addition of 12–48 equiv. of AcOH to $\lceil {}^n Pr_4 N \rceil \lceil RuO_4 \rceil$ in CH₃CN containing excess cyclohexane, the brown solution gradually turned green, and 16 mol% of cyclohexanone was produced within 1-2 h at 23 °C. The oxidation state of the ruthenium product was determined to be +6 (see below, Fig. S2†), hence the actual yield is 64%. Although the yield is independent of [AcOH], the rate of oxidation increases with increasing [AcOH] (Fig. 4); a plot of the initial rate versus [AcOH] gives a straight line. The initial rate is also doubled when [RuO₄] is doubled. A proposed reaction scheme is shown in eqn (5)-(7). The first step involves protonation of an oxo ligand of RuO₄ by AcOH, this step is supported by DFT calculations described below. The resulting [Ru(O)3(OH)] species is hydrogen-bonded to a second AcOH molecule to generate the active intermediate [AcOH·Ru(O)3(OH)] that oxidizes cyclohexane. The rate law is shown in eqn (8); at $K'[CH_3CO_2H] \langle 1,$ the rate law becomes that of eqn (9).

$$RuO_4^- + CH_3CO_2H \rightarrow [Ru(O)_3(OH)] + CH_3CO_2^-$$
 (5)

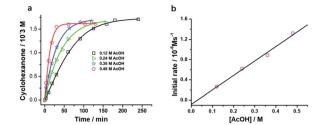


Fig. 4 (a) Effects of CH₃CO₂H on cyclohexane oxidation by RuO₄⁻ in CH₃CN. Conditions: [7 Pr₄N][RuO₄] (0.01 M), cyclohexane (1.0 M) in CH₃CN at 23 °C. (b) Plot of initial rate *versus* [AcOH]. (slope = (2.72 \pm 0.13) \times 10⁻⁶, *y*-intercept = -(3.33 \pm 3.82) \times 10⁻⁸, *r* = 0.9908).

$$[Ru(O)_3(OH)] + CH_3CO_2H \stackrel{\mathsf{K}'}{\rightleftharpoons} [CH_3CO_2H \cdot Ru(O)_3(OH)] \quad (6)$$

$$\left[\text{CH}_3 \text{CO}_2 \text{H} \cdot \text{Ru(O)}_3 (\text{OH)} \right] + c - \text{C}_6 \text{H}_{12} \xrightarrow{k'} \text{products} \tag{7}$$

Initial rate =
$$\frac{\textit{k'K'}[CH_{3}CO_{2}H]}{1 + \textit{K'}[CH_{3}CO_{2}H]}[RuO_{4}^{-}][c - C_{6}H_{12}] \quad (8)$$

At
$$K'[CH_3CO_2H] \langle 1 \rangle$$

Initial rate =
$$k'K'$$
[AcOH][RuO₄⁻][c-C₆H₁₂] = k_{AcOH} [AcOH]
[RuO₄⁻][c-C₆H₁₂] (9)

From the slope of Fig. 4b and using [RuO $_4$] = 0.01 M and [c-C $_6$ H $_{12}$] = 1.0 M, k_{ACOH} is found to be (2.72 \pm 0.13) \times 10⁻⁴ M⁻² s⁻¹ at 23 °C.

Cooperative activating effects of metal ions and AcOH

Remarkably, when the oxidation of cyclohexane by $\mathrm{RuO_4}^-$ was carried out in the presence of $\mathrm{Ca^{2^+}}$ and AcOH, both the rate and product yield were enhanced, as shown in Fig. 5. The amount of cyclohexanone produced by the $\mathrm{RuO_4}^-/\mathrm{Ca^{2^+}}/\mathrm{AcOH}$ system is 38 mol%, compared with ca. 16 mol% by both $\mathrm{RuO_4}^-/\mathrm{Ca^{2^+}}$ and $\mathrm{RuO_4}^-/\mathrm{AcOH}$ systems. In this case, the oxidation state of the ruthenium product was found to be +5 (see below, Fig. S3†), so this system functions as a two-electron oxidant and the actual yield is 76%, higher than the 64% using $\mathrm{Ca^{2^+}}$ or AcOH alone.

