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Lewis acid-activated oxidation of alcohols by permanganate†

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The oxidation of alcohols by $KMnO_4$ is greatly accelerated by various Lewis acids. Notably the rate is increased by 4 orders of magnitude in the presence of Ca^{2+}. The mechanisms of the oxidation of CH_3OH and $PhCH(OH)CH_3$ by MnO_4^- and $BF_3{\cdot}MnO_4^-$ have also been studied computationally by the DFT method.

The design of highly active metal oxo species that can mimic the reactivity of the iron oxo active intermediates in enzymes such as cytochrome P450 and methane monooxygenase continues to be a challenge for chemists.[1–3] Our strategy to generate highly oxidizing species is to make use of Lewis acids to activate metal oxo species that are otherwise relatively stable and unreactive.[4–8] For example, we have reported that the oxidation of alkanes by $KMnO_4$ in acetonitrile is accelerated by over seven orders of magnitude in the presence of BF_3.[4] In the absence of substrates BF_3/MnO_4^- undergoes an intramolecular O···O coupling reaction to generate O_2.[9] We report here that the oxidation of alcohols by $KMnO_4$ in CH_3CN is also greatly accelerated by various Lewis acids, including BF_3, $Sc(CF_3SO_3)_3$, $Zn(CF_3SO_3)_2$, $Ca(CF_3SO_3)_2$ and $Ba(CF_3SO_3)_2$.

A solution of $KMnO_4$ in CH_3CN reacts very slowly with CH_3OH at room temperature. The half-life ($t_{1/2}$) for the reaction of 1×10^{-4} M of $KMnO_4$ with 0.1 M CH_3OH in CH_3CN at 298 K is ~110 h, and we estimate that k_2, the second-order rate constant, is $\sim 1 \times 10^{-5}\ M^{-1}\ s^{-1}$. On the other hand, in the presence of BF_3, the oxidation of CH_3OH by $KMnO_4$ in CH_3CN occurs within seconds. There is a very rapid decrease in absorbance at around 550 nm, followed by a much slower decay; as monitored by UV/Vis stopped-flow spectrophotometry (Fig. S1, ESI†). The initial decay is too fast to be followed by stopped-flow spectrophotometry, we attribute this step to the formation of a BF_3/MnO_4^- adduct, as shown in eqn (1); while the second step is the oxidation of CH_3OH by the adduct. In the presence of excess BF_3 and CH_3OH, the decay of MnO_4^- at 526 nm (the second step) follows clean pseudo-first-order kinetics for over three half-lives (Fig. 1). The pseudo-first-order rate constant, k_{obs}, increases linearly with $[BF_3]$ (Fig. S2, ESI†). k_{obs} also increases with $[CH_3OH]$, but reaches saturation at high $[CH_3OH]$; and the plot of $1/k_{obs}$ *vs.* $1/[CH_3OH]$ is linear (Fig. 2). At 298 K, K_{CH_3OH} and kK_{BF_3} are found to be $(7.06 \pm 0.31) \times 10^2\ M^{-1}$ and $(2.67 \pm 0.07) \times 10^2\ M^{-1}\ s^{-1}$ respectively. These results are consistent with the reaction

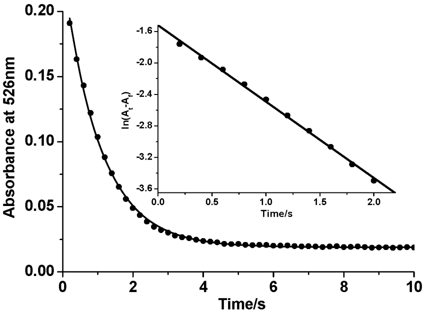

Fig. 1 Kinetic trace at 526 nm for the BF_3 (4.0×10^{-3} M) activated oxidation of CH_3OH (1.0×10^{-2} M) by $KMnO_4$ (1.0×10^{-4} M) in CH_3CN at 298 K. The inset shows the plot of $\ln(A_t - A_f)$ *vs.* *t*.

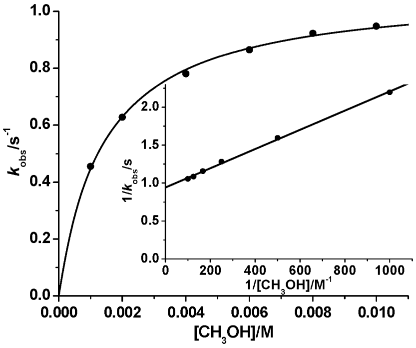

Fig. 2 Plot of k_{obs} *vs.* $[CH_3OH]$. $[BF_3] = 4.0 \times 10^{-3}$ M, $[KMnO_4] = 1.0 \times 10^{-4}$ M, $T = 298$ K. The inset shows the corresponding plot of $1/k_{obs}$ *vs.* $1/CH_3OH$ (slope $= (1.27 \pm 0.01) \times 10^{-3}$, y-intercept $= (9.43 \pm 0.02) \times 10^{-1}$, $r = 0.998$).

