Mechanisms for the oxidation of secondary alcohols by dioxoruthenium(VI) complexes

Zhao Wang, W. David Chandler, and Donald G. Lee

Abstract: Possible mechanisms for the oxidation of alcohols by dioxoruthenium(VI) complexes are critically evaluated. Rate constants for the reduction of *trans*-[(TMC)Ru^{VI}(O)₂]⁺⁺ (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) by substituted benzhydrols are correlated more satisfactorily with Hammett σ substituent constants ($\rho = -1.44 \pm 0.08$, $r^2 = 0.98$) than with σ^+ substituent constants ($\rho = -0.72 \pm 0.11$, $r^2 = 0.83$). Similar observations for the oxidation of substitued benzyl alcohols have recently been reported, confirming that the transition state for these reactions is not carbocation-like. Primary deuterium isotope effects indicate that cleavage of the α -C–H bond is rate-limiting. The lack of an observable O-D isotope effect and the ease of oxidation of ethers indicates that the presence of a hydroxyl is not essential. The previously reported observation that cyclobutanol is quantitatively converted into cyclobutanone by dioxoruthenium(VI) complexes eliminates free-radical intermediates from consideration as part of the mechanism, and negative entropies of activation ($-\Delta S^{\dagger} = 96-137$ J mol⁻¹ K⁻¹) suggest a structured transition state. Only two of eight possible reaction mechanisms considered were found to be consistent with the available data. A critical analysis of the available data indicates that a 2 + 2 (C—H + Ru=O) addition and a reaction initiated by ligand formation through the interaction of the reductant's HOMO with the oxidant's LUMO are the most likely reaction mechanisms.

Key words: oxidation, alcohols, ruthenium(VI), mechanism, substituent effects.

Résumé : On évalue d'une façon critique divers mécanismes possibles pour l'oxydation des alcools par des complexes de dioxoruthénium(VI). La corrélation entre les constantes de vitesse de réduction du *trans*-[(TMC)Ru^{VI}(O)₂]⁺⁺ (TMC = 1,4,8,11-tétraarétyl-1,4,8,11-tétraazacyclotétradécane) par des benzhydrols substitués est meilleure avec des constantes de substituants σ^+ de Hammett ($\rho = -1,44 \pm 0,08$; $r^2 = 0,98$) qu'avec des constantes de substituants σ^+ ($\rho = -0,72 \pm 0,11$; $r^2 = 0,83$). Des observations semblables ont été rapportées récemment pour l'oxydation d'alcools benzyliques substitués; elles confirment que l'état de transition de ces réactions ne ressemble pas à un carbocation. Les effets isotopiques primaires du deutérium indiquent que le clivage de la liaison C-H en α limite la vitesse. Le fait que l'on n'observe pas d'effet isotopique O-D et la facilité d'oxydation des éthers indiquent que la présence d'un groupe hydroxyle n'est pas essentielle. L'observation rapportée antérieurement à l'effet que le cyclobutanol peut être transformé quantitativement en cyclobutanone par les complexes de dioxoruthénium(VI) élimine la possibilité d'un mécanisme impliquant des intermédiaires radicalaires; par ailleurs, les entropies d'activation négatives ($-\Delta S^{\ddagger} = 96$ à 137 J mol⁻¹ K⁻¹) suggèrent la présence d'un état de transition structuré. On a trouvé que seulement deux des huit mécanismes réactionnels possibles sont en accord avec les données disponibles. Une analyse critique des données disponibles indique qu'une addition 2 + 2 (C-H + Ru=O) et une réaction initiée par la formation de ligand par interaction des OMHO du réducteur avec les OMBV de l'oxydant sont les mécanismes réactionnels les plus probables.

Mots clés : oxydation, alcools, ruthénium(VI), mécanisme, effets de substituants.

[Traduit par la rédaction]

Introduction

A knowledge of the redox properties of dioxoruthenium(VI) complexes, $[LRu(O)_2]^{++}$, where L is a neutral macrocyclic ligand, is important because of their potential use as stoichiometric or catalytic oxidants. The chemical and physical properties of

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¹ Author to whom correspondence may be addressed. Telephone: (306) 585-4247. Fax: (306) 585-4894. E-mail: dglee@meena.cc.uregina.ca these complexes, which can exist as either *cis* or *trans* isomers, have been studied in several laboratories including those of Che (1), Meyer (2), Drago (3), James (4), Groves (5), Morishima (6), Hirobe (7), and Jorgensen (8).