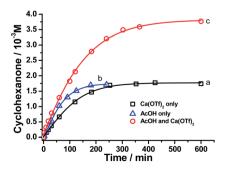


Fig. 5 Time trace for cyclohexane oxidation by $[^nPr_4N][RuO_4]$ (0.01 M) in CH₃CN at 23 $^{\circ}$ C in the presence of (a) 1 equiv. Ca²⁺, (b) 12 mol equiv. of AcOH and (c) 1 mol equiv. Ca²⁺ + 12 mol equiv. AcOH.

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The yield of cyclohexanone was increased to 92% when the amount of acetic acid was increased to 250 equiv. (CH₃CN/ AcOH: 6/1, Table 1). Note that in the absence of Ca(OTf)2, the yield of cyclohexanone did not increase with [AcOH], as illustrated in Fig. 4a. Similar cooperative effects of M²⁺ and AcOH were also found for other group 2 ions (Table 1), with a maximum yield of 99% observed for Sr²⁺/AcOH. However, no such cooperative effects were found for stronger Lewis acids such as BF3 and Sc(OTf)3, the yields remain the same in the absence or presence of AcOH. These results demonstrate the strong cooperative effects of relatively mild Brønsted and Lewis acid in activating a metal oxo species. Although the reaction rate is lower than that of BF₃ or Sc(OTf)₃, the Group 2 ion/AcOH combination is much more efficient in terms of product yield. Similar to the case of CF₃SO₃H discussed above, partial decomposition of RuO₄ occurs in the presence of a strong Lewis acid, hence resulting in lower yields.

The kinetics of cyclohexane oxidation by $RuO_4^-/Ca^{2^+}/AcOH$ were investigated. Saturation kinetics were also observed when $[Ca^{2^+}]$ was increased (Fig. 6). Based on Fig. 6 and the mechanisms proposed above for RuO_4^-/Ca^{2^+} and $RuO_4^-/AcOH$, the mechanism for this system can be represented by the following equations.

$$RuO_4^- + CH_3CO_2H \rightarrow [Ru(O)_3(OH)] + CH_3CO_2^-$$
(10)

$$[Ru(O)_3(OH)] + Ca(OTf)^+$$

$$+ CH_3CO_2H \stackrel{K''}{\rightleftharpoons} [Ca(OTf)^+ \cdot CH_3CO_2H \cdot Ru(O)_3(OH)]$$
(11)

$$\left[Ca(OTf)^{+} \cdot CH_{3}CO_{2}H \cdot Ru(O)_{3}(OH)\right] + c - C_{6}H_{12} \xrightarrow{k''} products$$
(12)

The rate-law is as shown in eqn (13):

Initial rate =
$$\frac{k''K''\left[Ca(OTf)_{2}\right]}{1+K''\left[Ca(OTf)_{2}\right]}\left[RuO_{4}^{-}\right]\left[AcOH\right]\left[c-C_{6}H_{12}\right]$$
(13)

Table 1 Oxidation of cyclohexane by $[^n Pr_4 N] [RuO_4] / Lewis acid in CH_3 CN/AcOH (6:1, v/v)^{\alpha}$

Entry a	Lewis acid	Yield of cyclohexanone d (%)	Time
1	Ca(OTf) ₂	92	5 h
2^b	Ca(OTf) ₂	92	5 h
3^c	Ca(OTf) ₂	91	5 h
4	$Sr(OTf)_2$	99	5 h
5	$Mg(OTf)_2$	86	5 h
6	$Ba(OTf)_2$	86	5 h
7	BF_3	42	3 min
8	$Sc(OTf)_3$	46	6 min

 $[^]a$ Conditions: $[^n\mathrm{Pr}_4\mathrm{N}][\mathrm{RuO}_4],$ 0.01 M; Lewis acid, 0.04 M; cyclohexane, 1.0 M; solvent, CH₃CN/HOAc (6:1, v/v); at 23 °C. b Under argon. c In the presence of 10 equiv. of BrCCl₃, only a trace amount of bromocyclohexane was detected. d Yield of cyclohexanone was calculated based on $[^n\mathrm{Pr}_4\mathrm{N}][\mathrm{RuO}_4]$ acting as two-electron oxidant. Yield = (mol of cyclohexanone)/(mol of $[^n\mathrm{Pr}_4\mathrm{N}][\mathrm{RuO}_4])\times2\times100\%$, no cyclohexanol was detected.

