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## Synergistic effects of $\text{CH}_3\text{CO}_2\text{H}$ and $\text{Ca}^{2+}$ on C–H bond activation by $\text{MnO}_4^-$ †

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The activation of metal-oxo species with Lewis acids is of current interest. In this work, the effects of a weak Brønsted acid such as  $\text{CH}_3\text{CO}_2\text{H}$  and a weak Lewis acid such as  $\text{Ca}^{2+}$  on C–H bond activation by  $\text{KMnO}_4$  have been investigated. Although  $\text{MnO}_4^-$  is rather non-basic ( $\text{p}K_a$  of  $\text{MnO}_3(\text{OH}) = -2.25$ ), it can be activated by  $\text{AcOH}$  or  $\text{Ca}^{2+}$  to oxidize cyclohexane at room temperature to give cyclohexanone as the major product. A synergistic effect occurs when both  $\text{AcOH}$  and  $\text{Ca}^{2+}$  are present; the relative rates for the oxidation of cyclohexane by  $\text{MnO}_4^-/\text{AcOH}$ ,  $\text{MnO}_4^-/\text{Ca}^{2+}$  and  $\text{MnO}_4^-/\text{AcOH}/\text{Ca}^{2+}$  are 1 : 73 : 198. DFT calculations show that in the active intermediate of  $\text{MnO}_4^-/\text{AcOH}/\text{Ca}^{2+}$ ,  $\text{MnO}_4^-$  is H-bonded to 3  $\text{AcOH}$  molecules, while  $\text{Ca}^{2+}$  is bonded to 3  $\text{AcOH}$  molecules as well as to an oxo ligand of  $\text{MnO}_4^-$ . Our results also suggest that these synergistic activating effects of a weak Brønsted acid and a weak Lewis acid should be applicable to a variety of metal-oxo species.

## Introduction

The chemistry of metal-oxo species has been of great interest to chemists because of the key roles they play in various chemical and biological systems.<sup>1–4</sup> In recent years, the use of Lewis acids to enhance the reactivity of metal-oxo species has attracted much attention,<sup>5,6</sup> especially after the discovery of a  $\text{Ca}^{2+}$  in the active site of the oxygen-evolving center (OEC) of photosystem II, which contains a manganese calcium oxo cluster ( $\text{Mn}_4\text{CaO}_5$ ).<sup>7,8</sup>

Various metal-oxo species are readily activated by strong Lewis acids such as  $\text{BF}_3$ ,  $\text{Sc}(\text{OTf})_3$  and other  $\text{M}^{3+}$  ions toward the oxidation of organic substrates.<sup>9–19</sup> There are also a number of studies on the interaction of relatively weak Lewis acids such as  $\text{Ca}^{2+}$  and other group II ions with metal-oxo species, and as expected their activating effects are much smaller than those of  $\text{Sc}(\text{OTf})_3$  or other  $\text{M}^{3+}$  ions.<sup>12,15,20–24</sup>

We recently reported the use of a weak Brønsted acid such as acetic acid in combination with a weak Lewis acid such as a group II ion to activate  $\text{RuO}_4^-$ .<sup>25</sup> We found a remarkable cooperative activating effect of these two acids on  $\text{RuO}_4^-$  toward the oxidation of alkanes. The oxo ligands in  $\text{RuO}_4^-$  are basic and can be protonated by  $\text{AcOH}$  to generate  $[\text{RuO}_3(\text{OH})]\text{OAc}^-$ , which readily abstracts H atoms from alkanes. In the presence of  $\text{Ca}^{2+}$ , a more active intermediate is formed with  $[\text{RuO}_3(\text{OH})]\text{OAc}^-$ , in which  $\text{Ca}(\text{II})$  binds to both  $\text{OAc}^-$  (which is H-bonded to

$\text{OH}$ ) and an oxo ligand. In this work, we have carried out experimental and theoretical investigations on the use of  $\text{AcOH}$  and  $\text{Ca}^{2+}$  to activate  $\text{MnO}_4^-$  toward cyclohexane oxidation.  $\text{MnO}_4^-$  was chosen because of the relevance of Mn in the OEC of photosystem II. Remarkably, a similar synergistic activating effect of  $\text{AcOH}$  and  $\text{Ca}^{2+}$  is also observed for this oxoanion, although  $\text{MnO}_4^-$  is much less basic than  $\text{RuO}_4^-$  and is not protonated by  $\text{AcOH}$ . Our results suggest that the synergistic effects of a weak Brønsted and a weak Lewis acid should be applicable to a variety of metal-oxo species.

## Results and discussion

### Effects of $\text{AcOH}$ on cyclohexane oxidation by $\text{KMnO}_4$

$\text{KMnO}_4$  does not react with cyclohexane at room temperature. However, upon addition of  $\text{AcOH}$  (3–9 M) to  $\text{KMnO}_4$  (0.011 M) in  $\text{CH}_3\text{CN}$  in the presence of cyclohexane (1.0 M) at 23 °C, the purple color of the solution gradually changed to brown. Analysis of the solution by GC-MS and GC-FID revealed the formation of cyclohexanone (38.8%), together with a small amount of cyclohexanol (2.2%). The yields were calculated based on  $\text{KMnO}_4$  acting as a 3-electron oxidant (product is a Mn(IV) species, see below).

Kinetics studies were carried out at constant  $[\text{KMnO}_4]$  (0.011 M) and  $[\text{cyclohexane}]$  (1.0 M) by monitoring the growth of cyclohexanone using a GC-FID (gas chromatograph-flame ionization detector). The increase in  $[\text{cyclohexanone}]$  follows pseudo-first-order kinetics (Fig. 1a), and the pseudo-first-order rate constant  $k_{\text{obs}}$  at  $[\text{AcOH}] = 3.0$  M was found to be  $4.3 \times 10^{-6} \text{ s}^{-1}$ .  $k_{\text{obs}}$  increases with increasing  $[\text{AcOH}]$  (3–9 M), and the plot of  $k_{\text{obs}}$  versus  $[\text{AcOH}]^2$  is linear (Fig. 1b), suggesting that

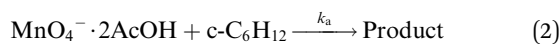
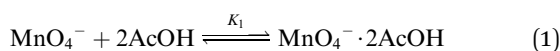
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under these conditions the active oxidizing species involves  $\text{MnO}_4^-$  binding to two molecules of  $\text{AcOH}$ . The reaction can be represented by eqn (1) and (2).



