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Application and Mechanistic Studies of a Water-Oxidation Catalyst in Alcohol Oxidation by Employing Oxygen-Transfer Reagents

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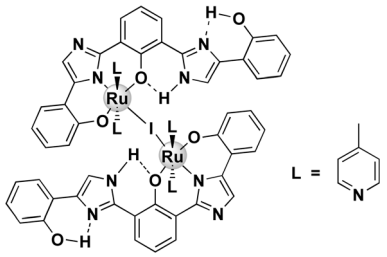
Abstract: By using a dimeric ruthenium complex in combination with *tert*-butyl hydrogen peroxide (TBHP) as stoichiometric oxidant, a mild and efficient protocol for the oxidation of secondary benzylic alcohols was obtained, thereby giving the corresponding ketones in high yields within 4 h. However, in the oxidation of aliphatic alcohols, the TBHP protocol suffered from low conversions owing to a competing Ru-catalyzed disproportionation of the oxidant. Gratifyingly, by switching to Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ triple salt) as stoichiometric oxidant, a more efficient and robust system was obtained that allowed for the oxidation of a wide range of aliphatic and benzylic secondary alcohols, giving the corresponding ketones in excellent yields. The mechanism for these reactions is believed to involve a high-valent Ru^V–oxo species. We provide support for such an intermediate by means of mechanistic studies.

Keywords: alcohols · biphasic catalysis · oxidation · Oxone · ruthenium

Introduction

Selective oxidation of alcohols into their corresponding aldehydes and ketones is a fundamental transformation in organic synthesis and is of major importance in both laboratory and industrial synthetic chemistry.[1] The transformations are still widely carried out with stoichiometric amounts of high-valent metal reagents such as Cr^{VI} and Mn^{VII}.[2] These protocols suffer from high costs, poor atom utilization, and production of stoichiometric amounts of toxic metal waste, thus making them unattractive from both an economical and environmental perspective. However, in recent decades, major efforts have been dedicated to developing new efficient catalytic oxidation protocols based on transition metals (e.g., Pd,[3] Ru,[4] Cu,[5] and Au[6]) that employ environmentally benign oxidants.

Recently, our group has developed and synthesized the dimeric ruthenium complex **1**, which displayed excellent activity as a water-oxidation catalyst (WOC) in chemical- and light-driven water oxidation.[7] The introduction of negatively charged ligands into WOCs lowers the redox potentials and allows for the formation of high-valent metal–oxo complexes. Furthermore, the bioinspired ligand was designed to withstand the highly oxidative conditions associated with water oxidation. The use of WOCs for the oxidation of organic substrates has lately attracted considerable interest,[8] and this has inspired us to investigate the potential applications of **1** for similar transformations. Herein, we report on the use of **1** in the oxidation of alcohols to their corresponding carbonyl compounds with various two-electron oxidants and provide support for a mechanism involving a high-valent Ru^V–oxo species.



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Results and Discussion

Initial screenings: A screening of suitable oxidants for Ru complex **1** was performed and the results are summarized in Table 1. Unfortunately, complex **1** exhibited poor solubility in most organic solvents, and among all the tested solvents only dichloromethane (CH_2Cl_2) was found to provide sufficient solubility. Some of the tested oxidants were slightly soluble in CH_2Cl_2, but this problem could be circumvented by employing a two-phase system consisting of CH_2Cl_2 and H_2O. Because of the oxidative stability of complex **1**, the reactions could be carried out under normal conditions without the use of an inert atmosphere.

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Table 1. Oxidation of 1-phenylethanol (**2a**) with ruthenium complex **1** by using different oxidants.[a]

Entry	Oxidant	Conv. [%][b]
1	H_2O_2	8
2	NaOCl	32
3	TBHP	55
4	iodosobenzene	>99
5	Oxone	>99[c]

[a] Conditions: **2a** (0.26 mmol), **1** (0.75 mol%), oxidant (1.04 mmol), CH_2Cl_2 (2.0 mL), H_2O (2 mL, pH 6), 40°C, 4 h. [b] Determined by GC analysis. [c] After 2 h.

Oxidants such as hydrogen peroxide (H_2O_2; Table 1, entry 1), sodium hypochlorite (NaOCl; Table 1, entry 2), and *tert*-butyl hydrogen peroxide (TBHP; Table 1, entry 3) all resulted in low to moderate conversion in the oxidation of 1-phenylethanol (**2a**) at 40°C. Furthermore, significant gas evolution could be observed from the reaction mixture when using these oxidants. The most probable reason seemed to be a disproportionation reaction of the oxidants, which led to the evolution of molecular oxygen.[9] A substantial decrease in pH (from pH 6 to 1) could also be observed during these reactions. This suggests that water oxidation could be a competing reaction, since it would involve an attack by H_2O on an intermediate metal–oxo species, ultimately generating molecular oxygen and protons. However, in the case of TBHP, the disproportionation reaction turned out to be slower. It was therefore possible to obtain higher conversions by adding the TBHP over one hour and slightly modifying the catalyst/oxidant loadings (see below). TBHP is inexpensive, has high oxygen availability, and the byproduct *tert*-butanol formed from the reaction can be easily separated from the product by evaporation. These advantages have led to the development of a wide variety of catalytic systems for the oxidation of alcohols that employ TBHP as stoichiometric oxidant.[10]

Employing iodosobenzene resulted in quantitative conversion after 4 h (Table 1, entry 4). However, from an economic and environmental point of view, the use of iodosobenzene is undesirable. Interestingly, the best result was obtained with Oxone ($2\,KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ triple salt), which resulted in quantitative conversion after only 2 h (Table 1, entry 5). Furthermore, in the reactions in which Oxone was employed, gas evolution was less pronounced than with other oxidants (see below).

