The Effect of Solvent on a Lewis Acid Catalyzed Diels-Alder Reaction, Using Computed and Experimental Kinetic Isotope Effects

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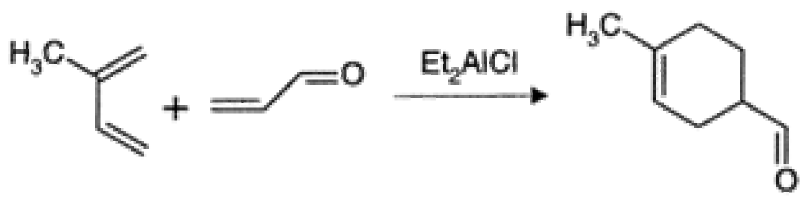
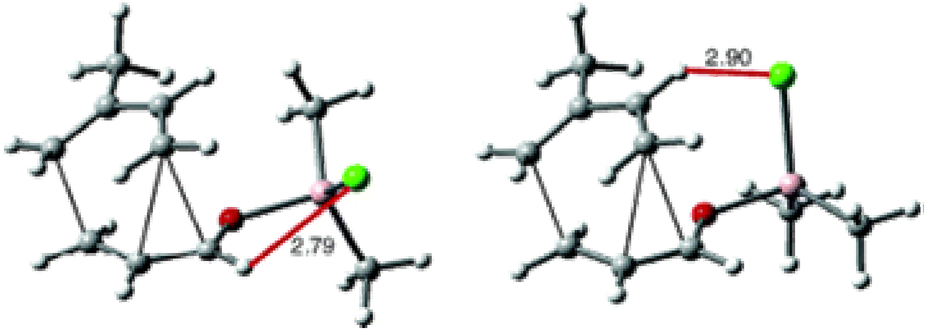
Abstract

- A new transition structure is reported for the Diels-Alder reaction of isoprene and acrolein catalyzed by a Lewis acid
- Including the effect of the solvent realigns the computed results with experimental data
- The newly predicted KIE data reaffirms the ability of theory and experiment to probe the mechanism and transition structure geometry of organic reactions





Overview

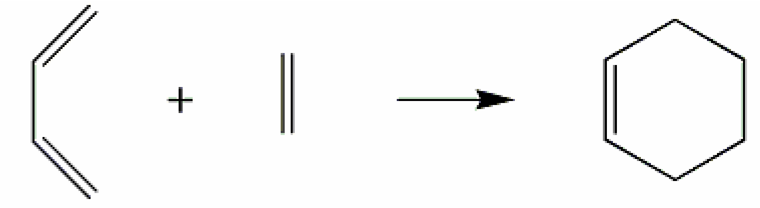
- Discussion of key points of reaction
  - Overview of transition structures
  - Discussion of organic chemistry involved
- Using Kinetic Isotope Effects (KIE) to investigate transition states
- Using ab initio calculations to investigate transition states
- Discussion of methods as applied in this experiment and the results

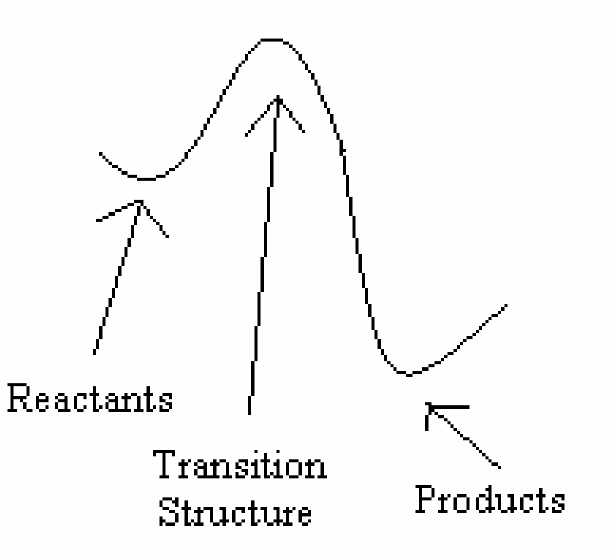
Scott Geyer:

