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MECHANISTIC INVESTIGATION OF ADDITIONS TO ALKENES BY USING CORRELATIONS

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MECHANISTIC INVESTIGATION OF ADDITIONS TO ALKENES
BY USING CORRELATIONS

A DISSERTATION APPROVED FOR THE
DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY

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List of Abbreviations

AO	-Atomic orbital
A-value	-Axial strain energy
c.l.	-Confidence level
EA	-Electron affinity
EDA	-Electron-donating group
ESR	-Electron spin resonance
ETS	-Electron transmission spectroscopy
EWA	-Electron-withdrawing group
GC	-Gas chromatography
GTO	-Gaussian-type orbital
HF	-Hartree-Fock
HOMO	-The highest occupied molecular orbital
I_a	-Associative interchange
I_d	-Dissociative interchange
IP	-Ionization potential
LCAO	-Linear combination of atom
LFERs	-Linear Free Energy Relationships
LUMO	-The lowest unoccupied molecular orbital
Met	-Metal
MNDO	-Modified neglect of diatomic overlap
MO	-Molecular orbital
NDDO	-Neglect of diatomic differential overlap
P	-Triphenylphosphine, PPh_3
PES	-Photoelectron spectroscopy
PM3	-Parameterized Model 3
RD	-Rate-determining
S	-Solvent
SCF	-Self-consistent field
STO	-Slater-type orbital
TS	-Transition state
UV	-Ultra violet

Abstract

We have conducted correlation studies on ten alkene addition reactions in this project in order to explore the substituent effects on alkene reactivity in these reactions. In these studies, we have correlated the relative reactivities of alkenes versus their measurable characteristics, such as the ionization potentials (IPs), the highest occupied molecular orbital (HOMO) energy levels, and sometimes, the lowest unoccupied molecular orbital (LUMO) energy levels, in order to determine the relative magnitudes of electronic and steric effects in the rate-determining step of the alkene addition. The results from our correlation studies indicate that the majority of the alkene reactions included in this project are electrophilic additions to alkenes either with significant steric effects, such as in acid-catalyzed hydration and complexation with solid iodine, or without significant steric effects, such as in chlorination, bromination, oxidation with chromyl chloride and with chromic acid, ISCN addition, and ICl addition. Only two reactions, oxidation with palladium chloride and homogeneous hydrogenation in presence of Wilkinson's catalyst, were found to be nucleophilic additions with significant steric effects. These results are helpful in predicting alkene relative reactivities in the alkene reactions based on the substituents on the C=C bonds. The patterns of correlation plots in some studies have also provided supportive evidence that helped us in differentiating between alternatively proposed mechanisms for studied alkene additions.

Chapter One

Introduction

1.1 The objective of the project

Alkenes readily react with a large variety of chemical reagents via addition to their carbon-carbon double bonds.[1,2] These reactions have been widely applied in organic syntheses, chemical industries, and many other relevant areas.[1-6] The chemical reactivity of the selected alkene toward the addition reaction is always the most important factor to be considered when applying an alkene addition into a practical process in order to achieve expected reaction rate and product yield. The objective of our research is to investigate the structural influence on chemical reactivities of alkenes toward their addition reactions.

The key step in an alkene addition reaction involves cleavage of its alkenyl π bond and the consecutive formation of new bonds between the alkenyl carbon atoms and the incoming species. The chemical reactivity of an alkene in an addition reaction is the measurement of its stability under the electrophilic attack from an electrophile in an electrophilic addition, or the nucleophilic attack from a nucleophile in a nucleophilic addition. The chemical reactivity of an alkene is directly related to the types (or properties), numbers, and relative positions of the substituents bound on the alkenyl carbon atoms. Therefore, a thorough exploration of the substituent effects on alkene reactivity toward a wide range of their addition reactions will advance the understanding of alkene addition reactions and meanwhile provide information useful in mechanistic and synthetic studies.

1.2 Chemical reactivity

Chemical reactivity is an important core subject in all chemistry related fields, especially in organic chemistry. The chemical reactivity of a reactant in a certain reaction can be measured quantitatively by the reaction rate constant (*k*) in a kinetically-controlled reaction or by the reaction equilibrium constant (*K*) in a thermodynamically-controlled reaction. Both constants (*k* and *K*) are related to the free energy changes in the reaction processes (eqs 1-1 and 1-2).[7]

$$\Delta G^{\ddagger} = - RT \ln (kh/\mathbf{k}T) \qquad (1\text{-}1)$$

$$\Delta G^{\circ} = - RT \ln K \qquad (1\text{-}2)$$

For eq 1-1, *k* is the reaction rate constant; $\Delta G^{\ddagger}$ is the free energy of activation for the reaction, which is the free energy difference between the transition state and the reactant (Fig 1-1); T is the temperature in degrees Kelvin (K); **k** is Boltzmann's constant; h is Planck's constant; and R is the universal gas constant.

For eq 1-2, *K* is the equilibrium constant; ΔG° is the free energy difference between the products and the reactants (Fig 1-1); T is the temperature in degrees Kelvin (K); and R is the universal gas constant.

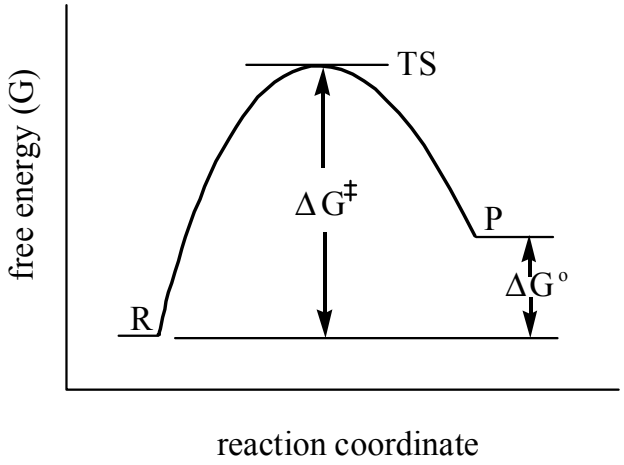


Figure 1-1. Schematic diagram showing the relationship between the two free energy parameters ($\Delta G^{\ddagger}$ and ΔG°) and the free energies of reactants (R), products (P), and transition state (TS) in a chemical reaction

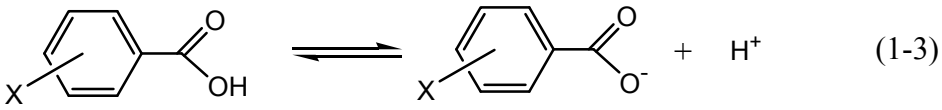
From eq 1-1, the logarithm of reaction rate *k* is proportional to free energy of activation $\Delta G^{\ddagger}$ in a kinetically-controlled reaction. A smaller the value of $\Delta G^{\ddagger}$ corresponds to a greater the reaction rate. A similar relationship is also observed between the logarithm of equilibrium constant *K* and free energy difference ΔG° in a thermodynamically-controlled reaction in eq 1-2. Therefore, if a structural change in a reactant results in a change of $\Delta G^{\ddagger}$ in a kinetically-controlled reaction or a change of ΔG° in a thermodynamically-controlled reaction, the relative reactivity of the reactant measured by reaction constant *k* or by equilibrium constant *K* will be changed correspondingly. A widely applied method in organic chemistry for evaluating substituent effects on chemical reactivity of substrates is Linear Free Energy Relationships (LFERs).

1.3 LFERs method

1.3.1 Hammett equation

Intensive studies about structural effects on chemical reactivity have found that the change of $\Delta G^{\ddagger}$ (or $\Delta G°$) due to introduction of a series of substituent groups in a reaction is, in many cases, directly proportional to that due to introduction of the same series of substituent groups in another reaction, which is termed as Linear Free Energy Relationships (LFERs).[7-10] Similar relationships between the logarithms of *k* (or *K*) of different reactions would also be expected due to the linear relationship between log *k* (or log *K*) and the correspondent free energy change $\Delta G^{\ddagger}$ (or $\Delta G°$) (eqs 1-1 and 1-2).

Hammett first quantified the effect of substituents by using the ionizations of substituted benzoic acids as model reactions (eq 1-3).[11,12]



(1-3)

Here, X is the substituent, on the *para* or *meta* position to the -COOH group, on the benzene ring. The substituent constant for X is defined as:

$$\sigma_X = \log (K_X/K_H) \qquad (1\text{-}4)$$

Here, K_X and K_H are the acidity constants at 25°C in water for the benzoic acid with a substituent X and benzoic acid without any substituent, respectively.

The relationship between this substituent constant σ_X and the relative reactivity of the reactant with the same substituent X in another reaction series can be expressed, for a kinetically-controlled reaction, as:

$$\log (k_X/k_H) = \rho \sigma_X \qquad (1\text{-}5)$$

Here, k_X and k_H are the reaction rate constants of the new reaction for the reactant with an X as the substituent and the reactant without any substituent, respectively.

For a thermodynamically-controlled reaction, it can be expressed as:

$$\log (K_X/K_H) = \rho \sigma_X \qquad (1\text{-}6)$$

Here, K_X and K_H are the equilibrium constants of the new reaction for the reactant with an X as the substituent and the reactant without any substituent, respectively. In both equations, parameter ρ is a proportionality constant, which measures the susceptibility of a given reaction series to the substituent effects. The two equations above (eqs 1-5 and 1-6) are known as the Hammett equations, which can be applied to predict rate or equilibrium constants for new reactions in the same series with different substituents based on some known rate or equilibrium constants.

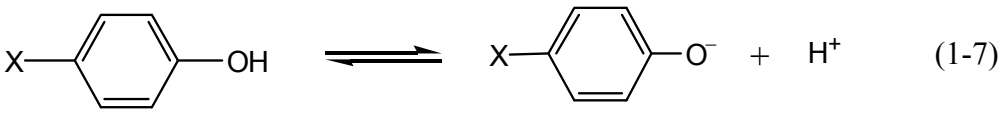
1.3.2 Extensions of Hammett equation

In order to make the Hammett equation applicable to a wider range of reactions, some other scales were developed later by following the approach similar

to the σ scale, but based on different reaction series. For instance, obvious deviations were observed when Hammett equation was applied in reactions in which the substituent can conjugate with the reaction center through the benzene ring. This is because the substituent effects in these reactions are due to both inductive and resonance effects, mainly the latter, while in the benzoic acid ionization, the substituent effects are only due to the inductive effects. The following two scales were developed in order to improve the application of LFERs method in these cases.

A. σ^- Scale

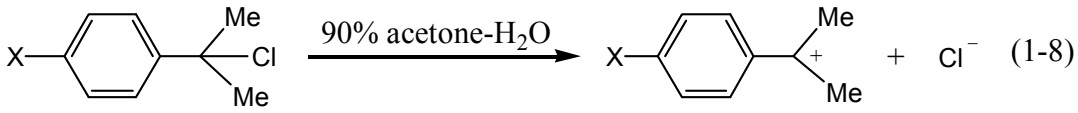
σ^- Scale is applied in reactions in which a negative charge is generated adjacent to the benzene ring. Ionization of *para*-substituted phenols is chosen as the model reaction of this scale (eq 1-7).[13] Similar to the σ scale, the substituent constant for group X is defined as $\sigma^- = \log (K_X/K_H)$.



(1-7)

B. σ^+ Scale

In contrast, σ^+ scale is applied in reactions in which a positive charge is generated adjacent to the benzene ring. Solvolysis of *t*-cumyl chloride is chosen as the model reaction of this scale (eq 1-8).[14] Similarly, the substituent constant for group X is defined as $\sigma^+ = \log (k_X/k_H)$.



(1-8)

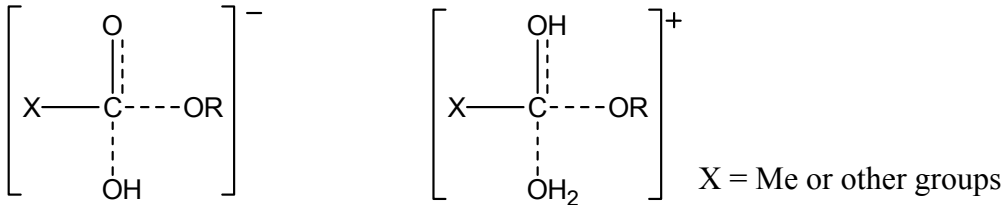
1.3.3 Separation of polar and steric effects

Steric effects on reactivities are not considered in the three scales described above, which would sometimes cause problems when LFERs methods are applied in aliphatic systems. In order to extend LFERs method to aliphatic systems, Taft later developed a procedure for separating polar and steric effects, based on basic and acidic hydrolysis of substituted acetate esters.[15,16] He found that electronic factors of the substituents have little effect on acidic hydrolysis of aliphatic esters. Therefore, substituent effects in this reaction could be considered only due to steric factors and so the steric constant could be defined as:

$$E_s = \log (k_X / k_0)_A \qquad (1\text{-}9)$$

Here, k_X and k_0 are rate constants for acidic hydrolysis of substituted acetate esters (XCOOR) and acetate ester (CH_3COOR). The subscript A denotes acidic hydrolysis.

In basic hydrolysis of substituted acetate esters, both polar and steric effects are found important. The steric effects in basic hydrolysis could be considered almost equal to those in acidic hydrolysis (E_s) since its rate-determining transition state structure (a) differs from that in acidic hydrolysis (b) by only two protons.



(a) (b)

Therefore, the difference of substituent effects between them could be considered as pure polar effects. Based on the above analysis, Taft defined a polar substituent constant σ* as:

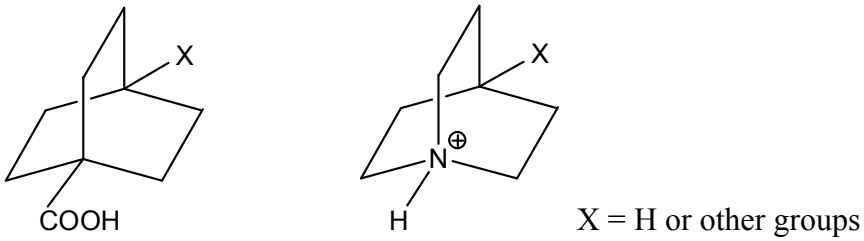
$$\sigma^* = [\log (k_X/k_0)_B - \log (k_X/k_0)_A] / 2.48 \qquad (1\text{-}10)$$

In eq 1-10, k_X and k_0 are rate constants for hydrolysis of substituted and unsubstituted acetate esters, respectively. Subscripts B and A refer to basic and acidic hydrolysis, respectively. Factor 2.48 was introduced here to make the σ* values into the same numerical range as Hammett's σ values. Finally, the general Taft equation for a studied aliphatic system could be expressed as:

$$\log (k_X/k_0) = \rho^* \sigma^* + \delta E_s \qquad (1\text{-}11)$$

In eq 1-11, k_X and k_0 are rate constants for the studied reaction of substituted and unsubstituted substrates, respectively. ρ* and δ are two proportionality constants that represent the susceptibilities of the studied reaction to the polar and steric factors, respectively. It should be pointed out that methyl, other than H, is used as reference substituent in Taft's σ* scale.

Two other different approaches measuring the polar substituent constants for aliphatic systems are based on the dissociations of the H^+ in 4-substituted bicycle[2.2.2]octanecarboxylic acids (a)[17,18] and in 4-substituted quinclidinium ion (b),[19] respectively. The substituent constants are named as σ' in the former system and as σ_I in the latter system. Both σ' and σ_I are believed to reflect only the polar (also named as inductive or field) effects of the substituents because neither steric nor resonance interaction between the substituent and the acid site could be possible in both cases.



(a) (b)

1.3.4 Dual-parameter substituent constants

Resonance contribution to the substituent effects plays a major role when direct conjugation exists between the reaction center and the substituent. This often causes problems in application of LFERs in systems which are influenced by polar and resonance effects differently. In order to solve this problem, an approach, decomposition of a substituent constant into polar and resonance effects, has been proposed[17,18] as shown in eq 1-12.

$$\sigma = fF + rR \qquad (1\text{-}12)$$

For eq 1-12, f is the sensitivity to field (polar) effects, F the pure field substituent effect constant, r the sensitivity to resonance effects, and R the pure resonance substituent constant. F and R are constant for an individual substituent over all reactions, but f and r are empirical weighting factors dependent on each reaction. Therefore, the linear free-energy relationship can be presented as eq 1-13 in this approach.

$$\log (k_X/k_0) = \rho\sigma = \rho fF + \rho rR \qquad (1\text{-}13)$$

1.3.5 Approximate nature of LFERs

Linear free energy relationships have been applied successfully over a wide range of reactions in organic chemistry. However, deviations from LFERs have also been found in many cases, which could be attributed to the approximate nature of LFERs. LFERs have been interpreted[20,21] as empirical approximate models with local validity only, rather than combinations of fundamental effects. Studies have shown that LFERs are very likely obeyed well among sufficiently similar processes. However, if the diversity between the processes is too large, this empirical model would collapse.[20]

The approximate nature of LFERs results from several possible sources. First, it is very common to correlate a series of reactions of aromatic compounds (for instance, ionizations of substituted benzoic acids) with reactions of aliphatic molecules in LFERs studies. The difference between substituent effects in an aromatic system and in an aliphatic system would possibly lead to deviation from

LFERs.[20] Second, deviation from LFERs would likely arise when a series of thermodynamically controlled equilibria (for instance, ionization of substituted benzoic acids) are correlated with kinetically controlled reactions. In this case, the reactivity of the reactants depends upon the free energy difference between the products and the reactants (ΔG°) in the former, while in the latter, the reactivity of the reactants depends upon the free energy of activation for the reaction ($\Delta G^\ddagger$). These two parameters might be nearly linear to each other over a limited region, but the linearity does not hold over a wide range.[22]

Another important factor causing deviation from LFERs is steric effects of the substituents, which are often ignored in many LFERs methods. In some cases, especially for aliphatic systems, steric effects are significant and complicated, dependent upon the number, position, size, and geometry of the substituents.[23,24] Taft has proposed an approach to separate the polar and steric effects in organic reactions based on two assumptions (see section 1.3.3). However, both assumptions, (a) only steric effects exist in acid catalyzed hydrolysis of acetate esters and (b) the steric effects are equal in both acid and base catalyzed hydrolyses of acetate esters, have been found not valid in many cases.[24] Finally, it should be pointed out that reaction conditions, for instance, solvent and temperature, would exert different influences on different reactions, which would also possibly cause deviation from LFERs in some cases.[20,21]

1.4 Steric effect measurements

In addition to Taft's method stated above, several other approaches for measuring the steric effects of different substituent groups on chemical reactivity have also been developed later. In one method, the monosubstituted cyclohexane derivatives are chosen as the model system.[25-27] The free-energy difference between equatorial and axial substituents on a cyclohexane ring, termed as the axial strain energy or A-value, is used to measure the steric effects of the correspondent substituent. In this case, the A-value equals zero if the substituent is H, since there is no free-energy difference between the two isomers. For all other substituents, the A-values are generally greater than zero because the equatorial isomers are favored over the axial ones.

Another method was developed based on the computational analysis of molecular mechanics methods for a series of chromium complexes, $Cr(CO)_5L$, where L represents one of the different ligands.[28] The computational van der Waals repulsive energy between the ligand L and $Cr(CO)_5$ fragment is defined as the ligand repulsive energy, E_R, which can be used as a measure of the steric effect of the correspondent ligand L. Generally, a larger ligand corresponds to a greater ligand repulsive energy. This method has been found applicable in both organometallic and organic chemistry.[29]

1.5 Research methodology

In this project, we intend to investigate not only electronic but also steric effects of the substituents on chemical reactivities of alkenes toward their addition

reactions. Dr. Nelson[30-39] has developed a technique to determine the relative magnitudes of electronic and steric effects of substituents in alkene additions by correlating the logarithms of relative rates (or equilibrium constants) of alkene additions versus alkene measurable characteristics. These measurable characteristics include alkene ionization potentials (IPs), the highest occupied molecular orbital (HOMO) energy levels, and the lowest unoccupied molecular orbital (LUMO) energy levels.

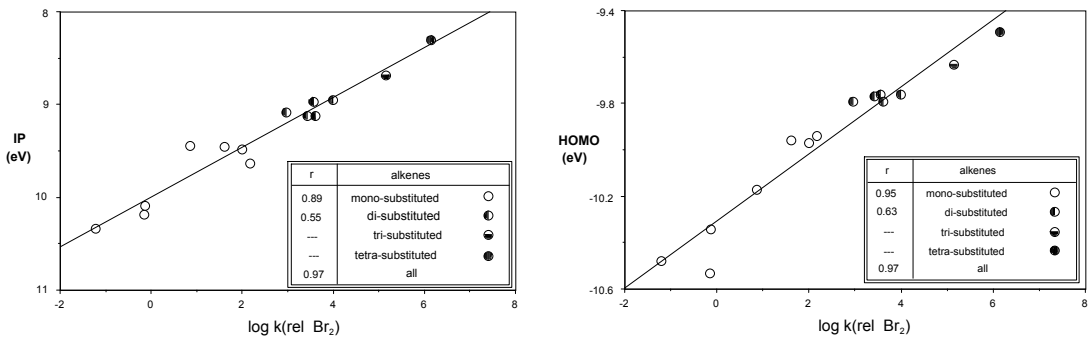
We have chosen alkene IPs, HOMO energy levels, LUMO energy levels to correlate the alkene relative reactivities in our research because an alkene addition is initiated either by an electrophilic attack from an electrophile on the alkene π bond, or by a nucleophilic attack from a nucleophile on the alkene empty π* orbital. In the former case, the stability of the alkene π bond can be measured by the alkene IP or HOMO energy level. In the latter, the ability for an empty alkene π* orbital to accept a nucleophilic attack can be measured by the alkene electron affinity (EA) or LUMO energy level. In our actual studies, only alkene LUMO energies are used because experimental alkene EAs are often not available in literature. Therefore, the chemical reactivities of alkenes toward addition reactions must be related directly to these measurable characteristics (IPs and HOMO/LUMO energies).

Furthermore, the substituents on alkene C=C bonds would affect the free energy level of the transition state of the reaction in the same way as they affect the properties (IPs and HOMO/LUMO energies) of alkenes. For example, an electron-donating group (EDG) lowers the IP of an alkene, and also lowers the free energy level of the transition state (or the energy of activation) for an electrophilic addition to

alkenes. Therefore, an EDG would accelerate the reaction, or in other words, would enhance the alkene reactivity. In contrast, the electron-withdrawing groups (EWG) would do the opposite.

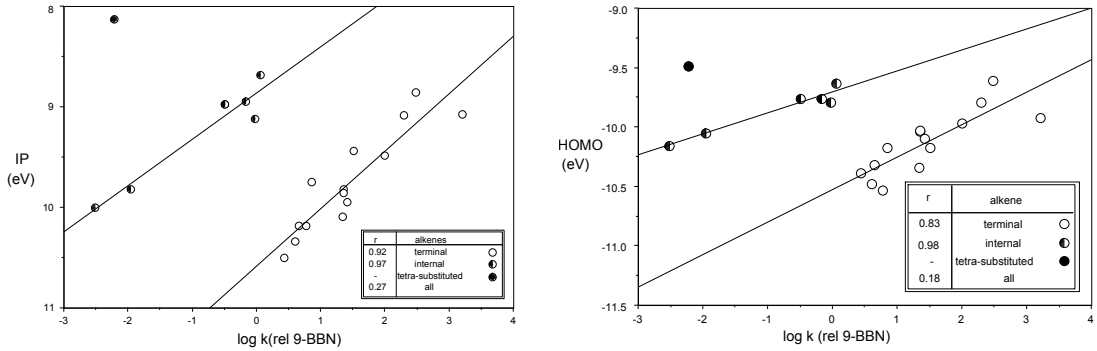
Another important reason for choosing these properties in our research is that the values of alkene IPs and HOMO/LUMO energies are influenced almost solely by the electronic effects of the substituents on the C=C bonds. As a result, these alkene characteristics can be considered as good measurements of pure electronic effects of the substituents on the alkene reactivity toward its addition reactions.

In order to explore the steric effects of the substituents on the reactivities of the alkenes toward an addition reaction, we correlate logarithms of the relative rates versus these alkene characteristics (IPs and HOMO/LUMO energies) among each group of sterically similar alkenes and also among all alkenes regardless of their steric requirements. Based on the patterns shown in the resulting correlation plots, the relative importance of electronic and steric effects on alkene reactivities toward the addition reactions can be elucidated.[40] If a single line of correlation is obtained among all alkenes, regardless of their steric requirements, alkene reactivities in this reaction depend predominantly upon electronic effects, and steric effects are relatively insignificant and negligible (Fig 1-2). The majority of alkene additions we have studied so far are found to belong to this category, for instance, bromination,[30,38] sulfenyl halide addition,[31] epoxidation,[31] dichlorocarbene addition,[34] nitrosyl chloride addition,[34] oxidation with osmium tetroxide,[34] oxidation with chromyl chloride,[35] oxidation with chromic acid,[35] chlorination,[38] and iodine chloride addition.[39]



(a) (b)

Figure 1-2. Plots of log k_{rel} values (a) versus alkene IPs and (b) versus alkene HOMO energy levels for alkene bromination, an electrophilic addition to alkenes without strong steric effects



(a) (b)

Figure 1-3. Plots of log k_{rel} values (a) versus alkene IPs and (b) versus alkene HOMO energy levels for alkene hydroborotion, an electrophilic addition to alkenes with strong steric effects

On the other hand, if a natural separation of sterically different alkene groups is observed in the correlation plots, it means that steric effects play a significant role in this reaction and the alkene reactivity depends upon both electronic and steric effects (Fig 1-3). Some alkene additions included in our study so far are found to

belong to this category, for instance, hydroboration,[30] oxymercuration,[30] silver ion complexation,[31] diimide reduction,[32] complexation with iodine,[38] and acid-catalyzed hydration.

Values of slopes of the correlation lines in the plots can provide information about whether the addition to the alkene is electrophilic or nucleophilic. Positive slopes in the plots of logarithms of relative rates versus alkene IPs or versus alkene HOMO energies indicate that the studied addition to alkene is electrophilic, i.e. a lower IP or higher HOMO energy corresponds to a greater reaction rate. In order to facilitate the comparison with the plots for HOMO energies, IP data are actually plotted in inverse order on the Y-axis in our studies. If negative slopes are observed in the plots of logarithms of relative rates versus alkene IPs or versus alkene HOMO energies, the studied reaction is very likely to be a nucleophilic addition to alkenes. In this case, we need to employ alkene LUMO energies (Fig 1-4), but not IPs or HOMO energies, to constitute the correlation plots, which could give information about substituent effects on alkene reactivities toward a nucleophilic addition to alkenes. Only three alkene reactions in our correlation studies, oxidation with permanganate,[33] Wacker oxidation,[36] and hydrogenation catalyzed by Wilkinson's catalyst,[37] have been found to be nucleophilic additions to alkenes. Alkene oxidation with permanganate gives correlation plot similar to Fig 1-4 (a), while both Wacker oxidation and hydrogenation catalyzed by Wilkinson's catalyst show plots similar to Fig 1-4 (b).

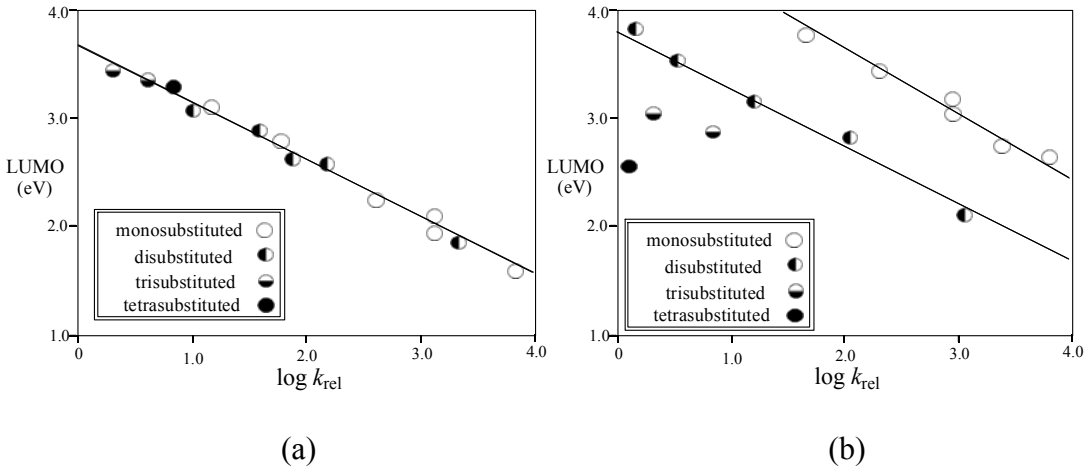


Figure 1-4. Schematic diagrams showing the plots of log k_{rel} values versus alkene LUMO energy levels for a nucleophilic addition to alkenes (a) without strong steric effects and (b) with strong steric effects

Electronic effects of the substituents affect electrophilic and nucleophilic additions to alkenes oppositely. For instance, an electron-donating substituent accelerates electrophilic additions, but decelerates nucleophilic additions. However, steric effects affect both electrophilic and nucleophilic additions in the same way, i.e. steric retardation.[41] The key process in an alkene addition is either an electrophilic or a nucleophilic attack from the incoming electrophile/nucleophile to the alkene C=C bond. Therefore, steric hindrance from the substituents on C=C bond would always retard the reaction more or less, depending on the transition structures. Many studies[41-48] on steric effects have also given evidence for the steric retardation in alkene additions.

The alkene relative rates used in our studies are either from previously published kinetic studies, or from our competitive reaction experiments. An example of the competitive reaction experiments, competitive hydration of alkenes, is

introduced in Chapter 2. Alkene experimental IP values were collected from literature. The alkene HOMO and LUMO energy levels in our study were calculated by using different molecular orbital (MO) methods. A detailed introduction about the computational MO methods employed in the project can be found in Chapter 5.

1.6 Linear regression

In our correlation studies, the method of least squares is employed to obtain the linear relationship between the relative reactivities (log k_{rel}) of alkenes and their measurable characteristics (IPs, HOMO/LUMO energies).[8,48] This method follows the rule that the sum of the squares of the deviations between observed and estimated values should be a minimum. Assuming the linear relationship between the two variables (x and y) can be simply written as:

$$y = \alpha x + \beta \qquad (1\text{-}14)$$

For eq 1-14, α and β are the slope and intercept of the line of correlation on the y axis in the plot, respectively.

In order to evaluate the correlation from the regression, the following parameters about this correlation still need to be calculated.

A. Correlation coefficient, r:

$$r = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}} \qquad (1\text{-}15)$$

For eq 1-15, (x_i, y_i) are a pair of the experimental data; $\bar{x}$ and $\bar{y}$ are the averages of x_i and y_i, respectively. The value of r is from 0 to 1; the greater the r value is, the better the regression equation fits to the data. If all data points fall on the correlation line perfectly, the value of r would be r = 1. Generally, r > 0.9 indicates a strong correlation between y and x.[49]

B. Standard deviation, s:

$$s = \sqrt{\frac{\sum_{i=1}^{n}[y_i - (\alpha x_i + \beta)]^2}{n-2}} \qquad (1\text{-}16)$$

For eq 1-16, n is the number of data pairs. The value of s is a measure of the scatter of the y values about the correlation line. The smaller the value of the standard deviation, the stronger is the correlation between y and x.

C. Confidence level, c.l.:

The confidence level gives the probability that the experimental data follow the relationship ($y = \alpha x + \beta$) from the regression. The calculation of confidence level

(c.l.) is based on the Student's t-test. First, the Student's t function is calculated by eq (1-17).

$$t = r\,[(n - 2) / (1 - r^2)]^{1/2} \qquad (1\text{-}17)$$

Then, the confidence level can be found from statistical tables[50] about the t distribution according to the value of t from eq 1-17 and the number of data sample. The confidence level of the correlation depends on both the correlation coefficient r and the number of the experimental data. The higher is the confidence level, the stronger is the correlation between y and x.

The regression procedure and plot drawing are actually performed by the computer programs which give the values of slope α, intercept β, standard deviation s, and correlation coefficient r due to the experimental data. The computer programs we employed in our research are Cricket Graph in the Macintosh computers and Sigma Plot in the PC computers.

1.7 Significance of the project

In our correlation studies, relative magnitudes of electronic and steric effects of substituents on reactivities of alkenes toward their additions can be ascertained by examining the patterns of the resulting correlation plots. These results are useful in predicting relative reactivities between different alkenes in an addition reaction semi-quantitatively, which is significant in organic syntheses and related industrial applications. In some cases, it is expected to react only one C=C bond but to leave

the others intact in an unconjugated diene or polyene molecule.[51-59] The priority order of additions of these different C=C bonds can also be predicted with the help of the results from our correlation studies.

The patterns of correlation plots in our studies are also useful in mechanistic studies in some cases.[35-37] In our correlation studies, reactions that gave different correlation plots follow different mechanisms, while reactions with similar mechanisms always gave similar correlation plots. In other words, electronic and steric effects are expected to be similar among reactions following similar mechanisms. Therefore, comparison of correlation plots obtained from different alkene additions, combined with the information of electronic and steric effects in these reactions, would help us to differentiate between alternative proposed reaction mechanisms.

This methodology is also relatively simple and convenient in comparison with the LFERs method in assessing substituent effects in alkene additions. Alkene IPs and HOMO/LUMO energies are characteristic properties of alkenes and independent of any specific reaction. This is an advantage over the LFERs method, in which an appropriate scale (σ, σ^+, σ^-, σ^*, σ', or σ_I) should be chosen for the studied reaction in order to obtain the correct results.

The method correlating relative reactivity (log *k* or log *K* values) of a series of alkene reactions versus alkene IPs,[60-73] versus alkene HOMO energy levels,[74-79] and versus alkene EAs[80-83] has also been employed in some studies for various purposes. Our methodology differs from those studies in that we focused on the separation of steric versus electronic effects by covering a wide range of alkenes bearing

substituents with different electronic and steric requirements in order to obtain the correct results. For instance, alkene hydroboration was considered to be a nucleophilic addition to alkenes in a previous study[72] by correlating alkene IPs versus logarithms of relative rates. However, a later study by Dr. Nelson,[30] by including more data points of alkenes with a wide range of different substituents, revealed that it is actually an electrophilic addition with strong steric effects. This result corrected the previous erroneous conclusion caused by using too few data points and covering alkenes bearing substituents without a wide range of electronic and steric requirements.

1.8 Development of the methodology

This correlation method, first established by Dr. Nelson,[30] had been successfully applied to many alkene additions reactions[30-34] when we began to work on this project. The majority of these alkene additions studied were found to be electrophilic additions to alkenes without significant steric effects, in which a single line of correlation with a positive slope was observed in the plot of logarithms of relative rates versus alkene IPs or versus alkene HOMO energies. For instance, alkene bromination,[30] epoxidation,[31] sulfenyl halide addition,[31] carbene addition,[34] oxidation with osmium tetroxide,[34] and nitrosyl chloride addition,[34] have been found to belong to this type. A number of alkene additions were found to be electrophilic addition with strong steric effects, in which nearly paralleled multiple lines of correlation with positive slopes were obtained in the correlation plots of log k_{rel} values versus alkene IPs or HOMO energies. This type of reactions include alkene

hydroboration,[30] oxymercuration,[30] silver ion complexation,[31] and diimide reduction.[32] Only one alkene reaction, oxidation with permanganate,[33] was found to be nucleophilic additions to alkenes without strong steric effects due to the single line of correlation with negative slope in the plot of logarithms of relative rates versus alkene IPs.

The main purposes of this project are to apply the correlation method to a greater variety of alkene addition reactions to assess its viability and meanwhile to obtain important mechanistic information about the selected addition reactions of alkenes. Based on the previous researches, we have carried out correlation studies in this project on ten different alkene reactions: acid-catalyzed hydration of alkenes, alkene oxidation with chromyl chloride,[35] alkene oxidation with chromic acid,[35] alkene oxidation with palladium chloride (the Wacker oxidation),[36] alkene homogeneous hydrogenation in presence of Wilkinson's catalyst,[37] chlorination of alkenes,[38] bromination of alkenes,[38] alkene complexation with molecular iodine,[38] iodine thiocyanate addition to alkenes,[39] and iodine chloride addition to alkenes.[39] All these studies, except for the acid-catalyzed hydration of alkenes, have been published in peer-reviewed journals[35-39] and have been the subject of several Awards,[84] including the Guggenheim Award,[84a] Fellow of the American Association for the Advancement of Science (AAAS),[84b] Chemical Heritage Foundation Oral History Interviewee,[84c] Society for the Advancement of Chicanos and Native Americans in Science (SACNAS) Distinguished Scientist Award,[84d] and University of Oklahoma Department of Chemistry J. J. Zuckerman Award for Research in Chemistry. In addition, this research has been used to explain addition reactions of

alkenes in chemistry textbooks.[85] A detailed introduction of these studies will be presented in the ensuing chapters.

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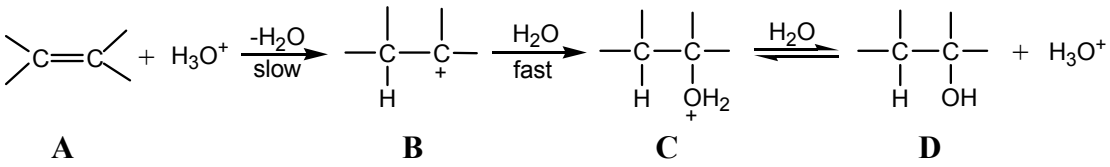
Chapter Two

Substituent Effects in Acid-Catalyzed Hydration of Alkenes

Abstract: A set of reaction conditions applicable to alkenes with different steric requirements (mono-, di-, tri-, and tetrasubstituted) was established in order to determine the relative reactivity of alkenes in acid-catalyzed hydration. The relative reaction rates for 19 alkenes were obtained through competitive reactions under the same condition. Correlation plots of logarithms of relative reaction rates for acid-catalyzed hydration of alkenes versus alkene IPs and versus alkene HOMO energies indicate that this reaction is an electrophilic addition to alkenes. Multiple lines of correlations among sterically similar groups of alkenes in the plots reveal that the alkene reactivity depends on both electronic and steric effects of the substituents on the alkene C=C bond. Comparison with other similar electrophilic alkene additions, which also depend on both electronic and steric effects, reveals that alkenes in hydration reaction form groups based on both the number and the relative position of substituents on the C=C bond, which is consistent with those in alkene hydroboration and oxymercuration. However, this observation is inconsistent with results for analogous investigations of some other sterically dependent alkene additions, such as diimide reduction and complexation with molecular iodine, in which alkenes form groups solely based on the number of substituents on the C=C bond. These two different grouping patterns can be rationalized by the differences in their transition structures of the rate-determining steps.

2.1 Introduction

The acid-catalyzed hydration of alkenes is a fundamental organic reaction. It converts an alkene into an alcohol by following Markovnikov's rule, i.e. the OH group is added to the more highly substituted carbon of the C=C bond. Acid-catalyzed hydration of alkenes have been intensively studied in many aspects.[1-39] The widely accepted mechanism for this reaction is shown in Scheme 2-1.[1-3]



Scheme 2-1. The reaction mechanism for acid-catalyzed hydration of alkenes

The first step, protonation of the alkenyl C=C bond of alkene **A** to give a carbocation intermediate **B**, is believed to be the rate-determining step of the reaction. Experimental studies[4,7,8] indicate that this is an irreversible step, but not a fast equilibrium. Kinetic studies[10,19,23,31,35] show that this reaction is first order in both alkene and hydronium ion, which also supports protonation of the C=C bond (**A→B**) as the rate-determining step. The carbocation intermediate **B** is then immediately captured by a water molecule to form a cationic intermediate **C**. The intermediate **C** releases a proton to a water molecule to regenerate a hydronium ion and produce the final alcohol product **D**.

The reaction has been found to be an electrophilic addition to alkenes;[1-2,19-23] electron-donating groups on C=C bonds accelerate the reaction, while electron-withdrawing groups decelerate it. However, there has not been reported a set of

experiment conditions that accommodates all differently substituted olefins (mono-, di-, tri-, and tetrasubstituted). This caused difficulty in analyzing steric effects of the substituents on alkene reactivity in this reaction. Therefore, it seems desirable for us to conduct a study that includes alkenes with different electronic and steric requirements under the same reaction conditions to investigate the relative importance of electronic and steric effects in this reaction. The alkene ionization potentials (IPs) were collected from literature, while the relative reaction rates were obtained from our competitive reaction experiments.

2.2 Competitive reaction experiments

2.2.1 Materials

All the alkenes used in this study were purchased from Wiley Organics and Aldrich Chemical Company. Internal standard alkanes were purchased from the Humphrey Chemical Company. All materials are the best available commercial grades. Aqueous solutions were prepared by using deionized water.

2.2.2 Instruments

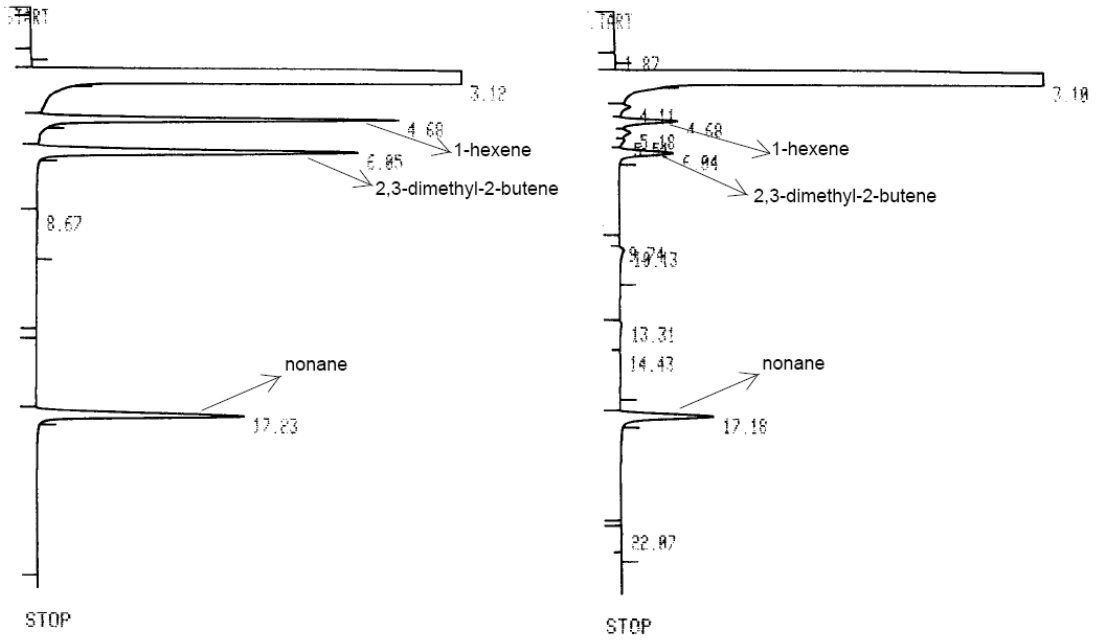
The GC analyses were carried out on a Hewlett-Packard 5890A gas chromatograph, which was connected to a Hewlett-Packard 3390A integrator for measuring the peak areas. The GC was equipped with a column of 3.66 meter packed with 10% SE-30 on 100/120-mesh Chromosorb W. The GC temperature was programmed as from 35°C (initial temperature, 5 minute) to 200°C (final temperature, 5 minute) at a rate of 5°C/min.

2.2.3 Experiment procedure

An alkene/standard solution, 2 alkenes (5 mmol for each) and nonane (2.5 mmol, as internal standard), was first analyzed by GC in order to determine the response factor F for each alkene (eq 2-1). In eq 2-1, F_X is the response factor for alkene X; n_{0X} and n_{0S} are the amounts (mole) of alkene X and internal standard S in the initial reactant solution, respectively; A_{0X} and A_{0S} are the areas of the peaks in the GC chromatogram for alkene X and for internal standard S, respectively.

$$F_X = \frac{n_{0S}}{A_{0S}} \bullet \frac{A_{0X}}{n_{0X}} \qquad (2\text{-}1)$$

The alkene/standard solution was then mixed with 3 mL of H_2SO_4 (60%) in a 50 mL round bottom flask equipped with a sidearm and a cold water condenser. The reaction mixture was stirred vigorously for a certain time (depending upon the reactivity) in a water bath at 50°C. Once stirring was stopped, the reaction mixture was moved into a bottle with 3.1g of solid KOH and 5 mL of ethanol, and was then submerged in an ice-water bath. The flask was washed with 4 mL of ethanol twice and the washing liquid was collected into the same bottle in the ice-water bath. The bottle was then vigorously shaken in the ice-water bath until all the white KOH pellets disappeared. The white precipitate (K_2SO_4) was then separated from the liquid phase by centrifugation. A sample from the liquid phase in the bottle was then used in GC analysis to determine the amounts of the residual alkenes in the final reaction mixture. Figure 2-1 gives an example of the GC chromatograms from a competitive reaction experiment.



(a) (b)

Figure 2-1. The GC chromatograms for competitive hydration of 2,3-dimethyl-2-butene versus 1-hexene: (a) initial reactants and (b) final reaction products

The residual amounts of the two alkenes in the final reaction mixture can be calculated by using eq 2-2. In eq 2-2, n_{fX} and n_{fS} are the amounts of alkene X and internal standard S in the product mixture, respectively; A_{fX} and A_{fS} are areas of the peaks in the GC chromatogram for alkene X and for internal standard S, respectively.

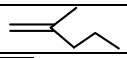
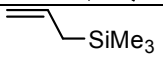
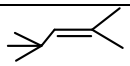
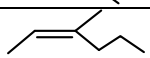
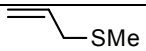
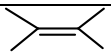
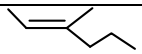
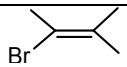
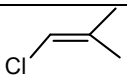
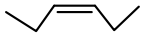
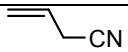
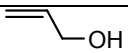
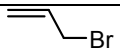
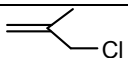
$$n_{fX} = \frac{n_{fS}}{A_{fS}} \bullet \frac{A_{fX}}{F_X} \qquad (2\text{-}2)$$

Finally, the relative reactivity of the two alkenes could be calculated by using the Ingold-Shaw equation (eq 2-3).[40] In eq 2-3, k_{rel} is the relative rate; k_X and k_Y are the rate constants for alkene X and for alkene Y, respectively.

$$k_{rel} = \frac{k_X}{k_Y} = \frac{\log n_{0X} - \log n_{fX}}{\log n_{0Y} - \log n_{fY}} \qquad (2\text{-}3)$$

Totally, 19 alkenes are included in our competitive reaction experiment. The relative rate for each pair of alkenes should less than 7 in order to keep maximum precision. The studied alkene pairs are listed as following: 2-propen-1-ol / 1-hexene, 3,3-dimethyl-1-butene / 1-hexene, 3-chloro-2-methylpropene / 1-hexene, 3-bromopropene / 2-propen-1-ol, 3-butenenitrile / 3-bromopropene, 1-chloro-2-methylpropene / 1-hexene, 3-(methylthio)-1-propene / 1-hexene, 2-bromo-3-methyl-2-butene / 3-bromopropene, *trans*-2-heptene / 1-hexene, *cis*-2-heptene / 1-hexene, *cis*-3-hexene / *trans*-2-heptene, 2,4,4-trimethyl-2-pentene / 2,3-dimethyl-2-butene, 2,3-dimethyl-2-butene / 1-hexene, 2-methyl-1-pentene / trimethyl-2-propenylsilane, trimethyl-2-propenylsilane / 2,4,4-trimethyl-2-pentene, *trans*-3-methyl-2-hexene / 1-hexene, *cis*-3-methyl-2-hexene / 1-hexene, and *trans*-3-hexene / *trans*-2-heptene. The reaction for each pair of alkenes is run in triplicate and the averages are used in our correlation study. The rates relative to 1-hexene for all alkenes from the experiment are listed in Table 2-1. The errors are calculated by using Student's t-test[41] with a confidence coefficient 90%.

Table 2-1. Relative rates from the competitive reaction experiments in H_2SO_4 (60%) at 50°C

No.	Alkene	Relative rates
1		9.20 ± 0.93
2		4.49 ± 0.16
3		2.53 ± 0.02
4		1.38 ± 0.07
5		1.29 ± 0.03
6		1.09 ± 0.06
7		1.03 ± 0.02
8		1.00
9		0.86 ± 0.06
10		0.70 ± 0.04
11		0.59 ± 0.02
12		0.46 ± 0.06
13		0.45 ± 0.02
14		0.40 ± 0.01
15		0.29 ± 0.03
16		0.23 ± 0.01
17		0.21 ± 0.01
18		0.17 ± 0.02
19		0.17 ± 0.03

Note: The relative rates in the table are relative to k_{rel} = 1.00 for 1-hexene.

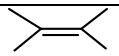
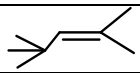
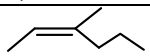
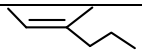
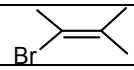
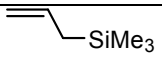
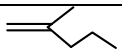
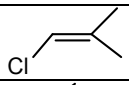
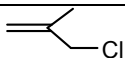
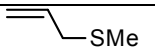
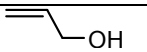
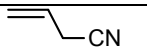
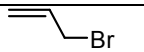
2.3 Correlation plots

Alkene experimental IPs, computational HOMO energy levels, and relative reaction rates of acid-catalyzed hydration of alkenes are listed in Table 2-2. Cyclic alkenes and aryl alkenes are not included in order to avoid complications due to ring strain or conjugation with the aryl group. Alkene IPs are collected from literature.

Alkene HOMO energies are given in Table 2-2 because experimental IPs for a number of alkenes in the table are not available in literature. Alkene HOMO energy levels are calculated by using the *ab initio* method at the HF/6-31G* level. The relative rates in Table 2-2 are converted from the results of our competition reaction experiment in Table 2-1, but relative to k_{rel} = 100 for 1-hexene.

Multiple lines of correlation were obtained in the plot of log k_{rel} values of acid-catalyzed hydration of alkenes versus alkene IPs (Fig 2-2). Good to excellent correlations[49] are observed for terminal alkenes (r_{ter} = 0.90) and for internal alkenes (r_{int} = 0.86), which are much better than the correlation coefficient calculated by including all alkenes regardless of degree of substitution (r_{all} = 0.44). The plot of log k_{rel} values versus alkene HOMO energies (not shown) gives correlations similar to those for alkene IPs, and the correlation coefficients for terminal alkenes, for internal alkenes, and for all alkenes regardless of degree of substitution are 0.80, 0.75, and 0.31, respectively.

Table 2-2. Alkene IPs (eV), HOMO energies (eV), and relative rates of acid-catalyzed hydration of alkenes in aqueous H_2SO_4 (60%) at 50°C

No.	Alkene	IP[a]	HOMO[b]	k_{rel}[c]
1		8.27	-8.70	103
2		8.48[d]	-8.89	253
3		8.53[e]	-8.77	129
4		8.53[e]	-8.77	86
5		8.61[f]	-8.98	70
6		8.95	-9.27	46
7		8.97	-9.28	40
8		8.97[g]	-9.20	45
9		8.97[h]	-9.20	17
10		9.00[i]	-9.60	449
11		9.08	-9.36	920
12		9.45	-9.65	138
13		9.48	-9.66	100
14		9.61[j]	-9.65	59
15		9.90[k]	-9.72	17
16		9.95[l]	-9.88	109
17		10.16[m]	-10.01	23
18		10.18[n]	-10.02	29
19		10.18[o]	-10.02	21

[a]Ref 42, unless otherwise noted. [b]*Ab initio* at the HF/6-31G* level by Christopher Brammer. [c]Relative to k_{rel} = 100 for 1-hexene. [d]Calculated by applying to the IP for 2-bromopropene a correction factor calculated as the difference between the IPs of 2-methylpropene and 2,3-dimethyl-2-butene: 9.58eV - (9.24eV – 8.27eV) = 8.61eV; Ref 42 and Chadwick, D.; Frost, D. C.; Katrib, A.; McDowell, C. A.; McLean, R. A. N. *Can. J. Chem*. **1972**, *50*, 2642-2651. [e]Calculated by applying to the IP for *cis*-4,4-dimethyl-2-pentene a correction factor calculated as the difference between the IPs of *cis*-2-butene and 2-methyl-2-butene: 8.92eV - (9.12eV – 8.68eV) = 8.48eV; Ref 42.

[f]Calculated by applying to the IP for *cis*-2-hexene a correction factor calculated as the difference between the IPs of *cis*-2-butene and 2-methyl-2-butene: 8.97eV - (9.12eV – 8.68eV) = 8.53eV; Ref 42. [g]Calculated by applying to the IP for chlorobutene a correction factor calculated as the difference between the IPs of butene and 2-methylpropene: 10.00eV - (9.63eV – 9.24eV) = 9.61eV; Refs 42 and 51. [h]IP for *cis*-2-hexene used as an approximation; Ref 42. [i]IP for *trans*-2-hexene used as an approximation; Ref 42. [j]Ref 43. [k]Ref 44. [l]Ref 45. [m]Ref 46. [n]Ref 47. [o]Ref 48.

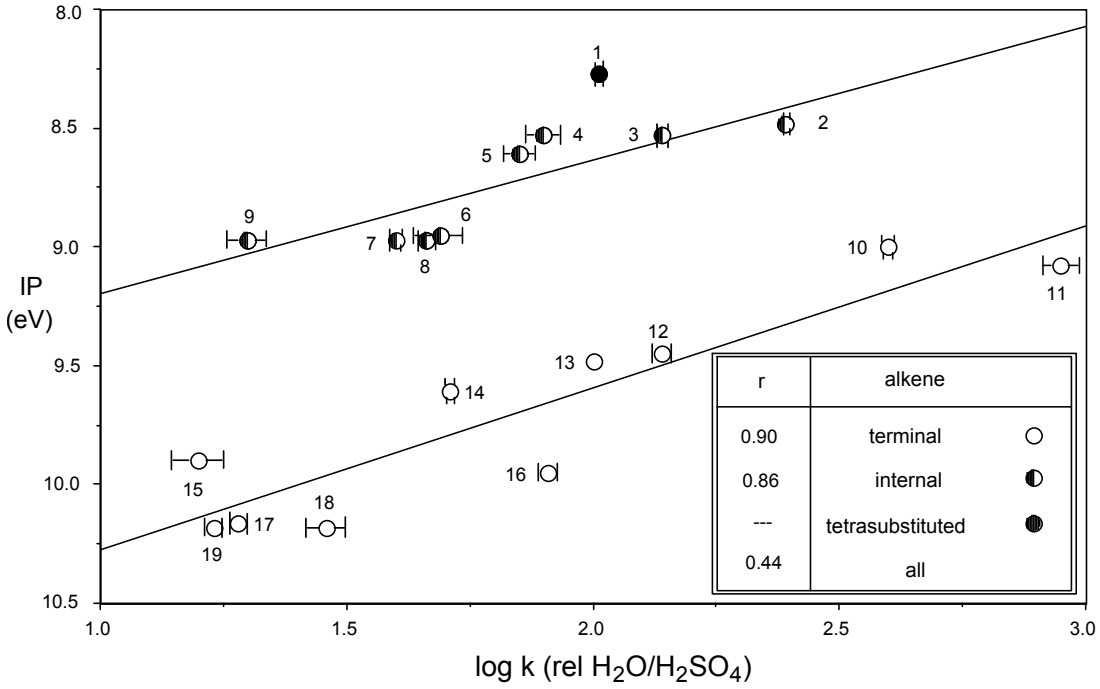
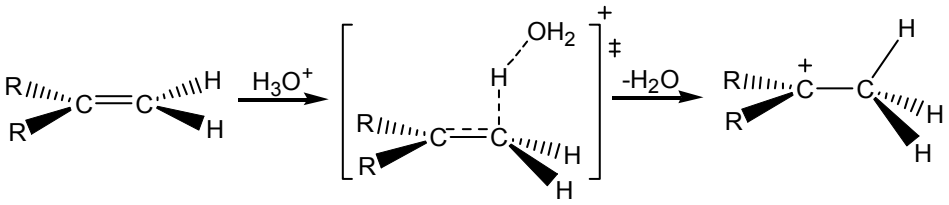


Figure 2-2. The plot of the log k_{rel} values for acid-catalyzed hydration of alkenes versus alkene IPs. Data are from Table 2-2. The y-axis IP data are plotted in inverse order to facilitate comparison with previous studies. Data points naturally fall into different sterically similar alkene groups. Correlation lines are given for terminal alkenes (IP = 10.99 – 0.68 log k_{rel}, r = 0.90, s = 0.21, and c.l. = 99.97%) and for internal alkenes (IP = 9.77 – 0.56 log k_{rel}, r = 0.86, s = 0.28, and c.l. = 99.23%).

