Ruthenium(IV)–Oxo Complexes: A Novel Hydrophobic Effect of Tertiary Phosphine Ligands on the Selective Oxidation of Alcohols

Mary E. Marmion and Kenneth J. Takeuchi *
Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214, U.S.A.

Kinetic and mechanistic studies on the oxidation of a series of alcohols by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ (bipy = 2,2′-bipyridine and ER_3 is a tertiary phosphine or arsine ligand) have been conducted in both aqueous and non-aqueous solutions. Under all conditions, the rate law shows a first-order dependence on both the alcohol and the ruthenium(IV)–oxo species. The rate of alcohol oxidation in aqueous solution is dependent on the hydrophobic nature of the target alcohol, where the second-order rate constant increases in the following order: methanol < ethanol < propan-1-ol < 2-methylpropan-1-ol < butan-1-ol < 3-methylbutan-1-ol < pentan-1-ol. The rate of alcohol oxidation is also strongly dependent on the tertiary phosphine ligand, where the rate of aqueous oxidation of allyl alcohol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ [$k = (1.68 \pm 0.02) \times 10^{-1}$ dm^3 mol^{-1} s^{-1}] is 250 times faster than the rate of oxidation by $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$ [$k = (6.7 \pm 0.3) \times 10^{-4}$ dm^3 mol^{-1} s^{-1}]. A primary isotope effect of $k_H/k_D = 10$, and secondary isotope effects of 1.4 per methyl group and 1.2 for the hydroxy group were observed for the aqueous oxidation of propan-2-ol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$, suggesting a concerted outer-sphere redox mechanism where a hydride ion is transferred from the target alcohol to the oxo ligand of the Ru^{IV}=O moiety. To account for the hydrophobic selectivity of alcohol oxidation by pnictogen–ruthenium(IV)–oxo complexes, a mechanism involving a preassociation of target alcohol and co-ordinated phosphine ligand prior to hydride transfer is proposed.

Owing to the importance of ruthenium–oxo complexes as redox agents,[1–7] we have synthesized novel ruthenium(IV)–oxo complexes containing tertiary phosphine ligands *cis* to the oxo moiety,[8] and have subsequently examined their abilities to act as stoicheiometric oxidants and as catalysts for oxidations.[9] The mechanistic interest in these phosphine–ruthenium(IV)–oxo complexes lies in their ability to act as two-electron, two-proton redox agents, which are selective, due to the electronic, steric, and hydrophobic versatility of the phosphine ligand. In contrast to most metal–oxo systems,[10] there are no internal reorganizational problems with these ruthenium(IV)–oxo complexes, for the same basic structure of the metal complex is maintained in the ruthenium-(IV), -(III), and -(II) oxidation states.[8] Thus, clear kinetic, thermodynamic, and mechanistic information regarding the oxidation of organic substrates by phosphine–ruthenium(IV)–oxo complexes can be obtained, given the straightforward redox and spectroscopic properties of these complexes.

We report here the results of a kinetic and mechanistic investigation of the oxidation of alcohols by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ (bipy = 2,2′-bipyridine and ER_3 = tertiary phosphine or arsine) in which the rate of oxidation was determined to be strongly dependent on the nature of the phosphine ligand and the solvent employed in the experiment. For example, the oxidation of primary alcohols by phosphine–ruthenium(IV)–oxo complexes displays a unique hydrophobic selectivity, based on the dependence of the alcohol oxidation rate constant with respect to alcohol hydrophobicity, phosphine hydrophobicity, and solvent. This observation is important, for although the kinetic and mechanistic aspects of transition-metal-assisted oxidations of alcohols have been extensively investigated,[4,7,10–12,†,22–24] and the influence of solvent effects on the kinetics of many organic,[25], inorganic,[26] and bioinorganic[27] reactions have received recent attention, no relationship between rate of substrate oxidation and substrate hydrophobicity has ever been reported. In addition, this hydrophobic selectivity may have relevance to cytochrome P-450 chemistry,[28] where the affinity of cytochrome P-450 for hydrocarbons increases with increasing lipophilicity, independently of the chemical structure of the hydrocarbon.[29] This behaviour is apparently due to the interactions between the hydrophobic cleft in which the haem resides, and the lipophilic hydrocarbon. In this way, cytochrome P-450 functions as a detoxifying agent, by oxidizing hydrophobic substances into hydrophilic substances.

Experimental

Materials.—The complexes $[Ru^{IV}O(bipy)_2(ER_3)][ClO_4]_2$ [ER_3 = PMe_3, PEt_3, PPr^i_3, $P(cyclo\text{-}C_6H_{11})_3$, PPh_3, or $AsPh_3$] and $[Ru^{IV}(^{18}O)(bipy)_2(PEt_3)][ClO_4]_2$ were synthesized as previously described.[8]

All alcohols and aldehydes were fractionally distilled over a drying agent immediately prior to use. $(CH_3)_2CHOD$ (98 + atom% D) and $(CD_3)_2CDOD$ (99 + atom% D) were purchased from the Aldrich Chemical Co. and used as received. $(CH_3)_2CDOD$ was prepared following the procedure of Leo and Westheimer,[30] by reduction of acetone with lithium aluminium deuteride. The reaction was quenched with D_2O, and the deuterium incorporation was verified by n.m.r. spectroscopy. Spectrograde methylene chloride (h.p.l.c./g.c.–m.s. pure) and acetonitrile (h.p.l.c. pure) were used as obtained from Fisher Scientific. Reagent-grade toluene and pentane were distilled before use. House distilled water was passed through Barnstead HN Combination (D8922) and HN Organic Removal (D8904) purification cartridges. Redistilled nitric acid (Aldrich) and sodium nitrate, as well as other simple salts, acids, and bases, were reagent quality and used without further purification. All buffer solutions were prepared as reported previously.[8]

