REVIEW COMMENTARY

RUTHENIUM TETRAOXIDE MEDIATED REACTIONS: THE MECHANISMS OF OXIDATIONS OF HYDROCARBONS AND ETHERS

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The reaction mechanisms for the RuO_4-mediated oxidations of saturated hydrocarbons and of ethers were investigated. For both groups of compounds the kinetic influence of the reaction medium and of substituents near the reaction centre was determined together with deuterium isotope effects. The results do not support reaction mechanisms with carbocation intermediates. Reactions by radical pair intermediates are only possible if these collapse at rates faster than $10^8 s^{-1}$. For the oxidation of hydrocarbons the data fit a two step mechanism, a pre-equilibrium followed by a rate-determining concerted reaction. The results from the oxidation of ethers can be explained by a concerted, S_E2-like type of reaction.

INTRODUCTION

Ruthenium tetraoxide is a powerful oxidant which reacts with a number of organic compounds. Carbon–carbon double bonds are cleaved producing ketones and carboxylic acids, alcohols are oxidized to ketones or carboxylic acids and ethers give esters, including lactones. Aromatic rings are usually cleaved to produce carboxylic acids. The use of RuO_4 in organic chemistry has been reviewed by several authors.[1] It is normally applied in catalytic amounts and a number of stoichiometric oxidants can be used, sodium periodate being the most common. For lipophilic compounds a two phase system consisting of CCl_4–CH_3CN–H_2O (2:2:3) (Sharpless[2] conditions) is often applied. Oxidations of hydrophilic compounds are carried out in aqueous solutions.

In spite of the synthetic importance of RuO_4-mediated oxidations, only a limited number of studies on the reaction mechanisms have been reported. We described the RuO_4-mediated derivatization of saturated hydrocarbons a few years ago[3] and later reported studies on the mechanism of this reaction.[4–6] In connection with this work, we have also studied the oxidation of ethers to esters.[7] This Review Commentary gives a summary of these studies.

DERIVATIZATION OF SATURATED HYDROCARBONS BY RuO₄

Ruthenium tetraoxide oxidizes a number of saturated hydrocarbons to the corresponding tertiary alcohols or ketones. The reaction is regioselective and, from a limited number of examples, appears to be stereospecific. The by-products from the reactions yielding alcohols are in most cases ketones from reactions on secondary C—H bonds. Typical results are given in Table 1.

From Table 1, it is evident that the RuO_4 oxidation of saturated hydrocarbons represents an important synthetic reaction. The results show that tertiary C—H bonds are more reactive than secondary bonds (entries 1, 2 and 4–6) except for substrates with the tertiary C—H bond situated at a bridgehead (Entry 3). There also appear to be some steric requirements of the reaction (compare the results of entries 4 and 5). The reaction takes place with retention of configuration (entries 4 and 6). No skeletal rearrangements take place in the oxidation of bridged polycyclic hydrocarbons (entry 8), except for cis- and trans-pinane (entries 9 and 10).

The results presented in Table 1 may be explained by several reaction mechanisms (Scheme 1): (a) hydrogen atom abstraction to give a radical pair intermediate; (b) hydride ion abstraction to give a carbocation intermediate; or (c) a concerted reaction mechanism. It should be emphasized that the structure of the transition state in route c serves as an illustration only.

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Table 1. RuO$_4$-mediated oxidations of saturated hydrocarbons

Entry	Substrate	Product	Yield (%)	Ref.
1			81[a]	3
2			85[a]	3
3			60[a]	3
4			90[b]	5
5			50[b]	5
6			100[b]	5
7			50[a]	8
8			69[a]	9
9			48[a]	10
10			26 and 29[a]	10

[a] Isolated yields.
[b] Initial yields (GC).
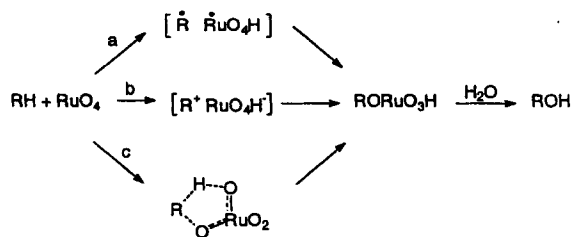
Scheme 1

