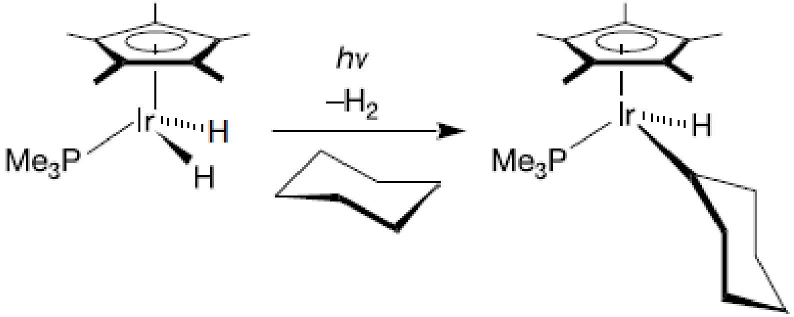
C-H BOND ACTIVATION

Focus on John Bercaw's early work

DEFINING "C-H ACTIVATION"

- Processes such as Friedel-Crafts alkylations or aromatic nitrations cleave a C-H bond by initial electrophilic attack on aromatic π-system and subsequent cleavage of the C-H bond by a base
- In contrast, "C-H activation" refers to reactions involving the cleavage of an unreactive C-H bond of alkanes, arenes, or alkyl chains by transition metal complexes to form products with M-C bond



Organotransition Metal Chemistry; Hartwig, J.; University Science books: California, 2010.
Janowicz, A. H. & Bergman, R. G. *J. Am. Chem. Soc.* **1982,** *104,* 352-354.

THE TARGET OF INTEREST -

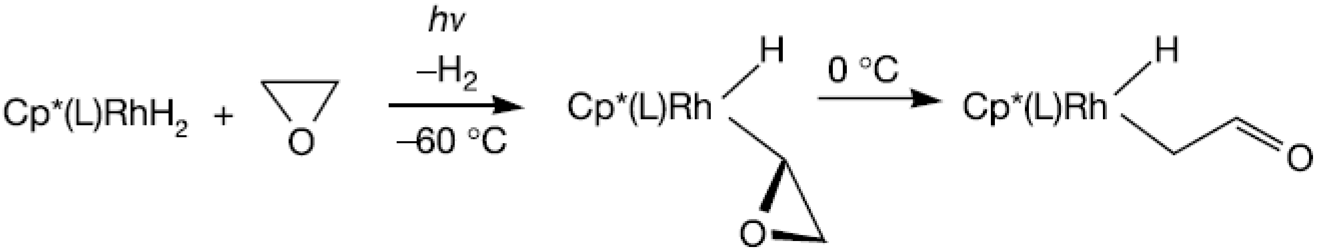
- Current major use of alkanes are for their energy content via combustion.
- They can also be cracked and degraded to valuable olefins but it is energy intensive.
- Standard organic reactions via radicals or carbonium ions occur less readily at primary C-H bonds than at secondary or tertiary C-H bonds

- - Is the selective cleavage of a C-H bond followed by its functionalization into a C-X bond (where X = OH, NH_2, aryl …) under mild conditions via a catalytic process

The Organometallic Chemistry of the Transition Metals; Crabtree, R. H.; John Wiley & Sons, Inc.: New Jersey, 2009.
Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.

GOALS AND CHALLENGES

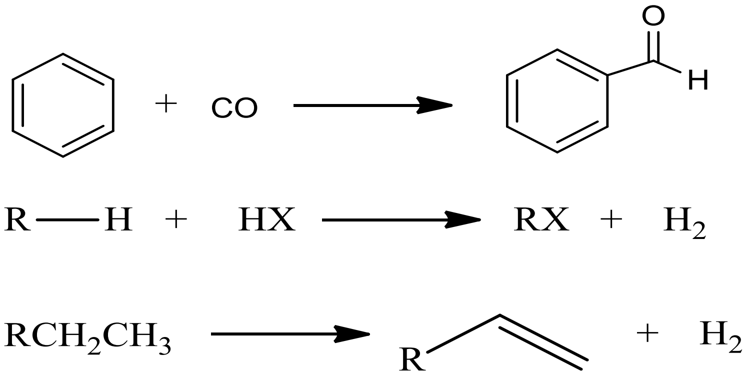
- Selective conversion of methane to methanol
- Replacement of strong terminal alkyl C-H bonds with a functional group
- Functional group on a desired product does not react more readily than the starting alkane



Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.
Wu, J. & Bergman, R. G. *J. Am. Chem. Soc.* **1989,** *111,* 7628-7630.