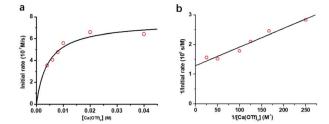


Fig. 6 (a) Plot of initial rate vs. $[Ca^{2+}]$ for the $Ca(OTf)_2/AcOH$ activated oxidation of cyclohexane (0.10 M) by RuO_4^- (0.01 M) in CH_3CN at 23.0 °C. (b) The corresponding plot of 1/initial rate vs. $1/[Ca^{2+}]$. Slope = (6.29 \pm 0.64) $\times 10^3$, y-intercept = (1.29 \pm 0.09) \times 10⁶, r = 0.9504. Conditions: RuO_4^- (0.01 M); cyclohexane (1.0 M); AcOH (0.12 M); $Ca(OTf)_2$ (0.002 M - 0.040 M).

From eqn (11) and Fig. 6b, K'' and k'' are found to be (2.05 \pm 0.31) \times 10² M⁻¹ and (6.49 \pm 0.45) \times 10⁻⁴ M⁻¹ s⁻¹, respectively. A similar cooperative effect was also found for Mg²⁺/AcOH (Fig. S4†). However, no increase in rate and yield were found for Sc³⁺/AcOH (Fig. S5†).

Ruthenium intermediates and products

Electrospray ionization mass spectrometry (ESI/MS) was employed to detect any intermediate formed between RuO_4^- and Ca^{2+} . The mass spectrum of $[^nPr_4N][RuO_4]$ in CH_3CN exhibits a single peak at m/z 166.1 due to RuO_4^- (Fig. S6†). Upon addition of 0.25 equiv. of $Ca(OTf)_2$, a new peak at m/z 653.9 appeared, which is assigned to $[RuO_4 \cdot Ca(CF_3SO_3)_2 \cdot CF_3SO_3H]^-$ (Fig. S7†). MS/MS of this ion (m/z 653.9) gives fragment peaks due to $CF_3SO_3^-$ (m/z 148.9) and RuO_4^- (m/z = 165.9) (Fig. S8†). This result provides evidence for the binding of Ca^{2+} to RuO_4^- .

The brown color of the solution of $[^nPr_4N][RuO_4]/Ca(OTf)_2$ gradually lightened during cyclohexane oxidation, eventually a dark brown precipitate was observed and the solution became colorless. The dark precipitate, which is probably a Ca^{2^+} -bridged polymeric species, was dissolved in 0.1 M HNO $_3$ and the solution was titrated spectrophotometrically with the strong oxidant $(NH_4)_2Ce(NO_3)_6$ (Ce(iv)). Upon addition of Ce(iv) to the ruthenium product solution, the characteristic vibronic-structured peaks at around 380 nm due to RuO_4 appeared, 26 and 2.3 \pm 0.3 equiv. of Ce(iv) was consumed (Fig. S2†). This result indicates that the oxidation state of Ru in the dark brown product is +6 and hence the Ca^{2^+}/RuO_4^- system acts as one-electron oxidant in the reaction with cyclohexane.

In cyclohexane oxidation by ["Pr₄N][RuO₄]/AcOH, the brown solution gradually turned dark green but no precipitate was observed. ESI/MS of the dark green solution shows the appearance of a peak at *m*/*z* 209 (Fig. S9†), which can be assigned to [Ru^{VI}O₃(AcO)]⁻. When CH₃CO₂H was replaced by CD₃CO₂D, the *m*/*z* 209 peak was shifted to *m*/*z* 212, indicating that the *m*/*z* 209 peak consists of 1 AcO⁻ ion. The assignment of +6 oxidation state to the ruthenium product is also supported by Ce(IV) titration, which consumes two equiv. of Ce(IV) to generate RuO₄. Hence the RuO₄⁻/AcOH system also functions a one-electron oxidant.

