The Palladium (II) – Catalyzed Homogeneous Oxidation of 1-Hexene

Margarita Kirova

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THE PALLADIUM (II) - CATALYZED HOMOGENEOUS OXIDATION OF 1-HEXENE

Recommended 4/14/92
(Date)

William G. Floyd
Director of Thesis
D.W. Atocum

Peter J. Hessley
Thomas K. Green

Approved May 8, 1992
(Date)

Elmer Gray
Dean of the Graduate College
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The Palladium(II)-catalyzed homogeneous oxidation of 1-hexene in methanolic medium has been studied, copper(II) chloride being used as cocatalyst. Aspects of the kinetics, mechanism and product composition were investigated in several series of oxidations involving variation of hexene concentration, oxygen partial pressure, Cu(II):Pd(II) ratio and concentration and temperature. The progress of the reaction was studied in the course of periodic sampling runs. Reaction products were identified by gas chromatography, and verified by means of GC/mass spectrometry. The expected product of 1-hexene oxidation was 2-hexanone; however, 3-hexanone occurs as a major coproduct, arising from concurrent Pd(II)-catalyzed isomerization of 1-hexene to 2-hexene. Isomerization is inhibited by excess copper(II) chloride. The overall oxidation is generally consistent with P. M. Henry's mechanism for Pd(II)-catalyzed alkene oxidations, the rate-limiting step being the \( \pi \)-to \( \sigma \)-rearrangement of the Pd(hexene) complex. The corresponding ketals (2,2-dimethoxyhexane and 3,3-dimethoxyhexane) were also found. Free hexanal was not detected in any oxidation product mixtures; when produced it was found as the dimethyl acetal. Chlorination products were not observed. A surprisingly sharp rate maximum was observed when copper(II) chloride concentration was varied. Two kinetic regions were found to occur in virtually all oxidations. An explanation is proposed for this behavior.
INTRODUCTION

A. Historical

Nearly a hundred years ago Francis Phillips\(^1\) reported that aqueous palladium(II) chloride reacts stoichiometrically with ethylene (as well as with other gases such as carbon monoxide). In the case of ethylene the products are acetaldehyde and palladium metal:

\[
\text{C}_2\text{H}_4 + \text{PdCl}_2 + \text{H}_2\text{O} \rightarrow \text{Pd}(0) + 2\text{HCl} + \text{CH}_3\text{CHO} \quad (1)
\]

A second useful reaction was reported by Camille Matignon\(^2\): noble metals such as palladium can be oxidized at ambient temperatures by molecular oxygen and aqueous hydrochloric acid. Reaction (2)

\[
\text{Pd}(0) + 2\text{HCl} + 1/2 \text{O}_2 \rightarrow \text{PdCl}_2 + \text{H}_2\text{O} \quad (2)
\]

can be seen as the sum of the oxygen oxidation of HCl catalyzed by transition metal surfaces (the old Deacon reaction):
and the oxidation of Pd(0) by molecular chlorine:

$$\text{Pd}(0) + \text{Cl}_2 \rightarrow \text{PdCl}_2$$  \hspace{1cm} (4)

In principle the combination of these reactions permits the continuous oxidation of ethylene to acetaldehyde by the combination of reactions (1) and (2). In practice, however, Matignon's experiment required several weeks to oxidize 0.23 g of Pd(0). Even with finely divided palladium metal this is a relatively slow reaction.

A German patent application filed in 1934 and issued in 1941 disclosed the third useful reaction. Copper(II) halides greatly accelerate the oxidation of Pd(0), by replacing reaction (2) with two faster reactions:

$$\text{Pd} + 2\text{CuCl}_2 \text{(aq)} \rightarrow \text{PdCl}_2 + \text{Cu}_2\text{Cl}_2$$  \hspace{1cm} (5)

$$\text{Cu}_2\text{Cl}_2 + 2\text{HCl} + 1/2 \text{O}_2 \rightarrow 2\text{CuCl}_2 + \text{H}_2\text{O}$$  \hspace{1cm} (6)

While the 1934 patent application was concerned solely with the oxidative removal of carbon monoxide, it provided a set of fast reaction steps needed for a novel catalytic oxidation of ethylene and other alkenes [reactions (1), (5)]
Twenty-five years later Juergen Schmidt, Reinhold Jira and their associates at Wackerchemie put this chemistry together and published the first of a major series of papers describing the catalytic oxidations of olefins by aqueous Pd(II)/Cu(II) systems. These reactions are popularly known as Wacker oxidations, and in their most familiar embodiment convert ethylene to acetaldehyde and higher α-olefins to methyl ketones, by the reaction scheme summarized below (using propylene as an example):

\[
\text{CH}_3\text{-CH} = \text{CH}_2 + \text{PdCl}_2 + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{-CO-CH}_3 + \text{Pd}(0) + 2\text{HCl} \quad (7)
\]

\[
\text{Pd}(0) + 2\text{CuCl}_2 \rightarrow \text{PdCl}_2 + \text{Cu}_2\text{Cl}_2 \quad (8)
\]

\[
\text{Cu}_2\text{Cl}_2 + 2\text{HCl} + 1/2 \text{O}_2 \rightarrow 2\text{CuCl}_2 + \text{H}_2\text{O} \quad (9)
\]

Summing these reactions:

\[
\text{CH}_3\text{-CH} = \text{CH}_2 + 1/2 \text{O}_2 \rightarrow \text{CH}_3\text{-CO-CH}_3 \quad (10)
\]

This chemistry has been shown to be applicable to a great many olefinic compounds, and under various conditions to lead to the preparation of a variety of products, often with useful conversions and selectivities. Since the overall reaction uses a very inexpensive oxidizing agent, molecular oxygen, to convert an organic chemical of relatively low value to a more valuable product, this class of reactions is of considerable
potential synthetic value.

The palladium(II)-olefin reactions studied in the past three decades have been carried out mainly in aqueous or glacial acetic acid systems, the latter following a different course and producing vinyl acetates. Some prior work has been done in alcoholic media, and will be reviewed later.

1. Aqueous Systems

(a) Syntheses. In aqueous systems commercial interest has focused upon the conversion of ethylene to acetaldehyde, and to a lesser extent upon the conversion of propylene and butenes to acetone and butanone. These reactions are sluggish at near-ambient temperature. Most synthetic work is carried out at temperatures of 60-140°C.

The concentration of PdCl₂ may be as low as 0.0005 M for kinetic studies, but is typically in the range 0.005-0.050 M in synthetic applications. When the reoxidation steps are fast and palladium is substantially maintained as Pd(II), overall rates are reported to be proportional to both alkene and palladium(II) chloride concentrations. Under these conditions pseudo-first-order rates at 25°C are in the range 0.01-0.1 min⁻¹. Various reoxidant salts have been used, the original CuCl₂ being the most common. Reoxidant concentra-
tions in the range 0.5-1.0 M are common, though both lower and higher concentrations are found. Other reoxidants used include FeCl₃⁷, benzoquinone⁷,₁³, H₆PMo₆V₆O₄₀ and a number of other heteropolyacids¹⁴,¹⁶, tert-butyl hydroperoxide and other alkyl hydroperoxides¹⁷,¹₈, H₂O₂¹⁹,₂₀, acetoin and benzil²¹.

Most applications of this reaction are 'one-pot', in which both alkene and oxygen are introduced and reactions (7)-(9) occur simultaneously. Under favorable conditions the reoxidant concentration can be dropped to 0.1 M or less without slowing the overall reaction. The 'two-pot' reaction avoids the potentially explosive olefin-oxygen mixture by reacting the olefin in one vessel, and continuously regenerating the reoxidant with oxygen in a separate vessel. In some of these applications the reoxidant concentration is as high as 1.5 M.

There have been two principal constraints to the commercialization of Wacker chemistry: the working liquid phase (typically PdCl₂ and CuCl₂ in acidified aqueous solution) is very corrosive, and the reaction produces unwanted byproducts in the form of chlorinated organics. The chlorination is not discussed mechanistically. It seems likely to be an oxidative chlorination by CuCl₂ of the enol forms of the carbonyl compound(s) formed in the main reaction.
High yields of the unwanted 3-chloro-2-butanone from reaction of butenes under Wacker conditions can be related primarily to two reaction variables: copper(II) chloride concentration and reaction temperature. Chlorobutanone yields from eleven oxidations of butylenes at 96-140°C range from 2% to 70% of total carbonyl products. The three worst cases (producing 40-70% of 3-chloro-2-butanone) entail reaction temperatures well above 100°C and/or CuCl₂ concentrations greater than 1.0 M. Conversely, the three best cases in this set (producing 2-6% 3-chlorobutanone) entail temperatures below 100°C and CuCl₂ concentrations of 0.7-0.9 M. Obviously, chlorobutanone formation can be further suppressed by carrying out the reaction at lower temperatures and/or by using less CuCl₂ or an alternative reoxidant, such as benzoquinone.

Oxidation runs affording high selectivities for the desired carbonyl compound and low amounts of α-chlorocarbonyl byproducts have indeed been made. Propylene reacted at 20°C with no CuCl₂ present gives 95% acetone. Ethylene reacts at 80°C with 0.43 M CuCl₂ present to provide acetaldehyde with a selectivity of 95%. Ethylene reacts at 95°C with aqueous PdSO₄ and Fe₂(SO₄)₃ to give acetaldehyde with 97% selectivity. Ethylene reacts with aqueous PdCl₂ and a heteropolyacid replacing the copper(II) salt, to give 96% selectivity for acetaldehyde. With a slightly better heteropolyacid, H₇PMo₇V₆O₄₀, the selectivity is 97%. The remaining 3-4% is
mostly acetic acid. The highest reported acetaldehyde selectivity, 99.1%, appearing in a Mitsubishi patent, was obtained in a reaction at 60°C with 0.90 M CuCl₂, 0.8 M HOAc and 0.3 M Zn(OAc)₂ added expressly to reduce chlorinated byproducts. Only 0.5% of chlorinated acetaldehydes were formed. (In a parallel run with ZnCl₂ replacing Zn(OAc)₂ the yield of chlorinated acetaldehydes was 1.1%.)

