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# Oxidative cleavage of cycloalkanones with dioxygen catalyzed by supported catalysts or homogeneous systems: Evidence for novel active ruthenium (II) and/or (III) species

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#### ABSTRACT

 $\alpha$ -Substituted cycloalkanones are oxidized to oxo-acids by low-nuclearity complexes (Cu<sup>2+</sup> or [VO<sub>2</sub>]<sup>+</sup>/[VO]<sup>2+</sup> – exchanged Nafion<sup>®</sup> beads), or homogeneous systems with ruthenium acetate complexes and [Ru(H<sub>2</sub>O)<sub>6</sub>] (tosylate)<sub>2</sub> in dioxygen (0.1 MPa) at 55–60 °C. The catalytic procedures compare well with previously described systems involving homogeneous catalysis with copper (II) or polyoxometalates such as "H<sub>8</sub>[PMo<sub>7</sub>V<sub>5</sub>O<sub>40</sub>]-aq". The results complement the widely used oxidative methods for ketone cleavage in cases when protons and transition metal salts are involved. A tentative dioxygenase mechanism, involving peroxygen species, is proposed for these reactions.

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# 1. Introduction

Despite the advantage of air or dioxygen as the final oxidant, there are relatively few methods which use homogeneous catalysts in the presence of  $O_2$  under mild conditions [1–3]. The oxidation of cyclic ketones is interesting especially for the synthesis of dicarboxylic acids: an industrially important process in the conversion of cyclohexanone into adipic acid, by nitric acid oxidation of KA oil or "olone" (cyclohexanone/cyclohexanol). Several improvements in the "nitric path" have been applied, particularly for the recycling of nitrogen oxides, but the formation of N<sub>2</sub>O, which cannot be reconverted to  $HNO_3$ , is reducing ozone in the atmosphere [1,4]. To overcome the disadvantages related to the use of HNO<sub>3</sub>, the oxidation of the olone mixture or of cyclohexane, by dioxygen, would be the ideal solution. The catalytic oxidative cleavage of ketones and  $\alpha$ -ketols with O<sub>2</sub> can be brought about by several transition metal catalysts: vanadium (V/IV), copper (II/I), iron (III/II), cerium (IV/III), manganese or cobalt (III/II), etc. instead of using stoichiometric oxidation with periodates, lead tetra-acetate or chromium (VI) compounds [4]. Copper systems in acidic media and Keggintype heteropolyacid complexes  $H_{3+n}[PMo_{12-n}V_nO_{40}]$  aq (denoted

HPA – *n* where *n* = 1–6) in the presence of dioxygen, are among the best bifunctional catalysts [1,4–11]. These precursors can be used in the oxidation of  $\alpha$ -ketols, benzylic ketones, 1-phenylalkanones, substituted cycloalkanones,  $\alpha$ -diols, cyclohexanone, KA oil and even natural compounds to prepare carboxylic acids [4–10]. The activity of the HPA – *n* is due, in part, to their Brönsted acidity and ability to take part in a variety of equilibria. The oxidative cleavage of cyclohexanone derivatives, a reaction which is atom economical, has been described with these precursors as a model of dioxygenases (no autoxidation reactions, no induction period, stoichiometry such that the ratio substrate/O<sub>2</sub>  $\simeq$  1; etc.) [4,10,11].

Many monomeric oxovanadium species ([VO{O-*i*-Pr}<sub>3</sub>], [{Ph<sub>3</sub>SiO}<sub>2</sub>VO<sub>2</sub>]<sup>-</sup>, VOSO<sub>4</sub>·aq [OV(acac)<sub>2</sub>], etc.) give the same chemistry as the HPA – *n* heteropolyacids, especially with  $\alpha$ -hydroxyketones [5–7,9,10]. In view of these facts, the catalytically active species were depicted as [VO<sub>2</sub>]<sup>+</sup> X<sup>-</sup> [6,10,11]. They are also the active catalysts (with H<sub>3</sub>O<sup>+</sup>) in the oligomerization of  $\varepsilon$ -caprolactone and  $\delta$ -valerolactone using heteropolyacid initiators [12]. Nafion<sup>®</sup>-supported copper (II) [13,14] and [VO<sub>2</sub>]<sup>+</sup>/[VO]<sup>2+</sup> [15] have been prepared. Ion pairs [–(SO<sub>3</sub><sup>--</sup>)<sub>x</sub>... [M]<sup>x+</sup>] (x=1 or 2) have been characterized (M=VO<sub>2</sub>, VO or Cu); they are active for aerobic oxidations [13,15]. It has been demonstrated that many mononuclear transition-metal-catalyzed C–C bond cleavages can be performed efficiently in the presence of dioxygen [1,4,11].