GOALS AND CHALLENGES

- Thermodynamically uphill – many catalytic processes with simple organometallic rxns are endothermic



ΔH = 1.7 kcal/mol

ΔH = 22 kcal/mol
$R = C_5H_{11}$, X = OH

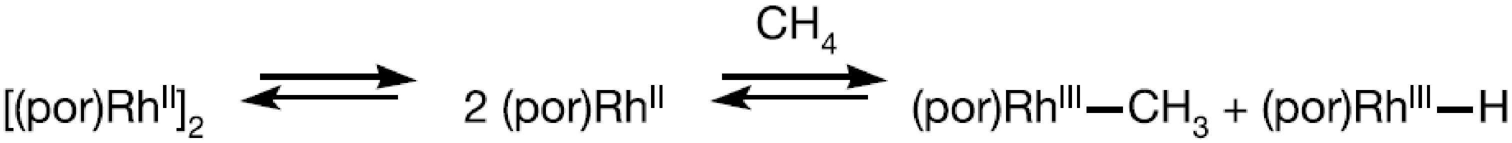
ΔH = 30 kcal/mol
$R = C_4H_9$

- Partial oxidations of alkanes are favored but many of C-H activation centers are highly sensitive to O_2 and other oxidants
- Pursant of systems that answer the demands of thermodynamics, chemial compatibilty, and selectivity

Organotransition Metal Chemistry; Hartwig, J.; University Science books: California, 2010
Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.

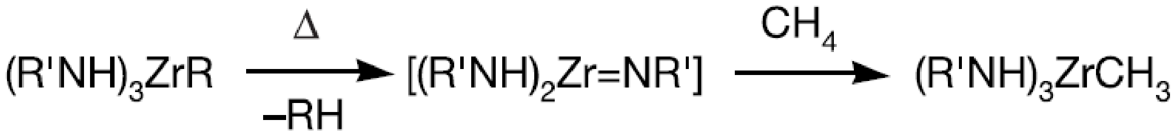
CLASSIFICATION OF REACTIONS

- Oxidative addition
- Sigma-bond metathesis
- Electrophilic activation
- Metalloradical activation
  - Complexes existing in monomer-dimer equilibrium can reversibly break alkane C-H bonds



$$[(\mathrm{por})\mathrm{Rh^{II}}]_2 \rightleftharpoons 2\ (\mathrm{por})\mathrm{Rh^{II}} \xrightleftharpoons{\mathrm{CH_4}} (\mathrm{por})\mathrm{Rh^{III}}{-}\mathrm{CH_3} + (\mathrm{por})\mathrm{Rh^{III}}{-}\mathrm{H}$$

- 1,2 – addition
  - Addition of an alkane to a metal-nonmetal double bond

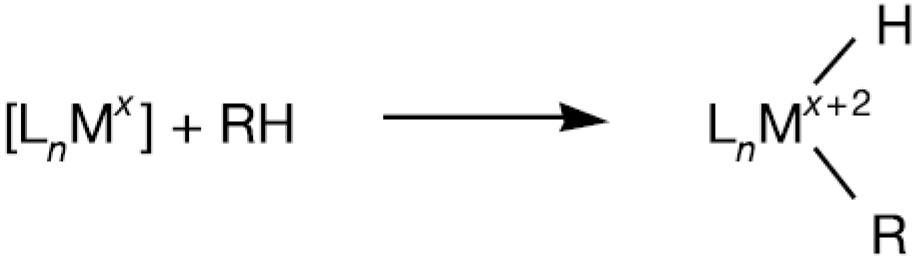


$$(\mathrm{R'NH})_3\mathrm{ZrR} \xrightarrow[-\mathrm{RH}]{\Delta} [(\mathrm{R'NH})_2\mathrm{Zr{=}NR'}] \xrightarrow{\mathrm{CH_4}} (\mathrm{R'NH})_3\mathrm{ZrCH_3}$$

Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.