For routes a and b, the stereochemical results could be explained by rapid reactions of the radicals or ions in a solvent cage. It should also be noted that nucleophiles were not incorporated into the products when the oxidations were carried out in acetone–water with e.g. acetate ions present,[6] although 5% of 2-chloro-*endo*-tetrahydrodicyclopentadiene was formed in the oxidation of *endo*-tetrahydrodicyclopentadiene in CCl_4–CH_3CN–H_2O in the presence of chloride ions and a phase transfer catalyst. In reactions carried out in CCl_4–CH_3CN without chloride ions present, no chlorinated products were observed.[4]

We have investigated the mechanism by several techniques and will first report the results of these investigations and then attempt to present a reaction mechanism.

Kinetic investigations

The oxidation of saturated hydrocarbons by RuO_4 showed second-order kinetics in both CCl_4–CH_3CN–H_2O and

acetone–water:[5,6]

$$-d[\text{substrate}]/dt = k_2[\text{substrate}][RuO_4]$$

The activation parameters for a representative selection of substrates are given in Table 2. The activation parameters were very similar for the investigated substrates and also for the two-solvent systems, as would have been expected if the same mechanism were operating in both systems.

From the kinetic data, it was also possible to calculate the reactivity of different types of tertiary and secondary C—H bonds in cyclohexane systems:[5] axial secondary C—H, relative rate 1; equatorial secondary C—H, 9; axial tertiary C—H, 47; and equatorial tertiary CH, 444. This comparison of the rates supports the impression from Table 1 of a steric requirement for the oxidation reaction.

Solvent effects

On oxidation of adamantane in a series of organic solvents with polarity varying from that of CCl_4–CH_3CN to nitrobenzene, the rate increased by only a factor of three. Furthermore, the oxidation of adamantane in acetone–water was only 40 times faster than that in CCl_4–CH_3CN.[6] *cis*-Decalin was oxidized in a series of acetone–water mixtures and in two acetonitrile–water mixtures. The rates were correlated with the Grunwald–Winstein Y values ($m = 0.31$) and with the Reichardt's $E_T(30)$ values (gradient = 0.17) for the oxidations in acetone–water. Both correlations indicated only a small degree of charge separation in the transition state (TS).[6,11]

Table 2. Activation parameters for RuO_4 oxidation of saturated hydrocarbons in CCl_4–CH_3CN–H_2O $(2:1:2)^a$ and in acetone–water $(3:1)^b$

Substrate	Solvent system	Log A	ΔH^* (kcal mol^{-1})	ΔS^* (cal K^{-1} mol^{-1})
	CCl_4–CH_3CN–H_2O	8·3	14·8	−24·6
	Acetone–water	8·9	14·0	−20
	CCl_4–CH_3CN–H_2O	8·4	16·6	−24·2
	CCl_4–CH_3CN–H_2O	9·3	16·2	−24·3
	CCl_4–CH_3CN–H_2O	7·9	14·7	−26·2
	Acetone–water	7·5	12·3	−26

[a] $[\text{Substrate}]_0 = 40$ mM, $T_{\text{average}} = 30.2\,°C$.
[b] $[\text{Substrate}]_0 = 25$ mM, $T_{\text{average}} = 32.4\,°C$.

Substituent effects

The effect of substituents on the rate of reaction was investigated by the oxidation of a series of 1-substituted adamantanes with RuO_4 in the two solvent systems CCl_4-CH_3CN and acetone-water (3 : 1). The rates of reaction were correlated with the Taft constants σ^* to give the reaction constants ρ^*. From the reactions of 1-substituted adamantanes, we obtained $\rho^* = -2\cdot1$ and $-2\cdot5$ for the reactions in acetone-water[6] and CCl_4-CH_3CN,[11] respectively. These results are comparable to the values obtained for the solvolysis of 3-substituted 1-adamantyl bromides ($\rho^* = -2\cdot7$)[12] and for 3-substituted 1-adamantyl tosylates ($\rho^* = -3\cdot1$).[13] On the other hand, typical S_N2 reactions, e.g. the solvolysis of primary tosylates, gave $\rho^* = -0\cdot74$.[14] The results from the RuO_4 oxidation of 1-substituted adamantanes therefore indicate a considerable development of positive charge in the TS.