Further work needed to develop this chemistry led to the discovery of novel catalysis systems: "Ru(III/II) complexes/solvent/O<sub>2</sub>" under non-demanding conditions.

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## 1.1. Why novel ruthenium precursors?

Ruthenium complexes have great potential for catalytic oxidation reactions of various organic compounds: ruthenium (VIII) species are strong oxidants, and low-valent ruthenium precursors can lead to middle-valent complexes with a variety of oxygen donors. One of the most famous results is the  $[Ru^{VI}(TMP)(O)_2]$ catalyzed (TMP = tetramesitylporphyrinato) aerobic epoxidation of cyclooctene which proceeds at 0.1 MPa of dioxygen in a dioxygenase mode (without the need for a coreductant), but this is probably the easiest common olefin to epoxidize, and also forms epoxide readily with dioxygen. A transient Ru(II) complex would be the species reactive towards dioxygen [16]. A ruthenium-containing polyoxometalate (POM), [{WZnRu2<sup>III</sup>(OH)(H2O)} (ZnW9O34)2]Q11 [17] (Q<sup>+</sup> = triooctylmethylammonium) and a sterically hindered ruthenium complex, cis-[Ru<sup>II</sup>(dmp)<sub>2</sub>(MeCN)<sub>2</sub>](PF<sub>6</sub>) (dmp=2,9dimethyl-1,10-phenanthroline) [18,19] are also effective for epoxidation with molecular oxygen, and may be acting initially as an inorganic dioxygenase catalyst. In some cases competing cleavage and epoxidation reactions were observed. Subsequent studies [17] suggest that the reaction proceeds by a radical-chain autoxidation mechanism rather than via the previously claimed all-inorganic dioxygenase catalysis mechanism. Worth mentioning also is the oxidation of 1-methylcyclohexene under conditions in which ruthenium (VIII) oxide, RuO<sub>4</sub>, can be generated catalytically and which gives 6-oxoheptanoic acid [20,21], while the "RuCl<sub>3</sub>·nH<sub>2</sub>O/MeCO<sub>3</sub>H/CH<sub>2</sub>Cl<sub>2</sub>/MeCN/H<sub>2</sub>O" system leads to α-ketol [21]:



Catalytic oxidative cleavage of vicinal diols and related oxidations by ruthenium-based pyrochlore oxides,  $A_{2+x} \operatorname{Ru}_{2-x} O_{7-y}$  (A=Pb, Bi; 0 < x < 1; 0 < y < 0.5) in 1.5 M NaOH ( $\simeq 0.7$  MPa O<sub>2</sub>; 25–55 °C) was claimed to occur at the gas–liquid–solid interfaces; Pb(IV), oxoruthenium species and basic media may contribute to the molecular events [22], since aerobic oxidation of cyclic ketones has been performed in alkaline solution [23]:



The oxidative cleavage of saturated  $\alpha$ -diols is of interest, due to its relevance to lignin oxidation; under mild conditions in acidic media, vanadium complexes are among the best precursors [24].

It should be noted that in neutral or basic medium at 80 °C [17] (*vide supra*) the stability of POM compounds may be suspect, and research should be carried out to determine the precursor integrity under such conditions. Monoxygenase-like systems for epoxidation have also been described: in the presence of dioxygen (ca. 0.1 MPa), at room temperature or at 40 °C, 1,2-dichloro-ethane (or toluene) solutions of olefins (*trans*-2-octene, (R)-(+)-limonene, 2-methyl-3-buten-2-ol, etc.) and *i*-PrCHO give the corresponding epoxides and *i*-PrCO<sub>2</sub>H in the presence of  $[Ru_3^{III}O(OAC)_6(H_2O)_3](OAc)$ ,  $[Ru_2^{II,III}(OAC)_4]Cl$ ,  $[Ru^{III}(NH_3)_5Cl]Cl_2$ ,  $[Ru^{II}(H_2O)_6](Me-C_6H_4-SO_3)_2\cdot 3H_2O$ , etc. Side-reactions are observed with Ru complexes at 40 °C, essentially C–C bond cleavage [25,26]. These old epoxidation reactions, with a sac-

rificial substrate, which can be initiated by numerous inorganic complexes or solids [25], were also developed in a perfluorinated solvent [27]. To the best of our knowledge, none of the ruthenium-catalyzed homogeneous oxidations using  $O_2$  as oxidant, or co-oxidant, imply carbon–carbon bond cleavage of ketones as the main reaction. These findings, combined with studies on oxoruthenium complex-catalyzed oxidations, prompted investigation of not-too-sophisticated ruthenium precursors. We report in this paper the use of molecular oxygen as stoichiometric oxidant in the metal-catalyzed conversion of  $\alpha$ -substituted ketones to keto-acids. Several precursors are considered (Scheme 1), with special attention to the Ru(II) aqua-complex [Ru(H<sub>2</sub>O)<sub>6</sub>] (Me-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub>)<sub>2</sub> (*vide supra*).