OXIDATIVE ADDITION

- Typical reactions for electron-rich, low-valent complexes of the late transition metals – Re, Fe, Ru, Os, Rh, Ir, Pt

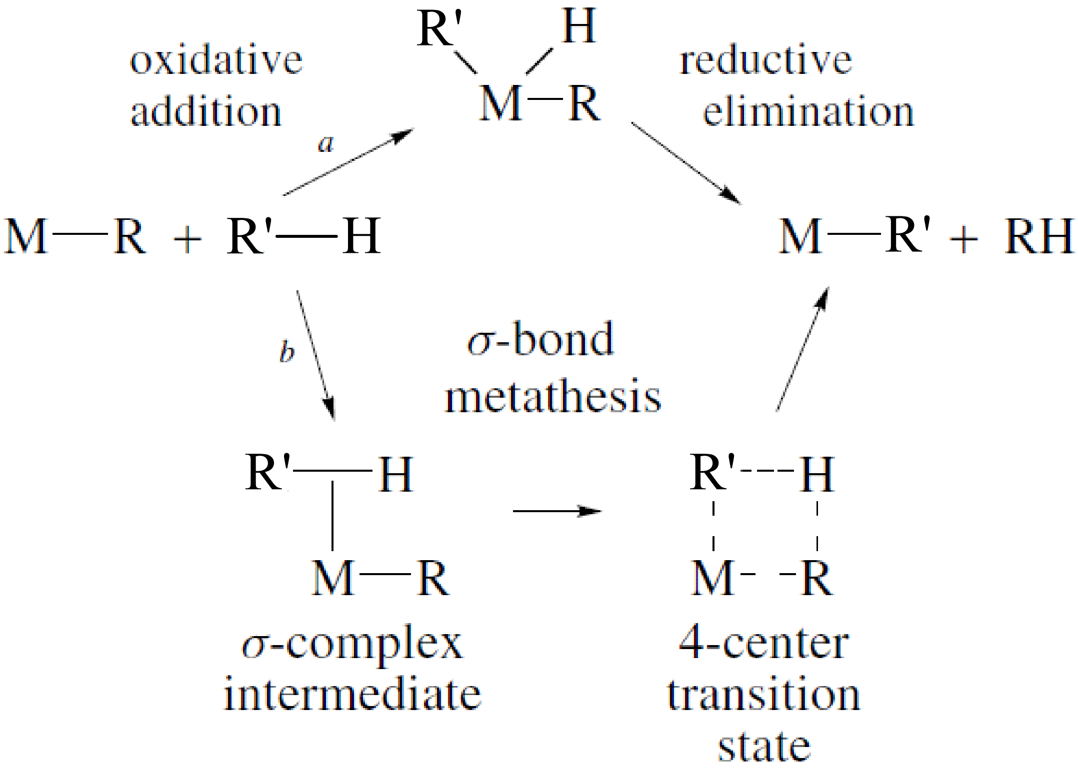


- The reactive species L_nM^x is generated *in situ* by thermal or photochemical decomposition from a precursor

Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.

SIGMA-BOND METATHESIS

- Transition metal complexes with d^0 configuration (ex: Cp_2ZrRCl, WMe_6) undergo a concerted process as oxidative addition is forbidden



The Organometallic Chemistry of the Transition Metals; Crabtree, R. H.; John Wiley & Sons, Inc.: New Jersey, 2009.

