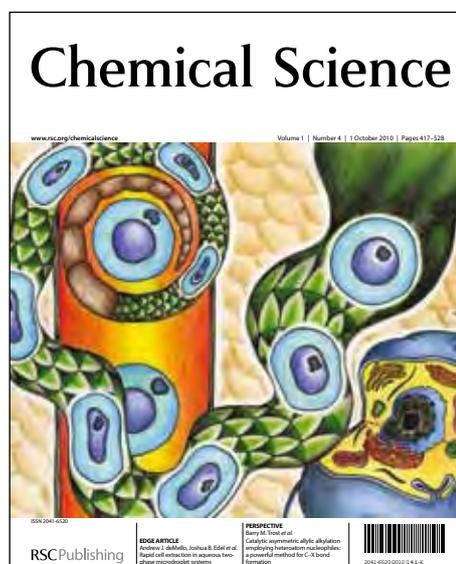


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ARTICLE

Hydrogen Atom Abstraction Reactions Independent of C-H Bond Dissociation Energies of Organic Substrates in Water: Significance of Oxidant-Substrate Adduct Formation

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Detailed kinetic studies on the oxidation reactions of organic substrates such as methanol with Ru^{IV}=O complexes as oxidants, formed electrochemically in water, have been conducted to elucidate the reaction mechanism. The rate constants of the oxidation reactions exhibited saturation behaviours relative to the substrate concentration, regardless of the oxidants and the substrates employed. This indicates the existence of the pre-equilibrium process based on the adduct formation between the Ru^{IV}=O oxidant and the substrate. Herein, we have experimentally confirmed that the driving force of the adduct formation is the hydrogen bonding between the oxidants and alcohols even in water. In addition, we have investigated the kinetic isotope effects (KIE) on the oxidation reaction using methanol and its deuterated derivatives and as a result observed moderate KIE values for the C-H bond of methanol. We have also revealed the independency of the reaction rates from the bond dissociation enthalpies of the C-H bonds of the substrates. This independency is probably derived from the tightly condensed transition state, whose energy level is strongly controlled by the activation entropy but less sensitive to the activation enthalpy.

Introduction

Catalytic oxidations of organic substrates with a high-valent metal-oxo complex have been intensively investigated¹⁻³ due to the interest for mechanistic insights into the enzymatic oxidations as observed in cytochrome P450^{4,5} and methane monooxygenase.^{6,7} Beyond the biological processes, efficient catalytic oxidation of organic compounds in aqueous solutions is one of the most required processes in the light of the development of environmentally benign procedure to attain useful primary and secondary products from abundant feedstock.⁸

Along this line, efficient oxidation systems have been developed with use of transition metal complexes as catalysts, involving high-valent metal-oxo complexes as reactive species.^{9,10} Among them, Ru^{IV}=O complexes have been intensively investigated as active species in oxidation reactions.¹¹⁻¹⁵ The Ru^{IV}=O complexes have been prepared *in situ* via proton-coupled electron-transfer (PCET) oxidation of the corresponding Ru^{II}-aqua complexes.^{16,17} Detailed kinetic studies on oxidation reactions of organic substrates have been frequently employed as strong tools to elucidate mechanisms of the oxidation reactions performed by metal-oxo complexes.¹⁸ Recently, the influence of the bond-dissociation enthalpy (BDE) of the C-H bond of a substrate,¹⁹ the BDE of the O-H bond formed for the oxo ligand of the oxidant,²⁰ and the

reduction potential of the oxidant²¹ on the reaction rates of the hydrogen abstraction reactions have been also intensively investigated. The oxidation reactions with synthetic metal-oxo complexes have been mainly performed in organic solvents, whereas knowledge of those in aqueous solutions has yet to be accumulated sufficiently.²² In addition, the effects of pre-equilibrium to form an adduct between the oxidant and a substrate on the reactivity of metal-oxo complexes have been rarely investigated,²³ despite the fact that the association equilibrium between an enzyme and the specific substrate plays very important roles in the enzymatic reactions.²⁴

Herein, we describe the oxidation reactions of organic substrates such as alcohols by Ru^{IV}=O complexes (1-3)¹⁵ (Fig. 1) in water under single-turnover conditions to elucidate the reaction mechanism on the basis of detailed kinetic analysis, and to discuss on the influence of BDEs of the substrates on the rate constants. In consequence, we have revealed the crucial impacts of an associative pre-equilibrium between the substrate

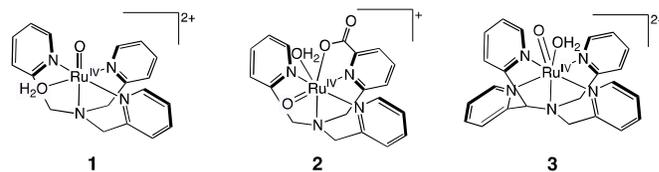


Fig. 1 Proposed structures of Ru^{IV}=O complexes, 1-3.

and the oxidant on the oxidation reactivity.