Oxone is an attractive oxidant owing to its high stability, simple handling, and low cost. It has been well studied in the literature as an oxidant for the Shi epoxidation reactions;[11] cleavage of alkenes[12] and alkynes[13] to ketones and carboxylic acids; α-hydroxylation of aryl alkyl ketones;[14] and in the oxidation of tertiary amines to the corresponding nitrones.[15] However, the examples of Oxone-based protocols for the oxidation of alcohols are scarce.

To prove that Ru complex **1** is responsible for the catalytic activity, control experiments with various oxidants were carried out in its absence. All control experiments exhibited no or minor conversions (<10%). The reaction was also tested with simpler ruthenium precursors, and the results are summarized in Table 2. The simpler ruthenium complexes displayed lower activity per molar equivalent of ruthenium than that of **1** when using either TBHP or Oxone as oxidant. However, when TBHP was used, the difference between complex **1** and $RuCl_3$ in the oxidation of 1-phenylethanol (**2a**) was found to be small. This can be explained by complex **1** being more efficient in catalyzing the disproportionation of TBHP than $RuCl_3$, which negatively affects its efficiency towards alcohol oxidation. However, when the oxidant is changed to the more stable Oxone that is less prone to undergo disproportionation, a significant difference in efficiency between **1** and $RuCl_3$ can be observed. To further prove this difference in efficiency, the reaction was also performed at room temperature. This resulted in a conversion of 48% after 1 h when using **1**, compared with 7% conversion when using $RuCl_3$. This difference in efficiency also holds true when comparing complex **1** and $RuCl_3$ in the reaction of the slower-reacting aliphatic alcohol, 2-octanol (not shown in Table 2). Performing the reaction under standard conditions at room temperature with **1** gave a conversion of 47% after 2 h, compared with 6% with $RuCl_3$.

Table 2. Oxidation of 1-phenylethanol (**2a**) with various ruthenium precursors.[a]

Entry	Catalyst	Conv. TBHP [%][b]	Conv. Oxone [%][b]
1	**1**	55	99[c] (48)[d]
2	$RuCl_3$	40	66 (7)[d]
3	RuO_2	4	10

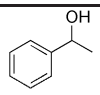
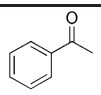
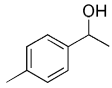
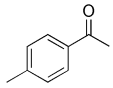
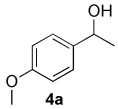
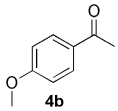
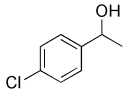
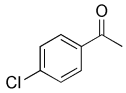
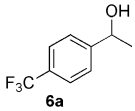
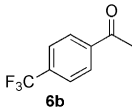
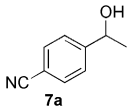
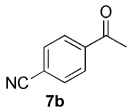
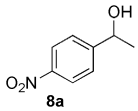
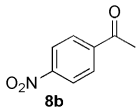
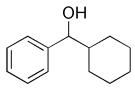
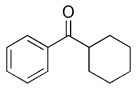
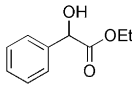
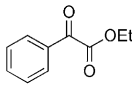
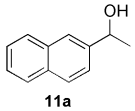
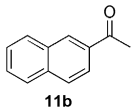
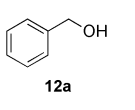
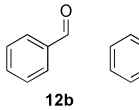
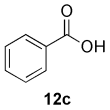
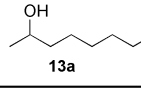
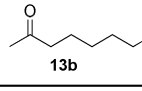
[a] Conditions (TBHP): **2a** (0.26 mmol), Ru (1.5 mol%), TBHP (1.04 mmol), CH_2Cl_2 (2.0 mL), H_2O (2.0 mL, pH 6), 40°C, 4 h. Conditions (Oxone): **2a** (0.26 mmol), Ru (1.5 mol%), Oxone (0.78 mmol), CH_2Cl_2 (2.0 mL), H_2O (2.0 mL, pH 6), 40°C, 4 h. [b] Determined by GC analysis. [c] After 2 h. [d] After 1 h at room temperature, under otherwise unchanged conditions as in [a].

For further studies of the substrate scope, we decided to investigate both TBHP and Oxone as terminal oxidants.

Oxidation using TBHP as stoichiometric oxidant: After further optimizations of the reaction conditions with TBHP as oxidant, we found the optimal amount of this oxidant to be 6 equivalents. The scope of the reaction was investigated, and the results are summarized in Table 3. Aryl methyl alcohols **2a**–**8a** (Table 3, entries 1–7) with varying electronic properties proved to be readily oxidized to their corresponding ketones by using this system. The bulkier cyclohexyl phenyl carbinol (**9a**; Table 3, entry 8) was also tolerated by this system, but the reaction was found to be slow, thereby resulting in a lower yield. The α-hydroxycarbonyl compound **10a** (Table 3, entry 9) and the naphthyl compound **11a** (Table 3, entry 10) were also oxidized in good to high yields.

