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DIRECT OXYGEN ATOM TRANSFER REACTIONS FROM MOLECULAR OXYGEN CATALYSED BY $[Ru(H_2O)_4Cl_2]$ AND Ru(III)-EDTA IONS*

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Oxidation of organic substrates by oxygen atom transfer from coordinated dioxygen is mediated by $[RuCl_2(H_2O)_4]^+$ ion and Ru(III)–EDTA complex which act as versatile catalysts in a variety of reactions. These reactions proceed by the insertion of the oxygen atoms of the coordinated dioxygen in the substrate/substrates with the formation of the oxidized product. The regenerated catalyst recombines with dioxgen to continue the catalytic cycle.

In some cases β-hydride abstraction from the substrate gives an oxidized product and a reduced metal ion species which is reoxidized by molecular oxygen in a fast step. The choice of β-hydride abstraction versus insertion depends on the *p*H and the nature of the substrate.

Key Words : Oxygen Transfer Reactions; Catalysis by Ruthenium Complexes

INTRODUCTION

THE selective oxidation of organic compounds has gained much importance in chemical industry in recent years.[1] These reactions in contrast to the free radical processes give high selectivity and specificity to the required product.[2] An important class of such reactions is the oxygen atom transfer reaction with metal dioxygen,[3–7] metal-peroxo[8–14] and metal-oxo[15–22] complexes as intermediates which offer non-radical pathways[2] for the selective oxidation of organic compounds.

The present paper deals with the insertion reactions of oxygen atom/atoms in an organic substrate mediated by $[Ru(H_2O)_4Cl]^+$ and Ru(III)-EDTA complexes. These reactions are models for oxygenases.

SINGLE OXYGEN ATOM TRANSFER REACTIONS

These reactions as exemplified by monooxygenases have a low valent metal ion such as Cu(I) in tysosinose or Fe(II) in cytochrome P-450 oxidase which forms a dioxygen complex 2 with molecular oxygen. This complex may be considered to be in equilibrium with a superoxo species 3 (Scheme I). An electron transfer to 3 reduces the superoxo to the peroxo complex 4. The monooxygenases avoid H_2O_2 by a very rapid concerted[23] oxygen atom transfer to the substrate (path A) or by a heterolytic cleavage of the O-O bond in 4 to form the oxo species 5 and

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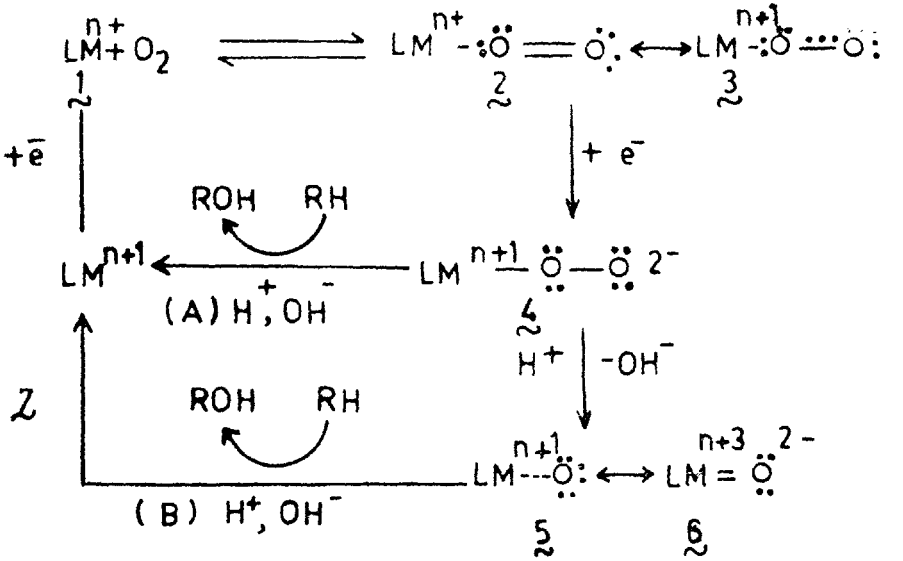
6 followed by a very rapid oxygen atom insertion in the substrate.[24,25] In both cases, one oxygen atom is transferred to the substrate followed by the other atom to OH^-. The oxidized substrate *R*OH leaves complex 7 which is reduced to the original low valent complex 1 by reduction with a second electron.