Deuterium isotope effect

From the rates of reaction of cis-decalin and perdeuterio-cis-decalin in CCl_4-CH_3CN, a KIE of 4.8 was obtained. Variable-temperature measurements indicated that quantum-mechanical tunnelling was not a significant contributor to this figure.[5] However, in perdeuterio-cis-decalin, there would be five deuterium atoms β to the reacting C-9 atom. If the RuO_4 oxidation proceeded by a hydride abstraction and the formation of a carbocation (route b, Scheme 1), the observed KIE would consist of both a primary and a considerable β-secondary KIE. The conformation of the 9-decalyl cation has been discussed.[15] From this, the empty p orbital would be almost parallel to three C—D bonds. This is the most favourable configuration for a β-secondary KIE and values of $1\cdot1$–$1\cdot2$ per deuterium atom would have been expected.[16]

To obtain the primary KIE, we oxidized adamantane and 1,3,5,7-tetradeuterioadamantane. For this system no secondary KIE is possible.[17] The observed KIEs for the cis-decalin and adamantane systems are given in Table 3 for both CCl_4-CH_3CN and acetone-water media.[5,11]

From this, the observed KIEs are very similar for both the cis-decalin and the adamantane systems. We therefore conclude that the observed KIEs are mainly primary KIEs with negligible secondary KIEs. We observed a considerable solvent effect on the KIEs, with larger values in acetone-water (Table 3). No solvent KIE was observed on the oxidation of adamantane in acetone-D_2O.[11]

Reaction mechanism

The available evidence may be summarized as follows:

1. The reaction is kinetically second order.
2. The reaction shows a large primary deuterium KIE and no or a negligible secondary KIE. The primary KIEs were larger in acetone-water than in CCl_4-CH_3CN.
3. The activation parameters and substituent effects are very similar in polar and non-polar media.
4. The reaction is subject to steric effects and takes place with retention of configuration. No foreign nucleophiles are incorporated into the products on reaction in acetone-water.
5. The polarity of the reaction medium has only a moderate influence on the rate of reaction.
6. A large negative substituent effect ρ^* is observed in both polar and non-polar reaction media.
7. No skeletal rearrangement takes place in the oxidation of bridged polycyclic hydrocarbons,[9] except for cis- and trans-pinane.[10]
8. No chlorinated products are formed from oxidations in CCl_4-CH_3CN.[4] Alkylcyclopropanes are oxidized to the corresponding alkyl cyclopropyl ketones.[8]

Point 8 shows that a hydrogen atom abstraction mechanism (Route a, Scheme 1) is possible only if a radical pair collapses in a solvent cage at a rate faster than 10^8 s^{-1}.[18] This path is not excluded from the present evidence.

Several points indicate that a reaction by hydride abstraction to give a carbocation intermediate (route b) is less plausible: if a carbocation were formed, it would have to be in an ion pair that collapsed before inversion could take place. The collapse would also have to be more rapid than reaction of the carbocation with a foreign nucleophile (point 4). However, even a reaction by an ion pair seems less likely from the small effect of solvent polarity (point 5) and the lack of a significant secondary KIE (point 2).

Table 3. Kinetic deuterium isotope effect (KIE) for the RuO_4-mediated oxidation of alkanes

Substrates	Solvent	KIE
AdH_4/AdD_4	CCl_4-CH_3CN-H_2O (2 : 1 : 2)	4·8(2)
cis-Decalin/cis-decalin-d_{18}	CCl_4-CH_3CN-H_2O (2 : 1 : 2)	4·8
AdH_4/AdD_4	Acetone-water (3 : 1)	7·8(1)
cis-Decalin/cis-decalin-d_{18}	Acetone-water (3 : 1)	6·8(4)

The lack of rearranged products from the oxidations of bridged polycyclic hydrocarbons (point 7) points in the same direction. The results from the pinane oxidations[10] deserve a special comment. Although rearranged products were observed, the results have been explained without the need for carbocation intermediates.[10] In that paper there was also the first report of an attack by RuO_4 on a methyl group. Although these and our own results seem to exclude carbocation intermediates, these may be important in the oxidations of other substrates better able to stabilize the carbocation formed.