We were also interested in investigating whether the protocol allowed for the oxidation of primary alcohols (Table 3, entry 11) and whether it was possible to obtain selectivity towards either the aldehyde or the carboxylic acid. Unfortunately, the reaction displayed poor selectivity when using

Table 3. Ruthenium-catalyzed oxidation of alcohols into carbonyl compounds by using TBHP as the oxidant.[a]

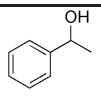
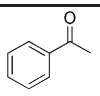
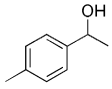
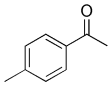
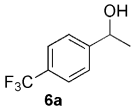
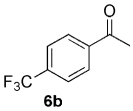
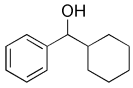
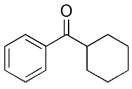
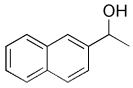
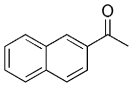
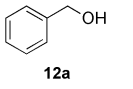
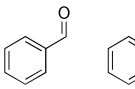
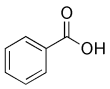
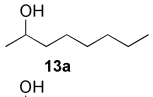
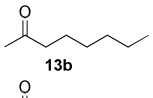
Entry	Substrate	Product	t [h]	Yield[b] [%]
1	 **2a**	 **2b**	4	82 (76)[c]
2	 **3a**	 **3b**	4	90
3	 **4a**	 **4b**	3	97 (90)[c]
4	 **5a**	 **5b**	4	89
5	 **6a**	 **6b**	4	84
6	 **7a**	 **7b**	4	93 (89)[c]
7	 **8a**	 **8b**	4	88
8	 **9a**	 **9b**	4	69
9	 **10a**	 **10b**	4	78
10	 **11a**	 **11b**	3	88
11	 **12a**	 **12b**  **12c**	4 4[d]	28/59 9/80
12	 **13a**	 **13b**	5	38

[a] Conditions: alcohol (0.26 mmol), **1** (0.75 mol%), TBHP (6 equiv), CH_2Cl_2 (2.0 mL), H_2O (2.0 mL, pH 6), 40°C. [b] Determined by GC, using dodecane as internal standard. [c] Isolated yield by column chromatography. [d] TBHP (9 equiv) was used.

the standard conditions with 6 equivalents of TBHP. A better selectivity was obtained by increasing the loading of TBHP to 9 equivalents, which resulted in 80% conversion to benzoic acid (**12c**). A drawback of this protocol is that it does not work well with aliphatic alcohols. Hence alcohol **13a** was not accepted by this system and the reaction stopped at low conversation (Table 3, entry 12).

Oxidation using Oxone as stoichiometric oxidant: Since the disproportionation reaction appeared to be significantly slower for Oxone, it was possible to use fewer equivalents of oxidant than in the TBHP protocol. After optimization of the reaction conditions, it was found that 3 equivalents of Oxone and 0.75 mol% of complex **1** was enough for an efficient oxidation in short reaction times. As shown in Table 4, aryl methyl alcohols, both electron rich and electron poor, were efficiently oxidized to their corresponding ketones in

Table 4. Ruthenium-catalyzed oxidation of alcohols into carbonyl compounds by using Oxone as the oxidant.[a]

Entry	Substrate	Product	t [h]	Yield[b] [%]
1	 **2a**	 **2b**	2	>99
2	 **3a**	 **3b**	2	>99
3	 **6a**	 **6b**	5	95
4	 **9a**	 **9b**	4	>99
5	 **11a**	 **11b**	10	82
6	 **12a**	 **12b**  **12c**	5 5[d]	43/38 22/78
7	 **13a**	 **13b**	4	>99
8	**14a**	**14b**	4	99
9	**15a**	**15b**	3	93
10	**16a**	**16b**	4	96[c]
11	**17a**	**17b**	3	89
12	**18a**	**18b**	4	>99[c]

[a] Conditions: Alcohol (0.26 mmol), **1** (0.75 mol%), Oxone (3 equiv), CH_2Cl_2 (2.0 mL), H_2O (2.0 mL, pH 6), 40°C. [b] Determined by GC, using dodecane as internal standard. [c] Decane as internal standard. [d] 6 equivalents Oxone.

excellent yields (Table 4, entries 1–3). However, in the case of alcohol **11a** (Table 4, entry 5), extended reaction times were required to obtain acceptable yields of 2-acetonaphthone (**11b**). The stability of Oxone also allowed for the extension of the protocol, towards aliphatic alcohols, which were not readily accepted by the TBHP protocol. The linear aliphatic alcohols 2-octanol (**13a**; Table 4, entry 7) and 2-decanol (**14a**; Table 4, entry 8) were oxidized to the corresponding ketones within 4 h. More sterically hindered aromatic (Table 4, entry 4) and aliphatic alcohols (Table 4, entries 9–12) were also well tolerated by this protocol and the corresponding ketones were obtained in high to excellent yields. In the case of **17a**, the formation of the Baeyer–Villiger byproduct was observed, which led to a slight decrease in the yield of this reaction. The oxidation of primary alcohols still proved to be difficult in terms of selectivity, and resulted in mixtures of the aldehyde and carboxylic acid (Table 4, entry 6).

Gas-evolution studies: To explain the difference in efficiency between the different oxidants, a gas-evolution study was performed by using mass spectrometry (Figure 1). H_2O_2, TBHP, and Oxone were chosen as oxidants for this study since they displayed different efficiencies in the catalytic alcohol oxidation.