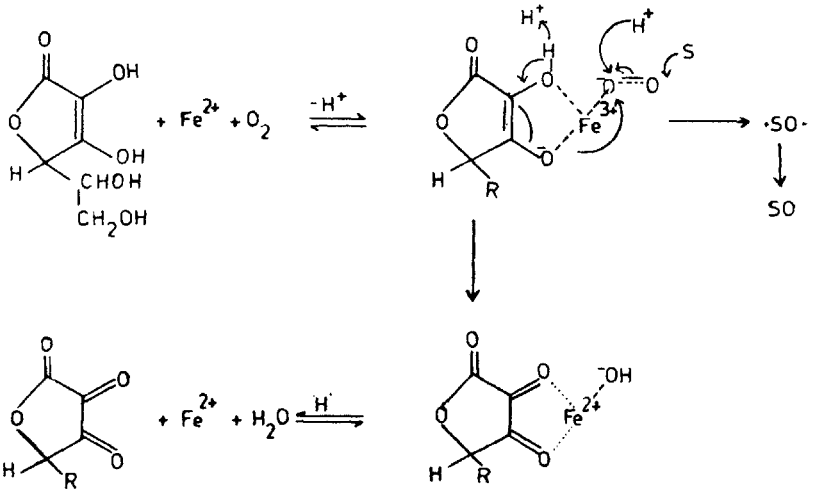
Scheme I

Model Monooxygenase Systems

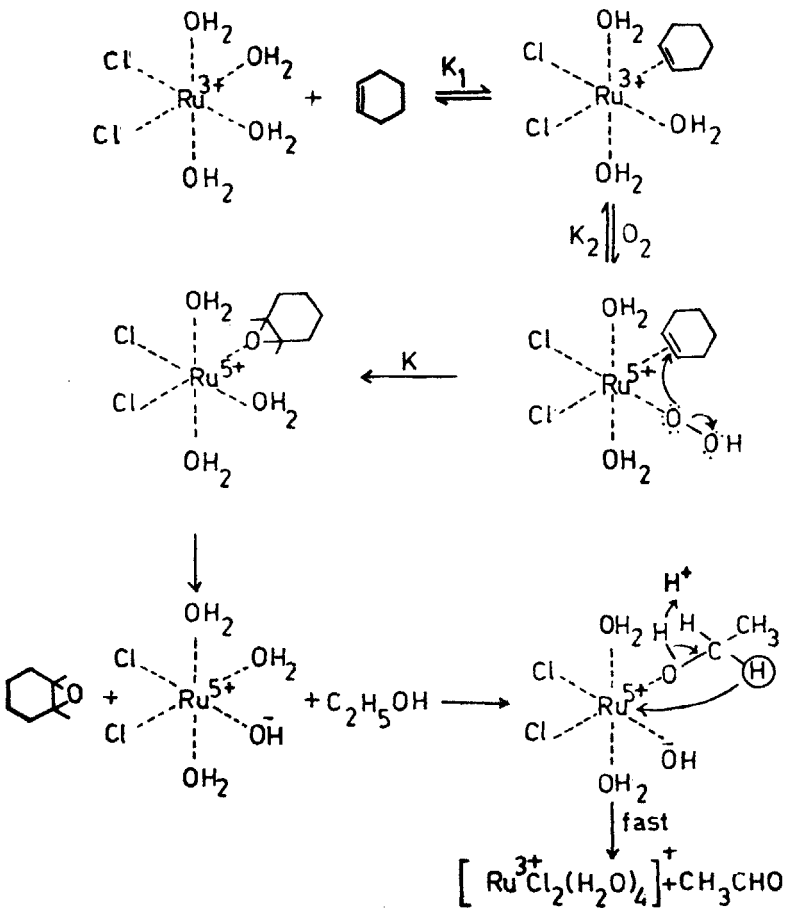
One of the earliest examples of the oxygen atom insertion reaction in organic substrates is the Udenfriends system,[26,27] which employs Fe(II)-EDTA, ascorbic acid and molecular oxygen. A variety of aromatic organic substrates like phenols, salicylic acid and amisole were used in the reaction. A reaction mechanism (Scheme II) was suggested[26] which involves a metal-ascorbate dioxygen complex 1 as an intermediate. The cleavage of the O-O bond under the influence of the metal ion results in the insertion of an oxygen atom into a C-H bond of a saturated substrate or epoxidation of an olefin. Though the intermediate metal-dioxygen complex is a suggestion,[1] no reasonable reaction mechanism can however be proposed without involving a dioxygen complex as an intermediate.

Epoxidation of Cyclohexene

We have carried out a modification[26] of Udenfriend's System in the epoxidation of cyclohexene by molecular oxygen catalyzed by $[RuCl_2(H_2O)]^+$ at *p*H 2. The rate of the reaction in first order with respect to cyclohexene, the catalyst and molecular oxygen concentrations. The reaction is stoichiometric in the absence of a reducing agent but becomes catalytic in the presence of ethyl alcohol which is



Scheme II



Scheme III

oxidized to acetaldehyde. Thus ethanol serves the same purpose as ascorbic acid in providing two redox equivalents to the reaction. The following mechanism is proposed[28] for the reaction (Scheme III).