Experimental

General.

Chemicals and solvents were used as received from Tokyo Chemical Industry (TCI) Co., Wako Chemicals, or Sigma-Aldrich Corp. unless otherwise mentioned. UV-Vis spectra were collected on a Shimadzu UV-3600 spectrophotometer, equipped with a temperature-controller, UNISOK UnispeKs. ^1H NMR spectra were recorded on a JEOL EX-270 spectrometer at room temperature and the chemical shifts of signals were determined with respect to residual proton signals of deuterated solvents. ^{19}F NMR spectra were recorded on a JEOL ECS-400 spectrometer at room temperature and potassium fluoride, whose saturated solution in D_2O was sealed into a glass capillary, was used as an internal reference ($\delta(^{19}\text{F}) = -125.30$ ppm). Electrochemical measurements were performed on an AUTOLAB PGSTAT12 potentiometer in Britton-Robinson (B.-R.) buffer (pH = 2–12) at room temperature. pH measurements were made using a Horiba pH-Meter F-51.

CD_3OH was formed *in situ* by addition of CD_3OD (deuteration percentage: 99.8%) into the solution of one of the three complexes **1–3** in B.-R. buffered H_2O . The oxidation of CH_3OD was done in the solution of CH_3OH in B.-R. buffered D_2O (deuteration percentage: 99.9%).

$\text{Ru}^{\text{IV}}=\text{O}$ complexes employed in this study and the BDE value.

The three $\text{Ru}^{\text{IV}}=\text{O}$ complexes employed here bear pyridylamine ligands, tris(2-pyridylmethyl)amine (TPA) for **1**,^{15a} *N,N*-bis(2-pyridylmethyl)-*N*-(6-carboxylato-2-pyridylmethyl)-amine (6-COO⁻-TPA) for **2**,^{15b} and *N,N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)-methylamine (N4Py) for **3**,^{15c} respectively. They exhibit the reduction potentials of $\text{Ru}^{\text{III/IV}}$ couples at +0.75, +0.68, +0.87 V vs SCE in B.-R. buffer at pH 1.8, respectively.¹⁵ Additionally, the $\text{p}K_{\text{a}}$ values for the protonation processes of the $\text{Ru}^{\text{III}}-\text{OH}$ complexes corresponding to **1** and **3** were determined to be 2.23 and 2.48, respectively.^{15,25} Based on the reduction potentials and the $\text{p}K_{\text{a}}$ values, the BDEs of $\text{Ru}^{\text{III}}-\text{OH}$ for **1** and **3**

were calculated with eq 1^{16c, 26} to be 82.7 and 84.7 kcal mol⁻¹, respectively (Fig. 2).

$$\text{BDE (kcal/mol)} = 1.37\text{p}K_{\text{a}} + 23.06E_{1/2} + 55.8 \quad (1)$$

Determination of product yields for the oxidation reactions with **1**

D_2O solution containing DSS (= 4,4-dimethyl-4-silapentane-1-sulfonic acid) (2.0×10^{-3} M) as an internal reference, $[\text{Ru}^{\text{II}}(\text{TPA})(\text{OH}_2)_2](\text{PF}_6)_2$ ^{15a} (2.0×10^{-3} M), $(\text{NH}_4)_2[\text{Ce}^{\text{IV}}(\text{NO}_3)_6]$ (4.0×10^{-3} M) was charged into an NMR tube, and then, a substrate (1.0×10^{-2} M) was added to the solution and stirred at room temperature for 1 h. The solution was analysed by ^1H NMR spectroscopy (Fig. S1 in Electronic Supplementary Information (ESI)), and the quantities of the products were estimated from the relative integrals of the ^1H NMR signals against that of the DSS signal. As results, the oxidation products were solely propionaldehyde for 1-propanol and acetone for 2-propanol and the yields against the oxidant were estimated to be 95% for propionaldehyde and 100% for acetone.

Kinetic studies on oxidation reactions with $\text{Ru}^{\text{IV}}=\text{O}$ species.