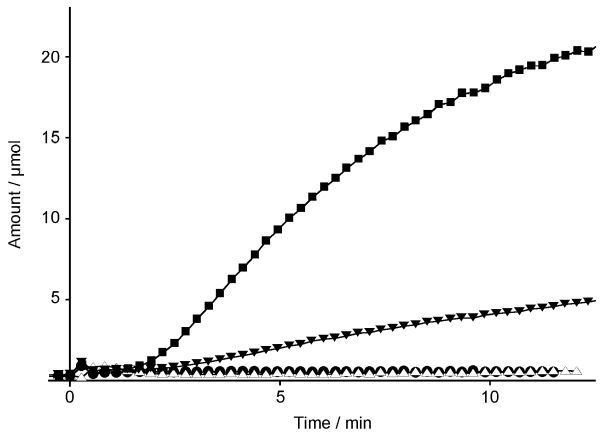


Figure 1. O_2 evolution during alcohol oxidation when using H_2O_2, TBHP, or Oxone as oxidants. Conditions: A deoxygenated solution of complex **1** (1.0 mM) and 1-phenylethanol (0.13 M) in CH_2Cl_2 (0.50 mL) was added to an aqueous solution of the oxidant (0.50 mL, 0.52 M): ●) no oxidant, Δ) Oxone, ▼) H_2O_2, and ■) TBHP as oxidant.

As expected, by means of mass spectrometry the gas could be identified as oxygen. Both H_2O_2 and TBHP, which were less efficient than Oxone, gave rise to significantly more oxygen evolution. However, the kinetics for the oxygen evolution were different for the two oxidants. In the case of THBP, a rapid generation of oxygen was observed, which approached 20 μmol after just 10 min. With H_2O_2, on the other hand, the evolution of oxygen was much slower, but the release remained constant for a longer time (3–4 h) and in the end approached the same amount as produced by TBHP. By contrast, only a minor evolution of oxygen could be observed when using Oxone, thus suggesting that almost no disproportionation reaction occurs in parallel with the alcohol oxidation. Measurements of the pH of the aqueous layer revealed that the pH changed from 6 to 1 upon addition of Oxone to the reaction. The explanation of the high stability of Oxone can probably be ascribed to its acidic nature. It is well known that the oxidation potential for water oxidation follows the Nernst equation, thus the oxidation potential of H_2O becomes significantly higher at lower pH values, and it is believed that it can therefore not compete with alcohol oxidation under highly acidic conditions.

Mechanistic studies: We believe that the catalytic cycle with Ru complex **1** and peroxides involves the generation of Ru–oxo intermediates through two-electron oxidation by oxygen-atom transfer. Ru–oxo intermediates are well known in the literature and are believed to be involved in several reactions, such as C–H bond activation,[16] epoxidation of alkenes,[17] alcohol oxidations,[8b,c,18] and water oxidation.[19]

To gain insight into the mechanism of the oxidation, a kinetic study was performed to investigate how the initial rate of the oxidation of 1-phenylethanol (**2a**) varied with varying concentrations of **1**. This was done by first mixing **2a** (0.26 mmol) with 0.25, 0.50, and 0.75 mol% of Ru complex **1** in CH_2Cl_2 (2 mL) and then adding Oxone (3 equiv) dissolved in water (2 mL) at room temperature. From the plots of initial rates versus catalyst concentration, it can be seen that the reaction displays a first-order dependence on the concentration of dimeric complex **1** (Figure 2). This would suggest that the reaction proceeds by means of mono-oxygenation of the complex, which is subsequently cycled in the reaction. Mono-oxygenation of catalyst **1** should produce a $Ru^{III,V}$ complex that rapidly disproportionates to a $Ru^{IV,IV}$ complex, which consequently should be the active catalyst.

The kinetics of the dependence of the substrate were also studied (Figure 3). By varying the concentration of the substrate and plotting the initial rates versus the concentration of the substrate, it was evident that the reaction also exhibited a first-order dependence on the substrate concentration. This implies that the substrate is involved in the rate-determining step(s).

The electrochemistry of complex **1** was further studied by cyclic voltammetry (CV). It was found that the oxidation of Ru^{III} to Ru^{IV} occurs at approximately 0.9 V versus the normal hydrogen electrode (NHE; Figure 4), whereas the further oxidation to Ru^{V} that corresponds to the oxo complex requires approximately 1.5 V.[7] However, when $[Ru(bpy)_3]^{3+}$ (bpy = 2,2′-bipyridyl) with an oxidation potential of approximately 1.2 V versus NHE was used as oxidant, no alcohol oxidation could be observed. Since the potential of $[Ru(bpy)_3]^{3+}$ is only sufficient to convert **1** to the $Ru^{IV,IV}$ state, a mechanism that involves such species can therefore be ruled out. In contrast, we favor a reaction path by which complex **1** undergoes rapid and reversible dissociation into two mononuclear species to form the iodide complex **1a** and the aqua complex **1b** prior to the mono-oxygenation event.