It has been observed in these studies that dioxoruthenium(VI) complexes can be used as oxidants for alcohols, alkenes, arenes, sulfides, amines, and phosphines. The products obtained from the oxidation of primary and secondary alcohols are aldehydes (7, 9–13) and ketones (9–14) respectively; from alkanes the products are alcohols (3, 10, 12) or ketones (10, 12); from alkenes the products are α , β -unsaturated ketones (10–13, 15), epoxides (5, 7, 10–13, 16), or products derived from the oxidative cleavage of the double bond (10, 11, 16); from arenes the products are α -phenyl alcohols (10, 12, 13, 16), aldehydes (11, 16, 17), ketones (10, 12, 16), or carboxylic acids (10), depending on the nature of the side

Scheme 1.

Single - electron transfer:

 $R_2CHOH + [LRu^{VI}(O)_2]^{++} \longrightarrow R_2CHOH^+ + [LRu^{V}(O)_2]^{++}$

Hydrogen atom transfers:

chain; from cyclic ethers the products are lactones (10); from sulfides the products are the corresponding sulfoxides (6, 7) or sulfones (7); from amines, dehydrogenated products (primarily nitriles and imines) are obtained (18); and from phosphines the products are the corresponding phosphine oxides (2, 6, 19, 20).

This paper reports the results obtained from a variety of experiments designed to provide a better understanding of the mechanism of the reaction between secondary alcohols and a typical dioxoruthenium(VI) complex, *trans*-[(TMC)Ru^{VI}(O)₂]⁺⁺ (TMC = 1.4.8.11-tetramethyl-1.4.8.11-tetraazacvclotetradecane). Eight theoretically possible reaction mechanisms have been considered: direct single-electron transfer from the alcohol to the oxidant, hydrogen atom or hydride ion transfer from either oxygen or carbon, 2 + 2 addition of a ruthenium oxo (Ru=O) to either the O—H or the α -C—H bond of the alcohol and ligand formation followed by a cyclic transfer of hydrogen. These possibilities, derived from the discussion by March (21a) and the theoretical work of Deng and Ziegler (22), Mayer and co-workers (23), and Rappe and Goddard (24) on the reactions of high valent transition metal compounds, have been summarized in Scheme 1.

Each of the mechanistic possibilities outlined in Scheme 1 has been examined in light of the rather large amount of experimental evidence currently available with respect to the reactions of dioxoruthenium(VI) complexes and alcohols. From such an analysis it is possible to eliminate several potential processes and to arrive at the "most likely" mechanisms.





Experimental section

Materials

Benzhydrol (α -phenylbenzenemethanol), 4-methylbenzhydrol, 4-chlorobenzhydrol, and 4,4'-dichlorobenzhydrol were obtained commercially (Aldrich) and purified by repeated crystallizations from a mixture of diethyl ether and hexane until sharp melting points in agreement with literature values were obtained. 2-Propanol was purified by distillation from calcium oxide. A middle fraction (bp 80.5–81.0°C) was collected and analyzed by use of GLC. The results indicated a purity of at least 99.9%.

4-Bromobenzhydrol, 4,4'-dimethylbenzhydrol, 4-fluorobenzhydrol, and 4-methoxybenzhydrol were prepared by reduction of the corresponding benzophenones with lithium aluminum hydride (25). The benzophenones were obtained from Aldrich. In a typical procedure, a flame-dried 300 mL three-necked flask, fitted with a magnetic stirrer and a dropping funnel, was charged with 0.3 g (8 mmol) of lithium aluminum hydride (J.T. Baker) and 100 mL of anhydrous ether. A solution of benzophenone (24 mmol) in anhydrous ether (50 mL) was added dropwise. The mixture was stirred under gentle reflux until the reaction was complete. The solution was then treated with 50 mL of ice water while cooling the reaction flask in an ice bath. The organic layer was separated and the aqueous layer extracted with ether $(2 \times 30 \text{ mL})$. The combined organic layers were dried over CaCl₂, filtered, and evaporated to give the corresponding benzhydrol in 85-93% yield. The products were repeatedly recrystallized from a solution of diethyl ether and hexane until sharp melting points were obtained and then identified from physical and spectral data. 4-Bromobenzhydrol, mp 62–63°C, lit. (26) 63–65°C; ¹H NMR (CDCl₃), δ: 2.12 (d, 1H), 5.74 (d, 1H), 7.36 (m, 9H); ¹³C NMR (CDCl₃), δ: 75.6, 121.4, 126.6, 127.9, 128.3, 128.7, 131.6, 142.8, 143.4. 4,4'-Dimethylbenzhydrol, mp 68.5-69.0°C, lit. (26) 69°C; ¹H NMR (CDCl₃), δ: 2.22 (d, 1H), 2.36 (s, 6H), 5.72 (s, 1H), 7.38 (M, 8H); ¹³C NMR (CDCl₃), δ: 21.2, 76.0, 126.5, 129.2, 137.2, 141.2. 4-Fluorobenzhydrol, mp 47-48°C; ¹H NMR (CDCl₃), δ: 2.41 (d, 1H), 5.78 (d, 1H), 6.99 (t, 2H), 7.28 (m, 7H); ¹³C NMR (CDCl₃), δ: 75.6, 115.5, 126.5, 127.8,

Fig. 2. Typical pseudo first-order plot for the oxidation of benzhydrol (0.670 M) by *trans*-[(TMC)Ru(O)₂]⁺⁺. Slope = $9.67 \times 10^{-5} \text{ s}^{-1}$, $r^2 = 0.999$.