Rate Law

$$\frac{[Ru\,Cl_2(H_2O)_4]^+_1[O_2]}{-d\,[O_2]/dt} = \frac{1}{kK_1K_2\,[S]} + \frac{1}{kK_2} + \frac{[O_2]}{k}$$

$k = 1.1 \times 10^{-3}$ min^{-1}

$K_1 = 4.0 \times 10^1$ M^{-1}

$K_2 = 2.7 \times 10^4$ M^{-2}

Hydroxylation of Cyclohexane

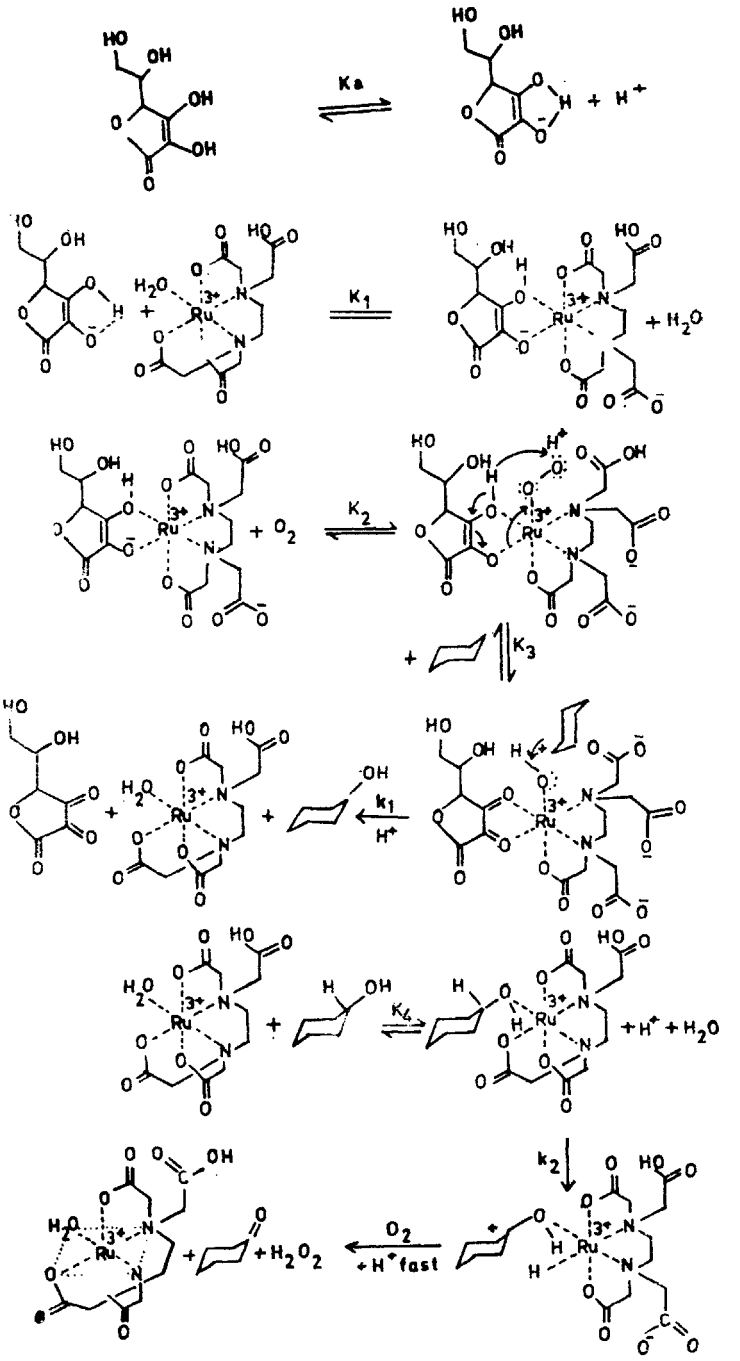
A ruthenium(III) analogue of Udenfriend's system; Ru(III)-EDTA, ascorbic acid, O_2 is a very efficient catalyst[29] for the hydroxylation of cyclohexane a cyclohexanol and its further oxidation to cyclohexanone. In the *p*H range 1.5–2.0 at 30° and mixed dixane-water system (μ = 0.1 KCl), the rate of the hydroxylation of cyclohexane is almost double that observed for the Fe(III)-EDTA, ascorbic acid O_2 system. The rate of the reaction is first order with respect to ascorbic acid, first order with respect to Ru(III)-EDTA and fractional order with respect to cycylohexane and molecular oxygen concentrations. A mechanism proposed for the reaction is shown in Scheme (IV).