## 2. Experimental

#### 2.1. Materials and apparatus

The organic chemicals (Aldrich), MoO<sub>3</sub>, V<sub>2</sub>O<sub>5</sub>, VOSO<sub>4</sub>·5H<sub>2</sub>O, NaIO<sub>4</sub>, HNO<sub>3</sub>, Pb (Prolabo), RuO<sub>2</sub>·aq, [Ru<sub>3</sub>O(OAc)<sub>6</sub>(H<sub>2</sub>O)<sub>3</sub>](OAc), [Ru<sub>2</sub>( $\mu$ -OAc)<sub>4</sub>]Cl (Engelhard, Compagnie des Métaux Précieux, min. 95%) H<sub>2</sub>SO<sub>4</sub>, H<sub>2</sub>SiF<sub>6</sub>, *p*-toluenesulfonic acid, HNO<sub>3</sub>, CH<sub>3</sub>COOH and commercial solvents, methanol and acetonitrile (Carlo Erba and Riedel-de Haën, respectively), were used without further purification. Nafion<sup>®</sup> NR50 (10–35 mesh) were obtained from Lancaster synthesis. Ion-exchange capacity of the 10–35 mesh materials is 0.8 meq H<sup>+</sup> g<sup>-1</sup>.

<sup>31</sup>P NMR spectra were recorded with 10 mm o.d. tubes on a Bruker WM250 apparatus operating at 101.2 MHz.

ESR spectra at the X-band were measured at 298 K with a Varian E4 spectrometer operating at 9.15 GHz and 100 kHz magnetic



Scheme 1. Schematic representation of the ruthenium complexes investigated.

field modulation (vanadium catalysts). Spectra at 77 K (copper (II)/Nafion<sup>®</sup>) were taken with a liquid nitrogen Dewar flask inserted into the ESR cavity of Bruker ESP300E spectrometer operating at 9.5 GHz with 100 kHz modulation. The beads were analysed in quartz tubes.

Structural analysis of the Nafion<sup>®</sup>-supported copper (II) samples was carried out by electron microscopy. A digital Leica S440 scanning microscope (SEM) equipped with a energy dispersive X-ray spectroscopy (EDS) unit was used to quantify the surface composition and homogeneity of ultramicrotomed sections ( $45 \text{ nm} \times 45 \text{ nm}$ ) of beads. This technique uses X-rays that are emitted by the samples as a consequence of the displacement of electrons by an electron beam; they are analysed by a TRACOR-NORAN-Voyager 1 spectrometer. Atomic compositions lead to the S/Cu ratios.

#### 2.2. Catalysis test

Typical experiments with the catalyst precursors were performed in an all-glass reactor vessel (40 mL) attached to a vacuum line, with a manometer and a gas inlet. This was charged with the vanadium (or copper or ruthenium) precursor ( $M \simeq 0.076$  mmol), the solvent (5 mL) and substrate (ca. 7.6 mmol). The mixture was stirred magnetically in O<sub>2</sub> for 24 h at 60 °C. Dioxygen uptake was determined by two gas burettes ( $2 \times 100$  mL). The number of moles of  $O_2$  taken up was calculated by the ideal gas law. The yields of keto-acids, or their esters (obtained in dinitrogen, using a large excess of refluxing methanol in the presence of sulfuric acid [7]) were determined by GC measurements. GC-MS analyses were performed on a TRACE GC 2000 gas chromatograph (OV 1701, 50 m capillary column) interfaced with a mass-selective detector (RTX5-MX). <sup>1</sup>H and <sup>13</sup>C NMR spectra and MS (70 eV or CI, NH<sub>3</sub>) data correspond to our previous findings [7,10,15,32]. Elemental analyses were performed at the CNRS Service Central d'Analyses, Lyon.