2.4 Substituent effects

Data points for alkenes in Fig 2-2 form three groups, corresponding to sterically different alkenes: terminal (monosubstituted and geminal disubstituted), internal (vicinal disubstituted and trisubstituted), and tetrasubstituted alkenes. These three groups correspond to proton bonding to CH_2, CHR, and CR_2 in the rate-determining step, respectively, so that the positive charge will reside on the more substituted carbon. In this way, the more stable (more highly-substituted) carbocation will be formed. The positive slopes of the correlation lines indicate the involvement of an electrophilic attack on the C=C bond in the rate-determining step of acid-catalyzed hydration of alkenes, which demonstrates consistency with previous studies.[1-3,19-23] The natural separation of sterically different alkene groups indicates the presence of significant steric effects in the rate-determining step of this reaction. The correlations among sterically similar alkenes indicate that relative reaction rates for acid-catalyzed hydration of alkenes are dependent upon both electronic and steric effects. The reaction rate increases as the alkene IP decreases within each sterically-similar alkene group, resulting in a positive slope for the correlation line of each group. This can be explained by the proposed[3,9,31,37] electrophilic attack of a hydronium ion upon the alkene double bond in the rate-determining step of this reaction (Scheme 2-1). The fact that 2-methyl-1-pentene (**11**) is in a separate group from *cis*-3-hexene (**6**) reveals different steric effects in geminal and vicinal disubstituted alkenes, as was observed in hydroboration[50] and oxymercuration.[50] This pattern agrees with the proposed[1,3,9,31,37] asymmetrical transition state structure in the

electrophilic attack of a H_3O^+ upon the less substituted carbon of the alkenyl C=C bond (Scheme 2-2).



Scheme 2-2. The structure of transition state in the rate-determining step of acid catalyzed hydration of alkenes

In Fig 2-2, two data points, trisubstituted 1-chloro-2-methylpropene (**14**) and tetrasubstituted 2-bromo-3-methyl-2-butene (**5**), fall in the terminal and internal groups respectively, but not the internal and tetrasubstituted groups respectively, as expected. This could probably be rationalized by the large difference in steric effects caused by the halogen atoms (Cl and Br) and by alkyl groups. For instance, the axial strain energies (the A-values) for Cl and Br, due to 1,3-diaxial interactions in an monosubstituted cyclohexane, are 0.53 and 0.48 kcal/mol, respectively, which are much smaller than that for a methyl (1.70 kcal/mol) or for a *t*-butyl (4.00 kcal/mol).[51] In addition, the ligand repulsive energies (E_R), due to the steric repulsion between a ligand L and the $Cr(CO)_5$ fragment in a complex $Cr(CO)_5L$, for these groups also show a similar trend. The E_R values for Cl and Br are 1.0 and 1.4 kcal/mol, respectively, which are much smaller than that for a methyl (18 kcal/mol) or for a *t*-butyl (90 kcal/mol).[52] Therefore, the steric requirements for CXH and CXR (X = Cl or Br; R = alkyl) on a carbon atom of the C=C bond would be expected to be similar

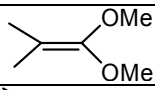
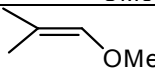
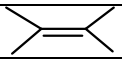
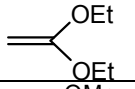
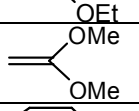
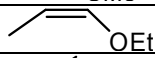
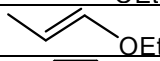
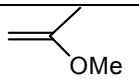
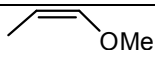
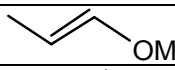
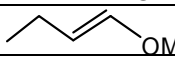
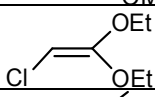
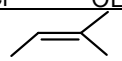
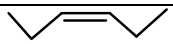
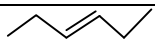
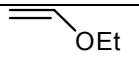
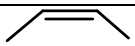
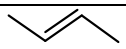
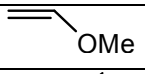
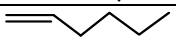
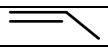
to those for CH_2 and CHR, respectively, but much weaker than those for CHR and CR_2, respectively.

2.5 Comparison with a previous study

In a previous study about substituent effects on alkene reactivities in acid-catalyzed hydration, Tidwell and coworker[22] collected rate data of acid-catalyzed hydration for various alkenes from different studies. In order to compare the rates, they converted the collected rates, which were obtained from reactions at different acidities, to the rates at the same acidity ($H_0 = 0.0$) by extrapolation. They found that the logarithms of the reaction rates correlate well with the alkene substituent constants ($\sum\sigma^+$) when terminal (mono- and 1,1-disubstituted) alkenes are included only and when 1,2-disubstituted alkenes are also included if an extra correction parameter are introduced for the β-substituent effects in 1,2-disubstituted alkenes. However, the correlation would be poor when they tried to include all alkenes, regardless of degree of substitution, especially when some tri- and tetrasubstituted alkenes included.

By using our methodology, we find that these rate data (see Table 2-3, only unconjugated acyclic alkenes included) correlate successfully with alkene IPs (Fig 2-3). Excellent correlations are observed for terminal alkenes ($r_{ter} = 0.97$), for internal alkenes ($r_{int} = 0.97$), and for tetrasubstituted alkenes ($r_{tetra} = 0.99$), which are much better than that for all alkenes regardless of degree of substitution ($r_{all} = 0.65$).

Table 2-3. Alkene IPs (eV), HOMO energies (eV), and relative rates of acid-catalyzed hydration of alkenes from Tidwell's study[22]

No.	Alkene	IP[a]	HOMO[b]	k_{rel}[c]
1		8.00[d]	-7.54	2.86×10^{10}
2		8.20[e]	-8.32	2.50×10^{7}
3		8.27	-8.70	3.39×10^{5}
4		8.30[f]	-8.11	9.90×10^{14}
5		8.44[g]	-8.18	1.49×10^{14}
6		8.53[d]	-8.62	4.72×10^{8}
7		8.55[d]	-8.73	1.57×10^{8}
8		8.57[d]	-8.65	3.30×10^{8}
9		8.58[d]	-8.70	2.24×10^{11}
10		8.60[h]	-8.70	2.51×10^{8}
11		8.62[i]	-8.65	7.16×10^{7}
12		8.65[d]	-8.63	9.41×10^{7}
13		8.67[j]	-8.22	1.49×10^{13}
14		8.68	-8.86	2.13×10^{5}
15		8.95	-9.27	1.76×10^{2}
16		8.97	-9.27	2.08×10^{2}
17		9.07[d]	-9.11	1.75×10^{9}
18		9.12	-9.26	82.4
19		9.12	-9.25	34.8
20		9.14[d]	-9.07	7.55×10^{8}
21		9.24	-9.39	3.68×10^{5}
22		9.48	-9.66	1.00×10^{2}
23		9.74	-9.72	49.0

[a]Ref 42, unless otherwise noted. [b]*Ab initio* at the HF/6-31G* level by Christopher Brammer. [c]Ref 22; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. The unit of rate constants is $M^{-1}S^{-1}$. [d]Ref 53. [e]Ref 54. [f]Ref 55. [g]Calculated by applying to the IP for 1,1-diethoxyethene a correction factor calculated as twice the difference

between the IPs of methoxyethene and ethoxyethene: 8.30eV + 2 (9.14eV – 9.07eV) = 8.44eV; Refs 53 and 55. [h]Calculated by applying to the IP for *cis*-1-ethoxypropene a correction factor calculated as the difference between the IPs of methoxyethene and ethoxyethene: 8.53eV + (9.14eV – 9.07eV) = 8.60eV; Ref 53. [i]Calculated by applying to the IP for *trans*-1-ethoxypropene a correction factor calculated as the difference between the IPs of methoxyethene and ethoxyethene: 8.55eV + (9.14eV – 9.07eV) = 8.62eV; Ref 53. [j]Calculated by applying to the IP for 1,1-diethoxyethene a correction factor calculated as the difference between the IPs of 1-butene and 1-chloro-1-butene: 8.30eV + (10.00eV – 9.63eV) = 8.67eV; Refs 42, 50, and 55.

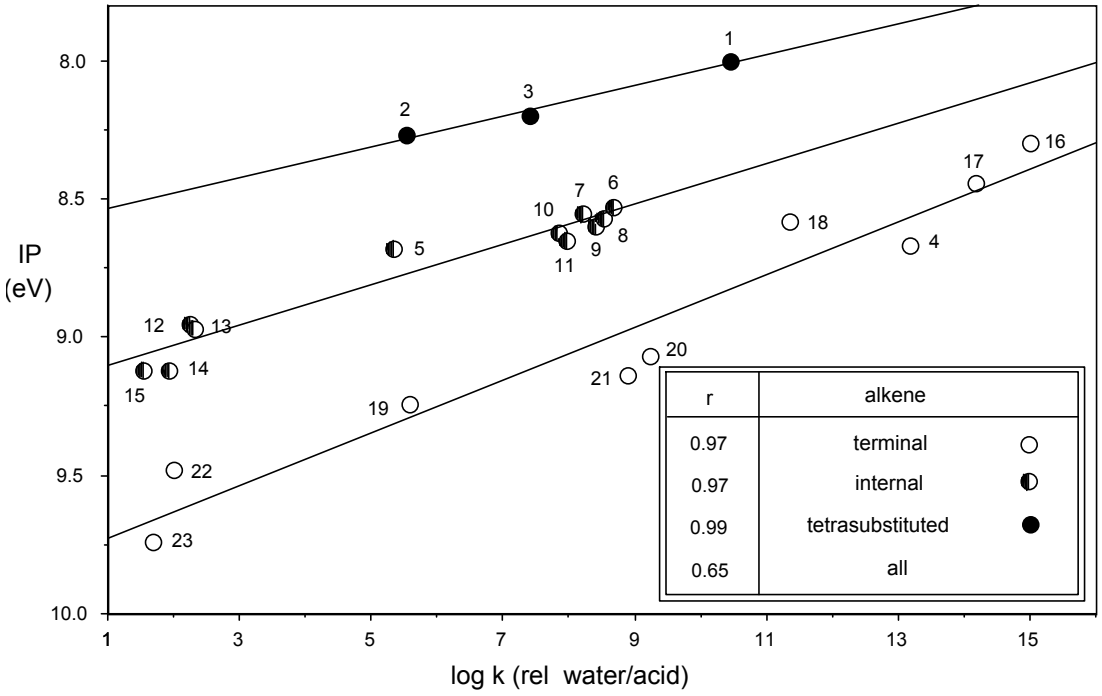
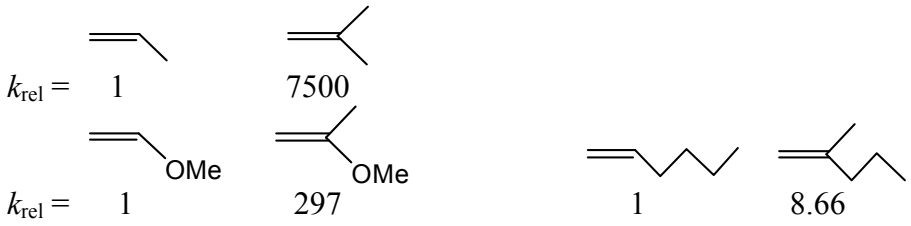


Figure 2-3. The plot of the log k_{rel} values for acid-catalyzed hydration of alkenes versus alkene IPs. Data are from Table 2-3. Data points naturally fall into different sterically similar alkene groups. Correlation lines are given for terminal alkenes (IP = 9.82 – 0.095 log k_{rel}, r = 0.97, s = 0.095, and c.l. = 99.98%), for internal alkenes (IP = 9.18 – 0.073 log k_{rel}, r = 0.97, s = 0.040, and c.l. = 99.98%), and for tetrasubstituted alkenes (IP = 8.59 – 0.056 log k_{rel}, r = 0.99, s = 0.060, and c.l. = 90.00%).

The correlation plot made by using data points from Tidwell's study[22] (Fig 2-3) shows multiple lines with positive slopes, which is similar to that made by using data points from our study (Fig 2-2), although we did not include the vinyl ethers because they are too reactive to control[55] under the competitive reaction conditions unless they are balanced with strong EWGs on the alkene C=C bond.[30] Careful comparison reveals that differences between these two studies still exist. For instance, the rate increase caused by adding a methyl on the geminal position of a monosubstituted alkene is much greater in Tidwell's study (a) than that in ours (b).

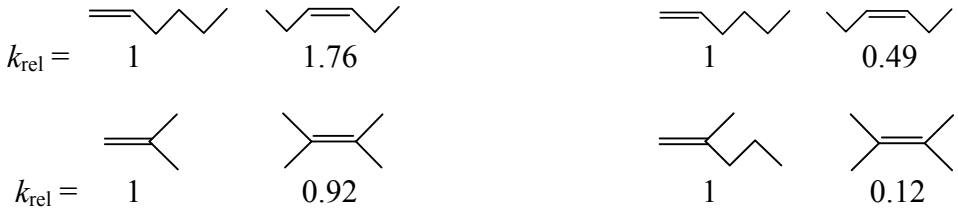


(a) (b)

Similarly, the rate decrease caused by adding a Cl on the vicinal position of an 1,1-disubstituted alkene is also much greater in Tidwell's study (c) than that in our study (d). Interestingly, just like the data point for 1-chloro-2-methylpropene in our study, the data point for trisubstituted 1-chloro-2,2-diethoxyethene (**13**) in Tidwell's study also fall in terminal group in Fig 2-3 probably due to the same reason stated above.

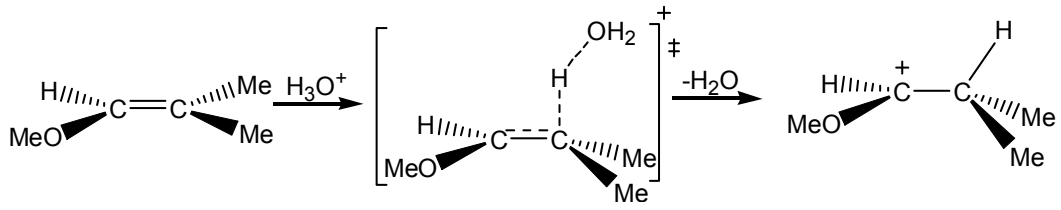
(c) (d)

Another difference is that the rate would increase when change a monosubstituted alkene into a vicinal disubstituted alkene or almost keep the same value when change a geminal disubstituted alkenes into a tetrasubstituted alkene in Tidwell's study (e). However, the rate would decrease remarkably in our study (f) in both cases. The differences between Tidwell's study and ours are most likely because their rate data were colleted from different studies under different reaction conditions and then converted by extrapolation, which may cause some inaccuracy.



(e) (f)

In Fig 2-3, data point for trisubstituted 1-methoxy-2-methylpropene (**2**) falls in the tetrasubstituted group, but not the internal group, as expected. This is because the rate-determining protonation here is initiated by the electrophilic attack of the hydronium ion to the alkenyl carbon with two methyl substituents to give a more stable carbocation intermediate (Scheme 2-3). In this way, the carbon atom with a methoxyl substituent bears a positive charge, which would be greatly stabilized through resonance with the methoxyl group. Therefore, the steric requirements of 1-methoxyl-2-methylpropene are similar to those of tetrasubstituted alkenes, but greater than those of internal alkenes in its acid-catalyzed hydration. The fact that this reaction finally gives an anti-Markovnikov product, 2-methylpropanal,[57] further confirms the explanation above.



Scheme 2-3. The transition structure and the resulting intermediate product of the rate-determining step of hydration of 1-methoxy-2-methylpropene

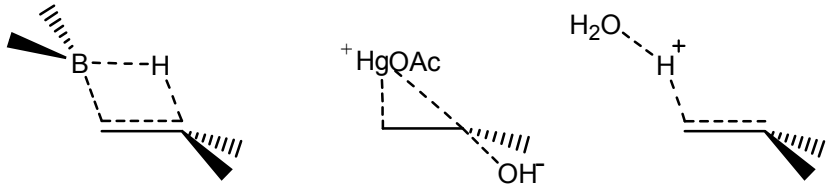
2.6 Comparison among similar electrophilic additions to alkenes

In the previous correlation studies conducted by Nelson's group, some reactions of alkenes, such as hydroboration,[50] oxymercuration,[50] silver ion complexation,[58] complexation with molecular iodine,[59] and diimide addition,[60] also showed multiple correlation lines with positive slopes. However, close scrutiny reveals that the alkenes forming the lines are grouped in two different ways. For example, in hydroboration and oxymercuration, the alkenes are grouped as terminal (monosubstituted and geminal disubstituted), internal (vicinal disubstituted and trisubstituted), and tetrasubstituted, just like what was done in acid-catalyzed hydration herein. Alternatively, in the studies of silver ion complexation, complexation with molecular iodine, and diimide addition, alkenes are grouped solely based on the number of the substituent groups attached to the alkene double bond: monosubstituted, disubstituted (including both vicinal and geminal), trisubstituted, and tetrasubstituted.

Comparing the two above types of grouping reveals that their difference is due to the placement of geminal and trisubstituted alkenes. In the first group (type 1), reaction rates are influenced predominantly by steric hindrance at the less highly-

substituted carbon of the C=C bond, which leads to a rate difference between geminal and vicinal disubstituted alkenes ($k_{gem} \neq k_{vic}$). In the second group (type 2), reaction rates are influenced almost equally by the steric hindrance at both alkenyl carbons, and thus resulting in $k_{gem} \approx k_{vic}$. The following analysis of the transition states observed for the pertinent reactions explains this phenomenon.

Reactions in which k_{vic} is much different from k_{gem} (type 1) have asymmetric transition state structures in their rate-determining steps. For example, the bonds being broken and formed with rate-determining transition state structures in hydroboration, oxymercuration, and acid-catalyzed hydration are arranged as a four-centered[61] parallelogram,[62] an irregular triangle,[50,63-65] and a zigzag[1,3] structure, respectively (Fig 2-4).



(a) (b) (c)

Figure 2-4. Asymmetric transition state structures in the rate-determining steps in (a) hydroboration, (b) oxymercuration, and (c) acid-catalyzed hydration

In these cases, if the rate-determining step is the first step, in the rate-determining transition state, the electrophile attacks the less substituted end of the C=C bond. If the rate-determining step is the second step, the complexed electrophile moves toward the less substituted end of the C=C bond. The alkyls in geminal disubstituted alkenes are far from the incoming electrophile, so the alkyls only have

significant rate-increasing electronic effects but comparatively smaller rate-retarding steric effects, and thus k_{gem} is greater than k_{vic}.

Type 2 reactions ($k_{gem} \approx k_{vic}$) have symmetrical structures for rate-determining transition states in kinetically controlled reactions, such as diimide reduction (Fig 2-5),[60,66] or for intermediates or products in equilibria, such as complexation with molecular iodine (Fig 2-6a)[59,67] and with silver ion (Fig 2-6b).[58,68]

Figure 2-5. Sterically equivalent transition state structures in diimide reduction

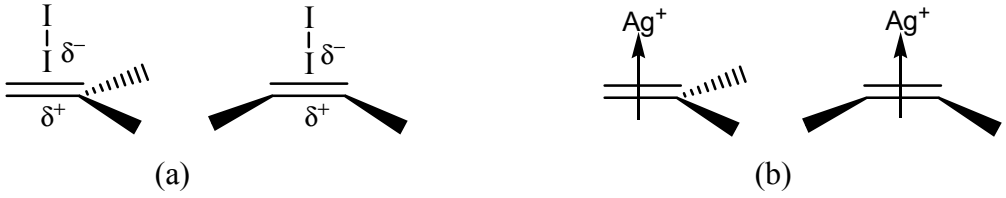


Figure 2-6. Sterically equivalent pairs of complexes in (a) complexation with molecular iodine and (b) silver ion complexation

Although disubstituted alkenes have similar relative rates in each of the reactions above, monosubstituted alkenes, trisubstituted alkenes, and tetrasubstituted alkenes each form an additional sterically-similar group in the plot for each reaction.[58-60]

$k_{gem} \approx k_{vic}$ is also necessarily the case for reactions giving plots with only one single line of correlation among all alkenes, regardless of degree of substitution, because the IP value of a vicinal alkene is similar to that of a geminal alkene with the

same substituents. This type of reaction includes epoxidation,[58] bromination,[59] chlorination,[59] carbene addition,[69] nitrosyl chloride addition,[69] oxidation with osmium tetroxide,[69] oxidation with chromyl chloride,[70] and oxidation with chromic acid.[70] In these cases, the correlation plot indicates that steric effects of alkyls, whether they are due to position or the degree of substitution, are relatively unimportant compared to electronic effects.

The common characteristics among acid-catalyzed hydration, hydroboration, and oxymercuration, classified as type 1 above, are that they have asymmetric rate-determining transition state structures and that the incoming electrophiles are located closer to the less-substituted carbon atom of the alkenyl double bond (Fig 2-4). This explains observations regarding these reactions in which steric effects cause grouping: (1) there are different steric effects between vicinal and geminal disubstituted alkenes; (2) trisubstituted alkenes fall in the same group as the internal alkenes (vicinal disubstituted), while geminal disubstituted alkenes fall in the same group with the monosubstituted (terminal) alkenes.

However, in the type 2 reactions, such as silver ion complexation, complexation with molecular iodine, and diimide addition, the rate-determining transition states are symmetrical structures (Figs 2-5 and 2-6). In these cases, the substituents attached to either carbon of the C=C bond are about the same distance from the incoming electrophile. Therefore, the steric and electronic effects in these reactions are dependent mainly upon the number and sizes, rather than positions, of the substituents attached to the alkene C=C bond. So, alkenes in these reactions are

grouped solely based on the number of substituents on the C=C bond, i.e. monosubstituted, disubstituted, trisubstituted, and tetrasubstituted alkenes.

2.7 Conclusion

A set of reaction conditions applicable for alkenes with different steric requirements (mono-, di-, tri-, and tetrasubstituted) was established for acid-catalyzed hydration. The relative rates of 19 alkenes were determined by competitive reactions. Correlation plots of logarithms of relative rates versus alkene IPs and versus alkene HOMO energies reveal that this reaction is an electrophilic addition to alkenes. The alkene reactivity depends upon both electronic and steric effects of the substituents on the C=C bond. Comparison with other sterically significant electrophilic additions demonstrates that the alkene grouping pattern observed in this reaction is characteristic of reactions with asymmetric transition state structures in the rate-determining steps. Reactions reported to have symmetric rate-determining transition states display alkene grouping solely based on the number of substituents on the alkene C=C bond.

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Chapter Three

Mechanistic Investigation on Alkene Reactions with Several Transition Metal Compounds via Correlations

Abstract: Several reactions of alkenes with transition metal compounds, including oxidation with chromyl chloride (CrO_2Cl_2), oxidation with chromic acid (H_2CrO_4), oxidation with palladium chloride ($PdCl_2/H_2O$), and homogeneous hydrogenation in the presence of Wilkinson's catalyst ($H_2/RhCl(PPh_3)_3$), have been studied mechanistically by using the correlation method in this chapter. Plots of logarithms of relative rates of alkene oxidation with CrO_2Cl_2 and with H_2CrO_4 versus alkene IPs and versus alkene HOMO energy levels demonstrate excellent correlations. Each plot shows a single line with positive slope among all studied alkenes, regardless of the steric requirements. The positive slopes of the lines indicate that both reactions are electrophilic additions to alkenes. The single lines of correlation in the plots demonstrate that electronic effects play a predominant role in the total substituent effects and steric effects are not important. In contrast, alkene oxidation with $PdCl_2/H_2O$ and alkene hydrogenation in the presence of $RhCl(PPh_3)_3$ both give multiple lines with negative slopes among sterically similar groups of alkenes in the plots of logarithms of relative rates versus alkene LUMO energy levels. The resulting plots indicate that these two reactions are nucleophilic additions to alkenes with significant steric effects. The relative reactivities of alkenes in the reactions depend upon both electronic and steric effects of the substituents. Results of these studies are also used to analyze proposed alternative mechanisms for the studied reactions.

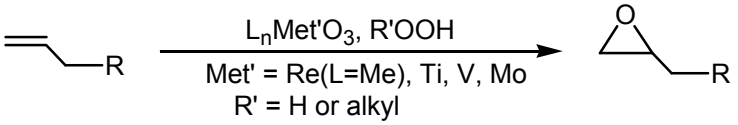
Studies included in this chapter have been published in three papers: (1) Nelson, D. J.; Li, R.; Brammer, C. *Journal of Physical Organic Chemistry* **2004**, *17*, 1033-1038; (2) Nelson, D. J.; Li, R.; Brammer, C. *The Journal of American Chemical Society* **2001**, *123*, 1564-1568; (3) Nelson, D. J.; Li, R.; Brammer, C. *Journal of Organic Chemistry*, **2005**, *70*, 761-767. Copies of the reprints of these papers are attached at the end of the dissertation.

3.1 Correlations in alkene oxidations with chromyl chloride (CrO_2Cl_2) and with chromic acid (H_2CrO_4)

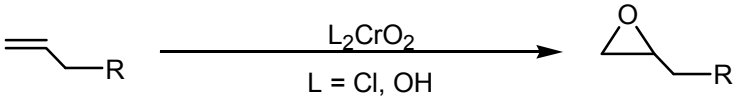
3.1.1 Introduction

Alkene oxidation by transition metal oxo compounds has been an important topic in organic chemistry for a long time.[1-3] Intensive mechanistic studies have been conducted both theoretically[4-20] and experimentally[21-25] during the past two decades. Among these compounds, chromium(VI) compounds, such as chromyl chloride (CrO_2Cl_2) and chromic acid (H_2CrO_4), are versatile oxidizing agents and can react with alkenes to give epoxides commonly and other products due to reaction conditions.[1-3,26-53] Interesting similarities and differences among reactions of alkenes with chromium(VI) compounds versus other d^0 transition metal oxo compounds have been noted recently.[11,16,41,43] In oxidizing alkenes, oxo compounds of Re(VII) (when L = Me),[11] Ti(IV),[54] V(V),[55] Cr(VI),[36] and Mo(VI)[56] each preferentially yields epoxides (eqs 3-1 and 3-2), while those of Re(VII) when L = Cp* (Cp* = C_5Me_5),[57] Mn(VII),[1] Ru(VIII),[58] Os(VIII),[59] and Tc(VII)[60] each preferentially yields *cis*-

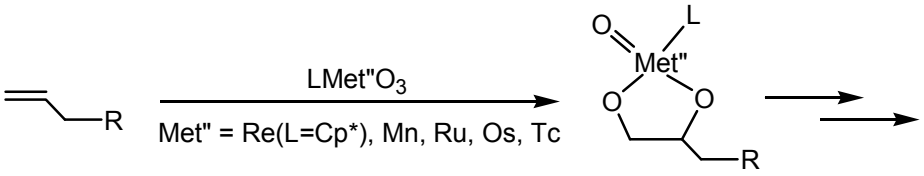
dihydroxyalkanes (eq 3-3).[11] In addition, some metal oxo compounds do not react directly with the alkenes, but with an additional oxygen source via an indirect pathway (eq 3-1); whereas, the others react with alkenes directly via a direct pathway (eqs 3-2 and 3-3).[11,16]



(3-1)



(3-2)



(3-3)

However, some of the above transition metal oxo compounds do not fit completely into either group Met' or Met". For example, it was noted[16,23] that $MeReO_3$ does not react directly with alkenes,[11] as do the compounds of Ti,[54] V,[55] and Mo.[56] However, Cp^*ReO_3 reacts directly with alkenes to give the metalladioxolane intermediates,[23,57] as do the compounds of Mn,[1] Ru,[58] Os,[59] and Tc,[60] but it does not yield diols as the final product,[23,57] as the latter compounds do.[1,58-60]

Another misfit is chromium Cr(VI) oxo compounds. Chromyl chloride, CrO_2Cl_2, has been likened[16] to other oxidizing metal compounds LMO_3, such as Os, Ru, and Mn. Chromium fits Met' in that it yields epoxides[1-3,36] as they do; but it does

not fit Met' in that it does not require an additional oxygen source to react with alkenes,[1-3,36] as they do.[11,54-56] Chromium is like Met" because its oxo compounds react directly with the olefins to give the metalladioxolane intermediates;[1-3] but it is unlike Met" because it does not give diols as final products,[1-3] as they do.[1,58-60]

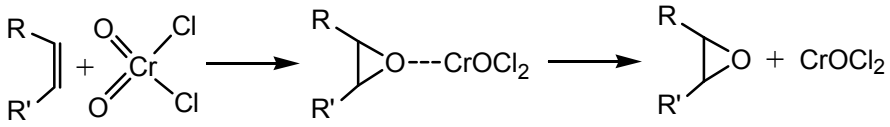
The above observations have led to mechanistic comparisons and contrasts of oxidation with chromium compounds versus those with compounds of Met" (Re, Mn, Ru, Os, and Tc).[11,36,41,43] As a result, many experimental[17,21,22] and theoretical studies[5,7-10,13-22,41,43] favor a proposed 2+3 mechanism over a proposed 2+2 mechanism. Due to comparisons and concerns stated above, questions about alkene oxidation by Cr(VI) oxo compounds linger (1) whether the 2+3 mechanism or the 2+2 mechanism is responsible for the products and (2) why the metalladioxolane intermediate would not yield diols as do compounds of the other metal Met", if the 2+3 mechanism operates with chromium compounds. In this section, we shall use our correlating technique to conduct a mechanistic exploration on chromyl chloride oxidation and chromic acid oxidation of alkenes, partly due to their importance in organic synthesis[1-3,26-31] and partly due to interest in their mechanisms.[1-3,32-53]

3.1.2 Oxidation with CrO_2Cl_2

The mechanism of chromyl chloride oxidation of alkenes has been investigated for decades.[1-3,32-46] The kinetic study[34] has determined the rate law of this reaction (eq 3-4), which is first order both in alkene and in chromyl chloride.

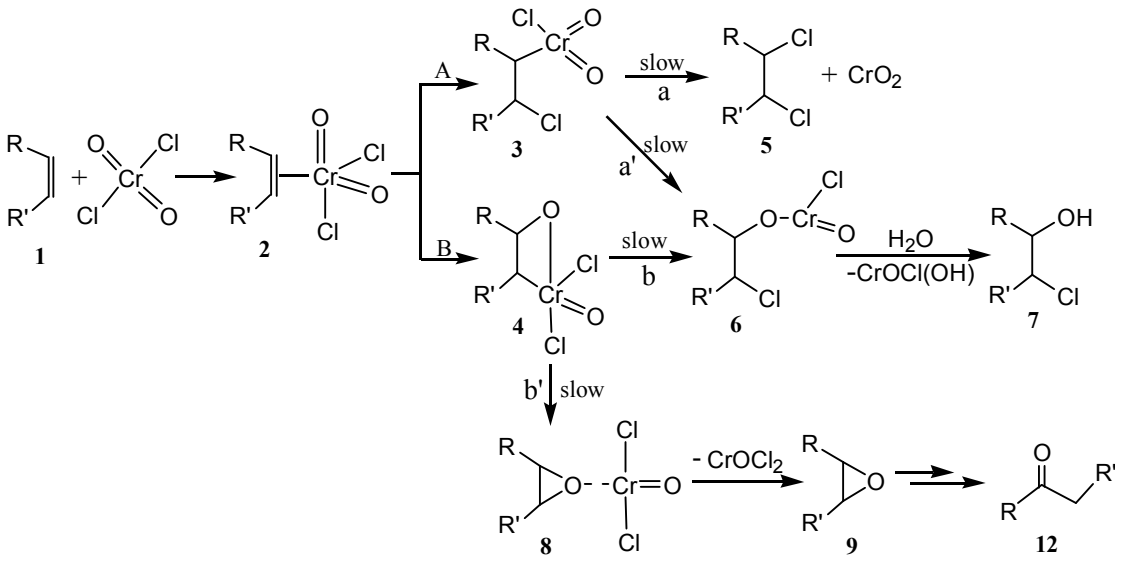
$$\text{Rate} = k\,[\text{alkene}]\,[CrCl_2O_2] \qquad (3\text{-}4)$$

At least four different mechanisms[1-3,32-46] have been suggested for this reaction. The first suggested mechanism was a "direct addition" mechanism (Scheme 3-1),[1-3] which was criticized due to its failure to explain all stereochemical aspects (such as the formation of the *cis*-chlorohydrin and the *cis*-dichloride) of chromyl chloride oxidation.[36,40]

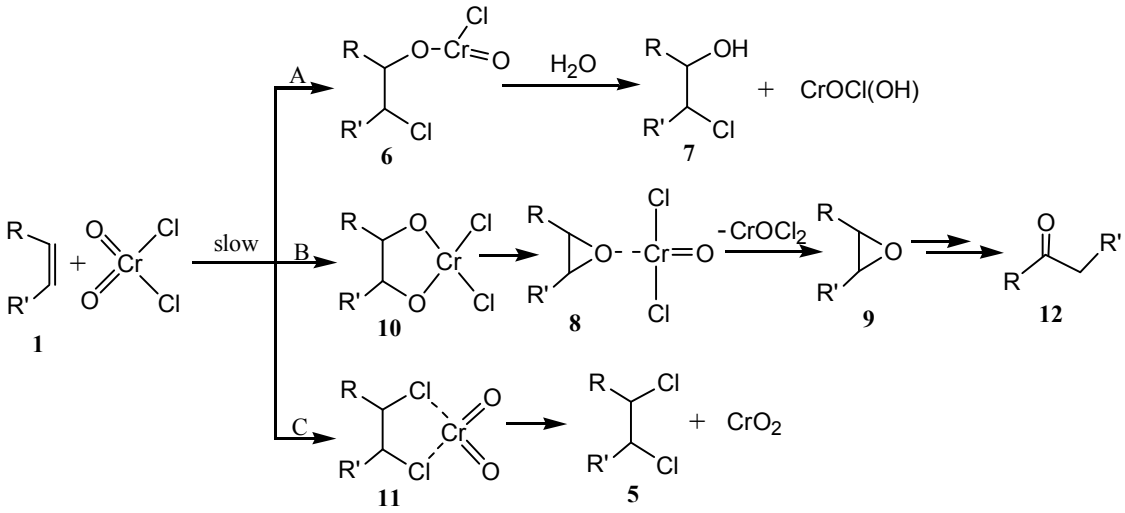


Scheme 3-1. The direct addition mechanism for CrO_2Cl_2 oxidation of alkenes

Two other different mechanisms were later proposed: (1) the 2+2 cycloaddition mechanism (Scheme 3-2),[3,36,40] and (2) the 2+3 cycloaddition mechanism (Scheme 3-3).[32-35] Recently, an ESR signal was observed in the oxidation of aryl substituted alkenes,[44,45] and a diradical was proposed as the intermediate giving rise to this result. However, the stereospecificity of these reactions has been used to argue against radical intermediates in the C-O bond forming steps. In addition, the alkenes considered in this report do not possess radical-stabilizing phenyl substitutions. Therefore, in this study, we only focus on the application of our results to the 2+2 and 2+3 mechanisms shown in Schemes 3-2 and 3-3.



Scheme 3-2. The 2+2 cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes



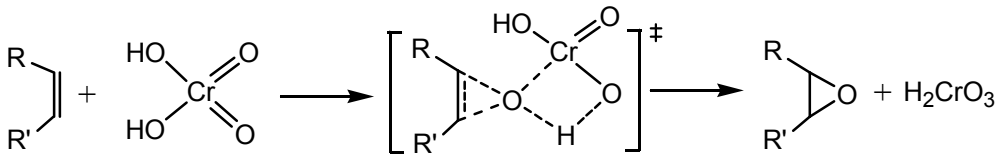
Scheme 3-3. The 2+3 cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes

The main difference between the two proposed mechanisms shown in Schemes 3-2 and 3-3 is in their rate-determining steps and characteristics of their transition state structures. In the 2+2 mechanism (Scheme 3-2), the decompositions

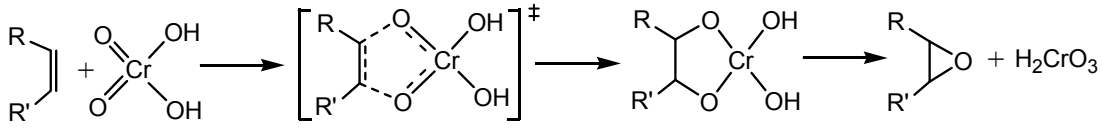
of intermediates **3** and **4** are proposed as rate-determining steps and four-membered cyclic transition state in the formation of these two intermediates (**3** and **4**).[43] In contrast, the 2+3 mechanism (Scheme 3-3) requires a five-membered ring transition state structure in the rate-determining formation of the five-membered cyclic intermediates.

3.1.3 Oxidation with H_2CrO_4

Chromic acid (H_2CrO_4) oxidation of alkenes produces epoxides or their higher oxidation level products.[1,48] Similar to alkene oxidation with chromyl chloride, H_2CrO_4 oxidation of alkenes is also first order both in alkene and in chromic acid.[48] A previous study[48] has fostered a mechanism involving a three-membered transition state structure (Scheme 3-4) similar to the "direct addition mechanism", which was previously discarded for CrO_2Cl_2 oxidation of alkenes. Another proposed mechanism[1,48] for the H_2CrO_4 oxidation invoked a five-membered cyclic intermediate (Scheme 3-5). It is analogous to the 2+3 mechanism for the chromyl chloride oxidation shown (**1→9**) in Scheme 3-3 (path B). A major difference between these two proposed mechanisms for chromic acid oxidation of alkenes is that the former suggests a direct single-step formation of an epoxide (Scheme 3-4), while the latter requires formation of a five-membered cyclic intermediate between the reactants and the epoxide product (Scheme 3-5). In this study, we shall discuss its mechanisms through comparison with those of chromyl chloride oxidation of alkenes.



Scheme 3-4. The direct addition mechanism for H_2CrO_4 oxidation of alkenes

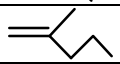
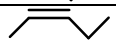
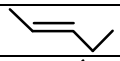
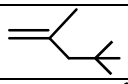
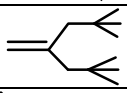
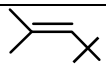
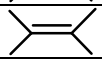


Scheme 3-5. The 2+3 cycloaddition mechanism for H_2CrO_4 oxidation of alkenes

3.1.4 Correlation plots

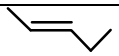
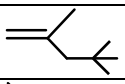
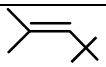
Relative rates of chromyl chloride oxidation of alkenes, alkene IPs, and alkene HOMO energies are shown in Table 3-1. Relative rates of chromic acid oxidation of alkenes, alkene IPs, and alkene HOMO energies are shown in Table 3-2. Relative rates for both reactions were converted from previous reports,[34,48] in which reaction rates were determined by following the disappearance of the Cr(VI) oxidation reagents in large excess of alkenes under pseudo first-order conditions. Experimental alkene IPs were collected from literature. The alkene HOMO energies were calculated by using the MNDO method.

Table 3-1. Alkene IPs (eV), HOMO energies (eV), and relative rates of chromyl chloride (CrO_2Cl_2) oxidation of alkenes

No.	Alkene	IP[a]	HOMO[b]	k_{rel}[c]
1		9.52	-9.94	1.22×10^2
2		9.51[d]	-9.95	88.0
3		9.48	-9.97	1.00×10^2
4		9.45	-9.96	5.36×10^2
5		9.43[d]	-9.95	77.0
6		9.12	-9.79	1.51×10^3
7		9.12	-9.78	1.38×10^3
8		9.08	-9.79	8.00×10^2
9		9.04	-9.77	1.48×10^3
10		9.04	-9.76	1.51×10^3
11		9.02	-9.75	1.05×10^3
12		8.91	-9.71	2.36×10^3
13			-9.78	7.54×10^2
14		8.83[e]	-9.64	1.38×10^5
15		8.68	-9.63	2.02×10^4
16		8.27	-9.49	3.91×10^5

[a]Ref 61, unless otherwise noted. [b]MNDO method by Christopher Brammer. [c]Ref 34; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. The unit of rate constants is $M^{-1}min^{-1}$. [d]Ref 62a. [e]Ref 62b.

Table 3-2. Alkene IPs (eV), HOMO energies (eV), and relative rates of chromic acid (H_2CrO_4) oxidation of alkenes

No.	alkene	IP[a]	HOMO[b]	k_{rel}[c]
1		9.74	-9.97	32.3
2		9.63	-9.94	52.0
3		9.52	-9.94	75.5
4		9.48	-9.97	1.00×10^2
5		9.45	-9.96	68.7
6		9.44	-9.94	94.2
7		9.24	-9.80	2.48×10^2
8		9.12	-9.79	2.86×10^2
9		9.12	-9.78	1.89×10^2
10		9.04	-9.76	2.46×10^2
11		8.97	-9.75	2.78×10^2
12		8.91	-9.71	3.44×10^2
13		8.83[d]	-9.64	1.10×10^3
14		8.68	-9.63	3.13×10^3
15		8.27	-9.49	1.60×10^4

[a]Ref 61, unless otherwise noted. [b]MNDO method by Christopher Brammer. [c]Ref 48; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. The unit of rate constants is $M^{-1}min^{-1}$. [d]Ref 62b.

Plots in Figs 3-1 and 3-3 show the similar correlations of log k_{rel} values versus alkene IPs for chromyl chloride oxidation of alkenes and for chromic acid oxidation of alkenes respectively. Each of them gives a single line with a positive slope and a good correlation coefficient among all alkenes, regardless of their steric requirements.

The plots of log k_{rel} versus alkene HOMO energies for both reactions (Figs 3-2 and 3-4) are essentially analogous to those of log k_{rel} versus alkene IPs (Figs 3-1 and 3-3). They also have single lines with positive slopes and show good correlations.

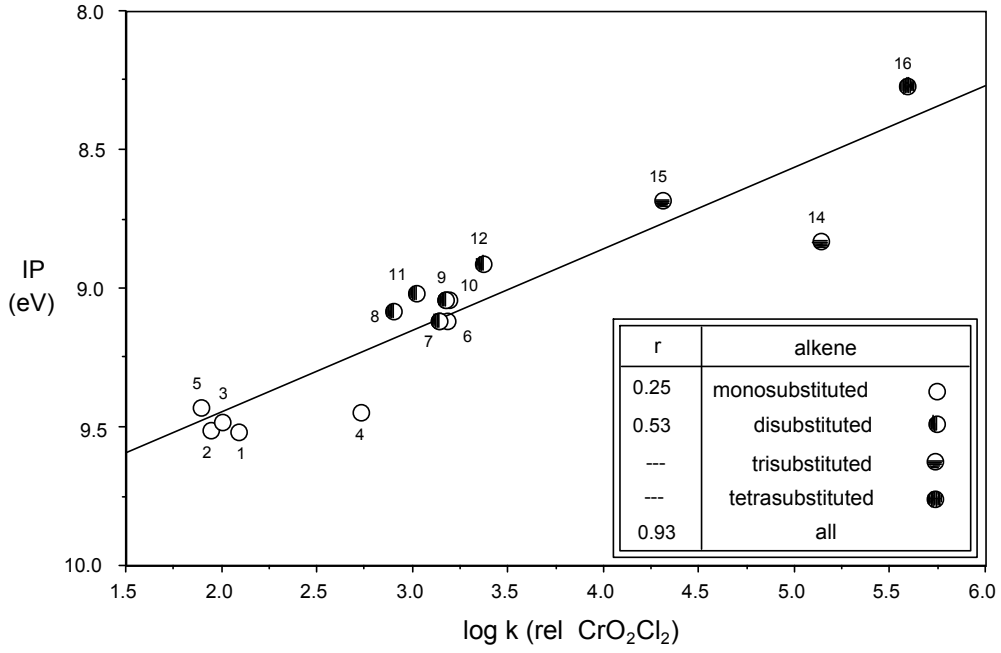


Figure 3-1. The plot of the log k_{rel} values versus correspondent alkene IPs for alkene oxidation with CrO_2Cl_2. Data are from Table 3-1. The y-axis IP data are plotted in inverse order to facilitate comparison with the plot for HOMO energies. All data points, regardless of steric requirements, lie on one line of correlation (IP = 10.04 – 0.29 log k_{rel}, r = 0.93, s = 0.110, and c.l. = 99.98%).

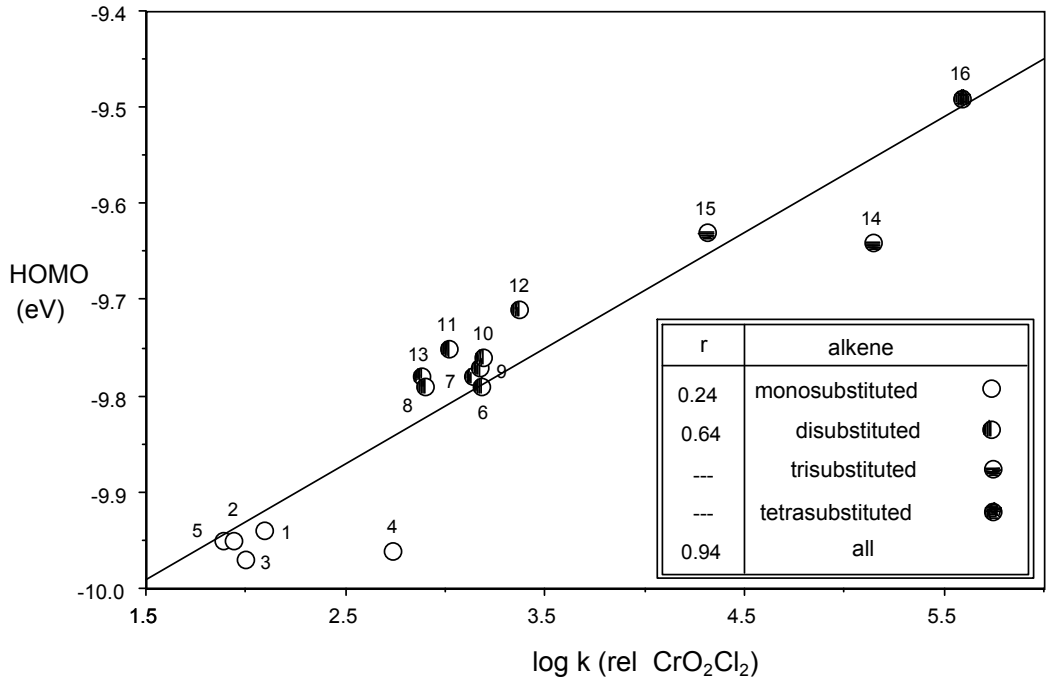


Figure 3-2. The plot of the log k_{rel} values for chromyl chloride oxidation of alkenes versus correspondent alkene HOMO energies. Data are from Table 3-1. All data points, regardless of steric requirements, lie on one line of correlation (E_{HOMO} = 0.12 log k_{rel} – 10.17, r = 0.94, s = 0.040, and c.l. = 99.98%).

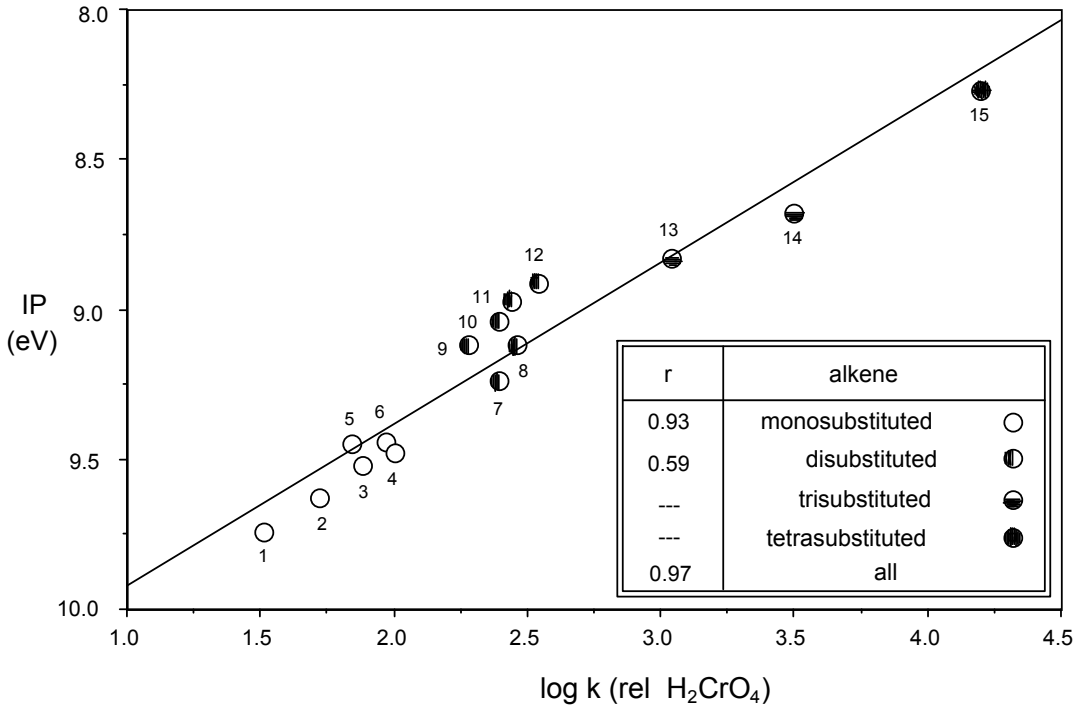


Figure 3-3. The plot of the log k_{rel} values for chromic acid oxidation of alkenes versus correspondent alkene IPs. Data are from Table 3-2. The y-axis IP data are plotted in inverse order to facilitate comparison with the plot for HOMO energies. All data points, regardless of steric requirements, lie on one line of correlation (IP = 10.46 – 0.54 log k_{rel}, r = 0.97, s = 0.101, and c.l. = 99.98%).

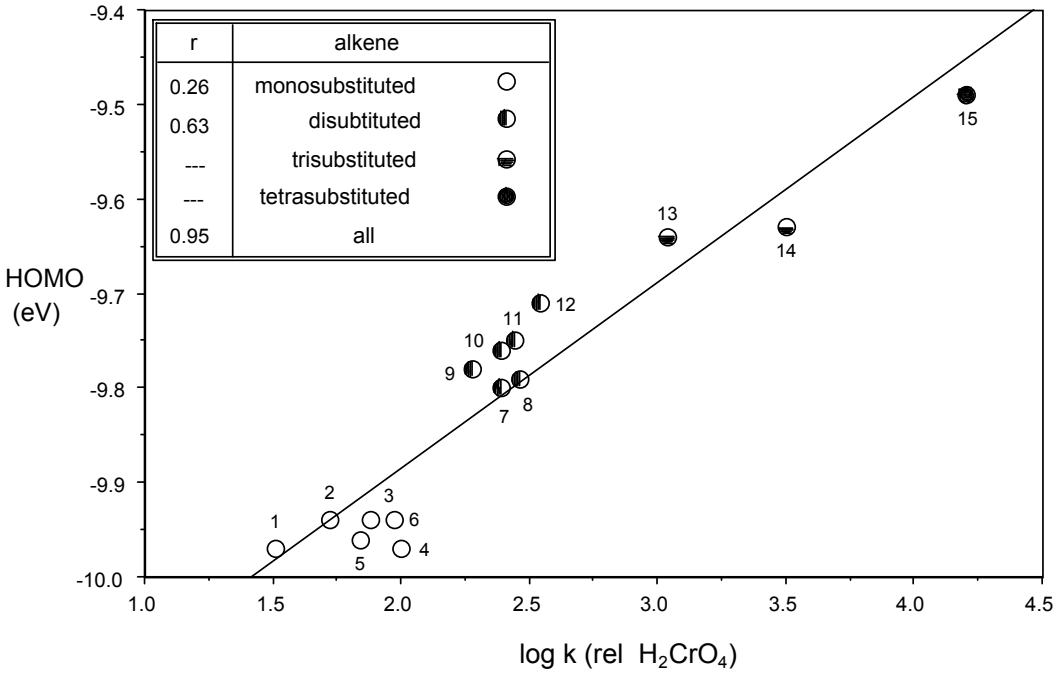


Figure 3-4. The plot of the log k_{rel} values for chromic acid oxidation of alkenes versus correspondent alkene HOMO energies. Data are from Table 3-2. All data points, regardless of steric requirements, lie on one line of correlation (E_{HOMO} = 0.20 log k_{rel} – 10.28, r = 0.95, s = 0.045, and c.l. = 99.98%).

3.1.5 Electronic versus steric effects

The good to excellent correlations have been observed in the plots of log k_{rel} values versus alkene IPs and versus alkene HOMO energies for both reactions. The overall trend is that alkenes with more alkyl substituents react faster. Data points in Figs 3-1 to 3-4 cluster according to the number of substituents on the alkene C=C bond. Among these groups, the relative reactivities show the following general trend: monosubstituted < disubstituted < trisubstituted < tetrasubstituted. The trend that increasing alkyl substitution on the alkene C=C bond increases the reaction rate in such cases could theoretically be rationalized in different ways, such as alkyl group

electronic effects or steric relief. These could operate either in a rate-determining step which involves the π bond or a reversible step which involves the π bond and precedes a rate-determining step if any exist. A discussion of each of these follows.

The clustering of the data points in Figs 3-1 to 3-4 could result from reactant uniformity, the fact that only simple olefins are included in the study. Alkenes with same number of alkyl substituents have similar IP values, and thus close relative reactivities because all alkyls have electron-donating abilities of similar magnitude. If some alkenes, functionalized with strong electron-donating and withdrawing substituents, were included in the study, then the data points would be spread out and not cluster into groups as seen in Fig 3-1 to 3-4. An example of this can be seen in alkene bromination (Fig 4-1), if the data points for the functionalized alkenes are omitted in this plot, an analogous clustering appears here also.

Electron-donating electronic effects of alkyl groups increase the rates of electrophilic additions to alkenes and decrease the rates of nucleophilic ones. Electronic effects of alkyl groups are of sufficient magnitude to play a major role in alkene additions, as has been observed in all our correlation studies. However, steric effects can be either significant or relatively insignificant, relative to the magnitude of the electronic effects, based on the nature and individual characteristics of the reaction.

If steric relief were important in the rate-determining step, then increasing alkyl substitution on the alkene C=C bond would increase the reaction rate due to steric effects of the substituents. Steric relief could be important if the rate-determining step led from, rather than to, a cyclic intermediate or transition state.

This possibility is less likely based on the following observation. As discussed in Chapter 1 (section 1.5), an alkene addition is usually retarded due to steric hindrance of the substituent(s) on the alkene C=C bond interacting with the incoming electrophile or nucleophile. Exceptions, i.e. steric acceleration, could exist, but are not common for alkene additions; we have observed none in our studies.

A determinant in the question of steric hindrance versus acceleration exists in the relative rates of cis/trans pairs in alkene additions. When the rate-determining step is formation of a cyclic intermediate or product the cis isomer is known to react faster.[35b] Therefore, a cis isomer reacting faster than its trans isomer has been taken as evidence of a rate determining step leading to, rather than from, a cyclic intermediate.[35b] Alkene addition reactions in which this relationship of cis/trans pairs has been observed include but are not limited to addition of bromine, addition of chlorine, addition of ISCN, hydration, ICl addition, etc. This faster reactivity is also seen in chromic acid oxidation of alkenes and chromium chloride oxidation of alkenes. Therefore, the explanation which better fits the existing data for these electrophilic alkene reactions is that electronic effects of the electron-donating alkyl groups play a dominant rate-increasing role, while steric effects are relatively insignificant. This is discussed in detail as it pertains to ISCN addition, in Section 4.3 of this dissertation (pages 160-165).