Under the condition that  $K_1 \ll 1$ , the rate-law is given by eqn (3).

$$\frac{d[\text{C}_6\text{H}_{10}\text{O}]/dt = k_{\text{obs}}[\text{MnO}_4^-] = K_1 k_a [\text{AcOH}]^2 [\text{c-C}_6\text{H}_{12}] [\text{MnO}_4^-] \quad (3)$$

From the slope of Fig. 1b,  $K_1 k_a = (4.73 \pm 0.19) \times 10^{-7} \text{ M}^{-2} \text{ s}^{-1}$  at 23.0 °C.

The kinetic isotope effect for cyclohexane oxidation determined by competitive oxidation of an equimolar mixture of *c*- $\text{C}_6\text{H}_{12}$  and *c*- $\text{C}_6\text{D}_{12}$  was found to be  $7.5 \pm 0.1$ , indicating C-H bond cleavage in the rate-limiting step.

### Effects of $\text{Ca}^{2+}$

The oxidation of cyclohexane by  $\text{KMnO}_4$  is also activated by  $\text{Ca}^{2+}$ . Upon adding  $\text{Ca}(\text{OTf})_2$  ( $5.5 \times 10^{-3}$  to  $4.4 \times 10^{-2} \text{ M}$ ) to  $\text{KMnO}_4$  (0.011 M) in  $\text{CH}_3\text{CN}$  containing cyclohexane (1.0 M), the purple color of the solution was gradually discharged together with the formation of a brown precipitate (Fig. 2). The UV/vis spectral changes indicate that there is no shift in the wavelengths of the peaks of  $\text{MnO}_4^-$ , just a gradual decrease in their absorbances (Fig. S1†). The same result was also observed in our earlier work on the effect of  $\text{BF}_3$  on  $\text{KMnO}_4$ .<sup>18</sup> The solution IR of  $\text{KMnO}_4$  and  $\text{KMnO}_4 + \text{Ca}(\text{OTf})_2$  in  $\text{CH}_3\text{CN}$  was also performed (Fig. S2†).  $\text{KMnO}_4$  shows a  $\text{M}=\text{O}$  stretch at  $904 \text{ cm}^{-1}$ , but this peak was not shifted upon addition of  $\text{Ca}(\text{OTf})_2$ ; presumably the binding of  $\text{Ca}^{2+}$  to  $\text{MnO}_4^-$  is relatively weak.

Analysis of the product solution by GC-FID and GC-MS revealed the formation of cyclohexanone (10.5%) and cyclohexanol (0.8%) in relatively low yields. The yields of products reached a maximum with just 1 equiv. of  $\text{Ca}^{2+}$ .

Kinetics studies were also carried out at various  $[\text{Ca}(\text{OTf})_2]$  but at constant  $[\text{KMnO}_4]$  (0.011 M) and  $[\text{cyclohexane}]$  (1.0 M). The increase in  $[\text{cyclohexanone}]$  follows pseudo-first-order

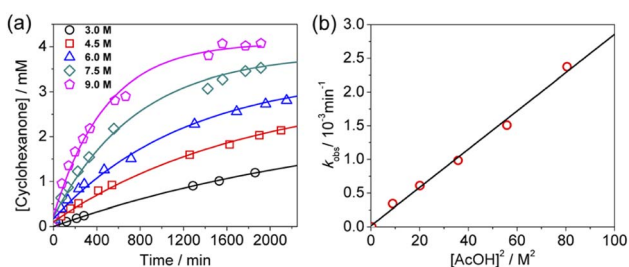


Fig. 1 (a) Time course for the production of cyclohexanone at various  $[\text{AcOH}]$ . Conditions:  $\text{KMnO}_4$ , 0.011 M; cyclohexane, 1.0 M; at 23 °C in  $\text{CH}_3\text{CN}$ . (b) Linear plot of  $k_{\text{obs}}$  vs.  $[\text{AcOH}]^2$ . Slope =  $(2.84 \pm 0.11) \times 10^{-5}$ , intercept =  $(2 \pm 5) \times 10^{-5}$ , and  $r^2 = 0.992$ .

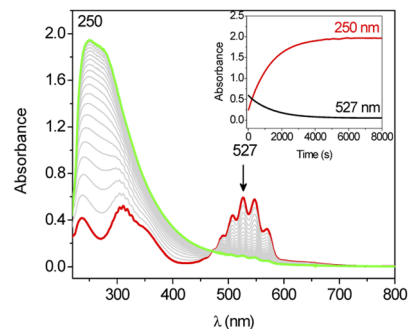
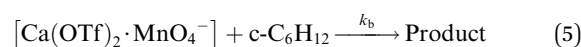
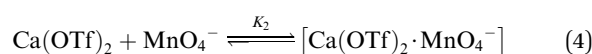


Fig. 2 UV-vis spectral changes for the reaction of  $\text{KMnO}_4$  ( $2.35 \times 10^{-3} \text{ M}$ ) with cyclohexane (1.0 M) in the presence of  $\text{Ca}(\text{OTf})_2$  ( $2.35 \times 10^{-3} \text{ M}$ ) in  $\text{CH}_3\text{CN}$  at 25 °C (1 mm UV cell was used in the measurement). The inset shows the change of absorbance at 250 nm and 527 nm versus time.

kinetics (Fig. 3a), but saturation kinetics were observed on increasing  $[\text{Ca}(\text{OTf})_2]$  (Fig. 3b), and the plot of  $1/k_{\text{obs}}$  versus  $1/[\text{Ca}(\text{OTf})_2]$  is linear. Kinetic studies were also conducted at various  $[\text{cyclohexane}]$  (Fig. 4a), while keeping both  $\text{Ca}(\text{OTf})_2$  and  $\text{KMnO}_4$  at 0.011 M. The plot of  $k_{\text{obs}}$  versus  $[\text{cyclohexane}]$  is linear with an intercept of  $(2.87 \pm 3.3) \times 10^{-4} \text{ s}^{-1}$  (Fig. 4b), which should be due to the decomposition of  $\text{KMnO}_4$  in the absence of cyclohexane. An independent experiment showed that in the presence of 1 equiv. of  $\text{Ca}(\text{OTf})_2$ , the absorbance of  $\text{KMnO}_4$  ( $2.82 \times 10^{-4} \text{ M}$ ) in  $\text{CH}_3\text{CN}$  at around 527 nm gradually decreased with time with a rate constant of  $(9.5 \pm 1.1) \times 10^{-4} \text{ s}^{-1}$  at 23 °C. Such a decomposition also accounts for the low yield of products. The kinetic results are consistent with a pre-equilibrium binding of  $\text{Ca}(\text{II})$  to  $\text{MnO}_4^-$  to form an intermediate, which then oxidizes cyclohexane, as represented by eqn (4) and (5), and the rate law is shown in eqn (6).