ELECTROPHILIC ACTIVATION

- Reactions classified as such result in functionalized alkanes without any observance of organometallic species, as illustrated in the equation below:

$$L_nM^{x+2}X_2 + R{-}H \longrightarrow [L_nM^{x}] + R{-}X + H{-}X$$

- $[M^{x+2}]$ is a late or post-transition metal (Pd^{2+}, Pt^{2+}/Pt^{4+}, Hg^{2+} , Tl^{3+}), usually in a strong polar medium such as water or anhydrous strong acid

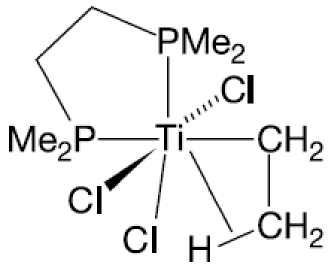
$$L_nM^{x+2}X_2 + R{-}H \longrightarrow [L_nM^{x+2}(R)(X)] + H{-}X$$

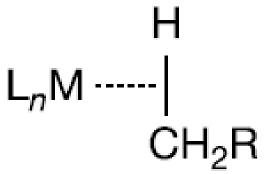
$$[L_nM^{x+2}(R)(X)] \longrightarrow [L_nM^{x}] + R{-}X$$

Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507.

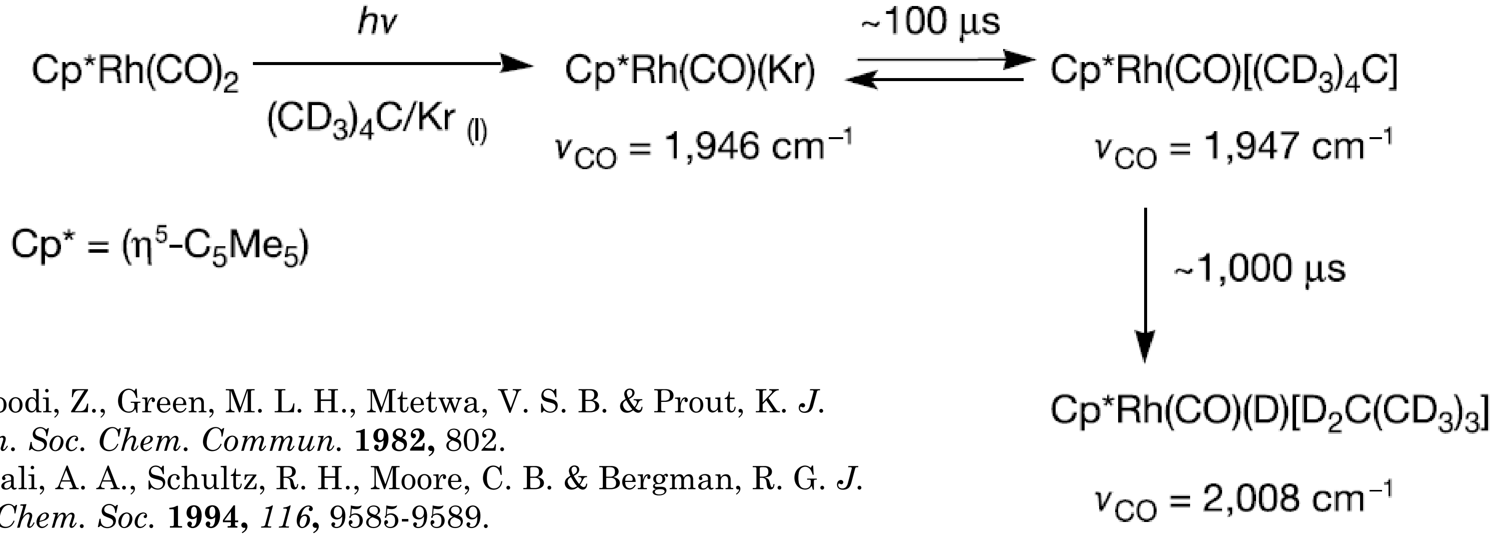
SIGMA COMPLEX: THE INITIAL INTERACTION

- Stable agostic complexes indicated that C-H bond activation occurred via the formation of σ-complex





- Vib. spectroscopic evidence of the transient species



Dawoodi, Z., Green, M. L. H., Mtetwa, V. S. B. & Prout, K. *J. Chem. Soc. Chem. Commun.* **1982,** 802.
Bengali, A. A., Schultz, R. H., Moore, C. B. & Bergman, R. G. *J. Am. Chem. Soc.* **1994,** *116***,** 9585-9589.