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† *e.g.* Oxidation by Br_2, permanganate, and Hg^{II},[13] Ru^{VI} and Ru^{VII} oxo complexes,[14] chromium,[15] $[Ag(bipy)_2]^{2+}$,[16] V^V and Mn^{III},[17] Co^{III},[18] Ce,[19] palladium,[20] and Mo^{VI}.[21]

Measurements.—U.v.–visible spectra were obtained on a Bausch and Lomb Spectronic 2000 spectrophotometer. Kinetic studies were determined spectrophotometrically using modified Beckman DU spectrophotometers which were retrofitted with Gilford accessories. The cell blocks in the spectrophotometers were maintained at constant temperature by the circulation of water from thermostatted water-baths. Product analyses were performed on a Hewlett-Packard gas chromatograph (g.c.) equipped with a mass spectrometry (m.s.) detector (model 5890A).

Kinetics Procedure.—The kinetics of the reactions were monitored spectrophotometrically at the wavelength maximum of the metal to ligand charge-transfer (m.l.c.t.) band of the Ru^{II} species which is formed upon reaction. Runs were made under pseudo-first-order conditions where the target substrate was in excess. In a typical experiment, the reaction was initiated by adding 2 cm^3 of the solution containing the oxidant (1×10^{-4} mol dm^{-3}) to 1 cm^3 of six different thermostatted solutions, which contained varying amounts of substrate (0.03—0.30 mol dm^{-3}). Each solution was mixed quickly in the cell with a disposable pipette and the absorbance *versus* time curve was then recorded using the chart drive as a time base.

Plots of $\ln [(A_\infty - A_0)/(A_\infty - A_t)]$ *vs.* time were linear, and the pseudo-first-order rate constants calculated using a least-squares treatment of the rate data according to equation (i), where A_∞ is the final absorbance at the completion of the reaction, A_0 is the initial absorbance, A_t is the absorbance measured at time t, and $k_{obs.}$ is the pseudo-first-order rate constant. The observed rate constants were then plotted *versus* substrate concentration to obtain the second-order rate constants. The accuracy of the measurements for all of the second-order rate constants was within 10% at a 95% confidence limit.

$$-\ln (A_\infty - A_t) = k_{obs.}t - \ln (A_\infty - A_0) \qquad \text{(i)}$$

Product Analysis.—The complex $[Ru^{II}(OH_2)(bipy)_2(ER_3)][ClO_4]_2$ was identified as the final ruthenium-containing product by an analysis of the u.v.–visible spectrum of the final solution. The organic products of the reaction were identified by g.c.–m.s. In a routine experiment, 0.025 mmol of $[Ru^{IV}O(bipy)_2(ER_3)][ClO_4]_2$ was dissolved in 2 cm^3 of solvent containing a 100-fold excess of substrate. The reaction mixture was stirred for 3 h after which time, an equal volume of pentane was added to reactions run in CH_2Cl_2, in order to precipitate the reduced metal complex. The remaining organic solution was analyzed by g.c.–m.s. For reactions run in CH_3CN or H_2O, pentane was added to extract the organic products, or the reaction mixture was injected directly into the g.c.–m.s. instrument. In all cases, toluene was added as an internal standard immediately prior to injection. G.c. calibration curves were prepared by quantitatively examining a series of standard solutions containing toluene and a reactant or product.

Table 1. Second-order rate constants for the oxidation of alcohols and aldehydes by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ in water at 25 °C

ER_3	Substrate	I/mol dm^{-3}	pH	10^4k/dm^3 mol^{-1} s^{-1}
PPh_3	Methanol	0.06	2.0	2.48
PPh_3	Ethanol	0.06	2.0	5.2
PPh_3	Propan-1-ol	0.06	2.0	7.9
PPh_3	2-Methylpropan-1-ol	0.06	2.0	8.8
PPh_3	Butan-1-ol	0.06	2.0	11.0
PPh_3	3-Methylbutan-1-ol	0.06	2.0	12
PPh_3	Pentan-1-ol	0.06	2.0	14.8
PPh_3	Propan-2-ol	0.06	2.0	23
		0.10	2.0	20
		0.25	2.0	20
		0.50	2.0	22
		0.75	2.0	21
		1.0	2.0	18
		1.5	2.0	15.2
		0.06	4.0	25
		0.06	6.8	24
PPh_3	Pentan-3-ol	0.06	2.0	84
PPh_3	Allyl alcohol	0.06	2.0	1 680
		0.06	4.0	1 630
		0.06	6.8	1 600
PEt_3	Allyl alcohol	0.06	2.0	6.7
$P(C_6H_{11})_3$	Allyl alcohol	0.06	2.0	16.9
PPr^i_3	Allyl alcohol	0.06	2.0	14
$AsPh_3$	Allyl alcohol	0.06	2.0	1 720
PPh_3	Benzyl alcohol	0.06	2.0	10 500
PEt_3	Benzyl alcohol	0.06	2.0	920
$AsPh_3$	Benzyl alcohol	0.06	2.0	4.6
PPh_3	Propionaldehyde	0.06	2.0	250
PPh_3	Butyraldehyde	0.06	2.0	220