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On the other hand, spectrophotometric titration of the product solution of Ca²⁺/AcOH/RuO₄ after cyclohexane oxidation shows that it consumes 3.1 \pm 0.2 equiv. of Ce($_{\rm IV}$), hence in this case the oxidation state of the Ru product is +5 and the system is a two-electron oxidant towards cyclohexane (Fig. S3†).

Mechanistic studies

The same results were obtained for cyclohexane oxidation carried out under argon or air (Tables 1 and S2†). Also, the addition of BrCCl₃, a radical scavenger, had little effects on the oxidation of cyclohexane, and only a trace amount of bromocyclohexane was detected (Tables 1 and S2†). These results indicate that no freely diffusing alkyl radicals are formed in the oxidation of cyclohexane by RuO₄⁻ in the presence of Ca²⁺ and/

The kinetic isotope effects (KIE) for cyclohexane oxidation by RuO₄ under various conditions were determined by competitive oxidation of an equimolar mixture of c-C₆H₁₂ and c-C₆D₁₂. The KIE for RuO₄⁻/Ca²⁺, RuO₄⁻/AcOH and RuO₄⁻/Ca²⁺/AcOH were found to be 6.4 \pm 0.2, 13.9 \pm 0.4 and 6.5 \pm 0.2, respectively. Such large KIEs are indicative of C-H bond cleavage in the ratelimiting step.

Based on the experimental results, the oxidation of alkane by RuO₄ in the presence of Lewis acid (LA) appears to be consistent with a mechanism that involves the initial binding of LA to RuO₄ to generate a precursor complex, which then reacts with alkane via a H-atom abstraction/O-rebound mechanism to generate the corresponding alcohol. Such a mechanism is commonly accepted for C-H bond activation by cytochrome P450 and various metal oxo species.30 However, since only ketones are detected in the present case, this suggests that the initially formed alcohol is rapidly oxidized to give the ketone. This is supported by a competitive experiment involving the oxidation of a mixture of cyclohexane and cyclopentanol (10:1) by RuO₄⁻/Ca²⁺, which resulted in the rapid and exclusive formation of cyclopentanone (Fig. S10†). No alkene or products derived from its oxidation were observed in the oxidation of alkane by RuO₄⁻/Ca²⁺, which rules out a dehydrogenation mechanism that has been shown to occur in alkane oxidation by non-heme iron(IV) oxo species.31 The binding of a Lewis acid to RuO₄⁻ enhances its oxidizing power, as observed in non-heme iron(IV) oxo complexes32 and manganese oxo clusters.16,17

Theoretical calculations

In order to obtain further insights into the activating effects of Ca(II) and AcOH on RuO₄-, the reaction mechanisms for the oxidation of cyclohexane catalysed by RuO₄⁻ in the presence of Ca(OTf)2 and/or AcOH have been theoretically studied by density functional theory (DFT). As a comparison similar studies with RuO₄ have also been carried out.

In the oxidation of cyclohexane by $[RuO_4]^-$ in CH_3CN (Fig. 7), cyclohexane and [RuO₄] first form an intermediate, INT1(RuO₄⁻), in which the two species are weakly attracted together ($[RuO_4\cdots C_6H_{12}]^-$). HAT then occurs from C_6H_{12} to Ru=O via a transition state TS1(RuO₄⁻) to form a second intermediate, INT2(RuO₄⁻). The reaction barrier ($\Delta G_{298}^{\ddagger}$) for the HAT is 26.8 kcal mol⁻¹ in CH₃CN. Such a large $\Delta G_{298}^{\ddagger}$ agrees with the experimental observation that RuO₄⁻ hardly reacts with cyclohexane at room temperature. The C1 of the cyclohexyl radical in INT2(RuO₄⁻) bears -0.93 electrons, consistent with a HAT process. The cyclohexyl radical then binds to another oxo ligand to generate an alkoxo intermediate [RuO2(OH) (OC_6H_{11})] via $TS2(RuO_4)$. It should be noted that the step after H-abstraction is not characterized as a rebound step, in contrast to cytochrome P450 and other mono-oxo species. Rather, another oxo group which is not used for H-atom abstraction combines with the carbon atom with a low barrier. Because of this reactivity pattern, a ruthenium-bound alkoxide instead of alcohol is formed as an intermediate. Then in the next step, proton transfer from Ru-OH to the alkoxide occurs via TS3(RuO₄⁻) to generate the cyclohexanol product. Similar reaction pathways are observed for cyclohexane oxidation by RuO4, except in this case no radical intermediate (INT2) is formed (Fig. S11†). The reaction barrier $(\Delta G_{298}^{\ddagger})$ is 17.8 kcal mol⁻¹, consistent with the experimental observation that RuO4 reacts readily with cyclohexane at room temperature.