The $\text{Ru}^{\text{IV}}=\text{O}$ species, **1**, **2** and **3** (0.5 mM) were generated in B.-R. buffer (pH 1.8) from the corresponding Ru^{II} -aqua complexes, respectively, through a bulk electrolysis as described in literature.^{15c} To the solution of the $\text{Ru}^{\text{IV}}=\text{O}$ complex generated were added substrates (CH_3OH and the deuterated derivatives, 1-propanol, 2-propanol, 4-methylbenzyl alcohol and sodium 4-ethylbenzenesulfonate (EBS)) with various concentrations at various temperatures. The reaction profiles were monitored by the rise of the absorption assigned to the resulting $\text{Ru}^{\text{II}}-\text{OH}_2$ complex at 620 nm for **1**, 630 nm for **2**, and 440 nm for **3** to determine pseudo-first-order rate constants ($k_{\text{obs}} / \text{s}^{-1}$).²⁷ All the time profiles of the absorbance changes obeyed the first-order kinetics and the pseudo-first-order rate constants were determined with various concentrations of the substrates (Fig. S3 and S5 in ESI).

The saturation behaviours of the k_{obs} values were analysed by using following equation:^{23,28,29}

$$k_{\text{obs}} = kK[\text{Sub}]/(1 + K[\text{Sub}]) \quad (2)$$

where K (M^{-1}) is the equilibrium constant for the pre-equilibrium, k (s^{-1}) is the first-order rate constant, and $[\text{Sub}]$ (M) is the concentration of a substrate used. Plots of k_{obs} vs. $[\text{Sub}]$ were fitted by eq. (1) to determine k and K values. The k and K values determined at various temperatures were used to provide corresponding Eyring and van't Hoff plots, respectively.

Results and discussion

Observation of the hydrogen-bonded adduct of the $\text{Ru}^{\text{IV}}=\text{O}$ complex

In the kinetic analysis of oxidation reactions of organic substrates with **1–3** as oxidants, we commonly observed saturation behaviours of the pseudo-first-order rate constants (k_{obs}) with respect to the concentration of substrates at all the temperatures examined, indicating the existence of pre-

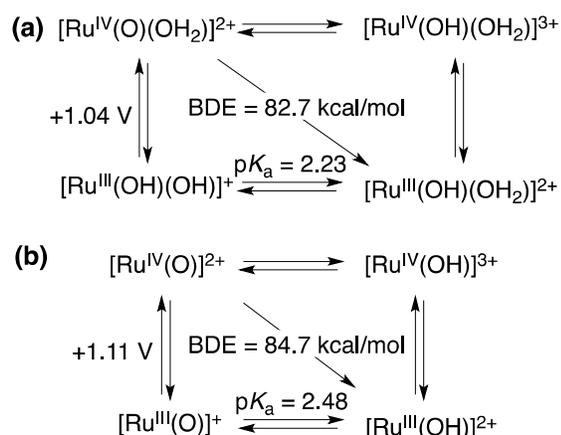


Fig. 2 Thermochemical square schemes for **1** (a) and **3** (b). The $\text{p}K_{\text{a}}$ values and the redox potentials are derived from ref. 15a and 15c and the redox potentials are recalculated as those relative to NHE.

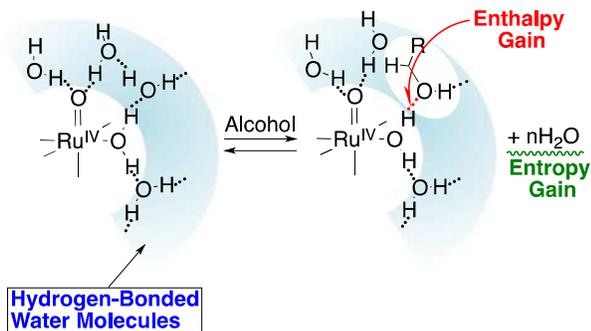
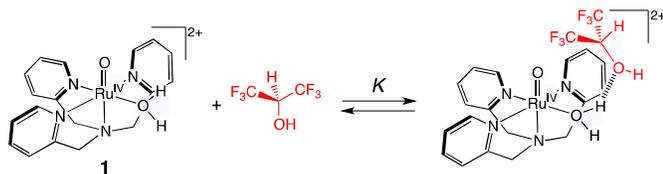


Fig. 3 Schematic description of the adduct structure for the pre-equilibrium processes.