128.2, 128.3, 128.6, 139.5, 143.0. 4-Methoxybenzhydrol, mp 65–66°C; ¹H NMR (CDCl₃), δ : 2.65 (d, 1H), 3.81 (s, 3H), 5.74 (d, 1H), 6.88 (d, 2H), 7.33 (M, 7H); ¹³C NMR (CDCl₃), δ : 55.3, 75.8, 113.9, 126.5, 128.0, 128.5, 136.0, 144.5, 159.5.

Benzhydrol- α -d and 2-propanol- α -d were prepared by the reduction of benzophenone and acetone with lithium aluminium deuteride (Aldrich). Benzhydrol- α -*d*, mp 67.5-68.0°C, was identified by use of NMR: ¹H NMR (CDCl₃), δ: 2.39 (s, 1H), 7.38 (m, 10H); ¹³C NMR (CDCl₃), δ: 126.6, 127.6, 128.5, 144.5. 2-Propanol- α -d was purified by distillation from calcium oxide, bp 80.0-80.5°C, and identified by NMR: ¹H NMR (CDCl₃), δ: 1.11 (s, 6H), 2.66 (br, 1H). Only one peak was detected in a GLC analysis indicating at least 99.9% purity. From the NMR integrals, the incorporation of deuterium was calculated to be 98%. 2-Propanol-O-d was prepared by repeatedly treating 2-propanol with D₂O. The product was identified by NMR; the ¹H NMR integrals indicated 96.7% incorporation of deuterium.

The oxidant was prepared in two forms, $[(TMC)-Ru^{VI}(O)_2](ClO_4)_2$ and $[(TMC)Ru^{VI}(O)_2](BF_4)_2$ using procedures previously described in the literature (27). Both salts reacted with alcohols at the same rate under any particular set of conditions, indicating that the identity of the anion has little influence on the reaction rate. The initial work was done with the perchlorate salt; however, on two occasions small explosions occurred when it was being transferred as a dry solid from the reaction flask in which it had been prepared to a storage vial. The explosions were sufficiently violent to shatter glassware and cause minor cuts to the hand of one of us (Z.W.). The fluoroborate salt proved to be much safer to work with.

Both salts were prepared starting from $K_2[Ru^{III}(Cl)_5H_2O]$, obtained from either Johnson Matthey or Strem Chemicals. Initially, 1.056 g (2.82 mmol) of $K_2[Ru^{III}(Cl)_5(H_2O)]$ was suspended in 150 mL of absolute ethanol and heated under reflux with vigorous stirring for 15 min. 1,4,8,11-Tetramethyl-1,4,8,11-tetraazacyclotetradecane, TMC (Aldrich, 0.92 g, 3.59 mmol), dissolved in 280 mL of ethanol was added dropwise to the refluxing suspension over a period of 6 h. After refluxing for an additional 12 h (overnight), the solution was

Table 1. Rate constants for the oxidation of 2-propanol and benzhydrol by [*trans*-(TMC)RuO₂]⁺⁺ in acetonitrile at 40°C.

Concentration (M)	$k_1 (\mathrm{s}^{-1} \times 10^5)^a$	$k_2 (\mathrm{M}^{-1} \mathrm{s}^{-1} \times 10^5)^b$
2.62	6.6 ± 0.6	2.5 ± 0.2
2.84	7.0 ± 0.3	2.5 ± 0.1
3.01	7.3 ± 0.1	2.4 ± 0.1
3.26	8.1 ± 0.1	2.5 ± 0.1
3.56	9.1 ± 0.1	2.6 ± 0.1
0.485	6.8 ± 0.3	14 ± 1
0.492	7.2 ± 0.5	15 ± 1
0.550	8.2 ± 0.1	15 ± 1
0.661	9.0 ± 0.6	15 ± 1
0.670	9.6 ± 0.2	14 ± 1
	Concentration (M) 2.62 2.84 3.01 3.26 3.56 0.485 0.492 0.550 0.661 0.670	$\begin{array}{c c} \mbox{Concentration (M)} & k_1 ({\rm s}^{-1} \times 10^5)^a \\ \hline 2.62 & 6.6 \pm 0.6 \\ 2.84 & 7.0 \pm 0.3 \\ 3.01 & 7.3 \pm 0.1 \\ 3.26 & 8.1 \pm 0.1 \\ 3.56 & 9.1 \pm 0.1 \\ 0.485 & 6.8 \pm 0.3 \\ 0.492 & 7.2 \pm 0.5 \\ 0.550 & 8.2 \pm 0.1 \\ 0.661 & 9.0 \pm 0.6 \\ 0.670 & 9.6 \pm 0.2 \end{array}$