While the oxidation of ethylene can produce only one carbonyl compound, most higher alkenes can produce at least two products, depending upon the orientation of the oxidative attack upon the carbon-carbon double bond. For simple α-olefins the two possible products are the methyl ketone and the aldehyde:

\[
R-\text{CH} = \text{CH}_2 + \frac{1}{2} \text{O}_2 \rightarrow R-\text{CO-CH}_3 \quad (11)
\]

\[
R-\text{CH} = \text{CH}_2 + \frac{1}{2} \text{O}_2 \rightarrow R-\text{CH}_2\text{CHO} \quad (12)
\]

When R is an alkyl group, or an aromatic ring with electron-donating substituents, reaction (11) predominates and typically accounts for 92-98% of the primary products. When R is an electron-withdrawing group, such as nitrile, or an aromatic ring with electron-withdrawing substituents, reaction (12) predominates.
In addition, higher olefins are likely to undergo significant isomerization under these conditions. All three linear butenes produce 2-butanone, along with small amounts of butyraldehyde. But 1-pentene is partly isomerized to 2-pentene by Pd(II) prior to reaction, and the resulting mixture of pentenes produces both 2- and 3-pentanone along with a small amount of pentanal. A few Wacker oxidations of higher alkenes have been reported to produce substantially a single product in high yield. For example, 4-methyl-1-pentene is converted to 4-methyl-2-pentanone with 91% selectivity\(^\text{27}\). This unusually high selectivity probably reflects factors which disfavor either the isomerization to the 2-pentene or (more likely) oxidation at the hindered C\(_3\) site. Palladium(II) under these conditions does not catalyze skeletal isomerizations.

In order to undergo Wacker oxidation, an alkene must have at least one hydrogen atom attached to each of the olefinic carbon atoms. While 4-methyl-1-pentene reacts readily, 2-methyl-1-pentene is unreactive. This unreactivity of 2-substituted 1-alkenes can be an advantage. The crude C\(_4\) fraction, containing all four butene isomers, reacts to produce essentially just one product, 2-butanone. Isobutylene passes through unreacted, along with any butane impurities.

(b). Palladium(II)-Chloride Equilibria. Chloride ion in
aqueous solutions strongly coordinates with palladium(II). The formation constants at 20-30°C have been reviewed by Aguilo. The value for the formation constant for the \( \text{PdCl}_4^{2-} \) species in the equilibrium:

\[
\text{PdCl}_3^{+} + \text{Cl}^- = \text{PdCl}_4^{2-}
\]

was found to be 63.1 L mol\(^{-1}\). The values for the corresponding formation constants for \( \text{PdCl}_3(\text{H}_2\text{O})^+ \), \( \text{PdCl}_2(\text{H}_2\text{O})_2^- \), and \( \text{PdCl}(\text{H}_2\text{O})_3^- \) are approximately 269, \( 7.08 \times 10^3 \), and \( 9.12 \times 10^5 \) L mol\(^{-1}\), respectively. There is virtually no cationic palladium(II) at free chloride ion concentrations above 0.010 M. At free chloride ion concentrations of 0.3 M and higher the palladium (II) is entirely anionic and nearly all in the \( \text{PdCl}_4^{2-} \) form.

For most traditional Wacker systems the reoxidant is a chloride salt of Cu(II) or Fe(III) and is typically present at 0.5-1.0 M. Copper and iron are both appreciably more electronegative than palladium, and their chloride salts in solution are good donors of chloride ion. Under typical Wacker conditions there exists a free chloride ion concentration of at least several tenths of a mole per liter. In the kinetic examinations of these oxidations, therefore, the initial dissolved palladium catalyst is believed to be in the form of the tetrachloropalladate(II) anion, \( \text{PdCl}_4^{2-} \).
(c) Kinetics. Aqueous reaction kinetics has been studied by three research groups: the Wackerchemie group noted above, a group led by I. I. Moiseev and M. N. Vargaftik at the Lomonosov Institute in Moscow, and a group led by Patrick M. Henry, now at Loyola University (Chicago).

For the oxidations of ethylene, propylene and the three linear butenes the overall kinetics follow the rate law:

\[ -\frac{d([\text{en}])}{dt} = k\frac{[\text{PdCl}_4^2^-][\text{en}]}{([\text{Cl}^-]^2[H_2O^-])} \]  \hspace{1cm} (14)

where [en] indicates olefin concentration. There are several qualifications to be noted regarding this expression:

1. The quotient \([\text{PdCl}_4^2^-]/[\text{Cl}^-]^2\) is equivalent to \(K_4[\text{PdCl}_3^-]/[\text{Cl}^-]\) and to \(K_3K_4[\text{PdCl}_2^-]\). Therefore these kinetics alone are not evidence that the tetrachloropalladate(II) anion is the reactive species.

2. In the presence of a substantial excess of chloride ion, Dozono and Shiba found departures from the above kinetics:

\[ -\frac{d([\text{en}])}{dt} = k\frac{[\text{PdCl}_2^-][\text{en}]/([\text{Cl}^-]^2[H_2O^-])} \]  \hspace{1cm} (15)
Under these conditions the extent of chlorination of Pd(II) is indeterminate.

(3) With quinone as the reoxidant and at a constant low chloride ion level, the observed kinetics are found to be simply:¹⁴,⁵⁰,⁵¹:

\[
-d(\text{en})/dt = k*[\text{Pd(II)}]*[\text{en}]
\]  

(16)

(4) Kolb and his coworkers¹³ report that the inverse square root dependency upon [Cl⁻] (equation 15) is true only when the H₃O⁺ concentration is greater than 0.6 M. At lower concentrations the oxidation rate is more nearly proportional to [Cl⁻]⁻¹.⁵. They also find that the inverse dependency upon [H₃O⁺] varies with both the alkene reactant and the hydronium ion concentration.

(5) All of these rate observations appear to have been made under conditions of fast reoxidation: in the system of reactions (1)-(5)-(6) the slow and rate determining step is always reaction (1). Under conditions of less efficient reoxidation it is evident that reoxidant species, dissolved oxygen concentration or oxygen partial pressure will necessarily enter into the overall kinetics.

(d) Mechanism. Palladium (II) has an electron
configuration $4d^8$ $5s^0$ and readily forms $d_{sp^2}$ square-planar complexes of coordination number 4. Moiseev suggested that alkenes dissolve in aqueous $\text{PdCl}_2$ solutions to form $\pi$-complexes, initially $\text{Pd(en)}\text{Cl}_3^-$, which in turn hydrolyze to $\text{Pd(en)}(\text{H}_2\text{O})\text{Cl}_2$\textsuperscript{8-10,32,33}. Much later the accurate measurement of dissolved olefinic gases in $\text{Pd(II)}$ salt solutions showed the actual existence of these 1:1 Pd-olefin complexes\textsuperscript{55}.

The following mechanism, developed by Henry\textsuperscript{11,12,40-42} is now generally accepted:

\[ \text{C}_2\text{H}_4(\text{aq}) + \text{PdCl}_4^{2-} \rightarrow (\text{C}_2\text{H}_4)\text{PdCl}_3^- + \text{Cl}^- \]  
(17)

\[ (\text{C}_2\text{H}_4)\text{PdCl}_3^- + \text{H}_2\text{O} \rightarrow (\text{C}_2\text{H}_4)\text{Pd(H}_2\text{O})\text{Cl}_2^- + \text{Cl}^- \]  
(18)

\[ (\text{C}_2\text{H}_4)\text{Pd(H}_2\text{O})\text{Cl}_2^- + \text{H}_2\text{O} \rightarrow (\text{C}_2\text{H}_4)\text{Pd(OH)}\text{Cl}_2^- + \text{H}_3\text{O}^+ \]  
(19)

\[ (\text{C}_2\text{H}_4)\text{Pd(OH)}\text{Cl}_2^- \rightarrow \text{ClPdCH}_2\text{CH}_2\text{OH} + \text{Cl}^- \]  
(20)

\[ \text{ClPdCH}_2\text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{CHO} + \text{Pd} + \text{HCl} \]  
(21)

In this scheme reactions (17), (18), (19) and (21) are fast, while reaction (20), the rearrangement from $\pi$-complex to $\sigma$-complex, is the slow and rate-determining step.

This mechanism not only supports the kinetics of
equation (15) but it is also consistent with the following observations:

(1) With perdeuterated ethylene, \( C_2D_4 \), only a secondary isotope effect is observed \([K_H/K_0 = 1.07]\). Thus the rate-determining step must not be the one in which C-H bond cleavage occurs.

(2) From this experiment with perdeuterated ethylene and others using \( D_2O \) it has been shown that all of the hydrogen atoms of the product come from the alkene. None come from the water. [This is consistent with equations (20) and (21)].

(3) Equations (17) and (18) account for chloride ion inhibition, and equations (19) and (21) for proton inhibition.

The details of the \( \pi \)-to-\( \sigma \)-complex transformation have been clarified by a study of the reaction of \( \text{cis-1,2-dideuterioethylene} \), in which the intermediate product was intercepted by carbon monoxide to form a \( \beta \)-propiolactone\(^{48} \). Isolation of \( \text{trans-2,3-dideuteriopropiolactone} \) showed that the hydroxypalladation step [reaction (20)] is stereospecifically anti, with the hydroxylating atoms coming from a water molecule outside of the Pd(II) coordination sphere.

The apparent stercrochemistry of reactions (20) and (21)
is shown in Chart 1. Reaction (20), the hydroxypalladation step, is the rate-limiting step. In the $\pi$-to-$\sigma$ conversion, the addition is anti, as required by the results of the dideuterioethylene experiment$^{48}$. As the olefin's $\pi$-electron pair shifts to enter into a $\sigma$-bond with palladium, the carbon which is left with a developing positive charge is the one best able to delocalize such a charge. This correctly predicts the predominant formation of methyl ketones from 1-alkenes, and the predominant formation of aldehydes from ethylenes and styrenes substituted with electron-withdrawing groups.

This mechanism specifies a nucleophilic attack upon the $\pi$-coordinated alkene. Alkenes are generally not very susceptible to nucleophilic attack. However, coordination entails the overlap of $\pi$-electron density with the empty $\text{dsp}^2$ orbital of Pd(II), resulting in a decrease in electron density between the olefinic carbon atoms, thereby rendering the complexed alkene much more susceptible to nucleophilic attack than would be the case for a free alkene molecule.

(e) Possible Side Reactions. The chlorination side-reaction noted above is probably a consequence of the well-known susceptibility of the enol form of methyl ketones to electrophilic attack:
\[
\text{RC(OH)CH}_2 = \text{CH}_2 + \text{Cl} \ldots \text{Cu}_2\text{Cl}_3 \rightarrow \text{RC(OH)CH}_2\text{Cl} \quad (22)
\]

\[
\text{RC(OH)CH}_2\text{Cl} + \text{H}_2\text{O} \rightarrow \text{RCOCH}_2\text{Cl} + \text{H}_3\text{O}^+ \quad (23)
\]

Under these generally acidic conditions another anticipated side-reaction is olefin hydration:

\[
\text{RCH} = \text{CH}_2 + \text{H}_2\text{O} \rightarrow \text{RCH(OH)CH}_3 \quad (24)
\]

This evidently is not an important source of byproducts; it is not mentioned in the major papers reviewed.