$$\begin{aligned} \frac{d[\text{C}_6\text{H}_{10}\text{O}]}{dt} &= k_{\text{obs}}[\text{MnO}_4^-] \\ &= \frac{k_b K_2 [\text{Ca}(\text{OTf})_2]}{(1 + K_2 [\text{Ca}(\text{OTf})_2])} [\text{c-C}_6\text{H}_{12}] [\text{MnO}_4^-] \quad (6) \end{aligned}$$

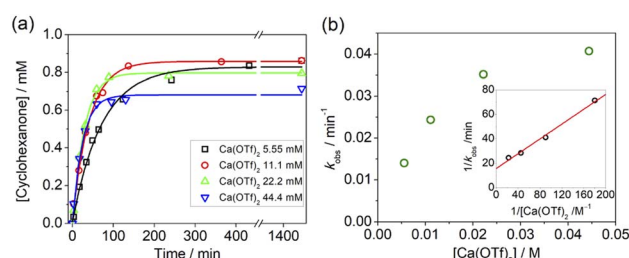


Fig. 3 (a) Time course for the production of cyclohexanone at various  $[\text{Ca}(\text{OTf})_2]$ . Conditions:  $\text{KMnO}_4$ , 0.011 M; cyclohexane, 1.0 M; at 23 °C in  $\text{CH}_3\text{CN}$ . (b) Plot of  $k_{\text{obs}}$  versus  $[\text{Ca}(\text{OTf})_2]$ . Inset: linear plot of  $1/k_{\text{obs}}$  vs.  $1/[\text{Ca}(\text{OTf})_2]$ ; slope =  $0.303 \pm 0.018$ , intercept =  $15.8 \pm 1.9$ , and  $r^2 = 0.99$ .



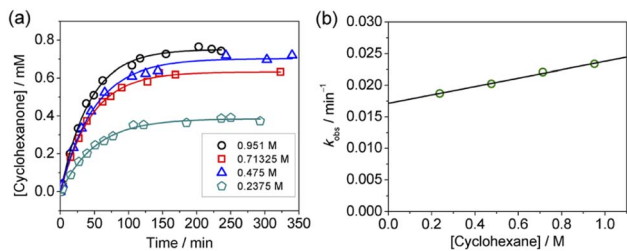


Fig. 4 (a) Time course for the production of cyclohexanone at various [cyclohexane]. Conditions:  $\text{KMnO}_4$  (0.011 M),  $\text{Ca}(\text{OTf})_2$  (0.011 M) and cyclohexane (0.238–0.951 M) in  $\text{CH}_3\text{CN}$  at 23 °C. (b) Plot of  $k_{\text{obs}}$  vs. [cyclohexane]. Slope =  $(6.64 \pm 0.29) \times 10^{-5}$ , intercept =  $(1.72 \pm 0.02) \times 10^{-2}$ , and  $r^2 = 0.994$ .

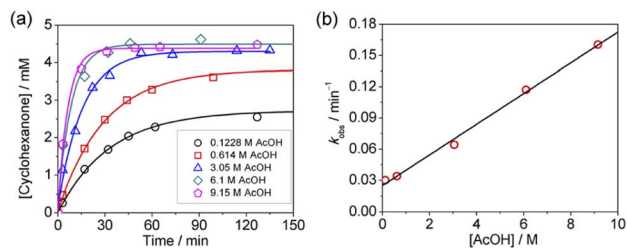


Fig. 5 (a) Time course for cyclohexanone production by  $\text{KMnO}_4$  (0.011 M) in the presence of cyclohexane (1.0 M), 1 equiv. of  $\text{Ca}(\text{OTf})_2$  (0.011 M) and various [AcOH] in  $\text{CH}_3\text{CN}$  at 23.0 °C. (b) Plot of  $k_{\text{obs}}$  vs. [AcOH]. Slope =  $(1.56 \pm 0.06) \times 10^{-2}$ , y-intercept =  $0.025 \pm 0.003$ , and  $r^2 = 0.995$ .

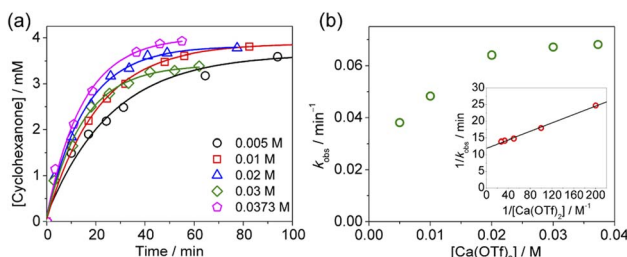


Fig. 6 (a) Time course for cyclohexanone production in  $\text{CH}_3\text{CN}$  at various  $[\text{Ca}(\text{OTf})_2]$ . Conditions: cyclohexane, 1.0 M;  $\text{KMnO}_4$ , 0.011 M; AcOH, 2.79 M.  $T = 23$  °C. (b) Plot of  $k_{\text{obs}}$  versus  $[\text{Ca}(\text{OTf})_2]$ . Inset: plot of  $1/k_{\text{obs}}$  versus  $1/[\text{Ca}(\text{OTf})_2]$ ; slope =  $(6.3 \pm 0.2) \times 10^{-2}$ , y-intercept =  $11.9 \pm 0.2$ , and  $r^2 = 0.995$ .

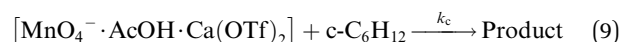
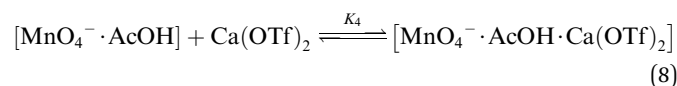
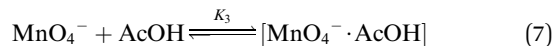
$K_2 = \text{y-intercept/slope of Fig. 3b} = (52.1 \pm 3.5) \text{ M}^{-1}$  and  $k_b = 1/\text{y-intercept} = (1.1 \pm 0.1) \times 10^{-1} \text{ M}^{-3} \text{ s}^{-1}$  at 23 °C.