The substituent effect, ρ^*, (point 6) was almost as large as those for S_N1 solvolysis reactions. In a one-step concerted reaction one would not expect such a large effect and we therefore also consider route c in Scheme 1 to be less likely. The sum of evidence therefore appears to exclude all three mechanisms in Scheme 1.

A fourth possibility would be two competing reactions, one by a carbocation intermediate, the other a concerted one (routes b and c in Scheme 1), the importance of each route depending on the reaction conditions.[5] However, we would have expected a larger secondary KIE and a larger substituent effect for the oxidations in the more polar medium. This was not observed and we therefore consider this explanation less likely.[11]

Consequently, the results are difficult to accommodate with any of the previously proposed mechanisms. We have therefore suggested the two step reaction path presented in Scheme 2. In this model, a complex is formed in a pre-equilibrium from the hydrocarbon and RuO_4. This complex then reacts in a concerted reaction to give the ruthenium ester, which is hydrolysed to the products under the reaction conditions.[6,11]

Owing to the electrophilic nature of RuO_4, one would expect a polar transition state. However, our own data do not give information on its structure. Waegel and co-workers[9,10] have discussed several possible structures for the transition state of concerted mechanisms with both four- and five-membered rings from a lateral approach of RuO_4. Another possibility would be an oxygen insertion reaction. This has been discussed for other oxygenation reactions of unactivated C—H bonds. However, no evidence has been found for this mode of reaction with oxometal systems.[19] The oxidation of saturated hydrocarbons with dioxiranes has been proposed to proceed by an oxygen insertion reaction,[20] but even this has been questioned lately.[21]

The evidence cited above can be explained by the two step reaction in Scheme 2: a reaction by this mechanism would show a large primary and no significant secondary KIE. A polar TS would be more symmetrical in the
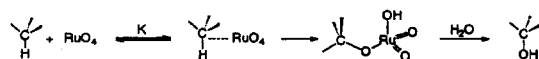
polar acetone–water medium than in CCl_4–CH_3CN, resulting in a larger KIE in the more polar medium. The pre-equilibrium would be dependent on the electron density in the complex-forming CH bond, explaining the large substituent effect and the relative reactivity of the different C–H bonds. The polarity of the reaction medium would not be important as there would be no large charge separation in the TS (point 5). This model would also explain the steric requirements, the retention of configuration observed (point 4) and the lack of rearrangement (point 7). Hydrocarbon–transition metal complexes have been discussed.[22]

OXIDATION OF ETHERS BY RuO_4

The RuO_4 oxidation of ethers gives esters, including lactones, in fair to good yields for methyl ethers, benzyl ethers and symmetric ethers. The preference for oxidation is $CH_2 > CH \gg CH_3$.[23] Schuda et al.[24] carried out a systematic study of the products and their stability from RuO_4 oxidation of benzyl ethers.

Lee and van den Engh[25] reported the kinetics and KIE of the oxidation of tetrahydrofuran (THF) in aqueous perchloric acid by a stoichiometric concentration of RuO_4. They found the reaction to be first order in THF and RuO_4, inversely dependent on h and dependent on the water concentration to the sixth power. From the rates of reaction of THF and perdeuterio-THF, a KIE of 1·4 was found and interpreted as a small primary KIE. Propan-2-ol and THF were oxidized at comparable rates and with almost identical activation parameters. From these data, they proposed a reaction with a hydride abstraction as the rate-determining step.[25]

Balavoine et al.[26] reported the catalytic oxidation of ethers with $RuCl_3$–OCl^- under phase-transfer conditions in CH_2Cl_2–H_2O. Together with the expected products, chlorinated compounds were obtained. Because of this, a one-electron transfer mechanism was proposed.

We wished to compare the results from the RuO_4 oxidation of saturated hydrocarbons with those from oxidation of ethers. For the oxidation of ethers, carbocations appeared as more likely intermediates, as indicated by Lee and van den Engh's results.[25] We applied the same strategy for the investigation of the ether oxidation as for the investigation of the oxidation of the saturated hydrocarbons. We chose benzyl methyl ether and substituted benzyl methyl ethers as the model substrates for the study. With these compounds, both substituent and steric effects could be investigated.