Based on the above analysis, it can be concluded that both chromyl chloride oxidation and chromic acid oxidation of alkenes are dependent predominantly upon electronic effects, while steric effects are relatively insignificant. Positive slopes of correlation lines in Figs 3-1 to 3-4 indicate that both reactions are electrophilic

additions to alkenes, i.e. a lower IP (or a higher HOMO energy level) corresponds to a greater reaction rate. Electron-donating substituents in the alkene C=C bond increase the rate of reaction, while electron-withdrawing substituents decrease the reaction rate in both cases.

3.1.6 Differentiation between the proposed mechanisms

One objective of this study was to determine whether our work could differentiate between the proposed mechanisms[3,40] for chromyl chloride oxidation of alkenes, the 2+2 mechanism (Scheme 3-2)[36-39] and the 2+3 mechanism (Scheme 3-3).[33-35, 41-43] The main differences between the two proposed mechanisms are in their rate-determining steps and characteristics of their transition state structures. In the 2+2 mechanism[36] (Scheme 3-2), decompositions of intermediates **3** and **4** are proposed as rate-determining steps,[43] and a four-membered cyclic transition state is proposed in the formation of each of the two intermediates **3** and **4**. In contrast, the 2+3 mechanism[33-35] (Scheme 3-3) involves five-membered cyclic transition state structures in the rate-determining formation[43] of intermediates **6**, **10**, and **11**.

In order to apply our analysis of steric and electronic effects to the mechanisms which had been proposed for chromyl chloride oxidation of alkenes, it was necessary to plot log k_{rel} values versus alkene IPs. Relative rates of chromyl chloride with various alkenes had been determined[34] in a study using an excess of alkenes, which yielded only carbonyl products under those conditions. Therefore, our analysis of the reaction by using these data is only pertinent to reactions, mechanisms, discussions, and reviews of this reaction under those conditions.[34] There have been

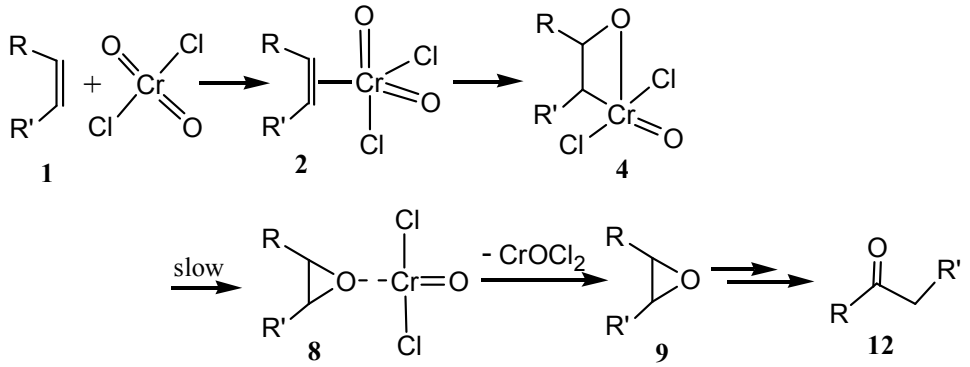
other studies and discussions of this reaction run under different conditions,[32] such as using an excess of chromyl chloride,[32] but our analysis is not applicable to those. One reason is because different products are obtained under those conditions, and this indicates operation of a different mechanism.

We used data from the chromyl chloride reaction with an excess of each alkene in order to explore steric and electronic effects in the chromyl chloride oxidation of alkenes, by plotting log k_{rel} values versus alkene IPs (Fig 3-1). The plot revealed a single line with positive slope and a good correlation coefficient among all alkenes. This indicates that the rate of this reaction is mainly determined by a step (or steps), in which (1) electrophilic attack upon the alkene π bond is involved, (2) alkene reactivity depends predominantly upon electronic effects of the substituents, and (3) steric effects in the alkenes studied are relatively insignificant. The results of this correlation study are useful in evaluating the rate-determining steps of this reaction. In order to demonstrate this application, we give below a step-by-step analysis of the proposed mechanisms in order to present experimental evidence to determine whether each step has an important influence on the rate of the reaction. We also discuss other studies and reviews of chromyl chloride oxidation of alkenes yielding carbonyls; some of these favored the former mechanism[36-39] and some the latter one.[33-35,41-43]

A. Analysis of the 2+2 mechanism (Scheme 3-6) to produce carbonyl products:

Only part of the mechanism shown in Scheme 3-2 is in operation in the reaction pertinent to our study, because only carbonyl compounds are produced under

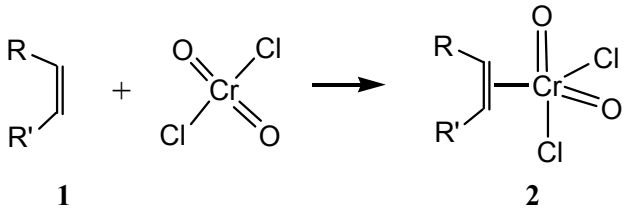
those conditions. The pertinent part of the mechanism is shown below in Scheme 3-6 and analyzed in the following sections.



Scheme 3-6. The 2+2 cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes to carbonyls

Step 1: Alkene coordination to the Cr center of the CrO_2Cl_2 (1→2)

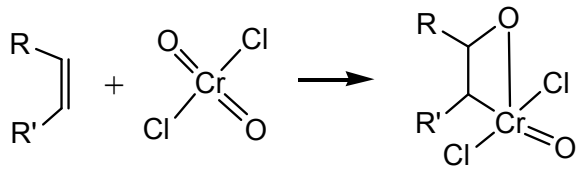
Not important: Three different opinions have been reported for this step — (1) either it does not occur,[43] (2) or it is a kinetically controlled fast reaction,[36] (3) or it is a fast equilibrium.[3,40]



Each of these possibilities is considered separately below, and experimental evidence shows none of these is capable of having an important influence on the reaction rate.

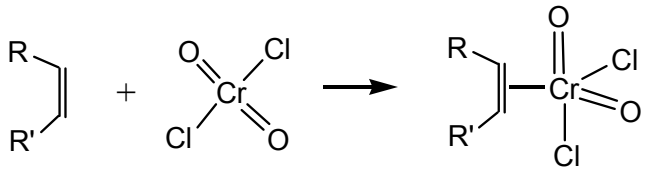
- Computational studies[43] suggest that complex **2** does not exist at all, and that the reaction of **1** + CrO_2Cl_2 proceeds directly to **4**. A DFT computational search[43] for a minimum corresponding to complex **2** on the PES (potential energy surface) of this reaction reported an inability to locate the complex. A more recent matrix isolation

study[53b] also supports the prediction that the complex of chromyl chloride and cyclohexene does not exist, although that reaction[53b] was run under conditions different from those used to determine the relative rates of chromyl chloride oxidation of alkenes.[34] If the complex does not exist, then this step would neither exist nor influence the reaction rate. The above mentioned computational study[43] also predicted that **1→4** is an irreversible step, followed by a rate-determining slow step to give **8**, which reacts further to yield the carbonyl compounds.



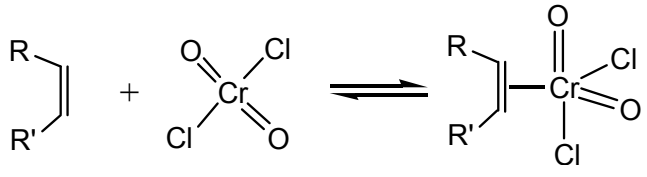
1 **4**

- Researchers, who proposed **1→2** as a mechanistic step,[36] proposed it as a kinetically controlled fast reaction prior to the rate-determining steps. In this case, complex formation will not influence the rate of the overall reaction.



1 **2**

- Some review articles[3,40] show complex **2** formation as an equilibrium, although no rationale or evidence was provided.



1 **2**

In this equilibrium, strong steric effects would be expected, as observed in comparable alkene complexations. For example, two other complexations have been reported previously,[63] one with silver ion (Ag^+) and one with molecular iodine (I_2). In both cases, multiple lines with positive slopes are observed in the plots of log K_{rel} values versus alkene IPs (Figs 3-5 and 3-6), which indicates the existence of strong steric effects.

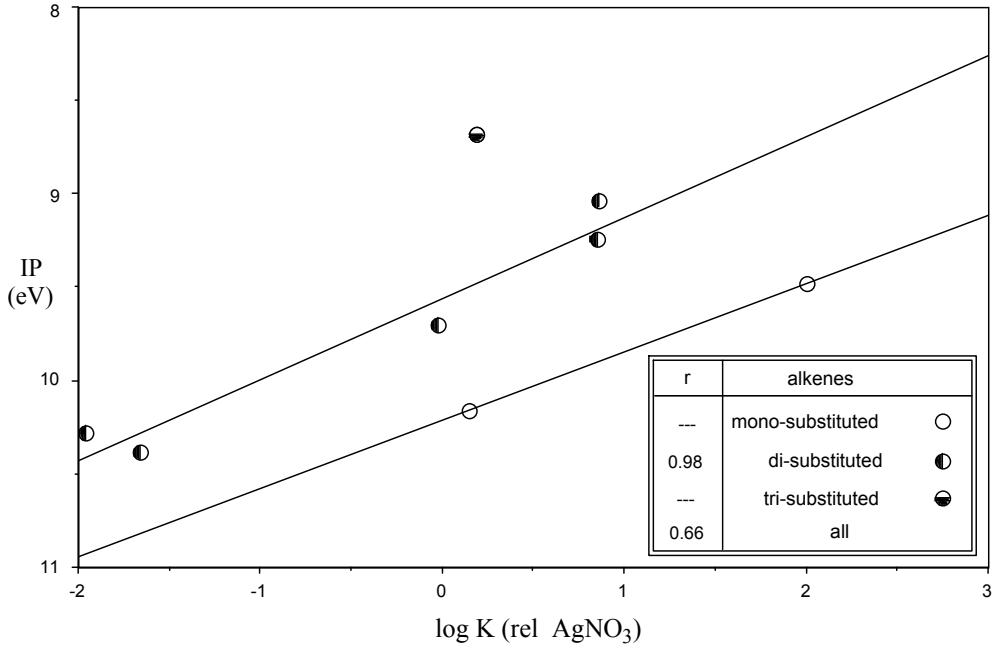


Figure 3-5. The plot of log K_{rel} values versus alkene IPs for alkene complexation with silver ion

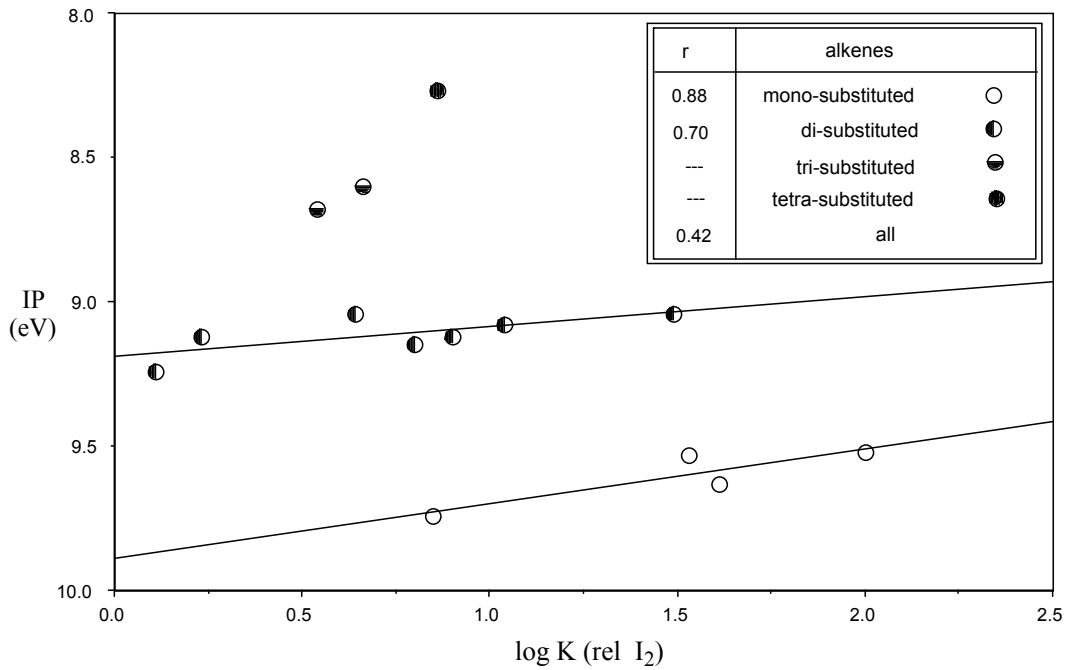
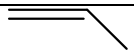
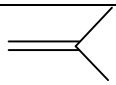
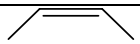
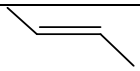
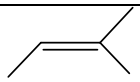


Figure 3-6. Plot of log K_{rel} values versus alkene IPs for complexation with molecular iodine.

Considering the greater steric requirements of CrO_2Cl_2 relative to those of I_2, greater steric effects would be expected in this reaction if this step influences it rate (Table 3-3). However, a single line of correlation is actually observed in the plot of experimental results for chromyl chloride oxidation; this indicates that steric effects in this chromyl chloride reaction are in fact relatively insignificant. Therefore, experimental evidence supports the conclusion that this complex does not exist or that it does not have an import influence on the rate of the reaction.

Table 3-3. Relative reactivities of alkenes in three reactions

Alkenes	Relative reactivity		
	CrO_2Cl_2	Ag^+	I_2
	100	100	100
	800	7.2	1.3
	1510	7.3	7.9
	1380	---	1.7
	20200	1.55	3.5

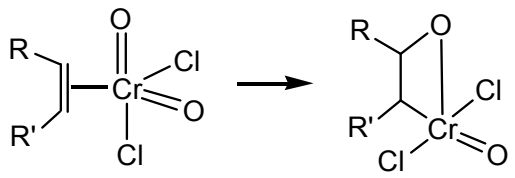
Data in Table 3-3 show that in chromyl chloride oxidation, reactivity of the alkene increases remarkably with the number of alkyl groups on the C=C bond. This indicates that alkene reactivity in this reaction depends predominantly upon the (rate-increasing and electron-donating) electronic effects of the substituents, while the (rate-retarding) steric effects of the substituents are much less important.

Conversely, opposite results have been reported[63a,b] in both complexation with silver ion and complexation with molecular iodine, which are also reported[63c,d] to be electrophilic reactions with alkenes. In these, alkene reactivity decreases dramatically upon increasing the number of alkyl groups on the C=C bond. This is because steric effects of substituents on the C=C bond play a more important role than electronic effects do in these reactions.

In conclusion, complexations with Ag^+ and with I_2 are equilibria and display an opposite trend from that observed for chromyl chloride oxidation of alkenes. This is evidence that the reaction step which predominantly influences the rate of chromyl

chloride oxidation of alkenes is not a complexation like that which occurs in complexation of an alkene with Ag^+ or with I_2.

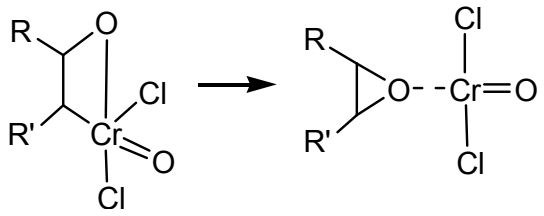
Step 2: Alkene insertion into the C=O bond to give intermediate 4 (2→4)



2 **4**

Not important: **2→4** is a nucleophilic reaction with an alkene C=C bond,[36] while the reaction has been shown experimentally to be an electrophilic addition to an alkene.

Step 3: Decomposition of intermediate 4 (4→8), which is proposed to be rate-determining in formation of a carbonyl product

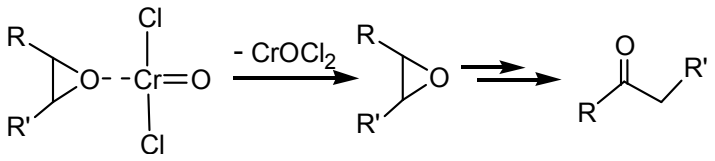


4 **8**

Not important: the alkene C=C bond is not directly involved in this step.[36] Although steric effects could influence this step more or less, the relative energy levels of the C=C bonds would be expected to have no effect on the rate in this reaction, because neither reactant nor product have a C=C bond; therefore no correlation between IP and log k_{rel} values would be expected. However, experimental

results of our studies show a correlation between alkene IPs and reaction rates. Therefore, experimental results do not support step **4→8** as a rate-determining step.

Step 4: Decomposition of intermediate 8 (8→9→12) to give the final carbonyl product

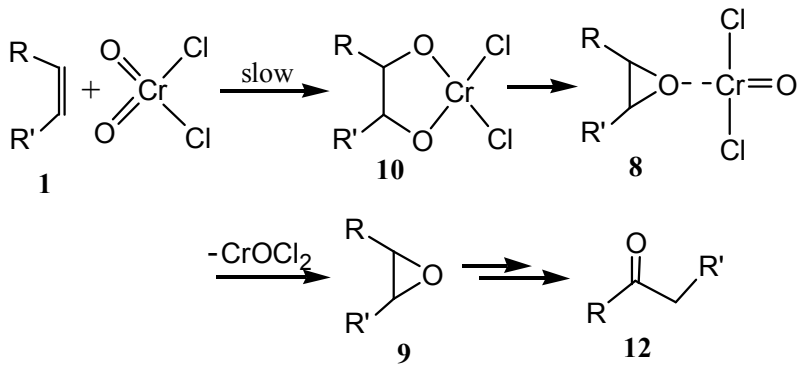


8 **9** **12**

Not important: this is a fast reaction[43] which takes place after the rate-determining step in the 2+2 mechanism.

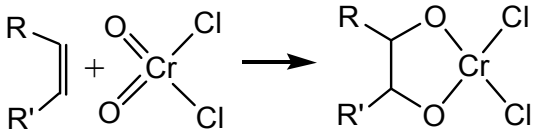
CONCLUSION: Based on the step-by-step analysis above, none of the mechanistic steps are predicted to have a significant influence on the reaction rate. Therefore, the results of our study are not consistent with the 2+2 mechanism which has been proposed for alkene oxidation with CrO_2Cl_2. This is regardless of whether complex **2** is formed or not, and if complex **2** is formed, then it is regardless of whether complex formation occurs via a kinetically controlled fast reaction or in a fast equilibrium.

B. Analysis of the 2+3 mechanism (Scheme 3-7) to produce carbonyl products:



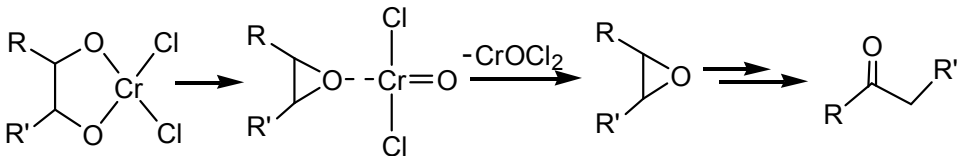
Scheme 3-7. The 2+3 cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes to carbonyls

Step 1: The 2+3 cycloaddition (1→10), which is proposed to be rate-determining in formation of a carbonyl



Possibly important: it is an electrophilic addition to alkenes[33-35] – an electrophilic attack by chromyl chloride on the alkene C=C bond. The proposal that this step is rate-determining[43] is consistent with the experimental results of our study (and others[33-35]) that the overall reaction is an electrophilic addition to alkenes.

Step 2: Decomposition of intermediate 10 to give the final carbonyl product (10→8→9→12)



10 **8** **9** **12**

Not important: these steps are fast reactions[43] which take place after the rate-determining step in the 2+3 mechanism.

Based on the step-by-step analysis of both proposed mechanisms, only one mechanistic step could influence significantly the rate of the reaction; this is the 2+3 cycloaddition (**1→10**), which is proposed to be rate-determining in formation of a carbonyl. Therefore, the results of our study support the 2+3 mechanism for alkene oxidation with CrO_2Cl_2.

Our investigations similarly indicate that the chromic acid oxidation of alkenes is also an electrophilic addition with a rate-determining step, which involves the alkene π electrons. The plot of log k_{rel} values versus alkene IPs for oxidation with H_2CrO_4 (Fig 3-3) is essentially analogous to that of CrO_2Cl_2 (Fig 3-1) with correlation coefficient $r_{all} = 0.97$. Our results are accommodated by either of the mechanisms in Scheme 3-4 or Scheme 3-5. One might argue to exclude the mechanism in Scheme 3-4 for the following reasons: (1) H_2CrO_4 is structurally similar to CrO_2Cl_2, (2) the two similar reagents might be expected to react in a similar manner, (3) an analogous mechanism for the CrO_2Cl_2 reagent was discarded, and (4) a mechanism similar to that in Scheme 3-5 also agrees with the results obtained by using the reagent CrO_2Cl_2.

3.1.7 Conclusion

A single line of correlation with a positive slope in each plot of log k_{rel} values versus alkene IPs and versus alkene HOMO energies (Figs 3-1 to 3-4) for oxidations of alkenes by using CrO_2Cl_2 and by using H_2CrO_4 demonstrates that (1) both reactions are electrophilic additions to alkenes and (2) these reactions depend predominantly upon electronic effects, while steric effects are relatively insignificant. The results of our study are consistent with the proposed 2+3 mechanism, in which formation of the five-member intermediate via an electrophilic attack of chromyl chloride on the alkene C=C bond is proposed to be the rate-determining step. However, the results of this study do not support the proposed 2+2 mechanism, in which the proposed rate-determining steps have no direct relationship with alkene C=C bonds.

3.2 Correlations in oxidation of alkenes with palladium chloride ($PdCl_2/H_2O$), the Wacker oxidation

3.2.1 Introduction

The majority of alkene additions are found to be electrophilic additions, in which the reactions are initiated with electrophilic attacks on the alkene π bonds from electrophiles. Most of our previous correlation studies were also focused on electrophilic additions to alkenes. However, for nucleophilic additions to alkenes, such as $PdCl_2$ oxidation and other additions related to transition metal complexes, which are characterized by inhibition of reaction rate by alkyl or other electron

donating substituents, there have been no clear measures of the relative importance of electronic and steric effects. Thus, it seems desirable for us to conduct correlation studies on this type of reactions to gain a deeper understanding of the reactions and meanwhile to explore the viability of this methodology in application to nucleophilic additions to alkenes.

There has been much interest in the mechanism of palladium chloride ($PdCl_2$) oxidation of alkenes (eq 3-5), partly due to the industrial importance[64-77] of the reactions in the synthesis of carbonyl compounds from corresponding alkenes (the Wacker oxidation[64,65]) and partly due to the interest in its mechanistic pathway.[64-112]

$$C_nH_{2n} + PdCl_2 + H_2O \rightarrow C_nH_{2n}O + Pd + 2HCl \qquad (3\text{-}5)$$

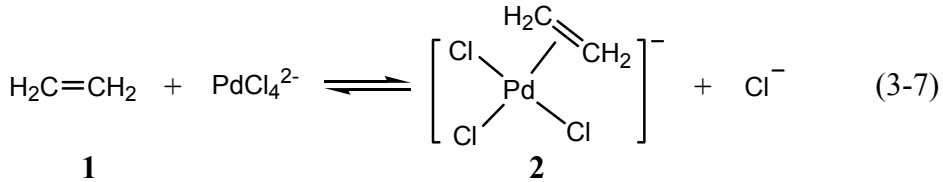
A kinetic study[70] has given the rate law of this reaction (eq 3-6), which is first order both in alkene and in palladium chloride if the acidity and concentration of chloride keep constant.

$$rate = \frac{k[PdCl_4^{2-}][alkene]}{[H^+][Cl^-]^2} \qquad (3\text{-}6)$$

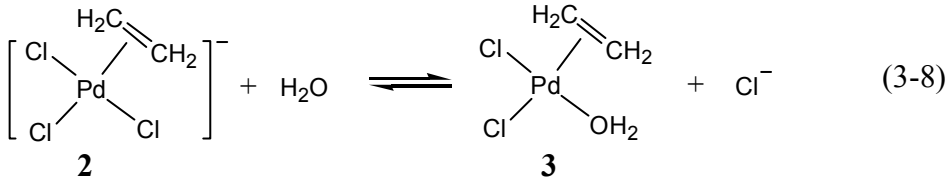
Multi-stepped pathway for this reaction has been generally suggested (eqs 3-7 to 3-12), although there has been disagreement over some mechanistic details and over the identity of the rate-determining step.[68-112] The first step (eq 3-7) of the reaction is alkene coordination with $PdCl_4^{2-}$ to give a palladium(II) complex **2**. The second step (eq 3-8) in the reaction sequence is generally accepted to be the nucleophilic replacement of a second chloride by water to give intermediate **3**. There seems to be agreement that the first two steps (eqs 3-7 and 3-8) in the reaction

sequence are fast equalibria.[68-112] However, two different pathways have been suggested for the ensuing step (**3**→**5**) (eqs 3-9 and 3-9').

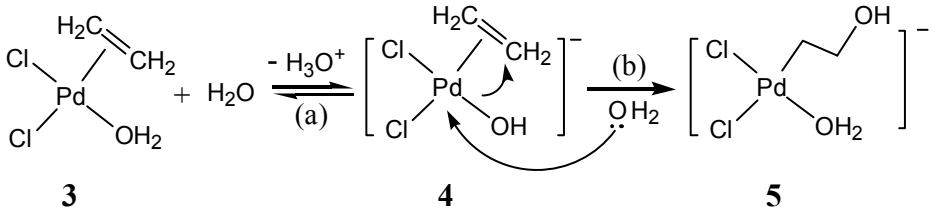
In the first pathway,[68-77] the alkene complex **3** deprotonates first to yield a negative hydroxymetal complex ion **4**, followed by rate-determining conversion of this intermediate complex anion **4** into a palladium(II) β-hydroxyalkyl species **5**, a process called hydroxypalladation (eq 3-9).[68-77] The second proposed pathway[96,97] is a rapid equilibrium in which an H_2O molecule directly attacks the C=C double bond to give the palladium β-hydroxyalkyl intermediate **5** (eq 3-9'), with the rate-determining step (**5**→**6**) following. This intermediate **5** loses a chloride ion to yield another β-hydroxyalkyl intermediate **6** (eq 3-10). The next step (eq 3-11) is a β-hydrogen elimination of the intermediate **6** to give a palladium enol π-complex **7**. Intermediate **7** then undergoes β-hydrogen addition to give the palladium α-hydroxyalkyl species **8**. Finally, the carbonyl product **9** is produced by deprotonation and dissociation (eq 3-12).



1 **2** (3-7)

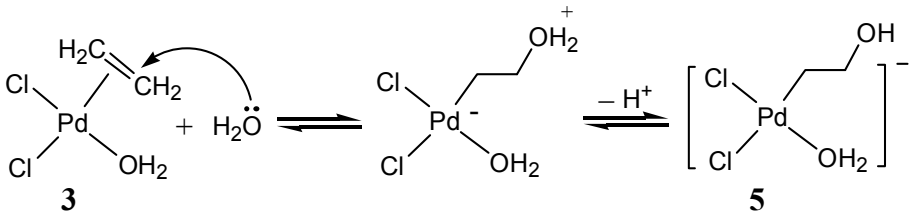


2 **3** (3-8)

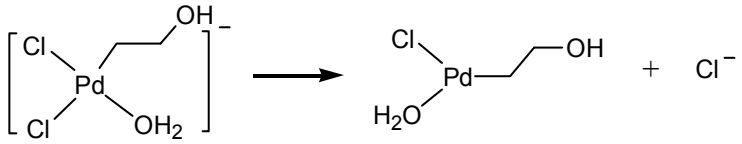


3 **4** **5** (3-9)

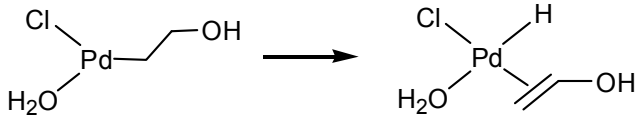
OR



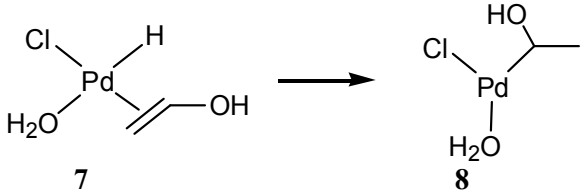
3 **5** (3-9')



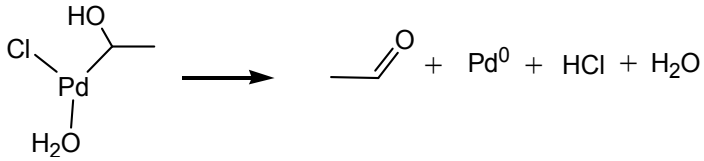
5 **6** (3-10)



6 **7** (3-11)



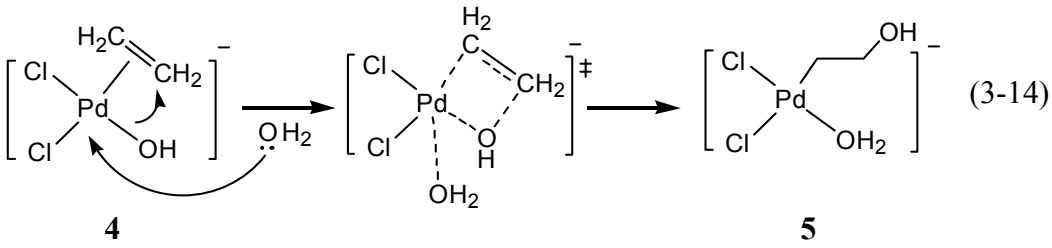
7 **8** (3-12)



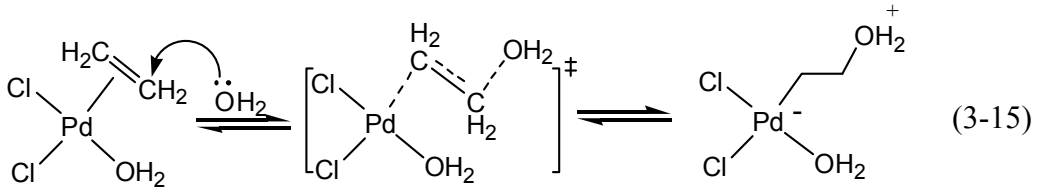
8 **9** (3-13)

Disagreement surrounding the identity of the rate-determining step has focused on whether the hydroxypalladation (**3**→**5**) is the rate-determining step or an

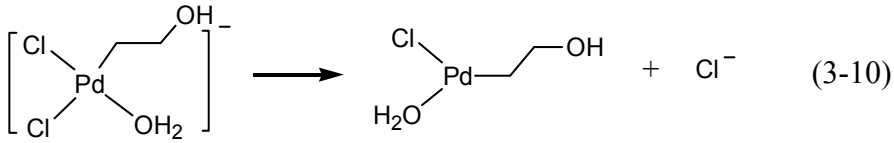
equilibrium immediately preceding the rate-determining step (**5**→**6**).[68-112] This is linked to a controversy over whether the attack by the nucleophile on the double bond in the hydroxypalladation step is internal (eq 3-14) or external (eq 3-15). One proposed mechanism, which has eq 3-14 as the rate-determining step, proceeds via internal nucleophilic attack on alkene π bond by a hydroxide that is coordinated to the metal center. Another proposed mechanism, which has eq 3-10 as the rate-determining step, specifies that the hydroxypalladation (eq 3-15) is initiated with a relatively fast external nucleophilic attack by a water molecule.



4 **5** (3-14)



3 (3-15)



5 **6** (3-10)

Henry proposed a concerted nonpolar four-center transition state[68] (eq 3-14) in the rate-determining step, similar to an I_a (associative interchange) process.[105] This

mechanism has been described as "a cis attack of coordinated hydroxide upon one of the double bond carbon atoms"[69] and "a nucleophilic intramolecular attack on the coordinated alkene."[102] Further investigation,[68-77] using a low concentration of chloride ion, showed that a combination of steric and electronic effects directs the mode of this hydroxypalladation step (eq 3-14).

In the second mechanism proposed, the hydroxypalladation step is not the rate-determining step but an equilibrium involving a relatively rapid external attack of a water molecule upon a carbon atom of the alkene double bond (eq 3-15).[96,97] Instead, the dissociation of a chloride ion Cl^- from the palladium β-hydroxyalkyl intermediate **5** (eq 3-10) is proposed to be the rate-determining step of the reaction.[96,97,103-105] However, data used to formulate these conclusions were obtained from reactions carried out under a high (≈ 3 M) chloride ion concentration, so these results may apply to a reaction other than that which is the subject of this study.

There may be some confusion surrounding the mechanism of this reaction because many of these reactions were not run under the exact conditions of the Wacker reaction.[64,65] For example, reactants often had different ligands on palladium[78-85] or used different nucleophiles;[86,95] it has been reported[73] that either of these can change the reaction mechanism. In addition, some studies[96-100] have been carried out with a much higher concentration of chloride (≈3 M) than is used in the traditional Wacker reaction (<1 M) developed by Smidt and co-workers[64,65] (while at Wacker Chemie laboratory). Initially, it was assumed[97] that using a chloride concentration different from that in the original Wacker oxidation would not likely change the steric course of the reaction. However, it was recently shown that this

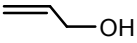
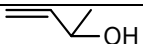
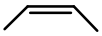
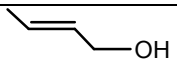
higher chloride concentration does indeed change the reaction mechanism, from syn addition at low [Cl^-] to anti addition at high [Cl^-].[73] Moreover, different products are obtained with the different chloride concentrations.[73] The relative reactivity data used for our study were obtained under the lower [Cl^-] (<1 M), so the studies[68-77] pertinent to this investigation are those carried out under analogous reaction conditions, including low chloride ion concentration. Therefore, only the pertinent studies[68-77] under analogous conditions will be used herein for comparison and analysis.

3.2.2 Correlation plots

Alkene IPs, HOMO energy levels, LUMO energy levels, and relative rates for the $PdCl_2$ oxidation of representative alkenes are shown in Table 3-4. The relative rates were converted from a previous kinetic study,[70] in which the reaction was carried out in low chloride concentration (<1M) at room temperature (25°C). Experimental alkene IPs were collected from literature. Alkene HOMO and LUMO energy levels were calculated by using the MNDO semi-empirical MO method.

Correlation lines with negative slopes were observed in the plots of log k_{rel} values versus alkene IPs (Fig 3-7) and versus HOMO energies (Fig 3-8), which indicate that this reaction is not an electrophilic addition to alkene C=C bonds, but a nucleophilic one. Therefore, we correlated log k_{rel} values versus alkene LUMO energies in Fig 3-9. The negative slopes in Fig 3-9 confirm that this reaction is a nucleophilic addition to alkenes; a lower LUMO energy level corresponds to a greater reaction rate within each sterically similar alkene group.

Table 3-4. Alkene IPs (eV), HOMO energies (eV), LUMO energies (eV), and relative rates of palladium chloride oxidation of alkenes

No.	alkene	IP[a]	HOMO[b]	LUMO[b]	k_{rel}[c]
1		10.52	-10.17	1.31	897
2		9.74	-9.97	1.12	241
3		9.63[d]	-9.93	1.14	103
4		9.63	-9.94	1.12	100
5		9.52[e]	-9.92	1.18	35.9
6		9.24	-9.80	0.99	44.9[f]
7		9.12	-9.79	0.93	76.9
8		9.12	-9.78	0.93	87.2
9		9.01[g]	-9.75	0.96	22.3

[a]Ref 61, unless otherwise noted. [b]MNDO method by Christopher Brammer. [c]Ref 70; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-butene. The unit of rate constants is M^2s^{-1}. [d]Ref 113. [e]Calculated by applying to the IP for 1-butene a correction factor calculated as the difference between the IPs of 1-propene and 2-propen-1-ol: 9.63eV - (9.74eV - 9.63eV) = 9.52eV; Ref 114a. [f]Ref 71. [g]Calculated by applying to the IP for 2-propen-l-ol a correction factor calculated as the difference between the IPs of 1-propene and *trans*-2-butene: 9.63eV - (9.74eV - 9.12eV) = 9.01eV; Refs 114a and 114b.

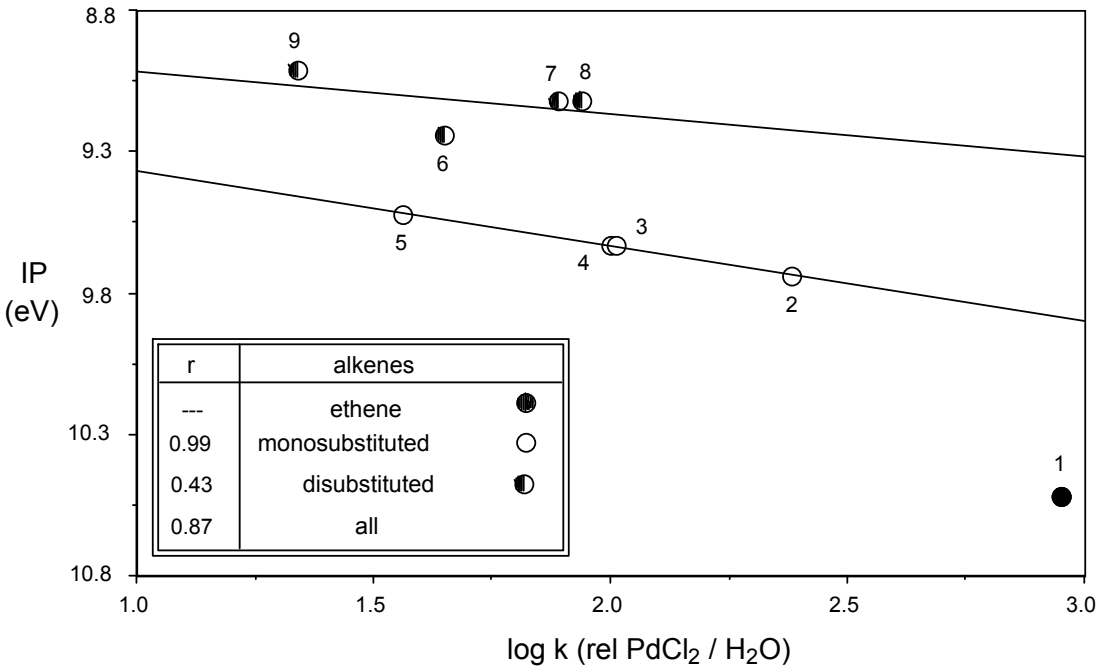


Figure 3-7. Plot of log k_{rel} values versus alkene IPs. Data are from Table 3-4. Negative slopes are obtained for correlation lines for sterically similar alkenes and for all alkenes, regardless of steric requirements, which indicates a nucleophilic addition to alkenes.

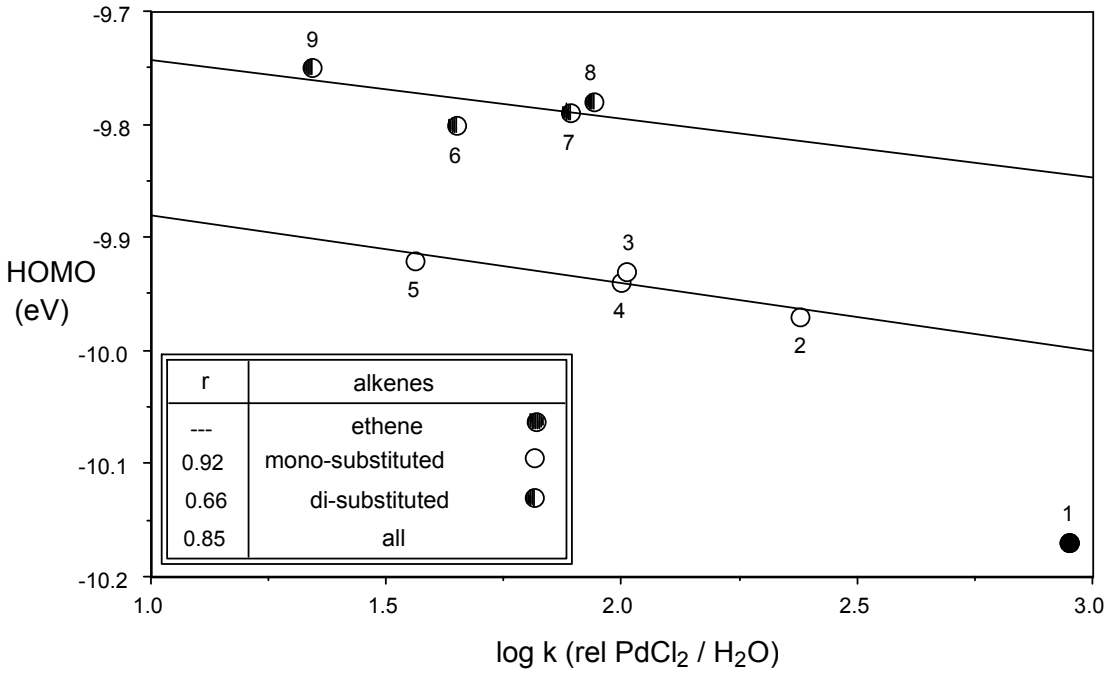


Figure 3-8. Plot of log k_{rel} values versus alkene HOMO energies. Data are from Table 3-4. Negative slopes are obtained for correlation lines for sterically similar alkenes and for all alkenes, regardless of steric requirements, which indicates a nucleophilic addition to alkenes.

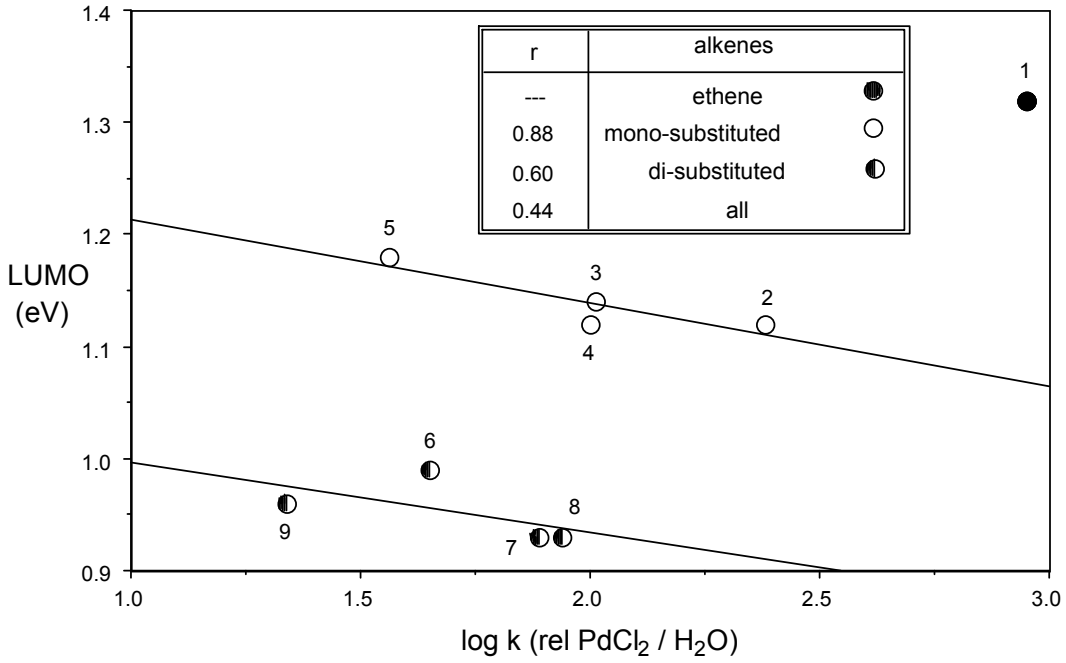


Figure 3-9. Plot of log k_{rel} values versus alkene LUMO energy levels. Data are from Table 3-4. Data points naturally fall into different sterically similar alkene groups. Correlation lines are given for monosubstituted alkenes (E_{LUMO} = 1.29 – 0.075 log k_{rel}, r = 0.88, s = 0.056, and c.l. = 90%) and for disubstituted alkenes (E_{LUMO} = 1.06 – 0.063 log k_{rel}, r = 0.60, s = 0.102, and c.l. = 60%).

3.2.3 Substituent effects

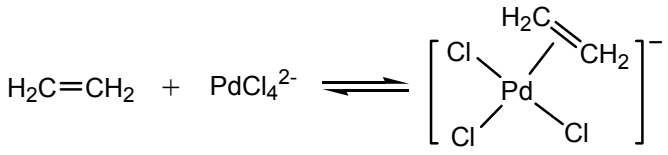
The negative slopes of correlation lines in Figs 3-7 to 3-9 reflect that the Wacker oxidation is a nucleophilic addition to alkenes. Within each sterically similar group of alkenes, a lower LUMO energy corresponds to a greater reaction rate. The natural grouping of data points for alkenes with different steric requirements in Fig 3-9 reveals that rates of this reaction depend upon not only electronic effects but also steric effects. For instance, the disubstituted alkenes react much slower than do those monosubstituted alkenes with similar LUMO energies because of their greater steric hindrance.

3.2.4 Mechanistic analysis of the Wacker oxidation

One goal of the mechanistic analysis was to determine whether our work could differentiate between the most likely proposed mechanisms for this reaction. A multi-step pathway (steps 1 to 7) has been suggested for the Wacker oxidation. However, debate surrounding the identity of the rate-determining step has focused on whether hydroxypalladation (**3**→**5**) is the rate-determining step[68] or an equilibrium preceding the rate-determining step (**5**→**6**).[96,97] This is linked to the question whether attack by the nucleophile on C=C in the hydroxypalladation is internal (**4**→**5**)[68] or external (**3**→**5**).[96,97]

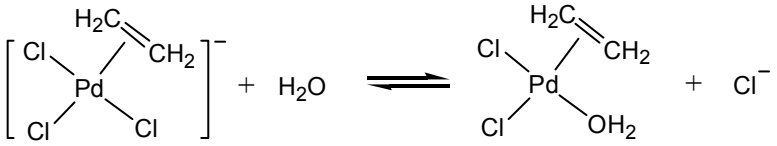
Proposed reaction mechanisms for Wacker oxidation:

Step 1



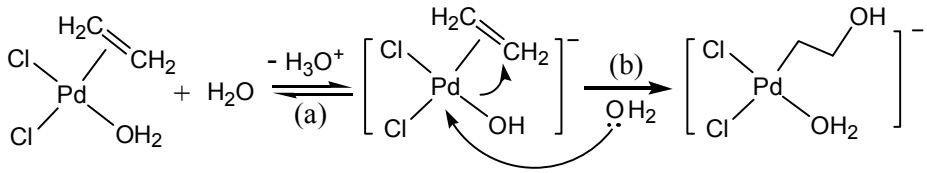
1 **2** (3-7)

Step 2



2 **3** (3-8)

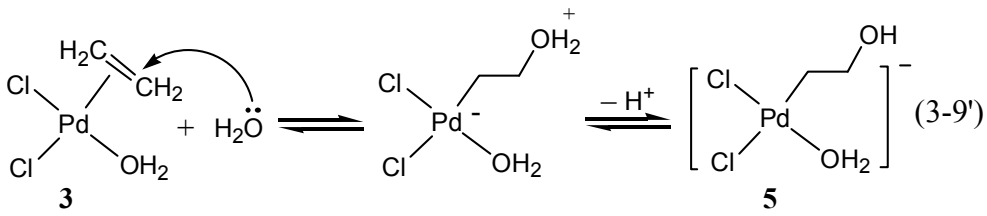
Step 3



3 **4** **5** (3-9)

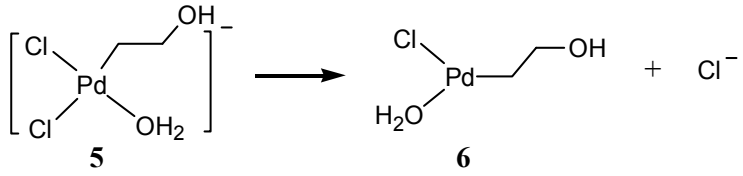
OR

Step 3'



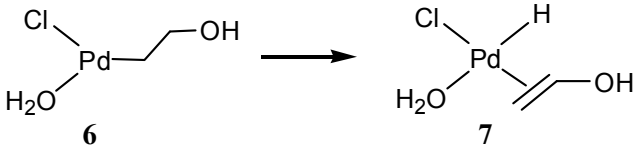
3 **5** (3-9')

Step 4



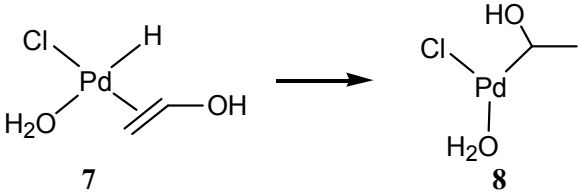
5 **6** (3-10)

Step 5



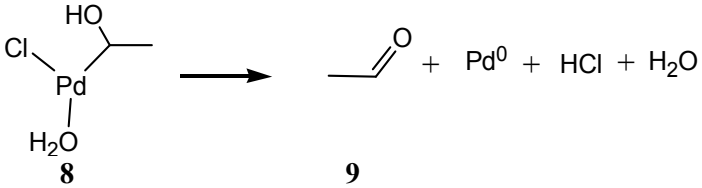
6 **7** (3-11)

Step 6



7 **8** (3-12)

Step 7



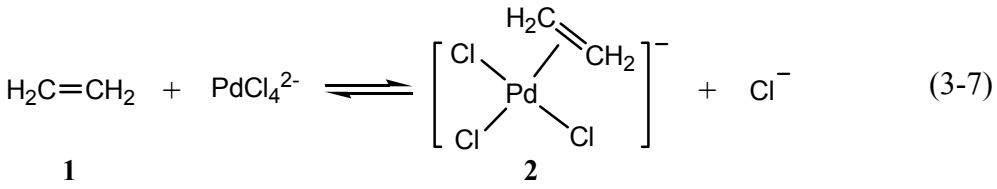
8 **9** (3-13)

In this section, evidence will be presented which supports internal attack (**4**→**5**) as the rate-determining step, rather than loss of chloride (**5**→**6**) preceded by an external attack (**3**→**5**) equilibrium. Our correlation study shows multiple lines with negative slopes in the plot of log k_{rel} values versus alkene LUMO energy levels for

the Wacker oxidation (Fig 3-9). This indicates that the overall reaction rate of the Wacker oxidation is mainly influenced by a step (or steps), in which nucleophilic attack upon the alkene C=C bond is involved and in which the alkene reactivity depends upon both electronic and steric effects of the substituents.

The results of our correlation study are helpful in considering the hydroxypalladation step and the rate-determining step of the reaction. The results of other mechanistic studies also give experimental evidence which should be considered in selecting which mechanism is more plausible. A step-by-step analysis of the proposed mechanisms presents the pertinent experimental evidence, which is useful in judging whether that step has an important influence on the rate of the reaction.

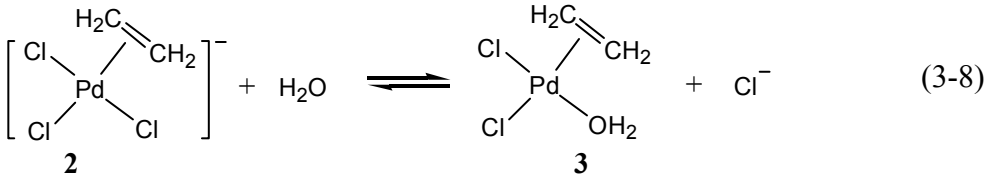
Step 1: Alkene displacement of Cl^- from the metal center of $PdCl_4^{2-}$



1 **2** (3-7)

- Not important: it is an electrophilic addition to an alkene C=C bond,[68,96,97] while experimental evidence indicates that the reaction with the alkene is nucleophilic.

Step 2: Replacement of chloride by a water molecule

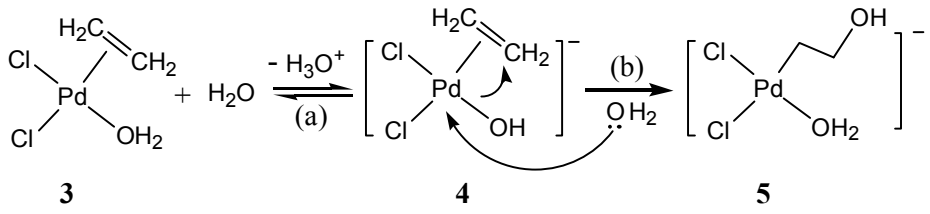


2 **3** (3-8)

- Not important: the alkene C=C bond is not directly involved in this step. Characteristics of the C=C bond would have little effect on this reaction, but experimental evidence indicates that substituents on C=C influence the reaction rate, both electronically and sterically.

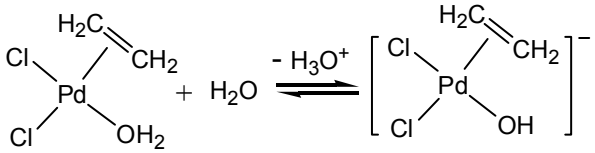
One member of the graduate Advisory Committee (MHA) has asked why Henry[71,72] did not discuss the equilibrium leading to formation of the trans isomer of **3** (**trans-3**). We believe this is because Henry realized that **trans-3** would be formed but would dissociate again, because it could not lead to product formation. It is common practice in organic chemistry not to write all possible equilibrium structures of a mechanism, but only to write those which lead to product formation.

Step 3: Hydroxypalladation by the internal attack mechanism[68]



3 **4** **5** (3-9)

Step 3a: Deprotonation of alkene complex 3



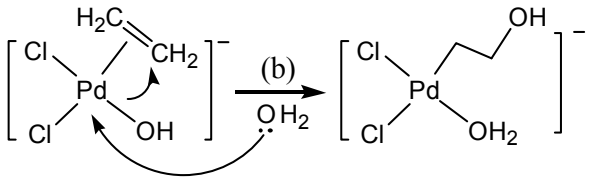
3 **4** (3-9a)

- Not important: the alkene C=C bond is not involved in this equilibrium. Therefore, substituents on the C=C bond would have little effect on this reaction, but

experimental evidence indicates that electron withdrawing substituents on C=C increase the rate.

One member of the graduate Advisory Committee (MHA) has asked why Henry[68] concluded that olefin structure would not be expected to have a significant effect (no "cis effect") on the equilibrium shown in eq 3-9a, which would produce the relative reactivities shown in Table 3-4. First, a "cis effect" is defined as "the effect of a ligand upon the rate of ligand replacement of the group cis to itself."[115a] In eq 3-9a, the H_2O ligand is not being replaced; it is being deprotonated. Therefore, the "cis effect" would not apply here. Second, we assume that Henry was aware that the effects of substituents drop off drastically after passing through three sigma bonds; the only functionality with an electronegative atom in his study was OH, and in each such functionalized alkene, the OH is two sigma bonds from the π system, which is itself two or three sigma bonds from the proton being abstracted (depending upon whether one considers the π-bonded olefin or the metallacyclopropane bonding extremes of compound 4).[115b] Third, although the trans effect is reported to be small, the cis effect is much smaller.[115a,c]

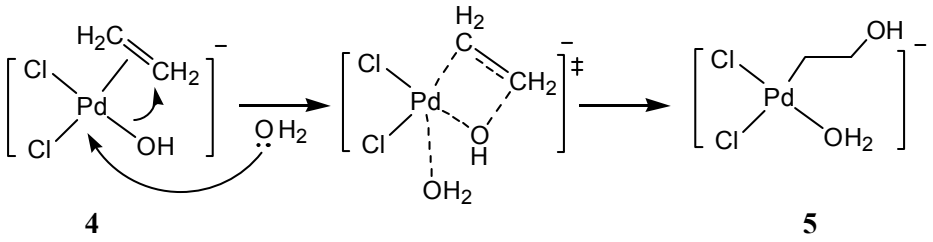
Step 3b: Addition of the coordinated OH^- to the alkene C=C bond to give 5



4 **5** (3-9b)

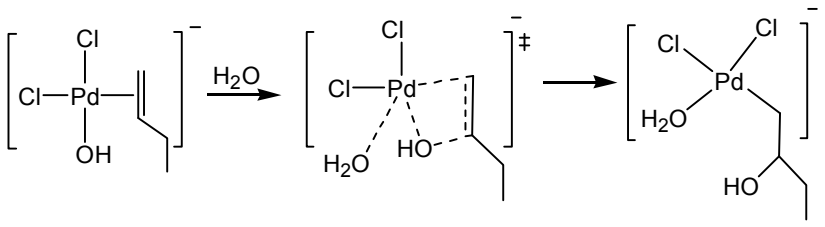
This step is important in determining the overall reaction rate because it is a reaction with the C=C bond and it is supported by a variety of experimental evidence:

- It is a nucleophilic addition to alkenes — an internal attack of the coordinated OH^- on the C=C bond coordinated to palladium (eq 3-14).[68] This is consistent with experimental evidence that the overall reaction is a nucleophilic attack upon the C=C bond.