^a Pseudo first-order rate constants

^b $k_2 = k_1 / [reductant].$

filtered hot, and the yellow filtrate evaporated to dryness. This product was redissolved in a minimum of hot 3 M HCl. Yellow crystals of *trans*-[(TMC)Ru^{III}(Cl)₂]Cl formed when the solution was allowed to slowly cool. After filtration and washing with cold 3 M HCl, a yellow crystalline product (0.70 g, 1.64 mmol, 58%) was obtained; $\lambda_{max} = 370$ nm, with a shoulder at 315 nm when dissolved in acetonitrile. A portion of this product (0.43 g, 0.95 mmol) and silver p-toluenesulfonate (0.77 g, 2.77 mmol) were heated at 60°C for 0.5 h in 35 mL of distilled water. A grey-white precipitate (AgCl), which formed immediately, was removed by filtration, and 50% H_2O_2 (9 mL) was added dropwise to the remaining yellow solution at 60°C. After 30 min the solution was cooled in an ice-water bath and an excess of NaClO4 added. The compound trans-[(TMC)Ru^{VI}(O)₂](ClO₄)₂, which slowly precipitated, was collected and recrystallized from hot (60°C) 0.1 M HClO₄. Crystalline product (0.23 g, 43%) was obtained. The spectrum of this product dissolved in acetonitrile was similar to that reported in the literature for other dioxoruthenium(VI) complexes: $\lambda_{max} = 228, 257, and 388 nm; lit. (13, 27) 223, 255,$ and 388 nm.

The compound *trans*-[(TMC)Ru^{VI}(O)₂](BF₄)₂ was prepared by first treating *trans*-[(TMC)Ru^{III}(Cl)₂]Cl (0.43 g, 0.95 mmol) with silver *p*-toluenesulfonate (0.77 g, 2.77 mmol) dissolved in 35 mL of distilled water and heating the mixture at 60°C for 0.5 h. The solution was filtered to remove AgCl, and 50% H₂O₂ (9 mL) was added dropwise to the yellow filtrate at 60°C. This solution was concentrated to two thirds of its volume and cooled in an ice-water bath. When an excess of saturated NaBF₄ solution was added, a precipitate formed slowly over several hours. Collection of the precipitate and recrystallization from hot (60°C) 0.1 M HBF₄ yielded *trans*-[(TMC)Ru^{VI}(O)₂](BF₄)₂ (0.12 g, 34%).

Plots of the concentration of this product in acetonitrile solutions vs. absorbance at 388 nm were precisely linear, as required by Beer's Law, with a slope of $\varepsilon = 539 \pm 5$.

The solvent, acetonitrile, used in these experiments was purified by stirring with $KMnO_4$ overnight and simple distillation. The distillate was then carefully redistilled over CaH_2 in a nitrogen atmosphere.

Kinetic method

Reaction rates were determined by monitoring spectral

Reductant	Oxidant ^a	Solvent	Temp. (°C)	$k_{\rm H}/k_{\rm D}$	Reference no.
CH ₃ CDOHCH ₃	trans-[LRu(O) ₂] ⁺⁺	CH ₃ CN	40	7.8 ± 0.5	This work
Ph ₂ CDOH	trans-[LRu(O) ₂] ⁺⁺	CH ₃ CN	40	21 ± 2	This work
PhCD ₂ OH	trans- $[L'Ru(O)_2]^{++}$	CH ₃ CN	25	19 ± 2	9
CD ₃ OD	trans- $[L'Ru(O)_2]^{++}$	CH ₃ CN	25	8 ± 1	9
CD ₃ CD ₂ OD	trans- $[L'Ru(O)_2]^{++}$	CH ₃ CN	25	8 ± 1	9
CD ₃ CDODCD ₃	trans- $[L'Ru(O)_2]^{++}$	CH ₃ CN	25	11 ± 1	9
CH ₃ CHODCH ₃	<i>trans</i> -[LRu(O) ₂] ⁺⁺	CH ₃ CN	40	1.0 ± 0.1	This work
CH ₃ CH ₂ OD	trans- $[L'Ru(O)_2]^{++}$	CH ₃ CN	25	1.0 ± 0.1	9
CH ₃ CH ₂ OD	<i>trans</i> - $[L'Ru(O)_2]^{++}$	D_2O	25	1.0 ± 0.1	9

Table 2. Kinetic deuterium isotope effects for the oxidation of alcohols by *trans*-dioxoruthenium(VI) complexes.

 a L is 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (TMC). L' is *N*,*N*'-dimethyl-6,7,8,9,10,11,17,18-octahydro-5*H*-dibenzo[en][1,4,8,12]dioxadiazacyclopentadecane.