#### 2.3. Preparation of " $H_8[PMo_7V_5O_{40}]$ aq" denoted HPA-5

The HPA-5 heteropolyacids were prepared according to described procedures [4,28-30]: a "peroxo-route" for preparing heteropolyacid mixtures of general formula " $H_{3+n}[PMo_{12-n}V_nO_{40}]$  aq". A solution of  $[PO_4\{Mo_2O_2(\mu O_2)_2(O_2)_2\}_2]^{3-}$  [31], and of the Mimoun species [MoO(O<sub>2</sub>)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>] was first obtained; then, a solution of the diperoxovanadate anion  $[VO(O_2)_2(H_2O)_2]^-$ , formed at 0°C, was added to the molybdenum(VI) solution at 0 °C. Decomposition of the peroxo-species led, after evaporation of water, to orange-red crystals of HPA-5. This method can also be used for n = 1-4, 6 and 8. Dioxygen is used to oxidize the solution which content vanadium (IV), in the presence of a slight excess of  $H_3PO_4$ , as in the reaction of HPA - n in catalytic systems for carbon–carbon bond cleavage of ketones and  $\alpha$ -ketols [5-7,11]. Molybdic oxide (28 mmol) was added to 30% hydrogen peroxide (20 mL). After reaction for 1 h at 50 °C, 1.2 mmol of H<sub>3</sub>PO<sub>4</sub> was added. The yellow lukewarm solution (solution A) was stirred for 30 min and then cooled at  $0\,{}^\circ C$   $V_2O_5$  (10 mmol) was reacted with 30 mL of  $H_2O_2$  (30%) at 0 °C with slow addition of the gel-like vanadium oxide (solution B). Solutions A and B were mixed slowly at 0°C. Evaporation, after dioxygen bubbling (24h) gave orange-red crystals. Elemental analysis is consistent with the formula "H<sub>8</sub>[PMo<sub>7</sub>V<sub>5</sub>VO<sub>40</sub>]·12H<sub>2</sub>O" or "PMo<sub>7</sub>V<sub>5</sub>O<sub>52</sub>H<sub>32</sub>" (1821.49): calcd. P1.70, Mo36.87, V13.98; found P1.65, Mo36.0, V13.4.

The HPA – *n* (solid or aqueous solutions) are multicomponent systems: they contain several polyanions, positional isomers of these, as well as monomeric metallo species such as the *cis*-dioxo cation  $[VO_2(H_2O)_4]^+$ , usually written as  $[VO_2]^+$ , and often traces of V(IV) ( $[VO]^{2+}$  species) [10]. The NMR measurements, confirm that the HPA-5 precursors are not pure heteropolyacids: they contain

a certain fraction of HPA-2, -3, -4 and -5 with several isomers and excess  $H_3PO_4$ .  $\delta^{31}P$ : -3.8; -3.6, -3.3; -2.9, -2.5; -2.3, -1.9; -1.7; -1.3, 0.5 ( $H_3PO_4/H_2PO_4^-$ ) [10].

# 2.4. Preparation of $[Ru(H_2O)_6]$ (tos)<sub>2</sub>; (tos = p-toluene sulfonate)

Hexa-aqua-ruthenium (II)*bis*(*p*-toluene sulfonate), [Ru(H<sub>2</sub>O)<sub>6</sub>] (Me–C<sub>6</sub>H<sub>4</sub>–SO<sub>3</sub>)<sub>2</sub>, was prepared according to the literature [32]. Its aqueous solutions are sensitive to dioxygen (*vide infra*) and to hydrolysis above pH  $\simeq$  6. C<sub>14</sub>H<sub>32</sub>O<sub>15</sub>S<sub>2</sub>Ru (551.55): calcd. C30.49, H4.75, S11.63, Ru18.32; found C30.10, H4.6, S11.5, Ru18.0. *Caution:* RuO<sub>4</sub> *is highly toxic. A well-ventilated fume cupboard must be used.* 

# 2.5. Supported-metal complexes by a ligand exchange reaction: Nafion $/[VO_2]^{+}/[VO_2]^{+}/CH_3CN$

They have been prepared with commercial Nafion<sup>®</sup> NR50 (10–35 mesh beads) in the H<sup>+</sup> form. Acidimetric titrations showed that their ion-exchange capacities are of the order 0.8 meq H<sup>+</sup> g<sup>-1</sup>. The required amount of vanadyl sulfate, VOSO<sub>4</sub>·5H<sub>2</sub>O, for 25% H<sup>+</sup> exchanged was introduced into 30 mL of acetonitrile. Nafion<sup>®</sup> ( $\simeq$ 1.00 g) was added, and the resulting mixture was stirred for 12 h at room temperature. The exchanged beads were separated by filtration, washed with MeCN (3 × 20 mL), then dried under vacuum. % H<sup>+</sup> exchanged was slightly lower (here 19%) as a result of chemical analysis (% S and % V). The native solids thus obtained have been characterized by EPR [15]. The spectrum is typical of vanadium (IV) species with high anisotropy and of mononuclear complexes.