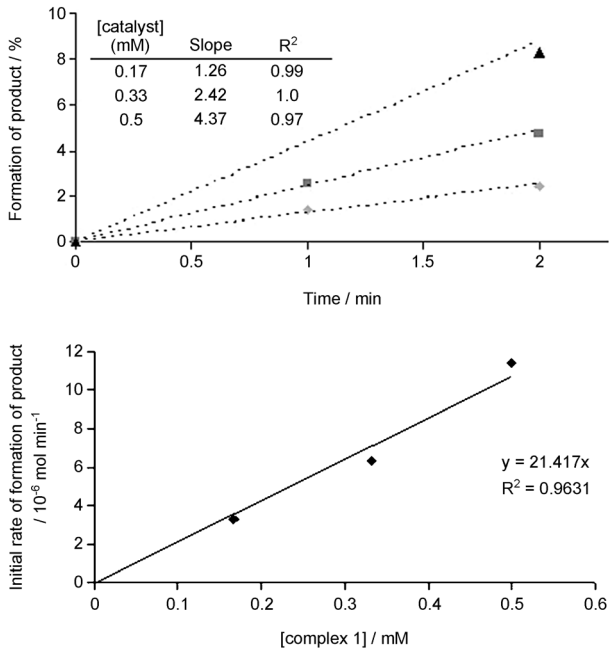


Figure 2. a) Kinetic plots for the oxidation of 1-phenylethanol (**2a**) into acetophenone (**2b**) by complex **1** versus time. Conditions: An aqueous solution of Oxone (0.39 M, 2.0 mL) was added to a solution of **1** (0.33, 0.67 or 1.0 mM), **2a** (130 mM), and dodecane (130 mM) in CH_2Cl_2 (2.0 mL). b) Initial rates for the formation of **2b** plotted against concentration of complex **1**; ◆) 0.17, ■) 0.33, and ▲) 0.50 mM.

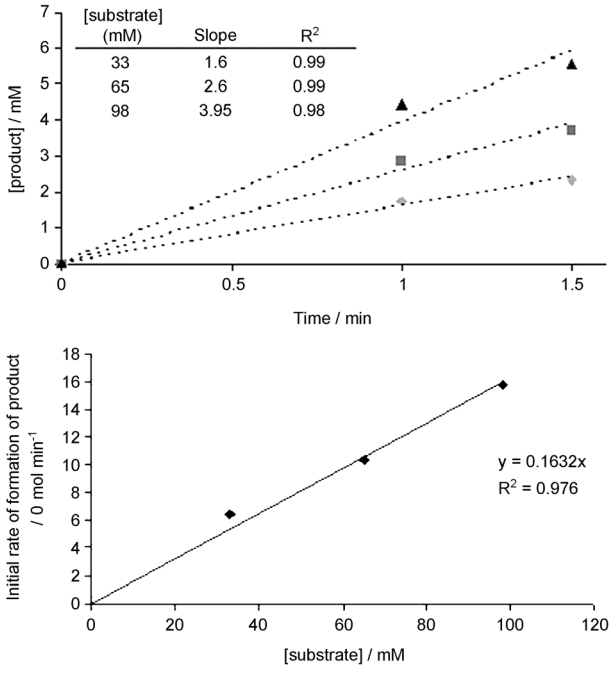


Figure 3. a) Kinetic plots for the oxidation of 1-phenylethanol (**2a**) into acetophenone (**2b**) by complex **1** versus time. Conditions: An aqueous solution of Oxone (0.39 M, 2.0 mL) was added to a solution of **1** (1.0 mM), **2a** (65, 130, or 195 mM), and dodecane (130 mM) in CH_2Cl_2 (2.0 mL). b) Initial rates for the formation of **2b** plotted against concentration of substrate **2a**; ◆) 33, ■) 65, and ▲) 98 mM.

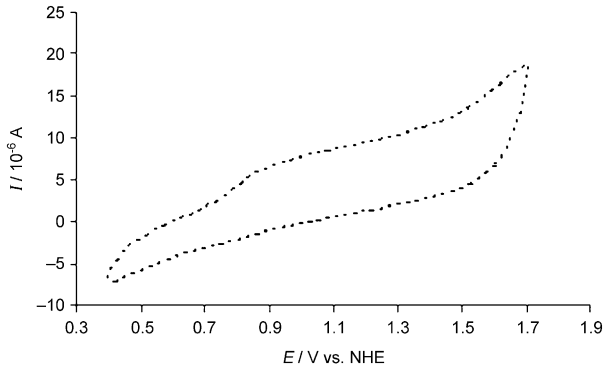


Figure 4. Cyclic voltammogram of complex **1** (0.1 mM) in CH_2Cl_2 recorded at a scan rate of 0.1 Vs^{-1} with Bu_4NPF_6 (0.1 M) as supporting electrolyte, using a glassy carbon disk (diameter 3 mm) as the working electrode, a platinum wire as counter-electrode, and $Ag/AgNO_3$ as the reference electrode.

This is supported by an earlier study performed on complex **1** by MS that showed two major peaks of essentially equal intensity, which corresponded to complexes **1a** and **1b**.[7] It is then proposed that complex **1b** is the mononuclear species that undergoes the subsequent mono-oxygenation by the two-electron oxidant, since the aqua ligand is expected to be more rapidly displaced by the oxo group than the iodide of complex **1a**. Strong support for this mechanism is derived from the fact that the formation of the relatively labile Ru^V–oxo species **1c** took place when treating a solution of Ru complex **1** in CH_2Cl_2 with 5 equivalents of aqueous Oxone or TBHP (see the Experimental Section for further details). The formation of complex **1c** was established by high-resolution mass spectrometry (HRMS), whereby a major peak was detected at *m*/*z* 526.0211, which could be assigned to the mononuclear Ru^V–oxo complex **1c** (Figure 5). It is noteworthy that no evidence for a corresponding Ru^{IV} species could be obtained by HRMS. To further support the possibility of a mononuclear Ru^V–oxo species being the active catalyst in the alcohol oxidation, we employed a mononuclear ruthenium catalyst that bears a great resemblance to **1b**.[20] To our delight, it was established that this mononuclear catalyst gave comparable results to that of dinuclear complex **1** in the oxidation of 1-phenylethanol (**2a**) when using Oxone as oxidant.