Dr. Jordan, Dr. Bahar

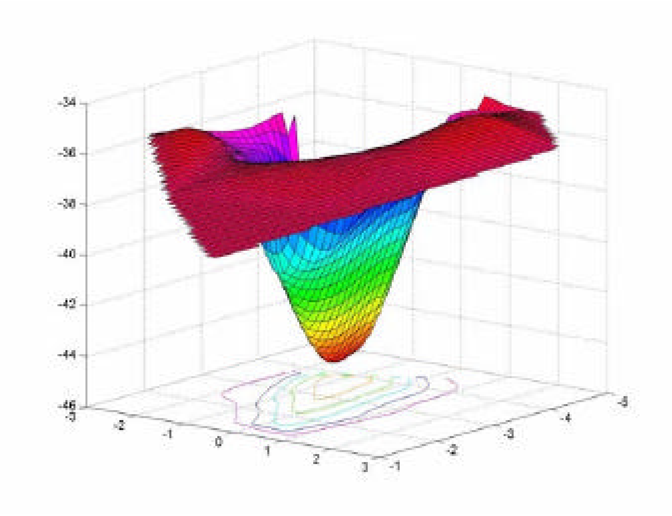
Potential Energy Surfaces

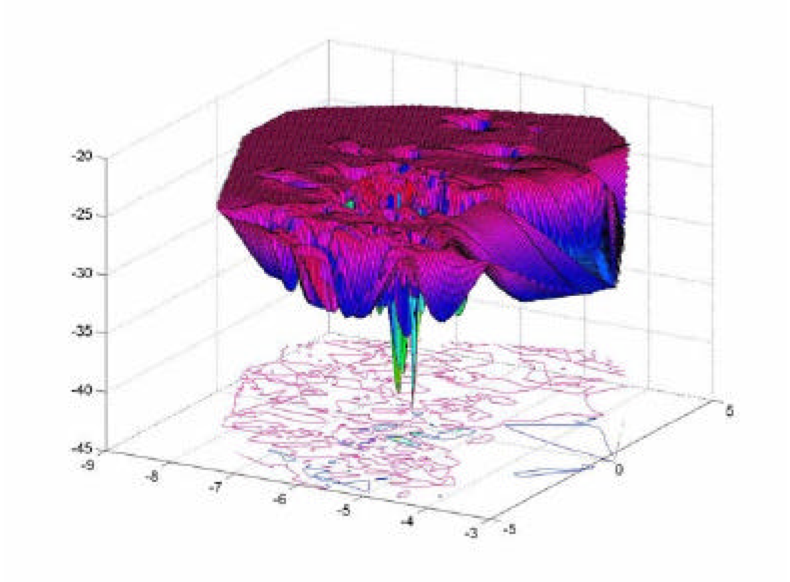
- Reactants and Products both exist in *local energy minima*
  - Bonds and structural conformation are in a manner to minimize energy
  - This is why they can be isolated and exist for extended periods of time
- To move from reactants to products involves going from one local minima to another
- The path that takes the least energy goes through a transition structure, where the system could move to both reactants and products *without more energy*

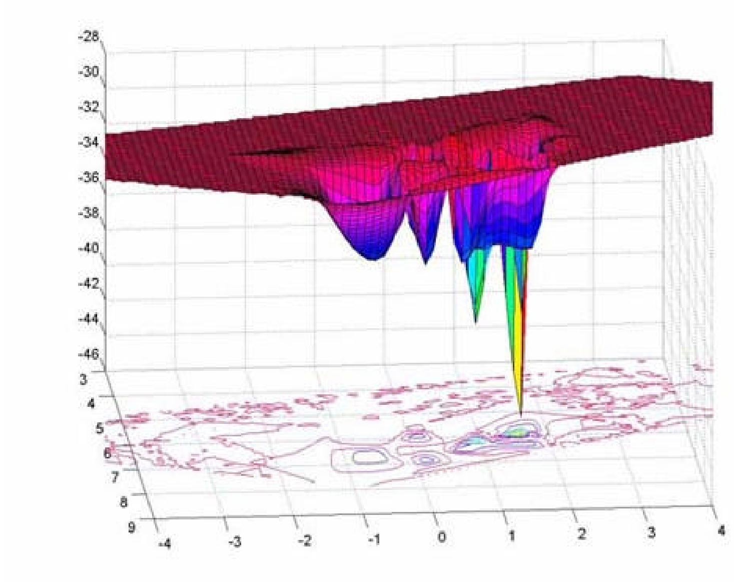




Previous Examples

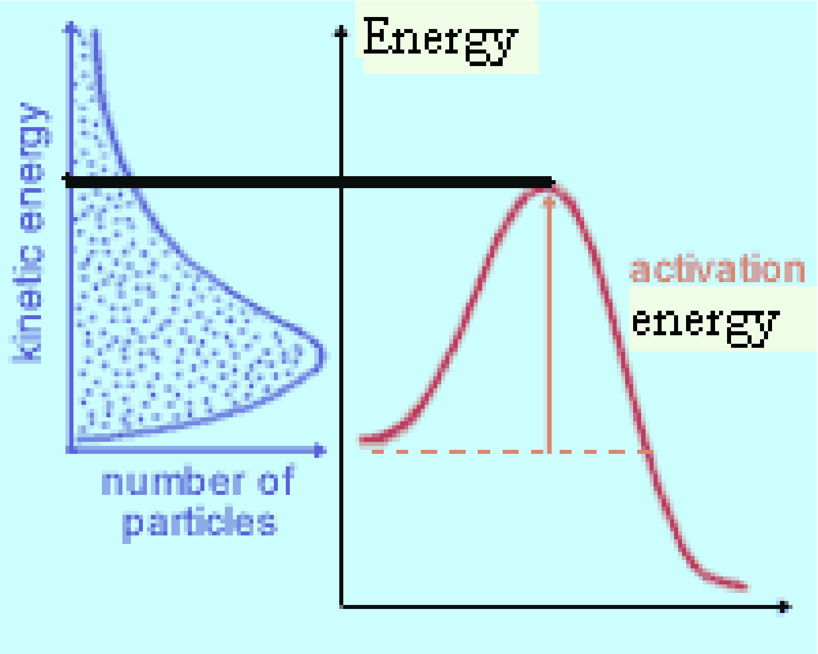






Activation Energy

- Transition State Theory relates the *activation energy* to the *rate of the reaction*