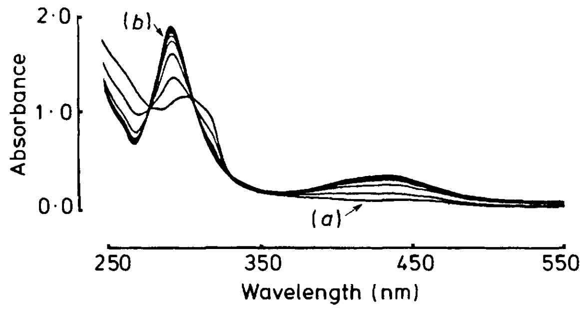

Figure 1. Spectral changes observed in the reaction of benzyl alcohol, 0.03 mol dm^{-3}, with $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ (5.0×10^{-5} mol dm^{-3}) in aqueous solution buffered at pH = 2.05 ($NaNO_3$–HNO_3). Spectra were recorded at 6-min intervals

Results

Kinetics and Spectrophotometry.—The reactions between $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ and alcohols are described in equations (1) and (2), where L_5 = 2 bipy + ER_3. In aqueous solution, these Ru^{IV}–oxo complexes react with aldehydes to yield the corresponding carboxylic acids. For all oxidations performed, the final spectrum, after the reactions were complete, corresponded exactly to that of $[Ru^{II}(OH_2)(bipy)_2(ER_3)]^{2+}$, or in acetonitrile, $[Ru^{II}(CH_3CN)(bipy)_2(ER_3)]^{2+}$, where in all cases there was a quantitative conversion of Ru^{IV} to Ru^{II} based on absorption coefficients. Spectrophotometric changes displayed no intermediate species, such as Ru^{III}, since all the intermediate spectra were isosbestic in nature, corresponding to a mixture of only the Ru^{II}– aqua and Ru^{IV}–oxo species (Figure 1).

$$[L_5Ru^{IV}{=}O]^{2+} + RCH_2OH \longrightarrow [L_5Ru^{II}\text{–}OH_2]^{2+} + RCHO \qquad (1)$$

$$[L_5Ru^{IV}{=}O]^{2+} + R_2CHOH \longrightarrow [L_5Ru^{II}\text{–}OH_2]^{2+} + R_2C{=}O \qquad (2)$$

The kinetics of all the alcohol and aldehyde oxidations were found to be strictly second order, first order both in substrate and oxidant. Values of the second-order rate constants for the oxidations of all substrates in aqueous and non-aqueous solutions are listed in Tables 1 and 2, respectively. Notably, in aqueous solution, the second-order rate constant is not sensitive to changes in pH over the range 2.0—6.8, or to variations in ionic strength from 0.06 to 1.0 mol dm^{-3}.

Table 2. Second-order rate constants for the oxidation of alcohols by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ in CH_3CN and CH_2Cl_2 at 25 °C

ER_3	Substrate	Solvent	$10^4k/dm^3\ mol^{-1}\ s^{-1}$
PPh_3	Methanol	CH_3CN	5.8
PPh_3	Ethanol	CH_3CN	16.3
PPh_3	Propan-1-ol	CH_3CN	30
		CH_2Cl_2	34
PPh_3	Butan-1-ol	CH_3CN	27
PEt_3	Butan-1-ol	CH_3CN	7.1
		CH_2Cl_2	24.3
PPh_3	Pentan-1-ol	CH_3CN	30
PPh_3	Propan-1-ol	CH_3CN	70
		CH_2Cl_2	69
PEt_3	Propan-2-ol	CH_3CN	13.5
		CH_2Cl_2	23
PPh_3	Allyl alcohol	CH_3CN	920
		CH_2Cl_2	2 500
PEt_3	Allyl alcohol	CH_3CN	1 100
		CH_2Cl_2	1 300
$P(C_6H_{11})_3$	Allyl alcohol	CH_2Cl_2	150
PPr^i_3	Allyl alcohol	CH_2Cl_2	227
$AsPh_3$	Allyl alcohol	CH_3CN	2 800
		CH_2Cl_2	2 800
PPh_3	Benzyl alcohol	CH_3CN	8 300
		CH_2Cl_2	5 500
PEt_3	Benzyl alcohol	CH_3CN	2 800
		CH_2Cl_2	2 500
$AsPh_3$	Benzyl alcohol	CH_3CN	6 800
		CH_2Cl_2	5 800

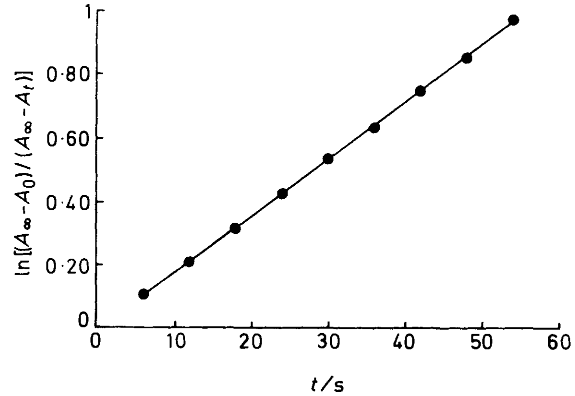

Figure 2. Plot of $\ln[(A_\infty - A_0)/(A_\infty - A_t)]$ *vs.* time for the oxidation of benzyl alcohol (5.93×10^{-3} mol dm^{-3}) by $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$ in CH_2Cl_2 at 25 °C. The linearity of the plot demonstrates that the reaction is first order in $[Ru^{IV}]$

Table 3. Kinetic isotope effects for the oxidation of propan-2-ol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ at 25 °C

Substrate	Solvent	$10^5k/dm^3\ mol^{-1}\ s^{-1}$	k_H/k_D
$(CH_3)_2CHOH$	H_2O[a]	230	—
$(CH_3)_2CHOD$	D_2O[a]	190	1.2
$(CH_3)_2CDOD$	D_2O[a]	19	12
$(CD_3)_2CDOD$	D_2O[a]	6.7	34
$(CD_3)_2CDOD$	CH_3CN	20[b]	36

[a] pH = 2.0, I = 0.06 mol dm^{-3}. [b] The reported value is an average k value, obtained from the equation, $k = k_{obs.}/[(CD_3)_2CDOD]$, for two $k_{obs.}$ values.