Kinetic investigations and reaction products

Benzyl methyl ether was oxidized by RuO_4 to methyl benzoate and benzoic acid in a 20 : 1 ratio. Benzoic acid was not formed by hydrolysis of the ester. The kinetics

Scheme 2

of the reaction were first order in substrate and RuO_4, as was observed for the oxidation of the hydrocarbons:

$$-d[\text{substrate}]/[dt] = k_2[\text{substrate}][RuO_4]$$

The reactions were performed in both CCl_4–CH_3CN and in nearly neutral (pH $\approx$ 4) aqueous media. RuO_4 was applied at ca 5 mol%.[7]

For the oxidation of benzyl methyl ether in acetone–water, a low activation enthalpy [$\Delta H^* = -8\cdot7$ kcal mol^{-1} (1 kcal $= 4\cdot184$ kJ)] and a large negative activation entropy ($\Delta S^* = -45$ cal mol^{-1} K^{-1}) were observed. The latter indicates a highly ordered TS. The activation entropy was considerably more negative than that obtained by Lee and van den Engh (-18 cal mol^{-1} K^{-1}).[25] This difference and others (see below) clearly show the dependence of the reaction on the applied conditions.

On oxidation of 4-methoxybenzyl methyl ether with RuO_4–$NaIO_4$ in CCl_4–CH_3CN, no chlorinated products were observed,[7] in contrast to the results reported by Balavoine et al.[26] from the oxidation of the same compound by $RuCl_3$–OCl^-.

Solvent effects

A change of reaction medium from the non-polar CCl_4–CH_3CN to the polar acetone–water increased the rate of oxidation of benzyl methyl ether by only a factor of five. The same lack of dependence of the polarity of the medium was observed on the oxidation of benzyl methyl ether in different acetone–water mixtures to give a Grunwald–Winstein m value of $0\cdot11$ and a Reichardt $E_T(30)$ value of $0\cdot08$.[7] Both of these values indicate only a low-polarity TS. A reaction by a carbocation intermediate would be expected to be considerably more sensitive to the polarity of the medium than that observed.

Substituent effects

The rates of the RuO_4 oxidations of 4-substituted benzyl methyl ethers and of 4-substituted α-methylbenzyl methyl ethers were correlated with the Hammet σ or σ^+ values to give the reaction constants in Table 4. The reaction

constants obtained were small and not very dependent on the solvent system.

The acid-catalysed hydrolysis of acetals is believed to proceed by a rate-determining formation of a carbocation/oxonium ion intermediate analogous to that expected from a RuO_4 hydride abstraction reaction. A reaction constant $\rho = -3\cdot3$ was obtained for the hydrolysis of substituted benzaldehyde acetals,[27] considerably more negative than the values in Table 4.

In acetone–water, α-methylbenzyl methyl ether reacted at one seventh of the rate of benzyl methyl ether.[7] This is in accordance with the results reported by Gosh et al.[28] and by Gore[1c]. However, for a reaction via a carbocation intermediate, the presence of the α-methyl group in α-methylbenzyl methyl ether would have been expected to increase, not to decrease, the rate of oxidation.

Solvent isotope effects

Benzyl methyl ether was oxidized with RuO_4 in perdeuterioacetone–D_2O. At 50% conversion, no deuterium was incorporated in either the substrate or products. From the rates of reaction in acetone–D_2O and acetone–H_2O, a solvent deuterium isotope effect, $k(H_2O)/k(D_2O) = 0\cdot86$, was observed.[29] As no incorporation of deuterium in the substrate or products was observed, this was probably the result of different solvent–solute interactions in the two solvents. Swain and Bader[30] concluded that a reaction of neutral reactants to give a charged intermediate, e.g. a carbocation, will show a normal solvent isotope effect. The observed inverse isotope effect was therefore not in accordance with a reaction via a carbocation intermediate.

Kinetic deuterium isotope effects

The kinetic deuterium isotope effects were calculated from the rates of reaction of benzyl methyl ether and its α-mono- and dideuteriated analogues (1, 2 and 3, Scheme 3). In Table 5 the relative rates of reaction of the three compounds are given.[7] From these observed rates, the KIEs were calculated (see discussion in the next section).