In the oxidation of cyclohexane by RuO₄⁻ in the presence of [Ca(OTf)]⁺, the reaction mechanism is similar. [Ca(OTf)]⁺ forms an intermediate, INT1(CaOTf), with RuO₄-; the Ca is bound to two oxo ligands. Due to the electron withdrawing effects of Ca(II) centre, the Ru-O bond lengths are changed from 1.740 (in RuO_4^- , Table S3†) to 1.775 (oxo bound to Ca) and 1.709 Å (free oxo) in INT1(CaOTf). HAT from C₆H₁₂ then occurs via the shorter and more electrophilic Ru=O bond. In this case there is no cyclohexyl radical intermediate, INT2(RuO₄-); HAT and binding of cyclohexyl radical to a second oxo occur in a single step. The $\Delta G_{298}^{\ddagger}$ for the oxidation of cyclohexane by [RuO₄(-CaOTf)] (Fig. 7 and Table S3,† entry 3), via TS1(CaOTf), is 18.5 kcal mol⁻¹. Such a lowering of 8.3 kcal mol⁻¹ is in agreement with the observed accelerating effect of Ca(II). We have also found the ΔG_{298}^{\dagger} for the oxidation of cyclohexane by [RuO₄(Ca)]⁺ (Table S3,† entry 5) is higher than that by [RuO₄(-CaOTf)], so $[RuO_4(Ca)]^+$ should not be the active species in the oxidation of cyclohexane.

In the presence of acetic acid, RuO₄⁻ is protonated to give INT1(AcOH), $[RuO_3OH(AcO)\cdots C_6H_{12}]$. The AcO is held by two additional AcOH molecules through hydrogen bonding (structures given in Table S3†). The Ru-OH bond distance is 1.858 Å; protonation results in shortening of two of the Ru=O from 1.740 Å (in RuO_4^-) to 1.709 Å. HAT by INT1(AcOH) occurs via one of the shorter and more electrophilic Ru=O; the resulting cyclohexyl radical then binds to Ru-OH···OAc to generate Ru bound cyclohexanol in the same step, INT2(AcOH). The ΔG_{298}^{3} for HAT from C₆H₁₂ to INT1(AcOH) via TS1(AcOH) is 15.2 kcal mol⁻¹, which is significantly lower than the $\Delta G_{298}^{\ddagger}$ for RuO₄ alone by 11.6 kcal mol⁻¹, in accordance with the experimentally observed accelerating effects of AcOH on RuO₄⁻.

In the presence of both [CaOTf]⁺ and AcOH, the intermediate with RuO₄⁻, INT1(CaOTf + AcOH), consists of AcO⁻ and Ca forming a chelate ring with Ru=O and Ru-OH, as well as three H-bonded AcOH molecules (Fig. 7 and Table S3,† entry 4). The free Ru=O bonds are further shortened to 1.692 Å. Accordingly

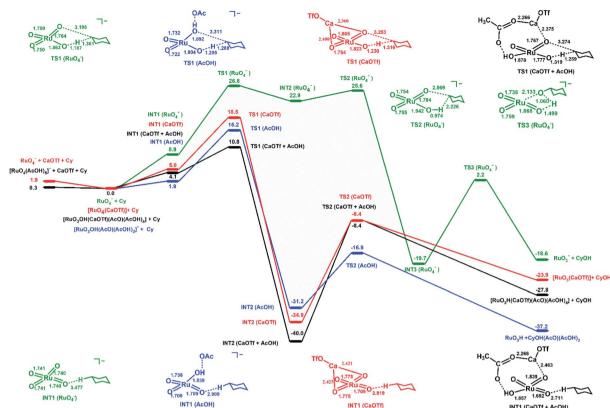


Fig. 7 PESs for cyclohexane oxidation by $[RuO_4]^-/[RuO_4(AcOH)]^-/[RuO_4(CaOTf)]/[RuO_4(AcOH)(CaOTf)]$ at the B3LYP level using LanL2TZ(f) basis set (Ru) and 6–311++G(d,p) basis set (non-metals). Relative 298 K Gibbs free energies in acetonitrile are given in kcal mol⁻¹. Not all acetic acid molecules are shown for simplicity.