The rate-determining step for the hydroxylation of cyclohexane is proposed to be an oxygen atom insertion in the C-H bond. An ionic mechanism[1] is suggested whereby a hydride transfer from cyclohexane to the coordinated oxygen atom produces OH^- and a carbonium ion. Migration of OH^- to the carbonium ion produces cyclohexanol and regenerates the catalyst. The mechanism is similar to that suggested by Groves and Puy[30] for the hydroxylation of cyclohexanol to 1,3-cyclohexanediol by Fe(II) + H_2O_2 system. The active species in this system is a ferryl ion $Fe^{IV} = O^{2-}$ which abstract a hydride ion stereospecificially from a C_3 carbon atom syn to the hydroxyl group. Subsequent transfer of the OH^- group to the carbonion in 3 results in the formation of *cis*-1,3-cyclohexane-diol 4 as shown in Scheme V.

The oxidation of cyclohexanol to cyclohexanone proceeds through a β-hydride shift from cyclohexanol to the metal complex to form an intermediate metal-hydride complex which breaks down on attack by molecular oxygen in a fast step to the catalyst and H_2O_2. The steps proposed for the oxidation of cyclohexanol catalyzed by Ru(III)-EDTA complex have been independently investigated at *p*H 2.00 in alcohol-water system at 30°. The rate data for Scheme IV are reported as:

Rate Law

$$\frac{[H_2A]\,[Ru(III)\,HL(H_2O)]}{-d\,[AH_2]/dt} = \frac{H^+\,(1 + k/k_2K_4[C_6H_{11}OH])}{k_1K_aK_1K_2K_3\,[C_6H_{12}]\,[O_2]} + \frac{[H_2A]}{k_1}\left(\frac{1}{K_2K_3\,[C_6H_{12}]} + \frac{1}{K_3\,[C_6H_{12}]} + 1\right)$$



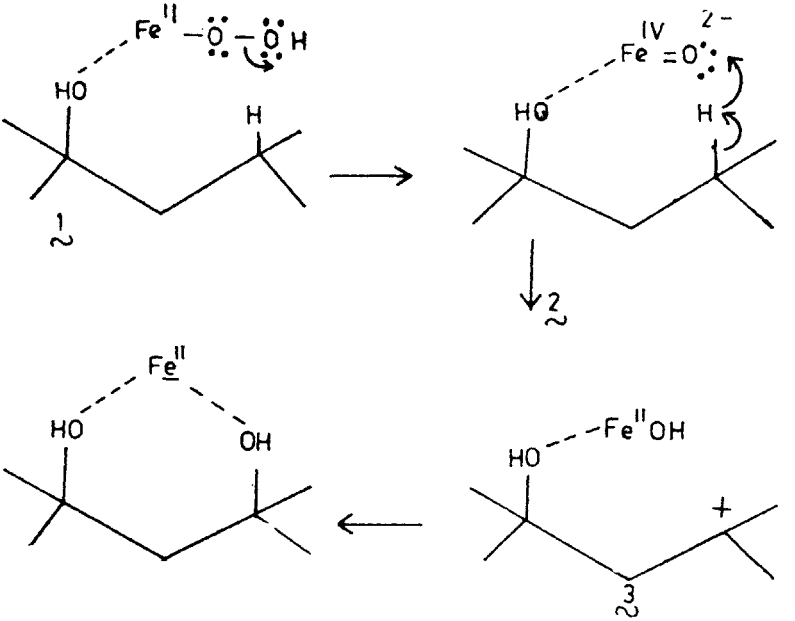
Scheme IV

$K_a = 11.22 \times 10^{-5}$ $k_1 = 9.76 \times 10^{-4}\ sec^{-1}$

$K_1 = 2.88 \times 10^3$ $k_2 = 5.66 \times 10^{-4}\ sec^{-1}$

$K_2 = 1.40 \times 10^3$ $K_4 = 2.45 \times 10^3$

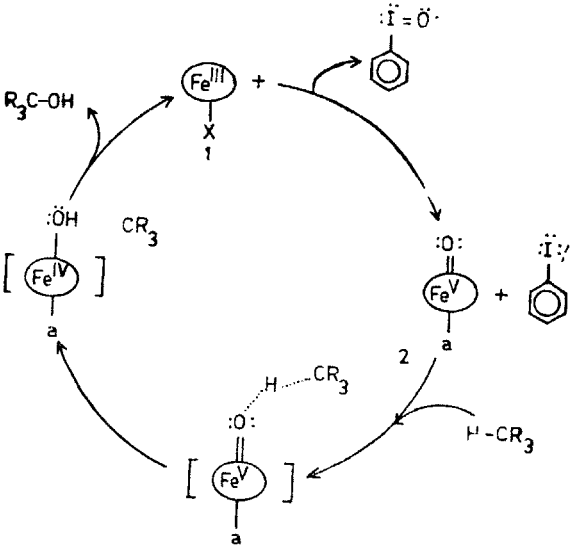
$K_3 = 2.00 \times 10^4$ $k = 7.66 \times 10^{-5}\ sec^{-1}$