4 **5** (3-14)

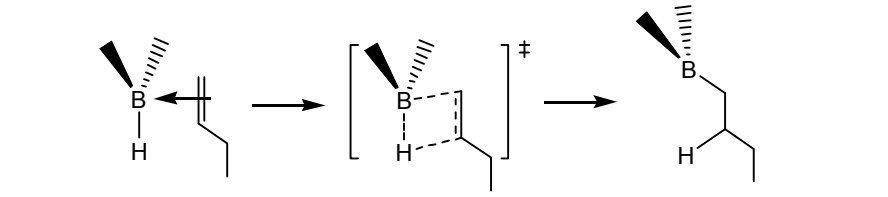
- A congested four-membered cyclic transition state is formed in this step (eq 3-14),[68] producing strong steric effects reducing the reaction rate. This is consistent with the experimental observation that the reaction rate depends upon steric effects as well as electronic effects of the substituents.
- Methyl ketones are the major products from terminal alkenes.[77,80,116] This is consistent with the internal attack mechanism for the hydroxypalladation step, in which the less hindered end of a terminal alkene is attached to Pd in intermediate **5a,** in order to minimize steric hindrance between the Pd complex and the alkene in the transition state[70] (eq 3-16).



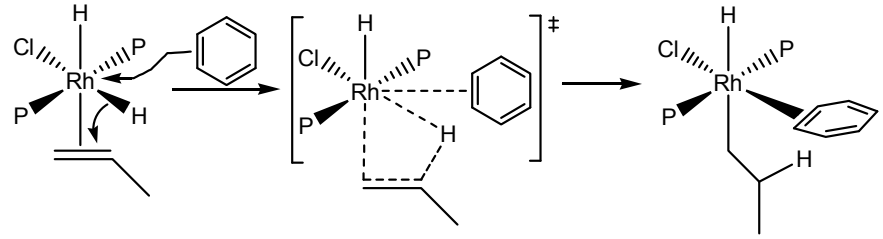
4a **5a** (3-16)

- Similar four-membered cyclic transition states are proposed in rate-determining steps for alkene hydroboration (eq 3-17) and for alkene hydrogenation catalyzed by

Wilkinson's catalyst (eq 3-18). In both cases, multiple lines have been observed in their correlation plots, which are similar to Fig 3-9. The similar correlation plots evidence similar electronic effects and strong steric effects among all three reactions. Comparable steric effects in these reactions suggest that they share some mechanistic characteristics, i.e. congested four-membered cyclic transition states in their rate-determining steps.

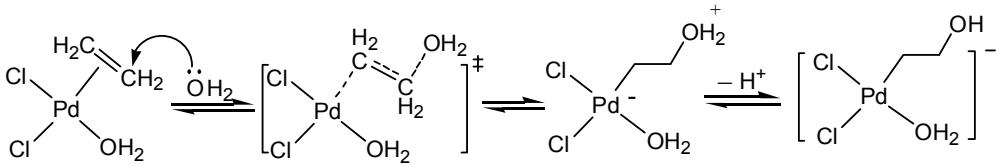


(3-17)



(3-18)

Step 3′: Hydroxypalladation by the external attack mechanism[96,97]



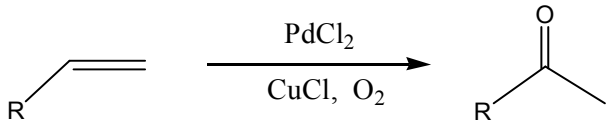
(3-15)

Not important: this is proposed to be a reversible external attack of a free water molecule upon the alkene C=C bond (**3**→**5**).[97]

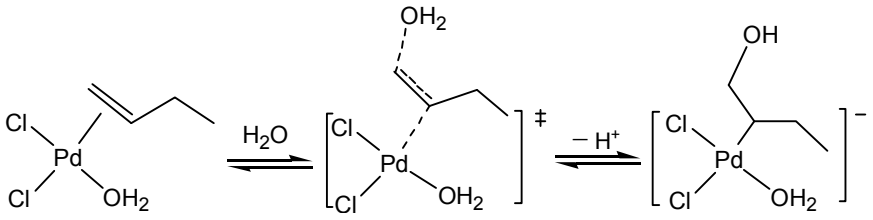
- The transition state of hydroxypalladation in the external attack mechanism is much less congested than the four-membered cyclic transition state in the internal attack mechanism. Therefore, steric effects on this equilibrium and consequently on the

overall reaction rate would be expected to be much lower, which is not consistent with the fact that steric effects on the rate of this reaction are strong. In oxymercuration, which has an analogous mechanism, introduction of methyl at the 2-position of a terminal alkene accelerates the reaction by a factor of 1000; this is opposite to that observed in the Wacker Reaction.

- Experiments[77,80,116] show that methyl ketones are the major products from terminal alkenes in the Wacker oxidation (eq 3-19). External attack by H_2O on a monosubstituted alkene in hydroxypalladation (eq 3-20) would favor the less hindered terminal carbon, in order to lower steric hindrance, giving aldehydes as major products.

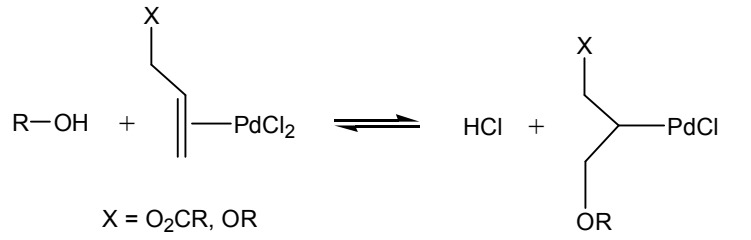


(3-19)



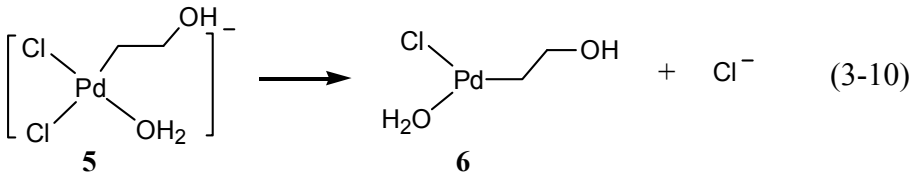
(3-20)

External attack is reported in other Wacker-like reactions, and in those cases, experimental results indicate attack at the terminal carbon. For example, in a palladium complex catalyzed reaction between a terminal alkene and an alcohol catalyzed via an external attack pathway, experimental evidence reveals that the alcohol attacks the less hindered terminal carbon of the C=C bond (eq 3-21).[117a]



(3-21)

Step 4: Chloride dissociation from intermediate 5

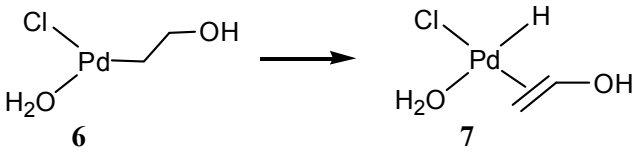


(3-10)

Not important:

- In the internal attack mechanism,[68] it is proposed to be a fast reaction after the rate-determining step and so would not affect the overall reaction rate.
- In the external attack mechanism,[97] it is considered to be the rate-determining step of the Wacker oxidation and dissociation of a ligand from a 4-coordinated intermediate **5** to give a 3-coordinated product **6**. This step does not involve the C=C bond. Moreover, in coordination chemistry,[117b] such a dissociation is expected to be sterically accelerated by bulky ligands. Therefore, increasing the degree of substitution on alkene C=C bond would increase the size of the hydroxyalkyl ligand in the 4-coordinated intermediate **5** and thus accelerate the rate-determining chloride dissociation (step 4). However, this is in contrast to the observation that this reaction is decelerated by increasing the degree of substitution on the alkene C=C bond.

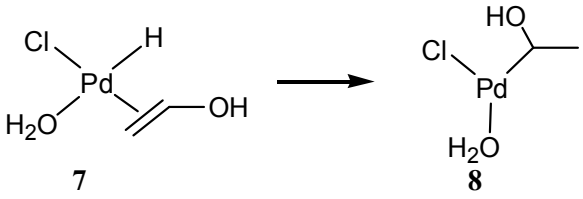
Step 5: β-Hydrogen elimination of intermediate 6



(3-11)

- Not important: it is a fast reaction after the rate-determining steps in both proposed mechanisms.[68,97]

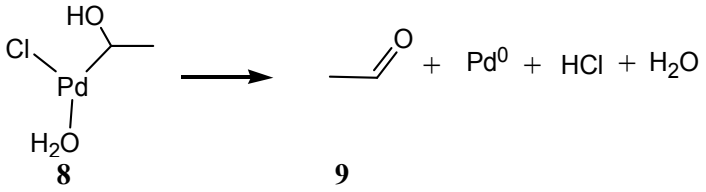
Step 6: β-Hydrogen addition of intermediate 7



(3-12)

- Not important: it is a fast reaction after the rate-determining steps in both proposed mechanisms.[68,97]

Step 7: Deprotonation and dissociation of intermediate 8



(3-13)

- Not important: it is a fast reaction after the rate-determining steps in both proposed mechanisms.[68,97]

Finally, based on the step-by-step analysis above, it can be concluded that the results of our correlation study favor the proposed internal attack mechanism and disfavor the proposed external attack mechanism for the Wacker oxidation.

3.2.5 Conclusion

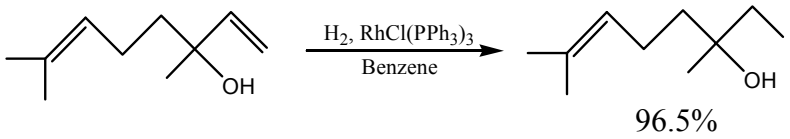
Plots of log k_{rel} values versus alkene LUMO energy levels reveal multiple nearly parallel lines of correlation with negative slopes, indicating that the Wacker oxidation is a nucleophilic addition to alkenes, dependent upon both electronic and steric effects. This result is consistent with the *syn* addition mechanism proposed by Henry in which the rate-determining step is the nucleophilic hydroxypalladation. However, the results of this study disfavor the mechanism proposed by Bäckvall and co-workers, in which the hydroxypalladation is considered to be an equilibrium via a *anti* attack of a water molecule to the alkene C=C bond and the rate-determining step is dissociation of a chloride from the hydroxypalladation adduct. Comparison of the results for $PdCl_2$ oxidation versus those for hydroboration and for oxymercuration, combined with consideration of the two mechanisms proposed for $PdCl_2$ oxidation, indicates that the *syn* addition mechanism for $PdCl_2$ oxidation of alkenes has similarities to that for hydroboration.

3.3 Correlations in homogeneous hydrogenation of alkenes in the presence of Wilkinson's catalyst, $RhCl(PPh_3)_3$

3.3.1 Introduction

Homogeneous hydrogenation of alkenes in the presence of $RhCl(PPh_3)_3$, tris(triphenylphosphine)chlororhodium(I), which was developed in 1965 by Wilkinson and coworkers and named as Wilkinson's catalyst,[126-128] has been extensively studied due to the interest in its mechanism[129-156] and in its application in organic syntheses.[157-164] Using modifications of Wilkinson's catalyst, homogeneous asymmetric hydrogenations, catalyzed by rhodium diphosphine chiral complexes, were developed later by Knowles[165-167] and Noyori.[168,169] Asymmetric hydrogenations enabled the production of a single predicted enantiomer, of great significance in the syntheses of pharmaceutical products.[152-155,165-169] One early industrial scale synthetic application was synthesis of L-DOPA, which is useful in the treatment of Parkinson's disease and which is produced by enantioselective hydrogenation of an α-amino acid catalyzed by a rhodium complex containing the chiral diphosphine ligand DiPAMP.[167] A wide range of similar catalysts has been applied widely in industrial syntheses of medical drugs and other materials.[152-155,165-169]

The basic hydrogenation of alkenes (eq 3-22) shows sensitive selectivity to different alkene C=C bonds with different substituents on it[157,161,162] and can be easily carried out under mild reaction conditions (room temperature and atmospheric pressure of H_2).[157-159]



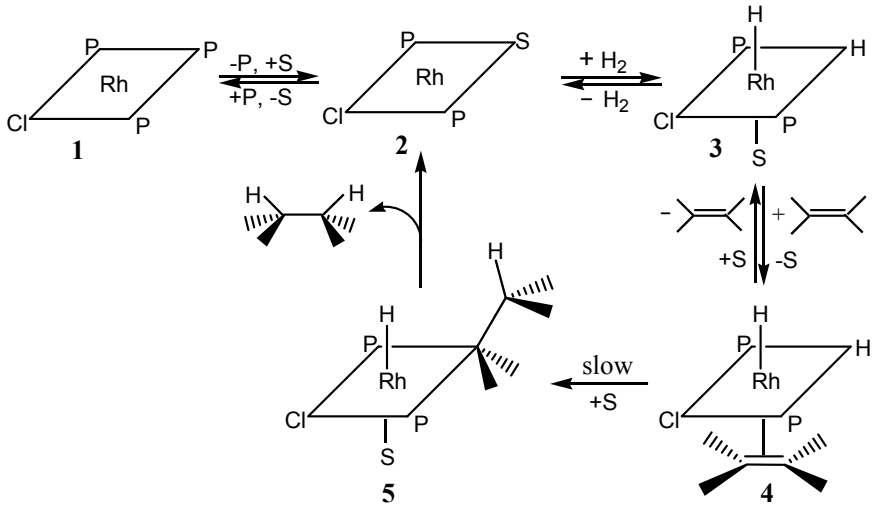
96.5% (3-22)

3.3.2 Proposed mechanisms

Several reaction mechanisms[146-151,153,156] have been proposed for this homogeneous hydrogenation catalytic cycle, but the "hydride route" (as opposed to the "alkene route"[157] or "substrate route"[136]) is believed to be the predominant pathway.[157] Three proposed "hydride route" mechanisms of this reaction are shown in Schemes 3-8, 3-9, and 3-10. Kinetic study[147] has given the rate law of this reaction (eq 3-23).

$$rate = \frac{Kk[alkene][RhH_2Cl(PPh_3)_2]}{[PPh_3] + K[alkene]} \qquad (3\text{-}23)$$

For eq 3-20, *k* is the rate constant for the rate-determining step, alkene insertion into the metal hydride bond. *K* is the equilibrium constant for the alkene coordination to the rhodium metal center. In the hydride route, the dihydride rhodium complex intermediate, $RhH_2Cl(PPh_3)_2$, is formed via a reversible oxidative addition of H_2 to rhodium catalyst (**2**⇄ **3** in Scheme 3-8 or **6**⇄ **7** in Scheme 3-9). Therefore, this reaction is first order in alkene, in hydrogen, and in rhodium catalyst.

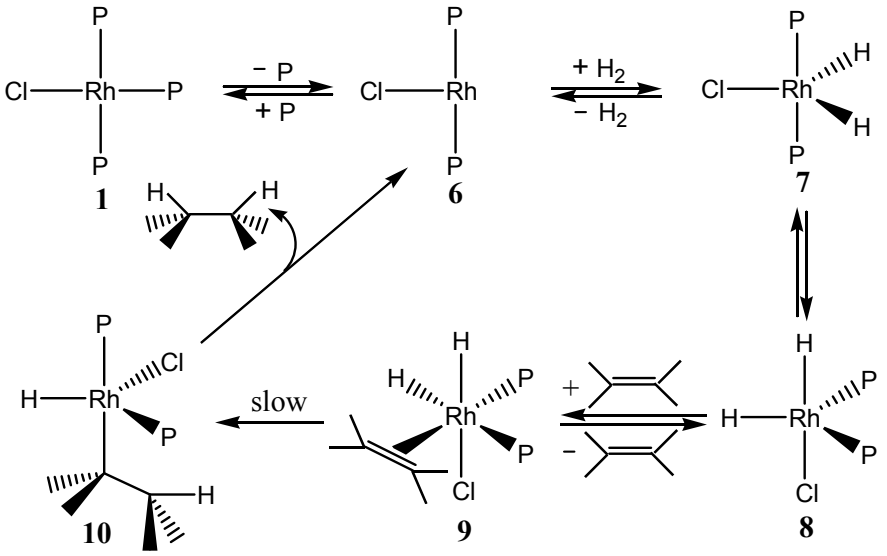


Scheme 3-8. A hydride route mechanism proposed for hydrogenation of alkenes by using Wilkinson's catalyst (P = PPh_3 and S = benzene as solvent)

There are five steps in the reaction sequence in Scheme 3-8:[147-151] (1) PPh_3 ligand dissociation **1**⇄ **2**; (2) oxidative addition of hydrogen (H_2) **2**⇄ **3**; (3) alkene coordination **3**⇄ **4**; (4) alkene migratory insertion into the Rh-H bond **4**→**5**; and (5) alkyl reductive elimination **5**→**2**. In this mechanism, the alkene insertion **4**→**5** is considered to be the rate-determining step,[146-151] and the key intermediate is **4**, an octahedral dihydride alkene complex $RhH_2Cl(alkene)(PPh_3)_2$. All other steps are fast relative to the alkene insertion **4**→**5**.[131-133,146-151] Positions occupied by S (S = solvent) in **2**, **3**, **5** are considered to be either vacant or coordinated to a solvent molecule.[147] Some later studies[157,170] tend to support the idea that a solvent molecule is associated with the Rh center at each of those positions.

A second hydride route mechanism (Scheme 3-9)[153] differs slightly regarding (a) the structures of the key intermediates (**9** in Scheme 3-9 versus **4** in Scheme 3-8) and (b) the involvement of the solvent molecules because no solvent molecule is

involved in this proposed mechanism. In this alternative mechanism, an isomerization (**7**⇄ **8**) precedes the formation of a key intermediate **9**, which possesses cis biphosphine ligands. All these first four steps (**1**⇄ **6**, **6**⇄ **7**, **7**⇄ **8**, and **8**⇄ **9**) are considered to be fast equilibria.[153] Then, the rate-determining alkene insertion (**9**→**10**) is followed by a fast alkyl reductive elimination (**10**→**6**) to give the final hydrogenated product and to regenerate **6**.[153,164]

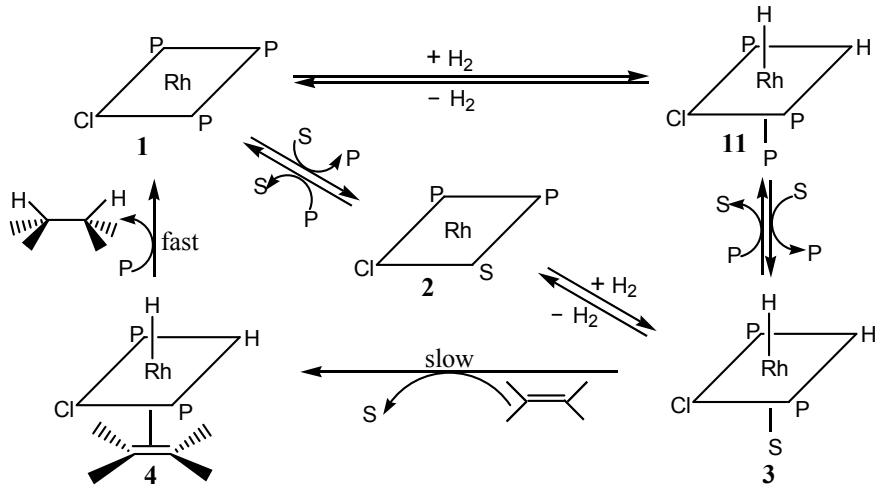


Scheme 3-9. A second hydride route mechanism with isomerization, proposed for hydrogenation of alkenes by using Wilkinson's catalyst (P = PPh_3)

In an *ab initio* computational mechanistic investigation[170-171] of the Scheme 3-8 pathway, the potential energy profile for the full catalytic cycle of alkene hydrogenation in the presence of the Wilkinson's catalyst was studied. The geometries of the transition states, as well as of the intermediates, were determined at the RHF/ECP level by using a variety of basis sets, for each step of the reaction cycle.

It was found that the alkene insertion step has the highest energy barrier in the full catalytic cycle of this reaction, predicting it to be the rate-determining step of this reaction. This conclusion is consistent with both mechanisms shown in Schemes 3-8 and 3-9.[146-151,153]

A third hydride route mechanism (Scheme 3-10)[156] was proposed based on kinetic analyses indicating that a solvent molecule S (S = benzene) is involved in the catalytic sequence. In this mechanism, the rate-determining step, which is preceded by four fast complexation equilibria[156] in two different routes (**1**⇄ **2**⇄ **3** and **1**⇄ **11**⇄ **3**), is formation of the 6-coordinate intermediate **4** (**3**→**4**). Then, this 6-coordinate intermediate **4** undergoes a fast decomposition to yield the alkane product and to regenerate Wilkinson's catalyst **1**.[156]



Scheme 3-10. The third hydride route mechanism (P = PPh_3, S = benzene as solvent)

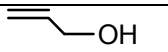
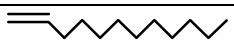
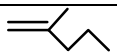
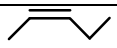
Another totally different mechanism for alkene hydrogenation in the presence of Wilkinson's catalyst and various Lewis acids, such as $AlCl_3$, BF_3, $AlPh_3$, etc., has

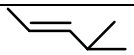
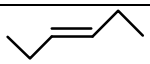
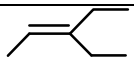
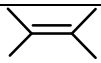
been proposed.[134] However, the reaction conditions used in that study are so different from those discussed above,[146-151,154,156] that this may constitute a different reaction, and a mechanistic comparison is probably invalid.

3.3.3 Correlation plots

Alkene experimental IPs, alkene computational LUMO energy levels, and relative rates for homogeneous hydrogenation of alkenes in the presence of Wilkinson's catalyst are given in Tables 3-5 and 3-6. The two sets of relative rate data in Tables 3-5 and 3-6 were converted from two previous studies,[172,173,176] in which both reactions were carried out under similar reaction conditions (at room temperature and using benzene as solvent). As was done previously, cyclic alkenes and aryl alkenes are excluded here in order to avoid complications due to ring strain or conjugation with phenyl. Experimental alkene IPs were collected from literature and the alkene LUMO energy levels were calculated by using *ab initio* method at HF/6-31G* level.

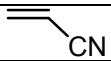
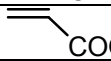
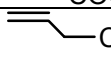
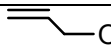
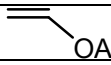
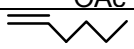
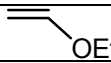
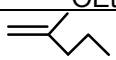
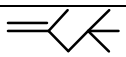
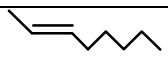
Table 3-5. Alkene IPs(eV), LUMO energy levels(eV), and relative rates of catalytic hydrogenation of alkenes by using Wilkinson's catalyst (A)

No.	alkene	IP[a]	LUMO[b]	k_{rel}[c]
1		10.16[d]	4.66	410[e]
2		9.59[f]	5.32	117.9
3		9.48	5.11	100
4		9.08	5.18	93.1
5		9.04	5.33	79.3
6		8.98	5.37	34.5

7		8.97	5.35	6.9
8		8.97	5.20	6.8[e]
9		8.57[g]	5.23	2.7[e]
10		8.27	5.36	1.4[e]

[a]Ref 61, unless otherwise noted. [b]*Ab initio* at HF/6-31G* level by Christopher Brammer. [c]Refs 172 and 173; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. The unit of rate constants is $mole^{-1}s^{-1}$. [d]Ref 174. [e]Ref 172; converted to relative rates from rates of H_2 consumption. [f]Calculated by applying to the IP for 1-decene, a correction factor calculated as the difference between the IPs of 1-decene and 1-octene: 9.51eV + (9.51eV – 9.43eV) = 9.59eV; Ref 175. [g]Calculated by applying to the IP for 3-ethyl-3-hexene, a correction factor calculated as the difference between the IPs of *cis*-2-pentene and *cis*-3-hexene: 8.48eV + (9.04eV – 8.95eV) = 8.57eV; Ref 61.

Table 3-6. Alkene IPs(eV), LUMO energy levels(eV), and relative rates of catalytic hydrogenation of alkenes by using Wilkinson's catalyst (B)

No.	alkene	IP[a]	LUMO[b]	k_{rel}[c]
11		10.91[d]	2.80	1470
12		10.72[d]	3.15	350
13		10.18[e]	4.22	490
14		10.16[f]	4.66	340
15		9.85[d]	4.47	160
16		9.48	5.11	100
17		9.15[g]	5.51	180
18		9.08	5.18	69
19		8.91	5.00	41
20		8.84	5.32	54
21		8.83	5.31	17

[a]Ref 61, unless otherwise noted. [b]*Ab initio* at HF/6-31G* level by Christopher Brammer. [c]Ref 176; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. [d]Ref 177. [e]Ref 178. [f]Ref 174. [g]Ref 179.

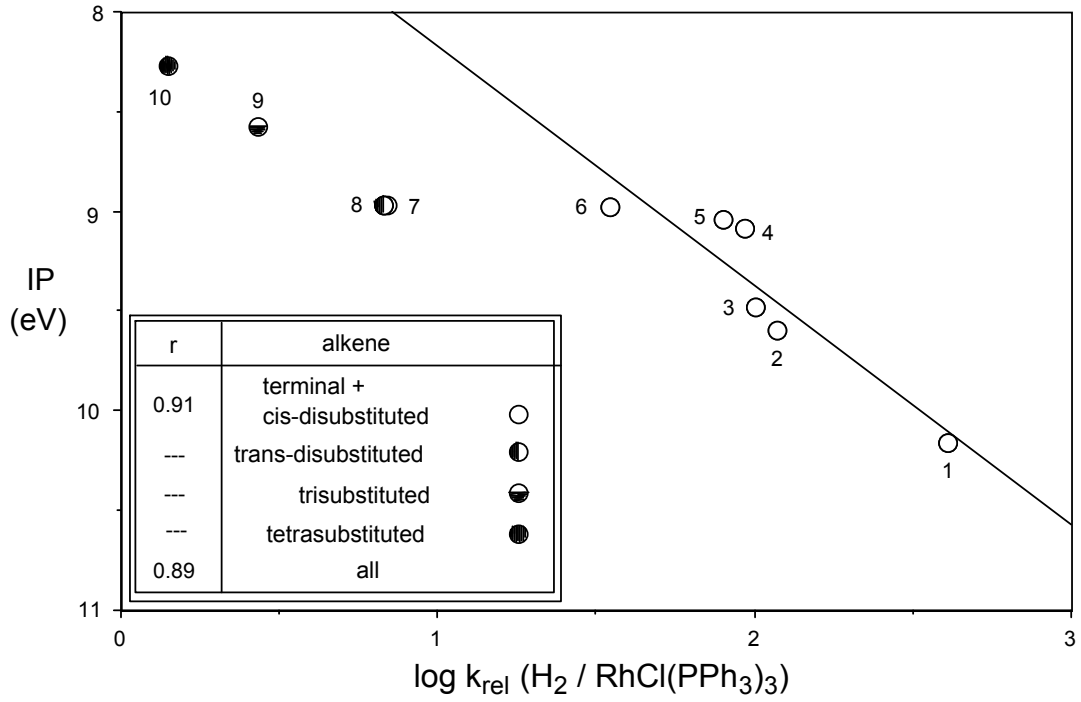


Figure 3-10. Plot of log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene IPs. Data used for this plot are given in Table 3-5. Negative slopes are obtained for correlation lines for sterically similar alkenes and for all alkenes, regardless of steric requirements, which indicates a nucleophilic addition to alkenes.

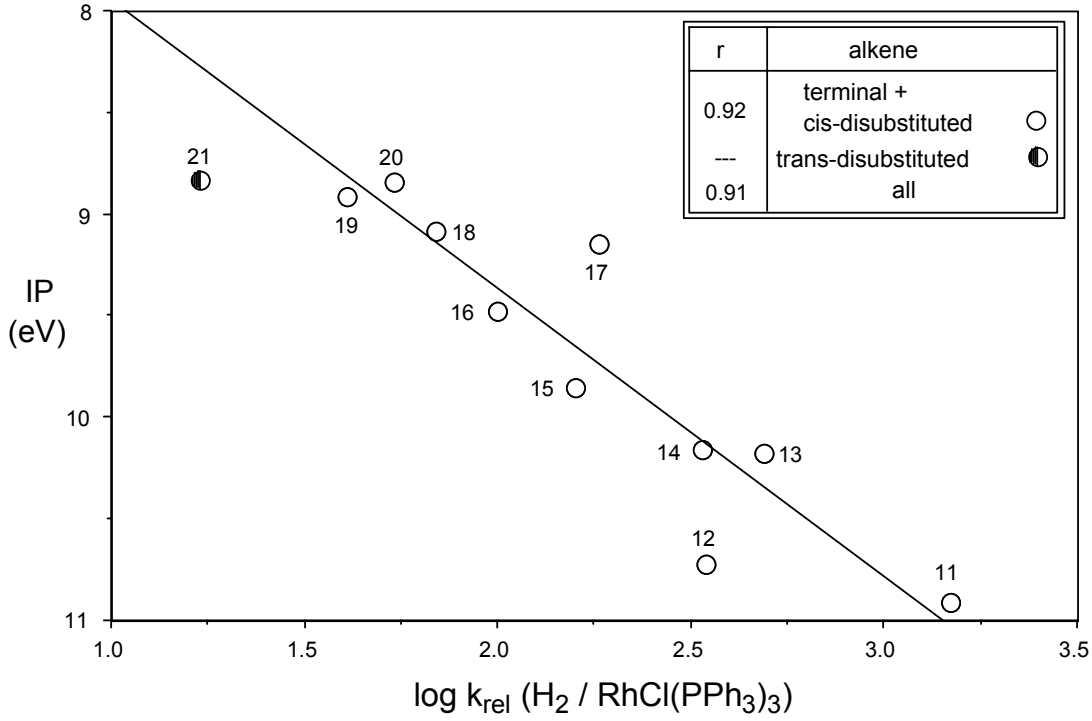


Figure 3-11. Plot of log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene IPs. Data used for this plot are given in Table 3-6. Negative slopes are obtained for correlation lines for sterically similar alkenes and for all alkenes, regardless of steric requirements, which indicates a nucleophilic addition to alkenes.

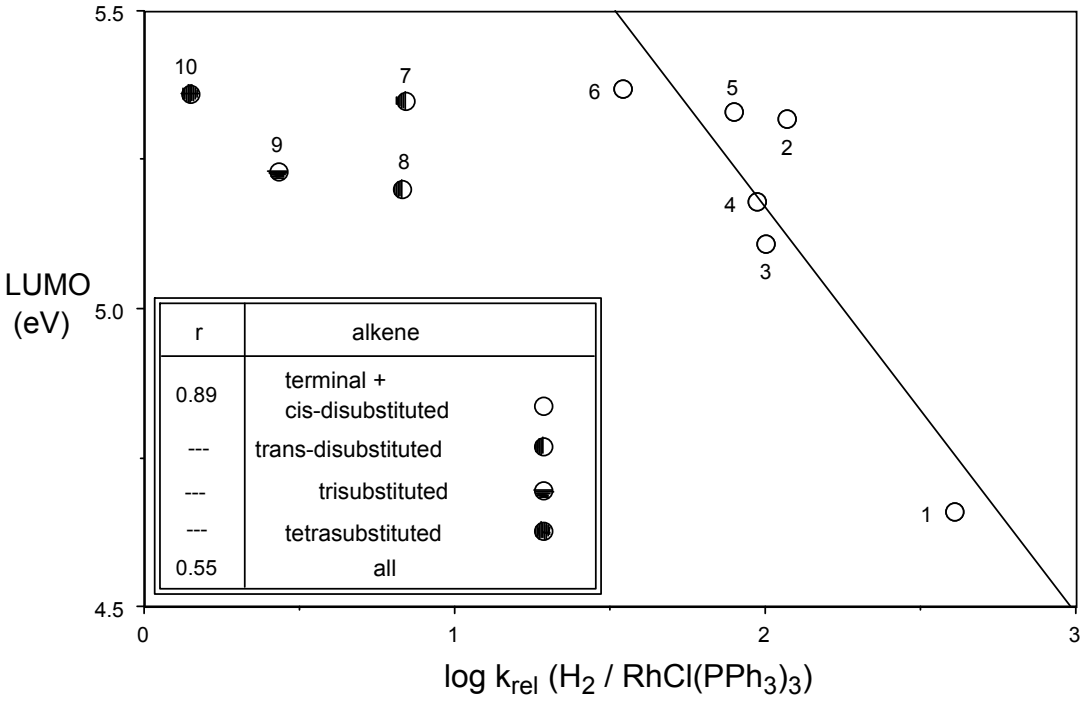


Figure 3-12. The plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene LUMO energies. Data used for this plot are given in Table 3-5. Data points for tetra-, tri-, and trans-disubstituted alkenes are naturally separated from those for terminal and cis-disubstituted alkenes. Correlation line is given for terminal and cis-disubstituted alkenes ($E_{LUMO} = 6.54 - 0.68 \log k_{rel}$, r = 0.89, s = 0.356, and c.l. = 98%).

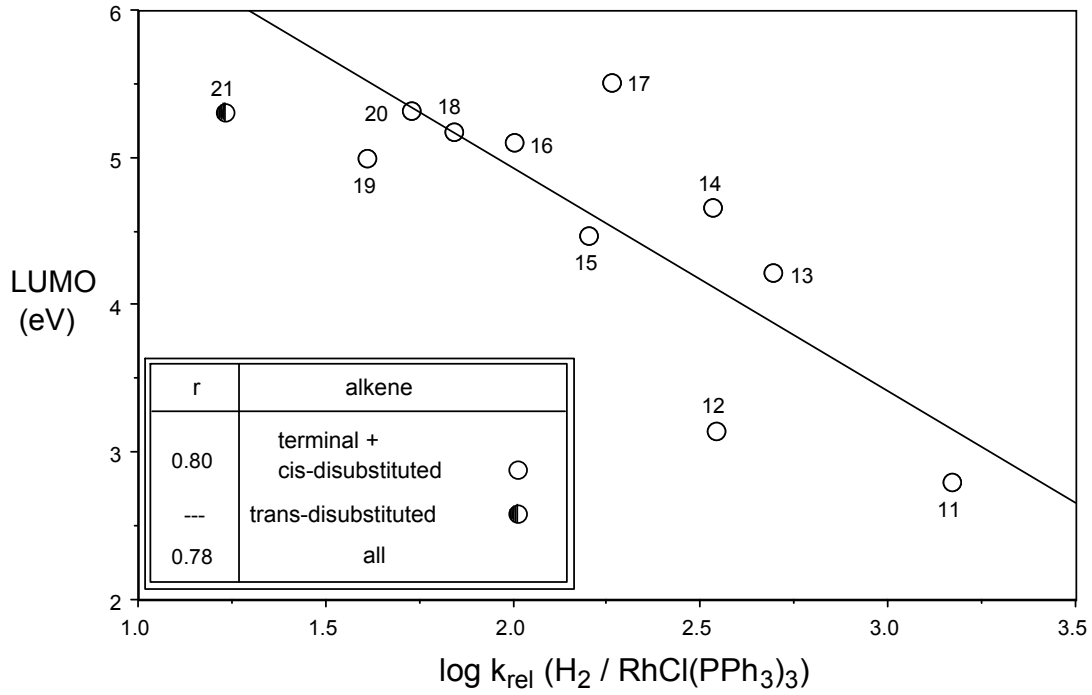


Figure 3-13. The plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene LUMO energies. Data used for this plot are given in Table 3-6. Similar to Fig 3-8, correlation line is given for terminal and cis-disubstituted alkenes (E_{LUMO} = 7.96 – 1.51 log k_{rel}, r = 0.80, s = 0.925, and c.l. = 99%).

Similar to the $PdCl_2$ oxidation of alkenes discussed in the previous section, negative slopes were also observed in the plots of log k_{rel} values versus alkene IPs for alkene hydrogenation (Figs 3-10 and 3-11). Therefore, alkene catalytic hydrogenation is also a nucleophilic addition to alkenes. We thus correlated the log k_{rel} values versus alkene LUMO energies to ascertain the relative importance of electronic and steric effects. Correlation lines of log k_{rel} values versus alkene LUMO energies for terminal and cis-disubstituted alkenes studied herein are shown in Figs 3-12 and 3-13. However, the data points for alkenes with different steric requirements, such as trans-disubstituted, trisubstituted, and tetrasubstituted alkenes, are deviant

from the line of correlation. The results of this correlation study indicate that the reaction rate this reaction depends upon both electronic and steric effects. The trend displayed in Fig 3-12 seems not very convincible because alkene **1** (allyl alcohol) is the only functionalized alkene in the sterically similar alkene group, and is obviously separated from the data points for the other olefins. However, in Fig 3-13, in which more than half of the alkenes are functionalized alkenes, a trend similar to that shown in Fig 3-12 is also observed, which confirms the validity of the results from Fig 3-12.

3.3.4 Substituent effects and mechanistic analysis

The negative slopes of the plots in Figs 3-12 and 3-13 agree with previous findings[180-183] that this reaction is a nucleophilic addition to alkenes, with a lower LUMO energy level corresponding to a higher reaction rate. The slopes in the plots are opposite to those in most of our previous investigations, which explored electrophilic additions. However, the correlation plots of this reaction is similar to that of $PdCl_2$ oxidation (multiple lines with negative slopes), which is also a nucleophilic addition reaction (see section 3.2).

The conclusion that the reaction rate in homogeneous hydrogenation catalyzed by $RhCl(PPh_3)_3$ is controlled predominant by a step involving nucleophilic attack on the alkene C=C bond is consistent with both the first and the second proposed mechanisms (Schemes 3-8 and 3-9).[147-151] These mechanisms have virtually identical rate-determining steps, each proposed to be an intramolecular alkene insertion into the Rh-H bond (**4→5** in Scheme 3-8 and **9→10** in Scheme 3-9). The structural changes during the insertion have been described[157] as a symmetrical alkene η^2-

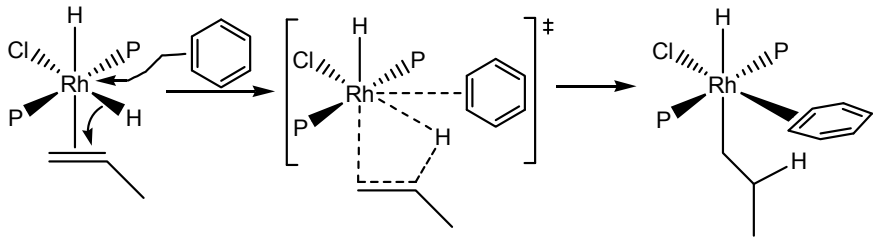
coordination, shifting to a η^1-coordinated species and picking up the hydride from the metal at its uncoordinated carbon. Therefore, the rate-determining steps are nucleophilic addition to alkenes in the first and second proposed mechanisms.[157,160] The alkene coordination to the rhodium metal center (**3**⇄ **4** in Scheme 3-8 and **8**⇄ **9** in Scheme 3-9) is the only step involving alkene C=C bond among all the equilibria prior to the rate-determining step. The alkene coordination step must play a minor role in determining the reaction rate because it is an electrophilic process, while the reaction is overall a nucleophilic addition to alkenes.

However, the results of our study disfavor the third proposed mechanism (Scheme 3-10),[156] in which alkene complexation to the metal center (**3**→**4** in Scheme 3-10) is predicted to be the rate-determining step. In this step, the alkene coordinates to the Rh center, which constitutes an electrophilic attack of Rh center on the alkene π bond. There is no alkene involved in all the equilibria prior to the proposed rate-determining step in this mechanism. Therefore, the results of our study do not support the third proposed mechanism.

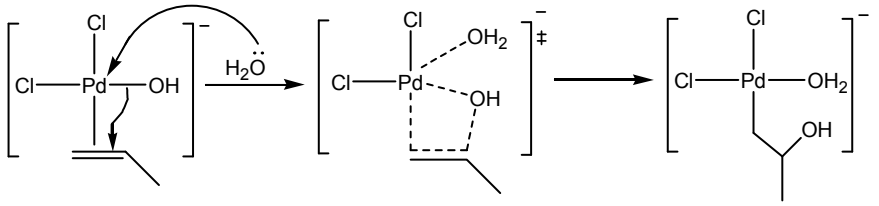
3.3.5 Comparison with Wacker oxidation

The catalytic hydrogenation of alkenes by using Wilkinson's catalyst has similarities to and differences from the $PdCl_2$ oxidation of alkenes (the Wacker Reaction): (1) the slopes of the lines in the plots of log k_{rel} values versus alkene LUMO energies for both reactions are negative, which indicates that both reactions are nucleophilic additions to alkenes; (2) the rate-determining steps in Scheme 3-8[147,148] and Scheme 3-9[153] are both alkene insertions into an Rh-H bond similar to

the alkene insertion into a Pd-OH bond in the $PdCl_2$ oxidation (eq 3-14); (3) the rate-determining steps both in catalytic hydrogenation in the presence of Wilkinson's catalyst (eq 3-24) and in the Wacker oxidation (eq 3-25) have been proposed to involve similar four-membered cyclic transition states; (4) data points in plots for $PdCl_2$ oxidation separate naturally into different sterically-similar alkene groups, as do those in the plots for alkene hydrogenation; and (5) geminal and vicinal cis-disubstituted alkenes fall into the same sterically similar group as the monosubstituted alkenes in alkene hydrogenation (Figs 3-12 to 3-13), while all disubstituted alkenes fall into a different group in $PdCl_2$ oxidation, which implies greater steric effects in the latter reaction.



(3-24)



(3-25)

The display of similar electronic effects in the two reactions is not surprising. Rh and Pd might be expected to form organic derivatives which have similar characteristics, based on their joint membership in the second triad of groups 9 and 10; they are both "platinum metals."[184,185] Similar nucleophilic characteristics in both reactions could be rationalized by the nucleophilic attacks upon one carbon atom of

the alkene double bonds by the nucleophilic hydride in the hydrogenation and by the nucleophilic hydroxide in the Wacker reaction.

The different steric effects in the two reactions could probably be derived from steric congestion at an alkene carbon atom, from steric congestion about the central metal, or from other sources. Several explanations for the differing steric effects in the transition states of the two reactions can be offered:

(A) The different sizes of the groups migrating to the alkene carbon must be considered; a hydroxide (-OH) is much larger than a hydride (-H), so its migration might be expected to cause greater steric congestion at the alkene carbon in Wacker reaction, as observed.

(B) The different sizes of the solvent molecules entering as ligands are significant. An entering benzene ligand might be expected to cause more congestion than an entering H_2O ligand (eqs 3-24 and 3-25). However, this is inconsistent with lower steric effects in the Wilkinson reduction than in the Wacker Reaction, so the entering solvent does not produce the observed steric effect in these reactions. This supports the practice of omitting solvent from mechanistic schemes drawn for this reaction, often done by Halpern[146-152] and by Brown.[153-155]

(C) The smaller steric effects in spite of a larger entering solvent ligand in alkene hydrogenation (eq 3-24) than in the Wacker reaction (eq 3-25) might also be explained by the former being an I_d (dissociative interchange[106]) process of an octahedral complex and the latter being an I_a (associative interchange[106]) process of a square planar complex. The designations "I_d process" and "I_a process" follow the generalized nomenclature for mechanisms of ligand exchange.[106] An I_d process has

both the entering and leaving ligands more dissociated and farther apart than an I_a process, as depicted in eqs 3-24 and 3-25. Although we have no experimental measurements to compare distances between the metals and entering ligands in the transition state structures, there are some data available for similar ground state molecules. Studies show that the average distance between Rh and the two coordinated benzene carbons in the product [Rh(η-C_5H_5){β,α,1,2-η-$C_6H_5C(Ph)=CH_2$}] is about 2.21 Å,[186] which is greater than the distance (2.10 Å) between Pd and O in the product [Pd(C_2H_4OH)(H_2O)Cl_2].[187,188]

(D) However, the calculated bond lengths of Pd-Cl and Pd-C are 2.30 Å and 2.20 Å[187] respectively in the four-membered transition state of the rate-determining insertion of $[PdCl_2H(C_2H_4)]^-$, while the calculated bond lengths of Rh-Cl and Rh-C are 2.30 Å and 2.21 Å,[170] respectively, in the four-membered transition state of the rate-determining insertion of [RhCl(PH_3)$_2$(C_2H_4)H_2]. These are almost identical and, therefore, would lead one to predict similar steric effects in the transition state structures in these two reactions.

(E) A theoretical calculation[189] predicts the Rh-C bond strength in Rh-C_2H_5 of 50.3 kcal/mol, which is higher than that of Pd-C bond in Pd-C_2H_5 (40.9 kcal/mol). The stronger developing Rh-C bond in the transition state structure might cause the alkene migratory insertion transition state in catalytic hydrogenation to be later with somewhat less steric effects than in the Wacker oxidation.

(F) Calculations[170] have predicted a late transition state for the hydrogenation of alkenes catalyzed by Wilkinson's catalyst, which is consistent with the prediction that the rate-determining step of this reaction is an endergonic process.[190,191] A late

transition state, in which only one carbon is significantly bonded to Rh and the Rh-H bond is nearly broken, could explain the reduced steric effects. Therefore, a later transition state in alkene hydrogenation by using Wilkinson's catalyst than in the Wacker oxidation might also contribute to slightly smaller steric effects in the former.

3.3.6 Conclusion

Negative slopes of correlation lines in the plots of log k_{rel} values versus alkene IPs and versus alkene LUMO energies are obtained for hydrogenation of alkenes by using Wilkinson's catalyst. This indicates that this reaction is a nucleophilic addition to alkenes. The natural separation of data points into sterically similar groups in each plot indicates that this reaction is dependent upon both electronic and steric effects. Results of this study are consistent with the two proposed mechanisms with an alkene migratory insertion into Rh-H bond as the rate-determining step, but inconsistent with a proposed alternative mechanism with coordination of an alkene to the metal center of a rhodium complex as the rate-determining step.

3.4 References

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Chapter Four

Substituent Effects in Alkene Halogenations

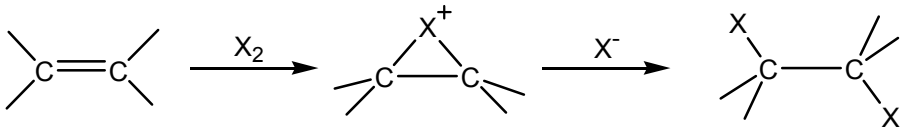
Abstract: In order to investigate the substituent effects in alkene halogenations, we have correlated relative reactivities of alkenes versus their IPs and HOMO energies for several different alkene halogenations in this chapter. Similarities and differences among these reactions are discussed. The plots for alkene bromination (Br_2) and chlorination (Cl_2) each shows a single line of correlation with positive slope among all alkenes, regardless of their steric requirements, which indicates that they are electrophilic additions to alkenes depending predominantly upon electronic effects. However, in interaction with iodine (complexation with I_2), each plot exhibits a natural separation into groups of similarly-substituted alkenes, which indicates that steric effects and electronic effects are both important here. The plots for ISCN addition to alkenes reveal that the alkene relative reactivity in this reaction depends mainly upon electronic effects, while steric effects also play an important role within each similarly-substituted alkene group. Steric effects are related to the relative position, size, and branching of alkyl substituents on C=C bonds in ISCN addition. Some interesting trends are observed through comparing ISCN addition to alkenes with ICl addition to alkenes and with alkene bromination and chlorination. Studies included in this chapter have been published in two different papers: (1) Nelson, D. J.; Li, R.; Brammer, C. *Journal of Organic Chemistry* **2001**, *66*, 2422-2428; (2) Brammer, C.; Nelson, D. J.; Li, R. *Tetrahedron Lett.* **2007**, *48*, 3237-3241. Copies of the reprints of the two papers are attached at the end of the dissertation.

4.1 Substituent effects on alkene reactivities in bromination and in chlorination of alkenes

4.1.1 Introduction

Additions of halogens X_2 (X = F, Cl, Br, and I) to C=C bonds of alkenes yield 1,2-dihalide products, which, termed as halogenation of alkenes, are very important reactions in organic chemistry.[1-2] The most widely applied and intensively studied alkene halogenations are additions of Br_2 (bromination) and Cl_2 (chlorination), whereas fluorination (F_2) and iodination (I_2) are less commonly used in practice because the former is too reactive to control while the latter is not reactive enough to give satisfactory yield of products.[1-4] Therefore, our correlation study in this section will only focus on bromination and chlorination of alkenes.

The rate-determining step in both bromination and chlorination is believed to be the formation of a three-membered cyclic halonium cation intermediate by an electrophilic attack of a halogen molecule on the C=C bond. This halonium intermediate is then quickly attacked by a nucleophile X^- to yield the final 1,2-dihalide products (eq 4-1).[1-4] Previous kinetic studies of bromination[5-16] and chlorination[17-19] of alkenes allow us to carry out correlation studies on these reactions to ascertain the relative importance of steric and electronic effects of substituents in the rate-determining steps.



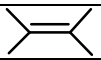
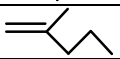
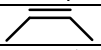
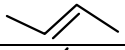
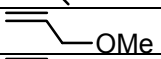
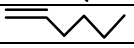
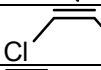
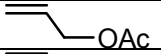
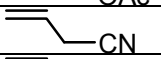
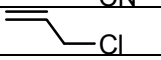
(4-1)

X = Cl, Br

4.1.2 Correlation plots

Table 4-1 lists experimental alkene IPs, computational alkene HOMO energy levels, and relative reaction rates of representative alkenes with bromine (Br_2) and chlorine (Cl_2). The relative rates for alkene bromination[5-16] and for alkene chlorination[17-19] were converted from previously reported kinetic data. The experimental alkene IP values were collected from literature. The alkene HOMO energy levels were calculated by using the MNDO method described in the previous study.[20]

Table 4-1. Alkene IPs (eV), HOMO energies (eV), and relative reaction rates of bromination and chlorination of alkenes

No.	alkene	IP[a]	HOMO[b]	Relative rates	
				Br_2[c]	Cl_2[d]
1		8.27	-9.49	1.40×10^6	4.30×10^7
2		8.68	-9.63	1.40×10^5	1.10×10^6
3		8.95	-9.76	9.76×10^3	
4		8.97	-9.76	3.57×10^3	
5		9.08	-9.79	895	
6		9.12	-9.79	4.05×10^3	6.30×10^3
7		9.12	-9.77	2.62×10^3	5.00×10^3
8		9.15	-9.79		1.60×10^4
9		9.24	-9.80		5.80×10^3
10		9.44[e]	-10.17	7.20[f]	
11		9.45	-9.96	40.48	115
12		9.48	-9.97	100	
13		9.63	-9.94	148	
14		9.74	-9.97		100
15		9.93[g]	-10.49		5.00×10^{-5}
16		10.09[h]	-10.34	0.72	
17		10.18[i]	-10.53	0.70	
18		10.34[i]	-10.48	0.06	0.300

[a]Ref 21, unless otherwise noted. [b]MNDO method by Christopher Brammer. [c]Refs 5-11; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. [d]Ref 17; k_{rel} values

are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. [e]Ref 22. [f]For the corresponding ethyl ether. [g]Ref 23. [h]Refs 24 and 25. [i]Ref 26.

Correlation plots of log k_{rel} values for alkene bromination versus alkene IPs and versus alkene HOMO energy levels are shown in Figs 4-1 and 4-2 respectively. The correspondent plots for chlorination of alkenes are shown in Figs 4-3 and 4-4. Since a higher IP corresponds to electron removal from a lower-energy molecular orbital, IP values were listed in increasing magnitude proceeding down each plot, in order to make the plots comparable to those using HOMO energy levels.

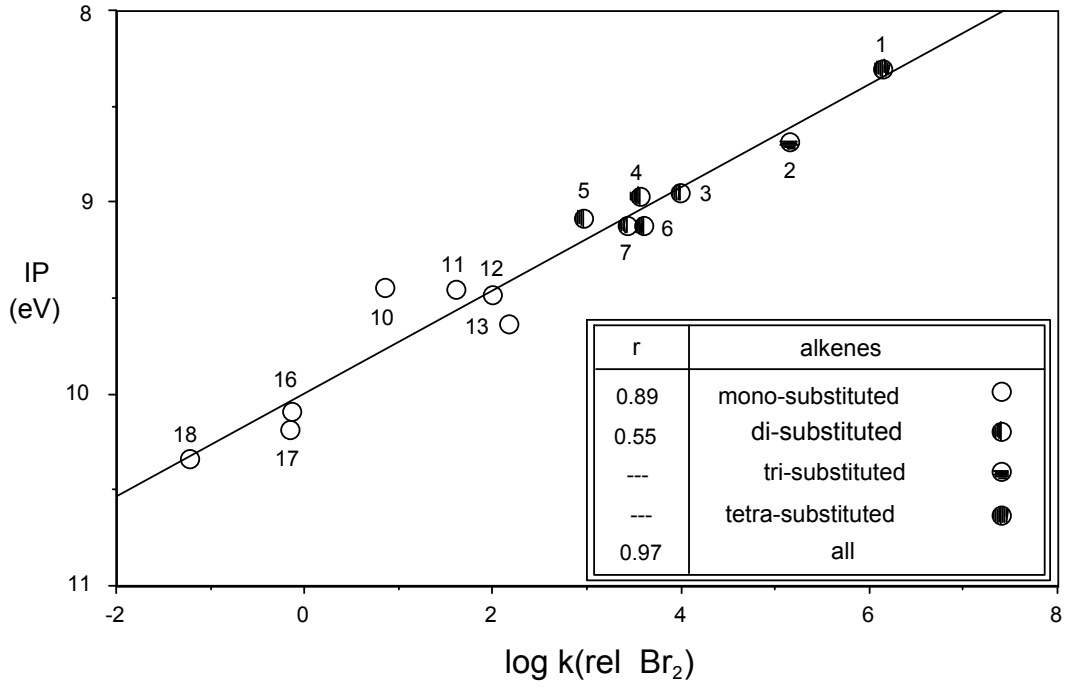


Figure 4-1. Plot of log k_{rel} values of alkene bromination versus alkene IPs for reaction conditions Br_2/NaBr/MeOH; data are from Table 4-1. All data points, regardless of steric requirements, lie on one line of correlation (IP = 9.99 – 0.27 log k_{rel}, r = 0.97, s = 0.057, and c.l. = 99.98%).