### Synergistic effects of AcOH and $\text{Ca}^{2+}$

The oxidation of cyclohexane in the presence of both AcOH and  $\text{Ca}^{2+}$  was investigated. As described above, the rate of oxidation of cyclohexane by  $\text{KMnO}_4/\text{AcOH}$  is second-order in  $[\text{AcOH}]$ . However, in the presence of just 1 equiv. of  $\text{Ca}(\text{OTf})_2$ , the rate becomes first-order in  $[\text{AcOH}]$  (Fig. 5).

On the other hand, at constant  $[\text{AcOH}]$  (2.79 M) and  $[\text{cyclohexane}]$  (1.0 M), saturation kinetics were observed on increasing  $[\text{Ca}(\text{OTf})_2]$ , and the plot of  $1/k_{\text{obs}}$  versus  $1/[\text{Ca}(\text{OTf})_2]$  is linear (Fig. 6).

These results are consistent with the reaction scheme shown in eqn (7)–(9).



For  $K_3 \ll 1$ , the rate law is

$$\frac{d[\text{C}_6\text{H}_{10}\text{O}]}{dt} = \frac{k_c K_3 K_4 [\text{Ca}(\text{OTf})_2]}{(1 + K_4 [\text{Ca}(\text{OTf})_2])} [\text{AcOH}][\text{MnO}_4^-][\text{c-C}_6\text{H}_{12}] = k_{\text{obs}} [\text{MnO}_4^-] \quad (10)$$

$K_4 = \text{y-intercept/slope of Fig. 6b inset} = 188.9 \pm 5.6 \text{ M}^{-1}$ . From the slope of Fig. 5b and using  $[\text{Ca}(\text{OTf})_2] = 0.011 \text{ M}$ ,  $K_3 k_c$  was calculated to be  $(3.85 \pm 0.15) \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$  (23 °C).

The kinetic isotope effect for cyclohexane oxidation by the  $\text{KMnO}_4/\text{AcOH}/\text{Ca}(\text{OTf})_2$  system was determined to be  $5.7 \pm 0.1$  by competitive oxidation of an equimolar mixture of  $\text{c-C}_6\text{H}_{12}$  and  $\text{c-C}_6\text{D}_{12}$ , indicating that C–H bond cleavage is the rate limiting step.

A comparison of the activating effects of AcOH,  $\text{Ca}(\text{OTf})_2$  and  $\text{AcOH} + \text{Ca}(\text{OTf})_2$  on cyclohexane oxidation by  $\text{KMnO}_4$  is shown in Table 1. The rate constant ( $k_{\text{obs}}$ ) for the oxidation of cyclohexane (1.0 M) by  $\text{KMnO}_4$  (0.011 M) in the presence of AcOH (3.0 M) at 23 °C was found to be  $5.73 \times 10^{-6} \text{ s}^{-1}$ . When AcOH was replaced by 1 equiv. of  $\text{Ca}(\text{OTf})_2$  (0.011 M), the rate constant

Table 1 Effects of AcOH,  $\text{Ca}(\text{OTf})_2$  and  $\text{AcOH} + \text{Ca}(\text{OTf})_2$  on the oxidation of cyclohexane by  $\text{KMnO}_4$  in  $\text{CH}_3\text{CN}$  at 23 °C<sup>a,b</sup>

|  | 3.0 M AcOH (275 equiv.)                  | 1 equiv. $\text{Ca}(\text{OTf})_2$ (0.011 M) | 1 equiv. $\text{Ca}(\text{OTf})_2$ + 3.0 M of AcOH |
|--|--|--|--|
| $k_{\text{obs}}$ (relative rate)           | $5.73 \times 10^{-6} \text{ s}^{-1}$ (1) | $4.21 \times 10^{-4} \text{ s}^{-1}$ (73)    | $1.14 \times 10^{-3} \text{ s}^{-1}$ (198)         |
| Oxidation state of Mn product <sup>c</sup> | $4.1 \pm 0.2$                            | $4.1 \pm 0.2$                                | $4.0 \pm 0.2$                                      |
| % Yield of cyclohexanone <sup>d</sup>      | 38.8                                     | 10.5   | 57.3   |
| Cyclohexanone/cyclohexanol                 | $18 \pm 1$                               | $14 \pm 1$                                   | $7 \pm 1$  |

<sup>a</sup> Reaction conditions:  $\text{KMnO}_4$ , 0.011 M, cyclohexane, 1.0 M,  $T = 23$  °C. <sup>b</sup>  $\text{KMnO}_4$  alone does not oxidize cyclohexane for >48 h at 23 °C. <sup>c</sup> The final oxidation state of the Mn product after oxidation was determined by iodometric titration. <sup>d</sup> % Yield was calculated based on  $\text{KMnO}_4$  acting as a 3-electron oxidant. Cyclohexanol is the minor product in all cases.



( $4.21 \times 10^{-4} \text{ s}^{-1}$ ) is 73 times faster, but the yield is much lower (10.5%). On the other hand, in the presence of both  $\text{Ca}(\text{OTf})_2$  and  $\text{AcOH}$ , the rate ( $1.14 \times 10^{-3} \text{ s}^{-1}$ ) increases by 198 fold relative to  $\text{AcOH}$  alone, and the product yield is also substantially increased to 57%, indicating synergistic effects of  $\text{AcOH}$  and  $\text{Ca}^{2+}$  in the activation of  $\text{MnO}_4^-$  toward C–H bond activation.

The rate constant for the oxidation of 1.0 M toluene by ( $^{18}\text{Bu}_4\text{N}$ ) $\text{MnO}_4$  was reported to be  $4.2 \times 10^{-7} \text{ s}^{-1}$  at  $25.0 \text{ }^\circ\text{C}$ .<sup>26</sup> As a comparison, we also investigated the oxidation of 1.0 M toluene by  $\text{KMnO}_4$  in the presence of 1 equiv.  $\text{Ca}(\text{OTf})_2$  and 3.0 M  $\text{AcOH}$ , and the rate constant was found to be  $5.2 \times 10^{-3} \text{ s}^{-1}$  at  $23 \text{ }^\circ\text{C}$  (Fig. S3†). Based on these data, the oxidation of toluene by  $\text{KMnO}_4/\text{Ca}^{2+}/\text{AcOH}$  is over 4 orders of magnitude faster than that of  $\text{MnO}_4^-$  alone.