Fig. 3. Hammett correlation, using σ substituent constants, for the oxidation of substituted benzhydrols by *trans*-[(TMC)Ru(O)₂]⁺⁺ at 40.0 ± 0.1 °C. Slope = -1.44 ± 0.08, r^2 = 0.978. Substituent constants were taken from March (21*b*). The effects when substituents are present in both rings were taken to be additive.

Fig. 4. Attempted Hammett correlation, using σ^+ substituent constants, for the oxidation of substituted benzhydrols by *trans*-[(TMC)Ru(O)₂]⁺⁺ at 40.0 ± 0.1°C. Slope = -0.72 ± 0.11, r^2 = 0.834. Substituent constants were taken from March (21*b*). The effects when substituents are present in both rings were taken to be additive.



Table 3. Hammett correlations for the oxidation of alcohols by dioxoruthenium(VI) complexes in acetonitrile.^a

Oxidant ^b	Reductant	Temp. (°C)	$\rho(r^2)^c$	$\rho^+(r^2)^d$	Reference
trans-[LRu(O) ₂] ⁺⁺	Ar ₂ CHOH	40	-1.44 (0.98)	-0.72 (0.83)	This work
trans- $[L'Ru(O)_2]^{++}$	ArCH ₂ OH	25	-1.51 (0.96)	-0.91 (0.87)	9 ^e
cis-[L"Ru(O) ₂] ⁺⁺	ArCH ₂ OH	25	-1.24 (0.99)	-0.75 (0.90)	16 ^e

^a Substituent constants were taken from ref. 21b.

^b L is 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (TMC). L' is N,N'-dimethyl-6,7,8,9,10,11,17,18-octahydro-5H-

dibenzo[en][1,4,8,12]dioxadiazacyclopentadecane. L" is N,N,N',N'-tetramethyl-3,6-dimethyl-3,6-diazaoctane-1,8-diamine.

^{*c*} Hammett ρ value obtained using σ substituent constants (r^2 is the correlation coefficient).

^d Hammett ρ value obtained using σ^+ substituent constants (r^2 is the correlation coefficient).

^e Correlations were recalculated using rate-constant data reported in these references.

changes as the reaction progressed. All measurements were made under pseudo first-order conditions with alcohol concentrations at least 100 times that of the oxidant. Each rate constant reported is the average of at least three determinations that agreed within $\pm 10\%$ or less. In a typical kinetic experiment, a quartz cuvette containing a 2.00 mL aliquot of

Fig. 5. Eyring plot for the oxidation of benzhydrol (0.504 M) by $[(TMC)Ru(O)_2]^{++}$. Slope = -6920 ± 370 K, intercept = 7.5 ± 1.2 , $r^2 = 0.989$.



approximately 1×10^{-3} M [(TMC)Ru^{VI}(O)₂]⁺⁺ in acetonitrile was placed in the thermostated cell compartment of a Hewlett Packard 8450A diode array spectrophotometer and held there until thermal equilibrium had been established. An excess of the alcohol, also dissolved in acetonitrile and thermostated at the same temperature, was added from a microliter syringe and, after thorough mixing, spectra recorded at equal time intervals. Sequential scans exhibited sharp isosbestic points at 334 nm and 404 nm (Fig. 1). The final spectrum was identical to that reported for [(TMC)Ru^{IV}O(CH₃CN)]⁺⁺ (13).

Results

Rate law

Plots of ln(absorbance – final absorbance) at 388 nm were linear (Fig. 2), indicating that the reaction is first order in oxidant. Second-order rate constants, calculated by division of the pseudo first-order rate constants by alcohol concentration (Table 1), were observed to be constant, indicating that the reaction is also first order with respect to the reductant. The rate law is therefore given by eq. [1].

[1] $-d[Ru^{VI}]/dt = k_2[Ru^{VI}][alcohol]$

Isotope effects

Kinetic isotope effects, determined for the oxidation of 2propanol-2-*d*, 2-propanol-*O*-*d* and benzhydrol- α -*d* are summarized in Table 2. The results reported from other laboratories for the oxidation of isotopically substituted alcohols by dioxoruthenium(VI) complexes have also been included in Table 2 for comparison purposes.

Substituent effects

The second-order rate constants for the oxidation of substituted benzhydrols by $[(TMC)Ru^{VI}(O)_2]^{++}$ were found to correlate well with Hammett σ values (Fig. 3), but not with the corresponding σ^+ values (Fig. 4). The negative ρ value (-1.44) indicates that the electron density on the α -carbon has decreased in the transition state; however, the lack of correlation with σ^+ values, observed in this and other studies, indicates

Table 4. Activation parameters for the oxidation of alcohols by dioxoruthenium(VI) complexes in acetonitrile.