All of the aldehyde byproducts produced from terminal olefins by reaction (12) will necessarily have \(\alpha\)-hydrogen atoms, and can be expected to undergo further oxidation to carboxylic acids and possibly acid-catalyzed aldol condensation reactions.  

In addition, if free radical autoxidation can take place in the reactor, the propagation chain for aldehydes will produce peracids, which react with free aldehydes to produce carboxylic acids, but also could react with the olefin [the Prilezhayev reaction\(^{49}\)] to produce epoxide. This product in acidic aqueous medium would be likely to undergo ring-opening to produce a glycol and possibly chlorohydrin(s).
2. Alcoholic Systems

(a) Synthesis. It was first shown in 1960 by Moiseev and his coworkers that Pd-complexed ethylene reacts readily with ethanol to produce acetaldehyde diethyl acetal and metallic palladium. In the presence of a reoxidant such as CuCl₂ or benzoquinone this becomes a catalytic process:

\[ C_2H_4 + 2ROH + 2C_6H_4O_2 \rightarrow CH_3CHO(OR)_2 + C_{12}H_{10}O_4 \]  \hspace{1cm} (25)

where \( C_{12}H_{10}O_4 \) is quinhydrone, which in the presence of oxygen is readily oxidized to regenerate benzoquinone:

\[ C_{12}H_{10}O_4 + \frac{1}{2} O_2 \rightarrow 2C_6H_4O_2 + H_2O \]  \hspace{1cm} (26)

The water formed in reaction (26) is removable as the ethanol-benzene-water ternary azeotrope. A twenty-minute reaction of ethylene (initially at 350 psi) with oxygen (20 psi) and ethanol containing per liter 1.67 g PdCl₂, 20 g CuCl₂ and 8.33 g concentrated HCl, at 127° yields after cooling and neutralization:

acetaldehyde and its acetal \hspace{1cm} 80.8 %
butenes \hspace{1cm} 10.9 %
acrolein \hspace{1cm} 4.0 %
ethyl acetate \hspace{1cm} 3.0 %
A representative group of synthetic reactions in alcoholic media are noted below:

A mixture of 25 mL 1-octene, 25 mL methanol, 1 mL p-cresol, 1 mg-mole PdCl₂ and 5 mg-mole CuCl₂·2H₂O was shaken under 3 atm. oxygen at 50° for 120 min, to afford an octene conversion of 81.4 % and an octanone selectivity of 98.5 %53,54.

When 1,4-Butanediol containing 0.028 M PdCl₂ and 0.586 M CuCl₂ was stirred for 40 min at 50°, initially under 300 psig of a 2:1 ethylene:oxygen mixture, a trace of free acetaldehyde was found, with a 99% selectivity for the cyclic acetal 2-methyl-1,3-dioxepane.21

Ethanolic solutions of PdCl₂, BiCl₃ and LiCl have been used for the oxidation of 2-octene to yield 2-octanone (selectivity 57%).56

Cyclopentene was reacted for 120 min at 50° with ethanolic PdCl₂ (0.020 M) and CuCl₂ (0.100 M) and under slightly superatmospheric oxygen pressure, providing a 98 % conversion with a 70 % selectivity for cyclopentanone56. A parallel run under 5 atm oxygen pressure provided a conversion of 99 % and selectivity of 96.8 %. Cyclohexene is less
reactive. With ethanolic PdCl$_2$ (0.020 M) and CuCl$_2$ (0.100 M) at 60° for 120 min, cyclohexene undergoes a 27% conversion with a selectivity for cyclohexanone of 74%.

In summary, in most cases of oxidations of higher alkenes with alcoholic PdCl$_2$ and CuCl$_2$, the free carbonyl compound is the principal product.

(b) Acetal and Ketal Equilibria. Aldehydes and most ketones undergo a rapid reversible reaction with alcohols under acidic conditions to form acetalts or ketals:

$$\text{RCHO} + 2\text{R'OH} \rightleftharpoons \text{RCH(OR')$_2$} + \text{H}_2\text{O}$$

When the concentrations of the components of this equilibrium expression are expressed in mole fractions, a dimensionless equilibrium constant $K_{(27)}$ can be used.

For monohydric alcohols this can be expressed as:

$$K_{(27)} = \frac{[\text{RCH(OR')$_2$}] \times [\text{H}_2\text{O}]}{[\text{RCHO}] \times [\text{R'OH}]^2}$$

Homer Adkins and his associates have made careful measurements of the values of $K_{(27)}$ for various combinations of aldehyde and alcohol$^{57,58}$. With an unhindered aldehyde and a primary alcohol, $K_{(27)}$ values at 25° fall between 1 and 6. $^{58}$ With
secondary alcohols $K_{(27)}$ is closer to 0.1, and with tert-butyl alcohol $K_{(27)}$ values are considerably smaller. Adkins' value for $\pi$-butyraldehyde $\pi$-butyl acetal is 1.2$^{58}$, while calculations from Lloyd's data give a value of 0.85$^{59}$, in reasonably good agreement.

Ketones react to give the corresponding ketals:

$$
\text{RCOR} + 2\text{R'OH} \rightarrow \text{R}_2\text{C(OR')}_2 + \text{H}_2\text{O}
$$

(29)

However, most ketals are destabilized by steric crowding, and consequently the corresponding equilibrium constants are much smaller. Thus mixtures of methyl ethyl ketone in substantially dry 1-butanol might be expected to form 2-butanone di(n-butyl) ketal, but in practice the species observed is the free ketone$^{21,59}$.

When the monohydric alcohol is replaced by a dihydric or polyhydric alcohol, especially one with alcoholic groups in vicinal or homovicinal positions, unstrained 1,3-dioxolanes or 1,3-dioxanes are formed. These cyclic acetals are quite stable; the equilibrium constants for cyclic acetal formation are greater by two or more orders of magnitude than those for the corresponding acyclic acetals. Equations (30) shows that the major product of oxidation of ethylene in ethylene glycol
to be 2-methyl-1,3-dioxolane, which is exactly what is found.

\[
\begin{align*}
\text{CH}_2\text{-OH} & + \text{C}_2\text{H}_4 + 1/2 \text{O}_2 \rightarrow \text{H}_2\text{O} + \text{CH}_2\text{-O}\text{-CH-CH}_3 \\
\text{CH}_2\text{-OH} & + \text{C}_2\text{H}_4 + 1/2 \text{O}_2 \rightarrow \text{H}_2\text{O} + \text{CH}_2\text{-O}\text{-CH-CH}_3
\end{align*}
\tag{30}
\]

Styrene in ethylene glycol yields chiefly 2-benzyl-1,3-dioxolane, a pleasant odorant ('odor of roses')\textsuperscript{60,70}. When 1-octene is warmed in 1,3-propanediol with PdCl\textsubscript{2} the reaction mixture contains both the expected 2-octanone and the cyclic ketal 2-n-hexyl-2-methyl-1,3-dioxane. Surprisingly, in view of the low yields of seven-membered ring compounds from other procedures, 1,4-butanediol when reacted with ethylene and PdCl\textsubscript{2} yields only a trace of free acetaldehyde along with a substantial amount of 2-methyl-1,3-dioxepane\textsuperscript{60}.

Glycerin can react to form both five-membered and six-membered rings, and with formaldehyde produces both 4-methyloldioxolane and 5-hydroxy-1,3-dioxane\textsuperscript{61}. The presence of a substituent at the 2-position on the ring, as would be found in the acetalization of acetaldehyde and higher aldehydes with glycerin, causes the dioxolane ring structure to be favored. The presence of two substituents at the 2-position on the ring, as would be found in the ketalization of acetone by glycerin, very strongly favors the dioxolane ring\textsuperscript{62-65}. Indeed, the oxidation of 1-hexene in glycerin,
thinned with methanol (in order to improve the mass transfer), yields not only 2-hexanone but also and principally 2-\(n\)-butyl-2-methyl-1,3-dioxolane-4-methanol. Similarly, oxidation of propylene in glycerin yields mainly 2,2-dimethyl-1,3-dioxolane-4-methanol\(^6\), marketed in Europe as a special-purpose solvent under the name 'Solketal'.

In summary, ethylene, styrene and negatively substituted ethylenes such as acrylonitrile react in alcohols to give mainly acetals. With monohydric alcohols, higher alkenes produce mainly the corresponding ketones, although under rigorously anhydrous conditions (which include abstraction of the water of reaction) good yields of ketals can be achieved. With dihydric and polyhydric alcohols the corresponding cyclic acetals and ketals (the 2-substituted 1,3-dioxolanes and 1,3-dioxanes) are easily formed. They are quite stable and are usually the principal observed products.

(c) Kinetics and Mechanism. Methanol, ethanol, ethylene glycol and the propanols lie between water and acetic acid with regard to dielectric constant. Reactivity in light alcoholic media should therefore be not entirely dissimilar from that in aqueous systems. Henry considers methanol sufficiently polar to stabilize by solvation the monomeric species of \(\text{Pd}(\text{II})\), as is the case in Wacker chemistry\(^6\). While
much is still not known about the Pd(II) –Cl' equilibria in methanol, Lee and Henry\textsuperscript{78} have shown that in methanol at 25\(^\circ\) and at chloride concentration greater than 0.1 M, the principal Pd(II) species is PdCl\textsubscript{4}\textsuperscript{2-}.

Factors Affecting Rate. Lee and Henry reported that, for the oxidation of ethylene in methanol, reaction rate increases with ionic strength up to a value of about 0.75, then falls off moderately at still higher ionic strengths\textsuperscript{12,78}. In the oxidation of cyclopentene to cyclopentanone, Takehira reports that the rate increases with increasing [Cl']\textsuperscript{56}, although the consensus from Moiseev\textsuperscript{8}, François\textsuperscript{68} and Henry\textsuperscript{66} is that Cl. retards oxidation rates.

Oxygen partial pressure is sometimes rate-limiting. Takehira, however, reports a surprising effect in cyclopentene oxidations. Under conditions such that alkene conversion is 98-99\% (50\(^\circ\) for 120 min with CuCl\textsubscript{2} co-oxidant), increasing the oxygen pressure from 115 to 490 kPa raises the selectivity from 70 \% to 96.8 \%\textsuperscript{56}.

