

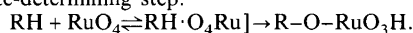
# The Mechanism of RuO<sub>4</sub>-Mediated Oxidations of Saturated Hydrocarbons. Solvent Effects and Substituent Effects\*

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Adamantane and *cis*-decalin have been oxidised by RuO<sub>4</sub> in organic solvents of different polarity. No large variations in the rate of reaction were observed. *cis*-Decalin was oxidised in a series of acetone–water mixtures. From these experiments, a Grunwald–Winstein *m*-value of 0.31 was obtained, indicating a non-polar transition state (TS) for the reaction. A series of 1-substituted adamantanes were oxidised with RuO<sub>4</sub>. A correlation of the rates of reaction with the Taft  $\sigma^*$  gave  $\rho^*$  of  $-1.68$  ( $-2.08$  excluding hydrogen as a substituent), indicating a polar TS. This contradicting evidence could be explained by two mechanisms: either by a hydride-abstraction reaction with the formation of an intimate ion pair or by a reaction with a pre-equilibrium formed from the hydrocarbon and RuO<sub>4</sub> followed by a concerted rate-determining step:



We have recently reported an investigation on the mechanism of the RuO<sub>4</sub>-mediated oxidation of saturated hydrocarbons. The reactivity of several hydrocarbons and the activation parameters for their oxidation were determined together with the kinetic deuterium isotope effect (KIE) for the reaction.<sup>1</sup> From the evidence presented, two mechanisms appeared possible, one via a cyclic transition state (TS) with a partial positive charge on the carbon atom (route a, Scheme 1) and one via a hydride-abstraction reaction and the formation of an ion pair (route b). The mechanism via a cyclic TS was first proposed by Waegell and coworkers.<sup>2</sup> They oxidised a series of bridged polycyclic hydrocarbons and observed no skeletal rearrangements which would have been expected for a cationic intermediate. We proposed the hydride-abstraction mechanism and the formation of an ion pair since the reactivity of the C–H bond decreased in the sequence tertiary > secondary >> primary and also because of the production of chloroalkanes during RuO<sub>4</sub> oxidation in the presence of chloride ions.<sup>3</sup> The magnitude of the KIE ( $k_{\text{H}}/k_{\text{D}} = 4.8$  for *cis*-decalin/*cis*-decalin-*d*<sub>10</sub>)<sup>1</sup> also appeared to be better explained by the linear TS leading to the ion pair than by a non-linear cyclic TS.<sup>1,3</sup> Reaction paths via hydrogen-atom abstraction or one-electron transfer have been excluded.<sup>3</sup>

In an attempt to differentiate between these two mechanisms we have now investigated the influence of the solvent on the rate of reaction and have also oxidised a

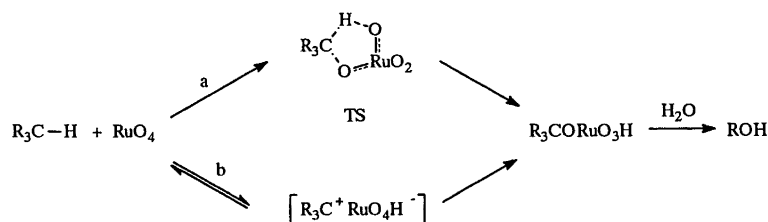
number of 1-substituted adamantanes. Both these series of experiments were expected to give information on the polarity of the TS. It might thereby be possible to differentiate between a carbocation-forming reaction and a concerted reaction with only a partial positive charge on the reacting carbon atom. The RuO<sub>4</sub> oxidations of hydrocarbons are first order in both substrate and RuO<sub>4</sub>.<sup>1</sup> However, the oxidations were performed under pseudo-first-order conditions with a constant concentration of RuO<sub>4</sub> owing to its rapid regeneration.<sup>3</sup>

## Results

**Solvent effects.** Oxidations of lipophilic organic compounds by RuO<sub>4</sub> are usually performed in a two-phase solvent system. The oxidation takes place in an organic solvent phase and the reduced ruthenium species is re-oxidised in the water phase by stoichiometric oxidants, e.g., periodates. Chlorinated solvents such as carbon tetrachloride and chloroform are commonly used.<sup>4</sup> An improvement of this procedure was introduced by Sharpless which consists of adding acetonitrile to the solvent system.<sup>5</sup>

In an introductory experiment we oxidised *cis*-decalin and adamantane in a series of organic solvents immiscible with water (Table 1). Owing to its insolubility, adamantane could not be reacted in all of the solvent systems. From Table 1 it is apparent that the rates of the reactions were not very dependent on the polarity of the solvent. Owing to the presence of acetonitrile the exact

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Scheme 1.