Scheme V

Metal oxo complexes as catalysts have been proposed earlier in a variety of oxygen atom transfer reaction.[15–25] In the hydoxylation of the saturated hydrocarbons cyclohexane and cycloheptane to the corresponding alcohols and ketones by Fe^{III} (TPP)Cl (TPP = tetraphenylporphyrin and iodosylbenzene an active $L\ Fe^{V} = O^{2-}$ species was reported[15] as an active intermediate. The hydroxylation of the hydrocarbon was proposed[15] to proceed by a homolytic cleavage of $R_3C\cdot$-$H\cdot$ bond to from $R_3C\cdot$ and $H\cdot$ free radicals. The $H\cdot$ free radical attacks $L\ Fe^{V}=O^{2-}$ to form $L\ Fe^{IV}$-OH which combines with R_3C^- to form the hydroxylated product R_3COH and the catalyst (Scheme VI).

Asymmetric epoxidation of prochiral olefins with chiral iron porphyrins was achieved[16] with iodosylbenzene as an oxidizing agent. Alkane hydroxylation and alkene epoxidation was reported[17] in the chloro substituted tetraphenyl-prophyrin Fe^{III} complexes in the presence of pentafluoroiodozylobenzene. Reaction of C^{III} (TPP) Cl with C_6H_5IO gives[18] the chromium(V) oxo complex $O = Cr^{V}$(Cl) TPP. The molybdyl species $Mo^{IV}(O)_2$ (L) and (Mo^{IV} OL (L = 2,6-bis-2,2-diphenyl-2-mertaptoethyl-pyridine) in DMF solution act[19] as models for the oxygen atom transfer molybdoenzymes. Lithium hypochlorite epoxidation of olefins catalyzed by



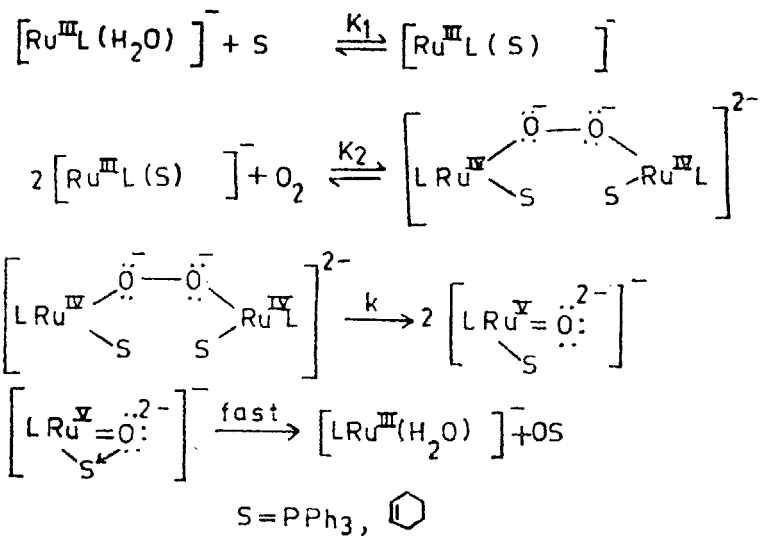
Scheme VI

Mn(TPP) Cl was reported[20] to proceed through a (TPP) $Mn^{V} = O^{2-}$ species. The transfer of the oxygen atom from the oxo species to the olefin was suggested[21] through an oxo-olefin intermediate which breaks down to the epoxide and catalyst in a rate determining step. It all these reactions free radical pathways are feasible[22,23] for the O-atom transfer reactions depending on the conditions of the reaction.

Homo-Oxygenation Reactions

Oxygen atom transfer reactions involving the transfer of both the oxygen atoms to two molecules of the same substrates are designated as homo-oxygenation reaction. Taqui Khan *et al.*[32] reported a catalytic oxygen atom transfer system involving molecular oxygen and the catalyst $[Ru^{III}(EDTA)H_2O)]^-$ for the oxidation of triphenylphosphine to triphenylphosphine oxide and cyclohexene to the epoxide. The rate of oxidation of PPh_3, cyclohexene is first order with respect to the substrate(s), first order with respect to Ru(III)-EDTA complex and one half order with respect to molecular oxygen concentration, supporting the formation of an intermediate μ-peroxo-complex $[Ru^{IV}(EDTA)(S)]_2O_2$ $\underset{\sim}{2}$ in the reaction (Scheme VII). The proposed rate determining step in the reaction is the formation of an intermediate ruthenyl species (EDTA) (S) $Ru^{V} = O^{2-}$ $\underset{\sim}{3}$ by the homolytic cleavage of the O-O bond in $\underset{\sim}{2}$. A fast inner sphere transfer of oxygen atom from $\underset{\sim}{3}$ to S forms OS and the catalyst is regenerated as depicted in Scheme VII.