# 2.6. Nafion<sup>®</sup>/Cu<sup>2+</sup>·aq/H<sub>2</sub>O

An amount of copper nitrate,  $Cu(NO_3)_2 \cdot 3H_2O(1.45 \text{ g or } 0.36 \text{ g})$ was introduced into 50 mL of distilled water. Nafion<sup>®</sup> NR 50 (4g) was added and the resulting mixture was gently stirred for 24h at room temperature. The maximum copper content of the beads in contact with excess Cu<sup>2+</sup> was ca. 80% of the total amount theoretically calculated for total neutralization, based on two sulfonic groups for each Cu<sup>2+</sup> ion. The exchanged beads were separated by filtration, repeatedly washed with distilled water until the pH of the washings was constant, then dried under vacuum [13,14]. The copper (II)-exchanged Nafion<sup>®</sup> as well as the recycled catalysts were characterized by scanning electron microscopy/and X-ray energy dispersion spectrometry (X-ray EDS) and EPR. The Cu and S signals of ultramicrotomed sections reveal that the copper distribution is quasi-uniform for the initially prepared Nafion<sup>®</sup>/Cu<sup>2+</sup> beads (S/Cu  $\simeq$  2.5). On the other hand, after the first and second catalytic runs, the S/Cu ratios are 3.48 and 3.49. These results argue in favour of a homogeneous distribution of the Cu sites in the beads and leaching of Cu(II) during the first run for the highly exchanged Nafion<sup>®</sup>, leading to low conversions and selectivities.

Two transitions are observed by EPR for the fresh and recycled catalysts: isolated cations are at  $g \simeq 2.18$  ( $\Delta m_s = 1$ ) and the half-field spin-forbidden signal ( $\Delta m_s = 2$ ) at ca. 1600 G, where the isolated cations are not expected to contribute; it corresponds to Cu<sup>2+</sup>...Cu<sup>2+</sup> dimers. In the dimer the Cu<sup>2+</sup> are probably ligated to the sulfonic groups of the Nafion network.

#### 3. Results and discussion

#### 3.1. Catalytic oxidative cleavage of 2-methylcyclohexanone

Results for the reactions of 2-methylcyclohexanone (1) with dioxygen and a variety of precursors are presented in Table 1. One important feature emerges for four different systems: further oxidative cleavage of the resulting keto-acids does not occur under these conditions (runs 1, 3, 5, 6). Experiments on the use of

Table 1

Oxidation of 2-methylcyclohexanon	e (1) to 6-oxohe	ptanoic acid (2), by	/ inorganic comi	plexes and dioxygen <sup>a</sup> .

Entry	Precursors	Solvent	$[H_{3}O]^{+}/M$	Conversion (%) <sup>b</sup>	Product yield (%) <sup>c</sup>	$TOF(s^{-1})$	Ref.
1	$[VO{O-i-Pr}_3]$	MeCN	0	62	56		[5,7]
2	$[n-Bu_4N][\{Ph_3SiO_2\}_2VO_2]$	MeOH	2 <sup>d</sup>	50	40		[10]
3	HPA-5	MeOH	1.6 <sup>e</sup>	100	97	$1.1  imes 10^{-3}$	g
4	Nafion <sup>®</sup> /[VO <sub>2</sub> ] <sup>+</sup> /[VO] <sup>2+</sup>	MeCN	7 <sup>f</sup>	80	67		[15] <sup>g</sup>
5	Cu(NO <sub>3</sub> ) <sub>2</sub> .aq	AcOH/H2O 4.5:0.5	-	98	96	$1.1  imes 10^{-3}$	g
6	Nafion <sup>®</sup> /Cu <sup>2+</sup>	MeCN	9	91	86		g
7	$[Ru_3^{III}O(OAc)_6(H_2O)_3](OAc)$	AcOH/H <sub>2</sub> O 4:1	-	95	75–83 <sup>h</sup>	$1.0  imes 10^{-3}$	g
8	[Ru <sub>2</sub> <sup>II/III</sup> (OAc) <sub>4</sub> ]Cl	AcOH/H <sub>2</sub> O 4:1	-	94	71–80 <sup>h</sup>	$1.0  imes 10^{-3}$	g
9	$[Ru(H_2O)_6](Me-C_6H_4-SO_3)_2$	AcOH/H2O 4:1	-	96	80-90 <sup>h</sup>	$1.0\times10^{-3}$	g

<sup>a</sup> Conditions: [M] (M = Cu or V or Ru), 0.076 mmol; 2-methylcyclohexanone, 7.6 mmol; solvent, 5 mL; p(O<sub>2</sub>): 0.1 MPa; reaction temperature, 60 °C; reaction time 24 h. <sup>b</sup> Conversion is percentage of the substrate consumed.

<sup>c</sup> Yield (%) is (mmol of (2) per mmol of (1) × 100) (determined after extraction – see Ref. [32]) and/or esterification – see Ref. [7].