During the last few years, extensive studies of ruthenium-catalyzed oxidation processes largely based on UV/Vis spectroscopy have been conducted.[8b,c,21] Therefore, the oxidation of complex **1** was also spectrophotometrically monitored by UV/Vis spectroscopy by subjecting it to 10, 20, and 30 equivalents of Oxone (Figure 6). The UV/Vis spectral titration of complex **1** upon oxidation of Oxone in an aqueous medium resulted in a bleaching of the broad absorption in the visible region. In these titrations, isosbestic points were observed at 205 and 216 nm. However, the UV/Vis experiment did not provide any unambiguous support for either the generation of a Ru^{IV} or a Ru^V species, since these species have similar absorption spectra.[21]

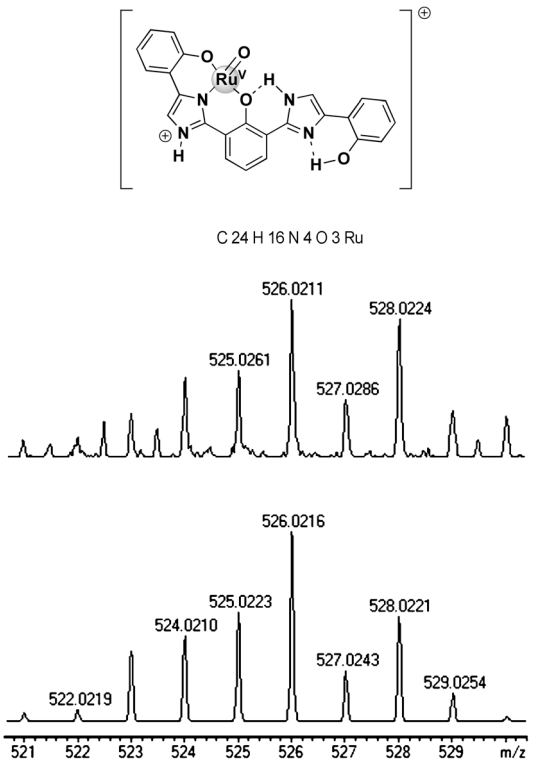


Figure 5. High-resolution mass spectra of the plausible active catalytic intermediate, Ru^{V}=O, obtained upon mixing catalyst **1** with Oxone (5 equiv; top) and calculated spectra (bottom).

It is also interesting to compare our results to those of Meyer and co-workers, who recently studied the oxidation of benzyl alcohol to benzaldehyde by using an Ru^{II} complex attached to a TiO_2 electrode. They found that the stepwise two-electron oxidation yields a Ru^{IV}–oxo complex, which is the active catalyst for the reaction.[8c] At low pH, the potential for oxidation of Ru^{II} to Ru^{III} is approximately 1.2 V versus NHE for Meyer's complex. The further oxidation to Ru^{IV} of approximately 1.5 V versus NHE is fairly similar to our potentials for the oxidation of Ru^{III} to Ru^{V}, which we can only reach by two-electron oxidation with Oxone. A difference between our results is that Meyer's complex selectively oxidizes benzyl alcohol to benzaldehyde, whereas our ruthenium complex **1** tends to give further oxidation to the carboxylic acid. It is not clear if these results demonstrate the occurrence of different mechanisms due to different spin states, or if our Ru^{V}–oxo species is a stronger oxidant than the corresponding Ru^{IV} species.

Based on our result, we suggest a mechanism according to Scheme 1, in which the dimeric Ru complex **1** reversibly dissociates into the two mononuclear complexes **1a** and **1b**. It is then assumed that, because of the coordinated iodide in complex **1a**, reaction with Oxone is much faster for complex **1b**, which gives the reactive Ru^{V}–oxo complex **1c**. This is then suggested to react with the alcohol substrate to give an alkoxy complex **1d**. After β-hydride elimination, the ketone is formed together with a Ru^{III}–hydroxy complex **1e**, which regenerates complex **1b** on protonation.