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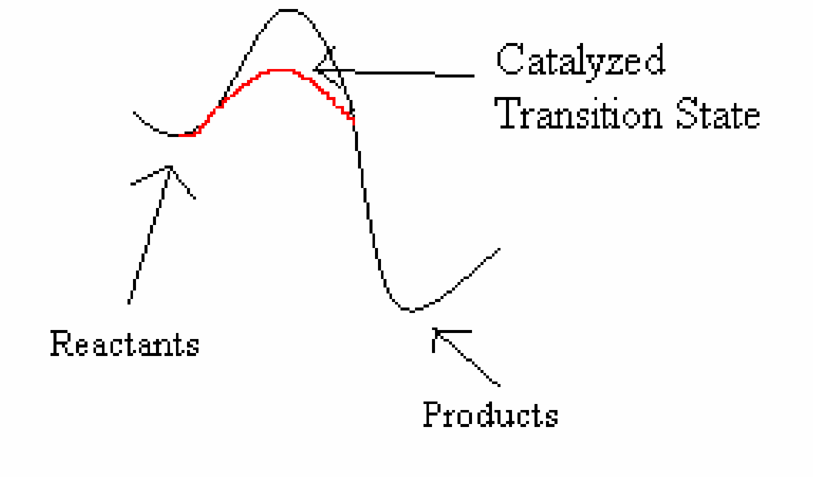
Higher reactants, gas phase le chatlier’s

Importance of Transition State

- There are numerous ways to go from products to reactants, but the path that takes the lowest amount of activation energy is the most important mechanistically
- Catalysts increase the rate of reaction by changing the energy landscape
- Knowledge of transition structures aids in the design of catalysts, etc.



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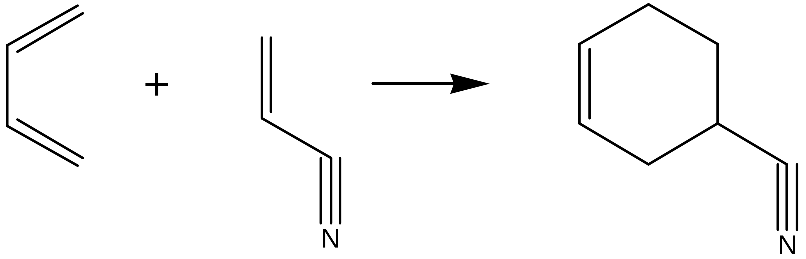
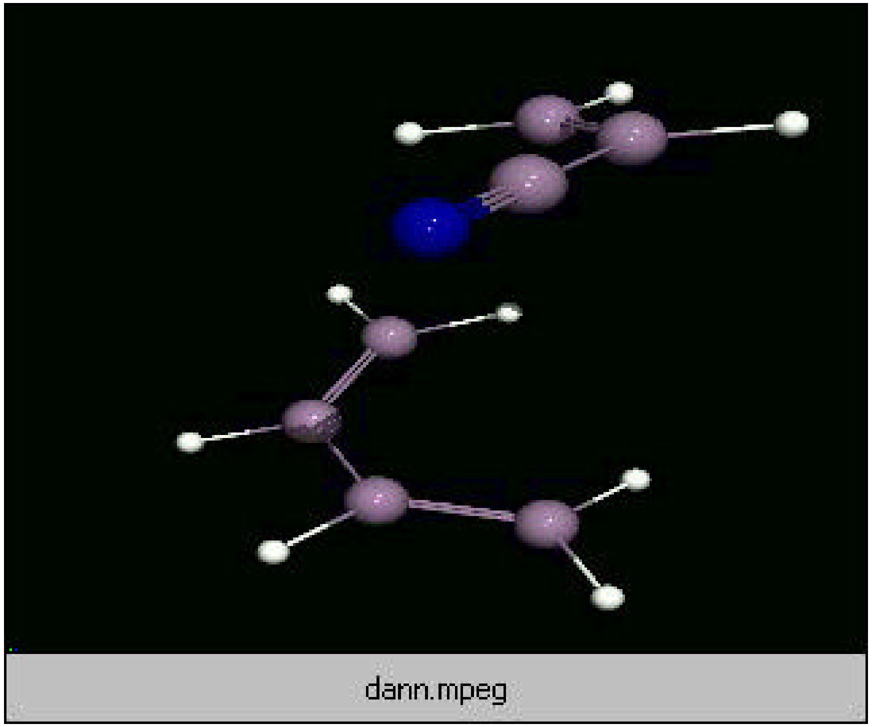
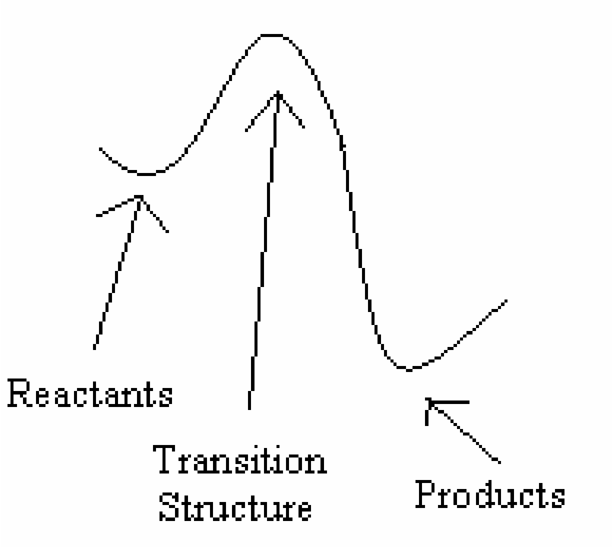
The Diels Alder Reaction