		ΔH^{\ddagger}	ΔS^{\ddagger}	Reference
Reductant	Oxidant ^b	(kJ/mol)	(J/mol K)	no.
Benzhydrol	trans-[LRu(O) ₂] ⁺⁺	58 ± 9	-137 ± 8	This work
2-Propanol	trans-[LRu(O) ₂] ⁺⁺	62 ± 5	-135 ± 2	This work
2-Propanol	cis-[L'Ru(O) ₂] ⁺⁺	54 ± 4	-109 ± 17	16
2-Propanol	<i>trans</i> - $[L''Ru(O)_2]^{++}$	50 ± 4	-117 ± 13	9
Cyclobutanol	cis-[L'Ru(O) ₂] ⁺⁺	59 ± 4	-92 ± 13	16
Benzyl alcohol	cis-[L'Ru(O) ₂] ⁺⁺	50 ± 4	-100 ± 13	16
Benzyl alcohol ^a	trans- $[L'''Ru(O)_2]^{++}$	35 ± 4	-96 ± 13	10
Benzyl alcohol	<i>trans</i> - $[L''Ru(O)_2]^{++}$	42 ± 4	-109 ± 13	9

^a Solvent: CF₃SO₃H.

^b L is 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (TMC). L' is N,N,N',N'-tetramethyl-3,6-dimethyl-3,6-diazaoctane-1,8-diamine. L" is N,N'-dimethyl-6,7,8,9,10,11,17,18-octahydro-5*H*-dibenzao[en][1,4,8,112] dioxadiazacyclopentadecane. L" is 5,5-dimethyl-2,2'-bipyridine.

that the transition state is not carbocation-like. Table 3 contains a comparison of the Hammett correlations for similar reactions of dioxoruthenium(VI) complexes that have been reported from other laboratories.

Activation parameters

The enthalpies and entropies of activation for the oxidation of 2-propanol and benzhydrol were determined from a study of the reaction rates at different temperatures. A typical Eyring plot has been reproduced in Fig. 5. The activation parameters that have been reported for other similar reactions are included in Table 4 for comparison purposes.

Discussion

There are at least two reasons why chemists wish to have a good understanding of reaction mechanisms: (i) a knowledge of the mechanism of a reaction provides an indication of the conditions that should be used to maximize the yield and rate of formation of a specific reaction product, and (ii) insights into the details of a particular reaction mechanism are often transferable to other reactions; i.e., there is a likelihood that all chemistry will ultimately be understandable in terms of a finite number of fundamental principles.

The reactions between high valent transition metal compounds (oxidants) and organic reductants are examples of important, often used processes for which the chemistry is not particularly well understood, despite a voluminous literature. The products obtained, in common with most redox reactions, could be produced via several possible mechanisms (21a), as summarized in Scheme 1 for the reaction under consideration. With such a multiplicity of viable mechanistic options available, it will likely be very difficult to "prove" that a particular mechanism is correct; the best that can be expected at this time is a critical evaluation of each possible mechanism in light of the available experimental evidence and the most current theoretical calculations. Using this approach several possibilities can be eliminated and the "most likely" mechanisms proposed. Ultimately, it is reasonable to expect that it may be possible to arrive at a unified mechanistic consensus that is applicable to a large number of redox reactions (28).

The observation made by Che and co-workers (12, 29), that

the only product obtained from the oxidation of cyclobutanol by dioxoruthenium(VI) complexes is cyclobutanone, indicates that free-radical intermediates are not involved. As discussed in detail elsewhere (16, 30–36), it is known that the internal strain of the cyclobutyl system causes it to open if free radical intermediates are formed. For example, acyclic products are obtained when cyclobutanol is oxidized by typical one-electron oxidants such as vanadium(V) (30, 31), manganese(III) (31), chromium(IV) (32), cerium(IV) (33), and ruthenium(VII) (34, 36), while cyclobutanone is obtained from typical two-electron oxidants such as ruthenium tetroxide (35), ruthenium(VI) (35, 36), chromium(VI) (32), and chromium(V) (32). The expected products from oxidations involving single-electron or hydrogen atom transfers would therefore be acyclic compounds (Scheme 2), while two-electron transfer reactions would result in the formation of cyclobutanone (Scheme 3).

Reaction mechanisms that involve cleavage of the O—H bond in the rate-limiting step are also eliminated from further consideration by the observation that there is no measurable kinetic deuterium isotope effect when the hydroxyl hydrogen

is replaced by deuterium (Table 2). This would include both hydrogen atom and hydride ion transfers from oxygen, as well as 2 + 2 (O-H + Ru=O) additions. The report that ethers, such as tetrahydrofuran, are readily oxidized by dioxoruthenium(VI) complexes (10, 29, 37) indicates that the presence of O-H groups in the structure of the reductant is not essential, in contrast to chromic acid oxidations (for example see ref. 38).