EARLY PLATINUM-CATALYZED C-H ACTIVATION

- Shilov & co-workers showed H/D exchange between alkanes and deuterated acid occured selectively at primary C-H bonds with Pt(II)

$$\mathrm{R{-}H} \xrightarrow[\mathrm{DClO_4,\ CH_3CO_2D,\ D_2O}]{\mathrm{K_2PtCl_4,\ 12\ mol\ \%}} \mathrm{R{-}D}$$

Alkane	Time (h)	% D found	Me – (%)	-CH_2- (%)	-CH- (%)
Methane	95	25			
Ethane	137	91	91		
Pentane	137	75	92	57	
2-methyl butane	137	69	83	37	9

Organotransition Metal Chemistry; Hartwig, J.; University Science books: California, 2010.

EARLY PLATINUM-CATALYZED C-H ACTIVATION

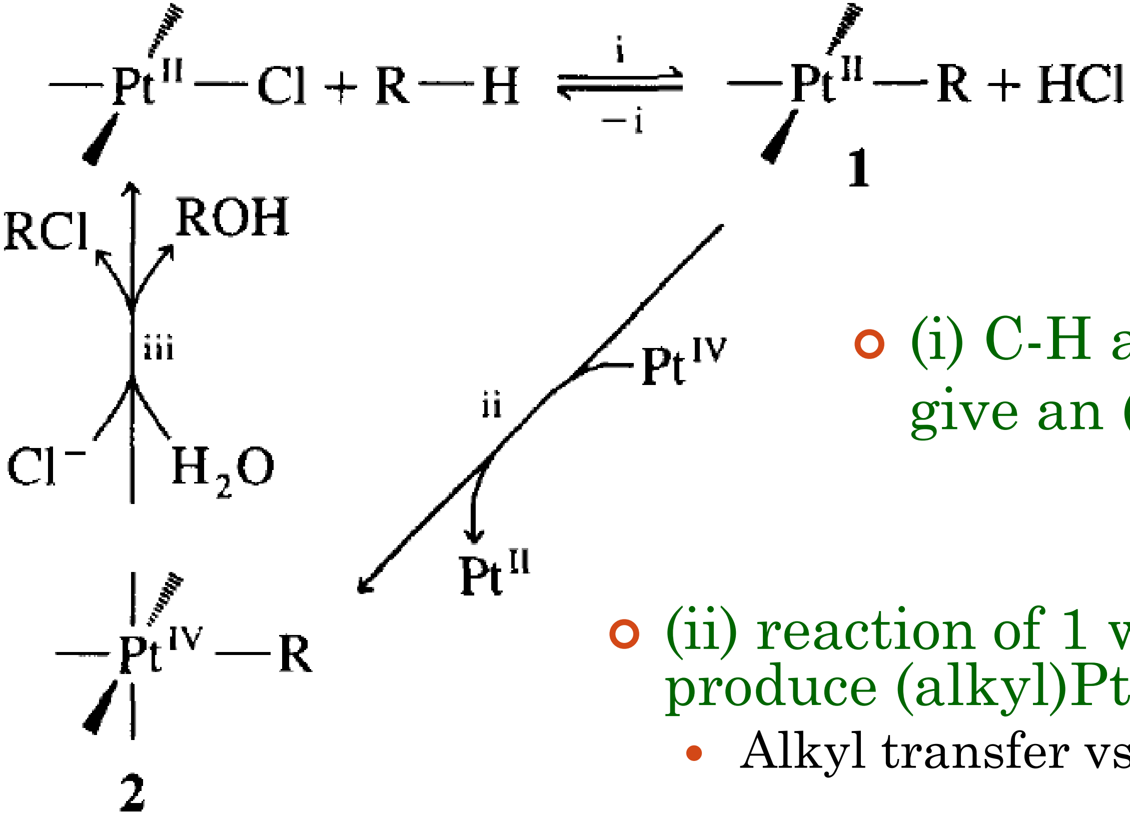
- With a Pt(IV) oxidant, Shilov also showed the oxidation of alkanes occurred via electrophilic mode of activation using the Pt(II) catalyst