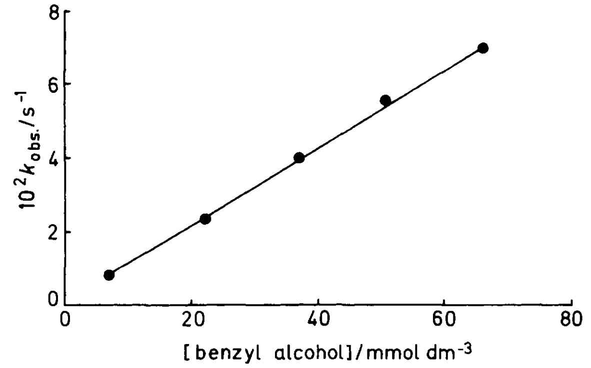

Figure 3. Plot of k_{obs} *vs.* alcohol concentration for the aqueous oxidation of benzyl alcohol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ at 25 °C, pH = 2.0 (nitrate buffer), I = 0.06 mol dm^{-3}. The linearity of the plot demonstrates the first-order dependence on [alcohol]

Based on these spectral observations and kinetic measurements, a rate law can be expressed as equations (3) and (4) where $k_{obs.}$ is the observed pseudo-first-order rate constant, k the second-order rate constant, and [S] the substrate concentration. A typical plot of $\ln[(A_\infty - A_0)/(A_\infty - A_t)]$ *vs.* time is shown in Figure 2 and a representative plot of the dependence of $k_{obs.}$ on substrate concentration is depicted in Figure 3. In most cases, the linear functions obtained from $k_{obs.}$ *vs.* [S] plots had small non-zero intercepts, indicating an instability of the oxidant in the solvent utilized in the experiment. No calculations were based on these intercepts, which were very small; however, the intercepts generally were equal to the slow rate of decomposition of the ruthenium(IV)–oxo complexes, in the absence of substrate, to the analogous ruthenium(II)–aqua complexes, in the solvent employed in the experiment.

$$-d[Ru^{IV}]/dt = +d[Ru^{II}]/dt = k_{obs.}[Ru^{IV}] \qquad (3)$$

$$k_{obs.} = k[S] \qquad (4)$$

Deuterium Labelling Studies.—Kinetic isotope effects were determined for the oxidation of $(CD_3)_2CDOD$, $(CH_3)_2CHOD$, and $(CH_3)_2CDOD$ by $[Ru^{IV}O(bipy)_2(PPh_3)][ClO_4]_2$, where a large primary isotope of k_H/k_D = 10 and secondary isotope effects of 1.4 for each methyl group and 1.2 for the hydroxy group were observed. These results, summarized in Table 3, are consistent with a hydrogen atom or hydride transfer mechanism,[31] where the reaction proceeds through a transfer from the α-carbon of the alcohol to the oxo group of the ruthenium(IV) centre, resulting eventually in the formation of a ruthenium(II)–aqua species and the corresponding aldehyde or ketone.

Substituent Effects.—Complexes of the type $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ appear very sensitive to the nature of substitution of the carbon atom at the site of oxidation. In general, benzylic and allylic alcohols were oxidized more rapidly than secondary alcohols which were oxidized faster than primary alcohols; the oxidation of methanol is almost immeasurably slow. Tertiary alcohols were unreactive under the conditions employed, implying that a hydrogen on the α-carbon of the alcohol is necessary for the reaction to occur.

As seen from Table 1, in aqueous solution, the rate of alcohol oxidation increases as the number of carbon atoms of the alcohol increases. In fact, a plot of the alcohol hydrophobicity, P,*[32–34] *versus* the second-order rate constants of the oxid-

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* P is a measure of substrate hydrophobicity, where an increasing P value is indicative of an increasing hydrophobic nature of the substrate. These values were determined by Hansch, where P describes the partitioning of the substrate between water and octan-1-ol (see refs. 32—34).

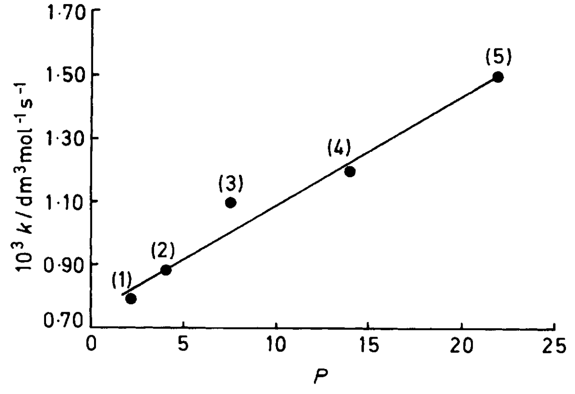

Figure 4. Correlation between the rate constant values, *k*, of primary alcohol oxidation by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ and alcohol hydrophobicity, *P*. Solvent = H_2O, pH = 2.0, I = 0.06 mol dm^3. (1) = Propan-1-ol, (2) = 2-methylpropan-1-ol, (3) = butan-1-ol, (4) = 3-methylbutan-1-ol, and (5) = pentan-1-ol

ation of propan-1-ol, 2-methylpropan-1-ol, butan-1-ol, 3-methylbutan-1-ol, and pentan-1-ol by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ (Figure 4), yields a linear relationship (r^2 = 0.97), where an increase in alcohol hydrophobicity, *P*, results in an increase in the second-order rate constant, *k*. Notably, in non-aqueous solvents, such as acetonitrile, there is little difference in the rate of substrate oxidation by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ for propan-1-ol ($k = 3.0 \times 10^{-3}$ dm^3 mol^{-1} s^{-1}), butan-1-ol ($k = 2.7 \times 10^{-3}$ dm^3 mol^{-1} s^{-1}), or pentan-1-ol ($k = 3.0 \times 10^{-3}$ dm^3 mol^{-1} s^{-1}).