A mechanism involving direct transfer of a hydride ion from the α -carbon would be in agreement with the observed isotope effects, but not with the Hammett studies reported here and elsewhere. The rate constants for such reactions (eq. [2]) should correlate better with σ^+ values (39), contrary to the experimental observations summarized in Table 3. In fact, any reaction in which the α -carbon is carbonyl-like (*sp*² hybridized) in the transition state should correlate better with σ^+ values. The correlation reported herein and those found in the literature are consistently better when σ values are used, the clear implication being that direct hydride transfer is not a likely mechanism.

$$[2] \qquad \operatorname{Ar}_{2}\mathsf{C}\mathsf{H}\mathsf{O}\mathsf{H} + [(\mathsf{T}\mathsf{M}\mathsf{C})\mathsf{R}\mathsf{u}^{\mathsf{V}\mathsf{I}}(\mathsf{O})_{2}]^{++} \longrightarrow \operatorname{Ar}_{2}\overset{+}{\mathsf{C}}\mathsf{O}\mathsf{H} + [(\mathsf{T}\mathsf{M}\mathsf{C}\mathsf{R}\mathsf{u}^{\mathsf{I}\mathsf{V}}(\mathsf{O}\mathsf{H})\mathsf{O}]^{+}$$

A mechanism in which the reaction is initiated by a 2 + 2 addition of a ruthenium oxo to the α -C—H bond, as has been proposed for several other oxidation reactions (40–42), is in agreement with the isotope effects reported in Table 2 and the Hammett studies summarized in Table 3. In this reaction (eq. [3]) the α -carbon remains sp^3 hybridized, eliminating the possibility of a direct resonance contribution from the substituents and therefore a lack of correlation with σ^+ values.

The observation (37) that the oxidation of tetrahydrofuran by dioxoruthenium(VI) complexes exhibits a primary isotope

effect and activation parameters $(k_{\rm H}/k_{\rm D} = 20 \pm 2, \Delta H^{\ddagger} = 59 \pm 4$ kJ mol⁻¹, $\Delta S^{\ddagger} = -117 \pm 13$ J mol⁻¹ K⁻¹) similar to those for the corresponding alcohol reactions (Tables 2 and 4) is also consistent with a possible 2 + 2 (C—H + Ru=O) addition mechanism. The α -hydrogens of ethers and alcohols are electronically similar and would therefore be expected to respond similarly to oxidants that cause C—H bond cleavage in the rate-limiting step.

It is also possible to consider a mechanism for conversion of the organometallic intermediate, **1**, into products. Two possibilities exist: (*i*) homolytic cleavage of the Ru—C bond would give a ruthenium(V) complex and a free radical that could subsequently undergo a hydrogen atom transfer as in eqs. [4] and [5], or (*ii*) heterolytic cleavage of the Ru—C bond to give a ruthenium(IV) complex and a cation that could transfer a proton to give the observed products as in eqs. [6] and [7].

$$[4] \qquad \begin{bmatrix} (TMC)^{OH}_{Ru} VI - CAr_2]^{++} \longrightarrow Ar_2 \dot{C}OH + [(TMC)^{Ru} V(OH)O]^{++} \\ 0 & OH \end{bmatrix}$$

$$[5] \qquad Ar_2 \dot{C}OH + [(TMC)^{Ru} V(OH)O]^{++} \longrightarrow Ar_2CO + [(TMC)^{Ru} V(OH)_2]^{++} \\ [6] \qquad \begin{bmatrix} (TMC)^{OH}_{Ru} VI - CAr_2]^{++} \longrightarrow Ar_2 \dot{C}OH + [(TMC)^{Ru} V(OH)O]^{+} \\ 0 & OH \end{bmatrix}$$

$$[7] \qquad Ar_2 \dot{C}OH \implies A_2CO + H^{+}$$

The reaction sequence in eqs. [4] and [5] involves formation of free-radical intermediates, which are considered to be unlikely because of the previously described observation that oxidation of cyclobutanol does not result in ring opening. It is, Scheme 2.

Single-electron transfer :



Hydrogen atom transfer from O-H:



Hydrogen atom transfer from C-H:



however, possible that the transfer of the hydrogen atom (eq. [5]) could occur more rapidly than ring opening, thereby precluding the formation of acyclic products. In such an event, the hydrogen atom transfer would have to take place rapidly before the free radical could diffuse out of the solvent cage enclosing it and the ruthenium(V) complex; diffusion out of the solvent cage would provide more than sufficient time for ring opening to occur.