<sup>d</sup> Addition of *p*-toluenesulfonic acid.

<sup>e</sup> No reaction without Brönsted acid (with onium salts).

<sup>f</sup> From % H<sup>+</sup> exchanged and % V. Products analysed by GC–MS. Internal standard: heptanoic acid.

<sup>g</sup> This work

<sup>h</sup> The low values refer to pure isolated product.

mononuclear species (runs 1, 2, 5) in homogeneous catalysis systems and comparison of conversions and selectivities with those obtained with HPA – n [4–10,24,28] has led us to consider methods for incorporating vanadium (V/IV) or copper (II) into polymeric materials such as Nafion<sup>®</sup> with [VO<sub>2</sub>]<sup>+</sup>/[VO]<sup>2+</sup> or Cu<sup>2+</sup> [14,15].

The oxidation of 2-methylcyclohexanone (1) to 6-oxoheptanoic acid (2) with pure dioxygen and Nafion<sup>®</sup> exchanged with  $Cu^{2+}$  [14] or [VO<sub>2</sub>]<sup>+</sup>/[VO]<sup>2+</sup> [15] were characterized by EPR: mononuclear or dinuclear moieties are the most likely active species interacting with SO<sub>3</sub><sup>-</sup> groups. The reaction was slower than for the homogeneous counterpart. Due to the high polarity of the products and the hydrophilic character of the matrix, solvents exert a major influence on product distribution; temperature and concentrations are also important for the supported catalysts. While the homogeneous copper (II)/acetic acid/water/O2 system is one of the best for the oxidation of (1) [4,7,33], acetonitrile has been found to be better than other solvents for supported catalysts, due to its effective coordination to the metal center as a labile ligand. The reduction of the activity of supported precursors as compared to homogeneous systems is partly related to diffusion limitations with Nafion<sup>®</sup> beads and to the local variation of the acidity function.

# 3.2. Limitations related to the choice of Nafion<sup>®</sup> beads and leaching behavior

2-Methylcyclohexanone does not lead to any significant leaching in acetonitrile when vanadium-exchanged Nafion<sup>®</sup> prepared in the same solvent is used. Under these conditions, the solid catalyst was reused three times without any loss of activity [15]. Yields were lower in the first reuse when the vanadyl salt, VOSO<sub>4</sub>·5H<sub>2</sub>O, was exchanged in water. The decrease is due to *extensive leaching* of the vanadium species in acetonitrile during the first test. Of all the materials tested, vanadyl-exchanged Nafion<sup>®</sup> beads prepared in acetonitrile were the most efficient catalysts for C–C bond cleavage of (1). For the best conditions [15], the conversion did not vary over four catalytic runs; no significant leaching of vanadium species was detected after the first and second runs on the 24% H<sup>+</sup>-exchanged polymers prepared in acetonitrile. The vanadium weight content remained constant (0.48–0.54%) [15]. To overcome diffusion limitations, other supports must be synthesized.

With copper (II)-exchanged Nafion<sup>®</sup>, diffusion limitations, and the formation of Cu<sup>2+</sup>...Cu<sup>2+</sup> pairs (*vide supra*) within the Nafion<sup>®</sup> beads led to lower the activity of these materials [13,14]. Whatever the substrate tested, the heterogeneous systems performed best with the smallest beads used: the grinding of Nafion<sup>®</sup>-NR50 polymer under cryogenic conditions and the use of acetonitrile (solvent) allowed better yields (85% at 65 °C with vanadium system, 90% with Cu(II)) and a marked reduction of vanadium (or copper) leaching, even after the catalyst had been used three times.

#### 3.3. The homogeneous systems revisited

To the best of our knowledge there is no long-lived efficient heterogeneous catalyst [1,4]; we have therefore re-examined some homogeneous systems. Evidence has been provided that the catalytically active species is  $[VO_2]^+$ , formed in the Nafion<sup>®</sup>/vanadium systems or via the partial dissociation of HPA – *n* with the release of  $VO_2^+$  or possibly  $VO^{2+}$  [29]. A mechanism based on coordination of the hydroxy oxygen of the substrate to  $[VO_2]^+$ , even at room temperature [6,8,9] (or with Cu<sup>2+</sup> species), was proposed to explain the experimental results on model substrates [5–11,13–15,33]. It is reasonable to assume that peroxo-derivatives can act as intermediates in the oxidative cleavage of C–C bonds [10,11,34,35].