the $\Delta G_{298}^{\ddagger}$ for HAT from cyclohexane *via* TS1(CaOTf + AcOH) is lowered to 10.8 kcal mol⁻¹, which is smaller than the value of 18.5 kcal mol⁻¹ and 15.2 kcal mol⁻¹, respectively, with Ca(OTf)⁺ or AcOH alone. This is in agreement with the observed cooperative activating effects of AcOH and Ca(II). HAT and binding of the resulting cyclohexyl radical to a Ca-bound oxo ligand occur in one step. Protonation by Ru-OH to the alkoxide then occurs to generate cyclohexanol. The potential energy surfaces (PES) for RuO₄/Ca(OTf)+, RuO₄/AcOH and RuO₄/Ca(OTf)+/AcOH are shown in Fig. S11.† The $\Delta G_{298}^{\ddagger}$ for HAT by RuO₄ alone is 17.8 kcal mol⁻¹, consistent with the experimental observation that RuO₄ is able to oxidize cyclohexane at ambient conditions. There are little or no changes in the Ru=O distances of RuO₄ upon binding to Ca(OTf)+ and/or AcOH, and there are only small changes in the reaction barriers, in agreement with experimental observations. This is in accordance with the Ru= O bonds being highly electrophilic and non-basic, hence there is little affinity for Lewis acids.

Conclusions

Our results demonstrate a remarkable cooperative effect of a weak Brønsted acid and a weak Lewis acid on the activation of a metal oxo species. RuO₄⁻, although in high oxidation state of +VII, is a weak oxidant due to stabilization by the four oxo ligands. However, it can be readily activated by a mild Lewis

acid such as Ca²⁺ or other group II metal ions, as well as a weak Brønsted acid such as CH₃CO₂H. The addition of both Ca²⁺ and CH₃CO₂H generates a highly efficient system that can oxidize unactivated C–H bonds with much higher yields than the use of strong Lewis acids such as Sc³⁺ or BF₃, with or without CH₃CO₂H. Such an observation may provide insights into the design of active oxidants based on metal oxo species in combination with relatively weak Brønsted and Lewis acids, especially if the metal oxo or the substrate is sensitive to strong acids. Our studies may also be relevant to oxidation by metal oxo species in biological systems, where only mild Brønsted acids such as alkanoic or amino acids, and mild Lewis acids such as Zn²⁺ or Ca²⁺, are present in cells. So may be highly efficient oxidizing systems can be generated in biological systems using this strategy.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- 1 T. Devi, Y.-M. Lee, W. Nam and S. Fukuzumi, *Coord. Chem. Rev.*, 2020, **410**, 213219.
- 2 Y. Liu and T.-C. Lau, J. Am. Chem. Soc., 2019, 141, 3755-3766.
- 3 S. Fukuzumi, Coord. Chem. Rev., 2013, 257, 1564–1575.
- 4 D. J. Vinyard, G. M. Ananyev and G. C. Dismukes, *Annu. Rev. Biochem.*, 2013, **82**, 577–606.
- 5 J. Yano and V. Yachandra, Chem. Rev., 2014, 114, 4175-4205.
- 6 J. D. Blakemore, R. H. Crabtree and G. W. Brudvig, *Chem. Rev.*, 2015, **115**, 12974–13005.
- 7 J. Barber, Chem. Soc. Rev., 2009, 38, 185-196.
- 8 Y. Umena, K. Kawakami, J.-R. Shen and N. Kamiya, *Nature*, 2011, 473, 55–60.
- 9 K. M. Davis, B. T. Sullivan, M. C. Palenik, L. Yan, V. Purohit, G. Robison, I. Kosheleva, R. W. Henning, G. T. Seidler and Y. Pushkar, *Phys. Rev. X*, 2018, 8, 041014.
- 10 Y. Pushkar, K. M. Davis and M. C. Palenik, J. Phys. Chem. Lett., 2018, 9, 3525–3531.
- 11 W. W. Y. Lam, S.-M. Yiu, J. M. N. Lee, S. K.-Y. Yau, H.-K. Kwong, T.-C. Lau, D. Liu and Z. Lin, *J. Am. Chem. Soc.*, 2006, 128, 2851–2858.
- 12 Y. Morimoto, H. Kotani, J. Park, Y.-M. Lee, W. Nam and S. Fukuzumi, *J. Am. Chem. Soc.*, 2011, 133, 403–405.
- 13 H. Yoon, H. Yoon, Y.-M. Lee, X. Wu, K.-B. Cho, R. Sarangi, W. Nam and F. S. Fukuzumi, *J. Am. Chem. Soc.*, 2013, 135, 9186–9194.
- 14 T. Devi, Y.-M. Lee, W. Nam and S. Fukuzumi, *J. Am. Chem. Soc.*, 2020, **142**, 365–372.
- 15 T. Devi, Y.-M. Lee, W. Nam and S. Fukuzumi, *J. Am. Chem. Soc.*, 2018, **140**, 8372–8375.
- 16 E. Y. Tsui, R. Tran, J. Yano and T. Agapie, *Nat. Chem.*, 2013, 5, 293–299.