Example:

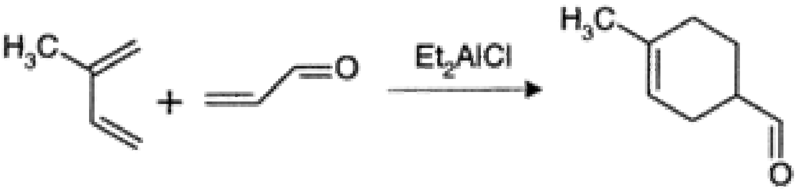




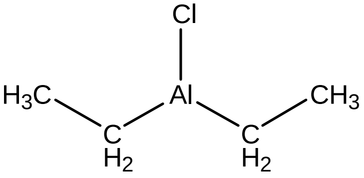


The Catalyzed Diels Alder Reaction

- The Lewis Acid Et_2AlCl is used to increase the reaction rate.
- How this actually occurs is what is under investigation



Et_2AlCl =



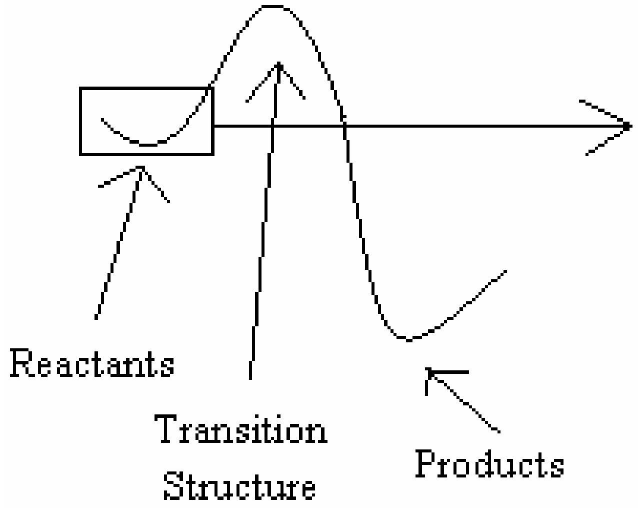
Kinetic Isotope Effects (KIE)

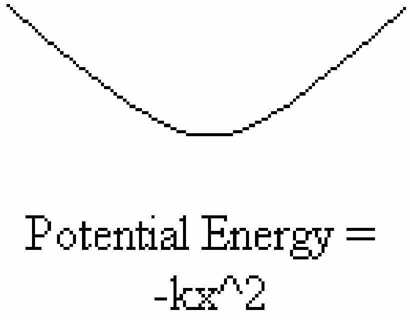
- Isotopes have same number of protons and electrons, but have with different mass
  - Ex. H- 1.008, D- 2.014, T- 3.016
- The Kinetic Isotope Effect is the change in the *reaction rate* when different isotopes are used
  - Isotopically labeled reagents can be synthesized and rates compared
  - NMR techniques that utilize the natural abundance of carbon 13, for example, have been employed
- The KIE is defined as (*rate of light isotope)/(rate of heavy isotope)*
  - Example: kH/kD = 1.5 if kH = 3, kD =2

Kinetic Isotope Effects:

Why the rate difference?

- Potential minima can be modeled as *harmonic oscillators*.
- For a quantum mechanical system, such as the local R-H bond, the solution of the energy must be derived from QM