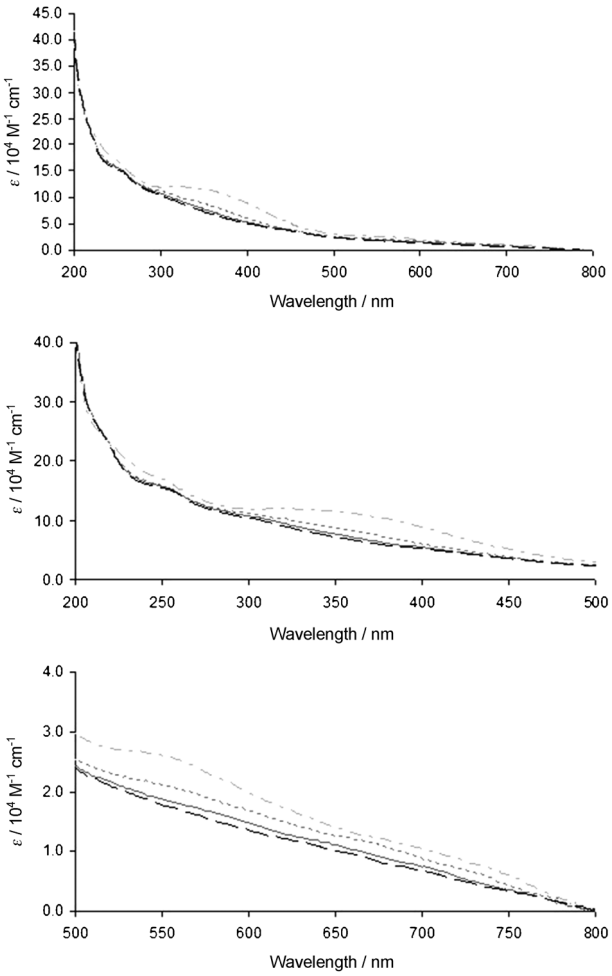
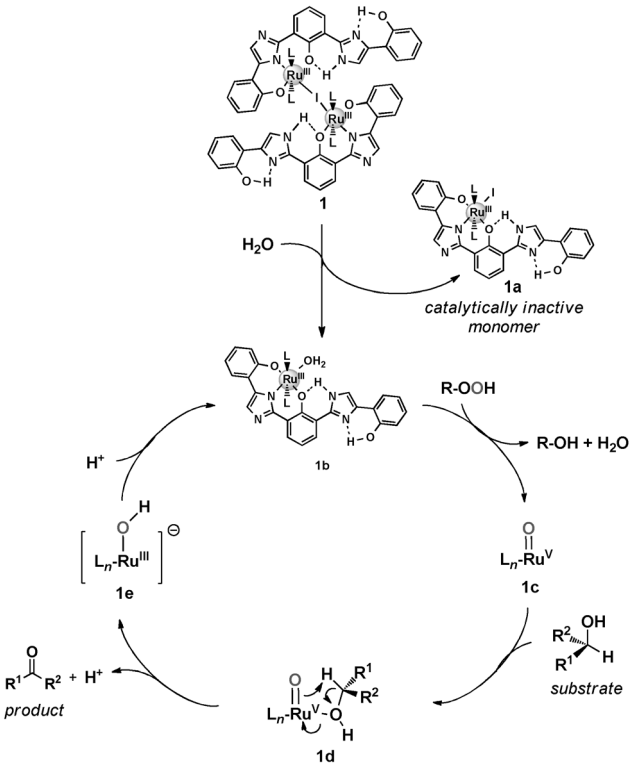


Figure 6. UV/Vis spectral changes of ruthenium complex **1** as a function of the addition of Oxone in H_2O. Conditions: Oxone (10, 20, 30 equiv) was added to an aqueous solution of complex **1** (6.6 μM, 3.0 mL). –•–•–) Complex **1** without any added oxidant, -----) 10 equivalents Oxone added, ——) 20 equivalents Oxone added, – – –) 30 equivalents Oxone added.

Conclusion

The water-oxidizing ruthenium complex **1** was successfully employed in the oxidation of secondary alcohols by using a variety of oxygen-transfer reagents. Of these, TBHP and Oxone showed the most promising results and two different oxidation protocols that involved **1** were developed. In the case of TBHP, a competing disproportionation reaction was observed, but this problem could be overcome by slow addition of the oxidant. The protocol was applied in the oxidation of benzylic secondary alcohols to give the corresponding ketones in good to high yields. When changing the oxidant from THBP to Oxone, a more efficient protocol was obtained, and the more stable oxidant Oxone allowed for an extension of the scope towards aliphatic as well as sterically hindered secondary alcohols. To explain the difference in reactivity for the different oxidants, gas-evolution measurements by mass spectrometry were conducted. Molecular oxygen could be detected when H_2O_2 and TBHP were used



Scheme 1. Proposed catalytic cycle for the oxidation of alcohols with complex **1a** and two-electron oxidants (**L**=4-picoline or tridentate ligand).

as oxidants. With Oxone, on the other hand, only a minor amount of oxygen was evolved. These results clearly demonstrate the difference in the kinetics between the disproportionation of the oxidant and in the catalysis of alcohol oxidation for the different oxidants. Furthermore, mechanistic studies were carried out to gain insight into the mechanism and to establish the identity of the catalytically active species. These studies favored a path that proceeds by means of a reversible dissociation of **1** into the iodo complex **1a** and the aqua complex **1b**. Subsequent mono-oxygenation of species **1b** resulted in the formation of the Ru^{V}–oxo species **1c**, which could be detected by high-resolution mass spectrometry. It is proposed that this species plays a key role in the catalytic mechanism of alcohol oxidation, and future work will be dedicated to studying the mechanism in greater detail with this catalyst and structurally similar ones (like those in Ref. [20]). We believe that these results will be of great value for the development and mechanistic understanding of future Ru catalysts in water oxidation as well as in organic transformations.