Primary alcohols are the most conducive to reaction, while tertiary alcohols are the least. With isopropyl and other secondary alcohols and Pd(II)/Cu(II) catalysis the selectivity for cycloalkene to cycloalkanone is also unfavorably affected\textsuperscript{56}. The presence of \(\alpha\)-branching of the
alcohol seems to be disadvantageous. Other factors being equal, most workers use the lower molecular weight alcohols. From a process viewpoint, however, it is usually advantageous to be able to distill the reaction product from the solvent-catalyst system. With this in mind, the use of diols such as ethylene glycol or propylene glycol may be convenient.

Water (CuCl₂ hydration water included) generally retards alcohol-based reactions. Takehiri found that even 2% added water depresses cyclopentene oxidation rates and conversions. This is also true for cyclohexene and other alkenes.

The size of the alkene reactant also influences rate. Vojtko et al. studied oxidation rates of the homologous series of 1-alkenes with PdCl₂ and HCl in aqueous 2-methoxyethanol, observing between C₇ and C₁₃ a smooth asymptotic decrease in rate with alkene molecular weight.

The ratio [CuCl₂]:[PdCl₂] at constant [Pd(II)] was studied in the range 0 to 1.0, in the course of a detailed examination of cyclopentene oxidation in ethanol. At 30° the reaction rate and the amount of ketone formed after four hours both increase sharply in the range 0.0 - 0.1, then show only a gradual further increase (about another 15%) as the ratio is increased from 0.1 to 1.0. Selectivity improves from 90% to 99+ % as that ratio increases. Oxygen consumption is flat
above a ratio of about 0.05. [Oxygen consumption stoichiometrically is 0.5 mole per mole of ketone or ketal product].

Takehira's group made a careful examination of FeCl₃ as a candidate reoxidant, vs. the more widely used CuCl₂. The results are unexpected and are not easily explained:

In cyclopentene oxidations, secondary alcohols result in slower reaction rates. However, with FeCl₃ the selectivity is also lower than with CuCl₂.

When water is added the oxidation rate is decreased. With FeCl₃ the selectivity is also depressed, while with CuCl₂ it is improved.

When oxygen pressure is increased from 1 to 5 atm., with FeCl₃ selectivity decreases from 99% to 75%, while with CuCl₂ it increases from 70% to 97%.

With cyclohexene oxidations, CuCl₂ affords a higher oxidation rate and a higher selectivity than FeCl₃ under identical conditions.

Takehira infers that there is a different primary oxidation mechanism operating with these two reoxidants.
Addition of a Lewis base (dimethylacetamide or N,N'-dimethylimidazolidinone) to ethanolic cyclohexene increases the overall reaction rate, but specifically increases secondary oxidation of cyclohexanone, leading to lower overall selectivity. This may be due to base promotion of the cyclohexanone enolization rate, as the enol tautomer is a likely starting point for secondary reactions\(^7\).

Coproducts and By-products. A few workers have carried out careful analyses of minor products formed along with the predominant acetals, ketals or ketones.

In the oxidation of ethylene in methanolic solutions of PdCl\(_2\), CuCl\(_2\) and HCl, heated to 127°, Schaeffer\(^5^2\) found in addition to acetaldehyde and its acetal (84.1 mole %) the following: methylal 4.0 %, butenes 3.9 %, methyl acetate 2.9 %, methyl formate 2.3 %, methyl ether 1.8 % and methyl vinyl ether 1.7 %. The methylal and methyl formate represent oxidation of the alcohol, not surprising at elevated temperatures\(^5^9\), and the methyl vinyl ether is the expected elimination coproduct of the acetal at high temperatures. However, the formation of 4 % butenes shows the presence of a quite different reaction, oxidative dimerization, while the presence of 3 % methyl acetate shows significant secondary oxidation of CH\(_3\)CHO.
Regarding the relationship of the dimethyl acetal and methyl vinyl ether, an opposite construction has been placed by François. His experiments with deuterated compounds led him to the conclusion that the vinyl ether is formed first. Another molecule of methanol then adds, according to this view, to form the acetal.

Ketley and Fisher conducted an interesting series of reactions with di-μ-chloro-dichlorobis(ethylene)palladium (I) under anaerobic conditions at room temperature.

\[
\begin{array}{c}
\text{(en)} \quad \text{Cl} \quad \text{Cl} \\
\text{Pd} \quad \text{Pd} \\
\text{Cl} \quad \text{Cl} \quad \text{(en)} \\
\end{array}
\]  

(I)

With methanol the major products are the expected acetaldehyde and acetal, along with about 1% chloromethane. With ethanol the products are similar, with the addition of 3% ethyl ether (shown by 14C isotope analysis to come from the alcohol). With tert-butyl alcohol a mixture was obtained, including 16% acetaldehyde and substantial alcohol products: 25% isobutylene and 20% tert-butyl chloride. This study reinforces the desirability of using primary alcohols as reaction media.
The oxidation of 1-octene in 1-propanol with PdCl$_2$ and CuCl$_2$ at 30°, 60° and 90° afforded octanone yields of 89%, 80% and 73% respectively$^{67}$. Coproducts were not identified. Pd(II) also catalyzes nonskeletal isomerization of alkenes. The yields, therefore, are mixtures of all three n-octanones. Distribution is as follows:

<table>
<thead>
<tr>
<th></th>
<th>2-octanone</th>
<th>3-octanone</th>
<th>4-octanone</th>
</tr>
</thead>
<tbody>
<tr>
<td>at 30°</td>
<td>98%</td>
<td>1.7%</td>
<td>trace</td>
</tr>
<tr>
<td>at 60°</td>
<td>85%</td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>at 90°</td>
<td>62%</td>
<td>25%</td>
<td>14%</td>
</tr>
</tbody>
</table>

The extent of alkene isomerization is thus seen to increase quite sharply with temperature.

The oxidation of styrene in ethanol at 30° typically produces phenylacetaldehyde diethyl acetal as the major product, accompanied by free phenylacetaldehyde and acetophenone, these three components making up 70 - 80% of the product mixture$^{67}$. Oxidation coproducts formed include ethoxystyrene, ethyl phenylacetate, benzaldehyde and ethyl benzoate.$^{70}$ Minor coproducts include 1-phenylethanol from acid hydration of styrene and α-chloroacetophenone from CuCl$_2$ chlorination. Another coproduct reported is styrene dimer (1,4-diphenylbutadiene), which is also obtained in the oxidation of styrene in glacial acetic acid$^{71}$. [Under rather
different conditions, with ethanolic PdCl$_2$ containing sodium methoxide, styrene yields acetaldehyde and both 1- and 2-ethoxystyrene$^{72}$.

In the oxidation of cyclopentene to cyclopentanone with PdCl$_2$ - CuCl$_2$ at 40°, selectivities are 80 - 97% and the principal coproducts are 2-cyclopenten-1-one and 3-ethoxy-2-cyclopenten-1-one, which together with cyclopentanone account for essentially all of the reacted cyclopentene$^{56}$. Under similar conditions at 60° cyclohexene is oxidized more slowly, with selectivities to cyclohexanone of about 70%. The main co-products are the corresponding 2-cyclohexen-1-one and 3-ethoxy-2-cyclohexen-1-one$^7$.

In summary, the co-products of alkene oxidations are mainly the following:

**Products of Further Oxidation** of the primary reaction product: esters from aldehyde products, products of oxidative dehydration of cycloalkanones (2-en-1-ones), and secondary oxidation products of cycloalkenones (3-alkoxy-2-en-1-ones) and of phenylacetaldehydes (benzaldehydes). Also, rarely, oxidative dimerization is observed, mainly in acetic acid medium.

**Alcohol Oxidation Products**, becoming more important at
high temperatures: to the corresponding acetal (dimethyl formal from methanol), and some further oxidation to the ester, especially when moisture is present to provide free aldehyde.

**Oxidative Chlorination Products**, from attack upon carbonyl compounds with available α-hydrogens, especially a problem for systems with high concentrations of $\text{CuCl}_2$. Rarely, under severe conditions, the alcohol solvent may undergo a non-oxidative substitution to produce an alkyl chloride.

**Elimination products**, e.g., alcohol elimination from acetal to produce vinyl ethers, acid catalyzed alcohol dehydration to produce ethers, and acid-catalyzed dehydration to produce alcohol-derived alkenes from tert-alkanols.

**Olefin Solvation Products**, especially olefin hydration when free mineral acid and water are present. With a highly polar solvent (ethylene glycol) and an olefin capable of forming a highly resonance-stabilized carbocation (e.g., styrene, forming the α-methylbenzyl cation), olefin solvation product may be significant. The corresponding electrophilic addition of an alcohol to an alkene is not known under these conditions.
Isomerization of a linear alkene reactant, with the resulting formation of mixed ketone position isomers (discussed above). Since the same Pd(II) ions which can bring about oxypalladation of linear olefins will also isomerize them, it is difficult to prepare pure 2-alkanones from higher linear α-olefins. The data available concerning the dependence of isomerization on temperature suggest that synthesis at the lowest feasible temperature may be the best approach for the preparation of nearly pure 2-alkanones.

There is relatively little solid mechanistic information for alcohol-based Pd-alkene oxidation systems. On the basis of kinetic analysis the species undergoing the rate-limiting reaction (for ethylene in methanol) is believed\textsuperscript{12,66} to start with the formation of an anionic π-complex:

\[
\begin{array}{c}
\text{Cl} \\
\text{Pd}(-) \\
\text{Cl} \quad \text{(II)} \\
\text{OMe}
\end{array}
\]

where (II) is a π-complexed anion in equilibrium with other Pd(II) species. Henry proposes the slow step to be a cis-attack from the MeO\textsuperscript{−} ligand, to form (III), which then undergoes a Pd-mediated internal hydride shift (as required by the deuterium isotope data), to form (IV) and then (V):
Intermediate (V) is then solvolyzed by methanol to yield the acetal and Pd(0).