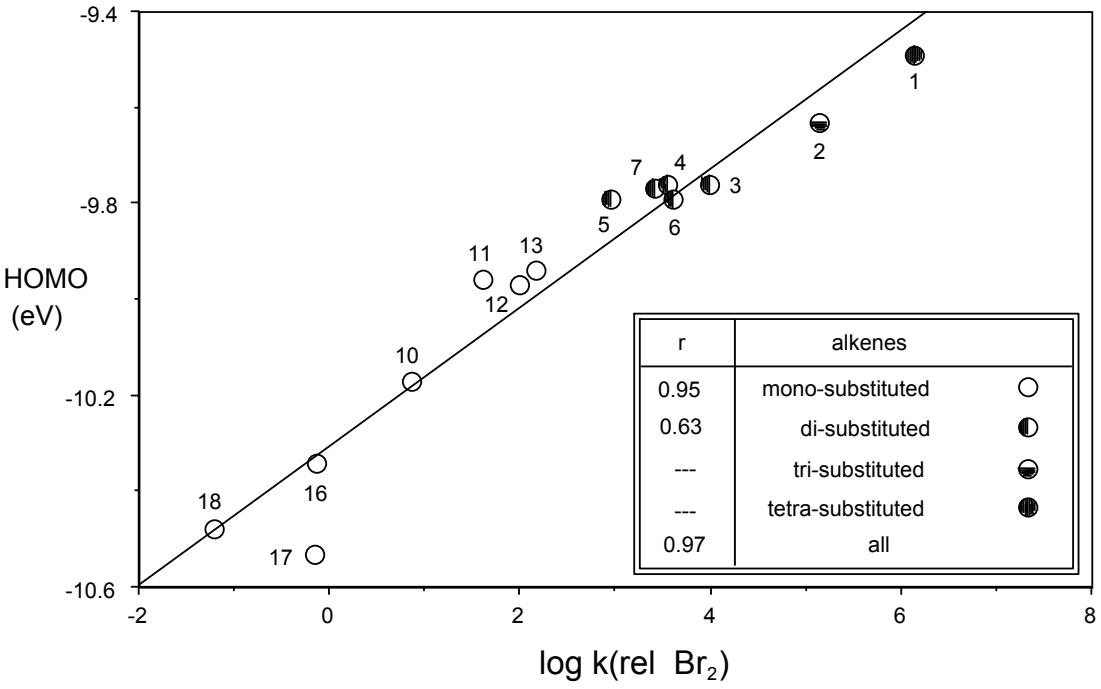


Figure 4-2. Plot of log k_{rel} values of alkene bromination versus alkene HOMO energies for reaction conditions Br_2/NaBr/MeOH; data are from Table 4-1. All data points, regardless of steric requirements, lie on one line of correlation (E_{HOMO} = 0.15 log k_{rel} - 10.31, r = 0.97, s = 0.034, and c.l. = 99.98%).

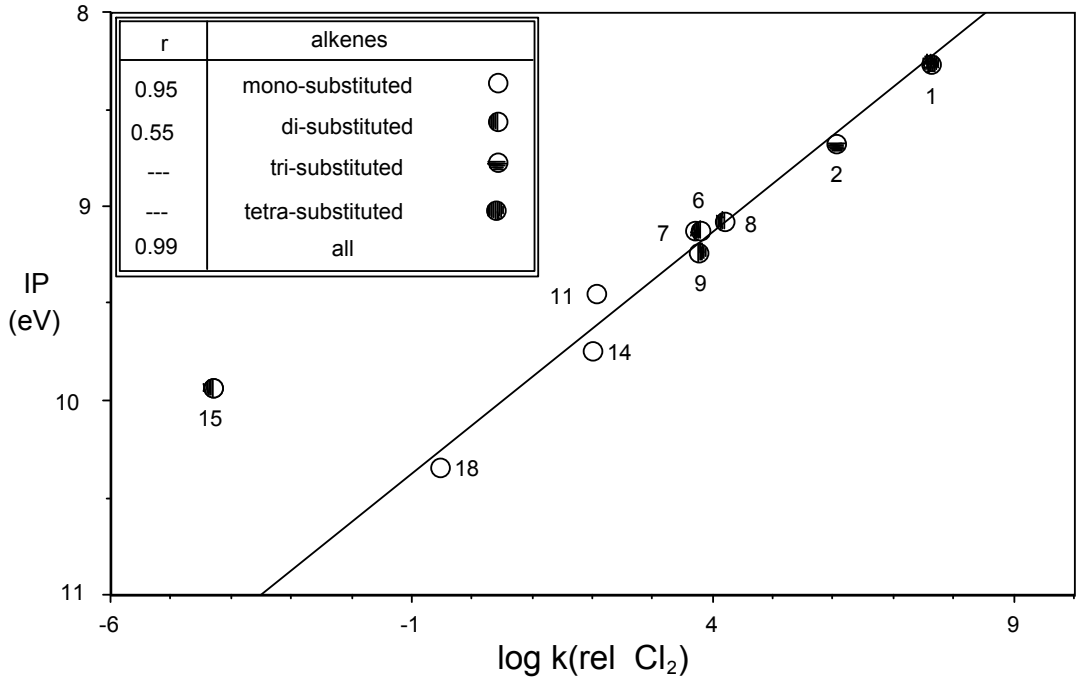


Figure 4-3. Plot of log k_{rel} values of alkene chlorination versus alkene IPs for reaction conditions Cl_2 gas/O_2/dark; data are from Table 4-1. Except for point **15**, all data points, regardless of steric requirements, lie on one line of correlation (IP = 10.13 – 0.25 log k_{rel}, r = 0.99, s = 0.061, and c.l. = 99.98%). Point **15** is not included in the line of correlation because of its obvious deviation from the line. If it was included, the correlation would be much weaker (IP = 9.75 – 0.16 log k_{rel}, r = 0.89, and s = 0.125). The deviation of IP from the line for point **15** would be over 4 times of standard deviation.

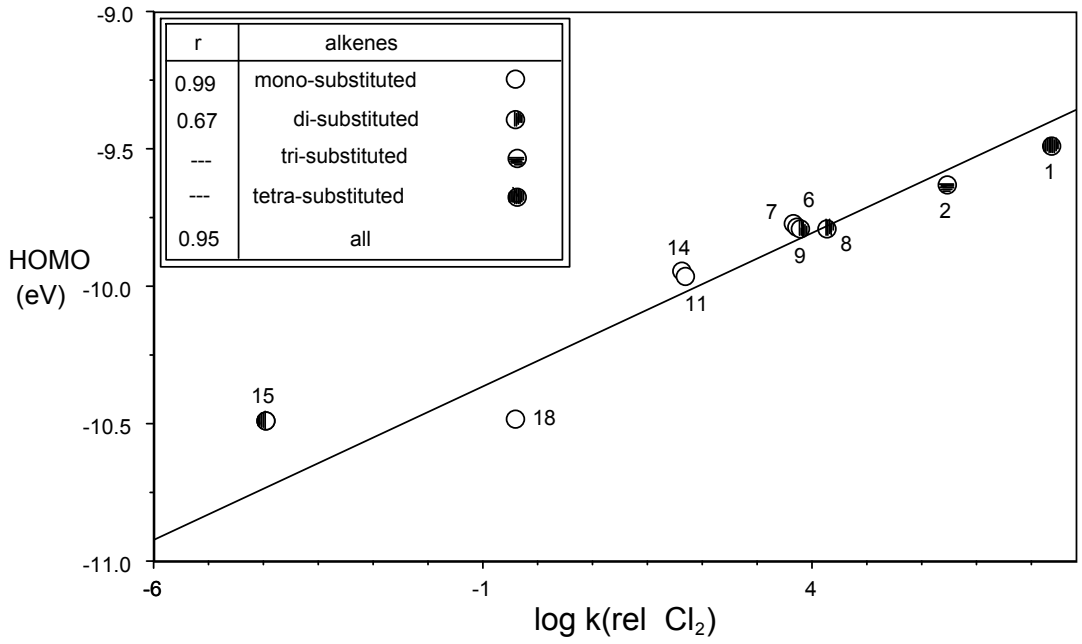


Figure 4-4. Plot of log k_{rel} values of alkene chlorination versus alkene HOMO energies for reaction conditions Cl_2 gas/O_2/dark; data are from Table 4-1. Except for point **15**, all data points, regardless of steric requirements, lie on one line of correlation (E_{HOMO} = 0.11 log k_{rel} - 10.25, r = 0.95, s = 0.059, and c.l. = 99.98%).

4.1.3 Alkene bromination

The plots of alkene IPs and HOMO energies versus log k_{rel} values for bromination (Br_2/NaBr/MeOH), shown in Figs 4-1 and 4-2 respectively, each has a single line of correlation with an good correlation coefficient among all alkenes, regardless of the degree of substitution about the C=C bond. In both cases, this correlation is better than those within groups of sterically similar alkenes, for instance, the mono-substituted alkenes and the di-substituted alkenes. Therefore, it could be concluded that electronic effects play a predominant role in the rate-determining step of this reaction, while steric effects are less important. The positive slopes in the plots indicate that this is an electrophilic addition of electrophile

bromine (Br_2) to the carbon-carbon double bonds of alkenes. Increasing electron-donating groups, such as alkyls, on alkene C=C bond would enhance the alkene HOMO energy level and lower the alkene IP value and thus increase the alkene reactivity in this reaction. In contrast, if the substituent is an electron-withdrawing group, the result is opposite. For instance, electron-withdrawing substituent groups, -Cl, -CH_2Cl, -CH_2CN, and -CH_2OAc in this study, all lead to lower reaction rates.

In a study reported by Dubois and Mouvier,[7] a two-parameter equation employing Taft's inductive constant (σ^*) and steric substituent constant (Es) was necessary to achieve a linear correlation because of the steric requirements of the substituents. In our study which includes alkenes with large substituents, for example, a *t*-butyl group in 3,3-dimethyl-1-butene (**11**), a linear correlation with the IPs was obtained; this means that this type of study may be more likely to give a suitable treatment without use of additional steric parameters.

Similar correlations and plots of alkene IPs versus log k_{rel} values for alkene bromination under other reaction conditions[17] (Br_2/HBr/CH_2Cl_2) also gave a single line of correlation regardless of the number of alkyl groups on the C=C bond and with an excellent correlation coefficient (r_{all} = 0.98) (plot not shown). However, data and plots (not shown) for bromination in the presence of HOAc[18] showed virtually no correlation for all alkenes (r_{all} = 0.26) or for sterically similar groups; it is unlikely that this is due to the acidic conditions, since bromination[17] using Br_2/HBr gave good results. Rather it is probably that each alkene included in the study using HOAc[18] had a functional group, which could offer conjugative stabilization directly to an alkenyl

carbon and could thereby stabilize a carbocation formed from the alkene; this could lead to involvement of mixed reaction mechanism pathways.

4.1.4 Alkene chlorination

The correlation plots (Figs 4-3 and 4-4) for chlorination (Cl_2 gas/O_2/dark[17]) show appearance similar to that for bromination. The best correlation is obtained by considering all alkenes as a single group with the correlation coefficients $r_{all} = 0.99$ for log k_{rel} values versus alkene IPs and $r_{all} = 0.95$ for log k_{rel} values versus alkene HOMO energies. This result implies that, similar to bromination, alkene chlorination is also an electrophilic addition to C=C bonds without significant steric effects. The reactivities of the alkenes in this reaction are interpreted[17,19] as compatible with a transition state which involves partial bonding of the chlorine molecule with both termini of the olefinic system and with little development of positive charge on one carbon, as in a π-complex.

In an alkene chlorination study by Poutsma,[17] it was found necessary to use only the σ* constant in order to achieve linear correlation. However, attempts to include allyl chloride and alkene with a bulky *t*-butyl substituent in that correlation gave less satisfactory correlation. In contrast, allylic compounds and alkenes with large substituents were included in the correlations study herein without problems.

Poutsma[17] warned of dangers in extrapolating from linear to branched alkenes since branching stabilizes possible carbocation formation. This could switch the mode of chloronium ion decomposition or switch the mechanism from one with a cyclic chloronium intermediate to one with an open carbocation. While we found no

problems achieving correlation with the branched olefins studied herein, we did find problems including aryl substituents, probably for that reason. We attempted to include 1,2-dichloroethene (**15**) in the plots, which was also excluded in Poutsma's study, but found that its point fell far from the correlation line. It is possible that the chlorine substitution directly on the double bond converts the reaction mechanism, in a manner similar to one of the mechanistic pathway changes discussed above, and thus the data points for **15** were not included in the correlation lines in Figs 4-3 and 4-4.

Chlorination data obtained using Cl_2/HOAc[18] were plotted versus alkene IPs and versus HOMO energies (plots not shown). Similar to the results obtained for bromination in the study using HOAc as solvent, we found no correlation for sterically similar groups or for all alkenes regardless of the degree of substitution in the plot of log k_{rel} values versus alkene IPs ($r_{mono\text{-}sub}$ = 0.83, $r_{di\text{-}sub}$ = 0.43, and r_{all} = 0.14). The results for log k_{rel} values versus alkene HOMO energies are essentially the same as those for versus alkene IPs. Once again, the alkenes included in this study[18] each had a functional group, which could offer conjugative stabilization with a carbocation and could lead to involvement of mixed reaction mechanism pathways.

4.1.5 Comparing chlorination with bromination

In the previous correlation study, we found that reactions with similar mechanisms always gave correlation plots with similar appearances. Chlorination and bromination both involve the formation of the halonium ion intermediate in their rate-determining steps, and so each plot of alkene IPs versus log k_{rel} values in both

reactions yields one single line with a positive slope, regardless of the steric requirements of the alkenes. The results indicate that the rate-determining step in each is an electrophilic addition influenced more by electronic effects than by steric effects.

However, careful analysis about the plots (Figs 4-1 to 4-4) or the data in Table 4-1 indicates that there still exist some differences in the relative importance of electronic and steric effects in these two reactions to some extent. For instance, the increase of relative rate caused by adding an extra methyl onto *cis*-2-butene (IP = 9.12 eV) to become 2-methyl-2-butene (IP = 8.68 eV) for alkene chlorination is five times greater than that for alkene bromination. Therefore, the electronic effects are stronger in chlorination than that in bromination, probably because chlorine is an electrophile stronger than bromine. The steric effects in bromination seem greater than those in chlorination, though the steric effects are not significant overall in both reactions. For example, the difference in relative rates between *cis*- and *trans*-2-butene (IP = 9.12 eV in both cases) in bromination is greater than that in chlorination, probably due to the greater steric requirements of bromine (Br_2) than those of chlorine (Cl_2) in the rate-determining transition states.

4.1.6 Conclusion

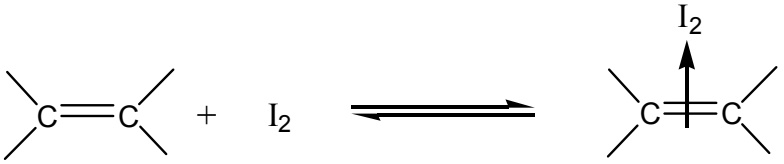
Alkene bromination and chlorination both give single lines of correlation with positive slopes in the plots of logarithms of relative rates versus alkene IPs and versus alkene HOMO energy levels. The results of this study indicate that both reactions are electrophilic additions to alkene C=C bonds, depending predominantly upon electronic effects in the rate-determining steps. Comparison between these two

reactions reveals that the electronic effects are stronger in chlorination than in bromination, while the steric effects in chlorination are weaker than in bromination. The difference in substituent effects between these two reactions could be rationalized with the strong electrophilicity and small size of chlorine (Cl_2), relative to those of bromine (Br_2).

4.2 Substituent effects in alkene complexation with iodine

4.2.1 Introduction

Adding I_2 to alkene C=C bonds to give 1,2-diiodo products, unlike alkene bromination and chlorination that are readily carried out under mild conditions, can only be achieved in the presence of UV irradiation or some catalysts under very low temperature.[2,27,28] Under normal conditions, iodine I_2 forms only complexes with alkenes (eq 4-2)[2,29,30] and other carbon-carbon π systems via thermodynamically controlled equilibria.[31] In this section, we investigated the substituent effects of a series of alkenes on their relative reactivity toward the complexation with solid molecular iodine (I_2).



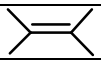
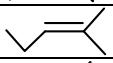
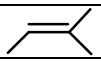
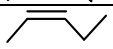
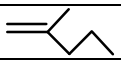
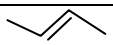
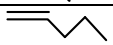
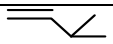
(4-2)

4.2.2 Correlation plots

A study of interaction between gaseous alkenes and solid iodine via a gas-solid chromatographic (GC) technique by coating solid iodine on the support material of a GC column has been reported by Cvetanović and co-workers.[30] The equilibrium

constants for the overall complexation process from their experiments were treated mathematically in two ways, not accounting for complexation with untreated support material and accounting for it. The relative values of the equilibrium constants treated in both ways, not accounting for complexation with support material (w/o support in Table 4-2) and with accounting for it (w/ support in Table 4-2), are listed in Table 4-2. Alkene IPs were collected from literature and HOMO energies were calculated by using the MNDO method.

Table 4-2. Alkene IPs (eV), HOMO energies (eV), and relative equilibrium constants of alkene complexation with solid iodine

No.	alkene	IP[a]	HOMO[b]	Relative reactivity[c]	
				K_{rel} (w/o support)	K_{rel} (w/ support)
1		8.27	-8.70	34	7.3
2		8.60[d]	-8.99	22	4.6
3		8.68	-8.86	9.6	3.5
4		9.04	-9.27	35	31
5		9.04	-9.21	6.6	4.4
6		9.08	-9.36	18	11
7		9.12	-9.26	9.6	7.9
8		9.12	-9.25	2.5	1.7
9		9.15	-9.37	8.8	6.3
10		9.24	-9.39	2.5	1.3
11		9.52	-9.62	100	100
12		9.53	-9.70	34	34
13		9.63	-9.70	40	41
14		9.74	-9.72	7.7	7.1

[a]Ref 21, unless otherwise noted. [b]MNDO method by Christopher Brammer. [c]Ref 30; K_{rel} values are relative to $K_{rel} = 1.00 \times 10^2$ for 1-pentene. [d]Estimated by applying to the IP for 2-methyl-2-butene a correction factor, which is the difference between the IPs of 2-butene and 2-pentene: 8.68eV – (9.12eV – 9.04eV) = 8.60eV; Ref 21.

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Similar plots of logarithms of relative equilibrium constants versus alkene IPs were shown in Figs 4-5 and 4-6. In both cases, regardless of consideration for untreated support material interaction, the data points fall into groups depending upon the steric requirements of the alkenes, giving multiple lines with positive slopes. In both plots, a much better correlation is obtained by using separate lines for monosubstituted alkenes ($r_{monosub}$ = 0.88 for both considering and not considering interaction with untreated support material) and for disubstituted alkenes (r_{disub} = 0.70 for considering interaction with untreated support and r_{disub} = 0.67 for not considering that interaction) than by considering all alkenes as one group regardless of degree of substitution on C=C bonds (r_{all} = 0.42 for considering interaction with untreated support material and r_{all} = 0.04 for not considering the interaction).

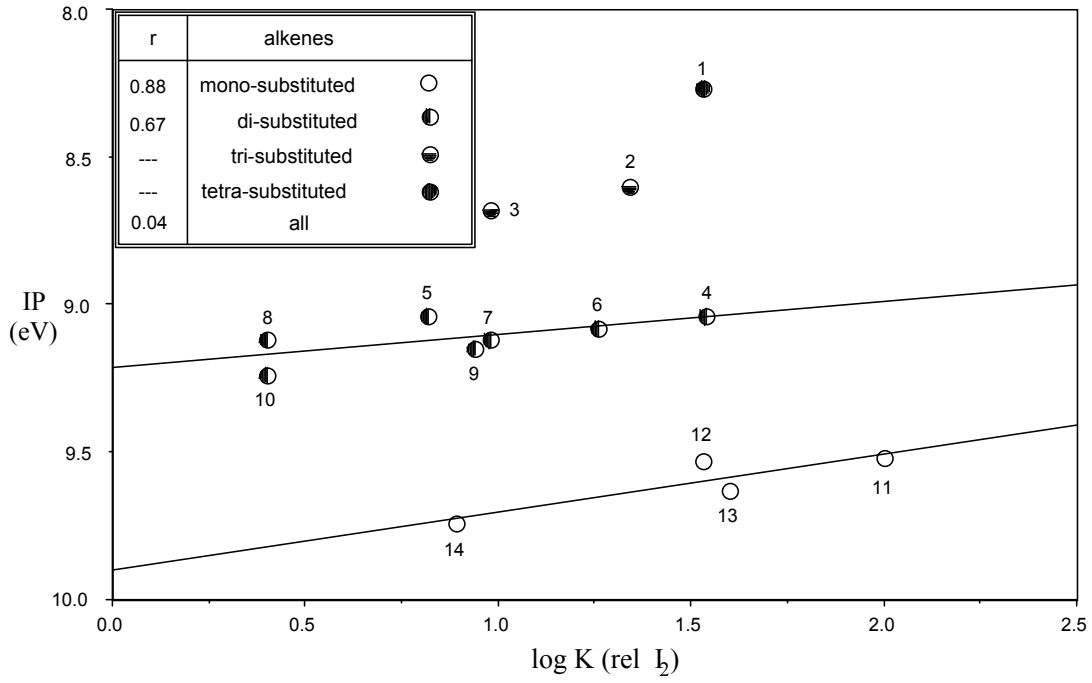


Figure 4-5. Plot of log K_{rel} values for the complexation of a series of alkenes with solid iodine versus alkene IPs. Complexation with untreated support material was not accounted for in this plot. Data are from Table 4-2. Data points naturally fall into different sterically similar alkene groups. Correlation lines are given for monosubstituted alkenes (IP = 9.90 – 0.20 log k_{rel}, r = 0.88, s = 0.117, and c.l. = 90%) and for disubstituted alkenes (IP = 9.21 – 0.11 log k_{rel}, r = 0.67, s = 0.055, and c.l. = 90%).

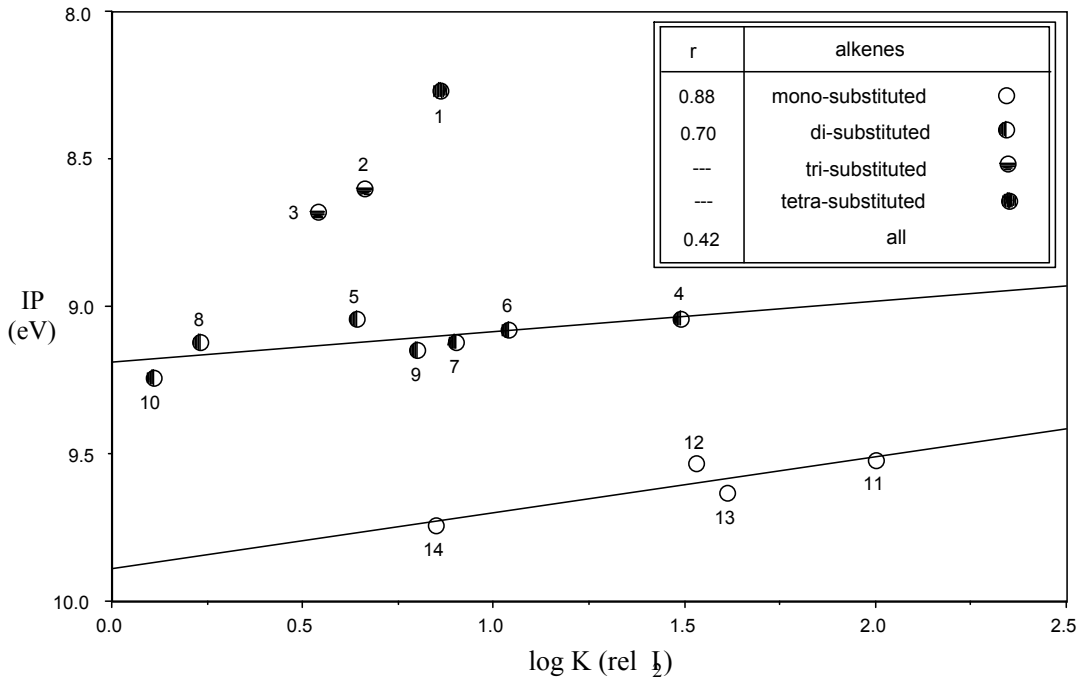


Figure 4-6. Plot of log K_{rel} values for the complexation of a series of alkenes with solid iodine versus alkene IPs. Complexation with untreated support material was accounted for in this plot. Data are from Table 4-2. Data points naturally fall into different sterically similar alkene groups. Correlation lines are given for monosubstituted alkenes (IP = 9.89 – 0.19 log k_{rel}, r = 0.88, s = 0.112, and c.l. = 90%) and for disubstituted alkenes (IP = 9.19 – 0.10 log k_{rel}, r = 0.70, s = 0.041, and c.l. = 90%).

4.2.3 Substituent effects

Multiple lines of correlation with positive slopes were obtained in plots of log K_{rel} values versus alkene IPs for alkene complexation with solid iodine (I_2) (Figs 4-5 and 4-6). The resulting plots indicate that complexation of alkenes with iodine is an electrophilic process that depends upon both electronic and steric effects. Within each sterically similar group of alkenes, the stability of the complexes of alkenes with iodine increases as the alkene IP value decreases.

As expected, the electrophilicity in iodine complexation is similar to that in alkene bromination and chlorination, as stated previously in this chapter. However, unlike alkene bromination and chlorination, multiple lines of correlation were obtained in the plots of log K_{rel} values versus alkene IPs for iodine complexation, which means that the relative reactivity of alkenes in complexation with iodine depends on both electronic and steric effects.

Different results for alkene complexation with iodine as opposed to those for alkene chlorination and bromination imply that they likely follow different mechanisms. Bromination and chlorination are kinetically controlled addition reactions and go to completion to produce final addition products. In contrast, the complexation with iodine is a thermodynamically controlled equilibrium and does not go to completion to give stable 1,2-diiodo products. Therefore, the plots obtained from complexation with iodine might be expected to resemble those of other alkene complexations rather than those of bromination and chlorination.

Alkene complexations with the silver ion ($AgNO_3$) and with mercury ion ($HgCl_2$) were previously studied by Nelson's group[32] by using the same methodology. Correlations or trends similar to alkene complexation with iodine were also observed in alkene complexations with silver ions and with mercury ions. Multiple lines of correlation with positive slopes in the plots of log K_{rel} values versus alkene IPs for these reactions indicate that they all involve electrophilic attack on alkene C=C bonds and the stabilities of the complex formed depend upon both electronic and steric effects.

4.2.4 Conclusion

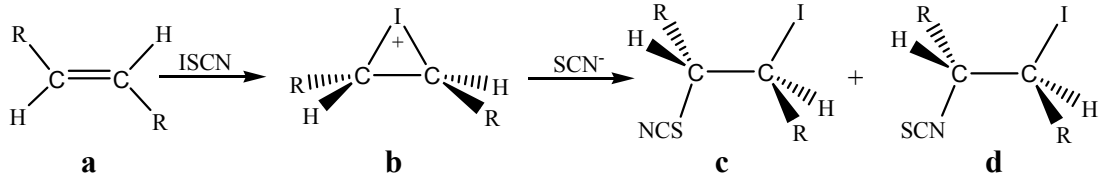
Alkene complexation with solid iodine on a gas-solid GC column results in grouping according to alkene steric requirements in the plots of alkene IPs versus log K_{rel} values. Correlation lines with positive slopes within each sterically similar group of alkenes were obtained in each plot. Results of this study demonstrate that iodine complexation, unlike bromination and chlorination, are dependent upon not only electronic effects but also steric effects, probably because it is a thermodynamically controlled equilibrium, but not a kinetically controlled completion addition. Instead of alkene bromination and chlorination, alkene complexation with some transition metal ions, such as Ag^{+} and Hg^{2+}, were found to result in correlation plots similar to those for alkene complexation with iodine, which suggests that these alkene complexations likely follow similar mechanisms.

4.3 Substituent effects in additions of ISCN and ICl to alkenes

4.3.1 Introduction

Adding iodine (I_2) directly to C=C bonds, as stated in previous sections, is not an effective way to produce organoiodine compounds, which are important in many areas, such as organic synthesis,[33,34] biochemistry,[35-37] biogeochemical reactions,[38-40] and environmental studies.[41-43] However, iodine incorporation is achievable via alkene additions of many iodine-containing compounds, such as ICl,[45-49] IBr,[44] IOAc,[44] IN_3,[50] and ISCN,[51-53] which are reported to undergo complete reactions with alkenes under mild reaction conditions. Thiocyanate has been termed as a

pseudohalogen anion,[54] because it has chemical properties similar to those of halogen anions; therefore, iodine(I) thiocyanate (ISCN) addition to alkenes (Scheme 4-1) might be expected to have characteristics similar to halogenations of alkenes. ISCN addition to alkenes yields *vic*-iodothiocyanates **c** and *vic*-iodoisothiocyanates **d,**[51-53] which can be used as intermediates in synthesizing some useful compounds, such as episulfides,[55,56] thiazolidin-2-ones,[56] 2-amino-2-thiazolines,[56] and 2-alkoxy-2-thiazolines.[57]



Scheme 4-1. ISCN addition to alkenes

The first step of ISCN addition to alkenes has been proposed[58-60] to be the formation of a bridged iodonium ion intermediate **b**, which is generally believed[61] to be the rate-determining step of the reaction (Scheme 4-1). Intermediate **b** does not undergo ring-opening prior to anti-attack by nucleophiles in the second step. There seems to be general agreement regarding the initial attack on the alkene double bond by the electrophilic ISCN molecule,[58-60] although controversy still exists about the exact species of nucleophile that reacts with the iodonium ion **b** in the second step[59-60] and about the distribution of the final anti-addition products.[57,58]

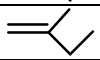
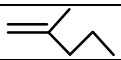
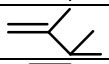
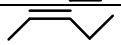
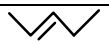
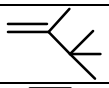
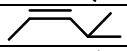
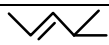
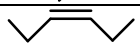
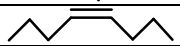
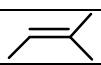
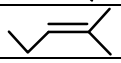
The analysis of substituent effects upon reactivity of alkenes toward ISCN addition to alkenes would provide new and useful information about its mechanism, since detailed mechanistic studies of this reaction are scarce to date. Its reaction pathway has been described[58-61] as similar to that for bromination or chlorination of

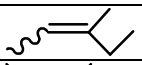
alkenes. Although the mechanisms for alkene bromination, chlorination, and ISCN addition are clearly not identical, it seems to be generally agreed that the rate-determining step in each precedes (not necessarily immediately) formation of the halonium ion.

4.3.2 Correlation plots

Relative reaction rates (k_{rel} values) of ISCN addition to alkenes, alkene IPs, and alkene HOMO energies are listed in Table 4-3. We examined the correlation of log k_{rel} values versus alkene IPs, and also the correlation of log k_{rel} values versus alkene HOMO energies because experimental IPs for some alkenes in Table 4-3 (**4**, **7**, **33**, and **34**) were not available in the literature. Alkene HOMO energies in Table 4-3 were calculated by using *ab initio* method at HF level with 6-31G* basis set.[62,63] Figs 4-7 and 4-8 give the plots of log k_{rel} values of ISCN addition to alkenes versus alkene IPs and versus alkene HOMO energies respectively. Their appearances are essentially analogous to each other.

Table 4-3. Alkene IPs (eV), HOMO energies (eV), and relative rates of additions of ISCN and ICl to alkenes

No.	Alkene	IP[a]	HOMO[b]	$k_{rel,\ ISCN}$[c]	$k_{rel,\ ICl}$[d]
1		10.52	-10.19		2.28
2		9.74	-9.72		40.5
3		9.63	-9.70	121	100
4		9.51[e]	-9.65	105	
5		9.53	-9.70	40.0	190
6		9.48	-9.66	100	
7		9.46[f]	-9.67	36.0	
8		9.45	-9.66	47.0	
9		9.45	-9.65	24.0	34.2
10		9.44	-9.61	137	
11		9.43[g]	-9.61	137	
12		9.40	-9.59	21.0	
13		9.24	-9.39	1.53×10^3	1.12×10^3
14		9.15	-9.37	1.84×10^3	2.14×10^3
15		9.12	-9.26	790	2.91×10^3
16		9.12	-9.25	411	934
17		9.08	-9.36	1.32×10^3	
18		9.07	-9.34	1.21×10^3	1.55×10^3
19		9.04	-9.27		4.15×10^3
20		9.04	-9.21		1.80×10^3
21		9.02	-9.17	521	1.36×10^3
22		8.98	-9.28		2.27×10^3
23		8.97	-9.28		1.10×10^3
24		8.97	-9.27	495	
25		8.95	-9.27	895	
26		8.92	-9.27		4.61×10^3
27		8.91	-9.25		50.6
28		8.84	-9.22	684	
29		8.83	-9.23	305	
30		8.77	-9.20	790	
31		8.76	-9.21	390	
32		8.68	-8.86	3.21×10^3	1.88×10^4
33		8.60[f]	-8.99	3.68×10^3	

34		8.59[i]	-8.78	2.53×10^3	
35		8.27	-8.70		3.74×10^4

[a]Ref 21, unless otherwise noted. [b]*Ab initio* at HF/6-31G* level, partially by Christopher Brammer. [c]Ref 64; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-hexene. [d]Ref 49; k_{rel} values are relative to $k_{rel} = 1.00 \times 10^2$ for 1-butene. The unit of rate constants is $M^{-2}s^{-1}$. [e]IP for 1-decene used as an approximation. [f]Calculated by applying to the IP for 1-pentene a correction factor, which is the difference between the IPs of *trans*-4-methyl-2-hexene and *trans*-2-hexene: 9.52eV– (8.97eV – 8.91eV) = 9.46eV; Ref 21. [g]Ref 65. [h]Calculated by applying to the IP for 2-methyl-2-butene a correction factor, which is the difference between the IPs of 2-butene and 2-pentene: 8.68eV– (9.12eV – 9.04eV) = 8.60eV; Ref 21. [i]Calculated by applying to the IP for 2-methyl-2-butene a correction factor, which is the difference between IPs of 2-methyl-1-propene and 2-methyl-1-butene: 8.68eV– (9.24eV – 9.15eV) = 8.59eV; Ref 21.

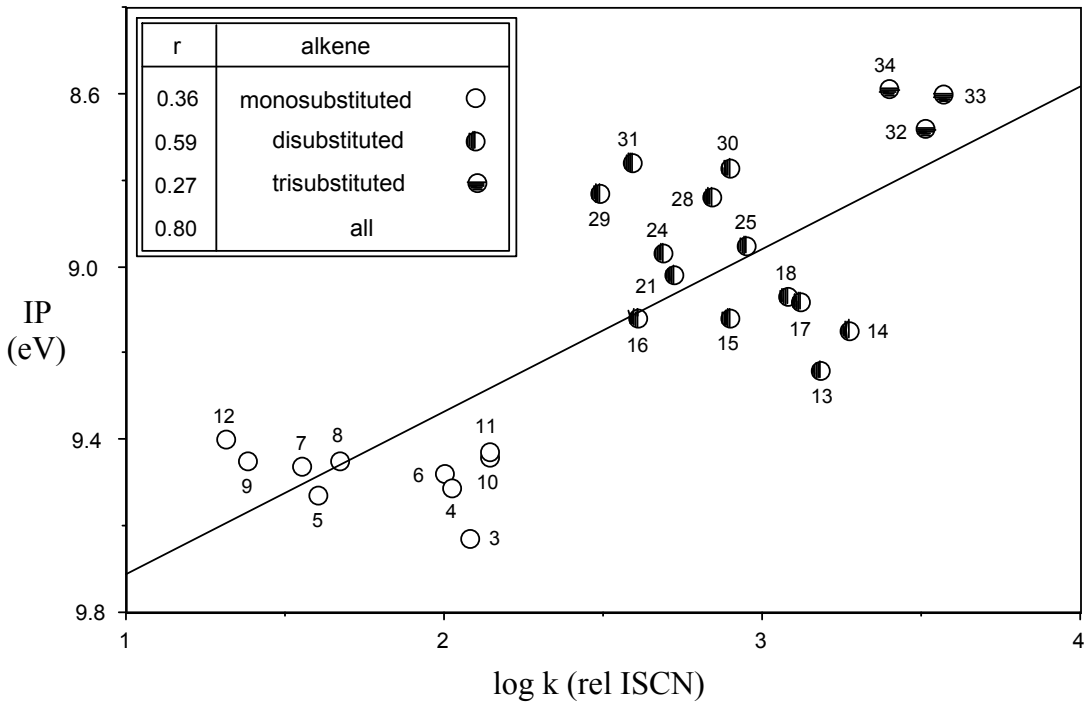


Figure 4-7. Plot of the log k_{rel} values for ISCN addition to alkenes versus alkene IPs. Data are from Table 4-3. Data points do not fall in the correlation line neatly, but cluster to three groups due to the numbers of the alkyl substituents on the alkene

double bonds. Within each sterically similar group, relative rates depend mainly upon the position(s) and size(s) (the branching) of alkyl substituent(s).

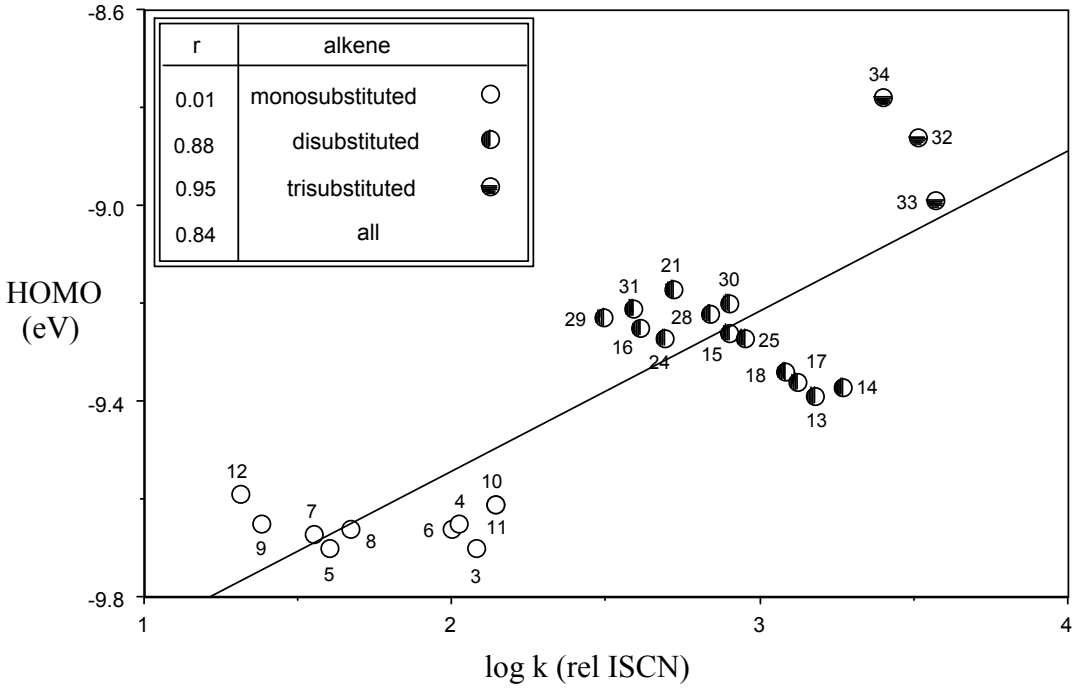


Figure 4-8. Plot of the log k_{rel} values for ISCN addition to alkenes versus alkene HOMO energies. Data are from Table 4-3. The trends shown here are essentially similar to those shown in the plot for alkene IPs.

4.3.3 Electronic effects versus steric effects

The overall trend shown in Figs 4-7 and 4-8 supports the proposal[61] that the rate-determining step of ISCN addition to alkenes is the first step, **a**→**b** in Scheme 4-1, in which the alkene π bond is attacked by electrophile ISCN to form a three-membered cyclic iodonium ion intermediate **b**. Increasing alkyl substitution on the double bond increases the reaction rate presumably due to the electron-donating electronic effects of the alkyl groups, rather than to steric effects, which would retard

the reaction rate. Enriching electron density on the alkenyl carbons makes their π electrons more loosely held and facilitates processes, which remove or reduce the electron density of the π bond. This manifests itself experimentally as a lower IP, as well as an increased rate of reaction with an electrophile.

Thus, the overall trend shown in Figs 4-7 and 4-8 indicates that electronic effects play a more significant role than do steric effects in the rate-determining step of the ISCN addition to alkenes. The above observations and inferences are similar to those made in alkene bromination and in alkene chlorination, but different from those in iodine complexation studied in previous sections of this chapter. This is probably because three-membered cyclic onium intermediates are formed in the kinetically controlled ISCN addition, bromination, and chlorination, whereas iodine complexation is only a thermodynamically controlled equilibrium, yielding only neutral I_2 complexes.

4.3.4 Patterns in the plot

The general pattern of alkene reactivity in ISCN addition displayed in Figs 4-7 and 4-8 is similar to that shown in many other electrophilic additions,[66] which depend upon only electronic effects: (1) the relative rates of trisubstituted alkenes are greatest because they have the lowest IPs or highest HOMO energy levels, (2) disubstituted alkenes react slower because they have higher IPs and a lower HOMO energy levels, and (3) the monosubstituted alkenes react slowest because they have the highest IPs and lowest HOMO energy levels.

However, the data points in the plots for ISCN addition (Figs 4-7 and 4-8) do not fall in the correlation line closely, but clearly cluster to three groups due to the numbers of the alkyl substituents on the alkene double bonds. Within each sterically similar group, relative rates depend mainly upon the position(s) and size(s) (the branching) of alkyl substituent(s) but not the alkene IP or HOMO energies. For example, in ISCN addition to disubstituted alkenes, the ordering according to relative reaction rates produces further subgroups: geminal alkenes (**13**, **14**, **17**, and **18** in Table 4-3 and Figs 4-7 and 4-8) > vicinal cis-alkenes (**15**, **25**, **28**, and **30**) > vicinal trans-alkenes (**16**, **24**, **29**, and **31**), as shown in Chart 4-1 (a). 2,3,3-Trimethyl-1-butene (**21**) reacts much slower than do other geminal alkenes, probably due to the bulky *t*-butyl group, which retards the reaction significantly. Similarly, the ordering of monosubstituted alkenes produces two subgroups: faster-reacting alkenes, each with a straight chain alkyl substituent (**3**, **4**, **6**, **10**, and **11**), and slower-reacting alkenes, each with a branched alkyl substituent (**5**, **7**, **8**, **9**, and **12**), as shown in Chart 4-1 (b).

(a) (b)

Chart 4-1. Orders of relative reactivity of alkenes in ISCN addition due to (a) positions and (b) branching of its substituent(s)

The dependence of relative reactivities of alkenes in ISCN addition upon the positions and branching of alkyl substituents within each sterically similar group of alkenes is quite different from what we observed in our other correlation studies,

where either a single line of correlation among all alkenes, regardless of the degree of substitution, or multiple lines of correlation among sterically similar alkenes was obtained.

4.3.5 Comparison with other alkene halogenations

Comparing the correlation plots for ISCN addition (Figs 4-7 and 4-8) with those for bromination and chlorination in the previous section reveals that although the plot of log k_{rel} values versus alkene IPs for each reaction displays a single line of correlation with positive slope, large differences still exist among them. In bromination and chlorination, all data points in each plot form a single correlation line with only very small deviations, indicating that their relative reaction rates depend predominantly on alkene IPs, regardless of degree of substitution and of position and size of substituents. However, as shown in Figs 4-7 and 4-8, the relative rates in ISCN addition depend upon not only alkene IPs or HOMO energies, but also positions and types of substituents within each sterically similar group, which account for the large deviations of the data points from the correlation line and worse correlation than those for bromination and chlorination.

In order to facilitate the comparison of substituent effects in ISCN addition with those in other similar halogenation reactions, plot of log k_{rel} values versus alkene IPs for ICl addition to alkenes is also given in Fig 4-9. Trends about the electronic and steric effects of the substituents in Fig 4-9 are similar to those shown in Fig 4-7 for ISCN additions. However, the correlation of log k_{rel} values versus alkene IPs for ICl addition is much better than that for ISCN addition, but still worse than those for

bromination or chlorination. The large deviation of **27** (*trans*-4,4-dimethyl-2-pentene) from the correlation line is probably due to the combination of its trans isomerism and the bulky *t*-butyl substituent.

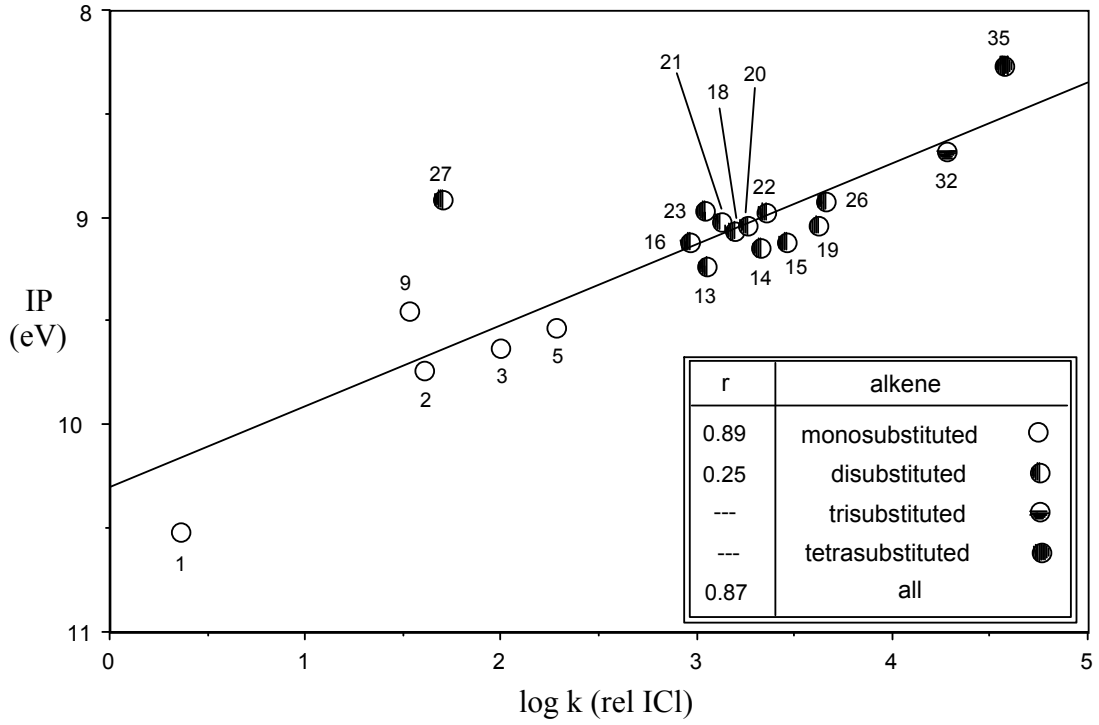


Figure 4-9. Plot of the log k_{rel} values for ICl addition to alkenes versus alkene IPs. Data are from Table 4-3. A much better correlation among all data points is obtained here (IP = 10.30 – 0.39 log k_{rel}, r = 0.89, and s = 0.162).

The differences among these alkene halogenations discussed above could be rationalized by the differences of the properties of these electrophiles. The electrophilicity order of Cl_2 > Br_2 > ICl > ISCN is probably the reason for the order of electronic effects in these reactions: chlorination > bromination > ICl addition > ISCN addition. The difference in size of ISCN > ICl > Br_2 > Cl_2 might account for the different steric effects among them: ISCN addition > ICl addition > bromination > chlorination. Because ISCN is the largest in size and smallest in electrophilicity,

steric effects would reasonably play a more important role in ISCN addition than in the other reactions, as has been observed. In contrast, Cl_2 and Br_2 are both strong electrophiles with small sizes and electronic effects thus play predominant roles in these reactions, while the steric effects are very weak and can be ignored. The relative importance of electronic and steric effects in ICl addition is between these two different cases. The relationship between steric effects and the sizes of electrophiles (XY) could be visualized clearly by the unsymmetrical three-membered cyclic transition state structure in the rate-determining step in Fig 4-10.

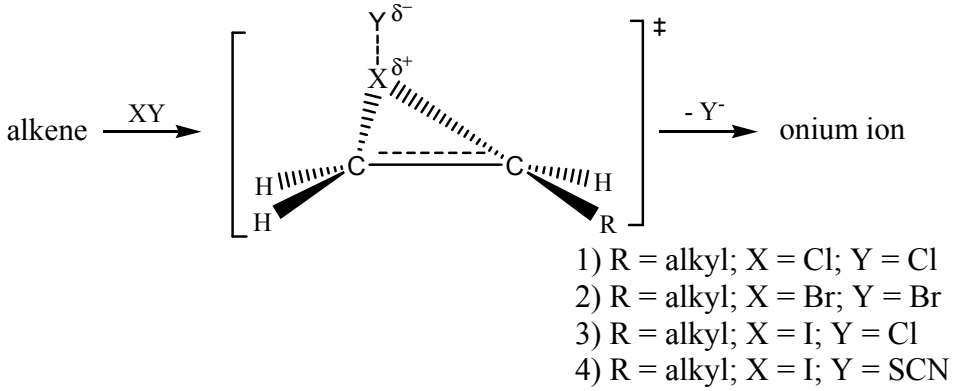


Figure 4-10. Possible unsymmetrical three-membered cyclic transition state structures in the rate-determining step of alkene halogenations

Such an unsymmetrical transition state could also explain the trends of relative reactivity in ISCN addition stated above: (1) a geminal disubstituted alkene has a less sterically hindered carbon atom in its double bond than a vicinal disubstituted alkene which has two equally sterically-hindered carbons; the geminal alkene therefore reacts faster, (2) a cis disubstituted alkene accommodates the entering electrophile molecule on the side with less steric hindrance and so reacts faster than a trans disubstituted alkene, and (3) a straight chain monosubstituted alkene is less sterically

hindered and reacts faster with the entering electrophile than a branched monosubstituted alkene. In addition, within each structurally similar subgroup of alkenes, increasing the size of an alkyl group borne by an alkene carbon increases two competing effects. These are (1) rate-increasing electronic effects, which lower the alkene IP, and (2) rate-retarding steric effects. The two effects obviously must cancel each other to some degree. This would explain why in ISCN addition, the reactivities of the alkenes in the same subgroup are closer to each other than one would expect based solely on their IPs. Similar subgrouping effects also observed in the other halogenations studied here but get weaker in the order of ICl > Br_2 > Cl_2 due to their size changes.

Steric effects caused by the branching of alkyl substituents could also be explained by Taft's[67] measurements about the electronic substituent constant σ* and the steric substituent constant E_s for alkyls groups. For instance, the σ* values of methyl, ethyl, *i*-propyl, and *t*-butyl are 0, -0.100, -0.190, and -0.300 respectively, while their E_s values are 0, -0.07, -0.47, and -1.54 respectively. It is apparent from these data that the ethyl group, compared to the methyl substituent, has very low steric effects for lack of branching, which could be mostly canceled by its increase in electronic effects. However, *i*-propyl and *t*-butyl groups show much stronger steric effects due to branching, which would outweigh their relatively less increased electronic effects and thus result in the obvious decrease of the relative reactivity of the alkenes when the steric requirements of the electrophile is great, such as in ISCN addition.

Complex intermediates prior to the formation of the onium ion in the rate-determining step have been proposed and identified for alkene bromination,[68,69] chlorination,[68,69] and ICl addition.[47-50] Therefore, similar complex intermediates might also be involved prior to the formation of the iodonium intermediate **b** in ISCN addition to alkenes (Scheme 4-1), although this could neither be confirmed nor excluded merely by the analysis of the electronic and steric effects in the rate-determining step in this study.

4.3.6 Conclusion

Interesting trends about relative reactivities of alkenes have been observed in the plot of log k_{rel} values versus alkene IPs for ISCN addition to alkenes. The overall trend shown in the plot indicates that this reaction is an electrophilic addition to alkenes and is dependent more upon electronic effects than upon steric effects in their rate-determining steps. However, within each sterically similar group, the reaction rates are also dependent upon the relative position and size (branching) of the alkyl substituents, which is quite different from what we found in the correlation studies on other alkene reactions.

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Chapter Five

Computational Methods

Abstract: Molecular orbital (MO) methods, including semi-empirical and *ab initio* methods, which have been applied in our correlation studies to calculate the alkene HOMO and LUMO energy levels, are first reviewed briefly in this chapter. The evaluation of five computational methods for 43 different alkenes (over two thirds functionalized) indicates that *ab initio* method with 6-31G* and 3-21G$^{(*)}$ basis sets can produce alkene HOMO and LUMO energy levels in relative order, almost matching those of experimental first ionization potentials (IPs) and electron affinities (EAs), respectively. Other studied methods can give only HOMO energy levels which correlate with experimental IPs well. However, the correlations between computational LUMO energy levels and experimental EAs are poor. The collected alkene experimental IPs/EAs and calculated HOMO/LUMO energy levels in Table 5-1, as well as the correlation plots in Figs 5-1 and 5-2, reveal the trends of substituent effects on alkene IPs (or HOMO energies) and on alkene EAs (or LUMO energies). These results are useful in predicting relative reactivities of alkenes toward an addition reaction according to the substituents on their C=C bonds. Calculations of HOMO and LUMO energies of alkenes in Table 5-1 were conducted in collaboration with Christopher Brammer.

5.1 Introduction

Ionization potentials (IPs) and electron affinities (EAs) of alkenes are important molecular parameters that closely relate to alkene characteristics and reactivities in addition reactions. These parameters are very useful in our studies correlating them to relative reactivities of alkenes toward their addition reactions, as stated in the previous chapters. However, experimental values of alkene IPs, and especially EAs, are in fact often unavailable in literature. In these cases, computational HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) energy level counterparts can be substituted for the experimental IPs and EAs respectively. This is because an alkene's first IP is related directly to its HOMO energy level[1-4] and similarly an alkene's first EA is related directly to its LUMO energy level.[1,2,5,6] Furthermore, the experimental data for alkene IPs and EAs collected from different reports might be inaccurate in some cases. Therefore, it seems necessary in our correlation studies to first obtain the computational HOMO and LUMO energies of the alkenes and then correlate their relative reactivities versus both the experimental alkene IPs/EAs and the computational alkene HOMO/LUMO energies. Comparison among the resultant correlation plots would help to avoid achieving false conclusions because of the possible inaccuracy of the experimental alkene IPs and EAs collected from literature.

The calculation of the HOMO and LUMO energies of a molecule is based on the solution of the Schrödinger equation (eq 5-1) for the molecule.[7-10]

$$H\Psi = E\Psi \qquad (5\text{-}1)$$

In this equation, H is the Hamiltonian operator, E is the system energy, and Ψ is the wavefunction of the molecule. The Schrödinger equation is a multivariate differential equation that can only be accurately solved for the simplest systems, for instance, a hydrogen atom or other similar one-electron systems. For other many-electron atoms and molecules, only approximate solutions can be achieved after making a number of approximations, which simplify the procedure solving the Schrödinger equation. The three approximations are:[8,9]

(1) The Born Oppenheimer approximation --- separates the nuclear and electron motions by assuming that the nuclei are stationary in a molecule. This approximation eliminates the nuclear kinetic energy terms and leads to a constant nuclear-nuclear potential energy term in eq 5-1.

(2) The Hartree-Fock approximation --- separates the electron motions by representing a many-electron wavefunction for a molecule as the product of all one-electron wavefunctions. This approximation simplifies the terms for the correlation between individual electrons.

(3) The LCAO approximation --- represents a molecular orbital (MO) in a linear combination of atom-centered basis functions (atomic orbitals, AOs), which is termed as the basis set.

Based on these approximations, Schrödinger equation can be solved for a molecule through iterative self-consistent field (SCF) computational procedures. The resultant solutions provide important information about the molecular structure, including the HOMO and LUMO energy levels. Two main streams of computational methods, semi-empirical and *ab initio* methods, have branched out from this point due

to whether introducing adjustable parameters into the calculation. In order to further simplify the calculation procedure, the semi-empirical methods make additional approximations and introduce adjustable parameters into the calculation. In contrast, *ab initio* methods are based merely on those three approximations and no adjustable parameters are needed in the calculations. Therefore, *ab initio* methods are generally more complicated and time consuming but also more reliable than the semi-empirical methods. Finally, it should be pointed out that it is almost impossible for the MO calculations to be carried out without the help of efficient computers.