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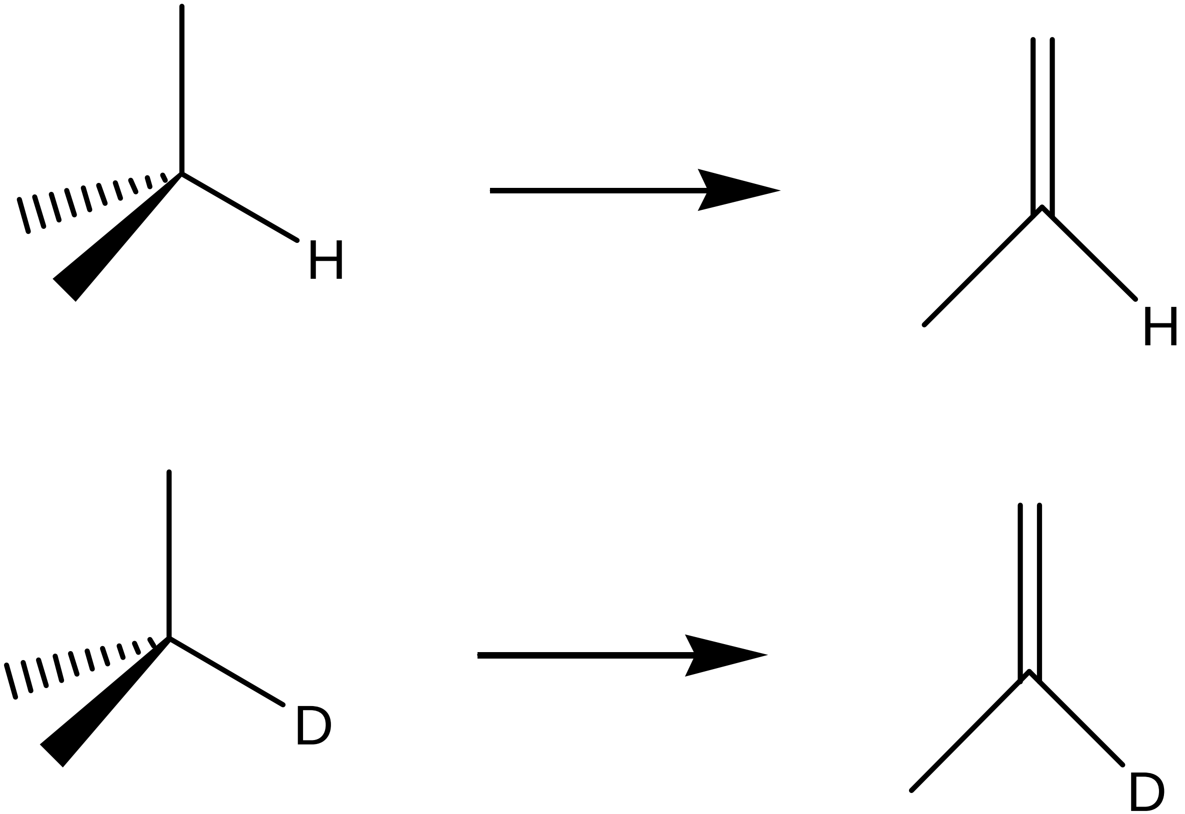
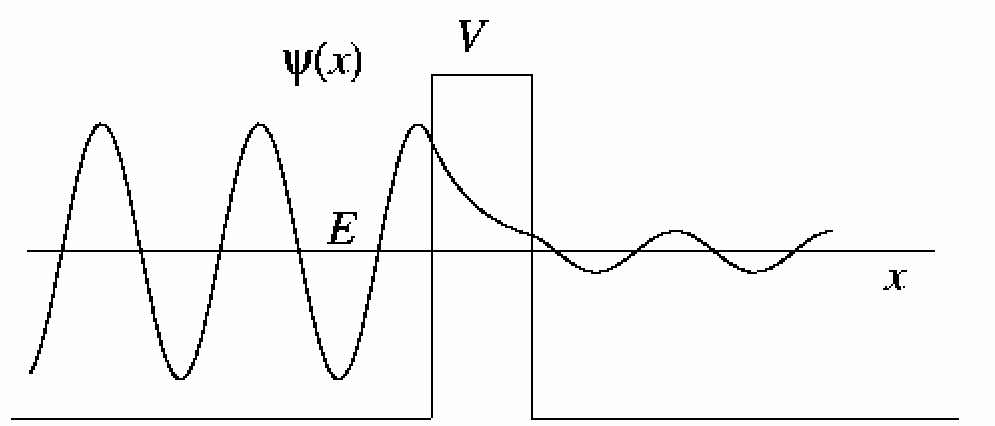
Example Of Secondary KIE



kH/kD = ?

Kinetic Isotope Effect:
QM tunneling and enzymes

- Full Quantum KIE effects include tunneling as well for light atoms, i.e. H, D, T.



- Research has been done to study if some of the effectiveness of certain enzymes on catalyzing reactions is due to their bringing together hydrogen donor and receiver close enough to allow hydrogen tunneling

Quantum *ab initio* methods

- Ab initio methods are based upon the explicit use of electrons.
- The Schrodinger equation can not be solved exactly for multiple electron systems.
- By making approximations to the Schrodinger equation, a system can be modeled over time, and energies, geometries and other molecular properties can be obtained.

Model Chemistries

- Model chemistries are functionally useful approximations, typically made of two parts for ab initio calculations:
  - Basis Sets: Describe the wavefunction of the electrons.
  - Methods: Approximate the Schrodinger equation
- Combined, these make up a specific level of theory.