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scheme shown in eqn (1)–(6). If CF_3CO_2H is replaced by BF_3, the rate is slower by $>10^3$ under the same conditions.

$$BF_3 + MnO_4^- \xrightleftharpoons{K_{BF_3}} [BF_3\cdot MnO_4]^- \quad (1)$$

$$[BF_3\cdot MnO_4]^- + CH_3OH \xrightleftharpoons{K_{CH_3OH}} [BF_3\cdot MnO_4\cdot CH_3OH]^- \quad (2)$$

$$[BF_3\cdot MnO_4\cdot CH_3OH]^- \xrightarrow{k} \text{products} \quad (3)$$

$$\text{Rate} = k_{obs}[MnO_4^-] \quad (4)$$

$$\text{Rate} = k\left(\frac{K_{BF_3}[BF_3]}{1 + K_{BF_3}[BF_3]}\right)\left(\frac{K_{CH_3OH}[CH_3OH]}{1 + K_{CH_3OH}[CH_3OH]}\right)[MnO_4^-] \quad (5)$$

$K_{BF_3}[BF_3] \ll 1$ (since no saturation kinetics were observed)

$$\text{Rate} = \frac{kK_{BF_3}K_{CH_3OH}[CH_3OH][MnO_4^-][BF_3]}{1 + K_{CH_3OH}[CH_3OH]} \quad (6)$$

The effects of other Lewis acids on the oxidation of CH_3OH by $KMnO_4$ have also been investigated at [Lewis acid] = 1×10^{-3} M. The rate law is: Rate = $k_2[MnO_4^-][CH_3OH]$ for these Lewis acids, and no saturation kinetics are observed. The observed saturation kinetics in the case of BF_3 is probably due to stabilization of the intermediate by RO–H···F–B hydrogen bonding, which is supported by DFT calculations described below. From Table 1 it can be seen that these Lewis acids accelerate the oxidation of CH_3OH by $KMnO_4$ by 3–7 orders of magnitude. The ability of Ca^{2+} to activate MnO_4^- by 4 orders of magnitude is of particular interest, because Ca^{2+} plays a key role in the $CaMn_4O_x$ active site in the oxygen evolving complex (OEC) in Photosystem II (PSII).[10–12]

The BF_3-activated oxidation of various other alcohols by $KMnO_4$ in CH_3CN has also been studied (Table 2). Rate saturation with respect to [ROH] is observed for all substrates, except 1-phenylethanol, where the rate increases linearly with [1-phenylethanol] from 0.001–0.01 M. Notably the rate constants are within a very narrow range, despite their large differences in C–H bond dissociation energies (BDFE) and hydride affinities (HA) (Table S1, ESI†). Table 3 shows product yields for selected alcohols. In the oxidation of cyclohexanol and benzyl alcohol, 2.5 mol of the carbonyl product is formed per mol of $KMnO_4$, suggesting that it functions as a 5-electron oxidant. The absence of broad absorptions in the range 400–600 nm due to colloidal MnO_2 and the inability of the final solution to oxidize I^- to I_2 are consistent with the product being Mn(II) rather than MnO_2. On the other hand, in the absence of BF_3, brown precipitate of MnO_2 was observed at the end of the reaction. In the oxidation of cyclobutanol by BF_3/MnO_4^-, cyclobutanone is formed exclusively, suggesting a two-electron hydride abstraction mechanism.[13] A deuterium isotope effect of 1.5 ± 0.2 was obtained for the oxidation of both methanol (k_{CH_3OH}/k_{CD_3OD}) and benzyl alcohol ($k_{C_6H_5CH_2OH}/k_{C_6D_5CD_2OH}$) by BF_3/MnO_4^-. These are much smaller than the corresponding values for other metal oxo species. For example, for $Ru(bpy)_2(py)(O)^{2+}$, the deuterium isotope effects are 9 and 50 for CH_3OH/CD_3OH and $C_6H_5CH_2OH/C_6H_5CD_2OH$, respectively.[14] However small deuterium isotope effects of 1.84 and 2.58 have been reported for known hydride transfer from $(CH_3)_2CHOH$ to Ph_3C^+ and HCO_2^-, respectively.[15]

Table 1 Rate constants at 298 K for the oxidation of CH_3OH by $KMnO_4$ in CH_3CN in the presence of various Lewis acids[a]