### Effects of other metal ions

The effects of other metal salts, including  $\text{Ba}(\text{OTf})_2$ ,  $\text{Mg}(\text{OTf})_2$ , and  $\text{Sc}(\text{OTf})_3$  on cyclohexane oxidation by  $\text{KMnO}_4$  in the presence of  $\text{AcOH}$  have also been investigated. As expected, both the rate and yield increase with increasing Lewis acidity of the metal ion (Fig. 7a and S4–S6†). The ratio of the rate constants obtained by GC for the 4 metal ions is found to be  $k(\text{Ba}^{2+}) : k(\text{Ca}^{2+}) : k(\text{Mg}^{2+}) : k(\text{Sc}^{3+}) = 1 : 4.8 : 10.4 : 228$ ; and the yields of cyclohexanone are 51% ( $\text{Ba}^{2+}$ ), 56% ( $\text{Ca}^{2+}$ ), 61% ( $\text{Mg}^{2+}$ ), and 75% ( $\text{Sc}^{3+}$ ). There is a fairly linear correlation of  $\log(\text{rate constant})$  with the  $\text{p}K_a$  of the metal ion in water,  $\text{Sc}^{3+}$  ( $\text{p}K_a = 4.3$ ),  $\text{Mg}^{2+}$  ( $\text{p}K_a = 11.2$ ),  $\text{Ca}^{2+}$  ( $\text{p}K_a = 12.7$ ), and  $\text{Ba}^{2+}$  ( $\text{p}K_a = 13.4$ ),<sup>27</sup> which is a measure of their Lewis acidity (Fig. 7b). Similar correlations of Lewis acid effects with their acidities have also been reported.<sup>15,23</sup>

### Nature of the manganese product

Addition of  $\text{Ca}(\text{OTf})_2$  to  $\text{KMnO}_4$  in  $\text{CH}_3\text{CN}$  gradually produced a brown solid and a colorless solution, irrespective of whether cyclohexane was present. When  $\text{AcOH}$  (3 M) was added to the resulting solution after cyclohexane oxidation, the brown solid dissolved but with only a small increase of 1–2% cyclohexanone. The oxidation state of Mn in the brown solution was determined

to be  $4.1 \pm 0.2$  by iodometric titration, which involves the addition of  $\text{NBu}_4\text{I}$  to reduce the  $\text{Mn}^{\text{IV}}$  product to  $\text{Mn}^{\text{II}}$  and then determining the amount of  $\text{I}_3^-$  formed by UV-vis spectrophotometry.<sup>28</sup>

Based on CHN elemental analysis, as well as K, Mn and Ca analysis by ICP-AES, it was found that the brown solids obtained from  $\text{MnO}_4^-/\text{Ca}(\text{OTf})_2$  (**1**) and  $\text{MnO}_4^-/\text{Ca}(\text{OTf})_2/c\text{-C}_6\text{H}_{12}$  (**2**) have similar compositions and are probably a  $\text{Mn}^{\text{IV}}-\mu(\text{O})-\mu(\text{Ca})$  polymer with an empirical formula close to “ $\text{Ca}_3\text{Mn}_7\text{O}_{14}(\text{H}_2\text{O})_{10}(\text{OTf})_6(\text{CH}_3\text{CN})_2$ ” (see the ESI†). The reason for the conversion of  $\text{Mn}^{\text{VII}}$  to  $\text{Mn}^{\text{IV}}$  in the absence of  $c\text{-C}_6\text{H}_{12}$  is not clear, presumably due to oxidation of the solvent.

We have carried out X-ray photoelectron spectroscopy (XPS) of **1** and **2** (Fig. S7 and S8†). In the  $\text{Mn}3s$  XPS spectra (Fig. S8†), the peak splitting of  $\Delta E = 4.8 \text{ eV}$  indicates that the oxidation state of Mn is +4.<sup>29</sup>

We have also determined the magnetic susceptibility of the solid samples of **1** and **2** using a magnetic balance. The  $\mu_{\text{eff}}$  for each Mn was found to be 3.96 and 4.05  $\mu_B$  for **1** and **2**, respectively, consistent with that of high spin  $\text{Mn}(\text{IV})$  with  $S = 3/2$ .

No brown precipitate was observed when cyclohexane oxidation was carried out in the presence of  $\text{AcOH}$ , irrespective of whether  $\text{Ca}(\text{OTf})_2$  was added. The Mn oxidation state of the brown solution determined by iodometric titration is again  $4.0 \pm 0.2$ . Presumably the brown solution contains colloidal  $\text{MnO}_2$ , as observed in alkane oxidation by  $\text{BF}_3/\text{MnO}_4^-$ .<sup>18</sup>

### Theoretical calculations

DFT calculations on the mechanisms of the oxidation of cyclohexane by  $\text{MnO}_4^-$ ,  $\text{MnO}_4^-/\text{AcOH}$ ,  $\text{MnO}_4^-/\text{Ca}(\text{OTf})_2^+$  and  $\text{MnO}_4^-/\text{AcOH}/\text{Ca}(\text{OTf})_2^+$  were performed. Solvent ( $\text{CH}_3\text{CN}$ ) effects have been included in the calculations.

The potential energy surfaces (PESs) for all calculated reactions are summarized in Fig. S9.† In the  $c\text{-C}_6\text{H}_{12}$  oxidation by  $\text{MnO}_4^-$  in  $\text{CH}_3\text{CN}$  (Fig. 8),  $c\text{-C}_6\text{H}_{12}$  and  $\text{MnO}_4^-$  first bind weakly together to form an intermediate  $[\text{MnO}_4 \cdots \text{C}_6\text{H}_{12}]^-$ , INT1( $\text{MnO}_4^-$ ). Hydrogen atom transfer (HAT) then occurs from