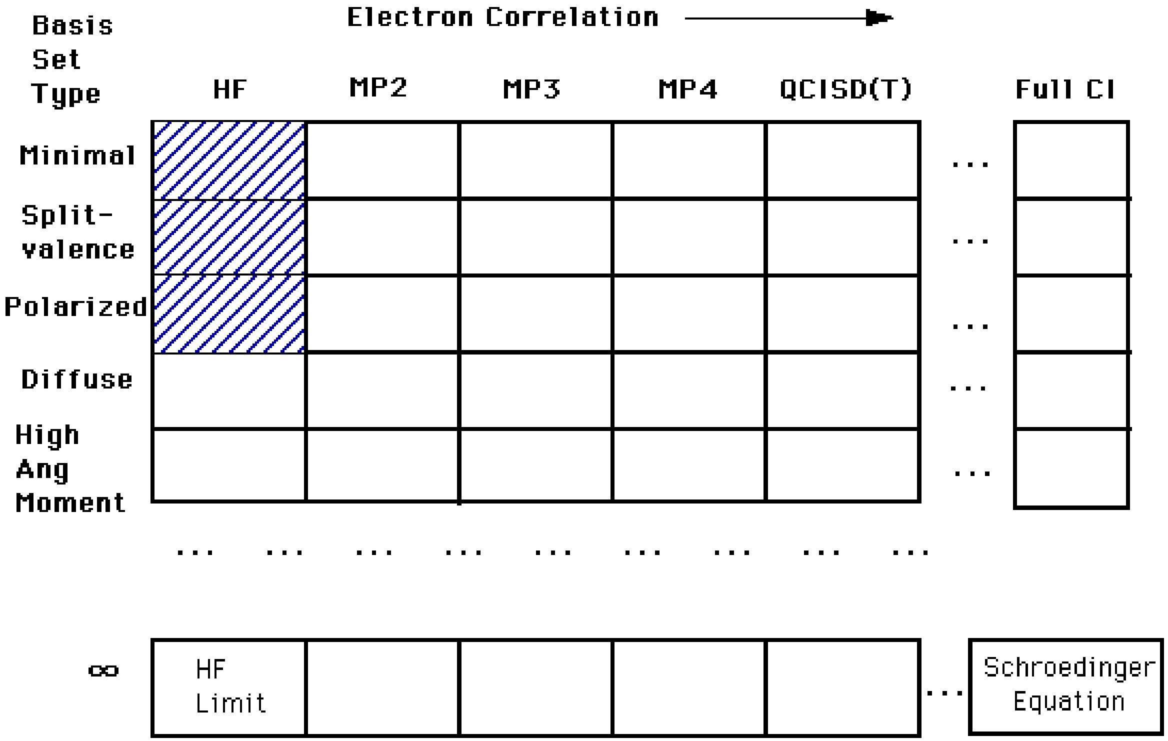
Basis Sets

- The size of a basis set refers to the number of atomic orbitals that are included in making up a molecular orbital.

Methods

- Hartree-Fock
  - Simplest, no electron correlation
- Moller Plesset Theory
  - Includes electron correlation

Ab initio calculations:
Diagram



Electron Correlation →

Basis Set Type	HF	MP2	MP3	MP4	QCISD(T)		Full CI
Minimal	▨					...	
Split-valence	▨					...	
Polarized	▨					...	
Diffuse						...	
High Ang Moment						...	
...	...	...	...	...	...	...	...
∞	HF Limit					...	Schroedinger Equation

All Calculations were done at the B3LYP/6-31G(d) level of theory

How it fits together:
Investigating a transition structure through KIE and ab initio approaches

- KIE values were experimentally obtained for the Lewis acid catalyzed diels alder reaction by Singleton at Texas A&M
- Ken Hock had suggested a transition structure, but it did not fit the experimental data.

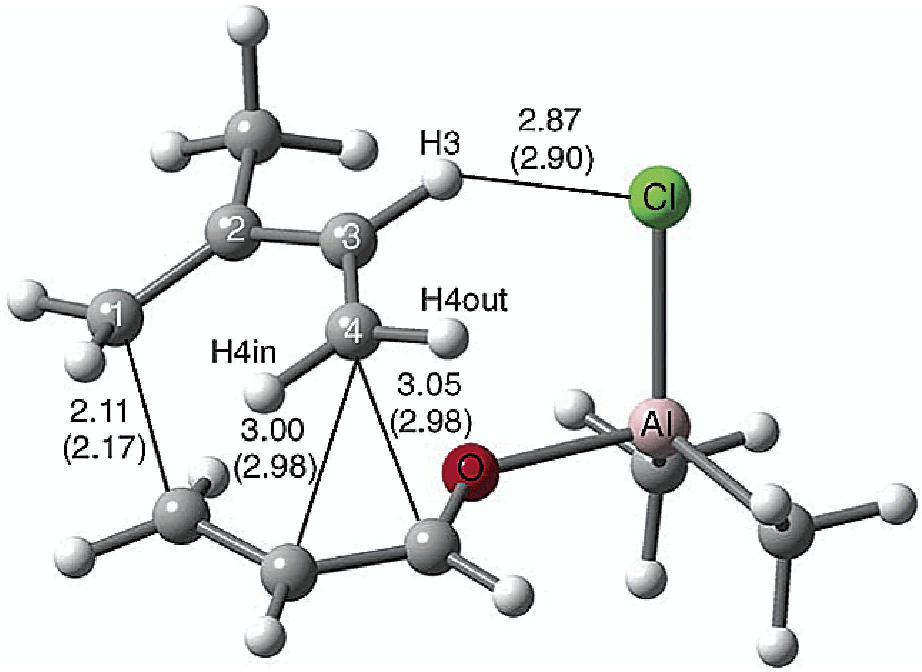


Table 1. The Experimental and Calculated KIEs (k_H/k_D or k_{12C}/k_{13C}) for the Lewis Acid Catalyzed Diels-Alder Reaction of Isoprene and Acrolein[1]