In the case of triphenylphosphine the oxidation to phosphine oxide was followed by ^{31}P nmr spectroscopy, triphenylphospine exhibits ^{31}P resonance peak at



Scheme VII

−5.38ppm. Oxidation of triphenylphosphine to phosphine oxide causes a downfield shift of the peak to 32 ppm. As shown in Fig. 1 the hight of the peak at −5.38ppm decreases and the one at 32ppm increases with time.

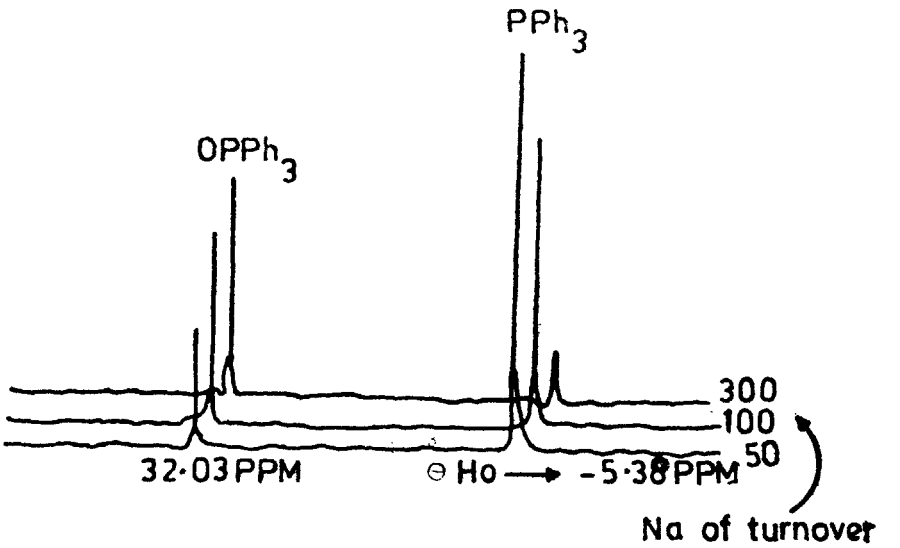


FIG 1

The rate data for PPh_3 and cyclohexene oxidation are :

Rate Law

$$\frac{[Ru^{III}(EDTA)(H_2O)]_T\,[O_2]^{1/2}}{-d\,[O_2]/dt} = \frac{1}{kK_1K_2S} + \frac{1}{kK_2} + \frac{[O_2]^{1/2}}{k}$$

$S = PPh_3$	$S =$ *Cyclohexene*
(1:1 dioxane-water) 35°	(1:1 alcohol-water) 30°
(μ = 0.1M KCl)	(μ = 0.1M KCl)
$K_1 = 28.0M^{-1}$	$K_1 = 27.0M^{-1}$
$K_2 = 1.0 \times 10^4\ M^{-2}$	$K_2 = 1.5 \times 10^3 M^{-2}$
$k = 2.3 \times 10^{-2}\ min^{-1}$	$k = 3.3 \times 10^{-4}\ min^{-1}$

Except a small difference of (5°) in the temperature and the dielectric constant effect of the medium, the equilibrium constant K_1 for the formation of mixed ligand PPh_3 in cyclohexene complexes is almost the same for the two π-acidic ligands. The difference however is manifested in the stability of the mixed ligand dioxygen complex K_2 which is more stable by a factor of 10 in PPh_3 than the cyclohexene complex, in accord with their π-acidities, PPh_3 > cyclohexene. The oxygen atom transfer rate k_1 to phosphine is about 100 times faster than the olefin because of the ease of cleavage of the O-O bond in the phosphine complex as compared to the olefin complex. The steps pertaining to O-O cleavage and oxygen atom transfer may be concerted and together correpond the slow step in the oxygen atom transfer to the substrate.

The epoxidation oxidation of allyl alcohol to glycidol by molecular oxygen is catalyzed[33] by $[RuCl_2H_2O_4]^+$ in the *p*H range 2–3. The reaction is first order with respect to the catalyst and allyl alcohol and one half order with respect to molecular oxygen concentrations. The formation of an intermediate μ-peroxo-Ru(IV)-allyl alcohol complex was proposed with an intramolecular transfer of oxygen atom from homolytic cleavage of the O-O bond to the double bond to form the epoxide as shown in Scheme VIII. The proposed intermediate oxo complex $[Ru^{5+}O^{2-}$ (HEDTA)] was directly obtained[34] by the reaction of iodosylbenzene with [Ru(HEDTA) Cl]$^-$ in aqueous solution.