equilibrium processes prior to the oxidations.¹⁵ The driving force for the adduct formation in the pre-equilibrium process was supposed to be hydrogen bonding between the lone pair of alcohol oxygen of the substrates and the O-H proton of the aqua ligand of the Ru^{IV}=O complex (Fig. 3).^{15,30} Thus far, however, no direct evidence has been provided to support the formation of hydrogen-bonded adduct between a Ru^{IV}=O complex and a substrate. Therefore, we performed titration experiments with the addition of the solution of **1** to that of 1,1,1,3,3,3-hexafluoro-propan-2-ol (hfp), which was employed as an inert alcohol against oxidation reactions,³¹ in water under acidic conditions. The various amounts of [Ru^{II}(TPA)(OH)₂](PF₆)₂ were added to D₂O (0.6 mL), which was acidified with HClO₄ to be pH 1.8, and then, 2 equiv of [Ru^{III}(bpy)₃](PF₆)₃ was added as an oxidant to each solution of [Ru^{II}(TPA)(OH)₂](PF₆)₂. The formation of **1** was confirmed with the paramagnetic ¹H NMR spectrum.^{15a} Subsequently, hfp (4 μL, 0.4 μmol) was added to each solution and the ¹⁹F NMR spectrum was measured. The ¹⁹F NMR signal due to the CF₃ groups of hfp was monitored to estimate the association constant. The chemical shift of the C¹⁹F₃ groups of hfp in D₂O (pH 1.8) was observed at δ(¹⁹F) = -78.67 ppm in the absence of **1**. The signal of the CF₃ groups exhibited downfield shifts upon increasing the concentration of **1**, indicating that the alcohol oxygen of hfp forms hydrogen bonding with the O-H proton of **1** as depicted in Scheme 1. The change of the chemical shifts for the ¹⁹F NMR signals of the CF₃ groups upon increasing the concentration of **1** was analysed with eq 3.³² The association constant (*K*) was

$$\Delta\delta = \frac{\Delta\delta_{\infty}}{2K[\text{Sub}]_0} \left\{ 1 + K[\mathbf{1}] + K[\text{Sub}]_0 - \left\{ (1 + K[\mathbf{1}] + K[\text{Sub}]_0)^2 - 4K^2[\mathbf{1}][\text{Sub}]_0 \right\}^{1/2} \right\} \quad (3)$$

determined to be $5.0 \times 10^2 \text{ M}^{-1}$ based on the titration curve (Fig. S7 in ESI). As well, the spectroscopic titration for **2** was also performed under the same conditions to observe similar chemical shift change to that observed for **1**. This result indicates that the chemical shift change observed for hfp is not



Scheme 1 The association equilibrium between **1** and hfp in water.

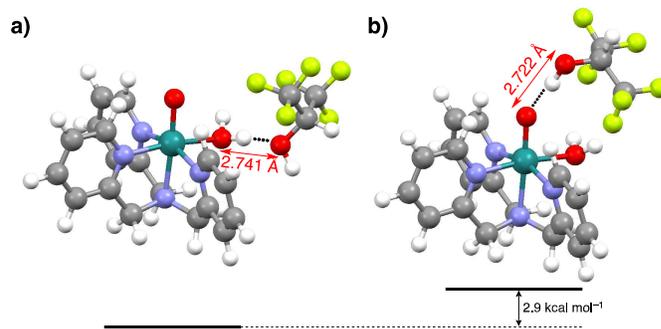


Fig. 4 DFT-optimized structures of the hydrogen-bonded adducts between **1** and hfp and the relative stabilization Gibbs energy.

due to paramagnetic contact shift but the formation of hydrogen bonding. The binding constant for **2** was also determined to be $3.6 \times 10^2 \text{ M}^{-1}$ (Fig. S7 in ESI) using eq 3. This result lends credence to the adduct formation between the Ru^{IV}=O complexes and alcohols even in water.

In addition, we confirmed the adduct formation by DFT calculations (Fig. 4). As initial structures for the calculations, two initial structures, which involve a hydrogen bond formed between the aqua ligand of **1** and the hydroxyl group of hfp, were prepared for the calculations. The optimization of one of the initial structure, which formed a hydrogen bond between one of the OHs of the aqua ligand of **1** and one of the lone pairs of the hydroxyl-oxygen of hfp, was converged to a solution (Fig. 4(a)). In contrast, the structure optimization started with the other initial structure, in which the hydrogen bond is formed between the lone pair of the aqua ligand of **1** and the O-H group of hfp, did not afford a well-converged solution maintaining the initial hydrogen-bonded structure but gave the structure as shown in Fig. 4(b) by changing the hydrogen-bonding position in the course of calculations. Consequently, the most favourable

Table 1 Thermodynamic parameters for the pre-equilibrium processes and activation parameters for the oxidation reactions of methanol and the deuterated derivatives, and 2-propanol with Ru^{IV}=O complexes.