Phosphine Effects.—The hydrophobicity of the phosphine ligand plays a dramatic role in controlling the rate of alcohol oxidation in aqueous solution. When a relatively hydrophilic phosphine ligand was employed, such as PMe_3, the trimethylphosphine–ruthenium(IV)–oxo complex was essentially non-reactive towards all alcohols in aqueous solution. $[\mathrm{Ru^{IV}O(bipy)_2(PEt_3)}]^{2+}$ was also unreactive towards primary and secondary alcohols, but did oxidize allyl alcohol and benzyl alcohol at relatively slow rates. Conversely, $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$, an oxidant containing a hydrophobic phosphine ligand, oxidizes all alcohols in aqueous solution at relatively fast rates. For example, the rate of allyl alcohol oxidation by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ ($k = 1.7 \times 10^{-1}$ dm^3 mol^{-1} s^{-1}) is *ca.* 250 times faster than the rate of allyl alcohol oxidation by $[\mathrm{Ru^{IV}O(bipy)_2(PEt_3)}]^{2+}$ ($k = 6.7 \times 10^{-4}$ dm^3 mol^{-1} s^{-1}), while in non-aqueous solvents, the rates of all alcohol oxidations by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ were only approximately two times faster than the rates of alcohol oxidations by the corresponding triethylphosphine complex. Notably, the rates of benzyl alcohol oxidation by both $[\mathrm{Ru^{IV}O(bipy)_2(AsPh_3)}]^{2+}$ and $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ were identical in non-aqueous solvents; however, in aqueous solution, the rate of benzyl alcohol oxidation doubled when $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ was utilized as the oxidant when compared with $[\mathrm{Ru^{IV}O(bipy)_2(AsPh_3)}]^{2+}$

Table 4. Activation parameters for the oxidation of alcohols by $[\mathrm{Ru^{IV}O(bipy)_2(ER_3)}]^{2+}$

ER_3	Substrate	Medium	$\Delta H^‡$/kcal mol^{-1} [a]	$\Delta S^‡$/cal mol^{-1} K^{-1} [a]
PPh_3	Propan-2-ol	H_2O [b]	11.1 ± 0.09	−33.0 ± 3.0
PPh_3	Propan-2-ol	CH_3CN	9.9 ± 1.0	−35.3 ± 3.4
PPh_3	Allyl alcohol	H_2O [b]	9.5 ± 0.5	−30.0 ± 2.0
PEt_3	Allyl alcohol	H_2O [b]	18.0 ± 0.3	−12.0 ± 8.0
PEt_3	Allyl alcohol	CH_3CN	7.0 ± 1.0	−40.0 ± 4.0
PEt_3	Allyl alcohol	CH_2Cl_2	11.0 ± 5.0	−26.0 ± 2.0

[a] cal = 4.184 J. [b] pH = 2, I = 0.06 mol dm^{-3}.

Table 5. Product studies for representative alcohol and aldehyde oxidations by $[\mathrm{Ru^{IV}O(bipy)_2(ER_3)}]^{2+}$

ER_3	Substrate	Solvent	Product
PPh_3	Propan-1-ol	H_2O*	Propionaldehyde
PPh_3	Propan-1-ol	CH_3CN, CH_2Cl_2	Propionaldehyde
PPh_3	Propionaldehyde	H_2O*	Propionic acid
PPh_3, PEt_3	Propan-2-ol	H_2O*	Acetone
PPh_3, PEt_3	Propan-2-ol	CH_3CN, CH_2Cl_2	Acetone
PPh_3, PEt_3	Benzyl alcohol	H_2O*	Benzaldehyde
PPh_3, PEt_3	Benzyl alcohol	CH_2Cl_2	Benzaldehyde
PPh_3, PEt_3	Allyl alcohol	H_2O*	Acrolein
PPh_3, PEt_3	Allyl alcohol	CH_3CN, CH_2Cl_2	Glycidol
PPh_3, PEt_3	Cyclobutanol	H_2O*	Cyclobutanone
PPh_3, PEt_3	Cyclobutanol	CH_3CN	Cyclobutanone

* pH = 2, I = 0.06 mol dm^{-3}.

Activation Parameters.—Activation parameters*[35] were determined from the slopes and intercepts of plots of ln (k/T) *versus* $1/T$, over the temperature range 5—35 °C, for a number of representative oxidations. The results obtained are given in Table 4. Clearly worth noting is the profound difference between the activation parameters obtained from the aqueous oxidations of allyl alcohol by $[\mathrm{Ru^{IV}O(bipy)_2(PPh_3)}]^{2+}$ and $[\mathrm{Ru^{IV}O(bipy)_2(PEt_3)}]^{2+}$, which is consistent with the dramatic difference in rate between these two reactions. This observation suggests that a change in mechanism may be occurring when PEt_3 is substituted for PPh_3 in these $\mathrm{Ru^{IV}{=}O}$ complexes. Also worth noting is the observation that the $\Delta H^‡$ and $\Delta S^‡$ values for the aqueous oxidation of propan-2-ol are consistent with the activation parameters determined for its oxidation by various oxidants, where there is a α-C–H bond breaking in the transition state.[4b,7b,7f,16,36]