	exp. 1[1]	exp. 2[1]	calcd
C1	1.030(3)	1.026(10)	1.031
C2	1.004(3)	1.006(9)	1.004
C3	1.001(2)	1.001(10)	1.000
C4	1.000(3)	1.001(10)	1.002
H1in + H1out	0.915(6)	0.916(7)	0.910
H3	0.965(5)	0.967(13)	0.934
H4out	0.978(6)	0.979(18)	0.986
H4in	0.951(4)	0.947(8)	0.968

Investigating a transition structure through KIE and ab initio approaches

- Another transition structure was modeled by changing the initial arrangement of the catalyst before doing the calculations
  - This structure was characterized by a planar, non traditional hydrogen bond
  - The KIE calculated theoretically agreed much more closely with the experimental KIE
- However, this structure was at a higher energy!
  - From before, the path that will be taken the vast majority of the time is the lowest in energy
  - Experimental KIE must be from path(s) taken a high percentage of the time

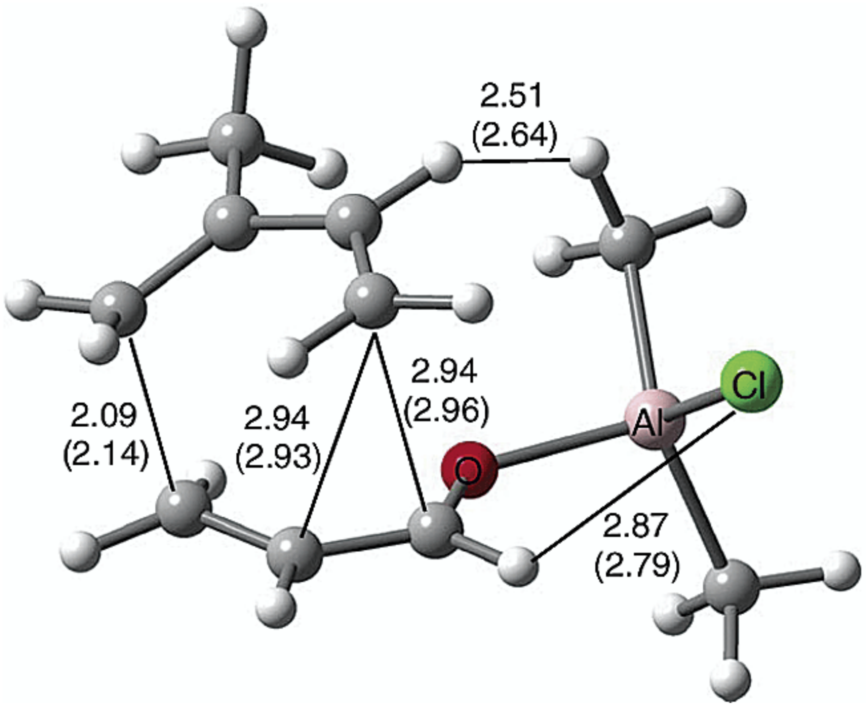


Table 2. Calculated KIEs (k_H/k_D or k_{12C}/k_{13C}) for the Two TSs of the Lewis Acid Catalyzed Diels-Alder Reaction of Isoprene and Acrolein at B3LYP/6-31G(d)[a]

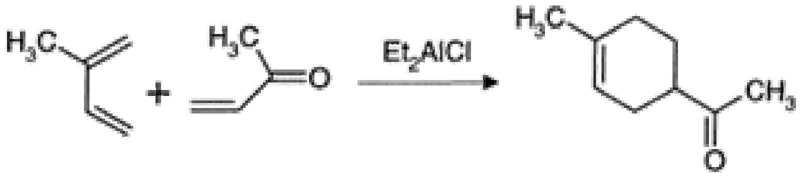
	Singleton/Houk TS	our TS	exp. 1[1]	exp. 2[1]
C1	1.032 [1.033]	1.032 [1.033]	1.030(3)	1.026(10)
C2	1.003 [1.002]	1.003 [1.002]	1.004(3)	1.006(9)
C3	0.999 [0.999]	0.999 [0.999]	1.001(2)	1.001(10)
C4	1.003 [1.003]	1.004 [1.003]	1.000(3)	1.001(10)
H3	0.943 [0.946]	0.964 [0.962]	0.965(5)	0.967(13)
H4out	0.985 [0.987]	0.975 [0.980]	0.978(6)	0.979(18)
H4in	0.963 [0.961]	0.968 [0.957]	0.951(4)	0.947(8)