oxidant	substrate	ΔH^\ddagger ^a	ΔS^\ddagger ^{b,c}	ΔH° ^a	ΔS° ^b
1	CH ₃ OH	20	-223	21	102
	CD ₃ OH	32	-189	6.9	54
	CH ₃ OD	25	-203	15	80
	<i>i</i> PrOH	25	-143	-21	-40
	<i>n</i> PrOH ^d	26	-197	-23	-4.8
2	CH ₃ OH	23	-211	15	81
	CD ₃ OH	38	-169	12	73
	CH ₃ OD	16	-238	23	108
	<i>i</i> PrOH	25	-146	-14	-13
	<i>n</i> PrOH ^d	25	-203	-29	-6.8
3	CH ₃ OH	15	-237	18	94
	CD ₃ OH	21	-224	15	88
	CH ₃ OD	12	-250	20	103
	<i>i</i> PrOH	21	-156	-14	-19
	<i>n</i> PrOH ^d	18	-225	-16	-2.6
[Ru ^{IV} (O)(tpy)(bpy)] ²⁺ ^e	<i>i</i> PrOH	38	-143	—	—

^a in kJ mol⁻¹. ^b in J mol⁻¹ K⁻¹. ^c At 298 K. ^d ref 15c. ^e ref 22.

Table 2 KIE values of the MeOH oxidation with **1–3** at various temperatures

oxidant	KIE	Temperature, K			
		281	289	297	305
1	$k_{\text{H}}/k_{\text{D}}$ for CH_3	3.3	2.6	2.5	2.1
	$k_{\text{H}}/k_{\text{D}}$ for OH	1.2	1.1	1.0	1.0
2	$k_{\text{H}}/k_{\text{D}}$ for CH_3	3.3	2.3	2.3	1.9
	$k_{\text{H}}/k_{\text{D}}$ for OH	1.0	1.1	1.1	1.2
3	$k_{\text{H}}/k_{\text{D}}$ for CH_3	2.1	1.8	1.7	1.8
	$k_{\text{H}}/k_{\text{D}}$ for OH	1.0	1.1	1.1	1.1

structure was suggested to be the structure depicted in Fig. 4(a), which involves the hydrogen bonding described in Scheme 1. The difference in the stabilization Gibbs energies of the two structures in Fig. 4 was estimated to be 2.9 kcal mol⁻¹.

Kinetic analysis of methanol oxidation

To investigate the reaction mechanisms of the substrate oxidation in detail, determination of the kinetic isotope effect (KIE) was conducted on the oxidation reactions of methanol and the deuterated derivatives (CD₃OH and CH₃OD) as substrates at various temperatures. The thermodynamic parameters for the pre-equilibrium processes and the activation parameters for the substrate oxidations were determined on the basis of the van't Hoff plots for the equilibrium constants and the Eyring plots for the rate constants (Table 1 and Fig. S4 and S6 in ESI), respectively. The activation and the thermodynamic parameters for the same substrate are quite similar to each other for the three different oxidants, indicating that the reaction proceeds via similar transition states for the three oxidants in terms of potential energies and structures.

According to the activation parameters, the activation Gibbs energy changes (ΔG^\ddagger) of the reactions are mainly controlled by the activation entropy terms (ΔS^\ddagger) and the contributions of the activation enthalpy terms (ΔH^\ddagger) to the transition states are not so large. For instance, $\Delta H^\ddagger = 20$ kJ mol⁻¹ and $T\Delta S^\ddagger = -66.5$ kJ mol⁻¹ were obtained for the reaction of CH₃OH as the substrate and **1** as the oxidant at 298 K. The negatively large $T\Delta S^\ddagger$ values suggest that the α -C-H bond in a hydrogen-bonded alcohol in the adduct of the pre-equilibrium process may be enforced to direct to the oxo-ligand to undergo PCET reactions as hydrogen atom transfer (HAT) *via* the formation of a tightly-condensed transition state (*vide infra*).^{15c}

In general, the KIE values were defined with the ratio of the rate constants ($k_{\text{H}}/k_{\text{D}}$) between those for the hydrogenated and deuterated substrates. As previously described,^{15,17} the KIE values for the hydroxyl groups, which were determined using CH₃OH and CH₃OD as substrates, were negligible all for the three oxidants (Table 2). The activation parameters for the oxidation reactions of CH₃OH and CH₃OD were almost identical in comparison with the values using the same oxidant (Table 1). In contrast, the oxidation rate constant for CD₃OH relative to that for CH₃OH showed larger KIE values (Table 2) and the activation enthalpies for the CD₃OH oxidations were larger than those for the CH₃OH oxidations. Therefore, the rate-determining step in the oxidation reactions involves the hydrogen abstraction from the methyl group of the methanol.^{15,17}