The epoxide is further oxidized to the aldehide by β-hydride abstraction in step k' ($k' >> k$) and the fast oxidation of intermediate by molecular oxygen. The rate data is summarized as follows :

Rate Law

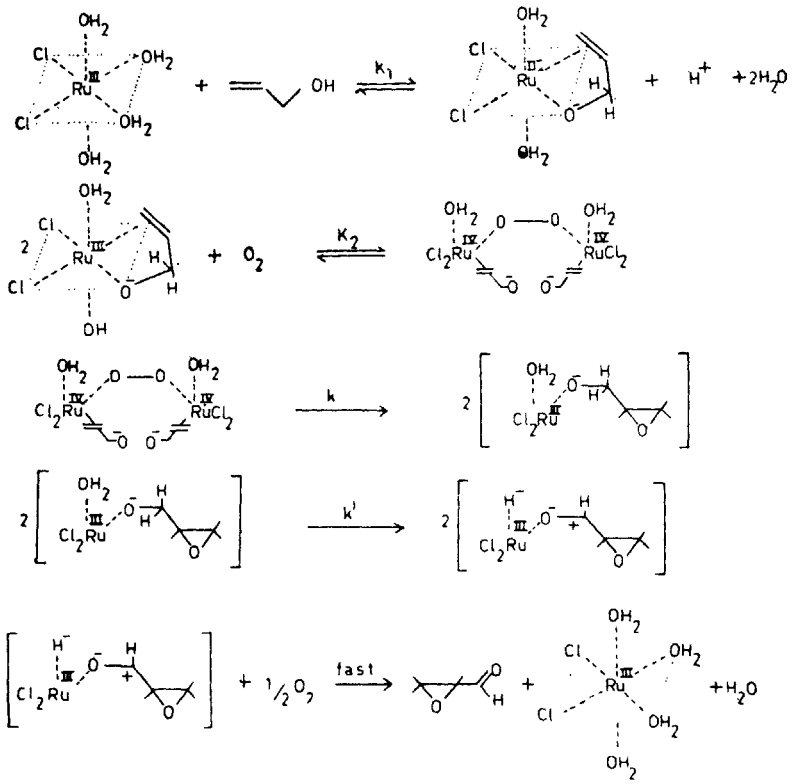
$$\frac{[RuCl_2(H_2O)_4]_T^+\,[S]\,[O_2]^{1/2}}{-d\,[O_2]/dt} = \frac{[S]}{kK_2} + \frac{[S]\,[O_2]^{1/2}}{k} + \frac{[H^+]}{kK_1K_2},$$

where

$K_1 = 8.0 \times 10^3\ M^{-1}$

$K_2 = 3.0 \times 10^2\ M^{-2}$

$k = 1.4 \times 10^{-5}\ min^{-1}$



Scheme VIII

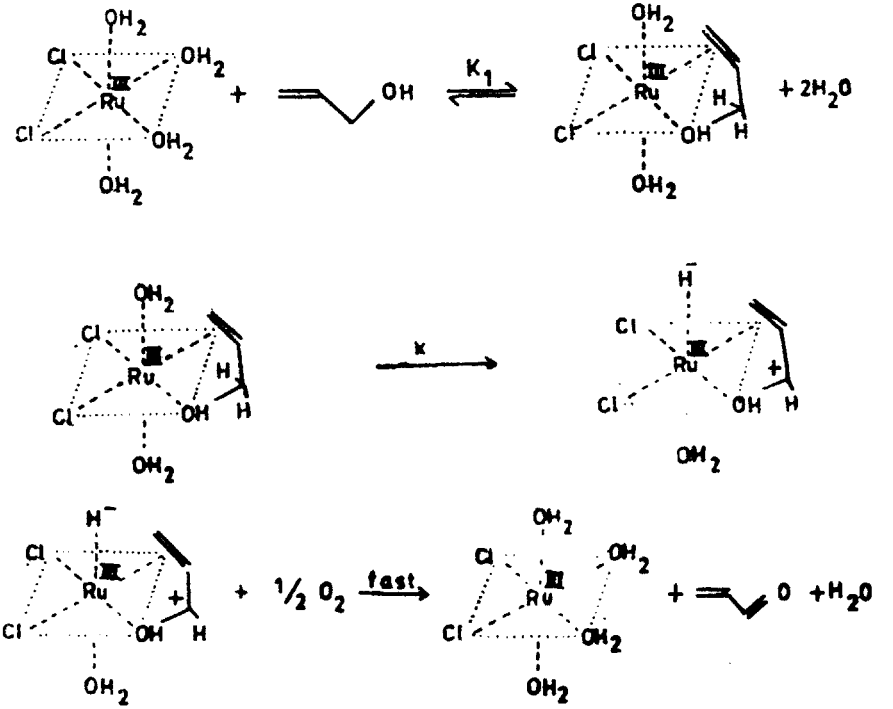
The formation constant of Ru^{III}-allyl alcohol complex is about a factor of 2.5×10^2 more stable than those of the mixed ligand complexes of PPh_3 and cyclohexene with Ru(III)-EDTA. This is expected because of the extra chelation of hydroxyethyl group to the metal ion. The dioxygen complex formation constant K_2 and the epoxidation rate k are however much lower than cyclohexene and PPh_3. This may be due to the hydrolysis of Ru(III) ion in aqueous solution which effectively reduces the concentration of the aquo metal ion in solution. The hydrolysis is maximum at *p*H 3.00.