$$\mathrm{RH} + \mathrm{PtCl_6}^{2-} + \mathrm{H_2O} \xrightarrow[120\ ^\circ\mathrm{C}]{\mathrm{PtCl_4}^{2-}} \mathrm{ROH} + \mathrm{RCl} + \mathrm{PtCl_4}^{2-} + 2\mathrm{HCl}$$

- Bercaw revisited this system in the 1990’s for a detailed mechanistic study of this C-H functionalization by Pt(II)/Pt(IV) mixture

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem*. **1995,** *504,* 75-91.

PROPOSED SCHEME AND INVESTIGATIONS

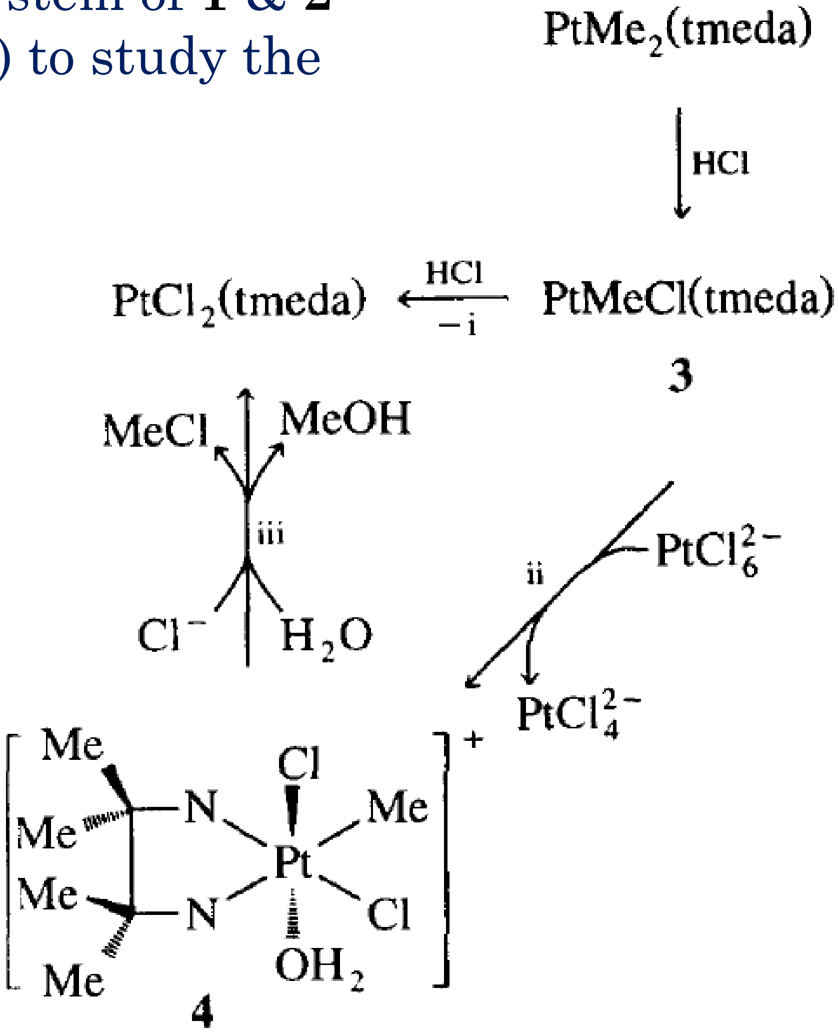


- (i) C-H activation by Pt^{II} to give an (alkyl)Pt^{II} **1** complex
- (ii) reaction of 1 with $PtCl_6^{2-}$ to produce (alkyl)Pt^{IV} **2** complex
  - Alkyl transfer vs. oxidation of RPt^{II}
- (iii) reaction of **2** with nucleophile to liberate product and regenerate Pt^{II}
  - Reductive elimination vs. external nucleophilic attack

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem.* **1995,** *504,* 75-91.