The rate determining $\sigma$-complex formation (III from II) can also be viewed as a step facilitated by both solvent and chloride ligand:

$$\text{Cl} \quad \text{Cl} \quad \text{Cl}$$
$$\downarrow \quad \downarrow \quad \downarrow$$
$$\text{Pd} \quad \text{H-Pd} \quad \text{Pd}$$
$$\text{Cl} \quad \text{Cl} \quad \text{Cl}$$

No other alternatives for the mechanism of this reaction have been presented in the literature reviewed.
EXPERIMENTAL

The Pd(II) catalyzed oxidation of 1-hexene was carried out in an apparatus, the schematic diagram of which is shown in Figure 1. Methanolic solutions were reacted under oxygen in a 500-ml round bottom flask immersed in a temperature-controlled bath (H) (average standard deviation of temperature over a 300 minute run was 0.12°). The flask was agitated by a 17 x 40 mm teflon clad magnetic ellipsoid driven by a 'Jumbo' magnetic stirrer (I) at 500 r.p.m. Prior to introducing the reagents in the flask, the latter was evacuated by a vacuum pump (F) and filled with 1 atm of pure oxygen from an oxygen cylinder (E), delivered into the flask by means of an oxygen reservoir bag (D). The pressure was measured in millibars by a digital pressure meter (A) and by a pressure transducer (B) the output of which was recorded continuously on a strip chart recorder for the 300-minute oxidation runs. The temperature was also recorded continuously and simultaneously by the same recorder. Each oxidation was commenced by charging the oxygen-filled flask with 25 mL of catalyst solution, followed by 25 mL of 1-hexene solution containing the internal standard chlorobenzene.
Figure 1

Oxidation Apparatus

A  Digital pressure gauge
B  to Vacuum ballast vessel
C  to Pressure transducer and recorder
D  to Oxygen ballast bag
E  to Oxygen cylinder
F  to Vacuum pump
G  Pressure-compensated addition funnel
H  Constant temperature bath
I  Jumbo magnetic stirrer
At the conclusion of each oxidation a portion of the product mixture was stabilized by combining 5 mL of the mixture with 2 to 5 mL of ammoniacal methanol (made up from three volumes of methanol per volume of concentrated aqueous ammonia). This mixture dissolves both Cu(II) and Pd(II) as inactive complexes and also stabilizes any acetals and/or ketals. The stabilized solution is saved for subsequent analyses.

Reaction products were identified by two methods. Routine analysis of all oxidation runs was carried out by gas chromatographic (GC) analysis, using a 3% OV-11 [poly(methyl-phenylsiloxane)] stationary phase on 80/100 mesh Supelcoport, packed in a 2m x 2 mm glass column, using a flame ionization detector, at 60°C isothermally. All oxidation mixtures contained chlorobenzene as an internal standard, and the retention times of all GC peaks were converted to relative retention times (r.r.t.). Figure 2 shows a typical gas chromatogram of a hexene oxidation product mixture. Authentic samples of 2- and 3-hexanone and their dimethyl ketals, and of hexanal and its dimethyl acetal, were also analyzed by GC. Provisional identifications were made by matching r.r.t.'s of the oxidation products with those of authentic samples. Identification was verified using selected oxidates and authentic samples by means of GC/mass spectrometry, using a
Figure 2

A Typical Gas Chromatogram of Hexene Products

A: Methanol
B: 1-Hexene
C: 3-Hexanone
D: 2-Hexanone
E: Chlorobenzene (internal standard)
F: 3,3-Dimethoxyhexane
G: 2,2-Dimethoxyhexane
Hewlett-Packard model 5970 mass selective detector, with the interfaced chromatograph fitted with a capillary column (0.25 mm x 25 m) wall coated with poly(methylphenylsiloxane).

Several series of oxidation runs were carried out at 30°C (except as noted otherwise), with the aim of investigating the effects of experimental variables upon reaction rate and product compositions. On the basis of 15 runs conducted to completion with measured quantities of hexene reactant, the effective system volume was calculated, and the ratio (mbar pressure drop) : (mmol oxygen per L liquid) was determined to be 3.151 ± 0.059. Turnover numbers [by definition, the number of hexene molecules reacting per atom of Pd per hour] were then calculated from initial pressure drop slopes.

The effect of varying 1-hexene concentration in methanol was investigated with a series of oxidations in which the initial hexene charge varied from 31 to 465 mmol/L (0.4% to 6.0% by volume). These runs were made with PdCl₂ 9.13 mmol/L, CuCl₂ 10.02 mmol/L, and initial oxygen pressure at 1 atm.

Oxygen partial pressure was varied from 179 mbar to 826 mbar (corrected for P_{water} at 50% R.H. for the air component, and for P_{MeOH}). This series was conducted with PdCl₂ 9.13 mmol/L, CuCl₂ 10.02 mmol/L, and initial 1-hexene 310.3 mmol/L.
Catalyst-cocatalyst concentration was studied by a series of runs containing varying amounts of a stock solution 0.100 M in both PdCl$_2$ and CuCl$_2$, such that Pd(II) and Cu(II) concentrations were varied in concert over the range 2.0 to 36.0 mmol/L. For this series initial 1-hexene was constant at 310.3 mmol/L and initial oxygen pressure was at 1 atm.

With PdCl$_2$ maintained at a constant concentration of 9.12 ± 0.01 mmol/L, the concentration of CuCl$_2$ cocatalyst was varied from 4.5 to 55 mmol/L (Cu/Pd ratio 0.5 to 6.1). Triplicate runs were made at CuCl$_2$ 10.0 mmol/L (Cu:Pd = 1.1). For these runs initial 1-hexene was constant at 155.1 mmol/L and initial oxygen pressure was 1 atm.

Temperature effects were studied with a series of oxidation runs conducted at temperatures between 20° and 50°C. For each run the concentration of PdCl$_2$ was 10.0 mmol/L, CuCl$_2$ 24.0 mmol/L, and initial 1-hexene 310.3 mmol/L; initial oxygen pressure was 1 atm.

Periodic sampling runs were carried out using a three-neck 500-mL round bottom flask in place of the two-neck flask. The third neck was connected to a sampling port fitted with a 2-mm i.d. teflon stopcock. After the flask was charged with the methanolic catalyst and 1-hexene solutions in the usual manner, the oxidation run was carried out with the oxygen
reservoir bag valve open, maintaining a constant oxygen pressure of 1 atm. throughout the run. Periodically the sampling port was opened and 1.0-mL samples were withdrawn using a syringe fitted with a 20-cm needle. Samples were immediately stabilized with an equal volume of methanolic ammonia, and saved for GC analysis. These runs were carried out with PdCl₂ 9.1 ± 0.01 mmol/L, CuCl₂ 10.0 or 30.5 mmol/L, initial 1-hexene 155.1 mmol/L, and oxygen continuously at atmospheric pressure (approximately 900 mbars after correcting for P_{\text{H₂O}}).
RESULTS

A. **Product Identifications**

GC Analyses were typically conducted for 30 minutes isothermally at 60°, yielding a product sequence (typical raw retention times in minutes) of methanol (0.65), hexene (1.05), 3-hexanone (6.5), 2-hexanone (7.1), chlorobenzene (11.1), 3,3-dimethoxyhexane (14.9), 2,2-dimethoxyhexane (16.6) and 1,1-dimethoxyhexane (25-26). Free hexanal was not detected in any oxidation product mixtures. When hexanal was produced in detectable amounts, it was always found in the acetal form. A typical gas chromatogram is shown in Figure 2 (page 37). Two pairs of peaks, methanol/hexene and 3-hexanone/2-hexanone, show only marginally acceptable separation. Column efficiency, based upon width at half height of the chlorobenzene peak, is ~ 1,750 theoretical plates.

Product quantitation made use of the internal standard, chlorobenzene. For the ketones, standard solutions were prepared of pure ketone and chlorobenzene in 4:1 methanol/water (the water having been added to suppress ketal
(formation). The response factor $f$ was determined as:

$$ f = \frac{A(\text{ketone}) \times C(\text{standard})}{C(\text{ketone}) \times A(\text{standard})} $$

where $A$ and $C$ are integrator area and concentration (mmol/L), respectively. Quadruplicate analyses of 2-hexanone yielded a $f$ value of $0.8287 \pm 0.0013$. With 3-hexanone the value of $f$ was identical within the standard error. Similar response calibrations for the two ketals, using anhydrous methanol and correcting for the amounts of free ketone, yielded a value of $f$ of $0.9241 \pm 0.0189$. The relative standard error for the free ketones, 0.16%, is acceptably low. That for the ketals, 2.0%, is larger than desirable. This arises partly from the accumulation of error in correcting for free ketone, but principally from the GC peaks themselves, characterized by long retention times and low peak slopes (Figure 2).

Gas chromatograph/mass spectrometer (GC/MS) identifications were made using the capillary column at 25° and 30°C. Table 1 shows the mass fragments used for identifications. The McLafferty rearrangement products are valuable corroborative evidence here. This rearrangement of a cationic species bearing the formal charge on the oxygen atom entails a $\beta$-$\gamma$ carbon-carbon scission with the concerted transfer of a $\delta$-hydrogen to the oxygen atom. The molecular ions of hexanal, 2-hexanone and 3-hexanone yield product fragments of m/e 44,
## Table 1

Hexene Product Identifications by GC-Mass Spectrometry

<table>
<thead>
<tr>
<th>r.r.t.¹</th>
<th>fraction</th>
<th>m/e and tentative identification of prod.²</th>
<th>molecule</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.59</td>
<td>30.8%</td>
<td>100 M⁺</td>
<td>3-HEXANONE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>72 McLafferty product</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>71 C₃H₇CO⁺</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>57 C₂H₅CO⁺, C₄H₉⁺</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>43 C₃H₇⁺,³</td>
<td></td>
</tr>
<tr>
<td>0.65</td>
<td>50.4%</td>
<td>100 M⁺</td>
<td>2-HEXANONE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>85 C₄H₉CO⁺</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>58 McLafferty product</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>43 CH₃CO⁺</td>
<td></td>
</tr>
<tr>
<td>[1.00]</td>
<td>---</td>
<td>114 ⁴³Cl-C₆H₅</td>
<td>CHLOROBENZENE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>112 ⁴³Cl-C₆H₅</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>77 C₆H₅⁺</td>
<td></td>
</tr>
<tr>
<td>1.34</td>
<td>2.1%</td>
<td>115 (M - CH₃O⁻)</td>
<td>3,3-DIMETHOXYHEXANE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>103 (M - C₃H₇⁻)</td>
<td></td>
</tr>
</tbody>
</table>

⁴ The mass of the molecule.
² Tentative identification.
<table>
<thead>
<tr>
<th>r.i.t.(^1)</th>
<th>fraction</th>
<th>m/e and tentative molecule of prod.(^2)</th>
<th>identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.49</td>
<td>11.2%</td>
<td>115 (M - CH(_3)O(^-))</td>
<td>2,2-DIMETHOXYHEXANE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>89 (M - C(_4)H(_9)(^+))</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>72 CH(_2)=C(CH(_3))OCH(_3)(^+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>59 CH(_3)-CHOCH(_3)(^+)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>43 CH(_2)CO(^+)</td>
<td></td>
</tr>
</tbody>
</table>

1. Relative retention time, referenced to the internal standard, chlorobenzene.
2. Based upon triplicate GC analysis of run 124 (1-Hexene 155 mmol/L in methanol, PdCl\(_2\) 9.13 mmol/L, CuCl\(_2\) 10.02 mmol/L, oxidized for 360 minutes at 30°C). An additional 5.4% of GC signal was dispersed among six minor and trace co-products.
3. This m/e signal may also arise from a McLafferty rearrangement of the butyryl cation (m/e 71).
58 and 72, respectively. In addition, α-scission of the two asymmetric ketones provides characteristic acyl cations of m/e 43 and 85 for 2-hexanone, 57 and 71 for 3-hexanone. Ketals were identified by the (M - CH₃O) peaks and by the characteristically strong (M - R₁) peaks [where R₁ is the larger alkyl group]. 2,2-Dimethoxyhexane yields m/e 89 (M - C₄H₉), and 3,3-dimethoxyhexane yields m/e 103 (M - C₃H₇). Chlorobenzene is easily identified by its molecular ions (m/e 112 and 114 in an intensity ratio of 3:1) and the strong (M - Cl) peak at m/e 77.