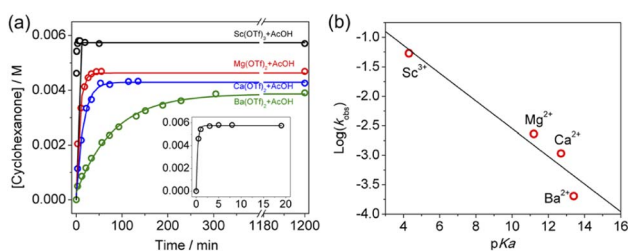


Fig. 7 (a) Time course for the production of cyclohexanone by  $\text{KMnO}_4$  (0.01 M)/ $\text{AcOH}$  (2.78 M)/ $c\text{-C}_6\text{H}_{12}$  (1.0 M) in the presence of 0.01 M of various metal salts. Pseudo-first-order fits give  $k_{\text{obs}}$ :  $\text{Sc}(\text{OTf})_3 = 5.4 \times 10^{-2} \text{ s}^{-1}$ ,  $\text{Mg}(\text{OTf})_2 = 2.3 \times 10^{-3} \text{ s}^{-1}$ ,  $\text{Ca}(\text{OTf})_2 = 1.1 \times 10^{-3} \text{ s}^{-1}$ , and  $\text{Ba}(\text{OTf})_2 = 2 \times 10^{-4} \text{ s}^{-1}$ . The inset shows the time course for  $\text{Sc}(\text{OTf})_3$ . (b) Plot of  $\log(k_{\text{obs}})$  vs.  $\text{p}K_a$  of metal ions.  $\text{Sc}^{3+}$  ( $\text{p}K_a = 4.3$ ),  $\text{Mg}^{2+}$  ( $\text{p}K_a = 11.2$ ),  $\text{Ca}^{2+}$  ( $\text{p}K_a = 12.7$ ), and  $\text{Ba}^{2+}$  ( $\text{p}K_a = 13.4$ ). Slope =  $-0.24 \pm 0.04$ , intercept =  $-0.2 \pm 0.5$ , and  $r^2 = 0.90$ .

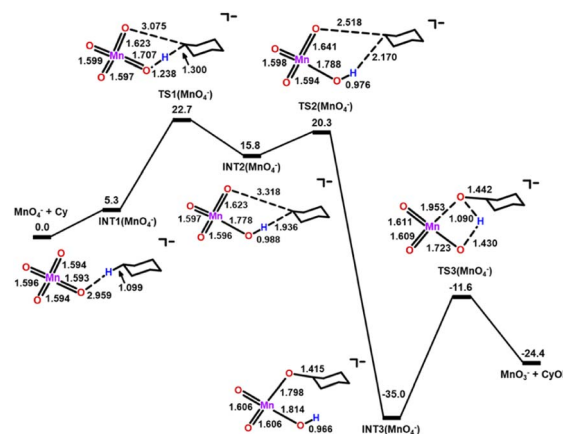


Fig. 8 PES and structures for cyclohexane oxidation by  $[\text{MnO}_4]^-$  at the B3LYP-D3(BJ)/def2-SVPD level. The relative 298 K Gibbs free energies in acetonitrile are given in  $\text{kcal mol}^{-1}$ .



$c\text{-C}_6\text{H}_{12}$  to  $\text{Mn}=\text{O}$  *via* a transition state,  $\text{TS1}(\text{MnO}_4^-)$ , to give a second intermediate,  $\text{INT2}(\text{MnO}_4^-)$ . The HAT step is rate-determining with a barrier height ( $\Delta G_{298}^\ddagger$ ) of 22.7 kcal mol $^{-1}$ . Such a high barrier suggests that  $\text{MnO}_4^-$  will hardly oxidize  $c\text{-C}_6\text{H}_{12}$  at room temperature. The carbon atom in the cyclohexyl radical of  $\text{INT2}(\text{MnO}_4^-)$  bears a  $-1.01$  electron spin, consistent with the spin distribution for a HAT. In the next step, the cyclohexyl radical binds to another  $\text{Mn}=\text{O}$  to generate an alkoxo intermediate  $[\text{MnO}_2(\text{OH})(\text{OC}_6\text{H}_{11})]^-$  *via*  $\text{TS2}(\text{MnO}_4^-)$ . Subsequently, proton transfer from  $\text{Mn}-\text{OH}$  to the alkoxide in  $\text{INT3}(\text{MnO}_4^-)$  occurs *via*  $\text{TS3}(\text{MnO}_4^-)$  to generate the cyclohexanol product. The reaction mechanism is similar to that of  $c\text{-C}_6\text{H}_{12}$  oxidation by  $\text{RuO}_4^-$  found in our previous study.<sup>25</sup>

In the presence of an acetic acid molecule (Fig. S10 $^\dagger$ ),  $\text{AcOH}$  and  $\text{MnO}_4^-$  first form  $\text{INT1}(\text{AcOH})$ ,  $[\text{MnO}_4(\text{AcOH})\cdots\text{C}_6\text{H}_{12}]^-$ , through a hydrogen bond. The  $\text{Mn}=\text{O}$  that is H-bonded to  $\text{AcOH}$  is elongated to 1.611 Å, while the other three  $\text{Mn}=\text{O}$  bonds become more electrophilic and shorter with distances of 1.587–1.590 Å, compared with the bond length of 1.594 Å in  $\text{MnO}_4^-$ . In  $\text{TS1}(\text{AcOH})$ , HAT occurs from  $c\text{-C}_6\text{H}_{12}$  to another free but shorter  $\text{Mn}=\text{O}$  bond (bond length = 1.588 Å). The  $\Delta G_{298}^\ddagger$  of  $\text{TS1}(\text{AcOH})$  is 20.4 kcal mol $^{-1}$ , which is 2.3 kcal mol $^{-1}$  lower than that of  $\text{TS1}(\text{MnO}_4^-)$ . The subsequent steps are similar to those in  $c\text{-C}_6\text{H}_{12}$  oxidation by  $\text{MnO}_4^-$ .

In the presence of three  $\text{AcOH}$  molecules, the  $\text{AcOH}$  molecules form hydrogen bonds with three  $\text{Mn}=\text{O}$  to give an intermediate,  $\text{INT1}(3\text{AcOH})$  (Fig. 9). The bond lengths of the H-bonded  $\text{Mn}=\text{O}$  are slightly elongated from 1.591 to 1.601 Å. HAT then occurs from  $c\text{-C}_6\text{H}_{12}$  to the free and more electrophilic  $\text{Mn}=\text{O}$  bond (bond length = 1.580 Å), with a  $\Delta G_{298}^\ddagger = 16.8$  kcal mol $^{-1}$ . Compared with  $c\text{-C}_6\text{H}_{12}$  oxidation by  $\text{MnO}_4^-$ , the  $\Delta G_{298}^\ddagger$  of HAT is further reduced by 5.9 kcal mol $^{-1}$ .