Table 1. Rate of reaction of *cis*-decalin and adamantane in different solvent systems, S–MeCN–H<sub>2</sub>O (2:1:2) at 30 °C [RH]<sup>0</sup> = 40 mM. [RuO<sub>4</sub>]<sup>0</sup> = 4.60 mM.

Solvent, S	$(k_{\text{obs}}/[\text{RuO}_4])/10^{-4} \text{ M}^{-1} \text{ s}^{-1}$	
	<i>cis</i> -Decalin	Adamantane
CCl <sub>4</sub>	9	14
CFCI <sub>3</sub> <sup>a</sup>	3	5
PhCN	37	—
CHCl <sub>3</sub>	19	38
CH <sub>2</sub> Cl <sub>2</sub>	22	44
PhNO <sub>2</sub>	26	—

<sup>a</sup> At 20 °C.

polarities of the different solvent systems were not known. However, nitrobenzene and benzonitrile ( $\epsilon = 35.74$ ,<sup>6</sup> 25.20<sup>7</sup>) are considerably more polar than, e.g., carbon tetrachloride and fluorotrichloromethane ( $\epsilon = 2.24$ , 2.28).<sup>6</sup> With a significant charge separation in the TS we would therefore have expected an increase in the rate of reaction by changing the solvent from carbon tetrachloride to nitrobenzene. This was not observed (Table 1).

To obtain quantitative data on the influence of the solvent, we oxidised *cis*-decalin in a series of water–acetone mixtures (Table 2). Adamantane was not soluble over the whole range of solvent mixtures.

The *m*-value from the Grunwald–Winstein equation [eqn. (1)] gives information on the degree of solvent assistance in nucleophilic substitution reactions and thereby indicates the degree to which the substrate undergoes unassisted ionization.<sup>8</sup> The equation originally used the solvolysis of *tert*-butyl chloride in 80% EtOH as the reference reaction. Later, the solvolysis of 1- and 2-adamantyl chlorides and sulfonates were used as reference reactions; the corresponding *Y*-values are referred to as *Y<sub>x</sub>*. The *Y<sub>x</sub>*-values for many solvent systems have been determined

Table 2. Rate of reaction of *cis*-decalin in acetone–water at 30 °C, [RH]<sup>0</sup> = 13 mM, [RuO<sub>4</sub>]<sup>0</sup> = 2.88 mM.

Vol% H <sub>2</sub> O	<i>Y</i> <sub>Tos</sub> <sup>a</sup>	$(K_{\text{obs}}/[\text{RuO}_4])/10^{-4} \text{ M}^{-1} \text{ s}^{-1}$
25 <sup>a</sup>	−0.50	149(7)
30	0.07	211(1)
40	0.66	338(25)
44	0.91	396(3)

<sup>a</sup> [RH]<sup>0</sup> = 25 mM.

and we have used the *Y<sub>x</sub>* values from the solvolysis reaction of 1-adamantyl tosylate in acetone–water, *Y*<sub>OTos</sub>) (The use of 1- or 2-adamantyl tosylates gives nearly the same *Y*<sub>OTos</sub> values).<sup>9</sup>

$$\log k_s/k_{\text{acetone-water}} = mY \quad (1)$$

From the data in Table 2, an *m*-value of 0.31 ( $r^2 = 0.997$ ) was obtained.

The use of the acetone–water mixture also allowed us to repeat the experiments with an added nucleophile present in the reaction medium which we reported with CCl<sub>4</sub>–water as medium.<sup>3</sup> In acetone–water it was possible to obtain a higher nucleophile concentration than in CCl<sub>4</sub>–CH<sub>3</sub>CN–water. We chose acetate ion as the foreign nucleophile. A higher yield of acetates than of chlorides from the reaction in CCl<sub>4</sub> was thus expected. However, no such products were observed and the reported results<sup>3</sup> may have been an artifact.

**Substituent effects.** To obtain information on the influence of substituents on the rate of reaction we oxidised a series of 1-substituted adamantanes in acetone–water 3:1 (Table 3). The primary products from the reaction were, in all cases, 3-substituted 1-adamantanols. In some cases these were oxidised further towards the end of the reaction, but the disappearance of the starting material always showed pseudo-first-order rate coefficients. The only directly formed by-products were 2-substituted adamantanones, always less than 1% by mass of the substituted adamantanols.

We have correlated the rate constants with  $\sigma^*$  values.<sup>10</sup> In cases where the  $\sigma^*$  values were not available we used the relationship  $\sigma_{I(x)} = 0.450 \sigma^*_{\text{XCH}_2}$ .<sup>11</sup> This correlation

Table 3. Rate of reaction of 1-substituted adamantanes with RuO<sub>4</sub> in acetone–water 3:1 at 30 °C, [RH]<sup>0</sup> = 25 mM, [RuO<sub>4</sub>]<sup>0</sup> = 2.88 mM.