B. Effect of Hexene Concentration

For this and the subsequent oxidation run series, it was found that there are two distinct reaction regions, based upon pressure drop: an initial region of linear drop, showing the maximum oxidation rate and permitting the calculation of maximum turnover number, and a second region characterized by an exponential drop, in which pressure follows the rate law:

\[ P = a + b \exp(-ct) \]

Constants \(a\) and \(b\) are parameters related to initial and final pressures; constant \(c\) is an empirical rate constant for the exponential region. Figure 3 illustrates these two regions in a typical oxidation.
Run 21
1-Hexene 4.0% v/v (310.3 mmol/L)

Initial slope (4 to 48 minutes):
$3.39 \pm 0.024$ mbar / min
$R^2 = 0.9995$  \hspace{1cm} df = 11

Exponential region (66 to 300 min):
$P = 536.7 + 388.5 \exp(-t / 85.151)$
$R^2 = 0.9994$  \hspace{1cm} $F = 18779$
The effect of varying hexene concentration is shown in Figure 4. With all but the lowest concentrations, an initial region of linear pressure drop was evident, corresponding to a turnover number of 7.1 - 7.4 hr\(^{-1}\). This was followed by a region of exponential decay of oxidation rate. With high initial concentrations of hexene, the linear range was extended. A quantitative summary of this series of runs is given in Table 2.

At hexene concentrations of 150 mmol/L (2% v/v) and greater the initial steady-state reaction rate is constant, and the estimated value of the exponential decay rate is also essentially constant. However, the total oxidation achieved in two hours continues to increase smoothly, as shown in Figure 4. This reflects the progressively greater period of fast 'linear' reaction.

C. Effect of Oxygen Pressure

Most oxidations in this study have been carried out with an initial oxygen pressure of about 900 mbar (actually at atmospheric pressure corrected for the partial pressure of methanol, 99.7 mbar at 30.0\(^{\circ}\)). Under these conditions little or no Pd(0) precipitation occurs, and the concentration of homogeneous Pd(II) catalyst can be taken as constant during any oxidation. When a series of runs is made with P\(^{o}\)\(_{\text{Oxygen}}\) of
Figure 4

Effect of 1-Hexene Concentration in Methanol at 30 deg C

![Graph showing the effect of 1-Hexene Concentration in Methanol at 30 deg C.]
Table 2

Effects of Varying Initial Concentration of 1-Hexene¹

<table>
<thead>
<tr>
<th>run charge, no.</th>
<th>conversion, mmol/L</th>
<th>initial slope</th>
<th>TN⁻¹, hr⁻¹</th>
<th>decay k, hr⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>31.0</td>
<td>13.8</td>
<td>0.3</td>
<td>1.3</td>
</tr>
<tr>
<td>17</td>
<td>62.1</td>
<td>34.8</td>
<td>2.3</td>
<td>9.6</td>
</tr>
<tr>
<td>19</td>
<td>93.1</td>
<td>58.0</td>
<td>2.5</td>
<td>10.3</td>
</tr>
<tr>
<td>108</td>
<td>155.1</td>
<td>114.8</td>
<td>3.4</td>
<td>14.1</td>
</tr>
<tr>
<td>21</td>
<td>310.3</td>
<td>187.8</td>
<td>3.4</td>
<td>14.1</td>
</tr>
<tr>
<td>15</td>
<td>465.4</td>
<td>237.6</td>
<td>4.1</td>
<td>14.7</td>
</tr>
</tbody>
</table>

¹ In methanol at 30°C with PdCl₂ 9.13 mmol/L, CuCl₂ 10.02 mmol/L, oxygen at atmospheric pressure

² after 120 minutes

³ Turnover Number, determined from initial slope
690 or less mbars, however, significant to heavy precipitation occurs within the first 30 minutes. Figure 5 shows the qualitative behavior of three runs in this series. The data of Table 3 includes initial rate estimates -- which are considered valid since they were measured before catalyst precipitation -- as well as other measurements which are not kinetically meaningful since the homogeneous catalyst concentration was unknown and changing during most of these runs.

D. Effect of Catalyst - Cocatalyst Concentration

The effect of variation of the catalyst-cocatalyst concentrations at constant initial hexene and oxygen are summarized in Table 4. The expectation is that with higher catalyst concentrations the reaction will proceed faster. This expectation in general has been realized. 1-Hexene oxidation is over 99% complete in 120 minutes at catalyst concentrations of 18 mmol/L and higher (Figure 6, solid triangles).

The initial slope is very low at 2 mmol/L catalyst, reflecting the second-order kinetic dependency upon catalyst-cocatalyst concentration for the Pd reoxidation step. While the initial slope increases steadily with increasing catalyst concentration, reaching 9 mbar min⁻¹ at 36 mmol/L, the
Figure 5

Effect of Oxygen Partial Pressure upon Hexene Oxidation at 30 deg C

Initial Oxygen: 197 mbar
Initial Oxygen: 512 mbar
Initial Oxygen: 910 mbar
Table 3
Effects of Oxygen Partial Pressure at 30°C

<table>
<thead>
<tr>
<th>run</th>
<th>$P_{oxygen}$</th>
<th>convn</th>
<th>initial</th>
<th>TN</th>
<th>decay $k^4$</th>
<th>pptn.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mbar</td>
<td>mmol/L</td>
<td>slope</td>
<td>hr$^{-1}$</td>
<td>hr$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>910</td>
<td>241.3</td>
<td>3.4</td>
<td>14.1</td>
<td>0.7</td>
<td>none</td>
</tr>
<tr>
<td>29</td>
<td>690</td>
<td>90.0</td>
<td>3.4</td>
<td>14.2</td>
<td>0.4</td>
<td>yes</td>
</tr>
<tr>
<td>27</td>
<td>512</td>
<td>76.7</td>
<td>2.8</td>
<td>11.6</td>
<td>0.4</td>
<td>yes</td>
</tr>
<tr>
<td>25</td>
<td>197</td>
<td>35.7</td>
<td>2.4</td>
<td>10.0</td>
<td>&lt;0.1</td>
<td>yes</td>
</tr>
</tbody>
</table>

1 With PdCl$_2$ 9.1 mmol/L, CuCl$_2$ 10.0 mmol/L, initial hexene 310.3 mmol/L

2 1-Hexene conversion after 300 minutes

3 Turnover number, determined from initial slope

4 Highly unreliable except for run 21, owing to Pd(0) precipitation
Table 4

Varying the Catalyst-Cocatalyst Concentration

<table>
<thead>
<tr>
<th>charge, mmol/L</th>
<th>conversion, mmol/L</th>
<th>initial slope</th>
<th>TN, hr⁻¹</th>
<th>decay k, hr⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>13.8</td>
<td>0.5</td>
<td>9.6</td>
<td>---</td>
</tr>
<tr>
<td>4.0</td>
<td>135</td>
<td>1.9</td>
<td>18.4</td>
<td>0.5</td>
</tr>
<tr>
<td>6.0</td>
<td>204</td>
<td>3.2</td>
<td>20.5</td>
<td>0.4</td>
</tr>
<tr>
<td>8.0</td>
<td>259</td>
<td>3.9</td>
<td>18.6</td>
<td>1.2</td>
</tr>
<tr>
<td>10.0</td>
<td>258</td>
<td>4.9</td>
<td>18.7</td>
<td>0.3</td>
</tr>
<tr>
<td>12.0</td>
<td>271</td>
<td>4.2</td>
<td>13.4</td>
<td>2.3</td>
</tr>
<tr>
<td>14.0</td>
<td>268</td>
<td>4.6</td>
<td>12.5</td>
<td>1.8</td>
</tr>
<tr>
<td>16.0</td>
<td>302</td>
<td>5.8</td>
<td>13.9</td>
<td>2.9</td>
</tr>
<tr>
<td>18.0</td>
<td>309</td>
<td>7.7</td>
<td>16.2</td>
<td>3.0</td>
</tr>
<tr>
<td>20.0</td>
<td>308</td>
<td>7.4</td>
<td>14.2</td>
<td>4.5</td>
</tr>
<tr>
<td>24.0</td>
<td>315⁴</td>
<td>8.3</td>
<td>13.1</td>
<td>4.5⁴</td>
</tr>
<tr>
<td>30.0</td>
<td>315⁴</td>
<td>8.3</td>
<td>10.5</td>
<td>4.7⁴</td>
</tr>
<tr>
<td>36.0</td>
<td>296⁴</td>
<td>9.1</td>
<td>9.6</td>
<td>1.1⁴</td>
</tr>
</tbody>
</table>

¹ In methanol at 30°C, [PdCl₂] = [CuCl₂], initial hexene 310.3 mmol/L, initial oxygen at atmospheric pressure
² Hexene converted (mmol/L) after 120 min.
³ Turnover Number, determined from initial slope
⁴ These data are questionable, owing to Pd precipitation.
Figure 6

Catalyst - Cocatalyst Concentration Effects upon 1-Hexene Oxidation

![Graph showing turnover number (TN) and rate constant (k(decay)) vs. palladium (II) and copper (II) concentrations.]