Lewis acid	$k_2/M^{-1}\ s^{-1}$	Rate acceleration[c]
None	$\sim 1 \times 10^{-5}$	
$Ba(CF_3SO_3)_2$	$(8.6 \pm 0.2) \times 10^{-2}$	8.6×10^3
$Ca(CF_3SO_3)_2$	$(1.12 \pm 0.03) \times 10^{-1}$	1.1×10^4
$Zn(CF_3SO_3)_2$	$(9.71 \pm 0.18) \times 10^{-1}$	9.7×10^4
$Sc(CF_3SO_3)_3$	$(1.35 \pm 0.02) \times 10^1$	1.3×10^6
BF_3[b]	$(7.6 \pm 0.4) \times 10^2$	7.6×10^7

[a] $KMnO_4$, 1.0×10^{-4} M; Lewis acid, 1.0×10^{-3} M. [b] BF_3, 4.0×10^{-3} M. [c] Ratio of k_2(Lewis acid/MnO_4^-)/k_2(MnO_4^-).

Table 2 Representative rate data for the oxidation of alcohols by $BF_3/KMnO_4$

Substrate	K_{ROH}[a]$/M^{-1}$	kK_{BF_3}[a]$/M^{-1}\ s^{-1}$
Methanol	$(7.06 \pm 0.31) \times 10^2$	$(2.67 \pm 0.07) \times 10^2$
Ethanol	$(1.50 \pm 0.04) \times 10^3$	$(6.07 \pm 0.09) \times 10^2$
2-Propanol	$(3.88 \pm 0.16) \times 10^2$	$(7.60 \pm 0.12) \times 10^2$
Cyclohexanol	$(4.90 \pm 0.24) \times 10^2$	$(2.08 \pm 0.51) \times 10^3$
2-Heptanol	$(1.72 \pm 0.14) \times 10^2$	$(6.80 \pm 0.21) \times 10^2$
1-Heptanol	$(5.58 \pm 0.25) \times 10^2$	$(1.69 \pm 0.27) \times 10^3$
Benzyl alcohol	$(3.23 \pm 0.61) \times 10^1$	$(6.00 \pm 0.44) \times 10^3$
1-Phenylethanol		$(4.28 \pm 0.05) \times 10^1$[b]
4-Chlorobenzyl alcohol	$(9.98 \pm 0.10) \times 10^1$	$(2.28 \pm 0.08) \times 10^3$
Cyclobutanol	$(4.52 \pm 0.09) \times 10^2$	$(6.22 \pm 0.04) \times 10^2$

[a] $KMnO_4$, 1.0×10^{-4} M; BF_3, 4.0×10^{-3} M; 298 K, CH_3CN. [b] This rate constant should be equal to $kK_{BF_3}K_{ROH}$.

Table 3 Product yields for the oxidation of alcohols by $KMnO_4/BF_3$[a,b]

Alcohol	Product	mmol (%yield)
Cyclohexanol	Cyclohexanone	0.020 (100)
Benzyl alcohol	Benzaldehyde	0.020 (100)
2-Heptanol	2-Heptanone	0.016 (80)
Cyclobutanol	Cyclobutanone	0.015 (75)

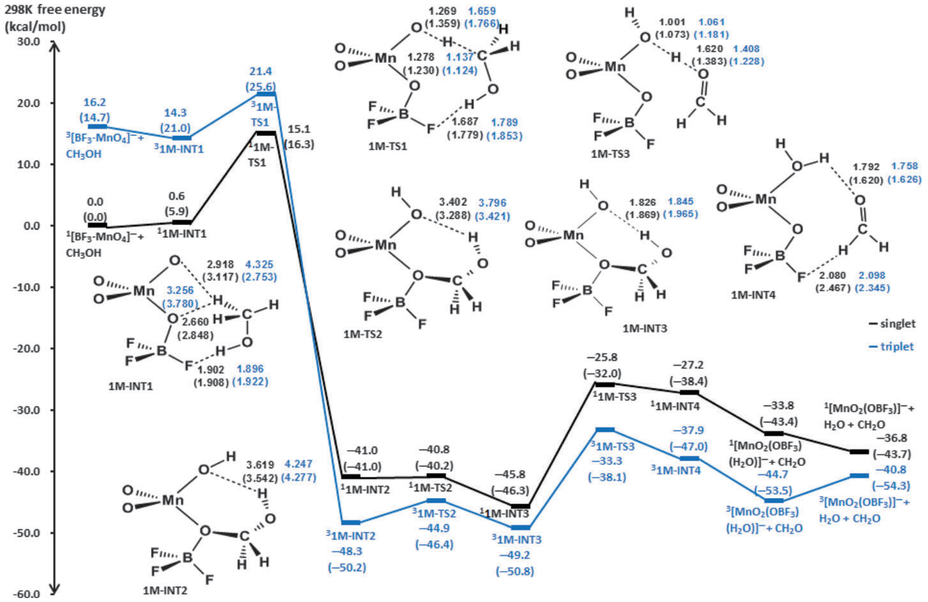
[a] $KMnO_4$, 0.008 mmol; BF_3, 0.12 mmol; alcohol, 0.8 mmol. T = 23 °C. Time = 15 min. All the reactions were carried out in CH_3CN (2 ml) under argon with chlorobenzene as internal standard. [b] Yields are calculated based on $KMnO_4$ acting as a 5-electron oxidant.