Product Studies.—Product analyses for various representative oxidations are given in Table 5. As previously mentioned, primary and secondary alcohols were oxidized to aldehydes and ketones, respectively, while in aqueous solution, aldehydes were oxidized to their corresponding carboxylic acids. Notably, carboxylic acids were not produced in the oxidation of primary alcohols, unlike more powerful oxidants, such as RuO_4.[1] This observation demonstrates that phosphine–ruthenium(IV)–oxo complexes are mild oxidants, which is advantageous since more powerful oxidants usually cause undesirable side reactions.[1,10]

The reactions between $[\mathrm{Ru^{IV}(^{18}O)(bipy)_2(PEt_3)}]^{2+}$ and various alcohols were carried out as described in the Experimental section. The extent of ^{18}O transfer was determined by g.c.–m.s., where the mass spectra of the products formed upon the reaction were compared with the mass spectra of the products obtained when $[\mathrm{Ru^{IV}(^{16}O)(bipy)_2(PEt_3)}]^{2+}$ was used as the oxidant. The mass spectra proved to be identical for each comparison, where the isotopic ratios for peaks representing oxygen-containing molecules or fragments remained the same. These results show that the oxygen atoms in the aldehyde and ketone products did not originate from the oxo moiety of the ruthenium(IV) complex, within the uncertainty of the experiment, which corroborates a hydrogen atom or hydride transfer mechanism.

Notably, the solvent utilized in the oxidation of allyl alcohol has a profound effect on the product formed, where the cor-

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* Activation parameters can be obtained from the pseudo-thermodynamic relationship:[35] $k_{\mathrm{reaction}} \doteq (k_B T/h)\, e^{-\Delta H^‡/RT} \cdot e^{\Delta S^‡/R}$.

responding aldehyde (acrolein) is produced in an aqueous medium, while the alcohol is oxidized to the corresponding epoxide [glycidol (2,3-epoxypropan-1-ol)] in both CH_2Cl_2 and CH_3CN. This indicates that a different mechanism, such as oxygen-atom transfer from the $Ru^{IV}=O$ to the olefinic group of the alcohol is occurring in non-aqueous solutions. The selective transition-metal-assisted oxidation of allylic alcohols to epoxy alcohols in related organic solvents has been previously reported.[21,37-40]

Discussion

Substrate Effects.—Based on the combination of rate law, kinetic isotope effects, hydrophobic effects, substituent effects, and product studies, the oxidation of alcohols in either aqueous or acetonitrile solution by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ [ER_3 = PEt_3, $P(cyclo\text{-}C_6H_{11})_3$, PPr^i_3, PPh_3, or $AsPh_3$] most likely occurs through a concerted outer-sphere redox mechanism between oxidant and substrate, where a hydrogen atom or hydride ion is transferred from the target alcohol to the oxo ligand of the ruthenium(IV)–oxo moiety. The fact that more hydrophobic alcohols exhibit a faster oxidation rate suggests that prior to alcohol oxidation, the target alcohol hydrophobically associates with the organic substituents of the *cis*-phosphine ligand, thus increasing the concentration of the alcohol in the vicinity of the oxo site, which results in a rate enhancement based on the hydrophobicity of the target alcohol. To reinforce this hypothesis, it should be noted that since the steric and electronic properties of the target alcohol that affect the rate of alcohol oxidation by $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ should be observed to a similar degree in either water or acetonitrile, then any relative differences in the rates of alcohol oxidation in water should be observed to a similar degree in acetonitrile. However, since little difference in rate constant is observed for the oxidation of propan-1-ol, butan-1-ol, and pentan-1-ol in acetonitrile, then it can be suggested that the hydrophobicity of the target alcohol is primarily responsible for the observed alcohol oxidation rate enhancements in aqueous media. The phosphine effects and solvent effects discussed below corroborate this hypothesis.

Phosphine Effects.—As noted previously, the rate of alcohol oxidation in aqueous solution is also very sensitive to the R substituents on the *cis*-phosphine ligand. Since the $Ru^{IV}=O$ moiety and the target alcohol must come into close proximity for oxidation to occur, the steric demands of the *cis*-phosphine ligand may be responsible for the dramatic changes in reactivity. However, phosphine steric effects apparently do not play a major role in determining the rate of alcohol oxidation in aqueous media, because the $Ru^{IV}=O$ complex containing the larger triphenylphosphine ligand (cone angle = 145°)[41] oxidizes allyl alcohol, in aqueous solution, 250 times faster than the $Ru^{IV}=O$ complex containing the less sterically hindered triethylphosphine ligand (cone angle = 132°).

The electronic effects of the phosphine ligand also cannot account for the sizeable rate difference for allyl alcohol oxidation in H_2O between $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ and $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$. The difference in reduction potential, in aqueous media, between these two oxidants is 70 mV, which was calculated from the difference between the average of the Ru^{IV}–Ru^{III} and Ru^{III}–Ru^{II} redox couples measured by cyclic voltammetry.[8] If a strict outer-sphere redox mechanism is assumed, the difference in activation energies between the two reactions is equal to this difference in reduction potentials (70 mV = 6.7 kJ). Thus, at 25 °C, the ratio of the rate constants for the two reactions, which have activation energies that differ by 6.7 kJ, is calculated from equation (5), where A is the Arrhenius factor, which is assumed to be constant, $E_{a2} - E_{a1}$ is the difference in activation energies (6.7 kJ), and the ratio of the second-order rate constants, k_1/k_2, is thus equal to 15.

$$k_1/k_2 = Ae^{-E_{a1}/RT}/Ae^{-E_{a2}/RT} = \exp[(E_{a2} - E_{a1})/RT] \quad (5)$$

Based on these observations, the marked change in reactivity which occurs upon changing substituents on the phosphine ligand cannot be rationalized simply in terms of the steric or electronic effects of the phosphine ligand. Thus, in aqueous media, steric, electronic, and hydrophobic phosphine ligand effects must determine the rate of alcohol oxidation, while in non-aqueous media, only the steric and electronic effects should be observed. Notably, in CH_2Cl_2 and CH_3CN, the electronic and steric effects almost cancel for the triphenylphosphine– and triethylphosphine–ruthenium(IV)–oxo complexes. Therefore, assuming that similar electronic and steric effects occur in both aqueous and non-aqueous media, the primary ligand effect which causes the large difference in rate of alcohol oxidation appears to be a hydrophobic phosphine ligand effect.