- ■ TN, hr\(^{-1}\)
- □ k(decay), hr
- ▲ 2-hr oxidation
turnover number, for which catalyst concentration appears in the denominator, quickly reaches a maximum at 4-6 mmol/L and thereafter falls gradually with increasing catalyst concentration (Figure 6, solid squares).

The exponential decay constant appears to increase linearly with catalyst concentration up to about 20 mmol/L. Oxidation runs with 24-36 mmol/L catalyst showed significant precipitation of Pd(0) at the conclusion of each run. Consequently the data obtained from these last three runs (Figure 6, crossed squares) must be viewed with great caution. As indicated in footnote 4 to Table 5, only the initial data from these high-catalyst runs are considered reliable.

Gas chromatographic analyses of reaction products showed very little compositional variation. The 2-hexanone peak in all cases accounted for 59-62% of the combined hexanones. [For this series, ketals were not measured. The true 2-hexanone fraction is greater when ketals are included in the analysis.]

E. Effect of the Cu(II) : Pd(II) Ratio

Results of the series of runs with varying concentrations of CuCl₂ and constant concentrations of (initial) hexene and PdCl₂ are summarized in Table 5. The initial linear regions of each run, and the corresponding turnover numbers, show
sharp and well-defined maxima at a Cu(II) : Pd(II) ratio of approximately 1.1 (see Figure 7), with maximum TN values of 12.7-14.2 hr\(^{-1}\). Turnover number values fall off sharply on each side of this maximum, reaching half-maximum values at ratios of 0.7 and 1.8.

The total conversion at 120 minutes shows a similar maximum, in the Cu:Pd ratio range 0.9 to 1.3, falling sharply for ratios below 0.8 and above 2.0.

The estimated values for the exponential decay constant appear to follow a similar relationship, with highest values for ratios in the range 0.8 to 1.5.

The two isomeric hexanones make up about 85% of the total product signal for all runs in this group. Selectivity for 2-hexanone varies over a narrow range, with the lowest values (53.4-55.5%) found at the highest Cu : Pd ratios. For lower ratios the average selectivity is 65%. There is a possibly significant maximum of 68% at a Cu : Pd ratio of 0.8.

Of the four runs with Cu : Pd ratios less than 1.10, two runs were conducted with the addition of make-up LiCl to maintain a constant total chloride concentration; the other two low-copper runs used no make-up chloride. The data of Table 5 suggest a slight retardation with LiCl addition at the
Table 5

Effect of Varying the Cu(II) : Pd(II) Ratio

<table>
<thead>
<tr>
<th>Ratio Cu/Pd</th>
<th>convn, mmol/L&lt;sup&gt;3&lt;/sup&gt;</th>
<th>TN&lt;sup&gt;2&lt;/sup&gt;, hr&lt;sup&gt;-1&lt;/sup&gt;</th>
<th>decay k, hr&lt;sup&gt;-1&lt;/sup&gt;</th>
<th>ketones selectivity % of tot for 2-isomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.50</td>
<td>18.2</td>
<td>1.5</td>
<td>---</td>
<td>84.5%</td>
</tr>
<tr>
<td>0.66&lt;sup&gt;4&lt;/sup&gt;</td>
<td>49.4</td>
<td>3.6</td>
<td>0.3</td>
<td>85.8%</td>
</tr>
<tr>
<td>0.80</td>
<td>113.2</td>
<td>9.7</td>
<td>1.5</td>
<td>81.4%</td>
</tr>
<tr>
<td>0.88&lt;sup&gt;4&lt;/sup&gt;</td>
<td>140.8</td>
<td>9.2</td>
<td>1.3</td>
<td>83.0%</td>
</tr>
<tr>
<td>1.10&lt;sup&gt;5&lt;/sup&gt;</td>
<td>132.5</td>
<td>13.8</td>
<td>0.8</td>
<td>85.7%</td>
</tr>
<tr>
<td>1.46</td>
<td>141.2</td>
<td>10.2</td>
<td>1.2</td>
<td>85.9%</td>
</tr>
<tr>
<td>2.00</td>
<td>103.7</td>
<td>5.4</td>
<td>0.7</td>
<td>85.9%</td>
</tr>
<tr>
<td>3.35</td>
<td>41.8</td>
<td>2.2</td>
<td>0.3</td>
<td>90.5%</td>
</tr>
<tr>
<td>6.06</td>
<td>29.8</td>
<td>1.2</td>
<td>0.3</td>
<td>85.1%</td>
</tr>
</tbody>
</table>

---

1 In methanol at 30°C, PdCl<sub>2</sub> 0.12 mmol/L, initial hexene 155.1 mmol/L, initial oxygen at atmospheric pressure

2 Turnover number, determined from initial slope

3 Hexene converted in 120 minutes

4 Makeup LiCl added to maintain Cl<sup>-</sup>:Pd<sup>**</sup> at 4.0

5 Median of three runs (repeatability ± 4.0% relative)
Figure 7

Effect of Cu : Pd Ratio upon Hexene Oxidation in Methanol

Turnover No. and k(decay), in hr⁻¹

Cu(II) : Pd(II) Ratio

mmol/L oxidized in two hours

TN, hr⁻¹  2-hr oxidation  k(expo decay)
Cu:Pd ratio of 0.88. In exploratory runs with PdCl₂ 6.0 mmol/L and hexene 310.3 mmol/L, the oxidation proceeded fairly well with 6.0 mmol/L CuCl₂ (TN 5.2 hr⁻¹, decay k 2.2 hr⁻¹). When the CuCl₂ concentration was reduced to 3.0 mmol/L and make-up LiCl (6.0 mmol/L) was added, the reaction was distinctly slower (TN 1.1 hr⁻¹, decay k 0.5 hr⁻¹).

F. Temperature Effects

The effect of temperature (20-45°C) is shown in Table 6. The extent of reaction (120-minute conversion) reaches a maximum at about 45° under these conditions; at 50° much of the palladium catalyst precipitates as Pd(0), and the overall conversion, as well as initial conversion rate, drops sharply. This is not surprising, since at 50°C P₇₅₅ is 554 mbar, so that Pₒ₂ in an atmospheric pressure reactor cannot exceed about 450 mbar. As is seen in Table 3 (p 52), the catalyst precipitates and the oxidation rate is depressed when Pₒ₂ falls below about 700 mbar, even at 30°.

The initial rate (shown in Table 6 as turnover number) shows a fairly sharp temperature dependency. Three of the four data are linear in an Arrhenius plot (Figure 8). Using all data the indicated activation energy of initial rate is estimated roughly to be 39 ± 10 kJ/mol.
Table 6

**Effects of Temperature upon 1-Hexene Oxidations**

<table>
<thead>
<tr>
<th>temp. °C</th>
<th>convn mmol/L</th>
<th>TN mmol/L</th>
<th>2-Hexanone</th>
<th>3-Hexanone</th>
<th>Hexanal</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.0</td>
<td>62.5</td>
<td>5.6</td>
<td>67.1%</td>
<td>25.2%</td>
<td>7.7%</td>
</tr>
<tr>
<td>30.0</td>
<td>241.8</td>
<td>13.9</td>
<td>68.9</td>
<td>24.7</td>
<td>6.4%</td>
</tr>
<tr>
<td>40.0</td>
<td>---</td>
<td>15.0</td>
<td>67.8</td>
<td>17.3</td>
<td>---</td>
</tr>
<tr>
<td>45.0</td>
<td>265.5</td>
<td>20.3</td>
<td>62.4</td>
<td>32.9</td>
<td>4.7%</td>
</tr>
<tr>
<td>50.0°</td>
<td>[69+]</td>
<td>[11+]</td>
<td>63.7</td>
<td>31.6</td>
<td>4.7%</td>
</tr>
</tbody>
</table>

---

1 Hexene 310.3 mmol/L in methanol with PdCl$_2$ 10.0 mmol/L, CuCl$_2$ 24.0 mmol/L, oxygen at atmospheric pressure
2 after 120 minutes
3 Turnover number, determined from initial slope
4 Pd(0) precipitation during run; fate and conversion data are unreliable
Figure 8

Effect of Temperature upon Turnover Number in Methanol

Slope \(-\frac{E(a)}{R}\) = -4.70 +/- 1.27

\(E(a) = 39 +/- 10 \text{ kJ/mol}\)
Gas chromatographic analysis identifies the three principal products, 2-hexanone (half of which occurs as the ketal, 2,2-dimethoxyhexane), 3-hexanone (about 15% of which appears as the ketal, 3,3-dimethoxyhexane) and hexanal (essentially all as the acetal, 1,1-dimethoxyhexane). The product compositions show only minor trends with increasing temperature: the 3-hexanone fraction increases from about 25% to about 32%; the hexanal fraction decreases from about 7% to about 5%; and the principal product, 2-hexanone, decreases from about 68% to about 63% as temperature is increased in this range.

In addition to $P_{\text{MeOH}}$ two other factors may contribute to the effective temperature ceiling of about 45° for this oxidation. As the Pd(II)-hexene reaction rate becomes too fast (TN exceeding 20 hr$^{-1}$), the $\text{CuCl}_2$-Pd(0) reoxidation step may be unable to keep the palladium essentially entirely in its oxidized Pd(II) state. At the same time, Cu(I) reoxidation is adversely affected by the declining solubility of oxygen as the atmospheric b.p. of methanol [65°] is approached.