The temperature dependence of the KIE of the oxidations with oxo-complexes **1–3** was also investigated in the temperature range of 281–305 K. The KIE values for the hydroxyl group were maintained to be *ca.* 1.1 in the

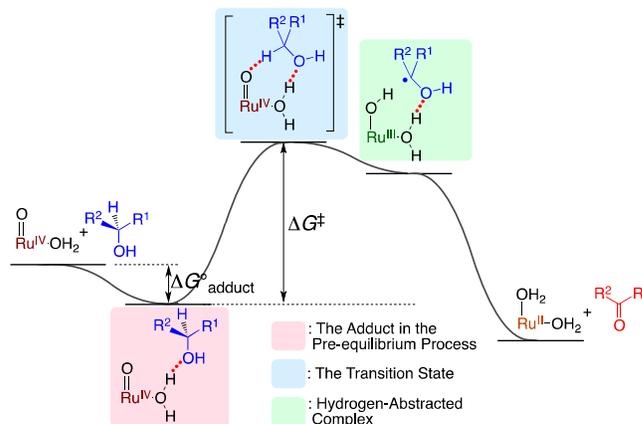


Fig. 5 A proposed energy diagram of the oxidation reaction of alcohols with a Ru^{IV}-oxo complex having an aqua ligand.

temperature range. On the other hand, KIE values for oxidations of CH₃OH and CD₃OH with **1–3** increased with decreasing temperature (Table 2). The KIE values for the methyl group obtained here were relatively small (1.8–3.3 for all the temperature range measured in this study). As for a hydrogen abstraction reaction involving tunnelling mechanism, it has been known to show a large $k_{\text{H}}/k_{\text{D}}$, at least larger than 7 at room temperature.^{33,34} As shown in Table 2, the largest KIE value for the oxidation reactions obtained here was 3.3, which was apparently smaller than 7, suggesting no tunnelling effect for the reactions reported here. Typically the magnitude of the KIE increases as the proton donor-acceptor distance increases.³⁵ The hydrogen donor-acceptor distances for the oxidation reactions with **1–3** should be preliminarily fixed as appropriate for HAT from the C-H moiety of the substrate to the metal-oxo moiety of the oxidant in the transition state (Fig. 5). Furthermore, KIE for hydrogen abstraction reactions from the methyl group of MeOH was demonstrated to become larger as temperature decreased, which is a normal tendency for hydrogen abstraction reactions without tunnelling, in the temperature range examined (Fig. S8 in ESI).³⁶

Dependence of the thermodynamic and kinetic parameters of the oxidation reactions on the substrates

Oxidation reactions of 2-propanol (*i*PrOH)³⁷ with complexes **1–3** were also conducted in this work (Fig. S5 and S6 in ESI). The values of the activation parameters for the 2-propanol oxidations were determined through variable-temperature kinetic measurements and were compared with those for 1-propanol (*n*PrOH) oxidations obtained in the previous reports (Table 1).^{15,38} The thermodynamic parameters of the pre-equilibrium processes (ΔH° and ΔS°) were significantly different between CH₃OH and *i*PrOH, whereas those of *n*PrOH¹⁵ and *i*PrOH were similar (Table 1). The ΔH° and ΔS° values for the CH₃OH oxidations were commonly positive, whereas those for *i*PrOH oxidations were negative. Thus, the adduct formation in the pre-equilibrium processes for *i*PrOH is dominated by the enthalpy term, whereas that for CH₃OH is governed by the entropy term. The cause of the differences in the thermodynamic parameters between CH₃OH and *i*PrOH for the pre-equilibrium processes can be ascribed to the difference in the solvation among the three substrates in water. *i*PrOH ($\epsilon = 19.9$) is less polar relative to CH₃OH ($\epsilon = 32.7$),³⁹ and the acceptor number of *i*PrOH ($A_{\text{N}} = 33.8$) is smaller than that of CH₃OH ($A_{\text{N}} = 41.3$),⁴⁰ although the donor numbers are

comparable ($D_N = 21.1$ for *i*PrOH, $D_N = 19$ for CH₃OH).⁴¹ Thus, CH₃OH should be strongly solvated in water, and moreover, forms strong hydrogen bonds with water molecules, whereas *i*PrOH is weakly solvated and the extent of the hydrogen bonding with water molecules should be moderate compared with that of CH₃OH. As a result, upon formation of the adduct of CH₃OH with the oxidant, a lot of water molecules are released, that should cause the entropy gain (Fig. 3), but the enthalpy gain by the adduct formation through the hydrogen bonding is offset by the enthalpy loss due to the cleavage of hydrogen bonds between CH₃OH and water molecules. On the other hand, the entropy gains for the pre-equilibrium process of *i*PrOH oxidations are not significant because *i*PrOH is less-solvated, but the formation of the strong hydrogen bonds of *i*PrOH with the oxidant affords the large enthalpy gain. The similarity in the parameters of the pre-equilibrium process for *n*PrOH¹⁵ to those for *i*PrOH can be ascribed to the similarity in the characteristics ($\varepsilon = 20.3$,³⁹ $A_N = 37.3$ ⁴⁰ and $D_N = 21.1$ ⁴¹ for *n*PrOH).