The second-order rate constants obtained for the oxidation of allyl alcohol in aqueous media by $[Ru^{IV}O(bipy)_2(PPr^i_3)]^{2+}$ (1.4×10^{-3} dm^3 mol^{-1} s^{-1}) and $[Ru^{IV}O(bipy)_2\{P(C_6H_{11})_3\}]^{2+}$ (1.7×10^{-3} dm^3 mol^{-1} s^{-1}) are also consistent with a mechanism involving a hydrophobic pre-association of the target alcohol with the phosphine ligand followed by oxidation by the $Ru^{IV}=O$ moiety. The complexes $[Ru^{IV}O(bipy)_2(PPr^i_3)]^{2+}$, $[Ru^{IV}O(bipy)_2\{P(C_6H_{11})_3\}]^{2+}$, and $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$ have identical reduction potentials in aqueous solution,[8] yet both $P(C_6H_{11})_3$ (cone angle = 172°) and PPr^i_3 (cone angle = 160°) are substantially bulkier than PEt_3, thus creating greater steric hindrance to the $Ru^{IV}=O$ active site. Therefore, the rate enhancement for allyl alcohol oxidation by $[Ru^{IV}O(bipy)_2\{P(C_6H_{11})_3\}]^{2+}$ and $[Ru^{IV}O(bipy)_2(PPr^i_3)]^{2+}$ relative to $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$ must be due to the increased hydrophobicity of the $P(C_6H_{11})_3$ and PPr^i_3 ligands. Notably, the second-order rate constants are very similar for allyl alcohol oxidation, in aqueous media, by $[Ru^{IV}O(bipy)_2(PPr^i_3)]^{2+}$ and $[Ru^{IV}O(bipy)_2\{P(C_6H_{11})_3\}]^{2+}$, which suggests that the hydrophobic nature of both phosphines, in the local vicinity of the $Ru^{IV}=O$ active site, must closely resemble each other. Finally, the steric effects of phosphine ligands can be observed, if the hydrophobic effects are removed through the use of a non-aqueous solvent. For example, the rates of allyl alcohol oxidation, in CH_2Cl_2, by $[Ru^{IV}O(bipy)_2\{P(C_6H_{11})_3\}]^{2+}$ (1.1×10^{-2} dm^3 mol^{-1} s^{-1}) and $[Ru^{IV}O(bipy)_2(PPr^i_3)]^{2+}$ (2.3×10^{-2} dm^3 mol^{-1} s^{-1}) are substantially slower than oxidation by $[Ru^{IV}O(bipy)_2(PEt_3)]^{2+}$ (1.3×10^{-1} dm^3 mol^{-1} s^{-1}), $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ (2.7×10^{-1} dm^3 mol^{-1} s^{-1}), and $[Ru^{IV}O(bipy)_2(AsPh_3)]^{2+}$ (2.8×10^{-1} dm^3 mol^{-1} s^{-1}). This implies that if the R substituents on the phosphine ligand are large enough, they may interfere with the approach of the target alcohol to the $Ru^{IV}=O$ moiety, thus causing steric effects to have a noticeable influence on the rate of reaction.

Solvent Effects.—The oxidation of alcohols by phosphine–ruthenium(IV)–oxo complexes displays a hydrophobic solvation effect, based on the dependence of the alcohol oxidation rate with respect to three considerations: alcohol hydrophobicity, phosphine hydrophobicity, and solvent. The term 'hydrophobic solvation' describes the phenomenon of the substrate leaving the bulk aqueous phase and associating with the R substituents of the phosphine ligand, thereby minimizing the surface area of both the substrate and the organic substituents of the phosphine ligand. The relief of ordered water around the substrate which occurs when the hydrophobic alcohol moves out of the bulk water implies that 'hydrophobic solvation' is entropically driven as suggested by Tanford.[33] This hypothesis is supported by the fact that bulk water, a hydrophobic substrate, and a hydrophobic ligand must all be present for this to occur. It is worth noting that large negative entropies of activation are obtained for these reactions, which may be partly due to the preassociation and selective orientational demands of the oxidant and target alcohol, prior to oxidation.

Notably, these reported phosphine, substrate, and solvent effects are consistent with a recent investigation of the substrate specificity of enzymes,[28] where substrate preference and oxidation rate were found to be entirely different in organic solvents as compared to aqueous solution, due to the hydrophobic interactions which occur only in water.