5.2 MNDO method

MNDO (modified neglect of diatomic overlap) method is a semi-empirical method first developed by Dewar and coworkers.[11,12] We have employed this method in calculating alkene HOMO and LUMO energies in several projects in this thesis because of its capability to yield reliable HOMO energies.[12] Moreover, the MNDO HOMO and LUMO energies of many alkenes have already been made available for us since this method had been applied in many previous studies in Dr. Nelson's research group.

In the MNDO calculation, in order to further simplify the computational procedure, only valence atomic orbitals (a minimal valence basis set) are included. Also, the core electrons together with the atomic nucleus are considered as a single entity (a point charge), which is termed as core approximation. In addition, all the terms (integrals) for overlap of atomic basis functions (AOs) on different atoms are eliminated in the calculation due to the NDDO (neglect of diatomic differential

overlap) approximation. Adjustable parameters are introduced in calculations of various electron repulsion integrals, which would compensate for the inaccuracy because of the approximations stated above. Values of these adjustable parameters are determined by fitting available experimental data, such as heats of formation, geometrical variables, dipole moments, and ionization potentials.

5.3 *Ab initio* methods

In some of our correlation studies, we have also employed the *ab initio* MO methods to calculate HOMO and LUMO energy levels of alkenes. Unlike in the semi-empirical methods, the *ab initio* MO methods are based solely on the three approximations stated in section 5.1 without introducing additional adjustable parameters into the computational procedure.[7-10] Therefore, the *ab initio* MO methods are more complicated but also more accurate than the semi-empirical MO methods.

Various *ab initio* methods differ in their employed basis sets, which are sets of atom-centered basis functions (AOs) used to construct the MOs. These basis functions are generally expressed as Gaussian basis functions (GTOs, Gaussian-type orbitals), $x^l y^m z^n \exp(\alpha r^2)$, which are developed from Slater-type orbitals (STOs), $N\exp(\alpha r)$.[8-10] Here, x, y, and z are the three coordinates; r is the vector distance between the electron and the nucleus; values of l, m, n, N, and α vary with different orbitals. Slater-type orbitals (STOs) are the AOs based on Hartree-Fock approximation that neglects the correlation between individual electrons.

The minimal basis set in *ab initio* calculation is STO-3G. In this basis set, each basis function (AO) is represented by a sum of three Gaussian functions which are specifically chosen to best fit Slater-type orbitals (STOs). However, this minimal basis set was found to be inadequate in many cases to describe non-spherical electron distribution in molecules. An approach to solve this problem is to split the valence functions into "inner" and "outer" components, each of which includes one or more Gaussian basis functions. For instance, in the 3-21G basis set, three Gaussian functions are used to represent each non-valence atomic orbital, while two and one Gaussian functions are used, respectively, to represent the "inner" and "outer" components of a valence atomic orbital. Similarly, the 6-31G basis set uses six Gaussian functions to represent each non-valence atomic orbital and three and one Gaussian functions, respectively, to represent the "inner" and "outer" components of a valence atomic orbital.

If the molecule possesses strong polarity, it would be necessary to incorporate an energetically low-lying d-type function into the basis set, which is indicated by adding an asterisk in the representation of a basis set. For example, in both 3-21G$^{(*)}$ and 6-31G*, d-type atomic orbitals have been involved in the construction of the basis sets. The parentheses in the former indicate that the d-type orbital incorporation is only applied to the second row and heavier elements. We have chosen 6-31G* basis set in our *ab initio* MO calculations, because we found from our evaluation studies for several MO methods that it could yield relatively more accurate alkene HOMO and LUMO energies.

5.4 Evaluation of the MO computational methods

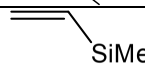
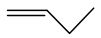
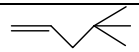
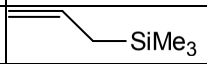
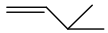
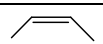
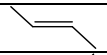
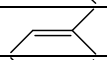
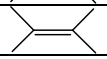
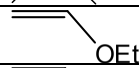
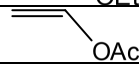
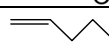
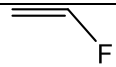
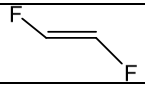
As stated above, since different approximations, parameterizations, and basis sets are adopted in different MO methods, the resulting HOMO and LUMO energy levels by different methods are expected to differ from each other. To evaluate the reliability of each method, a reliable approach is to compare the computational values obtained by this method with the correspondent experimental properties. Based on the direct relationships between alkene HOMO energy levels and IPs and between alkene LUMO energy levels and EAs, correlating computational alkene HOMO energy levels versus experimental IPs and LUMO energy levels versus EAs should each produce a nearly straight line, if the computational method is accurate enough. On the other hand, poor correlations between these parameters imply that the applied MO method is not reliable for producing computational alkene HOMO and LUMO energies.

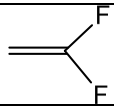
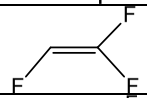
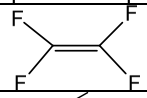
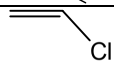
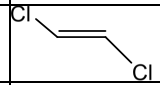
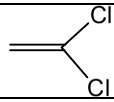
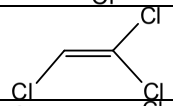
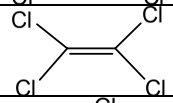
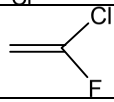
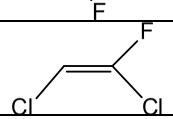
Listed in Table 5-1 are the experimental first IPs, EAs, and computational HOMO and LUMO energy levels by using five different MO methods for 43 alkenes (over two-thirds bearing functionalities). All alkenes studied herein were those that have experimental IPs[13-25] and EAs[26-35] reported in literature. The alkene IP values in Table 5-1 were measured from photoelectron spectroscopy (PES)[13-25] and EAs from electron transmission spectroscopy (ETS).[26-35] The negative values of EAs in Table 5-1 imply that the molecular anions formed from the impact of the alkene molecules by free electrons possess higher energy than the correspondent neutral molecules. Alkene HOMO and LUMO energy levels were calculated by using two semi-empirical methods (MNDO and PM3) and *ab initio* MO methods with three different

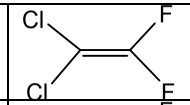
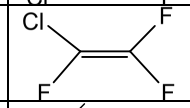
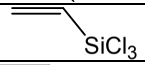
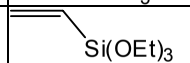
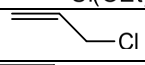
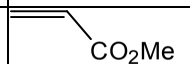
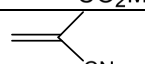
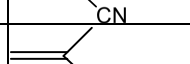
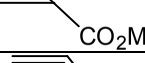
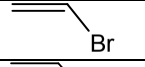
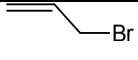
basis sets (STO-3G, 3-21G$^{(*)}$, and 6-31G*). PM3 (Parameterized Model 3) is a semi-empirical method,[9,35] similar to the MNDO method but with further parameterizations based on data from spectroscopy.

In order to evaluate the reliability of each MO method in calculating HOMO and LUMO energies of alkenes, we correlated the calculated alkene HOMO and LUMO energy levels versus the experimental IPs and EAs, respectively. The represented correlation plots for alkene IPs versus HOMO energies (*ab initio* with 6-31G* basis set) and for alkene EAs versus LUMO energies (*ab initio* with 6-31G* basis set) were shown in Figs 5-1 and 5-2 respectively.

Table 5-1. Alkene IPs, EAs, HOMO energies, and LUMO energies (eV)

No.	Alkene	IP	EA	STO-3G		3-21G(*)		6-31G*		PM3		MNDO	
				HOMO[x]	LUMO[x]	HOMO[y]	LUMO[y]	HOMO[y]	LUMO[y]	HOMO[y]	LUMO[y]	HOMO[z]	LUMO[z]
1		10.52[a]	-1.78[n]	-9.10	8.91	-10.33	5.08	-10.19	5.00	-10.46[x]	1.23[x]	-10.17	1.32
2		9.74[a]	-1.99[n]	-8.61	9.00	-9.83	5.31	-9.72	5.25	-10.10[x]	1.18[x]	-9.97	1.12
3		9.45[a]	-1.73[o]	-8.49	9.07	-9.71	5.08	-9.65	4.99	-10.23	1.19	-9.96	1.15
4		9.80[b]	-1.15[o]	-8.54	8.82	-10.01	4.39	-9.92	4.30	-9.86	0.96	-10.05	1.07
5		9.63[a]	-1.90[o]	-8.56	9.00	-9.79	5.22	-9.70	5.12	-10.15[x]	1.18[x]	-9.94	1.12
6		9.40[a]	-1.78[o]	-8.46	8.95	-9.69	5.04	-9.59	4.92	-10.00	1.20	-9.96	1.11
7		9.00[b]	-1.72[o]	-7.97	9.07	-9.72	5.02	-9.60	4.89	-9.29	0.72	-9.58	1.29
8		9.53[a]	-2.19[n]	-8.52	9.01	-9.77	5.24	-9.70	5.15	-10.26	1.17	-9.96	1.13
9		9.12[a]	-2.22[n]	-8.13	9.04	-9.36	5.25	-9.26	5.18	-9.67	1.11	-9.79	0.93
10		9.12[a]	-2.10[n]	-8.13	9.04	-9.34	5.24	-9.25	5.16	-9.65	1.11	-9.78	0.93
11		8.68[a]	-2.24[n]	-7.78	9.01	-8.93	5.12	-8.86	5.01	-9.40	1.06	-9.63	0.77
12		8.27[a]	-2.27[n]	-7.39	8.91	-8.78	5.46	-8.70	5.36	-9.10[x]	1.02[x]	-9.49	0.62
13		9.07[c]	-2.24[n]	-7.40	9.19	-9.27	5.52	-9.11	5.51	-9.46[x]	1.33[x]	-9.22	1.30
14		9.85[d]	-1.19[n]	-9.86	4.47	-9.92	4.39	-9.86	4.47	-9.95[x]	0.58[x]	-10.08	0.50
15		9.52[a]	-1.92[p]	-8.52	9.00	-9.74	5.08	-9.62	4.98	-10.03	1.17	-9.94	1.12
16		9.48[a]	-1.84[p]	-8.51	9.00	-9.75	5.21	-9.66	5.11	-10.11[x]	1.17[x]	-9.97	1.13
17		10.56[e]	-1.91[q]	-10.30	5.14	-10.57	5.01	-10.30	5.15	-10.60	0.71	-10.18	0.67
18		10.38[e]	-1.84[q]	-8.02	8.42	-10.75	4.84	-10.37	5.16	-10.54	0.21	-10.19	0.02

19		10.44[e]	-2.18[q]	-8.02	8.43	-10.75	4.89	-10.38	5.26	-10.54	0.23	-10.18	0.04
20		10.69[e]	-2.39[q]	-8.36	8.49	-10.90	5.07	-10.48	5.50	-10.76	0.23	-10.45	-0.01
21		10.54[e]	-2.45[q]	-7.87	8.19	-11.03	4.87	-10.52	5.52	-10.68	-0.25	-10.46	-0.62
22		10.56[e]	-3.00[q]	-7.69	7.95	-11.29	4.82	-10.66	5.81	-10.81	-0.69	-10.74	-1.26
23		8.80[a]	-1.51[r]	-8.01	9.04	-9.10	4.95	-9.11	4.83	-9.80	1.13	-9.78	0.91
24		10.00[f]	-1.28[s]	-9.09	7.81	-10.26	4.35	-10.14	4.37	-9.84	0.70	-10.39	0.59
25		9.91[f]	-0.80[s]	-9.20[aa]	6.85[aa]	-10.21	3.70	-10.08	3.79	-9.52	0.26	-9.78	0.03
26		9.93[f]	-1.11[s]	-9.16[aa]	6.90[aa]	-10.19	3.80	-10.08	3.92	-9.49	0.29	-10.49	0.38
27		10.16[f]	-0.76[s]	-9.37[aa]	6.97[aa]	-10.35	3.78	-10.23	3.86	-9.74	0.33	-9.84	0.14
28		9.75[f]	-0.59[s]	-9.37[aa]	6.14[aa]	-10.24	3.26	-10.12	3.43	-9.38	-0.04	-9.69	-0.38
29		9.58[f]	-0.30[s]	-9.49[aa]	5.47[aa]	-10.25	2.82	-10.12	3.05	-9.22	-0.32	-9.61	-0.76
30		10.21[g]	-1.51[s]	-8.98[aa]	7.63[aa]	-10.58	4.38	-10.35	4.61	-10.14	0.28	-10.14	0.05
31		9.80[h]	-1.17[s]	-9.00[aa]	6.73[aa]	-10.41	3.80	-10.20	4.10	-9.68	-0.10	-9.89	-0.47

32		9.93[g]	-1.32[s]	-8.72[aa]	6.63[aa]	-10.60	3.89	-10.28	4.45	-9.76	-0.46	-10.00	-0.96
33		10.26[g]	-1.97[s]	-8.29[aa]	7.21[aa]	-10.88	4.32	-10.44	5.06	-10.18	-0.57	-10.34	-1.10
34		9.24[a]	-2.19[t]	-8.23	9.00	-9.48	5.35	-9.39	5.28	-9.80[x]	1.12[x]	-9.80	0.99
35		11.00[i]	-0.52[u]	-10.44[aa]	6.05[aa]	-11.29	2.88	-11.21	2.85	-10.59	-1.19	-11.00	-0.20
36		10.16[j]	-1.11[u]	-8.81[aa]	8.58[aa]	-9.98	4.57	-10.06	4.30	-9.82[x]	0.88[x]	-10.45	0.79
37		10.34[k]	-1.13[v]	-9.26	7.40	-10.46	4.00	-10.35	4.12	-10.31[x]	0.53[x]	-10.48	0.21
38		10.74[d]	-0.49[v]	-8.86	6.42	-10.77	3.04	-10.70	3.15	-11.06[x]	-0.11[x]	-10.76	0.16
39		10.37[l]	-0.17[v]	-8.97	6.52	-10.36	2.94	-10.38	2.91	-10.50	-0.15	-10.43	-0.04
40		10.06[d]	-0.38[v]	-8.62	6.64	-10.22	3.13	-10.15	3.21	-10.52	0.08	-10.46	-0.06
41		9.90[j]	-1.17[w]	-7.86	8.27	-9.87	4.42	-9.71	4.44	-10.44[x]	-0.06[x]	-10.09	0.53
42		10.18[j]	-0.60[w]	-8.28	7.79	-10.26	4.18	-10.02	3.70	-10.49[x]	-0.21[x]	-10.32	0.10
43		9.58[m]	-1.31[w]	-7.71	8.34	-9.57	4.46	-9.43	4.43	-10.18[x]	-0.07[x]	-9.65	0.41

[a]Ref 13. [b]Ref 14. [c]Ref 15. [d]Ref 16. [e]Ref 17. [f]Ref 18. [g]Ref 19. [h]Calculated by applying to the IP for 1-chloro-1-fluoroethene a correction factor calculated as the difference between the IPs of 1,1-dichloroethene and trichloroethene: 10.21eV – (10.16eV – 9.75eV) = 9.80eV; Refs 18 and 19. [i]Ref 20. [j]Ref 21. [k]Ref 22. [l]Ref 23. [m]Ref 24. [n]Ref 25. [o]Ref 26. [p]Ref 27. [q]Ref 28. [r]Ref 29. [s]Ref 30. [t]Ref 31. [u]Ref 32. [v]Ref 33. [w]Ref 34. [x]Spartan '02 for Windows by Christopher Brammer. [y]MacSpartan plus. [z]Ampac by Christopher Brammer. [aa]Hyperchem 7 by Christopher Brammer.

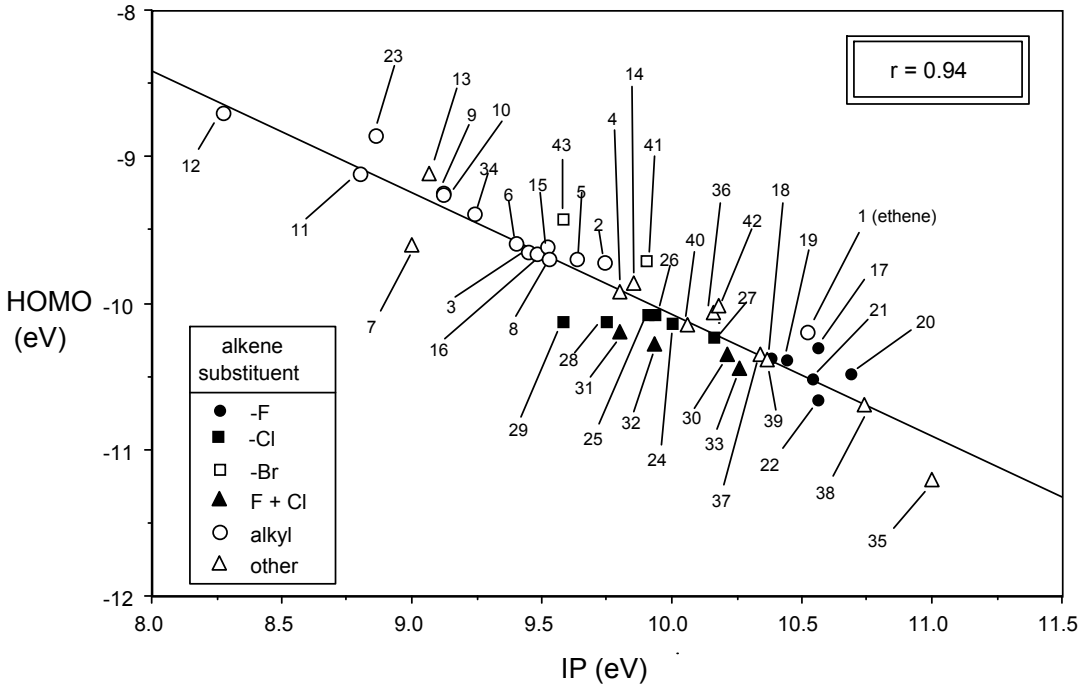


Figure 5-1. Experimental alkene IPs versus computational HOMO energies (*ab initio* with 6-31G* basis set); data are from Table 5-1. All data points lie on one line of correlation (E_{HOMO} = -0.83 IP – 1.78, r = 0.94, s = 0.446, and c.l. = 99.98%).

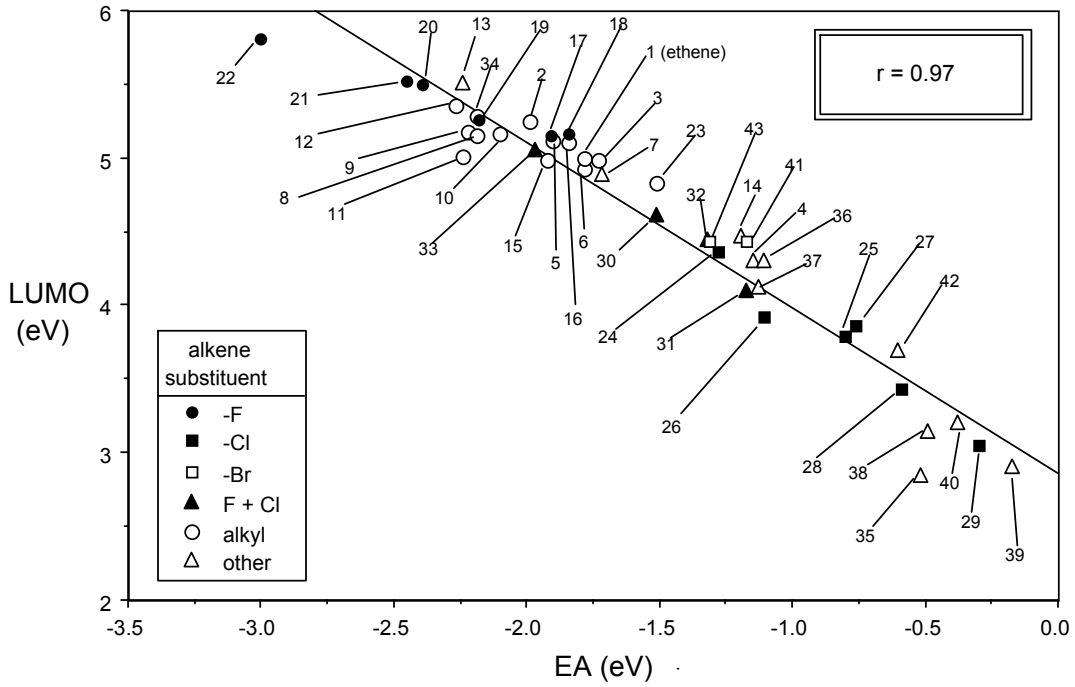


Figure 5-2. Experimental alkene EAs versus computational LUMO energies (*ab initio* with 6-31G* basis set); data are from Table 5-1. All data points lie on one line of correlation (E_{LUMO} = 2.87 – 1.12 EA, r = 0.97, s = 0.072, and c.l. = 99.98%).

The resulting correlation coefficients for these MO methods are listed in Table 5-2 in order to facilitate comparison; a higher correlation coefficient indicates that this method produces data, which are in a closer relative order to observed experimental values. The results in Table 5-2 show that all methods included herein, except for *ab initio* with STO-3G basis set, give good or excellent correlations for alkene HOMO energy levels versus IPs. However, only *ab initio* with 6-31G* and 3-21G$^{(*)}$ basis sets can give LUMO energies which correlate alkene EAs excellently and nearly excellently, respectively. Therefore, we have chosen *ab initio* method

with 6-31G* basis set to calculate alkene HOMO and LUMO energies in several projects.

Table 5-2. Correlation coefficients of alkene IPs versus HOMO energies and EAs versus LUMO energies for five different MO methods

No.	Method	Correlation coefficient (r)		Evaluation of r
		IP vs. HOMO	EA vs. LUMO	
1	STO-3G	0.49	0.62	Poor for both
2	3-21G$^{(*)}$	0.93	0.89	Excellent for HOMO Good for LUMO
3	6-31G*	0.94	0.97	Excellent for both
4	PM3	0.76	0.42	Good for HOMO
5	MNDO	0.83	0.45	Good for HOMO

5.5 Substituent effects on alkene IPs (or HOMO energies)

Different substituents on the alkenyl C=C bonds have different effects on alkene IPs (or HOMO energies). Understanding these substituent effects is important in predicting relative reactivities of alkenes with different substituents toward an electrophilic addition. The trends of substituent effects upon alkene IPs (or HOMO energies) can be observed explicitly by the correlation plot of alkene HOMO energy levels versus IPs in Fig 5-1, as well as the data given in Table 5-1.

(**i**) Alkyl substituents are weakly electron-donating groups; increasing the number of alkyl groups on the C=C bond raises the alkene HOMO energy level and lowers the alkene first IP. Therefore, 2,3-dimethyl-2-butene (**12)** with four alkyls attached to its C=C bond has the highest HOMO energy level and the lowest IP in Table 5-1 (and in Fig 5-1). Electron donating groups other than alkyls, such as -OEt in **13** and $-CH_2SiMe_3$ in **7**, raise the alkene HOMO energy level and lower the alkene first IP more than do alkyls.

(**ii**) Halogen substituents, which are overall electron withdrawing groups, exert two different effects upon alkene double bonds, inductive and conjugative; the former lowers the alkene HOMO energy level and increases the alkene IP, while the latter does the opposite. Table 5-1 and Fig 5-1 show that all examined alkenes, with Cl (**24**-**29**) and Br (**41** and **43**) directly attached to the C=C bonds, have slightly higher HOMO energy levels and lower IP values than their parent alkene (ethene **1**). This demonstrates that conjugative effects slightly outweigh inductive effects in chloro- and bromoalkenes. All examined alkenes bearing F (**17**-**22**) on the alkenyl carbons have HOMO energy levels and IP values similar to their parent alkene **1** (Table 5-1 and Fig 5-1); this indicates that conjugative effects are approximately equal to inductive effects and so they cancel each other. The alkenes with mixed Cl and F substituents (**30**-**33**) have IP (or HOMO energy) values between those of chloroalkenes and fluoroalkenes. For instance, the IP of 1,1-chlorofluoroethene (**30**) is lower than that of 1,1-difluoroethene (**20**) but higher than that of 1,1-dichloroethene (**27**). All examined haloalkenes generally have lower HOMO energy levels and higher IPs than alkenes with only alkyl substituents, showing a greater electron-donating character of alkyls relative to halogens.

(**iii**) Alkenes functionalized with other electron withdrawing groups examined herein, such as $-SiMe_3$, $-SiCl_3$, $-Si(OEt)_3$, $-CH_2Cl$, $-CO_2Me$, -CN, and $-CH_2Br$ (in **4**, **35**, **36**, **37**, **38** and **40**, **39**, and **42** respectively), are basically similar to haloalkenes. They generally have lower HOMO energy levels and higher IPs than alkenes with only alkyl substituents.

5.6 Substituent effects on alkene EAs (or LUMO energies)

Substituent effects upon alkene LUMO energy levels and EAs are, however, quite different from those upon alkene HOMO energy levels and IPs. Both data in Table 5-1 and the plot of alkene LUMO energy levels versus EAs (Fig 5-2) display the following trends, which is useful in predicting the relative reactivity of alkenes with different substituents toward a nucleophilic addition.

(**i**) Alkyl groups, relative to hydrogen in their parent alkene (ethene **1**), raise the alkene LUMO energy level and lower the alkene EA slightly. Therefore, all simple alkenes studied (**2**, **3**, **5**, **6**, **8-12**, **15**, **16**, **23**, and **34**) have slightly higher LUMO energies and lower EAs than those of parent alkene **1**.

(**ii**) Fluoroalkenes (**17-22**) have slightly higher LUMO energy levels and slightly lower EAs than their parent alkene **1**. For example, tetrafluoroethene **22** has the highest LUMO energy level and the lowest EA value.

(**iii**) Alkenes bearing chloro (**24-29**) and bromo (**41** and **43**) substituents on C=C bond experience effects upon LUMO energy levels and EAs which are opposite to those of fluoroalkenes and greater in magnitude, i.e., they have lower LUMO energy levels and higher EAs than their parent alkene **1**. For instance, tetrachloroethene (**29**) has a very low LUMO energy level and a very high EA relative to those of its parent alkene **1**. The LUMO energy levels and EAs of alkenes with mixed Cl and F substituents (**30-33**) are between those of chloroalkenes and fluoroalkenes. For instance, the EA of alkene **30** is higher than that of alkene **20**, but lower than that of alkene **27**.

(**iv**) Similarly to chloro- and bromoalkenes, alkenes in Table 5-1 which bear other electron withdrawing groups, such as $-SiMe_3$, $-SiCl_3$, $-Si(OEt)_3$, $-CH_2Cl$, $-CO_2Me$, -CN, and $-CH_2Br$ (in **4**, **35**, **36**, **37**, **38** and **40**, **39**, and **42** respectively), also have lower LUMO energy levels and higher EAs than their parent alkene **1**.

5.7 Conclusion

Correlation plots of experimental alkene IPs/EAs versus computational HOMO/LUMO energies from five computational MO methods showed that the capability of producing reliable alkene HOMO/LUMO energies by each method is quite different. *Ab initio* methods with 6-31G* and 3-21G$^{(*)}$ basis sets were found to be able to give both alkene HOMO and LUMO energy levels in relative order almost matching those of experimental first IPs and EAs respectively. Correlation plots of alkene IPs versus HOMO energies and EAs versus LUMO energies as well as the data listed in Table 5-1 reveal the trends of substituent effects on alkene IPs (or HOMO energies) and on alkene EAs (or LUMO energies). These trends are helpful in understanding the relative reactivities of alkenes with different substituents on their C=C bonds toward a certain addition reaction.

5.8 References

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Chapter Six

Conclusion

6.1 Summary of the project

In this project, we have applied the methodology, correlating relative reactivities of alkenes versus their measurable characteristics, such as IPs and HOMO/LUMO energies, in the mechanistic investigation on many important alkene reactions. The studied alkene reactions include (1) acid-catalyzed hydration, (2) oxidation with chromyl chloride, (3) oxidation with chromic acid, (4) oxidation with palladium chloride (the Wacker oxidation), (5) homogeneous hydrogenation in the presence of Wilkinson's catalyst, (6) bromination, (7) chlorination, (8) complexation with molecular iodine, (9) iodine thiocyanate addition, (10) iodine chloride addition. Based on these studies and the ones conducted previously by Dr. Nelson's group, a number of conclusions regarding this correlation method and the studied alkene addition reactions can be reached.

The results of these studies indicate that this correlation method is applicable for a wide range of alkene reactions, probably because an electrophilic/nucleophilic attack on alkene C=C bonds plays key role in most alkene additions. Good to excellent correlations have been observed in the plots of relative reactivities of the alkenes versus the alkene measurable properties (IPs and HOMO/LUMO energies) in most of our studies. From the resulting correlation plots, the substituent effects, including electronic and steric effects as well as their relative magnitudes, on alkene

reactivity in an addition reaction can be determined. These results are useful in predicting relative reactivities of different alkenyl C=C bonds toward an addition reaction, which is very important for synthetic purposes especially when two or more different alkenes are present simultaneously in the same reaction system or when an unconjugated diene or polyene with different C=C bonds reacts with a reagent.

In some cases, the results of the studies are also helpful in analyzing and understanding the proposed mechanisms with controversies for an alkene reaction, as shown in Chapter 3. Analyzing the substituent effects in the rate-determining step as well as in the preceding equilibria for the proposed alternative mechanisms sometimes may provide information valuable in differentiating between these mechanisms. For instance, the conclusion that alkene hydrogenation is a nucleophilic addition to alkenes can exclude the proposed mechanism in which the electrophilic coordination of the rhodium center with alkene C=C bonds is considered to be the rate-determining step. Instead, the mechanisms in which the nucleophilic alkene insertion into the Rh-H bond is considered as rate-determining step are favored.

The majority of the studied alkene reactions have been found to be electrophilic additions to alkenes, in which correlation lines with positive slopes are observed in the plots of log k_{rel} values versus alkene IPs or HOMO energies. This result indicates that alkene additions are initiated by electrophilic attacks from electrophiles to alkenes C=C bonds in most cases. In order to assess the validity of the methodology for nucleophilic additions to alkenes, we have also included two nucleophilic additions to alkenes, oxidation with palladium chloride (the Wacker oxidation) and homogeneous hydrogenation in the presence of Wilkinson's catalyst,

in this project by correlating log k_{rel} values versus alkene LUMO energies. Results of the study have proven the applicability of the methodology in nucleophilic additions to alkenes.

Steric effects of the substituents govern the pattern of the resulting correlation plots. Single lines of correlation have been obtained in more than half of the studied alkene reactions, in which steric effects are not significant and electronic effects play a predominant role. This type of alkene reactions studied includes (1) epoxidation, (2) sulfenyl halide addition, (3) carbene addition, (4) oxidation with osmium tetroxide, (5) oxidation with permanganate, (6) nitrosyl chloride addition, (7) oxidation with chromyl chloride, (8) oxidation with chromic acid, (9) bromination, (10) chlorination, and (11) iodine chloride addition. In contrast, owing to the strong steric effects, multiple lines of correlation have been obtained in the plots for the following alkene reactions: (1) hydroboration, (2) oxymercuration, (3) silver ion complexation, (4) diimide reduction, (5) acid-catalyzed hydration, (6) oxidation with palladium chloride (the Wacker oxidation), (7) homogeneous hydrogenation in the presence of Wilkinson's catalyst, and (8) complexation with molecular iodine.

The steric effects of substituents in alkene reactions are found to be dependent upon the rate-determining transition structure of the reaction. The symmetry of the structure of the rate-determining transition state also governs the grouping patterns of the alkene data points in the plots for those sterically important alkene additions. If the structure of the transition state is symmetrical in an alkene addition, for instance, in diimide reduction, silver ion complexation, and complexation with molecular iodine, a substituent would cause similar steric hindrance to the incoming electrophile

no matter on which carbon of the C=C bond it attaches. The alkene data points in the plots would separated into sterically similar groups based only on the number of the substituents on the C=C bond, i.e. mono-, di-, tri-, and tetrasubstituted alkenes. If the rate-determining state has an asymmetric structure in an alkene addition, for instance, in hydroboration, oxymercuration, and acid-catalyzed hydration, the incoming electrophile would be located closer to the less substituted carbon of the C=C bond to lower the steric hindrance from the substituents. In other words, the steric effects depend upon the steric requirements of the less substituted carbon of the C=C bond. In this case, the data points for the alkenes in the plots would be separated into sterically similar groups based on the steric requirements of the less substituted carbon of the C=C bonds, i.e. terminal (mono- and geminal disubstituted), internal (vicinal disub- and trisubstituted), and tetrasubstituted alkenes.

The relative magnitudes of electronic and steric effects in an alkene addition are also related to the electronic properties and steric requirements of the incoming electrophiles or nucleophiles. For example, we have studied alkene additions of several halogens and derivatives (Cl_2, Br_2, ICl, and ISCN) in Chapter 4. The results of the study demonstrate that the importance of electronic effects relative to the steric effects in these reactions follow an order of $Cl_2 > Br_2 > ICl > ISCN$. In alkene chlorination, electronic effects play a predominant role and steric effects are negligible. However, in ISCN addition, alkene reactivities depend upon not only electronic effects, but also steric effects in each group of sterically similar alkenes. The trends of relative importance of electronic and steric effects can be explained by

the order of their electrophilicity, $Cl_2 > Br_2 > ICl > ISCN$, and the order of their sizes, $ISCN > ICl > Br_2 > Cl_2$.

6.2 Directions for future studies

Based on the recent development, I believe that the future studies on this project should take the following two directions:

(1) Greater variety of alkene reactions should be included in this project to test the generality and limitation of the methodology and meanwhile to obtain information useful synthetically and mechanistically about the studied alkene reactions. Many alkene reactions that are significant in either organic syntheses or mechanistic studies have not been studied by using this method. Especially, more nucleophilic additions to alkenes should be included in the future study.

(2) The electronic and steric effects of the substituents in an addition to alkenes should be analyzed not only qualitatively but also semi-quantitatively by measuring the slopes and the extent of separation between the correlation lines for different sterically similar alkene groups. Quantitatively measuring the steric effects of the substituents on alkene reactivities in addition reactions would be a challenging, but very attractive target in the future study on this project.

Appendix: Copies of reprints of five published papers that correspond to the studies included in Chapters 3 and 4.

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Correlation of relative rates of chromyl chloride oxidation and chromic acid oxidation of acyclic alkenes versus alkene IPs and HOMOs†

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ABSTRACT: Plots of logarithms of relative reaction rates of chromyl chloride oxidation and of chromic acid oxidation of alkenes ($\log k_{rel}$ values) versus alkene ionization potentials (IPs) and versus their highest occupied molecular orbital energy levels (HOMOs) demonstrate excellent correlations. Each plot has a similar appearance and shows a single line with a positive slope. The results indicate that the rate-determining step of each title reaction involves an electrophilic attack on the alkene π-bond without significant steric effects; this supports a proposed $2+3$ cycloaddition mechanism and disfavors a proposed stepwise $2+2$ cycloaddition mechanism. Comparison is made with other d^0 transition metal complexes that oxidize alkenes. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: chromyl chloride; chromic acid; alkene oxidation; relative reaction rates; ionization potentials (IPs); electrophilic addition; cycloadditon of alkenes; electronic effects versus steric effects

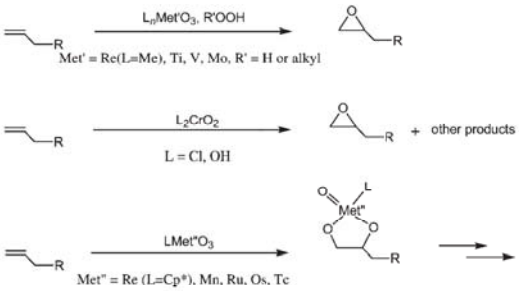
INTRODUCTION

We reported a method to differentiate the relative importance of electronic and steric effects in addition reactions of alkenes by correlating logarithms of relative reaction rates ($\log k_{rel}$ values) versus the alkene ionization potentials (IPs) and versus their highest occupied molecular orbital energy levels (HOMOs) and applied this method to a variety of important addition reactions of alkenes.[1a–i] This technique offers synthetically valuable information about addition reactions to one alkene in the presence of another differently functionalized alkene and sometimes enables selection from among the proposed mechanisms.[1h–i] Therefore, it seems desirable to investigate reactions with great mechanistic and synthetic importance, in order to gather additional information about that reaction.

Oxidation of alkenes by transition metal oxo compounds has been an important topic in organic and organometallic chemistry for a long time.[2a–c] Intensive mechanistic studies have been carried out both theoretically[2d–t] and experimentally[2u–y] during the past decade. Among them, chromium(VI) compounds, such as CrO_2Cl_2 and H_2CrO_4, have been shown to be versatile oxidizing agents, and their reactions with alkenes yield epoxides commonly and other products depending on the reaction conditions.[2a–c,3–6] In this study, we use the above technique to explore chromyl chloride oxidation and chromic acid oxidation of alkenes, partly because of their importance in organic synthesis[2a–c,3,4] and partly because of interest in their mechanisms.[2a–c,5,6]

BACKGROUND

Interesting similarities and differences among reactions of alkenes with complexes of chromium(VI) versus those of other d^0 transition metals have been noted recently.[2k,p,5j,l] In oxidizing alkenes, complexes of Re(VII) (when L = Me),[2k] Ti(IV),[7] V(V),[8] Cr(VI)[5e] and Mo(VI)[9] each yields epoxides preferentially, while those of Re(VII) when L = Cp* (= C_5Me_5),[10] Mn(VII),[2a]



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Ru(VIII),[11] Os(VIII)[12] and Tc(VII)[13] each preferentially yields *cis*-dihydroxyalkanes.[2k]

The point has been made[2k,p] that in some epoxidations, $L_nMet'O_3$ does not react directly with the alkene, but with an additional oxygen source, which may be necessary to effect the reaction; in these cases, the addition proceeds by an indirect pathway.

Some of the above metals do not fit completely into either group Met′ or Met″. For example, it was noted[2p,w] that $MeReO_3$ compounds do not react directly with olefins,[2k] as do oxidizing compounds of Ti,[7] V[8] and Mo.[9] However, Cp*ReO_3 is proposed to react with alkenes to give a $2+3$ addition product,[2w,10] as are the compounds of Mn,[2a] Ru,[11] Os[12] and Tc[13], but the former does not yield diols as the final product,[2w,10] as the later compounds do.[2a,11,12,13]

Another misfit is chromium. Chromyl chloride has been likened[2p] to other oxidizing metal complexes LMO_3, such as Os, Ru and Mn. Chromium fits Met′ in that it yields epoxides[2a–c,5e] as the others do; but it does not fit Met′ in that it does not require a peroxide to react with alkenes,[2a–c,5e] as the Os, Ru and Mn do.[2k,7,8,9] Chromium is like Met″ because its compounds react directly with the olefin[2a–c] in a proposed[5a–d] $2+3$ addition as do Os, Ru and Mn; but it is unlike Met″ because it does not give a diol as a product,[2a–c] as the others do.[2a,11,12,13]

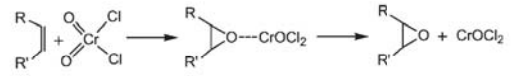
The above observations have spawned comparisons and contrasts of oxidation with chromium compounds versus those with compounds of Met″ (Re, Mn, Ru, Os and Tc).[2k,5e,j,l] As a result, proposals that these oxidations of alkenes proceed via $2+3$ reactions have been shared by many of these compounds, Cr,[5j,l] Os,[14] Re(L = Cp),[2j,k] Mn,[2p] Tc.[13]

There have been many experimental reports,[2q,u,v] theoretical reports,[2e,g–j,m–r,5j,l] and analyses[2s,v] favoring the $2+3$ mechanism over the $2+2$. Among these, density functional theory (DFT) calculations[2g–j,n–r,5j,l] predicted that the $2+2$ mechanism has a much higher activation energy than that of the $2+3$ mechanism in reactions of many such compounds, which led to the conclusion that the latter is more likely. In many[2g–j,n–r,5j,l] of the DFT calculations, the most stable point on the energy surface was the $2+3$ adduct,[2g–j,n–r,5j,l] which might be expected to hydrolyze to diols.[2n,5o] Owing to comparisons and concerns such as those noted above, questions linger as to (1) whether the $2+3$ mechanism or the $2+2$ mechanism is responsible for the products and (2) if the $2+3$ mechanism operates with chromium complexes, why the metalladioxylate intermediate would not yield diols as do complexes of the other metal Met″.

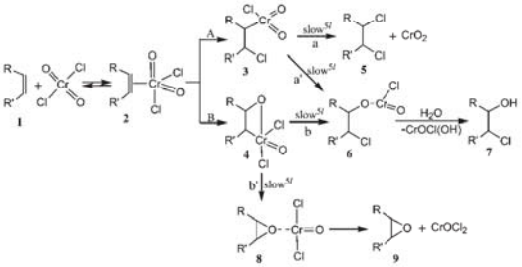
Oxidation using CrO_2Cl_2

The mechanism of chromyl chloride oxidation of alkenes has been investigated for decades.[2a–c,5] At least four[2a–c,5a–e,m,n] different mechanisms have been suggested for this reaction. The first suggestion was a 'direct addition' mechanism (Scheme 1),[2a–c] which was criticized due to its failure to explain all stereochemical aspects (such as the formation of the *cis*-chlorohydrin and the *cis*-dichloride) of chromyl chloride oxidation.[5e,i] Two other different mechanisms were then proposed: (1) the $2+2$ cycloaddition mechanism (Scheme 2)[2c,5e,i] and (2) the $2+3$ cycloaddition mechanism (Scheme 3).[5a–d] Recently, an ESR signal was observed in the oxidation of aryl substituted alkenes,[5m,n] and a diradical was proposed as the intermediate giving rise to this result. However, the stereospecificity of these reactions has been used to argue against radical intermediates in the C—O bond forming steps. In addition, the alkenes considered in this paper do not possess radical-stabilizing Ph substitutions. Therefore, in this study, we focus on the application of our results to the rate-determining steps of the mechanisms shown in Schemes 2 and 3.

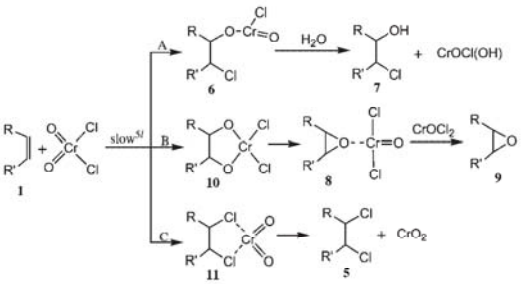
The main difference between the two proposed mechanisms shown in Schemes 2 and 3 is in their rate-determining steps and characteristics of their transition-state structures. In the $2+2$ mechanism (Scheme 2), the



Scheme 1. The direct addition mechanism for CrO_2Cl_2 oxidation of alkenes[2a–c,5l]



Scheme 2. The $2+2$ cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes[2c,5e,i,l]



Scheme 3. The $2+3$ cycloaddition mechanism for CrO_2Cl_2 oxidation of alkenes[5a–d,l]

decompositions of intermediates **3** and **4** are proposed as rate-determining steps.[5l] None of these transformations involves alkene π-electrons. In contrast, the $2+3$ mechanism (Scheme 3) requires a five-membered ring transition-state structure in the rate-determining formation of the intermediates and all involve breaking the alkene π-bond.

Oxidation using H_2CrO_4

Chromic acid (H_2CrO_4) oxidation of alkenes produces epoxides or their higher oxidation level products.[2a,6b] A kinetic study of this reaction fostered a mechanism involving a three-membered transition-state structure (Scheme 4),[6b] similar to the 'direct addition mechanism' that was previously discarded for CrO_2Cl_2 oxidation of alkenes. Another proposed mechanism[2a,6b] for the H_2CrO_4 oxidation invoked a five-membered intermediate (Scheme 5). It is analogous to the $2+3$ mechanism for the chromyl chloride oxidation shown (**1** → **9**) in Scheme 3 (path B). A major difference between these two proposed mechanisms for chromic acid oxidation of alkenes is that the former suggests a direct single-step formation of an epoxide (Scheme 4), while the latter requires formation of a five-membered intermediate between the reactants and the epoxide product (Scheme 5). In this study, we shall discuss its mechanisms through comparison with those of chromyl chloride oxidation of alkenes.

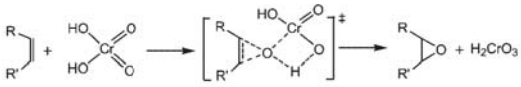
RESULTS AND DISCUSSION

Relative rates[5c] of chromyl chloride oxidation of alkenes, alkene IPs[15] and alkene HOMOs are shown in Table 1. Relative rates[6b] of chromic acid oxidation of alkenes, alkene IPs[15] and alkene HOMOs are shown in Table 2. Both reaction rates were determined by following the disappearance of the Cr(VI) oxidation reagents under pseudo-first-order conditions (large excess of alkene).[5c,6b] As in our previous studies,[1] cyclic alkenes and aryl alkenes are omitted in order to avoid complications due to ring strain or conjugation with the aryl group. Because the IP for compound 13 in Table 1 was not available in the literature, we calculated HOMOs for all alkenes to enable a check to be made using data for all compounds. The alkene HOMOs were calculated in the same manner as reported previously.[1a] Figures 1 and 2 show the similar correlations of $\log k_{rel}$ values versus alkene IPs for chromyl chloride oxidation of alkenes and for chromic acid oxidation of alkenes, respectively. Each shows a single line with a positive slope and an excellent[16] correlation coefficient ($r_{all} = 0.93$ in Fig. 1, $r_{all} = 0.97$ in Fig. 2). The plots (not shown) of $\log k_{rel}$ versus alkene HOMOs for both reactions are essentially analogous to Figs 1 and 2. They also have single lines with positive slopes and show excellent correlations ($r_{all} = 0.94$ for the chromyl chloride oxidation and $r_{all} = 0.95$ for the chromic acid oxidation). Correlation coefficients for all alkenes (r_{all} values) are calculated from individual values for the alkenes.

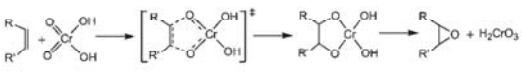
Table 1. IPs, HOMOs and relative rates of chromyl chloride (CrO_2Cl_2) oxidation of alkenes

No.	Alkene	IP (eV)[a]	HOMO (eV)	k_{rel}[b]
1		9.52	−9.94	1.22×10^2
2		9.51[c]	−9.95	88.0
3		9.48	−9.97	1.00×10^2
4		9.45	−9.96	5.36×10^2
5		9.43[c]	−9.95	77.0
6		9.12	−9.79	1.51×10^3
7		9.12	−9.78	1.38×10^3
8		9.08	−9.79	8.00×10^2
9		9.04	−9.77	1.48×10^3
10		9.04	−9.76	1.51×10^3
11		9.02	−9.75	1.05×10^3
12		8.91	−9.71	2.36×10^3
13			−9.78	7.54×10^2
14		8.83[d]	−9.64	1.38×10^5
15		8.68	−9.63	2.02×10^4
16		8.27	−9.49	3.91×10^5

[a] Ref. 15a, unless otherwise noted.
[b] Ref. 5c.
[c] Ref. 15b.
[d] Ref. 15c.



Scheme 4. The direct addition mechanism for H_2CrO_4 oxidation of alkenes[6b]



Scheme 5. The $2+3$ cycloaddition mechanism for H_2CrO_4 oxidation of alkenes[6b]

Table 2. IPs, HOMOs and relative rates of chromic acid (H_2CrO_4) oxidation of alkenes

No.	Alkene	IP (eV)[a]	HOMO (eV)	k_{rel}[b]
1		9.74	−9.97	32.3
2		9.63	−9.94	52.0
3		9.52	−9.94	75.5
4		9.48	−9.97	1.00×10^2
5		9.45	−9.96	68.7
6		9.44	−9.94	94.2
7		9.24	−9.80	2.48×10^2
8		9.12	−9.79	2.86×10^2
9		9.12	−9.78	1.89×10^2
10		9.04	−9.76	2.46×10^2
11		8.97	−9.75	2.78×10^2
12		8.91	−9.71	3.44×10^2
13		8.83[c]	−9.64	1.10×10^3
14		8.68	−9.63	3.13×10^3
15		8.27	−9.49	1.60×10^4

[a] Ref. 15a, unless otherwise noted.
[b] Ref. 6b.
[c] Ref. 15c.

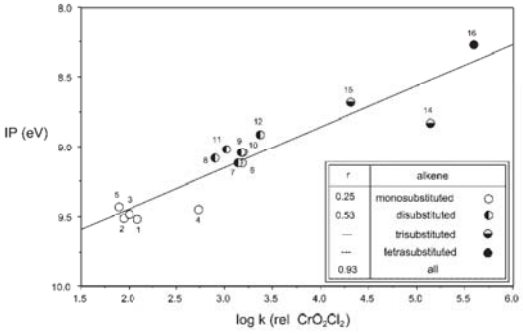


Figure 1. The plot of the $\log k_{rel}$ values for chromyl chloride oxidation of alkenes versus correspondent alkene IPs. Data are given in Table 1. Correlation coefficients (*r* values) are given in the legend for monosubstituted alkenes, for disubstituted alkenes and for all alkenes regardless of the degree of substitution about the double bond. The *y*-axis IP data are plotted in inverse order to facilitate comparison with the HOMO plots and previous studies

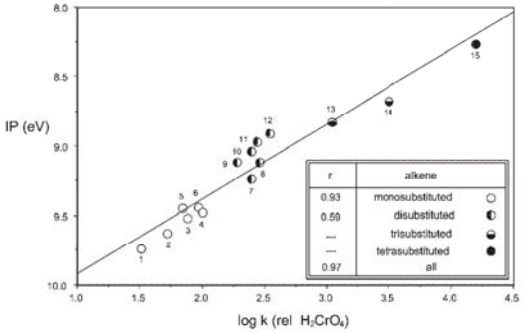


Figure 2. The plot of the $\log k_{rel}$ values for chromic acid oxidation of alkenes versus correspondent alkene IPs. Data are from Table 2

Steric effects and electronic effects

The excellent[16] correlation of $\log k_{rel}$ values versus alkene IPs and versus alkene HOMOs in each plot indicates that the rate-determining step of each reaction involves the alkene π-electrons. Each plot has a single line of correlation, regardless of the degree of alkene substitution, so there is no natural separation due to steric requirements of the alkenes, which has sometimes been observed in other additions to alkenes.[1a,b,d,g,h] This provides evidence that both chromyl chloride oxidation and chromic acid oxidation of alkenes are dependent more upon electronic effects than steric effects in their rate-determining steps.

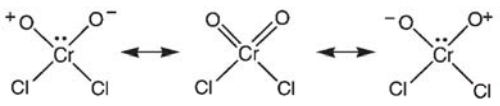
All correlation lines in Figs 1 and 2 have positive slopes; in each reaction a lower IP (or a higher HOMO) corresponds to a greater reaction rate. Therefore, the rate-determining step, in chromyl chloride oxidation of alkenes and in chromic acid oxidation of alkenes, involves electrophilic attack upon the π-bond of the alkene. Electron-donating substituents in the alkene increase the rate of reaction using either reagent, and electron-withdrawing ones decrease it.

Differentiating between the proposed mechanisms

Many studies have attempted to differentiate between the $2+2$ mechanism versus the $2+3$ mechanism for chromyl chloride oxidation of alkenes.[5f,g,h,j,l] Some have favored the former mechanism,[5f,g,h] and have some favored the latter.[5j,l] The results of our current study indicate that the rate-determining step in the oxidation of alkenes, by using chromyl chloride or chromic acid, is an electrophilic attack upon the alkene π-bond. This disfavors the $2+2$ mechanism for chromyl chloride oxidation of alkenes, because in this mechanism (Scheme 2) the only electrophilic step is the formation of the chromyl chloride alkene complex (**1** → **2**), which is

generally agreed[2c,5i] not to be the rate-determining step, but a fast equilibrium. Neither of the two proposed[5l] sets of rate-determining steps in the 2 + 2 mechanism are viable possibilities, because they are not electrophilic processes involving the alkene π-bond; the formation of intermediates **3** and **4** from **2** (**2** → **3** and **2** → **4** in Scheme 2) are nucleophilic processes. The decomposition of these intermediates (**3** → **5**, **3** → **6**, **4** → **6** and **4** → **8** in Scheme 2) has no direct relationship to the alkene π-bond IPs and any mechanism with these as the rate-determining steps can be excluded. Ziegler's calculations[5l] predicting that these are indeed the rate-determining steps excludes the 2 + 2 mechanism (Scheme 2) in this reaction, in analog with calculations[2g–j,n–r] for other metal complex oxidations of alkenes using similar computational methods.

Our analysis that the rate-determining step is an electrophilic process involving attack upon the alkene π-bond supports the 2 + 3 mechanism (Scheme 3). Electrophilic attack by the reactant CrO_2Cl_2 could be visualized by using one of its resonance structures in which an oxygen atom carries a positive charge.[5e]



Our investigations similarly indicate that the chromic acid oxidation of alkenes is also an electrophilic addition with a rate-determining step which involves the alkene π-electrons. The plot of $\log k_{rel}$ values versus alkene IPs for oxidation with H_2CrO_4 (Fig. 2) is essentially analogous to that of CrO_2Cl_2 (Fig. 1) with correlation coefficient $r_{all} = 0.97$. Our results are accommodated by either of the mechanisms in Scheme 4 or Scheme 5. One might argue to exclude the mechanism in Scheme 4 for the following reasons: (1) H_2CrO_4 is structurally similar to CrO_2Cl_2; (2) the two similar reagents might be expected to react in a similar manner; (3) an analogous mechanism for the CrO_2Cl_2 reagent was discarded and (4) a mechanism similar to that in Scheme 5 also agrees with the results obtained by using the reagent CrO_2Cl_2.

What explanations can be offered for the production of products other than diols? One possibility is that in the 2 + 2 mechanism, the first step is actually the rate-determining step, although the results of Ziegler's study work against this. Another possibility is that the 2 + 3 adduct reacts via a pathway other than hydrolysis to diols. This second possibility has been the subject of recent studies.[5m,n,o] The observation of an ESR signal in the reaction of the Cr(V) intermediate complex with CrO_2Cl_2: alkene = 2:1[5m,n,o] suggests that, for the 2 + 3 adducts of CrO_2Cl_2 and of H_2CrO_4, instead of hydrolysis, perhaps an alternate reaction pathway involving diradicals is favored.

CONCLUSION

A single line in each correlation plot of $\log k_{rel}$ values versus alkene IPs (Figs 1 and 2) and versus alkene HOMOs ($r_{all} = 0.94$ and 0.95) for the oxidation of alkenes by using CrO_2Cl_2 and H_2CrO_4 demonstrates that (1) the rate-determining step of each reaction involves the alkene π-electrons and (2) these reactions are more dependent upon electronic effects than upon steric effects. Their positive slopes indicate that the rate-determining step in each reaction is an electrophilic addition. Our study supports the 2 + 3 mechanism and disproves the 2 + 2 mechanism with the rate-determining step that has been proposed for it.

Acknowledgement

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Correlation of Relative Rates of $PdCl_2$ Oxidation of Functionalized Acyclic Alkenes versus Alkene Ionization Potentials, HOMOs, and LUMOs

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Abstract: Investigations of the title reaction, carried out by plotting logs of the relative reaction rates vs IPs, vs HOMOs, and vs LUMOs, reveal multiple nearly parallel lines of correlation with small negative slopes in each. Overall, the natural grouping into monosubstituted and disubstituted alkenes gives better correlations than that obtained by using all alkenes. Comparison with analogous plots for other reactions indicates that the mechanism for this reaction has similarities to that for hydroboration, the major difference being that the lines in the plots for hydroboration have positive slopes, indicating an electrophilic rate-determining step involving the π electrons, while those for the title reaction have small negative slopes, indicating a nucleophilic rate-determining step. Of the two reaction mechanisms proposed for the title reaction, only one has a nucleophilic attack at the complexed alkene as the rate-determining step, and therefore, this work supports that reaction mechanism.