In order to gain more insight into the mechanism of alcohol oxidation by Lewis acid/$KMnO_4$, DFT calculations have been performed on the oxidation of CH_3OH and $PhCH(OH)CH_3$ by $KMnO_4$ and $BF_3{\cdot}MnO_4^-$. The reaction barriers (ΔG^{o}_{298}) in gas phase and in acetonitrile are summarized in Table 4. The reaction barriers are substantially lowered in the presence of BF_3, consistent with the observed accelerating effects.

The singlet and triplet potential energy surfaces (PESs) for the oxidation of CH_3OH by $[BF_3{\cdot}MnO_4]^-$ is shown in Scheme 1. CH_3OH and $[BF_3{\cdot}MnO_4]^-$ first form an intermediate

Table 4 Reaction barriers ($\Delta G^{\neq}_{298}$, in kcal mol^{-1}) for the oxidation of methanol and 1-phenylethanol by MnO_4^- and $[BF_3{\cdot}MnO_4]^-$ in gas phase and in acetonitrile

$\Delta G^{\neq}_{298}$	Gas phase	PCM (acetonitrile)
Methanol oxidation		
MnO_4^-	20.3	26.1
$BF_3{\cdot}MnO_4^-$	15.1	16.3
1-Phenylethanol oxidation		
MnO_4^-	16.7	24.4
$BF_3{\cdot}MnO_4^-$	20.4	16.7



Scheme 1 Potential energy surface for the oxidation of CH_3OH by $[BF_3{\cdot}MnO_4]^-$ at the B3LYP level using LanL2DZ basis set for transition metal (Mn) and 6-311++G(d,p) basis set for nonmetal atoms. Relative 298 K Gibbs free energies in gas phase and in acetonitrile (in parentheses) are given in kcal mol^{-1}.

(^{1}1M-INT1), $[(MnO_3)(OBF_3)(CH_3OH)]^-$, followed by hydride transfer to form (^{3}1M-INT2), $[MnO_2(OH)(OBF_3CH_2OH)]^-$. The hydride transfer step occurs with a reaction barrier of ΔG^o_{298} = 16.3 kcal mol^{-1} in CH_3CN *via* ^{1}1M-TS1 and forms ^{3}1M-INT2 by singlet-triplet PES crossing. This hydride transfer is followed by combination of the resulting carbocation with $Mn{-}OBF_3$ to form a very stable intermediate ^{3}1M-INT2 and the ΔG^o_{298} of the hydride abstraction is −56.1 kcal mol^{-1} relative to ^{1}1M-INT1 (in CH_3CN). The intermediate ^{3}1M-INT3, formed by internal rotation of hydroxyl groups in ^{3}1M-INT2, undergoes proton transfer from the hydroxyl group of the alcohol to Mn–OH to form ^{3}1M-INT4. INT4 then decomposes to CH_2O, H_2O and $^3MnO_2(OBF_3)^-$, the latter Mn(V) species presumably undergoes disproportionation to give Mn(VII) and Mn(IV). The mechanism of 1-phenylethanol oxidation by $BF_3{\cdot}MnO_4^-$ is similar to that of methanol, except because of the bulkiness of $PhCH(OH)CH_3$, the BF_3 is required to bind to a free manganese oxo group that is not directly involved in bonding interactions with the CH_3OH molecule during the redox process (ESI†). Apparently this leads to a smaller effect of BF_3 on the reaction barrier (Table 4), resulting in CH_3OH and $PhCH(OH)CH_3$ being oxidized at similar rates, despite their large differences in BDFE and HA.

In conclusion, we have reported a number of novel effects of Lewis acids on the oxidation of alcohols by MnO_4^-. First, rate accelerations of 3–7 orders of magnitude are observed. Second, MnO_4^- usually functions as a 3-electron oxidant in organic solvents, but in the presence of Lewis acids it may function as a 5-electron oxidant, apparently Lewis acids can also activate the intermediate MnO_2 to carry out further oxidation.

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