A mechanism consisting of reaction [3], followed by either [4] and [5] or [6] and [7], is consistent with the observed rate law, the products from the oxidation of cyclobutanol, the isotope effects, and the Hammett study. It is also consistent with the observed activation parameters (Table 4). A 2 + 2 addition (eq. [3]) would be expected to exhibit a negative entropy of activation in common with most combination reactions that require an organized transition state and result in the loss of one translational degree of freedom. The low enthalpy of activation is also consistent with a 2 + 2 addition of a ruthenium oxo bond to a C—H bond because the energy required for bond cleavage would be partly compensated for by the concurrent formation of new O—H and Ru—C bonds.

There is, however, a theoretical difficulty associated with the 2 + 2 (C—H + Ru=O) mechanism. Frontier molecular orbital theory suggests that oxidation reactions of this type should involve an initial interaction between the reductant's HOMO and the oxidant's LUMO. The oxidant's LUMO in this case would be an Ru=O π^* antibonding orbital (28), while the reductant's HOMO would be an oxygen 2*p*-nonbonding orbital. Since the LUMO would be centered primarily on the metal, it is predicted on the basis of this theory that the initial reaction would involve ligand formation as in eq. [8].



Scheme 3.

Hydride transfer from C-H:







<u>C-H</u> + <u>Ru=O</u> addition followed by a transfer of 2 electrons :



O-H + Ru=O addition followed by a transfer of 2 electrons :



Ligand formation would be followed by proton transfer as in eq. [8] to give 4, which is formally the 2 + 2 (O—H + Ru=O) addition product. The amounts of 3 and 4 present would be controlled by the relative pK_{BH^+} values for the two compounds. However, the lack of an observable O-D isotope effect (Table 2) suggests that 4 may not be part of the reaction sequence leading to product formation. The aforementioned fact that tetrahydrofuran is readily oxidized by dioxoruthenium(VI)

complexes also indicates that a proton transfer would not be an essential part of the reaction if this is the correct mechanism.

The intermediates **3** and **5** for alcohol and ether oxidation, respectively, would decompose to yield oxidized products by a cyclic transfer of hydrogen as depicted in eqs. [9] or [10] and [11]. This mechanism is similar to one recently proposed by Espenson and co-workers (43) for the oxidation of alcohols by $[Cr = O]^{++}$. It is also in general agreement with the theoretical

description of the reaction between methanol and oxidants



containing chromium or ruthenium oxos recently published by Deng and Ziegler (22).

Conclusions

The electron flow in these reactions has been indicated as if it involved hydride transfer; however, for cyclic redox mechanisms it is not possible to specify the direction of electron flow, nor whether it occurs by single- or double-electron shifts. The assumption that the oxygen bears a positive charge in the transition state is consistent with the negative Hammett ρ value and with the observation that electronic substituent effects correlate with σ rather than σ^+ values. Since the positive charge is not located adjacent to the aromatic ring in intermediate **3**, direct resonance interactions are not possible.

In common with the 2 + 2 (C—H + Ru=O) reaction mechanism discussed previously, the mechanism defined by eqs. [8] and [9] would be consistent with the unfavorable entropies of activation and the low enthalpies of activation summarized in Table 4. The cyclic, well-organized transition state would be expected to result in an unfavorable entropy of activation and the simultaneous bond making and breaking would be consistent with a low enthalpy of activation. The significant C-D isotope effect and the lack of an observable O-D isotope effect are also consistent with this mechanism.

Both the 2 + 2 (C—H + Ru=O) addition mechanism (eq. [3]) and the ligand association mechanism (eq. [8]) require the introduction of a new ruthenium ligand into the octahedral complex, $[(TMC)Ru^{VI}(O)_2]^{++}$. In eq. [3] the new ligand is attached through carbon to give an organometallic intermediate, while in eq. [8] the new ligand is attached through oxygen giving a ruthenate ester intermediate. Whether these new ligands would be introduced by associative or dissociative mechanisms (44) cannot be determined conclusively on the basis of the experimental evidence currently available. However, the observation made by Che et al. (9) that complexes with more flexible acyclic tetraaza ligands react faster by several orders of magnitude than the corresponding cyclic tetraaza ligands suggests that a dissociative mechanism with loss of an *N*-donor ligand may be most likely (45).

The experimental and theoretical information available with respect to the oxidation of alcohols by dioxoruthenium(VI) complexes is not compatible with several possible redox mechanisms including a single-electron transfer and direct hydrogen atom or hydride ion transfers from either carbon or oxygen. The available information is consistent with both a 2 + 2 (C—H + Ru=O) mechanism (eqs. [3]–[7]) or attachment of the alcohol as a ligand on Ru, followed by a cyclic transfer of hydrogen from the reductant to the oxidant as in eqs. [8] and [9]. Currently available information does not permit a choice between these two possibilities; however, the latter appears to be more consistent with theoretical considerations.

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