The activation Gibbs energy changes of the oxidation reactions are mainly controlled by the activation entropy terms and the contributions of the activation enthalpy terms to the transition states are not so large (Table 1). For instance, $\Delta H^\ddagger = 20$ kJ mol⁻¹ and $T\Delta S^\ddagger = -66.5$ kJ mol⁻¹ were obtained for the oxidation of CH₃OH by **1** at 298 K. The negatively large ΔS^\ddagger values suggest that the α -C-H bond in a hydrogen-bonded alcohol in the adduct of the pre-equilibrium process may be enforced to direct to the oxo-ligand to undergo PCET reactions as hydrogen atom transfer (HAT) *via* the formation of a tightly-organized transition state (Fig. 5).^{15c}

Evans-Polanyi plot for the oxidation reactions

Despite the difference in BDE values among CH₃OH (96.0 kcal mol⁻¹), *i*PrOH (90.0 kcal mol⁻¹) and *n*PrOH (93.7 kcal mol⁻¹),⁴² the activation parameters (ΔH^\ddagger and ΔS^\ddagger) are almost the same for the oxidations of all the three substrates (Table 1). This indicates that the rate constants for the oxidation reactions with complexes **1–3** and the energy levels of the transition states are not or, if any, very slightly dependent on the BDEs of the C-H bonds of the substrates. To confirm the independence of the reaction rates (k) from BDEs of the substrates, as observed in the oxidation reactions of the three alcohols, we determined the rate constants at 298 K with **1** as the oxidant for five substrates having different BDE values (Fig. S10 in ESI); methanol (BDE = 96.0 kcal mol⁻¹), *n*PrOH (93.7), *i*PrOH (90.0), 4-methylbenzyl alcohol (87.5), sodium 4-ethylbenzene-sulfonate (EBS) (84.6).⁴² A plot of $\log k$ against BDE values of the C-H bonds to be cleaved in the substrates showed a linear correlation (Fig. 6). In general, the linear relationship between the second-order rate-constant and BDE of the substrate has been known as the Bell-Evans-Polanyi (BEP) relation as expressed by eq 1.⁴³ In most cases, oxidation reactions of C-H

$$E_a = \alpha\Delta H^\circ + C \quad (1)$$

$$\Delta H^\circ = \text{BDE}_{\text{C-H for substrate}} + \text{BDE}_{\text{O-H for oxidant}} \quad (2)$$

bonds with high-valent metal-oxo complexes obeyed the BEP relation to give the coefficient $\alpha \sim 0.5$ and oxidation reaction of a substrate having a larger BDE value proceeded slowly.^{10a,44} In sharp contrast, the rate constants for the oxidation reactions with **1** were almost independent of the BDE values of the substrates and the slope of the plot in Fig. 6, that is, α was very

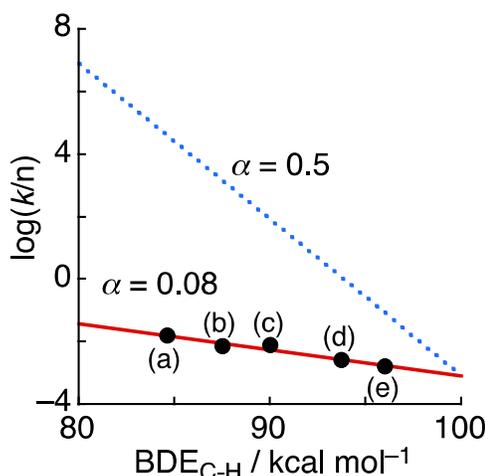


Fig. 6 A plot of the $\log(k/n)$ (n : the number of equivalent C-H hydrogen atoms) at 298 K for the oxidation of five substrates (a: EBS, b: 4-methylbenzyl alcohol, c: *i*PrOH, d: *n*PrOH, e: methanol) with **1** against BDEs of C-H bonds to be cleaved in the substrates.

small to be 0.08.