Further Mechanistic Considerations.—As mentioned earlier, given the large kinetic primary isotope effect, there are two reasonable mechanisms for the rate-determining redox step which follows the preassociation of reactants. One is hydride transfer, which is a synchronous transfer of a proton and two electrons from the alcohol, followed by a fast proton transfer (Scheme 1). The proton that is transferred subsequent to the hydride transfer most probably originates from the target alcohol, since $[Ru^{IV}O(bipy)_2(ER_3)]^{2+}$ is reduced to $[Ru^{II}(OH_2)(bipy)_2(ER_3)]^{2+}$ in the oxidation of alcohols in dry methylene chloride solution.

$$[Ru^{IV}O(bipy)_2(ER_3)]^{2+} + R_2CHOH \xrightarrow{k} [Ru^{II}(OH)(bipy)_2(ER_3)]^{+} + R_2\overset{+}{C}OH$$

$$[Ru^{II}(OH)(bipy)_2(ER_3)]^{+} + R_2\overset{+}{C}OH \xrightarrow{\text{fast}} [Ru^{II}(OH_2)(bipy)_2(ER_3)]^{2+} + R_2C{=}O$$

Scheme 1.

The second plausible mechanism is a hydrogen atom transfer in the initial step, followed by a rapid outer-sphere electron transfer and a proton transfer (Scheme 2). It should be noted that the secondary isotope effects of $k_H/k_D = 1.2$ and 1.4, which are observed in aqueous media for the hydroxy group and each methyl group, respectively, are indicative of a linear hydride or hydrogen atom transfer, where the secondary carbon atom, hydride or hydrogen atom, and the oxo ligand are linear during the rate determining step.[31]

$$[Ru^{IV}O(bipy)_2(ER_3)]^{2+} + R_2CHOH \xrightarrow{k} [Ru^{III}(OH)(bipy)_2(ER_3)]^{2+} + R_2\dot{C}OH$$

$$[Ru^{III}(OH)(bipy)_2(ER_3)]^{2+} + R_2\dot{C}OH \xrightarrow{\text{fast}} [Ru^{II}(OH_2)(bipy)_2(ER_3)]^{2+} + R_2C{=}O$$

Scheme 2.

We are not able unequivocally to distinguish which mechanism is operative in our substrate oxidations, given the present data; however, a hydrogen atom transfer appears less likely, on the basis of the experimental evidence. First, the isosbestic nature of the spectral changes observed during oxidation indicates that the loss of Ru^{IV} is exactly equal to the formation of Ru^{II}. Although the existence of Ru^{III} intermediates cannot be ruled out completely, for it is possible that they do not build up to appreciable concentrations or they are too short-lived to be evidenced spectrophotometrically, there are no indications of free radical interventions. For example, the oxidation of cyclobutanol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ yields cyclobutanone, which is characteristic of two-electron oxidants.[4b] With one-electron transfer agents, such as Cr^{IV}, Ce^{IV}, Mn^{III}, and V^{V}, C–C bond cleavage occurs, and non-cyclic products are obtained.[15c,17b] In addition, the large substituent effects of the alcohols on the rate of oxidation may suggest a concerted two-electron oxidation, since one-electron oxidants are known to be relatively insensitive to the structure of the target alcohol.[17–19]

There is the possibility that the reaction of propan-2-ol and $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ occurs through the initial formation of an alcohol–oxidant complex intermediate, analogous to Cr^{VI} oxidations, where the oxidation of sterically hindered secondary alcohols proceeds through chromate ester formation.[10,15b] However, such a mechanism does not seem reasonable when one considers the absence of observable intermediates, the slow rate of oxo exchange of the complex with H_2O, and the lack of proton dependence on the rate of reaction.

Notably, the oxidation of propan-2-ol by $[Ru^{IV}O(bipy)_2(PPh_3)]^{2+}$ appears to be similar in several respects to alcohol oxidation by RuO_4,[4a] $Na[RuO_4]$,[4b] OsO_4,[19] Br_2, MnO_4^-, and Hg^{2+},[13] carbonium ions,[36] $[Ru^{IV}O(terpy)(bipy)]^{2+}$ (terpy = 2,2′:6′,2″-terpyridyl),[7b] and $[Ru^{IV}O(bipy)_2(py)]^{2+}$ (py = pyridine),[7f] which all suggest that oxidation occurs through a two-electron, hydride transfer. Some of the common features are: (1) all reactions were first-order in oxidant and alcohol concentrations; (2) all oxidations displayed a large primary isotope effect when the hydrogen on the α-carbon was replaced by deuterium; (3) when investigated, the oxidation of cyclobutanol gave cyclobutanone as the primary product; (4) for the oxidation of propan-2-ol by metal–oxo complexes, similar activation parameters were obtained, where entropy was characteristically highly unfavoured; (5) the second-order rate constants for the oxidation of propan-2-ol, in aqueous media, by $[Ru^{IV}O(bipy)_2(py)]^{2+}$ and $[Ru^{IV}O(terpy)(bipy)]^{2+}$, are also independent of pH and ionic strength over the ranges investigated.

Conclusions

The results obtained here show that one of the real advantages of incorporating phosphine ligands into ruthenium(IV)–oxo complexes lies in the hydrophobic nature of the tertiary phosphine ligands. In the oxidation of alcohols, where phosphine–ruthenium(IV)–oxo complexes act as electron/proton oxidants, we have proposed that the hydrophobic phosphine ligand prevents water solvation of the oxo ligand. Thus, in aqueous solution, the substrate must leave the aqueous phase and enter the desolvated region immediately around the $Ru^{IV}{=}O$ moiety in order to react with the ruthenium centre. This apparent ability to induce kinetic and mechanistic changes by simply varying the organic substituents of the phosphine ligand is noteworthy, for it suggests that one may ultimately generate high selectivity of substrate oxidation based on solvent and hydrophobicity of substrate and phosphine ligand. In addition, this proposed hydrophobic mechanism may be applicable to cytochrome P-450 chemistry, where it can be envisioned that the function of the hydrophobic cleft in which the haem resides is similar to the function of the phosphine ligand in these ruthenium(IV)–oxo complexes.

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