Substituent	$\sigma^*$	$(K_{\text{obs}}/[\text{RuO}_4])/10^{-4} \text{ M}^{-1} \text{ s}^{-1}$	<i>r</i> <sup>2</sup>
H	0.49	265.3	0.996
OH	0.56	66.3	0.998
NHAc	0.58	58.0	0.998
Ac	0.62	51.0	0.996
Br	0.98	9.06	0.994
Cl	1.02	6.91	0.996
CN	1.24	2.50	0.776

gave  $\rho^* = -1.68$  ( $r^2 = 0.952$ ) or  $\rho^* = -2.08$  ( $r^2 = 0.9997$ ) if the value for  $R = H$  was omitted as suggested by Schleyer.<sup>12</sup>

## Discussion

From the present investigation we have conflicting pieces of evidence.

1. The polarity of the solvent had only a small effect on the rate of reaction.
2. Substituents present in the hydrocarbon exercise a considerable influence on the rate of reaction.
3. No incorporation of nucleophiles present in the acetone-water medium was observed.

In addition to this, the following observations have been made earlier.<sup>1</sup>

4. The reaction is kinetically second order with a rather low activation enthalpy and a large negative activation entropy.
5. The reaction shows a primary KIE.
6. The reactivity of C-H bonds decrease in the series *tert.* > *sec.* >> *primary*.
7. The oxidation takes place with retention of configuration.

To this can be added:<sup>2</sup>

8. No skeletal rearrangements took place during the oxidation of bridged polycyclic hydrocarbons.

*The solvent effect (Point 1).* The Grunwald-Winstein  $m$ -value of 0.31 obtained may be compared with those from other reactions. The solvolysis of 1-adamantyl tosylate in acetone-water, a reaction that proceeds without solvent assistance and by the formation of a carbocation has — by definition — an  $m$ -value of 1. On the other hand, typical  $S_N2$  reactions such as the solvolysis of ethyl or methyl tosylates give  $m_{EW}$  of 0.26 and 0.23, respectively.<sup>13</sup> Low Grunwald-Winstein  $m$ -values have been reported for reactions with carbocation intermediates, e.g., 0.42–0.53 for the solvolysis of vinyl chlorides and 0.34 for vinyl bromides.<sup>14</sup> However, these low values were explained by the high temperature of the reaction (120°C). With adjustment for this they came close to the normal value for reactions with carbocation intermediates (0.7–1).<sup>14</sup> Even solvolysis reactions via intimate ion pairs show normal  $m$ -values: 0.93 for pinacolyl brosylate and 1.23 for 1-adamantyl tosylate (from  $Y$  values based on 2-adamantyl tosylate).<sup>13</sup> The observed  $m$ -value for the oxidation reaction (0.31) therefore indicated only a small charge separation in the TS.

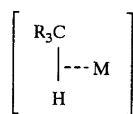
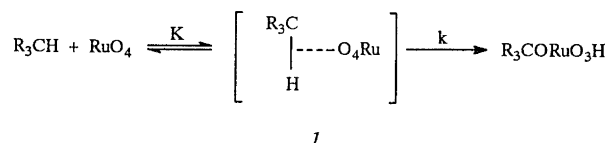
However, the Grunwald-Winstein equation was developed for substitution reactions. The correlations have been shown to depend, among other things, on the leaving group and in our case there was no such traditional group. The observed  $m$ -value may not therefore be unambiguously interpreted although the observed value together with the results from the reactions in organic solvents (Table 1) suggest a non-polar TS for the oxidation.

*The substituent effect (Point 2).* The  $\rho^*$ -values ( $-1.68$  including hydrogen as a substituent,  $-2.08$  excluding it<sup>12</sup>) obtained from the reactions in acetone-water (Table 3) are comparable to the values obtained for the solvolysis of 3-substituted 1-adamantyl bromides ( $\rho^* = -2.70$ , values for H omitted)<sup>12</sup> and the solvolysis of 3-substituted 1-adamantyl tosylates ( $\rho^* = -3.07$  after correlating the rates with  $\rho^*$ ).<sup>15</sup> On the other hand, typical  $S_N2$  reactions like the solvolysis of primary alkyl tosylates gave  $\rho^* = -0.742$  and the reaction of thiophenolates with primary alkyl bromides gave a  $\rho^*$  of  $-0.606$ .<sup>10</sup> The results from the oxidation of 1-substituted adamantanes therefore indicated a considerable charge separation in the TS of the reaction.

There is thus conflicting evidence from these two sets of experiments and also from those reported earlier (Points 4–8). The concerted mechanism<sup>2</sup> with a cyclic TS appears to be in conflict with the large negative  $\rho^*$  observed for the oxidation of substituted adamantanes. A cyclic TS without a charge separation also fails to explain the reaction order in Point 6.