Work with cyclanone derivatives, other than  $\alpha$ -ketols, and HPA - n suggested that the Brönsted acidity is a key parameter [6,7,10,28]. High degrees of conversion are obtained in the presence of HPA – n (n = 2–5), which means that their redox and acidic properties are better tuned: protons catalyze the formation of the corresponding enol of the substrate, and it is known that the redox potential of the V(V)/V(IV) couple increases with acidity [28], so the reactions should proceed better in acidic media. With an available OH group, the oxidative system described can be regarded as a model of dioxygenases [10,11]. Thus, it appeared that several lownuclearity species help initiate the catalytic oxidative cleavage of ketones and  $\alpha$ -ketols with dioxygen. For the first time, ruthenium precursors have been found to be efficient in homogeneous catalysis for the oxidative cleavage of (1) under aerobic conditions (runs 7–9). The yields of (2) are comparable to, although slightly lower than, those obtained with the best systems reported so far using ruthenium-substituted heteropolyanions with sodium periodate as oxidant [36], but here we use ruthenium (III) and/or (II), and in particular the mononuclear ruthenium (II) hexa-aqua-complex and dioxygen.

Usually, the ratio of dioxygen uptake to substrate of about 1.095 (0.90–1.15) suggests a single oxidative cleavage process; interestingly, no induction period is observed (Fig. 1). We are certainly closer to the true catalyst in all these cases; only minor subsequent cleavage of the resulting oxo-acid or of intermediates can occur under these conditions. We proposed that this reaction is analogous to biological oxidations catalyzed by catechol dioxygenases [10,11]. It is known that  $[Ru(H_2O)_6]^{2+}$  is readily oxidized by dioxygen or air to the yellow  $[Ru(H_2O)_6]^{3+}$  [37,38]; the water molecule

#### Table 2

Product yields from the oxidation of cyclic ketones by  $[Ru(H_2O)_6]_2$  (tosylate)<sub>2</sub> and dioxygen<sup>a</sup>.



<sup>a</sup> Reaction conditions: [Ru(H<sub>2</sub>O)<sub>6</sub>] (Me-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub>)<sub>2</sub>, 0.076 mmol; ketone, 7.6 mmol. Solvent AcOH: 4 mL, H<sub>2</sub>O: 1 mL; 55 °C; p(O<sub>2</sub>)=0.1 MPa.

<sup>b</sup> Conversion is percentage of the substrate consumed.

<sup>c</sup> Yield (%) is mmol of keto-acid per mmol of substrate × 100. Products analysed by GC–MS, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. Internal standard: heptanoic acid.

in the +2 ion can be readily replaced by  $X^-$  anions and by neutral ligands such as MeCN, DMSO, etc. [39].

These observations, previous [25] and new results (Table 1) led us to consider the tosylate salt as the most convenient precursor. Another point of interest is the reduction of  $O_2$  to  $H_2O_2$  by a series of ruthenium (II) complexes in aqueous acids [40].

# 3.4. Catalytic oxidative cleavage of some $\alpha$ -substituted cycloalkanones

As shown in Table 2, the use of the Ru(II) tosylate/dioxygen/acetic acid-water catalytic system can be extended to other substituted cycloalkanones with one or two alkyl substituents or a phenyl group. Treatment of 2,4-



**Fig. 1.** Consumption of dioxygen in the reaction of 2-methylcyclohexanone (7.6 mmol) in AcOH/H<sub>2</sub>O (4 mL/1 mL); dioxygen 0.1 MPa; reaction temperature  $60 \,^{\circ}$ C. Curve A: [Ru<sub>3</sub>O(OAc)<sub>6</sub>(H<sub>2</sub>O)<sub>3</sub>](OAc); curve B: [Ru(H<sub>2</sub>O)<sub>6</sub>] (Me-C<sub>6</sub>H<sub>4</sub>-SO<sub>3</sub>)<sub>2</sub>.

dimethylcyclopentanone (run 2) gives 3-methyl-5-oxohexanoic acid in good yield. 2-Phenylcyclohexanone produces mainly 5benzoylvaleric acid (run 3). Among the by products are benzoic acid ( $\leq 6\%$ ) and 5-benzoylpentanal ( $\leq 4\%$ ). 2,6-Dimethylcyclohexanone gives 2-methyl-6-oxoheptanoic acid, the only product of the direct oxidative cleavage of the substrate (run 4). Worth noting again is the ratio of dioxygen uptake to substrate of about unity (0.90–0.98) which argues in favor of a single major oxidative cleavage process; minor reactions were observed only with 2-phenylcyclohexanone. This catalytic procedure compares well with previously described systems involving vanadium or copper precursors [5,32].

Much emphasis has been placed on selectivity rather than rate, yet both are important in practice. A ruthenium system which achieves higher TOF than  $1.0 \times 10^{-3} \text{ s}^{-1}$  must be sought.