β-Hydride Elimination Reactions

One of the examples of the effect of *p*H on the course of an oxidation reaction is the oxidation[33] of allyl alcohol by molecular O_2 catalyzed by $[Ru(H_2O)_4\ Cl_2]^+$ in the *p*H range 1–2. The rate of oxidation of allyl alcohol is first order with respect to catalyst and substrate, directly proportional to H^+ ion concentration and independent of the concentration of molecular oxygen. The product of the oxidation of allyl alcohol in this *p*H range is pure acrolein.

In the proposed[33] mechanism (Scheme IX) allyl alcohol forms a complex with $[Ru(H_2O)_4\ Cl_2]^+$ in a preequilibrium step with $\log K_1 = 3.90$ at 30°. A rate-

determining β-hydride transfer from allyl alcohol to Ru(III) within the Ru(III)-allyl alcohol complex results in the formation of a Ru(III)-hydride. The existence of metal-hydride as an intermediate had been proposed earlier[31] in the oxidation of cyclohexanol to cyclohexanone by molecular oxygen catalyzed by Ru(III) chloride and by Harrod *et al.*[35,36] in the chloride catalyzed hydrogenation of unsaturated compounds. The Ru(III)-hydride is then oxidized by molecular oxygen in a fast step to give H_2O, acrolein and the catalyst.



Scheme IX

Rate Law

$$\frac{-\mathrm{d}\,[C_2]}{\mathrm{d}t} = kK_1\,[RuCl_2\,(H_2O)_4]^+\,[CH_2{=}CH{-}CH_2\,OH],$$

where

$$K_1 = 8.0 \times 10^3\ M^{-1}$$

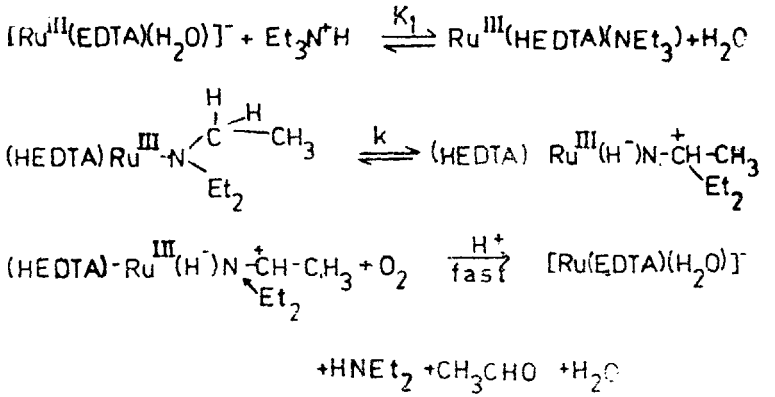
and

$$k = 1.0 \times 10^{-5}\ min^{-1}.$$

Oxidation of Triethylamine

The oxidation of triethylamine by molecular oxygen catalyzed by Ru(III)-EDTA in the *p*H range 1.5 to 2.5 (μ = 0.1M KCl) at 35° proceeds[37] with the dealkylation of

the amine. The major products of the reaction are diethylamine and acetaldehyde. In the *p*H range investigated, protonated triethylamine reacts with Ru(III)-EDTA to form a ternary complex (Scheme X). In the rate-determining step β-hydride transfer takes place from triethylamine to Ru(III) in the mixed ligand Ru(III)-EDTA-triethylamine complex. The Ru(III)-hydride is then oxidized by molecular oxygen in a fast step to give the oxidized product, diethyl amine and acetaldehyde.



Scheme X

Rate Law

$$\frac{[RuL]_T}{d[Et_3N^+H]/dt} = \frac{1}{k_2K_1[Et_3N^+H]} + \frac{1}{k}$$

$$\text{Log } K_1 = 1.14$$

$$k = 6 \times 10^{-2} \text{ min}^{-1}$$

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