I. Introduction

We have developed a technique[1] for correlating measurable characteristics in addition reactions with alkenes in order to gain information which is useful mechanistically and synthetically. We have applied this technique to several reactions: hydroboration,[1a] oxymercuration,[1a] bromination,[1a,g,h] diimide addition,[1b] oxidation with permanganate,[1c] epoxidation,[1d] sulfenyl halide addition,[1d] mercuric chloride complexation,[1d] silver ion complexation,[1d,h] carbene addition,[1e] nitrosyl chloride addition,[1e] oxidation with osmium tetroxide,[1e] chlorination,[1g,h] and complexation with iodine.[1g,h] This technique offers (1) a procedure to determine relative magnitudes of steric and electronic effects in the rate-determining step, (2) a relatively simple way to predict the effects of substituents on reaction rates for synthetic purposes, and (3) a method to choose between alternative proposed reaction mechanisms in some cases. In investigations[1] of other additions to alkenes, we applied this simple method by correlating the logs of the relative reaction rates (log k_{rel} values) with the alkene ionization potentials (IPs), with their highest occupied molecular orbital energies (HOMOs), and in some cases with their lowest unoccupied molecular orbital energies (LUMOs). In those investigations, reactions with similar mechanisms gave correlation plots which were similar in appearance. To develop further this new technique and to elucidate synthetically and mechanistically important information from experimental or from computational data, we apply the technique to important reactions with a variety of mechanisms. For nucleophilic addition reactions, such as $PdCl_2$ oxidation and other transition metal additions, which are characterized by inhibition of rate by alkyl substitution and nonselective mode of addition, there have been no clear measures of the relative importance of electronic and steric effects; this technique provides such quantitative information.[2] Thus, it is desirable to investigate similarly the $PdCl_2$ oxidation of representative functionalized alkenes, because this is an important reaction for which is indicated a mechanism of a type which we have not treated previously, and the reaction is suited to our analysis method.

II. Background

There has been much interest[3−12] in the mechanism of palladium chloride ($PdCl_2$) oxidation (eq 1) of acyclic alkenes.

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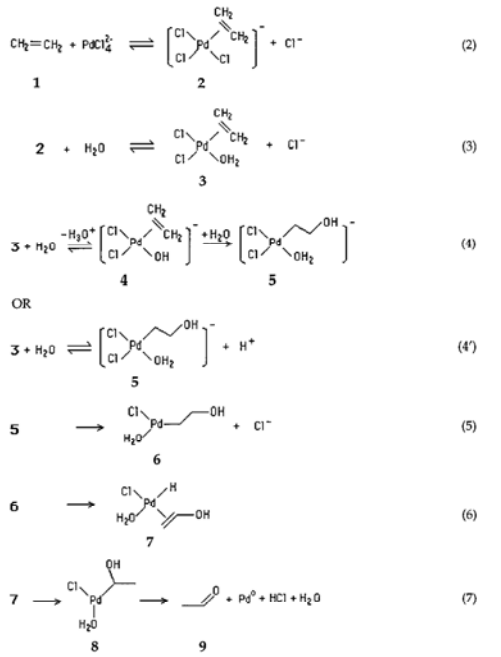
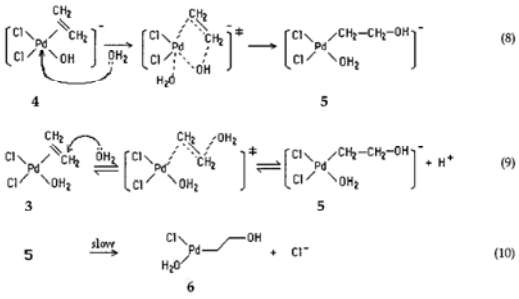
This is in part due to the industrial importance[3,4] of the reaction in the synthesis of carbonyl compounds from corresponding alkenes (the Wacker oxidation[3a,b]) and in part due to the interest in its mechanistic pathway.[3−12]

$$C_nH_{2n} + PdCl_2 + H_2O \rightarrow C_nH_{2n}O + Pd(0) + 2HCl \quad (1)$$

The steps of the reaction are now generally considered to be those shown below (eqs 2−7), although there has been disagreement over some mechanistic details and over the identity of the rate-determining step.[4−12] The first step (eq 2) of the reaction is alkene coordination to give a palladium(II) complex **2**. The next step (eq 3) in the reaction sequence is generally accepted to be the nucleophilic replacement of a second chloride by water to give intermediate **3**. There seems to be agreement that the previous equilibrium steps (eqs 2 and 3) in the reaction sequence are fast relative to the rates of the subsequent steps.[4−12] However, two different pathways have been suggested for the following step (**3** → **5**) (eqs 4 and 4′). In the first pathway,[4] the alkene complex **3** deprotonates first to a negative hydroxymetal complex ion **4** (eq 4), followed by rate-determining conversion of the palladium(II) alkene π-complex into a palladium(II) β-hydroxyalkyl species **5**, a process called hydroxypalladation (eq 4).[4] The second proposed pathway[7a,b] is a rapid equilibrium in which a H_2O molecule attacks the C=C double bond directly to give the palladium β-hydroxyalkyl intermediate 5 (eq 4′), with the rate-determining step following. The palladium β-hydroxyalkyl intermediate **5** then loses a chloride ion (eq 5) to yield another β-hydroxyalkyl intermediate **6**. The next step (eq 6) is β-hydrogen elimination of the intermediate **6** to give a palladium enol π-complex **7**. Compound **7** then undergoes β-hydrogen addition to give the palladium α-hydroxyalkyl species **8**. Finally, the carbonyl product **9** is produced by deprotonation and dissociation (eq 7).

Much debate surrounding the identity of the rate-determining step has focused on whether the hydroxypalladation (**3** → **5**) is the rate-determining step or an equilibrium immediately preceding the rate-determining step (eq 5).[4−12] This is linked to a controversy over whether the attack by the nucleophile on the double bond in step 4 is internal (eq 8) or external (eq 9). The proposed mechanism which has eq 8 as the rate-determining step proceeds via internal nucleophilic attack, while the proposed mechanism which has eq 10 as the rate-determining step specifies a relatively fast thermodynamic external nucleophilic attack preceding the rate-determining step.





Henry proposed a concerted nonpolar four-center transition state[4a] (eq 8) in the rate-determining step, similar to an I_a process.[11b] This mechanism has been described as "a cis attack of coordinated hydroxide upon one of the double bond carbon atoms" [4b] and "a nucleophilic intramolecular attack on the coordinated alkene".[9] Further investigation,[4] using a low concentration of chloride ion, showed that a combination of steric and electronic effects directs the mode of this hydroxypalladation step (eq 8).

In the second mechanism proposed, the hydroxypalladation step (eq 8) is not the rate-determining step but is a reversible procedure involving a relatively rapid external attack of a water molecule upon a carbon atom of the alkene double bond (eq 9).[7a,b] Instead, the loss of a chloride ion Cl^- from the palladium

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Table 1. IPs, HOMOs, LUMOs, and Relative Rates of Palladium Chloride Oxidation of Alkenes

No.	alkene	IP (eV)[a]	HOMO (eV)	LUMO (eV)	k_{rel} $PdCl_2$[b]
1		10.52	-10.17	1.32	897
2		9.74	-9.97	1.12	241
3	OH	9.63[c]	-9.93	1.14	103
4		9.63	-9.94	1.12	100
5	OH	9.52[d]	-9.92	1.18	35.9
6		9.24	-9.80	0.99	44.9[e]
7		9.12	-9.79	0.93	76.9
8		9.12	-9.78	0.93	87.2
9	OH	9.01[f]	-9.75	0.96	22.3

[a] Reference 13a. [b] Reference 4c. [c] Reference 13b. [d] Calculated by applying to the IP for 1-butene a correction factor calculated as the difference between the IPs of 1-propene and 2-propen-1-ol: 9.63 eV − (9.74 eV − 9.63 eV) = 9.52 eV, ref 15. [e] Reference 4d. [f] Calculated by applying to the IP for 2-propen-l-ol a correction factor calculated as the difference between the IPs of 1-propene and *trans*-2-butene: 9.63 eV − (9.74 eV − 9.12 eV) = 9.01 eV; refs 13c and 15.

β-hydroxyalkyl intermediate **5** (eq 10) is proposed to be the rate-determining step of the reaction.[7a,b,10,11] However, data used to formulate these conclusions were obtained from reactions carried out under a high (≃3 M) chloride ion concentration, so these results may apply to a reaction other than that which is the subject of this report.

There may be some confusion surrounding the mechanism of this reaction because many of these reactions were not run under the exact conditions of the Wacker reaction.[3a,b] For example, reactants often had different ligands on palladium[5] or used different nucleophiles;[6] it has been reported[4f] that either of these can change the reaction mechanism. In addition, some studies[7] have been carried out with a much higher concentration of chloride (≃3 M) than is used in the traditional Wacker reaction (<1 M), developed by Smidt and co-workers[3a,b] (while at Wacker Chemie laboratory). Originally, it was assumed[7b] that using a chloride concentration different from that in the original Wacker oxidation would not be likely to change the steric course of the reaction. However, it was recently shown that this higher chloride concentration does indeed change the reaction mechanism, from syn addition at low [Cl^-] to anti addition at high [Cl^-].[4f] Moreover, different products are obtained with the different chloride concentrations.[4f] The relative reactivity data used for our study were obtained under the lower [Cl^-] (<1 M), so the studies[4] pertinent to this investigation are those carried out under analogous reaction conditions, including low chloride ion concentration. Therefore, only those pertinent studies[4] under analogous conditions will be used herein for comparison and analysis.

III. Results

Relative rates[4c,d] for the $PdCl_2$ oxidation of representative alkenes and alkene IPs[12] are shown in Table 1. As in our previous studies,[1] cyclic alkenes and aryl alkenes are omitted in order to avoid effects due to ring strain or conjugation with phenyl; only acyclic alkenes without aryl functionalities are included in this study. HOMOs and LUMOs, also given in Table 1, were calculated as described below.

The plot of the log k_{rel} values for $PdCl_2$ oxidation of alkenes versus their corresponding IPs (Figure 1) reveals a natural grouping of data for monosubstituted and disubstituted alkenes. Lines show a good-to-excellent correlation ($r_{monosubstituted} = 0.99$, $r_{disubstituted} = 0.43$) within each sterically similar group, with a small natural separation between the two lines so formed. The correlation obtained by considering data for all alkenes regardless of degree of substitution is $r_{all} = 0.87$. Within each group of alkenes, the relative reaction rates increase as the IPs increase, giving a line with negative slope. Figure 2 shows similar correlations of log k_{rel} values versus the HOMOs of the corresponding alkenes ($r_{monosubstituted} = 0.92$, $r_{disubstituted} = 0.66$, $r_{all} = 0.85$). Similar to the IP data, within each group of sterically similar alkenes, relative reaction rates increase as the HOMO energies decrease. The negative slopes of the lines in the plots using IP and HOMO values indicate a nucleophilic attack upon the complexed alkene in the rate-determining step. Therefore, we also determined the LUMO energies in order to ascertain whether there was a similar correlation. In Figure 3, a correlation with the alkene LUMOs shows results somewhat more definitive than those obtained with IPs or with the HOMOs ($r_{monosubstituted} = 0.88$, $r_{disubstituted} = 0.60$, $r_{all} = 0.44$). Considering the data from all three plots, the correlations within sterically similar groups are somewhat better than those obtained with all data points regardless of degree of substitution.

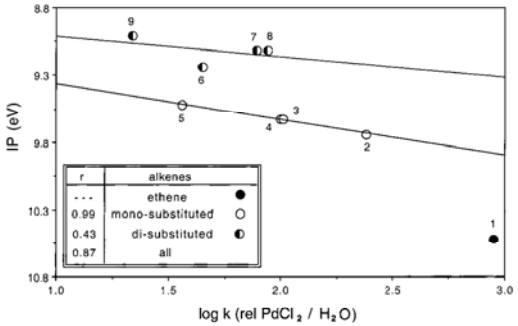


Figure 1. Plot of the log k_{rel} values for $PdCl_2$ oxidation of alkenes versus their corresponding IPs. Data are from Table 1. Lines of correlation for monosubstituted alkenes and for disubstituted alkenes are shown. Correlation coefficients r are given in the legend for monosubstituted alkenes, for disubstituted alkenes, and for all alkenes regardless of the degree of substitution about the double bond. The y-axis IP data are plotted in inverse order so that data reflecting lower π-electron energies appear at the bottom of the plot, to facilitate comparison with the plots of HOMOs and of LUMOs.

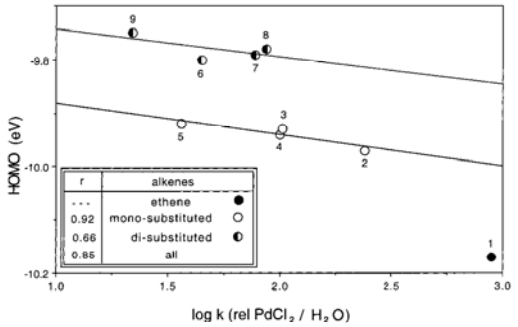


Figure 2. Plot of log k_{rel} vs HOMO analogous to that shown in Figure 1.

IV. Discussion

A. Nucleophilic vs Electrophilic. The lines of correlation in the plots (Figures 1 and 2) show an opposite (negative) slope compared to the results of most of our previous investigations,

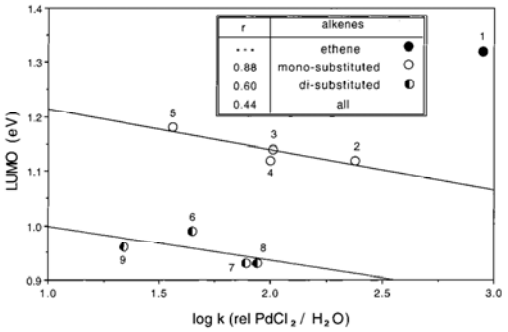


Figure 3. Plot of log k_{rel} values vs LUMO analogous to that shown in Figure 1.

which were of electrophilic reactions with positive slopes, such as bromination,[1a] hydroboration,[1a,g,h] oxymercuration,[1a] diimide reduction,[1b] and chlorination.[1g,h] These results are similar to those found for nucleophilic reactions such as permanganate oxidation[1c] and conversion of the adsorbed form of the alkene on molecular iodine or silver ion to the complexed form,[1h] although the slopes of the lines are smaller for this reaction. The negative slope, reflecting a nucleophilic attack at the alkene carbons, is in agreement with Henry's proposed rate-determining step for the $PdCl_2$ oxidation of alkenes, which invokes attack by OH^- at the complexed alkene. The small magnitude of the slope indicates that the reaction is not as dependent upon IP as other nucleophilic reactions which we have investigated previously.[1c,h] Nevertheless, this is interesting and important since we have not previously found another system which gives plots with multiple lines of negative slope.

The nucleophilicity of the rate-determining step of this reaction is relevant to the recent debate surrounding the mechanism of the $PdCl_2$ oxidation of alkenes,[4−11] i.e., whether the rate-determining step is eq 8[4,8,9] or eq 9.[7a,b,10,11] Henry's most recent mechanistic studies[4f,g] indicate that the rate-determining step is eq 8, the nucleophilic hydroxypalladation step leading from the π-complex. Our results support this conclusion, since the lines in our plots each have a negative slope, characteristic of a nucleophilic reaction.[1c,g]

The other proposed rate-determining step, the dissociation of Cl^- (eq 5), has no direct relation to the π-bond in the alkene. Our results, which indicate a correlation with molecular orbital energies, disfavor that step as the rate-determining step. They are inconsistent with the mechanism proposed by Bäckvall and co-workers, in which the hydroxypalladation is an equilibrium process, and the rate-determining step is loss of chloride from the hydroxypalladation adduct **5** (eq 5). These conclusions, which account for the appearance of the plots for this reaction and for Henry's findings,[4] also fit the patterns which were established by our previous studies.

B. Mechanism of Formation of the C−O Bond. There have been conflicting proposals for the mechanism by which the C−O bond is formed in eq 4 or 4′; some reports propose an internal migration of OH to a carbon of the complexed alkene (eq 4),[4,8,9] and some propose an external attack by H_2O upon a carbon of the complexed alkene (eq 4′).[7a,b,10,11] Our work cannot differentiate between external vs internal attack directly. However, our work does show that the rate-determining step for the reaction with low $[Cl^-]$ is a nucleophilic addition to an alkene, and in the proposed mechanism involving nucleophilic addition to an alkene (eq 8), the C−O bond is formed via internal migration. Conversely, the step involving external attack is proposed to be a rapid equilibrium[7a,b,10,11] (eq 9) preceding a rate-determining step (eq 10), which neither is nucleophilic nor involves the alkene π-electrons. Therefore, our work indirectly supports internal migration of OH to the complexed alkane.

C. Relative Magnitudes of Steric versus Electronic Effects. Additional patterns drawn from our previous studies of additions to alkenes can be used for comparison to help differentiate between eqs 8 and 10 as the rate-determining step for the palladium chloride oxidation of alkenes. In previous studies of single-step reactions leading to three-center products or reactions involving three-center intermediates, we often find two types of plots of log k_{rel} values vs alkene IPs. Type 1: If the rate-determining step leads *to* a three-center intermediate or product, a correlation involving all alkenes regardless of steric effects is indicated by a single line of correlation in the analogous plot of log k_{rel} vs IP or HOMO.[1] Type 2: If the rate-determining step leads *from* a three-center π-complex, then plotted data appear in groups dependent upon the steric requirements of the alkenes.[1d]

Since plotted data for palladium chloride oxidation of alkenes appear in groups dependent upon the steric requirements of the alkenes, these results support a reaction mechanism[4] more similar to the type 2 mechanism, with the rate-determining step leading *from* the π-complex, as depicted in eq 8. A correlation with all alkenes regardless of steric effects would favor formation of a π-complex, similar to the reaction shown in eq 2, as the rate-determining step of this reaction. The natural separation into two sterically similar groups supports the postulation that the rate-determining step of this reaction is dependent upon both steric and electronic effects. These conclusions, regarding the rate-determining step and the steric and electronic effects upon it, are similar to those reported by Henry et al.[4c,f]

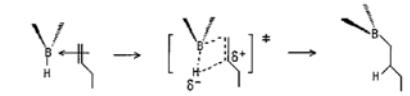
The log k_{rel} values for substituted alkenes **6**−**9** are faster than would be predicted on the basis of IP alone. Because the IP reflects the electronic but not the steric effects of the substituents, the steric effects in palladium chloride oxidation may be responsible for the reaction rate being different than would have been expected solely on the basis of the IP. If this is the case, then the steric effects of the substituents on the double bond carbon atoms do not decelerate the decomposition of the Pd(II) β-hydroxyalkyl, but accelerate it. The steric effects of the alkenes might be expected to affect the rate of the hydroxypalladation step (eq 8), since the Pd(II) group complexed to the alkene is quite large and could therefore create steric congestion. Steric acceleration in the rearrangement from the π-complex would occur when the complex is more sterically congested than the transition state structure which follows. A similar analysis of hydroboration or of oxymercuration reveals steric deceleration, which indicates a transition from a less to a more sterically hindered structure. This might indicate that the π-complex in hydroboration is looser and less sterically congested (eqs 10 and 11).[14]

(13) (a) Masclet, P.; Grosjean, D.; Mouvier, G.; Dubois, J. *J. Electron Spectrosc. Relat. Phenom.* **1973**, *2*, 225−237. (b) Katrib, A.; Rabalais, J. W. *J. Phys. Chem.* **1973**, *77*, 2358−2363. (c) Klasnic, L.; Ruscic, B.; Sabljie, A.; Trinajstic, N. *J. Am. Chem. Soc.* **1979**, *101*, 7477−7482.

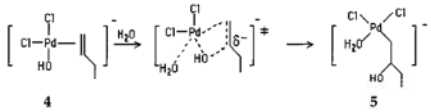
(14) (a) Brown, H. C. *Hydroboration*; W. A. Benjamin, Inc.: New York, 1962; p 13. (b) Dewar, M. J. S.; McKee, M. L. *Inorg. Chem.* **1978**, *17*, 1075−1082. (c) Sundberg, K. R.; Graham, G. D.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1979**, *101*, 2863−2869. (d) Nagase, S.; Ray, N. K.; Morokuma, K. *J. Am. Chem. Soc.* **1980**, *102*, 4536−4537. (e) Clark, T.; Schleyer, P.v. R. *J. Organomet. Chem.* **1978**, *156*, 191−202. (f) Dasgupta, S.; Datta, M. K.; Datta, R. *Tetrahedron Lett.* **1978**, *15*, 1309−1312. (g) Seyferth, D. *Prog. Inorg. Chem.* **1962**, *3*, 210. (h) Streitwieser, A. J.; Verbit, L.; Bittman, R. *J. Org. Chem.* **1967**, *32*, 1530−1532.

D. Compare and Contrast Similar Reactions. The $PdCl_2$ reaction has similarities to and differences from hydroboration and oxymercuration: (1) The plot for each shows a separation into groups of sterically similar alkenes, with each group dependent upon the steric requirements of the alkenes. (2) Increased substitution on the alkene causes a rate decrease in all three reactions. (3) The slopes of the lines in the plots are negative in $PdCl_2$ oxidation but positive in hydroboration and oxymercuration. (4) In each reaction, the π-electrons are complexed to the metal via a dative bond which changes to a formal σ bond through the transition state. (5) A four-center transition state in the rate-determining step preceded by a three-center π-complex has been proposed for each reaction.[1,4a,14] (6) However, palladium chloride oxidation demonstrates effects consistent with steric acceleration in rearrangement from the π-complex while hydroboration and oxymercuration results are consistent with steric deceleration.

The similarities suggest that the steric and electronic requirements of the internal migration could be analogous to those of hydroboration (eqs 10 and 11), and those of the external attack could be analogous to oxymercuration (eqs 12 and 13). The following comparison between the mechanisms involving four-center transition states in palladium chloride oxidation proposed originally by Henry (eq 11),[4a] and in hydroboration proposed originally by Brown (eq 10),[14a] is striking.[16]



(10)



(11)

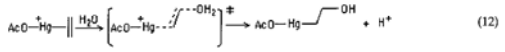
4 5

The external attack mechanism in $PdCl_2$ oxidation (eq 13) is also similar to that in oxymercuration (12), except that eq 12 is proposed to be the rate-determining step in oxymercuration, while eq 13 is *not* proposed to be the rate-determining step in $PdCl_2$ oxidation.

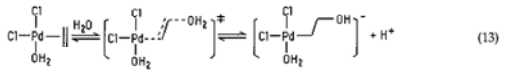
However, comparing eqs 12 and 13 is not warranted for at least three reasons: (1) the reaction shown in eq 13 is not proposed as a rate-determining step, (2) the rate-determining step in the proposed mechanism which includes step 13 is not a nucleophilic process, and (3) the mechanism by which the C−O bond is formed in eq 4 has been determined recently by Henry to be internal attack in the presence of low [Cl^-] and external attack with high [Cl^-].[4f] This conclusion fits nicely our results for this reaction using low [Cl^-] as well as analogies with other reactions predicted from the patterns determined in our previous studies.

(15) Yamazaki, T.; Kimura, K. *Bull. Chem. Soc. Jpn.* **1975**, *48,* 1602−1607.

(16) A reviewer noted that a similar unsymmetrical transition state has been previously proposed for nucleophilic attack upon olefins complexed to other transition metals: (a) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1981**, *103,* 4308−4320. (b) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102,* 6148−6149.

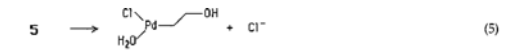


(12)



(13)

3 5



(5)

6

The electrophilic nature of the electronic effects in hydroboration and in oxymercuration manifests itself as a slope opposite to that for oxidation by using palladium chloride, a nucleophilic reaction. However, a linear relationship of the electronic effects is apparently intact in all three reactions.

V. Theoretical Procedure

The HOMOs and LUMOs of the alkenes were calculated by using MNDO in the same manner as reported previously.[1a] In each case, the eigenvectors were examined to ensure that the HOMO and LUMO correspond to the carbon−carbon π- and π^*-orbitals, respectively. The HOMOs for the allylic alcohols each pertain to the geometry having the O−C−C=C dihedral angle equal to 0°. We found that these geometries yield the lowest-magnitude HOMO values for the allylic alcohols and give the best correlation with log k_{rel} values. For some allylic alcohols having both HOMO and IP data available, the use of HOMO values for other conformers was explored; these data were not used because the correlation between HOMO and IP values was diminished in those cases.

VI. Conclusion

Plots of log k_{rel} values vs IPs, vs HOMOs, and vs LUMOs reveal multiple nearly parallel lines of correlation with negative slopes in each, indicating that the rate-determining step of this reaction is a nucleophilic process. Although the present results cannot distinguish between anti and syn additions, they do indicate that the rate-determining step is a nucleophilic addition. This result is consistent with the mechanism proposed by Henry in which the rate-determining step is nucleophilic hydroxypalladation. It is inconsistent with the mechanism proposed by Bäckvall and co-workers, in which the hydroxypalladation is a rapid equilibrium and the rate-determining step is loss of chloride from the hydroxypalladation adduct. Comparison of the plots for $PdCl_2$ oxidation versus those for hydroboration and for oxymercuration, combined with consideration of the two mechanisms proposed for $PdCl_2$ oxidation, indicates that the mechanism for $PdCl_2$ oxidation of alkenes at low [Cl^-] has similarities to that for hydroboration. The method of analysis reported herein also provides a simple way to predict relative reactivities of functionalized alkenes for synthetic purposes, based on the electronic and steric characteristics of the substituents.

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Using Correlations to Compare Additions to Alkenes: Homogeneous Hydrogenation by Using Wilkinson's Catalyst

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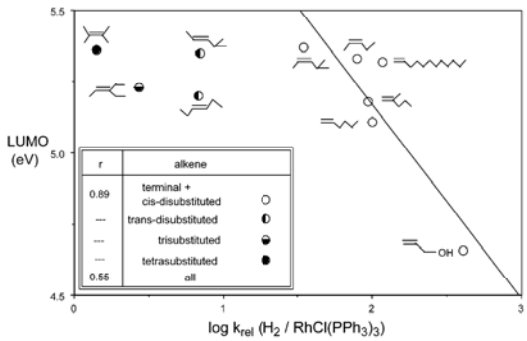

Plots of the logarithms of relative rates of homogeneous catalytic hydrogenation of alkenes (log k_{rel} values) by using Wilkinson's catalyst versus their ionization potentials (IPs) and versus their lowest unoccupied molecular orbital energy levels (LUMOs) display good-to-excellent correlations. The correlations indicate that the rate-determining step of this reaction is a nucleophilic addition to the alkene double bond, which is dependent upon both electronic effects and steric effects. This conclusion is in agreement with only two of three previously proposed mechanisms for the reaction, effectively ruling out one in which the rate-determining step involves electrophilic addition to the alkene. Characteristics of the analysis using these correlations are compared and contrasted with other additions to alkenes, such as the Wacker oxidation, to probe patterns in transition state characteristics.

Introduction

In this study, we apply to homogeneous catalytic hydrogenation by using Wilkinson's catalyst a relatively new technique that can reveal mechanistic similarities of alkene addition reactions by comparing their correlation plots. This simple method[1a−h] ascertains the relative importance of electronic and steric effects in addition reactions of alkenes by correlating logarithms of relative reaction rates (log k_{rel} values) versus the alkene ionization potentials (IPs), versus their highest occupied molecular orbital energy levels (HOMOs), and sometimes versus their lowest unoccupied molecular orbital energy levels (LUMOs). This technique provides synthetically useful information about the selectivity of a reaction toward

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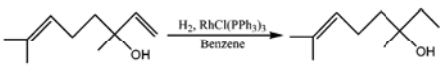
different types of alkene π bonds.[1a−h] In some cases, it has enabled mechanism selection from a group of proposed mechanisms. Examples of reactions of alkenes in which this was done are (1) classifying the mechanism of oxymercuration as being similar to hydroboration rather than bromination,[1b] (2) analyzing the three-membered cyclic intermediate (or product) mechanism in alkene bromination, arylsulfenyl chloride addition, oxidation via peracetic acid, and dichlorocarbene addition versus the four-membered cyclic intermediate mechanism in nitrosyl chloride addition,[1a,e] (3) selecting one of two proposed mechanisms for oxidation by using palladium chloride,[1g] and (4) supporting a 2 + 3 cycloaddition mechanism but disfavoring the 2 + 2 cycloaddition mechanism for alkene oxidation by chromyl chloride, by chromic acid, and by osmium tetroxide.[1h] In each study, we used the rationale that reactions with similar mechanisms give correlation plots that are similar in appearance. It is desirable to investigate similarly more reactions of mechanistic and synthetic importance, not only to gather additional information about the reactions but also to explore further the application of this analysis technique. Therefore, we report the application of this technique to the homogeneous catalytic hydrogenation of alkenes by using Wilkinson's catalyst, as a result of the interest in its mechanism[2−5] and its synthetic[6a−f] and industrial[6g,h] importance.

Background

Homogeneous catalytic hydrogenation of alkenes in the presence of Wilkinson's catalyst $RhCl(PPh_3)_3$, developed in 1965 by Wilkinson and co-workers,[7] is a widely studied[2−7] homogeneous catalytic hydrogenation method used in organic synthesis[6a−f] and reported to be industrially important.[6g,h] Using modifications of Wilkinson's catalyst, homogeneous asymmetric hydrogenation reactions, catalyzed by rhodium diphosphine chiral complexes, were developed later by Knowles[8a−c] and Noyori.[8d,e] This synthetic method enabled the production of a single predicted enantiomer, of great significance in the syntheses of pharmaceutical products.[3g,4b,c,8] One early industrial scale synthetic application was synthesis of L-DOPA, which is useful in the treatment of Parkinson's disease and which is produced by enantioselective hydrogenation of an α-amino acid catalyzed by a rhodium complex containing the chiral diphosphine ligand DiPAMP.[8c] A wide range of similar catalysts has been applied widely in industrial syntheses of drugs and other materials.[3g,4b,c,8]

The basic reaction (eq 1) shows sensitive selectivity to different alkene double bonds with different substituents on it[6a,e,f] and can be easily carried out under mild reaction conditions (room temperature and atmospheric pressure of H_2).[6a−c]



96.5% (1)

Several different reaction mechanisms[3a−f,4a,5] have been proposed for this homogeneous hydrogenation catalytic cycle, but the "hydride route" (as opposed to the "alkene route"[6a] or "substrate route"[2h]) is believed to be the predominant pathway.[6a] Three proposed hydride route mechanisms of this reaction are shown in Schemes 1−3.

There are five steps in the reaction sequence in Scheme 1:[3b−f] (1) PPh_3 ligand dissociation **1** ⇌ **2**; (2) hydrogen oxidative addition **2** ⇌ **3**; (3) alkene coordination **3** ⇌ **4**; (4) alkene migratory insertion into the Rh−H bond **4** → **5**; and (5) alkyl reductive elimination **5** → **2**. In this mechanism, the alkene insertion **4** → **5** is considered to be the rate-determining step,[3a−f] and the key intermediate is **4**, an octahedral dihydride alkene complex $RhH_2Cl(alkene)(PPh_3)_2$. All other steps are fast relative to the alkene insertion **4** → **5**.[2c−e,3a−f] Positions occupied by S (S = solvent) in **2**, **3**, **5** are considered to be either vacant or coordinated to a solvent molecule.[3b] Some later

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(3) (a) Halpern, J.; Wong, C. S. *J. Chem. Soc., Chem. Commun.* **1973**, *17*, 629−630. (b) Halpern, J.; Okamoto, T.; Zakhariev, A. *J. Mol. Catal. A* **1976**, *2*, 65−68. (c) Halpern, J. *Inorg. Chim. Acta* **1981**, *50*, 11−19. (d) Halpern, J.; Okamoto, T. *Inorg. Chim. Acta* **1984**, *89*, L53-L54. (e) Halpern, J. In *Organotransition-Metal Chemistry*; Ishii, Y., Tsutsui, M., Eds.; Plenum: New York, 1975; pp 109−117. (f) Halpern, J. *Trans. Am. Crystallogr. Assoc.* **1978**, *14*, 59−70. (g) Halpern, J. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; Vol. 5, pp 41−69.

(4) (a) Brown, J. M.; Evans, P. L.; Lucy, A. R. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1589−1596. (b) Brown, J. M.; Evans, P. L. *Tetrahedron* **1988**, *44*, 4905−4916. (c) Brown, J. M. *Chem. Soc. Rev.* **1993**, *22*, 25−41.

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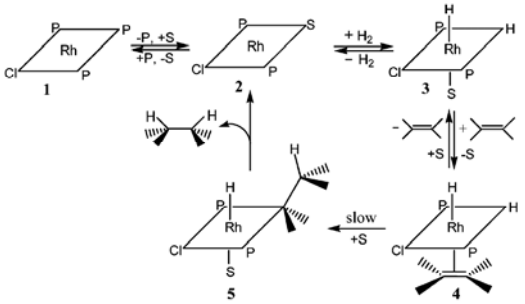
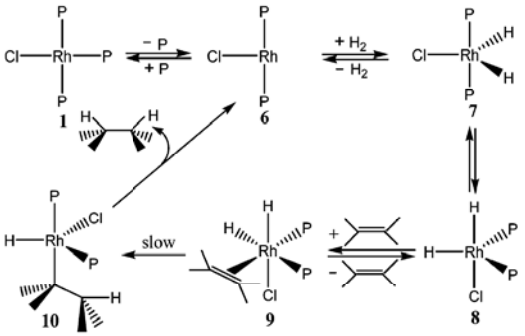
(7) (a) Young, J. F.; Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *J. Chem. Soc., Chem. Commun.* **1965**, *7*, 131−132. (b) Osborn, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711−1732. (c) Lawson, D. N.; Osborn, J. A.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1733−1736. (d) Jardine, F. H.; Osborn, J. A.; Wilkinson, G. *J. Chem. Soc. A* **1967**, 1574−1578. (e) Montelatici, S.; van der Ent, A.; Osborn, J. A.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 1054−1058.

(8) (a) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 5946−5952. (b) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 2567−2568. (c) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106−112. (d) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932−7934. (e) Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629−631.

SCHEME 1. First Hydride Route Mechanism Proposed for Hydrogenation of Alkenes by Using Wilkinson's Catalyst[3b−f] (P = PPh_3 and S = Benzene as Solvent)



SCHEME 2. Second Hydride Route Mechanism with Isomerization, Proposed for Hydrogenation of Alkenes by Using Wilkinson's Catalyst[4a] (P = PPh_3).

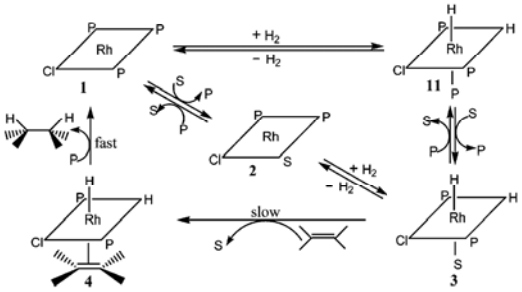


studies[6a,9a] tend to support the idea that a solvent molecule is associated with the Rh center at each of those positions.

A second hydride route mechanism[4a] differs slightly regarding (a) the structures of the key intermediates (**9** in Scheme 2 versus **4** in Scheme 1) and (b) the involvement of the solvent molecules because no solvent molecule is involved in this proposed mechanism. In this alternative, an isomerization (**7** ⇄ **8**) precedes the formation of a key intermediate **9**, which possesses *cis* biphosphine ligands. All of these first four steps (**1** ⇄ **6**, **6** ⇄ **7**, **7** ⇄ **8**, and **8** ⇄ **9**) are considered to be fast equilibria.[4a] Then, the rate-determining alkene insertion (**9** → **10**) is followed by a fast alkyl reductive elimination (**10** → **6**) to regenerate **6**.[4a,6h]

In an ab initio computational mechanistic investigation[9a,b] of the Scheme 1 pathway, the potential energy profile for the full catalytic cycle of alkene hydrogenation by Wilkinson's catalyst was studied. The geometries of the transition states as well as of the intermediates were determined at the RHF/ECP level by using a variety of basis sets, for each step of the reaction cycle. It was found that the alkene insertion step has the highest energy barrier in the full catalytic cycle of this reaction, predicting it to be the rate-determining step of this reaction. This conclusion is consistent with both mechanisms shown in Schemes 1 and 2.[3a−f,4a]

SCHEME 3. Third Hydride Route Mechanism[5] (P = PPh_3, S = Benzene as Solvent)[a]



[a] Stereochemistry was not specified and is given solely to facilitate comparison with structures in Schemes 1 and 2.

A third hydride route mechanism[5] (Scheme 3) was proposed on the basis of kinetic analyses indicating that a solvent molecule S (S = benzene) is involved in the catalytic sequence and that the rate-determining step, which is preceded by four fast complexation equilibria[5] in two different routes, is formation of the 6-coordinate intermediate **4**. Then, this 6-coordinate intermediate **4** undergoes a fast decomposition to yield the alkane product and to regenerate Wilkinson's catalyst **1**.[5]

Another totally different mechanism for alkene hydrogenation in the presence of Wilkinson's catalyst and various Lewis acids, such as $AlCl_3$, BF_3, $AlPh_3$, etc., has been proposed.[2f] However, the reaction conditions used in that study[2f] are so different from those discussed above[3a−f,4b,5] that this may constitute a different reaction, and a mechanistic comparison is probably invalid.

Results and Discussion

A. Correlation Patterns Probe Addition Reaction Mechanisms. Information about electronic and steric effects is revealed from the plots of log k_{rel} values versus IPs. The IP is an appropriate comparator because it is a measure of the amount of energy required to remove an electron from the π bond and because it is independent of steric effects. Most of our previously studied reactions gave good-to-excellent correlations with positive slopes;[1a−c,e,f,h] some of the resulting plots each had a single line of correlation,[1a,b,e,f,h] and some each had nearly-parallel lines of correlation.[1a−c,f]

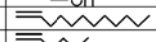
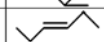
In this way, these correlation plots gave information about steric effects in the reactions. Reactions of alkenes (such as bromination,[1b,f] epoxidation,[1a] carbene addition,[1e] oxidation by chromyl chloride and by chromic acid,[1h] etc.) that lack significant steric effects display in their plots of log k_{rel} values versus IPs a single correlation line consisting of all alkenes, regardless of degree of substitu-

(9) (a) Daniel, C.; Koga, N.; Han, J.; Fu, X. Y.; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 3773−3787. (b) Koga, N.; Daniel, C.; Han, J.; Fu, X. Y.; Morokuma, K. *J. Am. Chem. Soc.* **1987**, *109*, 3455−3456. (c) Hornback, J. M. *Organic Chemistry*; Brooks/Cole: New York, 1998; p 259. (d) Connors, K. A. *Chemical Kinetics*; VCH: New York, 1990; p 223.

(10) (a) Dewar, M. J. S.; McKee, M. L. *Inorg. Chem.* **1978**, *17*, 1075−1082. (b) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4907−4917.

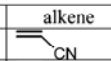
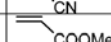
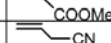
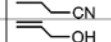
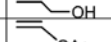
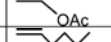
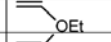
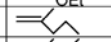
(11) Nelson, D.; Dewar, M. J. S.; Buschek, J. M.; McCarthy, E. *J. Org. Chem.* **1979**, *44*, 4109−4113.

TABLE 1. IPs(eV), LUMOs(eV), and Relative Rates of Catalytic Hydrogenation of Alkenes by Using Wilkinson's Catalyst, $RhCl(PPh_3)_3$

No.	alkene	IP[a]	LUMO	k_{rel}[b]
1		10.16[c]	4.66	410[d]
2		9.59[e]	5.32	117.9
3		9.48	5.11	100
4		9.08	5.18	93.1
5		9.04	5.33	79.3
6		8.98	5.37	34.5
7		8.97	5.35	6.9
8		8.97	5.20	6.8[d]
9		8.57[f]	5.23	2.7[d]
10		8.27	5.36	1.4[d]

[a] Reference 13a, unless otherwise noted. [b] References 7d, 12a. [c] Reference 13b. [d] Reference 7d; converted to relative rates from rates of H_2 consumption. [e] Reference 13c. [f] Reference 13d.

TABLE 2. IPs(eV), LUMOs(eV), and Relative Rates of Catalytic Hydrogenation of Alkenes by Using Wilkinson's Catalyst, $RhCl(PPh_3)_3$

No.	alkene	IP[a]	LUMO	k_{rel}[b]
11		10.91[c]	2.80	1470
12		10.72[c]	3.15	350
13		10.18[d]	4.22	490
14		10.16[e]	4.66	340
15		9.85[c]	4.47	160
16		9.48	5.11	100
17		9.15[f]	5.51	180
18		9.08	5.18	69
19		8.91	5.00	41
20		8.84	5.32	54
21		8.83	5.31	17

[a] Reference 13a, unless otherwise noted. [b] Reference 12b. [c] Reference 13f. [d] Reference 13g. [e] Reference 13b. [f] Reference 13h.

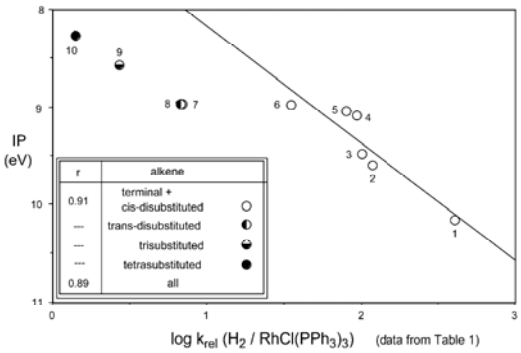


FIGURE 1. Plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene IPs. Data used for this plot are given in Table 1. Correlation coefficients (r values) are given in the legend for terminal alkenes + *cis*-disubstituted alkenes and for all alkenes regardless of the degree of substitution about the double bond. The correlation line in this plot refers to terminal alkenes and *cis*-disubstituted alkenes only. The *y*-axis IP data are plotted in inverse order to facilitate comparison with previous works.

tion. Reactions of alkenes with significant steric effects (such as hydroboration,[1b] oxymercuration,[1b] silver ion complexation,[1a] diimide addition,[1c] etc.) give plots with multiple lines of correlation.

However, for the reaction of alkenes with $PdCl_2/H_2O$,[1g] we found multiple lines with negative slopes in the plots of alkene IP versus log k_{rel} value. The lines indicated a good-to-excellent correlation. Initially, in this nucleophilic addition, we planned to explore a correlation between log k_{rel} values and alkene electron affinities (EAs), but EAs are not readily available for a large selection of alkenes. However, calculated alkene LUMOs are good estimates for experimental EA values[10,11] if a suitable computational method is selected. Therefore, using a selection of computational methods, we examined the correlation of calculated alkene LUMOs versus experimental alkene EAs and used the method (6-31G*) that gave the best agreement.[1i]

Previous studies indicated that reactions with similar rate-determining transition-state structures yield correlation plots that have similar slopes and numbers of lines. Reactions that have different rate-determining transition-state structures usually yield different types of correlation plots, but this is not necessarily the case. As clarification, if different types of plots are obtained, then rate-determining transition states in the reactions concerned must have significant differences; however, similar correlation plots do not necessarily indicate similar rate-determining transition-state structures.

B. Correlation in Hydrogenation of Alkenes by Using Wilkinson's Catalyst. Relative reaction rates[7d,12a,b] for homogeneous hydrogenation of alkenes in the presence of Wilkinson's catalyst, alkene IPs,[13a–h] and alkene LUMOs are given in Tables 1 and 2. As was done previously,[1] cyclic alkenes and aryl alkenes are excluded here in order to avoid complications due to ring strain or conjugation with phenyl.

The plots in Figures 1–4 show good-to-excellent[14] correlations of log k_{rel} values versus alkene IPs and versus alkene LUMOs for the terminal alkenes and *cis*-disubstituted alkenes. However, the data points for alkenes with different steric requirements, such as *trans*-disubstituted, trisubstituted, and tetrasubstituted alkenes, are deviant from the correlation lines, which indicates that the rate-determining step of homogeneous

(12) (a) James, B. R. *Homogeneous Hydrogenation*; John Wiley & Sons: New York, 1973; pp 198–287. Allyl cyanide is not included in the plot because its data point falls far from the correlation line, probably as a result of the interaction of the cyanide group and the Rh metal center of the catalyst. (b) Candlin, J. P.; Oldham, A. R. *Discuss. Faraday Soc.* **1968**, *46*, 60–71.

(13) (a) Masclet, P.; Grosjean, D.; Mouvier, G.; Dubois, J. *J. Electron Spectrosc. Relat. Phenom.* **1973**, *2*, 225–237. (b) Katrib, A.; Rabalais, J. W. *J. Phys. Chem.* **1973**, *77*, 2358–2363. (c) Calculated by applying to the IP for 1-decene, a correction factor calculated as the difference between the IPs of 1-decene and 1-octene: 9.51 + (9.51 − 9.43) = 9.59 eV; ref 13e. (d) Calculated by applying to the IP for 3-ethyl-3-hexene, a correction factor calculated as the difference between the IPs of *cis*-2-pentene and *cis*-3-hexene: 8.48 + (9.04 − 8.95) = 8.57 eV; ref 13a. (e) Hiraoka K. *J. Phys. Chem.* **1981**, *85*, 4008–4015. (f) Houk, K. N.; Munchausen, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 937–946. (g) Willett, G. D.; Baer, T. *J. Am. Chem. Soc.* **1980**, *102*, 6774–6779. (h) Friege, H.; Klessinger, M. *J. Chem. Res., Synop.* **1977**, 208–209.

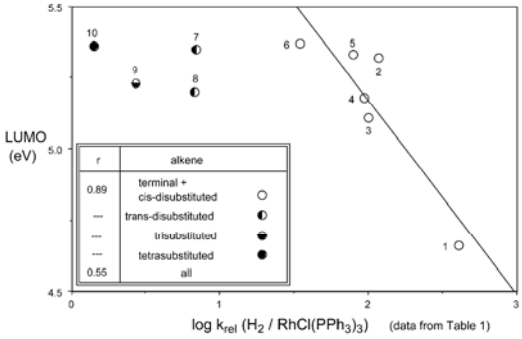


FIGURE 2. Plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene LUMOs. Data used for this plot are given in Table 1. The correlation line in this plot refers to terminal alkenes and *cis*-disubstituted alkenes only.

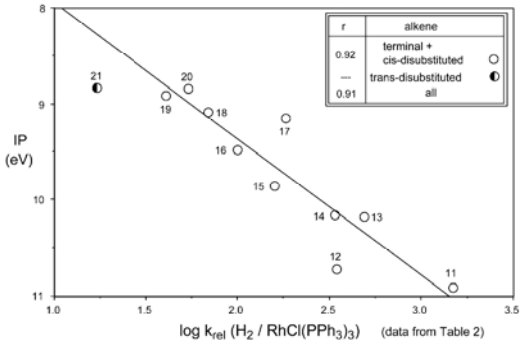


FIGURE 3. Plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene IPs. Data used for this plot are given in Table 2. The correlation line in the above plot refers to terminal alkenes and *cis*-disubstituted alkenes only.

hydrogenation of alkenes in the presence of Wilkinson's catalyst is dependent upon both steric effects and electronic effects. The correlation line in each plot of Figures 1−4 is for terminal alkenes and *cis*-disubstituted alkenes that have similar steric requirements in this reaction, but not for all alkenes regardless of the degree of substitution of the alkene double bonds. Although in some plots it seems that the plot with all alkenes gives just as good results as the plot with terminal + *cis*-disubstituted alkenes, this is not the case for all figures. However, the plot with terminal alkenes + *cis*-disubstituted alkenes gives at least "good"[14] correlation in each case.

C. Nucleophilic versus Electrophilic Characteristics. The negative slopes of the plots in Figures 1−4 agree with previous findings[15a−d] that the rate-determining step in this reaction is a nucleophilic process, with a

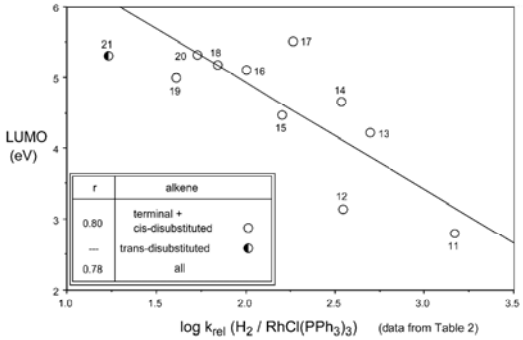


FIGURE 4. Plot of the log k_{rel} values for homogeneous hydrogenation of alkenes by using Wilkinson's catalyst versus corresponding alkene LUMOs. Data used for this plot are given in Table 2. The correlation line in the above plot refers to terminal alkenes and *cis*-disubstituted alkenes only.

higher IP or lower LUMO corresponding to a higher relative reaction rate. The slopes in the plots are opposite to those in most of our previous investigations[1a−h] which explored electrophilic additions. However, the correlation in this reaction is similar to that of $PdCl_2$ oxidation (multiple lines with negative slopes),[1g] which is also a nucleophilic addition reaction.

The conclusion that the rate-determining step in homogeneous catalytic hydrogenation involves nucleophilic attack on the alkene is consistent with both the first and the second proposed mechanisms (Schemes 1 and 2).[3b−f,4a] These mechanisms have virtually identical rate-determining steps, each proposed to be an intramolecular alkene insertion (**4** → **5** in Scheme 1 and **9** → **10** in Scheme 2). The structural changes during the insertion have been described[6a] as a symmetrical alkene η^2-coordination, shifting to a η^1-coordinated species, and picking up the hydride from the metal at its uncoordinated carbon. The proposed rate-determining step is a nucleophilic addition,[6b,d] which our results support.

However, the above conclusion disfavors the third proposed mechanism (Scheme 3),[5] in which alkene complexation (**3** → **4** in Scheme 3) is predicted to be the rate-determining step. In this step, the alkene displaces benzene and coordinates to the Rh center, which constitutes an electrophilic attack of Rh on the alkene; our results, which indicate a rate-determining nucleophilic attack on the alkene, are at odds with this proposed mechanism.

D. Comparison with Other Similar Addition Reactions. The catalytic hydrogenation of alkenes by using Wilkinson's catalyst has similarities to and differences from the $PdCl_2$ oxidation of alkenes (the Wacker reaction): (1) the slopes of the lines in the log k_{rel} versus IP and log k_{rel} versus LUMO plots of both reactions are negative, which indicates that both reactions are nucleophilic addition reactions; (2) the rate-determining steps in Scheme 1[3b,c] and Scheme 2[4a] are both alkene insertion processes similar to that for $PdCl_2$ oxidation;[16a−c] (3) the rate-determining steps in catalytic hydrogenation in the presence of Wilkinson's catalyst (eq 2) and in the Wacker

(14) Rowntree, D. *Statistics Without Tears*; Scribner: New York, 1981; p 170.

(15) (a) Burger, B. J.; Santarsiero, B. D.; Trimmer, M. S.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 3134−3146. (b) Doherty, N. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 2670−2682. (c) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102*, 6148−6149. (d) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4308−4320.

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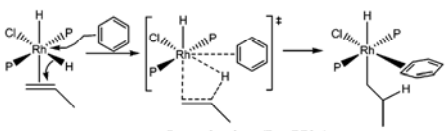
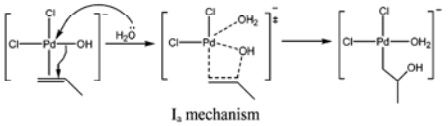
oxidation (eq 3) have been proposed to involve similar four-center transition states; (4) data points in plots for





$PdCl_2$ oxidation[1g] separate naturally into different sterically similar alkene groups, as do those in the plot for alkene hydrogenation, although some differences still exist between them; and (5) geminal and vicinal cis disubstituted alkenes fall into the same sterically similar group as the monosubstituted alkenes in hydrogenation (Figures 1−4), whereas all disubstituted alkenes fall into a different group in $PdCl_2$ oxidation,[1g] which implies greater steric effects in the latter for reasons that cannot be specified.

The display of similar electronic effects in the two reactions is not surprising. Rh and Pd might be expected to form organic derivatives that have similar such characteristics, based on their joint membership in the second triad of groups 9 and 10; they are both "platinum metals".[17] Similar nucleophilic characteristics in both reactions could be rationalized by the nucleophilic attacks upon one carbon atom of the alkene double bonds by hydride in the hydrogenation and by hydroxide in the Wacker reaction.

The different steric effects in the two reactions could be derived from steric congestion at an alkene carbon, from steric congestion about the central metal, or from other sources. Several explanations for the differing steric effects in the transition states of the two reactions can be offered:

(A) The different sizes of the groups migrating to the alkene carbon must be considered; OH is larger than H, so its migration might be expected to cause greater steric congestion at the alkene carbon in that reaction, as observed.

(B) The different sizes of the solvent molecules entering as ligands are significant. An entering benzene ligand might be expected to cause more congestion than an entering H_2O ligand (eqs 2 and 3). However, this is inconsistent with lower steric effects in the Wilkinson reduction than in the Wacker Reaction, so the entering solvent does not produce the observed steric effect in these reactions. This supports the practice of omitting solvent from mechanistic schemes drawn for this reaction, often done by Halpern[3] and by Brown.[4]

(C) The smaller steric effect despite a larger entering solvent ligand in alkene hydrogenation (eq 2) than in the Wacker reaction (eq 3), might also be explained by the former being an I_d (dissociative interchange[18]) process of an octahedral complex and the latter being an I_a (associative interchange[18]) process of a square planar complex. The designations "I_d process" and "I_a process" follow the generalized nomenclature for mechanisms of ligand exchange;[18] an I_d process has both the entering and leaving ligands more dissociated and farther apart than in an I_a process as depicted in eqs 2 and 3. Although we have no experimental measurements to compare distances between the metals and entering ligands in the transition-state structures, there are some data available for similar ground-state molecules. Studies show that the average distance between Rh and the two coordinated benzene carbons in the product [Rh(η-C_5H_5){β,α,1,2-η-$C_6H_5C(Ph)=CH_2$] is about 2.21 Å,[19a] which is greater than the distance (2.10 Å) between Pd and O in the product $[Pd(C_2H_4OH)(H_2O)Cl_2]$.[19b,c]

(D) However, the calculated bond lengths of Pd−Cl and Pd−C are 2.30 and 2.20 Å,[19b] respectively, in the four-membered transition state of the rate-determining insertion of $[PdCl_2H(C_2H_4)]^-$, and the calculated bond lengths of Rh−Cl and Rh−C are 2.30 and 2.21 Å,[9a] respectively, in the four-membered transition state of the rate-determining insertion of $[RhCl(PH_3)_2(C_2H_4)H_2]$. These are almost identical and, therefore, would lead one to predict similar steric effects in the transition-state structures in these two reactions.

(E) A theoretical calculation[19d] predicts the Rh−C bond strength in Rh−C_2H_5 of 50.3 kcal/mol, which is higher than that of Pd−C in Pd−C_2H_5 (40.9 kcal/mol). The stronger developing Rh−C bond in the transition state structure might cause the alkene migratory insertion transition state in catalytic hydrogenation to be later with somewhat less steric effects than in the Wacker oxidation.