# 3.5. Proposed mechanism

The selectivities obtained in the presence of transition metal complexes (here with ruthenium (II) and/or (III)) are consistent with a metal-catalyzed conversion of (1) to (2). The lack of induction period and the substrate/O2 stoichiometry of about unity also support a mechanism (Scheme 2) based on coordination of the hydroxy oxygen to the active species. Unfortunately, incorporation of <sup>18</sup>O into products from <sup>18</sup>O<sub>2</sub> (99% CEA) is not conclusive: the concentration of <sup>18</sup>O-labelled **2** depends drastically upon the water content and protic solvent [41]. 2-Methylcyclohexanone (1) reacts in the enol form [6,7,10,11] since addition of weak or, especially, strong acids accelerate the oxidation (the protons can also increase the redox potential of the oxidizing species). The scheme represents a formally closed catalytic cycle, although it is likely that other steps occur and that the equilibria are more complex. The reaction considers a catalytically active ruthenium (III) species,  $[Ru^{III}(O_2CMe)_n]$ , this species may contain additional ligands such a coordinated



Scheme 2. Proposed mechanism for the catalytic C–C bond cleavage of 2methylcyclohexanone by ruthenium (III/II) systems.

water. The reaction starts with the coordination of the enol to produce the enolate (I). The "free proton" and one-electron transfer from the carbon atom to the ruthenium moieties give rise to the formation of (II) which is a ruthenium (II) donor–acceptor complex. Proton transfer occurs through deprotonation–protonation with participation of protic solvent, substrate or water. There is an unpaired electron on the organic ligand; in the presence of dioxygen (II) would react with  $O_2$ .

We assume that the peroxyl radical formed after addition of  $O_2$  to the carbon atom in (II) would add to the Ru(II) centre to form a Ru(III) peroxo-derivative (III) or (III'). In this step, a ROO<sup>•</sup> radical oxidizes Ru(II) to Ru(III). The reduction of  $O_2$  by Ru(II) complexes [40] according to:

 $2Ru(II) + 2H^+ + O_2 = 2Ru(III) + H_2O_2$ 

in aqueous acids, may be relevant to the mechanism with a ruthenium peroxo-complex, similar to that previously proposed with vanadium catalysts [6,10,42,43] (III) can decompose by homolytic fission of O–O bonds. We propose that homolytic C–C bond cleavage in (**IV**) occurs simultaneously, possibly through a six-membered transition state. After a few stages formally depicted as steps (**IV**) $\rightarrow$  (**V**), 6-oxoheptanoic is formed and the catalytic cycle is closed.

proposed А similar mechanism has been for FeCl<sub>3</sub>/O<sub>2</sub>/MeOH/cycloalkanones [44]. These reactions are reminiscent of biological oxidations catalyzed by catechol dioxygenases [10,43]. It should be noted that this type of mechanism relates to the C-C bond splitting in substituted phenols and catechols under the action of O<sub>2</sub> and catalyzed by enzymes. Thus oxidative systems based on ruthenium (III/II) complexes may be considered as biomimetic models of dioxygenases: synthetic catechol dioxygenases have also been proposed with RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> [45] (maximum turnover was about 20, but with formation of OPPh<sub>3</sub>).

#### 4. Conclusion

The above results show the formation of novel ruthenium (II) and/or (III)-dioxygen systems to promote carbon–carbon cleavage in a tentatively assigned dioxygenase mode, although some minor competing processes can occur. "Radicals are far more frequently involved in oxygenation reactions than originally assumed; in fact, they appear almost omnipresent" [46], and short-lived radicals can be transient species [10,11] for facile catalysis with appropriate substrates such as  $\alpha$ -ketols [6,7,9]. It is difficult to establish by EPR the intermediates formed in the Ru(II)/HOAc–H<sub>2</sub>O/O<sub>2</sub> catalysis system, which can involve several equilibria.

Under anaerobic conditions, there is no C–C bond cleavage of the cycloalkanones. To the best of our knowledge, there is no firm evidence for Ru(IV)-peroxide formation from  $d^6$  Ru(II) precursors, while the peroxo-bridged Ru<sup>III</sup>O<sub>2</sub>Ru<sup>III</sup> species are still to be detected [17].

Current work in our laboratory is aimed at expanding the scope and applications of this new C–C bond cleavage methodology [43] and to preparing ruthenium phosphates and [LiRuPO<sub>4</sub>], an analogue of [LiFePO<sub>4</sub>], with high specific surface area, to develop heterogeneous catalysts with site isolation, stabilized anionic species and supported  $Ru_x$  catalysts with low-leaching. What is clear from this work is that there are many ways of cleaving cycloalkanones with oxidizing agents, and that options for catalyst development are far greater than previously recognized.

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