- 17 E. Y. Tsui and T. Agapie, *Proc. Natl. Acad. Sci. U.S.A.*, 2013, **110**, 10084–10088.
- 18 M. M. Najafpour, T. Ehrenberg, M. Wiechen and P. Kurz, *Angew. Chem., Int. Ed.*, 2010, **49**, 2233–2237.
- 19 M. Wiechen, I. Zaharieva, H. Dau and P. Kurz, *Chem. Sci.*, 2012, 3, 2330–2339.
- 20 S. Bang, Y.-M. Lee, S. Hong, K.-B. Cho, Y. Nishida, M. S. Seo, R. Sarangi, S. Fukuzumi and W. Nam, *Nat. Chem.*, 2014, 6, 934–940.
- 21 H. Du, Po-K. Lo, Z. Hu, H. Liang, K.-C. Lau, Y.-N. Wang, W. W. Y. Lam and T.-C. Lau, *Chem. Commun.*, 2011, 47, 7143–7145.
- 22 L. Ma, W. W. Y. Lam, P.-K. Lo, K.-C. Lau and T.-C. Lau, *Angew. Chem., Int. Ed.*, 2016, 55, 3012–3016.
- 23 T.-C. Lau and C.-K. Mak, *J. Chem. Soc., Chem. Commun.*, 1993, 766–767.
- 24 S.-M. Yiu, Z.-B. Wu, C.-K. Mak and T.-C. Lau, *J. Am. Chem. Soc.*, 2004, **126**, 14921–14929.
- 25 S.-M. Yiu, W.-L. Man, X. Wang, W. W. Y. Lam, S.-M. Ng, H.-K. Kwong, K.-C. Lau and T.-C. Lau, *Chem. Commun.*, 2011, 47, 4159-4161.
- 26 W. P. Griffith, Ruthenium Oxidation Complexes: Their Uses as Homogenous Organic Catalysts, Springer, 2011.
- 27 W. P. Griffith, S. V. Ley, G. P. Whitcombe and A. D. White, *J. Chem. Soc., Chem. Commun.*, 1987, 1625–1627.
- 28 S. J. Hawkes, J. Chem. Educ., 1996, 73, 516.
- 29 E. A. Seddon and K. R. Seddon, *The Chemistry of Ruthenium*, Elsevier, Amsterdam, 1984, vol. 52.
- 30 J. L. McLain, J. Lee and J. T. Groves, *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*. Imperial College Press, London, 2000.
- 31 K.-B. Cho, X. Wu, Y.-M. Lee, Y. H. Kwon, S. Shaik and W. Nam, *J. Am. Chem. Soc.*, 2012, **134**, 20222–20225.
- 32 W. Nam, Y.-M. Lee and S. Fukuzumi, *Acc. Chem. Res.*, 2014, 47, 1146–1154.