The hydride abstraction mechanism<sup>1</sup> with a carbocation intermediate is in accordance with the results from the substituent effect investigation but appears to be in conflict with the results from the solvent effect investigation. The observations in points 3, 7 and 8 above exclude free carbocations but not cations as part of ion pairs in the reaction. The stereochemical results (Point 7) would demand an intimate ion-pair that collapses at a higher rate than inversion. The experiment with added acetate ion (Point 3) and the lack of rearrangements of strained molecules (Point 8) also require an ion pair to collapse at a high rate.

The presented evidence may be explained by two models. If we assume that the Grunwald-Winstein equation cannot be applied to the present reaction as this is not a solvolysis reaction, the experimental data will fit mechanism b in Scheme 1: an intimate ion pair is produced by a hydride abstraction. This then collapses at a higher rate than other reactions of the carbocation (reactions with external nucleophiles, rearrangements or inversion of configuration, see above). However, this would require the



Scheme 2.

solvent polarity not to be important for the rate of formation of the ion pair.

In the second model, the hydrocarbon and RuO<sub>4</sub> are in a rapid established equilibrium with a complex and this complex then reacts in a rate-determining concerted step (Scheme 2).

The rate of formation of the ruthenate ester would then be:

$$d[\text{R-O-RuO}_3\text{H}]/dt = k[\text{RH}\cdot\text{O}_4\text{Ru}]$$

and the equilibration constant:

$$K = [\text{RH}\cdot\text{O}_4\text{Ru}]/[\text{RH}][\text{RuO}_4]$$

From these two equations one obtains:

$$d[\text{R-O-RuO}_3]/dt = kK[\text{RH}][\text{RuO}_4]$$

or:

$$-d[\text{RH}]/dt = kK[\text{RH}][\text{RuO}_4]$$

The reactions were run under pseudo-first-order conditions with constant [RuO<sub>4</sub>].<sup>1</sup> We therefore have:

$$k_{\text{obs}} = kK[\text{RuO}_4] \text{ and } kK = k_{\text{obs}}/[\text{RuO}_4].$$

The complex [RH·O<sub>4</sub>Ru] would be analogous to the hydrocarbon-metal complexes which have been postulated for hydrocarbon oxidations by transition metal and formulated as **2** (Scheme 2).<sup>16-18</sup> The formulation of the hydrocarbon-RuO<sub>4</sub> complex would then be as shown in **1** (Scheme 2) with an interaction between the carbon-hydrogen bond and the strongly electrophilic oxygen atoms of RuO<sub>4</sub>. The strength of such a complex would be dependent on the electron density of the carbon-hydrogen bond and thereby on the substituents on the carbon atoms in the vicinity of this bond (Table 3). This dependence would also explain the tertiary/secondary/primary reactivity relationship of the oxidised C-H bond (Point 6 above). The acetone-water composition would not have a large influence on the equilibrium constant: there would be no charge separation during its formation and in every case the concentrations of water and acetone were very large compared with that of the hydrocarbon. There would therefore be no significant change in the competition by the solvents for complex formation by a change in the solvent composition.

With a concerted rate determining step (Scheme 2), the rate constant *k* would not be very dependent on the polarity of the reaction medium (Point 1). The other points above are also in accord with this model. With a cyclic TS, there would be no inversion of configuration, no incorporation of added nucleophiles and no skeletal rearrangements of strained molecules.

**Conclusion.** During the oxidation of saturated hydrocarbons by RuO<sub>4</sub> only a small solvent effect was observed but a large effect of the substituents on the hydrocarbon. These results and those reported earlier<sup>1-3</sup> can be explained either by a hydride-abstraction reaction and formation of an intimate ion pair which collapses rapidly to give the ruthenate ester (route b in Scheme 1) or by a model in which the hydrocarbon and RuO<sub>4</sub> are in a pre-equilibrium with a hydrocarbon-RuO<sub>4</sub> complex. This complex then reacts by a cyclic concerted mechanism to produce the ruthenate ester. This is subsequently hydrolysed to the product alcohol (Scheme 2).

## Experimental

The methods used for the kinetic investigations and the analyses have been reported.<sup>1</sup> All the reactions were run in the presence of excess sodium periodate (stoichiometric oxidant). The reoxidation of RuO<sub>2</sub> to RuO<sub>4</sub> has been shown to be rapid on the timescale of this reaction and the concentration of RuO<sub>4</sub> was therefore assumed to be constant.<sup>1,3</sup> In accordance with this, all the oxidations showed pseudo-first-order kinetics. The products of the reactions were identified by comparison with authentic substances or by standard spectroscopic and chromatographic methods. The experiment with acetate ions present was performed in acetone-water 3:1 with a sodium acetate concentration of 40 mM and [*cis*-decalin]<sup>0</sup> = 40 mM. The other conditions as in Table 2.

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