(F) Calculations[9a] have predicted a late transition state for the hydrogenation of alkenes catalyzed by Wilkinson's catalyst, which is consistent with the prediction that the rate-determining step of this reaction is an endergonic process.[9c,d] A late transition state, in which only one carbon is significantly bonded to Rh and the Rh−H bond is nearly broken, could explain the reduced steric effects. In this case, electronic effects would also not be significant, because little distortable π electron density would remain in the transition state structure. This would agree with the correlation plot, i.e., closely spaced multiple lines with small slopes. Thus, a later transition state in alkene hydrogenation by using Wilkinson's catalyst than in the Wacker oxidation might also contribute to slightly smaller steric effects in the former.

It should be added that rates of catalytic reactions may not represent only the barrier of the rate-determining step, as has been assumed in the above discussion; they can be a more complex mixture, driven by the distribution of catalyst among active and inactive species. However, in this case, excellent correlations are obtained, suggesting that here a factor other than catalyst distribution prevails.

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Conclusion

Negative slopes of correlation lines in the plots of log k_{rel} values versus IPs and versus LUMOs are obtained for hydrogenation of alkenes by using Wilkinson's catalyst. This supports previous findings that the rate-determining step of this reaction is a nucleophilic alkene addition. The multiple lines in each plot indicate that the reaction is dependent upon both electronic effects and steric effects in its rate-determining step. The method of analysis employed in this study demonstrates a simple way to predict relative reactivities of functionalized alkenes based on electronic and steric characteristics of the alkene substituents; this information will be useful in designing syntheses requiring selective reaction of one alkene functionality in the presence of another.

Acknowledgment. We are grateful to the John Simone Guggenheim Foundation and the National Science Foundation for support of this research.

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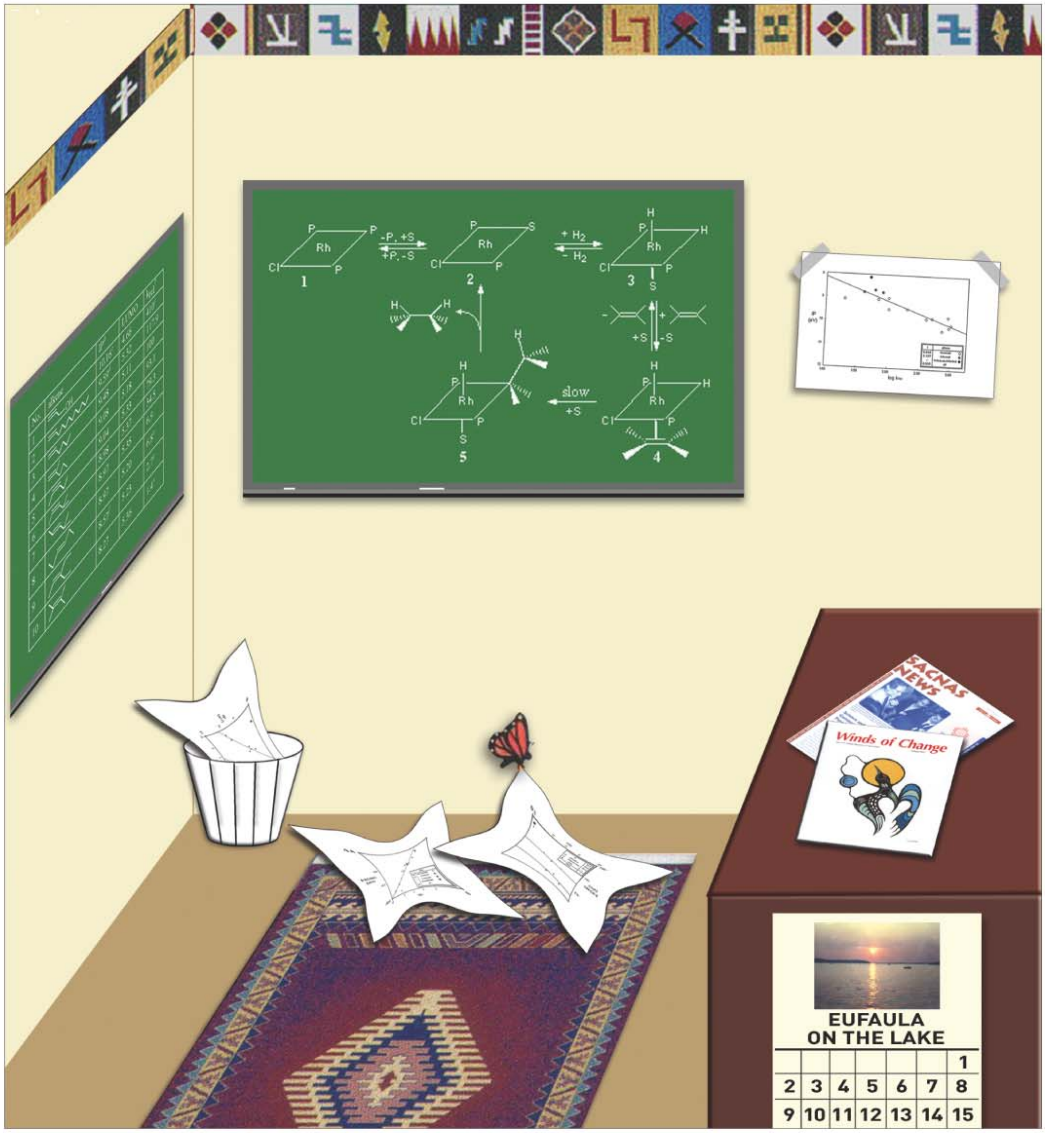

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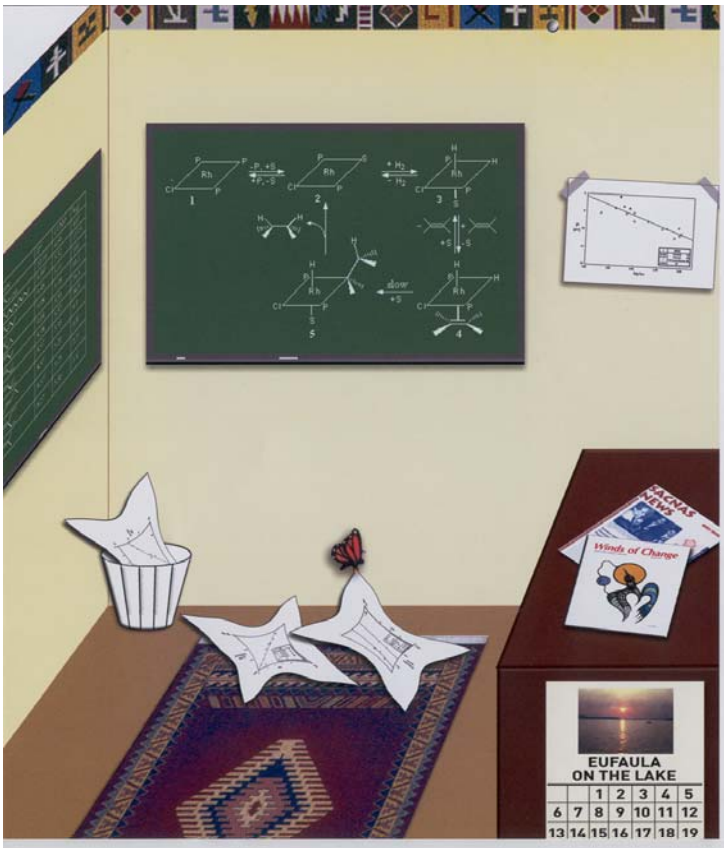

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Using Correlations to Compare Additions to Alkenes: Homogeneous Hydrogenation by Using Wilkinson's Catalyst

DONNA J. NELSON, RUIBO LI, AND CHRISTOPHER BRAMMER

J. Org. Chem.; 2005; 70(3) pp 761 - 767; (Article)
DOI: 10.1021/jo048968r

Comparing correlations of logs of relative reaction rates versus alkene HOMO and LUMO energies reveals that reactions with similar electronic and steric effects have similar shapes in their plots; this can sometimes be used to select among proposed reaction mechanisms. The rate-determining step of homogeneous hydrogenation of alkenes catalyzed by Wilkinson's catalyst is revealed to be a nucleophilic addition to the alkene double bond, which depends upon both electronic and steric effects of the substituents.
See Nelson and co-workers, p 761.

september

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
	AUGUST '06 / OCTOBER '06				1	2
3	4 *Labor Day*	5	6	7	8	9
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17	18	19	20	21	22 *Rosh Hashanah (begins at sundown)*	23 *Ramadan begins*
24	25	26	27	28	29	30

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Correlation of Ionization Potentials and HOMO Energies versus Relative Reactivities of Cl_2, of Br_2, and of I_2 with Representative Acyclic Alkenes. Comparison with Other Additions to Alkenes

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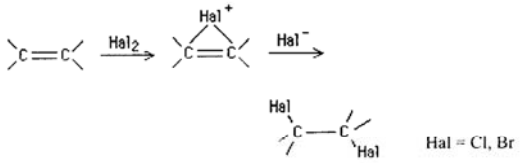
Plots of log k_{rel} versus IP or versus HOMO for the title reactions are presented; similarities and differences among the reactions are discussed. The Cl_2 and Br_2 data each show a single line of correlation with positive slope for all alkenes regardless of the steric requirements; increasing substitution at the double bond increases the reaction rate, indicating an electrophilic reaction. Each plot of the I_2 data calculated for adsorption exhibits a natural separation into groups of similarly substituted alkenes, in which increased substitution reduces the rate. Within each group, a good-to-excellent correlation is observed, with a lower IP generally corresponding to a higher relative rate. The results indicate that the relative magnitude of the steric requirements about the double bond is similar to that of the electronic effects in iodination. Plot shapes for iodination are compared to those of other reactions, such as hydroboration, oxymercuration, complexation with Ag^+, and complexation with $MeHg^+$.

I. Introduction

We have correlated measurable characteristics in addition reactions with alkenes in order to gain information which is useful mechanistically and synthetically. We have applied this technique to several reactions: hydroboration,[1a,b] oxymercuration,[1a,b] bromination,[1a,c] diimide addition,[1d] oxidation with permanganate,[1e] epoxidation,[1f] sulfenyl halide addition,[1f] mercuric chloride complexation,[1f] silver ion complexation,[1e,f] carbene addition,[1g] nitrosyl chloride addition,[1g] oxidation with osmium tetroxide,[1g] and the Wacker oxidation.[1h] The technique can often (1) determine relative magnitudes of steric and electronic effects in the rate-determining step; (2) predict, in a simple way, the effects of substituents on reaction rates for synthetic purposes; and (3) select between alternative proposed reaction mechanisms, in some cases. The previous investigations[1] applied this simple method by correlating the logarithms of the relative reaction rates (log k_{rel} values) with the alkene ionization potentials (IPs) and with their highest occupied molecular orbital energies (HOMOs); reactions with similar mechanisms gave correlation plots which were similar in appearance. To develop further this new technique and to elucidate synthetically and mechanistically important information from experimental or computational data, we apply the technique to important reactions with a variety of mechanisms.

Independent rate studies of chlorination,[3] bromination,[4] and iodination[5] of alkenes allow examination and comparison of steric and electronic effects caused by increasing the degree of substitution at the doubly bonded carbons of acyclic alkenes. In bromination, such steric effects are smaller than electronic effects since one line of correlation is obtained which includes all alkenes, regardless of the degree of substitution at the double bond.[1a,4] For chlorination, in nonpolar media and free from radical contributions,[3] relative rates parallel those of bromine addition, and the plot obtained is similar, as expected (eq 1).



Studies of alkene iodination explored the adsorption (A ⇌ B) of the olefin with solid iodine on a GC column to give the charge-transfer complex B, and complexation (B

* Corresponding author.

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(2) Masclet, P.; Grosjean, D.; Mouvier, G.; Dubois, J. *J. Electron Spectrosc. Relat. Phenom.* **1973**, *2*, 225−37.

(3) (a) Poutsma, M. L. *J. Am. Chem. Soc.* **1965**, *87*, 4285. (b) de la Mare, P.; Bolton, R. *Electrophilic additions to unsaturated system*; Reaction Mechanisms in Organic Chemistry Monograph 4; Elsevier: New York, 1966; pp 73−112. (c) Bartlett, P. D.; Sargent, G. D. *J. Am. Chem. Soc.* **1965**, *87*, 1297. (d) A reviewer pointed out that the deviations of the values from linearity could also be due to errors in the IPs, HOMOs, or k_{rel} values.

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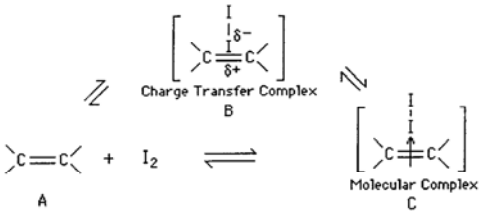
⇌ C) from the adsorbed alkene B to give the molecular complex C.[5]



Comparing the relative steric and electronic effects of these reactions would increase their synthetic utility.

We previously contrasted the bromination of alkenes against hydroboration,[1a] oxymercuration,[1a] and a number of other reactions of alkenes involving three-membered intermediates or products.[1b,c] We determined that hydroboration and oxymercuration each had multiple lines in the plots, grouping alkenes with steric effects which were of the same order of magnitude.[1a] However, bromination gave one line for all alkenes, indicating that the steric effects in that reaction were of the same order of magnitude for all of the alkenes studied, similar to what was observed for the other reactions involving three-membered intermediates.[1b,d] To explore the effectiveness of this procedure and increase the synthetic utility of the reaction, it seemed desirable to determine if these results for bromination are also applicable to the reactions of alkenes with chlorine and iodine; we report the results of that comparison herein.

II. Background

The general procedure[1] for gathering information about the relative magnitudes of steric versus electronic effects in the transition state of the rate-determining step, and therefore about the mechanistic pathway, is the following: (1) relative rates of reaction (k_{rel} values) of a number of representative alkenes, with a broad range of electronic and steric properties are determined; (2) ionization potentials (IPs), highest occupied molecular orbital energies (HOMOs), and in some cases, lowest unoccupied molecular orbital energies (LUMOs) are obtained, because these are relatively insensitive to steric effects; (3) log k_{rel} values of the alkenes are plotted against the alkene π IPs, HOMOs, or LUMOs; (4) plots and correlation coefficients are examined for linearity and number of lines, with each line representing a group of alkenes having steric effects with similar orders of magnitude in that reaction; and (5) plot shapes are compared with those from other reactions in order to ascertain similarities.

In our previous investigations of addition reactions of representative acyclic alkenes.[1] a plot of IPs or HOMO energies versus the logarithm of relative rates shows a natural grouping of data points corresponding to the number of alkyl groups attached to the double bond. Data for the groups of more highly substituted alkenes fall together in the portion of the plot corresponding to lower relative rates of reaction. The rate retardation for more highly substituted alkenes must be due to the rate-retarding steric effects over-riding the rate-increasing, electron-donating electronic effects of the alkyl groups.

In contrast, other addition reactions of acyclic alkenes give only one line in such plots, regardless of the degree of substitution. In these, the reaction rates are of the same order of magnitude regardless of the degree of substitution about the double bond.[1] In these cases, the overall effect of increasing the degree of substitution is rate-increasing, which means that electronic effects override the steric effects.

III. Results and Discussion

Table 1 lists k_{rel} values of representative acyclic alkenes with chlorine,[3] bromine,[4] and iodine.[5] It also lists alkene IPs and HOMOs. In designated cases, IPs were not available and had to be determined through comparison with HOMOs, which were calculated as described previously.[1a] Plots of alkene IPs or HOMOs versus log k_{rel} values are shown in Figures 1−4. Since a higher IP value corresponds to electron removal from a lower-energy molecular orbital, IPs were listed with increasing magnitude proceeding down each plot, in order to make the plots comparable to those using HOMO energy levels.

A. Bromination. Although we did not include so many large substituents on the alkenes in our previous alkene bromination study,[1a] we have included them in this study. Each of the plots of alkene IP and HOMO versus log k_{rel} for bromination[4a−g] (Br_2/NaBr/MeOH), shown in Figure 1, has one line of correlation with $r = 0.97$. In both plots, this correlation is better than those found within groups of sterically similar alkenes. In a study reported by Dubois and Mouvier,[4c] it was necessary to utilize a two-parameter equation, employing Taft's inductive σ^* constant and steric substituent constant, to achieve a linear correlation because of the steric requirements of the substituents. In the study reported herein, which includes alkenes with large substituents, a linear correlation with the IPs was again obtained; this means that this type of study may be more likely to give a suitable treatment without use of additional steric parameters.

Similar correlations and plots (not shown) of IP versus log k_{rel} values for bromine addition under other conditions[3a] (Br_2/HBr/CH_2Cl_2) gave one line of correlation regardless of the number of alkyl groups on C=C and with an excellent correlation coefficient ($r = 0.98$). Data and plots (not shown) for bromine addition in the presence of HOAc[3b] showed virtually no correlation for all alkenes ($r = 0.26$) or for sterically similar groups; it is unlikely that this is due to the acidic conditions, since bromination[3a] using Br_2/HBr gave good results. Rather, it is probably the case that each alkene included in the study using HOAc[3b] had a functional group which could offer conju-

(4) (a) Collin, V. G.; Jahnke, U.; Just, G.; Lorenz, G.; Pritzkow, W.; Rolling, M.; Winguth, L.; Dietrich, P.; Doring, C. E.; Houthal, H. G.; Wiedenhoft, A. *J. Prakt. Chem.* **1969**, *311*, 238. (b) Walisch, W.; Dubois, J. E. *Chem. Ber.* **1959**, *92*, 1028. (c) Dubois, J. E.; Mouvier, G. *Tetrahedron Lett.* **1963**, 1325. (d) Dubois, J. E.; Schwarcz, A. *Tetrahedron Lett.* **1964**, 2167. (e) Dubois, J. E.; Goetz, E. *Tetrahedron Lett.* **1965**, 303. (f) Dubois, J. E.; Barbier, G. *Tetrahedron Lett.* **1965**, 1217. (g) Dubois, J. E.; Mouvier, G. C. R. *Hebd. Seances Acad. Sci. (Paris)* **1964**, *259*, 2101. (h) Grosjean, D.; Mouvier, G.; Dubois, J. E. *J. Org. Chem.* **1976**, *41*, 3872. (i) Cerichelli, G.; Grande, C.; Luchetti, L.; Mancini, G.; Bunton, C. *J. Org. Chem.* **1987**, *52*, 5167−5171. (j) Acharya, D.; Das, M. *J. Org. Chem.* **1969**, *34*, 2828−2831. (k) Fukuzumi, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 2783−2791. (l) Popov, A. *Halogen Chemistry*; Gutmann, V., Ed.; Academic Press: London, 1967; p 225.

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Table 1. Alkene IPs, HOMOs, and Relative Reactivities for Reactions with Chlorine, Bromine, and Iodine

				Relative reactivity					
no.	alkene	IP[a] (eV)	HOMO energy level	Cl_2[b]	Br_2[c]	I_2[d]			
						with support adsorp	with support complex	without support adsorp	without support complex
1		8.27	-9.49	4.3×10^7	1.40×10^6	7.3	3.6	34	16.4
2		8.68	-9.63	1.1×10^6	1.40×10^5	3.5	4.5	9.6	11.9
3		8.95	-9.76		9.76×10^3	31[e]	32[e]	35[e]	33[e]
4		8.97	-9.76		3.57×10^3	4.4[e]	4.3[e]	6.6[e]	6.4[e]
5		9.08	-9.79	1.6×10^4[f]	895	11.0	4.8	18	7.8
6		9.12	-9.79	6.3×10^3	4.05×10^3	7.9	23	9.6	28
7		9.12	-9.77	5.0×10^3	2.62×10^3	1.73	5.0	2.5	7.2
8		9.24	-9.78	5.8×10^3		1.26	5.2	2.5	10
9		9.44[g]	-10.17		7.20				
10		9.45	-9.96	115	40.48	34[h]	43[h]	34[h]	44[h]
11		9.48	-9.97		100	100[i]	100[i]	100[i]	100[i]
12		9.63	-9.94		148	41	118	40	117
13		9.74	-9.97	100		7.1	73	7.7	78
14		9.93[j]	-10.49	5×10^{-5}					
15		10.09[k]	-10.34		0.72				
16		10.18[l]	-10.53		0.7				
17		10.34[l]	-10.48	0.30	0.06				

[a] All IPs, including those in footnotes, are first IPs from ref 2, unless otherwise noted. [b] Reference 3a. [c] Reference 4a–g. [d] Reference 5. [e] Data for the corresponding 2-pentenes; IP's = 9.04 eV (cis) and 9.04 eV (trans). [f] Data for 2-methyl-1-butene; IP = 9.15 eV. [g] Reference 6. [h] Data for 3-methyl-1-butene; IP = 9.52 eV. [i] Data for 1-pentene; IP = 9.48 eV. [j] Reference 7. [k] Reference 8. [l] Reference 9.

gative stabilization directly to an alkenyl carbon and could thereby stabilize a carbocation formed from the alkene; this could lead to the involvement of mixed reaction mechanism pathways.

Last, we should note that this treatment does not consider the effect of the simultaneous reaction of Br_3^- with alkenes. Although the rate of reaction of Br_3^- is slower than that of Br_2, the difference in rate is not sufficient to justify disregarding it.[4i,j] However, comparisons of these reactions have shown not only that substituents affect the two reactions similarly and only in differing magnitudes,[4j,k] but also that the effects of the substituents are roughly parallel.[4k] The fact that the results obtained for chlorination are similar to those obtained for bromination, as will be seen below, also supports the conclusion that the effects must be roughly parallel, since the formation of Cl_3^- is unimportant in that system.[4l]

B. Chlorination. The plots (Figure 2) for chlorination (Cl_2(g)/O_2/dark[3a]) each show that the best correlation is obtained by considering all alkenes as a single group with the correlation coefficients $r = 0.99$ (IP) and 0.95 (HOMO). This result is very similar to that for bromination. The reactivities of the alkenes in this reaction are interpreted[3a,c] as compatible with a transition state, which involves partial bonding of the chlorine molecule with both termini of the olefinic system, and with little development of positive charge on one carbon, as in a π complex. This transition state is preferred to one which involves attack at a single terminus with development of carbocation character on one carbon; this conclusion is also very similar to that for bromination.

Because the chlorination study[3a] included only one compound with a large substituent, the authors found it necessary to use only the σ^* constant in order to achieve linear correlation. However, attempts to include allyl chloride in that correlation gave less satisfactory results. In contrast, allylic compounds and alkenes with large substituents were included in our previous study and are included in the correlations reported herein, both without problems.

As in the previous chlorination study, the position of the alkyl substituent on the double bond has little effect on the rate; there is little difference among the chlorination or bromination data for isobutene, *cis*-2-butene, and *trans*-2-butene, but there is a large difference between the chlorination and bromination data for both methylpropene and 2-methylbutene.

Poutsma warned of dangers in extrapolating from linear to branched alkenes since branching stabilizes possible carbocation formation, this could switch the mode of chloronium ion decomposition or switch the mechanism from one with a cyclic chloronium intermediate to one with an open carbocation. While we found no problems achieving correlation with the branched olefins studied herein, we do find problems including aryl

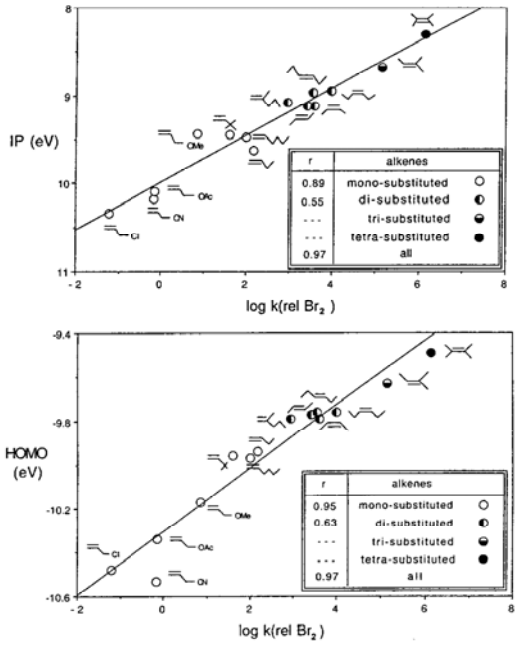

Figure 1. (a) Plot of log k_{rel} Br_2 versus IP for reaction conditions Br_2 /NaBr/MeOH; ref 4a–g. (b) Plot of log k_{rel} Br_2 versus HOMO for reaction conditions Br_2/NaBr/MeOH; ref 4a–g.

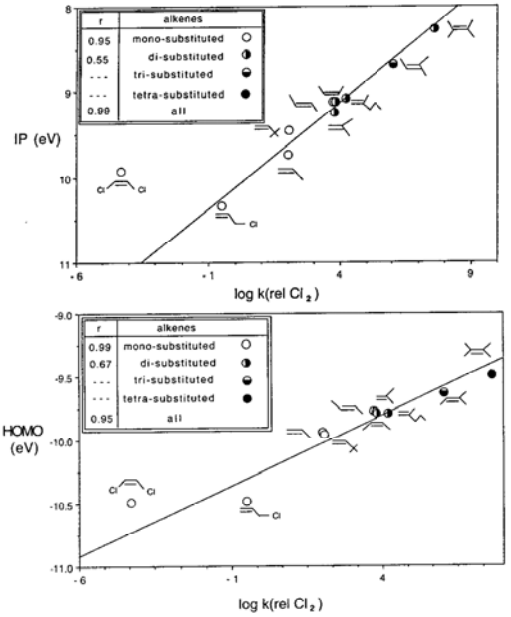

Figure 2. (a) Plot of log k_{rel} Cl_2 versus IP for reaction conditions Cl_2(g)/O_2/dark; ref 3a. (b) Plot of log k_{rel} Cl_2 versus HOMO for reaction conditions Cl_2(g)/O_2/dark; ref 3a.

substituents, probably for that reason. Although data for dichloroethene were not included in Poutsma's correlation,[3] we attempted to include it here and found that its point fell far off the correlation line (Figure 2). It is possible that the chlorine substitution directly on the double bond converts the reaction mechanism in a manner similar to one of the mechanistic pathway changes discussed above.

Chlorination data, obtained using Cl_2/HOAc,[3b] were plotted versus IPs[7,11] (or HOMO, values in parentheses). As with the results obtained for bromination in the study using HOAc, we found no correlation for sterically similar groups, $r = 0.83$ (0.16) and $r = 0.43$ (0.41), or for all alkenes. $r = 0.14$ (0.36) (plots not shown). Once again. the alkenes included in this study[3b] each had a functional group which could offer conjugative stabilization with a carbocation and could lead to involvement of mixed reaction mechanism pathways.[3d]

C. Iodination. Results for iodination[5] (by using I_2 on GC column support material) are different from those for bromination and chlorination. Studies of the interaction of olefins with molecular iodine were carried out by using a gas chromatographic technique. These explored the complexation equilibria of the olefin interacting with solid iodine on the column: an equilibrium corresponding to adsorption of the gaseous alkene molecules on solid iodine (A ⇌ B), and an equilibrium between the adsorbed alkene and the complexed alkene (B ⇌ C). Each equilibrium was treated mathematically in two ways, accounting for complexation with untreated support and not accounting for it. For adsorption (A ⇌ B), regardless of consideration for untreated support interaction, the data points group depending upon the steric requirements of the alkenes (Figure 3a,b), giving multiple lines with a positive slope. In the plots for these equilibria, a much better correlation is obtained by using separate lines for monosubstituted alkenes ($r = 0.78$ when considering interaction with untreated support and $r = 0.79$ when not considering it) and for disubstituted alkenes ($r = 0.73$ considering interaction with untreated support and $r = 0.70$ not considering interaction) than by considering all alkenes as one group ($r = 0.36$ considering interaction with untreated support and $r = 0.06$ not considering interaction).

For the second equilibrium (between the adsorbed alkene and the complexed alkene, B ⇌ C), regardless of consideration for untreated support interaction, a better correlation is shown in Figure 3c,d with one line of negative slope containing data for all alkenes, irrespective of their steric requirements ($r = 0.76$ considering interaction with untreated support and $r = 0.62$ not considering interaction). The negative slope in each of the plots in Figure 3c,d indicates that the product has an increased amount of electron density in the π bond. One explanation for this phenomenon, which has been

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(10) (a) Muhs, M. A.; Weiss, F. T. *J. Am. Chem. Soc.* **1962**, *84*, 4697. (b) Cvetanović, R. J.; Duncan, F. J.; Falconer, W. E.; Irwin, R. S. *J. Am. Chem. Soc.* **1965**, *87*, 1827.
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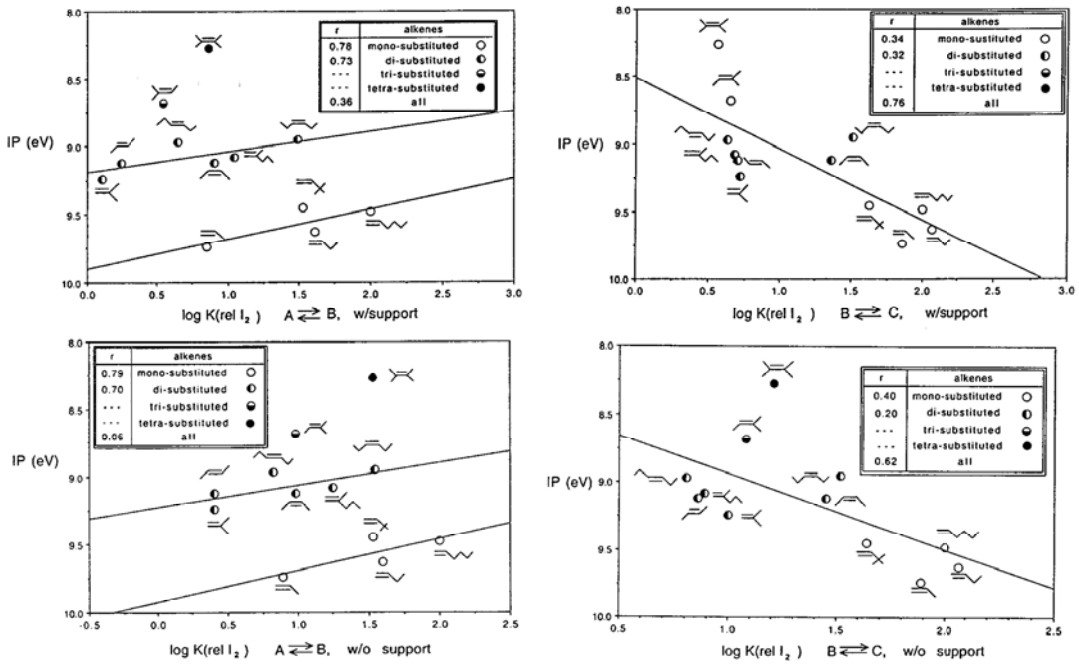

Figure 3. (a) Plot of log K_{rel} I_2 versus IP for adsorption (A ⇌ B) of I_2 on GC column support material; ref 5. (b) Plot of log K_{rel} I_2 versus IP for adsorption (A ⇌ B) of I_2 on GC column support material, interaction with support mathematically removed; ref 5. (c) Plot of log K_{rel} I_2 versus IP for complexation (B ⇌ C) of I_2 on GC column support material; ref 5. (d) Plot of log K_{rel} I_2 versus IP for complexation (B ⇌ C) of I_2 on GC column support material, interaction with support mathematically removed; ref 5.

proposed in other systems,[5,10b,12] is that back-bonding from the electrophile (here I_2) to the alkene could be absent in the adsorbed form B and present in the complex C.

Electrophilic character in the adsorption step (A ⇌ B), and nucleophilic character in the complexation from adsorption (B ⇌ C), reveal information regarding the direction and character of electron transfer in these steps. One explanation for these data, which agrees with eq 2, is that electron density is transferred from the alkene to iodine in the adsorption step (A ⇌ B), and there is a net increase in the amount of electron density in the π bond in going from the adsorbed alkene to the complexed one (B ⇌ C). Perhaps the transfer of electron density from iodine to the alkene via back-bonding is more important in the complexed form than in the adsorbed form.

The manifestation of grouping according to alkene steric requirements for adsorption (Figure 3a,b), but not for complexation starting from the adsorbed alkene (Figure 3c,d), might seem surprising because adsorption should be a "looser" interaction, with the molecules farther apart and reduced steric effects. However, because complexation is from the adsorbed alkene, perhaps there would be little additional congestion incurred in this transformation so no grouping according to steric requirements would appear in the plots.

Different results for iodination as opposed to those for chlorination and bromination might seem surprising at first, but they are easily explained. Bromination and chlorination are addition reactions which go to completion. The reaction with iodine does not go to completion because it is unfavorable entropically and is endothermic; it is a reversible complexation reaction in which the equilibrium favors the reactants. Therefore, the plot obtained from reaction with iodine might be expected to resemble those of other alkene complexations instead of those of bromination and chlorination.

D. Comparison to Complexation with Metal Ions or with Organometals. Comparison of the plots for iodination versus those for complexation with the silver ion ($AgNO_3$)[1f,5,10a] reveals similarity (Figure 4a,b). Correlation of log K_{rel} I_2 versus alkene IP gives different results depending upon the equilibrium which is being considered. The plot for A ⇌ B shows groups of data which form multiple lines, having a positive slope and corresponding to alkenes with different steric requirements; that for B ⇌ C shows one line with a negative slope, independent of alkene steric requirements. Correlation of log K_{rel} Ag^+ versus alkene IP can also give a different plot appearance, depending upon the experimental method used to obtain the equilibrium constant data. Like the results for the reaction with I_2, these are multiple lines with a positive slope or one line with a negative slope.

As we reported[1f] earlier, if Ag^+ complexation data are obtained by allowing the alkene to become distributed between two liquid phases, then the plot (shown in ref 1f) has multiple lines, each with a positive slope and corresponding to a group of sterically similar alkenes.

(12) Bach, R. D.; Weibel, A. T.; Patane, J.; Kevan, L. *J. Am. Chem. Soc.* **1976**, *98*, 6237.

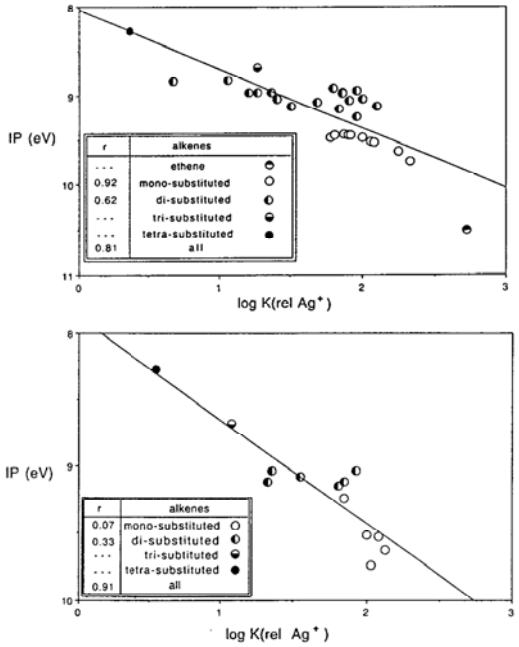

Figure 4. (a) Plot of log K_{rel} Ag^+ versus IP for adsorption (A ⇌ B) of Ag^+ on GC column support material; ref 10a. (b) Plot of log K_{rel} Ag^+ versus IP for adsorption (A ⇌ B) of Ag^+ on GC column support material; refs 5, 10.

That plot pertains to the complexation equilibrium[10a] (A ⇌ C) between the free alkene plus Ag^+ and the complexed alkene. However, it appears to be similar to that for the adsorption of the alkene on iodine (A ⇌ B) shown in Figure 3a,b. This similarity in plots is apparent although the equilibria being examined are not reported to be the same. There are at least two possible explanations for this. (1) The overall complexation of alkene with Ag^+ in solution proceeds via the adsorbed form (i.e., A ⇌ B ⇌ C) but reflects the steric requirements of the reactant alkenes. (2) Formation of the product is by direct complexation from the free alkene A ⇌ C, which accommodates (and reflects) the steric requirements of the alkene.

Plots for alkene adsorption (A ⇌ B) with iodine (Figure 3a,b) and silver ion[1f] are somewhat similar to the plots obtained for oxymercuration and hydroboration of alkenes,[1a] except for the placement of data for 1,1-disubstituted alkenes and trisubstituted alkenes. In the adsorptions, 1,1-disubstituted alkenes are in a "disubstituted alkenes" group with 1,2-disubstituted alkenes, and trisubstituted alkenes are separate; in oxymercuration and hydroboration, 1,1-disubstituted alkenes are in a "terminal alkenes" group with 1-hexene, and 1,2-disubstituted alkenes are in an "internal alkenes" group with the trisubstituted alkenes. It is interesting that these plots would be so similar even though the former two are equilibria reactions and the latter two are kinetically controlled reactions.

Equilibrium data for silver ion complexation which correspond to B ⇌ C are determined by GC.[5,10a] Plots of log K_{rel} vs IP or HOMO give one line of correlation with a negative slope (Figure 4a,b), regardless of the steric requirements of the alkenes ($r = 0.81$[10a] and $r = 0.91$,[5] respectively). Plotted data from either study of the equilibrium, between the alkene adsorbed on Ag^+ and the alkene complexed with Ag^+ (B ⇌ C), is similar to the analogous plots for iodination (also B ⇌ C). As in the case of the iodination adsorption to complexation equilibrium (B ⇌ C), the negative slope indicates the product has an increased amount of electron density in the π bond. Cvetanović[5] made note of the similarity between I_2 complexation and Ag^+ complexation (both give plots with one line of negative slope, B ⇌ C), as well as of the nucleophilic character of the Ag^+ complexation. He attributed[10b] the latter to a back-donation of electrons to the olefin from the silver ion; this is similar to our discussion for iodination above.

Bach[12] also noted a similarity between the results of calculations for alkenes complexed with methylmercury cation and those with silver ion. He explained that "the bonding in silver and mercury π complexes is due largely to overlap of the filled π orbital of the alkene with the vacant s orbital of the metal. The amount of $d\pi-p\pi$ back bonding of metal electron density with the antibonding π orbital of the alkene is minimal."[12] He also cited differences between the effect of increasing alkyl substitution on the alkene in the data for the reactions of alkenes with methylmercury cation (rate increasing in gas phase by ion cyclotron resonance) and in those for complexation with silver ion (rate decreasing in solution). These gas phase (ICR) data do not collect in sterically similar groups, which is in contrast with the behavior of the oxymercuration data (multiple lines, positive slopes),[1a] which leads to comparable intermediates in solution. The appearance of the plot (not shown, single line, positive slope, $r = 0.85$) obtained from the gas phase (ICR) data[12] for complexation with $MeHg^+$ is also at odds with those from the gas phase (GC) data for complexation with Ag^+ (B ⇌ C, single line, negative slope)[5,10a] or with I_2 (adsorption A ⇌ B, multiple lines, positive slope, Figure 3a,b; complexation B ⇌ C, single line, negative slope, Figure 3c,d).[5] This indicates that the intermediate and/or the mechanism involved in the reaction with $MeHg^+$ is not the same as that in the reaction with Ag^+ or I_2.

E. Summary of Patterns in Plot Appearance and Reactions. The following patterns appear in the above reactions. (1) Chlorination and bromination are similar in that the rate-determining step is the formation of the halonium ion, and the plot of IP versus log k_{rel} yields one line with a positive slope regardless of the steric requirements of the alkenes. The plots indicate that the rate-determining step in each is an electrophilic addition influenced more by electronic effects than by steric effects. (2) Adsorption with iodine (A ⇌ B) and complexation with silver ion in solution (A ⇌ C) are similar because plots of IP versus log k_{rel} give lines of correlation with positive slope and with data grouped according to the degree of alkene substitution: monosubstituted, disubstituted, and trisubstituted. (3) Upon including in the mathematical treatment of the data an equation which relates the equilibrium constant of adsorption of gaseous alkene molecules on solid iodine to the equilibrium constant of complexation with solid iodine of alkene molecules physically adsorbed on solid iodine, the appearance of the plots for iodination switches from multiple lines with positive slope to one line with negative slope. (4) Equilibria (B ⇌ C) for complexation from the

adsorbed form in the reaction of alkenes with I_2 or Ag^+ cause the best correlation line in each plot of IP versus log k_{rel} to be one line with negative slope, which includes data for all alkenes regardless of steric requirements. (5) Switching the phase of reaction with Ag^+ or mercuronium ion generation from solution to gas phase causes the correlation lines in the IP versus log K_{rel} plots to switch from multiple lines of positive slope to one line of positive slope. (6) Little back-bonding has been predicted in complexes with Ag^+ or HgX^+, and back-bonding is not possible in hydroboration. However, back bonding in complexes of alkenes with Ag^+ or I_2 would explain the change in slope in going from adsorption (positive, electrophilic) to complexation (negative, nucleophilic). It is not clear that those conclusions can necessarily be used to predict the significance of back-bonding in complexation with other metal ions or molecules. (7) Oxymercuration and hydroboration give results similar to those in (2) except that the data are grouped according to whether there is an unsubstituted end of the double bond, terminal vs internal instead of monosubstituted vs disubstituted.

IV. Conclusion

Chlorination and bromination give plots of alkene IP versus log k_{rel} which are characteristic of typical electrophilic additions to alkenes. Iodination gives plots which are dependent upon the treatment of the data to reflect adsorption or complexation of the alkene on solid I_2. Adsorption of the alkene on iodine results in grouping according to alkene steric requirements in the plots of alkene IP versus log K_{rel}, whereas complexation from the adsorbed alkene shows no such grouping. Data for reactions of alkenes with I_2 and with Ag^+ appear to be similar to each other, but different than those for reactions that give mercuronium ions; this may be due to changing reaction conditions.

Reactions considered herein, with similar mechanisms and steric and electronic requirements in the rate-determining step, give plots similar in appearance. Therefore, it follows that it should be possible to use correlations and plots such as the ones in this report to gather information about and/or to distinguish between reaction mechanisms and intermediates which are under consideration for a given reaction. One example is to differentiate in iodination between adsorption (A $\rightleftharpoons$ B), which has no back-bonding and gives multiple lines with positive slope in the plot, versus complexation from the adsorbed form (B $\rightleftharpoons$ C), which is predicted to have a small, but significant, amount of back-bonding and gives a single line of negative slope in the plot. Another example is to differentiate between a kinetically controlled reaction in which electronic effects have a greater influence than steric effects, such as bromination, which has a single line of positive slope in the plot, versus adsorption (A $\rightleftharpoons$ B) or complexation (B $\rightleftharpoons$ C) of iodine, which have plots as described in the previous sentence. Examples of the use of this technique to differentiate between a reaction involving a three-center intermediate I or product P with the rate-determining step leading to I or P (giving a plot with one line of positive slope) versus one with the rate-determining step leading from I or P (giving a plot with multiple lines of positive slope) have been reported.[1]

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Substituent effects in addition of iodine thiocyanate to alkenes

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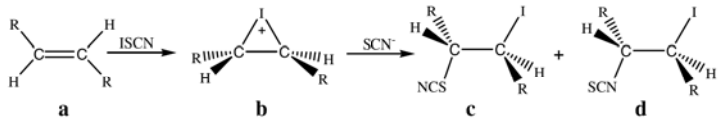
Abstract—The plots of logarithms of relative rates of ISCN addition to alkenes versus alkene IPs and versus alkene HOMO energies reveal that the alkene relative reactivity depends upon both electronic and steric effects of the substituents. Steric effects are related not only to the degree of substitution on the C=C bond but also to the relative position, size, and branching of alkyl substituents.

Organoiodine compounds play a significant role in many areas, such as, organic synthesis,[1] biochemistry,[2] biogeochemical reactions,[3] and environmental studies.[4] Adding I_2 to alkenes might initially seem to be a simple way to introduce iodine into an organic compound, but this reaction actually can only be carried out photochemically under very low temperatures (below −40 °C) to give diiodo products that are decomposed quickly at room temperature.[5,6] However, iodine incorporation is achievable via alkene addition of an iodine-containing compound, such as ICl,[7] IF,[8a] IN_3,[8b] INO_3,[8c] IOAc,[8d] INCO,[8e] ISeCN,[8f] and ISCN;[9] these are reported to undergo complete reaction under mild reaction conditions. One iodine-containing compound, which is often used in alkene addition, is ISCN.[9–13] Its reaction (Scheme 1) yields *vic*-iodothiocyanates **c** and *vic*-iodoisothiocyanates **d**, which are used as intermediates in synthesizing useful compounds, such as episulfides,[10,11] thiazolidin-2-ones,[12] 2-amino-2-thiazolines,[12] and 2-alkoxy-2-thiazolines.[13a]

The first step of ISCN addition to alkenes is proposed[13] to be the formation of a bridged iodonium ion intermediate **b**, which is generally believed[14] to be the rate-determining step of the reaction (Scheme 1). It is reported that intermediate **b** does not undergo complete ring-opening prior to anti attack by nucleophiles in the second step.[13] There seems to be general agreement regarding initial attack on C=C by electrophilic ISCN,[13] although controversy still exists about the exact species of nucleophile that attacks iodonium ion **b** in the second step and about the final anti addition product distribution.[13] Similarly to ISCN addition, additions of other iodine-containing compounds[7,8] to alkenes normally also yield vicinal anti addition products. Therefore, the reaction mechanisms of additions of these iodine-containing compounds might have some aspects in common and so further comparison may reveal additional similarities. Of the iodine-containing compounds listed above, there seem to be few kinetic studies on additions to a wide range of alkenes, but those of ISCN[15] and ICl[7] have been reported. We present here, the analysis of substituent effects upon alkene reactivity toward ISCN addition to alkenes and a comparison with ICl addition; this might provide useful information about the reaction mechanism, since detailed



Scheme 1. ISCN addition to alkenes.

Keywords: Iodine thiocyanate; Additions to alkenes; Correlations; Substituent effects.
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mechanistic studies about the title reaction are still somewhat scarce.

Alkene IPs, HOMO energy levels, and relative rates of ISCN and ICl additions to alkenes are listed in Table 1. Alkene HOMO energies were calculated,[17] because experimental IPs for some alkenes in Table 1 were not available in the literature. We report ab initio (HF level, 6-31G* basis set) values here because they correlated best versus alkene IPs, in our calculations by a variety of computational methods.[18c] Cyclic and aryl alkenes are excluded in order to avoid complications due to ring strain or conjugation with aryl groups. Figure 1a shows the plot of $\log k_{rel}$ values of ISCN addition to alkenes versus alkene IPs. The plot of $\log k_{rel}$ values versus alkene HOMO energies in Figure 1b is essentially analogous to that in Figure 1a. The overall trend of relative reactivity of alkenes shown in Figures 1a and b support the suggestion[14] that the rate-determining step of ISCN addition to alkenes is the first step, **a**→**b** in

Table 1. Alkene IPs, HOMO energies, and relative rates of ISCN and ICl additions to alkenes

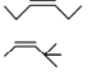
No.	Alkene	IP[a] (eV)	HOMO (eV)	$k_{rel,ISCN}$[b]	$k_{rel,ICl}$[c]
1		10.52	−10.19		2.28
2		9.74	−9.72		40.5
3		9.63	−9.70	121	100
4		9.51[d]	−9.65	105	
5		9.53	−9.70	40.0	190
6		9.48	−9.66	100	
7		9.46[e]	−9.67	36.0	
8		9.45	−9.66	47.0	
9		9.45	−9.65	24.0	34.2
10		9.44	−9.61	137	
11		9.43[f]	−9.61	137	
12		9.40	−9.59	21.0	
13		9.24	−9.39	1.53×10^3	1.12×10^3
14		9.15	−9.37	1.84×10^3	2.14×10^3
15		9.12	−9.26	790	2.91×10^3
16		9.12	−9.25	411	934
17		9.08	−9.36	1.32×10^3	
18		9.07	−9.34	1.21×10^3	1.55×10^3
19		9.04	−9.27		4.15×10^3
20		9.04	−9.21		1.80×10^3
21		9.02	−9.17	521	1.36×10^3
22		8.98	−9.28		2.27×10^3
23		8.97	−9.28		1.10×10^3
24		8.97	−9.27	495	
25		8.95	−9.27	895	
26		8.92	−9.27		4.61×10^3
27		8.91	−9.25		50.6
28		8.84	−9.22	684	

Table 1 (*continued*)

No.	Alkene	IP[a] (eV)	HOMO (eV)	$k_{rel,ISCN}$[b]	$k_{rel,ICl}$[c]
29		8.83	−9.23	305	
30		8.77	−9.20	790	
31		8.76	−9.21	390	
32		8.68	−8.86	3.21×10^3	1.88×10^4
33		8.60[g]	−8.99	3.68×10^3	
34		8.59[h]	−8.78	2.53×10^3	
35		8.27	−8.70		3.74×10^4

[a] Ref. 16a, unless otherwise noted.
[b] Ref. 15.
[c] Ref. 7a.
[d] IP for 1-decene used as an approximation. Ref. 16a.
[e] Estimated by applying to the IP for 1-pentene a correction factor, which is the difference between the IPs of *trans*-4-methyl-2-hexene and *trans*-2-hexene: 9.52 eV − (8.97 eV − 8.91 eV) = 9.46 eV. Ref. 16a.
[f] Ref. 16b.
[g] Estimated by applying to the IP for 2-methyl-2-butene a correction factor, which is the difference between the IPs of 2-butene and 2-pentene: 8.68 eV − (9.12 eV − 9.04 eV) = 8.60 eV. Ref. 16a.
[h] Estimated by applying to the IP for 2-methyl-2-butene a correction factor, which is the difference between IPs of 2-methyl-1-propene and 2-methyl-1-butene: 8.68 eV − (9.24 eV − 9.15 eV) = 8.59 eV. Ref. 16a.

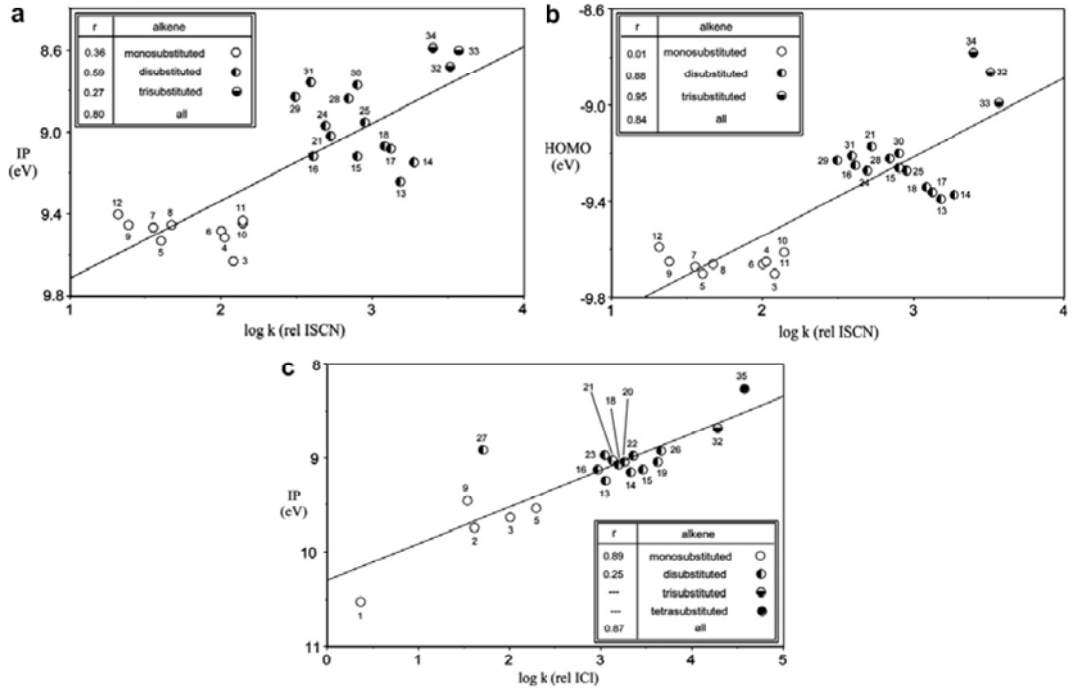


Figure 1. Plots of logarithms of relative rates of (a) ISCN addition to alkenes versus alkene IPs, (b) ISCN addition to alkenes versus alkene HOMO energies, and (c) ICl addition to alkenes versus alkene IPs. *Y*-Axis IP data are plotted in inverse order to facilitate comparison with the plot of HOMO energies. The data points in the plots are coded according to the steric similarities given by the number of alkyl groups attached to the double bond: mono-, di-, tri-, and tetrasubstituted.

Scheme 1, in which the alkene π bond is attacked by the electrophile ISCN to form a three-membered cyclic iodonium ion intermediate **b**. Increasing alkyl substitution on the alkenyl double bond increases the reaction rate, presumably due to the electron-donating electronic effects of the alkyl groups, rather than to steric effects, which should retard the reaction rate. This would be expected because enriching electron density on the alkenyl carbons makes their π electrons more loosely held and facilitates processes which remove or reduce π electron density. This manifests itself experimentally as a lower IP, as well as an increased rate of reaction with an electrophile.

The general pattern of relative reactivity of alkenes observed in ISCN addition has some similarities to our previous studies of electrophilic additions,[18a,b] which depended mainly upon electronic effects: (1) the relative rates of trisubstituted alkenes are greatest because they have the lowest IP values, (2) disubstituted alkenes react slower because they have higher IP values, and (3) the monosubstituted alkenes react slowest because they have the highest IP values. However, unlike those previous studies, the data points in the plots in Figures 1a and b do not fall on a correlation line neatly, but clearly cluster into three groups according to number of alkyl substituents on the C=C bond. Within each group, relative rates depend greatly upon position, size, and branching of alkyl substituents, as well as the alkene IP or HOMO energy values. For example, in ISCN addition to disubstituted alkenes, the ordering according to reaction rates produces further subgroups: geminal alkenes (**13**, **14**, **17**, and **18**) > vicinal *cis*-alkenes (**15**, **25**, **28**, and **30**) > vicinal *trans*-alkenes (**16**, **24**, **29**, and **31**). 2,3,3-Trimethyl-1-butene (**21**) reacts much slower than do other geminal alkenes probably due to the bulky *t*-butyl group, which may retard the reaction significantly. Similarly, the ordering of reaction rates of monosubstituted alkenes produces two subgroups: faster-reacting alkenes, each with a straight chain alkyl substituent (**3**, **4**, **6**, **10**, and **11**), and slower-reacting alkenes, each with a branched alkyl substituent (**5**, **7**, **8**, **9**, and **12**). The relationship between alkene reactivity and the position, size, and branching of its alkyl substituents in ISCN addition is quite different from what we observed in our previous studies.[18a,b] In those either (1) a single line of correlation among all alkenes regardless of the degree of substitution and of the positions and sizes of the substituents, or (2) multiple lines of correlation among similarly-substituted alkenes regardless of the positions and sizes of the substituents was obtained. Therefore, this study demonstrates that, in addition to the degree of substitution of the alkene C=C bonds, the position, size, and branching of substituents can be a major part of the total steric effects upon the reactivity in some alkene additions.

The plot of alkene IPs versus $\log k_{rel}$ values of ICl addition is given in Figure 1c. The overall trend here is similar to that shown in Figures 1a and b for ISCN additions, that is, the reaction rate increases as more alkyl substituents are introduced onto the C=C bond. However, the clustering and subgrouping of the data points observed in ISCN addition are less apparent here and $\log k_{rel}$ values correlate alkene IPs better in ICl addition than in ISCN addition. Additions of ICl,[7] Br_2,[19] and Cl_2,[19] are more complicated than ISCN addition; the proposed mechanism for each involves several steps. Therefore, one might expect a lower correlation in these reactions than in ISCN addition. Surprisingly, ISCN addition appears to have the worst correlation.[18b] Reasons which might account for the unexpected result include (1) the substituent effects are spread across multiple reaction steps in the addition of ICl, Br_2, and Cl_2 and (2) ISCN is lower in electrophilicity, but larger in size than those halogens, which enhances the relative importance of steric effects.

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