G. Periodic Sampling Runs

The results of oxidations conducted with periodic
Table 7
Hexene Oxidations with Periodic Sampling

<table>
<thead>
<tr>
<th>minutes</th>
<th>2-hexanone (^2)</th>
<th>3-hexanone (^2)</th>
<th>total</th>
<th>ratio (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>7.0</td>
<td>1.5</td>
<td>9.1</td>
<td>6.1</td>
</tr>
<tr>
<td>40</td>
<td>12.3</td>
<td>3.8</td>
<td>16.2</td>
<td>3.2</td>
</tr>
<tr>
<td>60</td>
<td>14.7</td>
<td>6.0</td>
<td>20.7</td>
<td>2.4</td>
</tr>
<tr>
<td>140</td>
<td>28.7</td>
<td>16.7</td>
<td>45.5</td>
<td>1.7</td>
</tr>
<tr>
<td>180</td>
<td>33.1</td>
<td>20.8</td>
<td>53.8</td>
<td>1.6</td>
</tr>
<tr>
<td>250</td>
<td>43.2</td>
<td>30.1</td>
<td>73.3</td>
<td>1.4</td>
</tr>
<tr>
<td>300</td>
<td>47.8</td>
<td>35.4</td>
<td>83.2</td>
<td>1.4</td>
</tr>
<tr>
<td>---------</td>
<td>----------------</td>
<td>----------------</td>
<td>-------</td>
<td>----------</td>
</tr>
<tr>
<td>9.6</td>
<td>14.7</td>
<td>5.7</td>
<td>20.4</td>
<td>2.6</td>
</tr>
<tr>
<td>20</td>
<td>25.9</td>
<td>12.1</td>
<td>38.0</td>
<td>2.1</td>
</tr>
<tr>
<td>40</td>
<td>44.3</td>
<td>22.7</td>
<td>67.1</td>
<td>2.0</td>
</tr>
<tr>
<td>60</td>
<td>61.7</td>
<td>33.1</td>
<td>94.8</td>
<td>1.9</td>
</tr>
<tr>
<td>80</td>
<td>68.5</td>
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<td>100</td>
<td>71.9</td>
<td>40.7</td>
<td>112.6</td>
<td>1.8</td>
</tr>
<tr>
<td>180</td>
<td>74.3</td>
<td>42.3</td>
<td>116.7</td>
<td>1.8</td>
</tr>
<tr>
<td>240</td>
<td>83.2</td>
<td>43.5</td>
<td>126.7</td>
<td>1.9</td>
</tr>
<tr>
<td>300</td>
<td>71.4</td>
<td>41.0</td>
<td>112.4</td>
<td>1.7</td>
</tr>
</tbody>
</table>

\(^1\) At 30°C, 1-hexene 155.1 mmol/L in methanol
\(^2\) Free ketone and dimethyl ketal combined
\(^3\) Ratio = [total 2-hexanone]/[total 3-hexanone]
Figure 9
Hexanone Formation at 30.0 deg C
PdCl₂ 9.11 mmol/L  CuCl₂ 30.55 mmol/L

9a. Ketone Formation Rates

9b. Isomer Ratios
sampling are summarized in Table 7. Oxidation 122 was conducted with a Cu(II) : Pd(II) ratio of 3.35. As expected from the data of Figure 7 (p. 58), this oxidation is somewhat retarded by the excess of CuCl₂. As can be seen in Figure 9a, the concentrations of both hexanones increase essentially linearly with time. A plot of the ratios of 2-hexanone to 3-hexanone (Figure 9b) shows that the earliest oxidation produces a great preponderance of 2-hexanone. As the reaction proceeds, the cumulative ratio of 2-hexanone : 3-hexanone falls from about 6.0 to less than 1.5, while the differential ratio falls essentially to unity.

Oxidation 124 is similar to 122 except only for the Cu(II) : Pd(II) ratio, which for this reaction was 1.10. Figure 10a shows that hexanone formation is initially linear with time. After about an hour the oxidation slows as hexene conversion approaches completion. Again the early ratios of 2-hexanone to 3-hexanone (Figure 10b) are relatively high, though not as high as in Run 122. At later stages in the oxidation, the cumulative ratio falls to a constant value near 1.7, while the differential ratio falls to approximately unity. An interpretation of these observations is given in the following section.
Figure 10

Hexanone Formation at 30.0 deg C
PdCl₂ 9.13 mmol/L CuCl₂ 10.02 mmol/L

10a. Ketone Formation Rates

Ratios of 2-Hexanone to 3-Hexanone
PdCl₂ 9.13 mmol/L CuCl₂ 10.02 mmol/L

10b. Isomer Ratios
A. Kinetic inferences

The overall picture of the reaction suggested by these data is:

\[
\begin{align*}
(e_n) + \text{Pd(II)} & \quad K \quad k \quad \text{fast} \\
& \quad A \quad \rightarrow \quad B' \quad \rightarrow \quad \text{ketone mixture} \\
& \quad k_i \\
(e_n') + \text{Pd(II)} & \quad K' \quad k' \quad \text{fast} \\
& \quad A' \quad \rightarrow \quad B' \quad \rightarrow \quad \text{ketone mixture}
\end{align*}
\]

where \( A \) and \( B \) are the \( \pi \)- and \( \sigma \)-complexes shown in Chart 1, \( k_i \) is the nonskeletal isomerization rate constant, proceeding via the \( \pi \)-allylic intermediate, and \( A' \) and \( B' \) are the corresponding complexes of the isomerized hexene (\( \text{cis} \)- and \( \text{trans} \)-2-hexene). Values of \( k, K \) and \( k_i \) can be estimated or roughly approximated from the data obtained. [The further isomerization to 3-hexene and its oxidation to 3-hexanone are not shown.]

Most of these oxidations exhibit an initial linear slope. This slope is substantially proportional to Pd(II) concentration up to about 10 mmol/L. The rate-limiting step is not Pd(II) regeneration, and is independent of hexene.
concentration above about 150 mmol/L. The oxidation rate increases with increasing [Pd(II)] but the turnover number is constant at 19 hr\(^{-1}\) through the range 4-10 mmol/L (Table 4, p. 53). This observation is consistent with the view that the rate-limiting step is a \(\pi\)-to-\(\sigma\) rearrangement of the Pd(hexene) complex, \([A \rightarrow B\) in Chart 1 (p. 15)].

For \(A \rightarrow B\) in the linear region of oxidation, \(\dot{\Delta} \approx [\text{Pd(II)}]\). With [Pd(II)] at 10 mmol/L and \(k = TN = 19\ \text{hr}^{-1}\),

\[
\frac{dX}{dt} = k[A] = k[\text{Pd(II)}] = 0.19\ \text{mol L}^{-1}\ \text{hr}^{-1}
\]

The exponential decay portion of the oxidation is found at hexene concentrations below about 100 mmol/L. Here \([A] + [\text{Pd(II)}]\), and must be estimated using hexene (H) and the equilibrium constant \(K\):

\[
[A] = K*[\text{Pd(II)}-A]*[H-A] \approx K*[\text{Pd(II)}-A]*[H]
\]

\[
\frac{dX}{dt} = k*[A] = k*K*[\text{Pd(II)}-A]*[H]
\]

where \(K \approx \frac{A}{([\text{Pd} - A]*[H])}\)

If \(K = 50\ \text{L mol}^{-1}\), for example, \(A\) at hexene concentrations of 50, 100 and 200 mmol/L is 7.1, 8.32 and 9.1 mmol/L, roughly in accord with the observed transition to exponential decay.
The rate of consumption of hexene in this region of exponential decay is approximated by:

\[ \frac{d[H]}{dt} = -\kappa[H] \]

(where \( \kappa = k^*K^*[Pd(II)-A] \)) which integrates to the form

\[ [H] = H^0 \exp(-\kappa t), \]

exactly as has been shown empirically.

The nominal product of 1-hexene oxidation is 2-hexanone. Small amounts of hexanal are expected, and are found. But the major coproduct in all oxidations is 3-hexanone. This coproduct arises from concurrent Pd(II)-catalyzed isomerization of 1-hexene to 2-hexene, thermodynamically favored \([\Delta G_f \approx -12 \text{ kJ/mol}\])]. The \( \pi \)-complex of 2-hexene \((A')\) can form two different \( \sigma \)-complexes, one decomposing to 2-hexanone and the other to 3-hexanone. As these ketones are thermodynamically comparable \([\Delta H_f \approx 1 \text{ kJ/mol}\])], the assumption can be made that the oxidation of 2-hexene leads to approximately equal amounts of 2- and 3-hexanone.

The data of Table 7 and Figures 9b and 10b show two particular points of interest. First, since 3-hexanone is an important product after several hours' oxidation, \( k \) cannot be much greater than \( k_1 \), and may be less than \( k_1 \). Yet 2-hexanone is clearly the major initial reaction product. This suggests that \( k' \) is relatively slow. If \( A' \) forms equal amounts of 2-
and 3-hexanone, then the presence of 35% 3-hexanone in product mixtures (Tables 5 and 7) implies that roughly 70% of the oxidation has proceeded via isomerization to 2-hexene(s). This point could be clarified by capillary GC analysis, which would permit the separate determination of the hexene isomers during oxidations.

B. General Notes on the Reaction

The literature reviewed suggests several oxidation coproducts which in fact have not been observed in the present study: acids and esters$^{14,52}$, $\alpha$-chloroketones$^{22,28}$, alkenones$^{7,56}$, and alkene dimers, ethers, and solvation products$^{52,69,71}$. In the present work no traces of methyl caproate or of chlorohexanones could be found. There may be several reasons for this. Hexanal is fully tied up as the acetal. 2-Hexanone is partially tied up as the dimethyl ketal. Of greater importance with regard to the absence of chlorination products is the quite low concentrations of CuCl$_2$ — well below 0.1 M and for many oxidations close to 0.01 M — and the low temperatures of these reactions. In the absence of free strong acid, and at the low temperatures used, no methyl hexyl ethers were found.

There is a surprisingly sharp optimum observed for CuCl$_2$ concentration (Tables 5, 7), and also an optimum range in
total \( \text{PdCl}_2-\text{CuCl}_2 \) concentrations (Table 4). Addition of \( \text{LiCl} \) tends to retard oxidation. Taken together, these observations suggest that the chloride ion, a good ligand, can preempt the coordination sites needed by the weak ligand hexene. \( \text{PdCl}_2 \) is readily formed in both aqueous and alcoholic solutions. The present results suggest that hexene oxidation proceeds best when there is just enough chloride ion available to solubilize \( \text{Pd(II)} \) as \( \text{Pd(L)Cl}_3 \) and to serve as an electron-transfer bridging ligand in \( \text{Pd reoxidation}. \)

Most studies of palladium(II)-catalyzed alkene oxidation, in both water and alcohols, have focused upon ethylene and propylene. The present study is the first investigation to our knowledge which examines in detail the oxidation of a higher \( 1 \)-alkene. The principal characteristics are:

1. The reaction proceeds readily under very mild conditions.
2. Only carbonyl compounds and their ketals are found.
3. Two distinct kinetic regions are consistently found.
4. The magnitude of the concurrent \( \text{Pd(II)} \)-catalyzed migration of the alkene double bond is evident.
5. The data of Table 7 and Figures 9 and 10 may provide a clue to the suppression of isomerization and hence to a modification which would permit the preparation of single ketone isomers with high selectivity.
6. This modification could greatly increase the synthetic value of this group of reactions.
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