In the presence of  $[\text{Ca}(\text{OTf})]_2$  (Fig. 10),  $\text{Ca}(\text{II})$  binds to two of the  $\text{Mn}=\text{O}$  bonds to form  $\text{INT1}(\text{CaOTf})$ ,  $[\text{MnO}_4(\text{CaOTf})\cdots\text{C}_6\text{H}_{12}]^-$ . The two  $\text{Mn}=\text{O}$  bonds that bind to  $\text{Ca}(\text{II})$  in  $\text{INT1}(\text{CaOTf})$  are longer (1.611 and 1.615 Å) than the unbound  $\text{Mn}=\text{O}$  bonds (1.576 Å) in  $\text{INT1}(\text{MnO}_4^-)$ , as a result of the electron withdrawing effect of  $\text{Ca}(\text{II})$ . Subsequent HAT from  $c\text{-C}_6\text{H}_{12}$  to an unbound

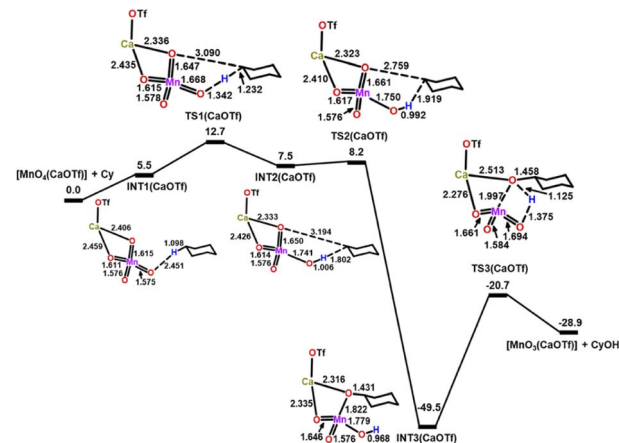


Fig. 10 PES and structures for cyclohexane oxidation by  $[\text{MnO}_4(\text{CaOTf})]^-$  at the B3LYP-D3(BJ)/def2-SVPD level. The relative 298 K Gibbs free energies in acetonitrile are given in kcal mol $^{-1}$ .

$\text{Mn}=\text{O}$  occurs with a  $\Delta G_{298}^\ddagger$  of 12.7 kcal mol $^{-1}$  *via*  $\text{TS1}(\text{CaOTf})$ , which is lower than that of  $\text{MnO}_4^-$  and  $\text{MnO}_4^-/3\text{AcOH}$  by 10.0 and 4.1 kcal mol $^{-1}$ , respectively; consistent with the experimental observation that the accelerating effect of  $\text{Ca}(\text{II})$  is much higher than that of  $\text{AcOH}$ .

The activation barrier is further lowered when both  $[\text{Ca}(\text{OTf})]^+$  and  $\text{AcOH}$  are present. In the presence of one molecule of  $[\text{Ca}(\text{OTf})]^+$  and three molecules of  $\text{AcOH}$ , each  $\text{AcOH}$  is H-bonded to one  $\text{Mn}=\text{O}$ , while the  $[\text{Ca}(\text{OTf})]^+$  is bonded to each  $\text{AcOH}$  and one  $\text{Mn}=\text{O}$  to form a relatively stable intermediate,  $\text{INT1}(\text{CaOTf}/3\text{AcOH})$ , as shown in Fig. 11. HAT then occurs from  $c\text{-C}_6\text{H}_{12}$  to the free and shortest  $\text{Mn}=\text{O}$  bond with the lowest  $\Delta G_{298}^\ddagger$  of 9.7 kcal mol $^{-1}$  ( $\Delta G_{298}^\ddagger = 11.5$  kcal mol $^{-1}$  for one  $\text{Ca}(\text{OTf})^+$  and one  $\text{AcOH}$ , Fig. S11 $^\dagger$ ), in agreement with the observed synergistic activating effects of  $\text{AcOH}$  and  $\text{Ca}(\text{II})$ . It should be noted that in this case HAT results in the direct formation of the alkoxo intermediate without going through a cyclohexyl radical intermediate.

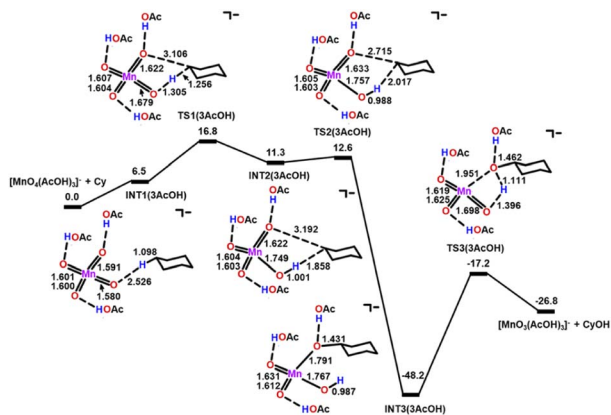


Fig. 9 PES and structures for cyclohexane oxidation by  $[\text{MnO}_4(\text{AcOH})_3]^-$  at the B3LYP-D3(BJ)/def2-SVPD level. The relative 298 K Gibbs free energies in acetonitrile are given in kcal mol $^{-1}$ .

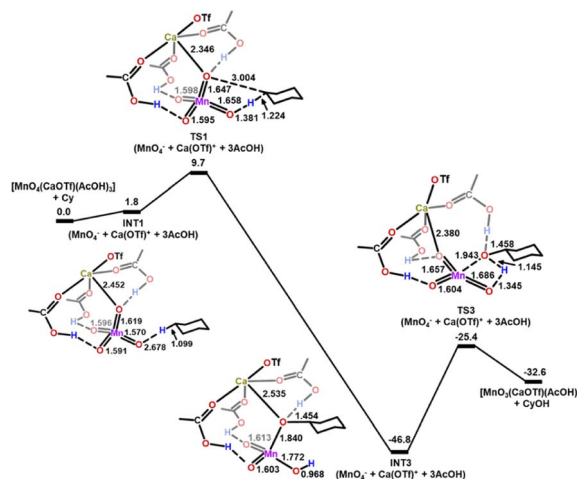


Fig. 11 PES and structures for cyclohexane oxidation by  $[\text{MnO}_4(\text{CaOTf})(\text{AcOH})_3]^-$  at the B3LYP-D3(BJ)/def2-SVPD level. The relative 298 K Gibbs free energies in acetonitrile are given in kcal mol $^{-1}$ .