Experimental Section

Materials and methods: All reagents were obtained from commercial suppliers. They were of analytical grade or higher and were used without further purification. Complex **1** was prepared as previously described.[7] The reactions were monitored by thin layer chromatography (TLC) using silica-gel-coated plates with indicator (Merck, silica gel 60). Column chromatography was performed on silica gel (Grace Division, Davsil, 0.035–0.070 mm) if not mentioned otherwise. After chromatography the fraction was pooled, evaporated to dryness, and dried under vacuum. ^{1}H and ^{13}C NMR spectroscopy were recorded using a Bruker Avance spectrometer at 400 and 100 MHz, respectively. Chemical shifts are reported in ppm relative to the residual solvent peak ($CDCl_3$; $\delta_H=7.26$ ppm and $\delta_C=77.0$ ppm). GC analysis was performed using a Varian 3800 gas chromatograph with CP-Chirasil-Dex CB (25 m×0.32 mm×0.25 μm) column. Identification of products by NMR spectroscopy and GC was done by comparison to references of authentic samples obtained from commercial suppliers. The UV/Vis absorption spectra were measured using a CARY 300 Bio UV/Vis spectrophotometer.

Electrochemistry: Cyclic voltammetry (CV) was measured using an Autolab potentiostat with a GPES electrochemical interface (Eco Chemie) with a glassy carbon disk (diameter 3 mm) as the working electrode, a platinum wire as counter electrode, and $Ag/AgNO_3$ as the reference electrode. The electrolyte used was 0.1 M Bu_4NPF_6 in CH_2Cl_2. Potentials in CH_2Cl_2 are versus NHE by using the Fc^{+}/Fc couple (0.630 V) as standard.

General procedure for oxidation of alcohols using TBHP as oxidant: Complex **1** (3.0 mg, 2.0 μmol), dodecane (44.3 mg, 0.26 mmol), and substrate alcohol (0.26 mmol) were dissolved in a 1:1 mixture of CH_2Cl_2/H_2O (4 mL, pH 6). The reaction was heated to 40 °C and aqueous TBHP (70 wt %, 1.56 mmol) was added slowly over 1 h, after which the reaction was allowed to stir for the appropriate time. The reaction was followed by removal of periodical aliquots for GC analysis, and the yield of the reaction was determined against an internal standard (dodecane).

General procedure for oxidation of alcohols using Oxone as oxidant: Complex **1** (3.0 mg, 2.0 μmol), dodecane (44.3 mg, 0.26 mmol), and substrate alcohol (0.26 mmol) were dissolved in a 1:1 mixture of CH_2Cl_2/H_2O (4 mL, pH 1). The reaction was heated to 40 °C and Oxone (0.78 mmol) was added, after which the reaction was allowed to stir for an appropriate time. The reaction was followed by removal of periodical aliquots for GC analysis and the yield of the reaction was determined against an internal standard (dodecane).

Oxygen-evolution measurements: The mass spectrometer consisted of three separate parts connected by gas valves: a reaction chamber, a gas handling system (GHS), and a mass spectrometer (MKS Spectra Products, Microvision Plus, 0–100 mass units) in ultra high vacuum (base pressure 2×10^{-10} mbar). A rough pump was used to evacuate the GHS, so the pressure can be regulated within 0.1–1000 mbar. By using this setup, the enclosed volume in the reaction chamber was continuously probed by the mass spectrometer by means of an inlet through the leak valve. The change over time of the measured pressure of masses 0–100 in the mass spectrometer was then converted to the amount in the enclosed volume by calibrating the system. Any leakage of air could be continuously measured by mass spectrometry (by observing an increase in both O_2 and N_2).

A solution that consisted of complex **1** (1 mM) and 1-phenylethanol (0.13 M) was prepared in CH_2Cl_2. This solution was then deoxygenated by bubbling with N_2 for at least 15 min before being used in the experiments. In a typical run, an aqueous solution of the oxidant (0.5 mL, 0.52 M) was placed in the reaction chamber and the reaction chamber was evacuated with a rough pump. He (42 mbar) was then introduced into the system. After a couple of minutes, the deoxygenated catalyst solution (0.50 mL) was injected into the reaction chamber. The generated oxygen gas was then measured and recorded versus time by mass spectrometry.

Kinetic studies of catalytic alcohol oxidation:

Catalyst dependence: An aqueous solution of Oxone (0.39 M, 2 mL) was added to a CH_2Cl_2 solution (2 mL) that contained complex **1** (0.33, 0.67, or 1.0 mM), alcohol **2a** (130 mM), and dodecane (130 mM). The reactions were performed at room temperature and were followed by removal of periodical aliquots for GC analysis after 1–2 min by using dodecane as internal standard.

Substrate dependence: An aqueous solution of Oxone (0.39 M, 2 mL) was added to a solution of complex **1** (1.0 mM), alcohol **2a** (65, 130 or

195 mM), and dodecane (130 mM) in CH_2Cl_2 (2 mL). The reactions were performed at room temperature and were followed by removal of periodical aliquots for GC analysis after 1–2 min by using dodecane as internal standard.

Mass spectrometry studies of catalytic intermediates: Complex **1** (0.5 mg, 0.33 μmol) and Oxone (0.2 mg, 1.66 μmol) were mixed in CH_2Cl_2/H_2O (2 mL). The reaction mixture was stirred for 5 min before aliquots were injected and analyzed by mass spectrometry.

General procedure for UV/Vis spectrophotometric studies of ruthenium complex 1: Complex **1** was dissolved in H_2O (66 μM) by the use of sonification. The resulting solution was further diluted to give a concentration of 6.6 μM. This solution (3 mL) was added to a cuvette and was then analyzed by UV/Vis spectrophotometry. Oxone in H_2O (10 mM, 20 μL) was then added in portions (10, 20, and 30 equiv) to this sample, and the spectral changes were followed by UV/Vis spectrophotometry.

Acknowledgements

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