Table 4. Hammett ρ and ρ^+ constants from the RuO_4-mediated oxidation of 4-substituted benzyl methyl ethers at 30 °C in CCl_4–CH_3CN–H_2O (2:1:2) and in acetone–water (3:1)

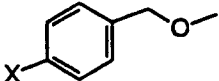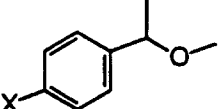| Substrate	Solvent system	ρ	ρ^+
	CCl_4–CH_3CN–H_2O	$-1\cdot3(1)$	$-0\cdot93(4)$
	Acetone–water	$-1\cdot7(3)$	$-1\cdot1(2)$
	Acetone–water	$-1.1(1)$	$-1\cdot0(2)$

Table 5. Relative rates of RuO_4-mediated oxidations of benzyl methyl ether and its mono- and dideuteriated isomers (1, 2, 3) in CCl_4–CH_3CN–H_2O (2 : 1 : 2)[a] and in acetone–water (3 : 1)[b]

Substrate	CCl_4–CH_3CN–H_2O	Acetone–water
$ArCH_2OCH_3$	8·4	40·0
$ArCHDOCH_3$	4·1	18·2
$ArCD_2OCH_3$	1	4·9

[a] $[Substrate]_0 = 40$ mM, $[RuO_4] = 2·6$ mM.
[b] $[Substrate]_0 = 25$ mM, $[RuO_4] = 1·44$ mM.

We also reacted THF and perdeuterio-THF with RuO_4 in acetone–water. For this system, a KIE of 7·0 was observed,[7] much larger than that reported by Lee and van den Engh[25] (1·4). This again stresses the importance of the reaction conditions for the reaction pathway.

Reaction mechanism

We believed that the RuO_4 oxidation of ethers was more likely to proceed via a carbocation intermediate than the corresponding oxidation of saturated hydrocarbons. However, as in that case, no unambiguous evidence was obtained:[7]

1. The reaction is kinetically second order.
2. The reaction shows one large and one smaller deuterium isotope effect.
3. The reaction shows a small enthalpy of activation and a large negative entropy of activation.
4. The rate of reaction is only moderately sensitive to substituents on the benzene ring.
5. The rate of reaction is only marginally sensitive to the polarity of the medium.
6. Chlorine is not abstracted from CCl_4 during the reaction. Oxidation of cyclopropylmethyl methyl ether gave no rearranged products.

A hydrid abstraction reaction was proposed by Lee and van den Engh.[25] For the oxidation of the benzyl ethers 1–3 we would have the route shown in Scheme 3. From this, we obtain

$$k_{obs}(1) = 2k_H^H$$

$$k_{obs}(2) = k_H^D + k_D^H$$

$$k_{obs}(3) = 2k_D^D$$
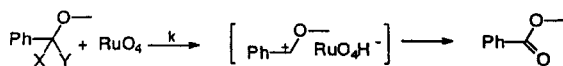
X = Y = H: 1
X = H, Y = D: 2
X = Y = D: 3

Scheme 3

where the subscript denotes the atom left on the benzylic carbon and the superscript that removed. If it is assumed that identical primary and secondary KIEs are acting in the reactions of both monodeuteriated (2) and dideuteriated (3) methyl benzyl ether, we obtain

$$k_{obs}(1)/k_{obs}(3) = KIE_{prim}KIE_{sec}$$

$$2[k_{obs}(2)/k_{obs}(1)] = 1/KIE_{prim} + 1/KIE_{sec}$$

where KIE_{prim} is the primary and KIE_{sec} the secondary kinetic isotope effect. These equations then give $KIE_{prim} = 6·1(4)$ and $KIE_{sec} = 1·3(1)$ for reaction in acetone–water and $KIE_{prim} = 6·9(6)$ and 1·2(2) for reaction in CCl_4–CH_3CN. These figures represent a primary KIE and a rather large secondary KIE. The large KIE_{sec} indicates a close to sp^2-hybridized intermediate. However, the effects of solvent and substituents on the reaction rates were much smaller than expected for a hydride abstraction reaction to give a carbocation intermediate. Although the smaller KIE could be interpreted as an α-secondary KIE, the other data are not in agreement with a carbocation reaction (points 4 and 5).