Table 2 Activation barrier ( $\Delta G_{298}^\ddagger$ , kcal mol<sup>-1</sup>) for the oxidation of *c*-C<sub>6</sub>H<sub>12</sub> by RuO<sub>4</sub><sup>-</sup> and MnO<sub>4</sub><sup>-</sup> under various conditions

|                         | RuO <sub>4</sub> <sup>-</sup> | MnO <sub>4</sub> <sup>-</sup> |
|-------------------------|-------------------------------|-------------------------------|
| No additive             | 26.8                          | 22.7                          |
| AcOH                    | 15.2                          | 16.8                          |
| Ca <sup>2+</sup>        | 18.5                          | 12.7                          |
| AcOH + Ca <sup>2+</sup> | 10.8                          | 9.7                           |

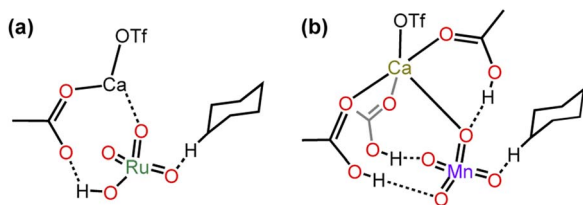


Fig. 12 Structures of the intermediates (a) RuO<sub>4</sub><sup>-</sup>/AcOH/Ca(OTf)<sub>2</sub> and (b) MnO<sub>4</sub><sup>-</sup>/AcOH/Ca(OTf)<sub>2</sub>.

$\Delta G_{298}^\ddagger$  was also determined experimentally by performing kinetics studies at 20–50 °C. From the Arrhenius plot  $\Delta G_{298}^\ddagger$  was found to be  $10.4 \pm 0.6$  kcal mol<sup>-1</sup>, in agreement with the calculated value (Fig. S12†).

We have also calculated the TS barrier heights for hydroxylation *via* a rebound mechanism and they are higher than those of the TS forming the alkoxo intermediate by 2–3.4 kcal mol<sup>-1</sup> (Table S1†).

#### Activating effects of Ca<sup>2+</sup>/AcOH on MnO<sub>4</sub><sup>-</sup> vs. RuO<sub>4</sub><sup>-</sup>

Although MnO<sub>4</sub><sup>-</sup> and RuO<sub>4</sub><sup>-</sup> are isostructural with similar  $E^0$  (0.56 V and 0.59 V, respectively), there is a great difference in the basicity of their oxo ligands; MnO<sub>4</sub><sup>-</sup> is a weak base ( $pK_a$  of HMnO<sub>4</sub> is -2.25),<sup>30</sup> whereas RuO<sub>4</sub><sup>-</sup> is a much stronger base. Although the  $pK_a$  of HRuO<sub>4</sub> is not known, RuO<sub>4</sub><sup>-</sup> is readily protonated by weak acids such as AcOH to give [RuO<sub>3</sub>(-OH)(AcO)<sup>-</sup>], which readily undergoes HAT with *c*-C<sub>6</sub>H<sub>12</sub> with a barrier that is lower than that of RuO<sub>4</sub><sup>-</sup> by >10 kcal mol<sup>-1</sup> (Table 2).<sup>25</sup> In contrast, MnO<sub>4</sub><sup>-</sup> is not protonated by AcOH. Nevertheless, AcOH can still exert a moderate activating effect on HAT by MnO<sub>4</sub><sup>-</sup> through H-bonding with the oxo ligands, with the activation barrier lowered by 6 kcal mol<sup>-1</sup> compared with MnO<sub>4</sub><sup>-</sup> alone. On the other hand, Ca<sup>2+</sup> has a higher activating effect on MnO<sub>4</sub><sup>-</sup> than on RuO<sub>4</sub><sup>-</sup> (lowering of the barrier is 10 vs. 8 kcal mol<sup>-1</sup>). Remarkably, for both complexes the presence of AcOH and Ca<sup>2+</sup> together shows a similar synergistic activating effect, resulting in a lowering of the HAT barrier by 16 and 13 kcal mol<sup>-1</sup> for RuO<sub>4</sub><sup>-</sup> and MnO<sub>4</sub><sup>-</sup>, respectively. DFT calculations show that Ca(II) forms a MO<sub>4</sub><sup>-</sup>/AcOH/Ca(II) active intermediate by binding to AcO<sup>-</sup>/AcOH and an oxo ligand (Fig. 12).

## Conclusions

In conclusion, we have demonstrated synergistic activating effects of a weak Brønsted acid such as acetic acid and a weak Lewis acid such as Ca<sup>2+</sup> on MnO<sub>4</sub><sup>-</sup>. Although MnO<sub>4</sub><sup>-</sup> is rather

non-basic, it can readily be activated by AcOH + Ca<sup>2+</sup> toward HAT of *c*-C<sub>6</sub>H<sub>12</sub>, resulting in a lowering of the barrier by 13 kcal mol<sup>-1</sup>. Remarkably, such a cooperative effect on MnO<sub>4</sub><sup>-</sup> is similar to that on RuO<sub>4</sub><sup>-</sup>, despite a great difference in the basicity of the two metal-oxo species, which should lead to vastly different affinities toward acids. Our studies suggest that such a synergistic activation is a general phenomenon which may occur in various other metal-oxo species.

The combination of a weak Brønsted and a weak Lewis acid is a potentially useful strategy for the activation of a metal-oxo species toward oxidation of various organic compounds, particularly for substrates that may contain functional groups that are sensitive to strong acids. It is possible that this synergistic activating effect on metal-oxo species may also occur in biological systems, where only relatively mild Brønsted acids and Lewis acids (metal ions) are present.

## Data availability

The datasets supporting this article have been uploaded as part of the ESI.†

## Author contributions

C. K. M. designed and carried out the experiments, analysed the data and wrote the manuscript. T. C. L. designed the experiments and wrote the manuscript. H. S. performed the experiments and helped in the analysis of the data and preparation of the manuscript. L. C., Y. P. and K. C. L. performed computational studies and wrote the manuscript.

## Conflicts of interest

There are no conflicts to declare.

## Note added after first publication

This article replaces the version published on 26/09/2022, which contained errors in the position of the equilibrium constants in equations 1, 4, 7 and 8.

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