To date, some exceptional cases have been reported, where the BEP relation was not valid.⁴⁵ Tanko and co-workers have discussed the causes of the insensitivity of the rate constants to BDEs of C-H bonds of substrates⁴⁶: They have indicated that the systems controlled by the activation entropy (ΔS^\ddagger) exhibit slight dependence of the reaction rates on BDEs of substrates and instead accessibility to the reaction points, orientation of the reactants and the pathways of HAT are controlling factors for the hydrogen abstraction processes. In our case, the energy levels of the transition states are mainly governed by the activation entropies (Table 1), and the reaction rates were insensitive to the BDE changes of the C-H bonds, since the C-H bond of the substrate should be intact at the transition state (Fig. 5). In addition, the orientations of the substrates in the oxidant-substrate adducts should be fixed by the hydrogen bonding formed in the pre-equilibrium process, attaining the advantageous molecular arrangements for the hydrogen abstraction. Thompson and Meyer have reported the activation parameters for the oxidation of *i*PrOH by $[\text{Ru}^{\text{IV}}(\text{O})(\text{tpy})(\text{bpy})]^{2+}$ (tpy = 2,2':6',2''-terpyridine, bpy = 2,2'-bipyridine) in water,²² indicating the negatively large activation entropy ($\Delta S^\ddagger = -143$ J mol⁻¹ K⁻¹ at 298 K, Table 1) similar to the cases of **1–3**, suggesting the adduct formation between the Ru^{IV}=O complex and *i*PrOH prior to the oxidation in water.²² On the other hand, for the oxidation of cumene with $[\text{Ru}^{\text{IV}}(\text{O})(\eta^3\text{-H}^+\text{TPA})(\text{bpy})]^{3+}$ in CH₃CN, in which no adduct formation was suggested and KIE was determined to be 12, the contribution of the ΔH^\ddagger and $T\Delta S^\ddagger$ terms to ΔG^\ddagger was almost identical; $\Delta H^\ddagger = 42$ kJ mol⁻¹ and $T\Delta S^\ddagger = -39$ kJ mol⁻¹ at 298 K.⁴⁷ Since the contribution of the entropy term is relatively small in the latter case, the reaction rates are dependent on the BDE to show the significant KIE value.

After the formation of the entropy-controlled transition state, the hydrogen abstraction reactions from the substrate to the Ru^{IV}=O complex spontaneously occur to afford the corresponding Ru^{III}-OH complex and the H-abstracted radical species of the substrate (Fig. 5),⁴⁸ despite the fact that the hydrogen abstraction process is energetically unfavourable (uphill) process. The intermediate state after the hydrogen

abstraction is estimated to be energetically stable relative to the transition state. In fact, the enthalpy changes (ΔH_{abst}) to form the radical species, which can be calculated by the difference of the BDE values between the Ru^{III}-OH complex and the C-H bond of the substrate, is sufficiently small compared to the free-energy difference of the transition state: For instance, the BDE difference between **1** and CH₃OH having the highest BDE value among the substrates studied here was estimated to be 56 kJ mol⁻¹. Additionally, the radical species should be also more stable than the transition state in terms of entropy, because the restricted orientation observed at the transition state is lost after the hydrogen abstraction. The following reactions also proceed smoothly led by the stability of the products, *i.e.*, the Ru^{II}-OH₂ complex and aldehydes or ketones.

Conclusions

Herein, we have experimentally confirmed the formation of a hydrogen-bonded adduct with a Ru^{IV}=O complex and an alcohol prior to the oxidation in water at the first time. Furthermore, we have demonstrated the significance of the adduct formation in the hydrogen abstraction reaction to promote the reactions regardless of BDEs of the C-H bonds to be cleaved. On the basis of the negatively large activation entropy (ΔS^\ddagger), the PCET reactions from the substrates to complexes **1–3** have been proposed to proceed *via* tightly organized transition states. All the observations can be elucidated by the formation of the oxidant-substrate adduct in the pre-equilibrium process, whose structure is strictly organized by hydrogen bonding to offer large contribution of ΔS^\ddagger to the transition state relative to that of ΔH^\ddagger . This work provides a strong basis to elucidate the reactivity of a high-valent metal-oxo complex in oxidation reactions of organic molecules, especially those involving oxidative C-H bond functionalization in water.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Details of DFT calculations, ¹H NMR spectra of the oxidized product of 2-propanol, UV-Vis spectral changes in the course of oxidation reactions, plots of the reaction rates against the substrate concentrations, van't Hoff and Eyring plots, titration curves of ¹⁹F NMR signals, MS spectrum of the decomposed product of **2** are included. See DOI: 10.1039/b000000/x/

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