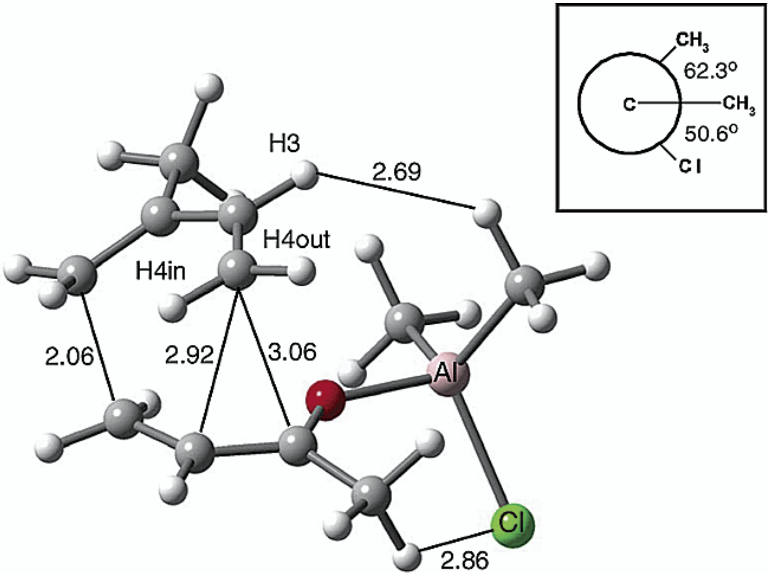
Solving the Energy Discrepancy: Solvent Effects

- The modeling was done with only the 2 reactants and catalyst initially for both transition states
- The effects of solvation by water were not included
- Upon including the effects of solvation, the energy of the second, KIE agreeing structure *drops below that of the other*
- This means the the second transition structure suggests a new, experimentally valid mechanism

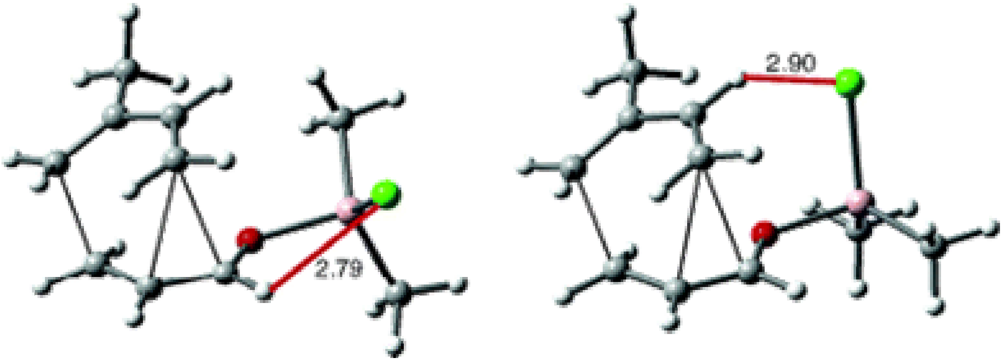
Testing the structure for a second case

- Another calculation was done to see if the same orientation of the Lewis acid catalyst might be valid for a molecule which could not participate in the non standard H-bonding
- This calculation showed the steric effects now dominated the configuration, and these also allowed for a similar catalyst arrangement.





Abstract:



A new transition structure for the Diels-Alder reaction between isoprene and acrolein catalyzed by Et_2AlCl is found to reconcile reported discrepancies between computed and observed secondary kinetic isotope effects (KIEs). Including the effect of solvent realigns the computed results with experiment demonstrating the importance of nonbond interactions at transition structures. Comparison of experimental and newly predicted KIE data reaffirms the ability of theory and experiment to probe the mechanism and transition structure geometry of organic reactions.

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The Diels-Alder Reaction and "Aromatic" Transition States

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Application of KIE to Biological System:

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Amnon Kohen

http://cricket.chem.uiowa.edu/~kohen/journal/prkm.pdf

Enzyme Catalysis: Beyond

Classical Paradigms

Amnon Kohen and Judith P. Klinman

http://pubs.acs.org/cgi-bin/gap.cgi/achre4/1998/31/i07/pdf/ar9701225.pdf

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Gustavo E. Davico

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Kinetic Isotope Effects in the N2O Decomposition over NiO

Peter Z¡ emva, Antonija Lesar, Ivan Kobal,* and Marjan Senegac¡nik

http://pubs.acs.org/cgi-bin/article.cgi/jpcbfk/2001/105/i19/pdf/jp002920+.pdf

Carbon-13 Kinetic Isotope Effects in CO Oxidation by Ag

Ivan Kobal, Uwe Burghaus,§ Marjan Senegac¡nik, and Nives Ogrinc

http://pubs.acs.org/cgi-bin/article.cgi/langd5/1999/15/i18/pdf/la981309n.pdf

Temperature-Dependent Kinetic Isotope Effects in the Gas-Phase Reaction: OH + HBr

Veronica I. Jaramillo and Mark A. Smith

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Obtaining KIE values experimentally:

Simultaneous Determination of Intermolecular and Intramolecular 13C and 2H Kinetic Isotope Effects at Natural Abundance

Daniel A. Singleton* and Michael J. Szymanski

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Measuring Kinetic Isotope Effects Of Carbon At Natural Abundance

Reported by John D. Baird

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Computational Chemistry and Guassian

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C. David Sherrill

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The Four Sources of Error in Ab Initio Calculations

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