The results in point 6 are analogous to those from the oxidation of saturated hydrocarbons: a reaction by hydrogen atom abstraction and formation of a radical pair cannot be excluded. However, the radical pair would have to collapse at a rate faster than 10^8 s^{-1}.[18] With this short lifetime, the radical pair would have a partial covalent bond and the benzylic carbon would not be close to sp^2 hybridized. We would therefore not expect a large secondary KIE for such a reaction. From the observed isotope effect of 1·3, we find this path less likely. Balavoine et al.[26] proposed a one-electron transfer mechanism for the ether oxidation based on the presence of chlorinated products. However, these may have been caused by the use of hypochlorite as stoichiometric oxidant. They would therefore be artefacts without significance for the reaction mechanism.[7]

Two more mechanisms will be discussed, a one-step concerted reaction and a two-step reaction involving a pre-equilibrium followed by a concerted rate-determining step (routes d and e, Scheme 4).[7]

For Route d, the attack of RuO_4 would have to be at the front of the reacting carbon atom with a TS similar to those of some aliphatic electrophilic substitution reactions (S_E2). In one S_E2 reaction, the acidic decomposition of (di-n-octyl)mercury, an α-secondary KIE, of 1·1 per deuterium atom was observed,[31] smaller than that observed by us. However, the other points would fit well with route d.

The results may in principle be explained by a two-step reaction, a pre-equilibrium followed by a rate-determining concerted step (route e, Scheme 4). From
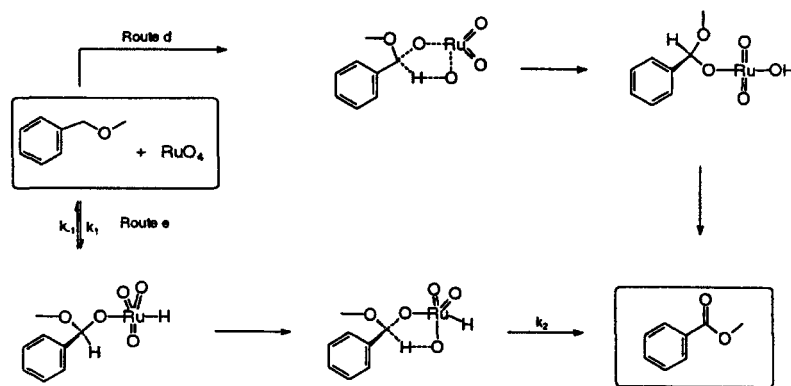
Scheme 4

route in Scheme 4, we obtain

$$k_{obs}(1) = 2(k_1^H k_2^H)/(k_{-1}^H + k_2^H)$$

$$k_{obs}(2) = k_1^H k_2^D/(k_{-1}^H + k_2^D) + k_1^D k_2^H/(k_{-1}^D + k_2^H)$$

$$k_{obs}(3) = 2(k_1^D k_2^D)/(k_{-1}^D + k_2^D)$$

If $k_2^H \ll k_{-1}^H$, $k_2^H \ll k_{-1}^D$, $k_2^D \ll k_{-1}^H$ and $k_2^D \ll k_{-1}^D$, then

$$k_{obs}(1) = 2K^H k_2^H$$

$$k_{obs}(2) = K^H k_2^D + K^D k_2^H$$

$$k_{obs}(3) = 2K^D k_2^D$$

where the superscripts denote the atom removed and the subscripts the rate constants in Scheme 4. From these equations, two deuterium isotope effects are obtained, 6·1 and 1·3 for the oxidations in acetone–water. The smallest would presumably apply to the pre-equilibrium and the largest to the concerted step.[7] After the publication of this work, a pK_a of Cp*$_2$RuH$^+$ of 4·3 has been reported.[32] A high-valence poly-oxygenated species such as the intermediate from the pre-equilibrium in route e (Scheme 4) would probably be considerably more acidic than this. The reversible step in route e is therefore not likely.

CONCLUSION

The results of the investigation of the reaction mechanism of the RuO$_4$ mediated oxidations of saturated hydrocarbons can be explained by a two-step reaction mechanisms, a pre-equilibrium followed by a rate-determining concerted step (Scheme 2). For the oxidation of ethers, a concerted reaction mechanism with an S_E2-like transition state fits the experimental results (Scheme 4, route d). Reactions by radical or carbocation intermediates are less likely for both types of reaction.

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