MECHANISTIC STUDY VIA A MODEL SYSTEM

- An analogous ligand substituted system of **1** & **2** (minus the intial alkane activation) to study the features of the proposed scheme
- Oxidation of **3** by $PtCl_6^{2-}$ in water gives $MePt^{IV}$(tmeda) complex **4**
- **4** then reacts with aqueous chloride at elevated temperatures to give methyl chloride and methanol along with $PtCl_2$(tmeda)



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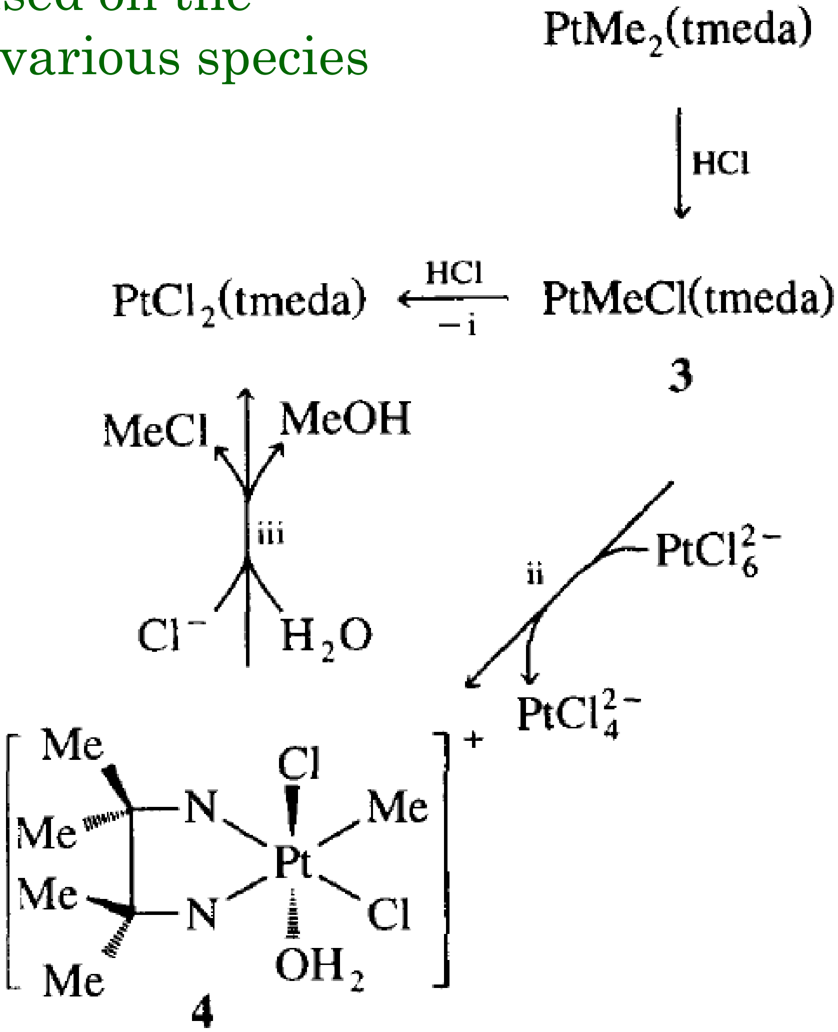
MECHANISTIC STUDY VIA A MODEL SYSTEM

- The structure of **4** was proposed based on the following ^{1}H NMR spectral data of various species
- **4** shows four separate signals for methyls on tmeda, two with large ^{195}Pt satellites
- **3** shows two separate signals for methyls on tmeda, with one having a large ^{195}Pt satellites
- Oxidation of **3** by Cl_2 gives only two tmeda methyl signals, presumably a $PtMeCl_3$(tmeda) species



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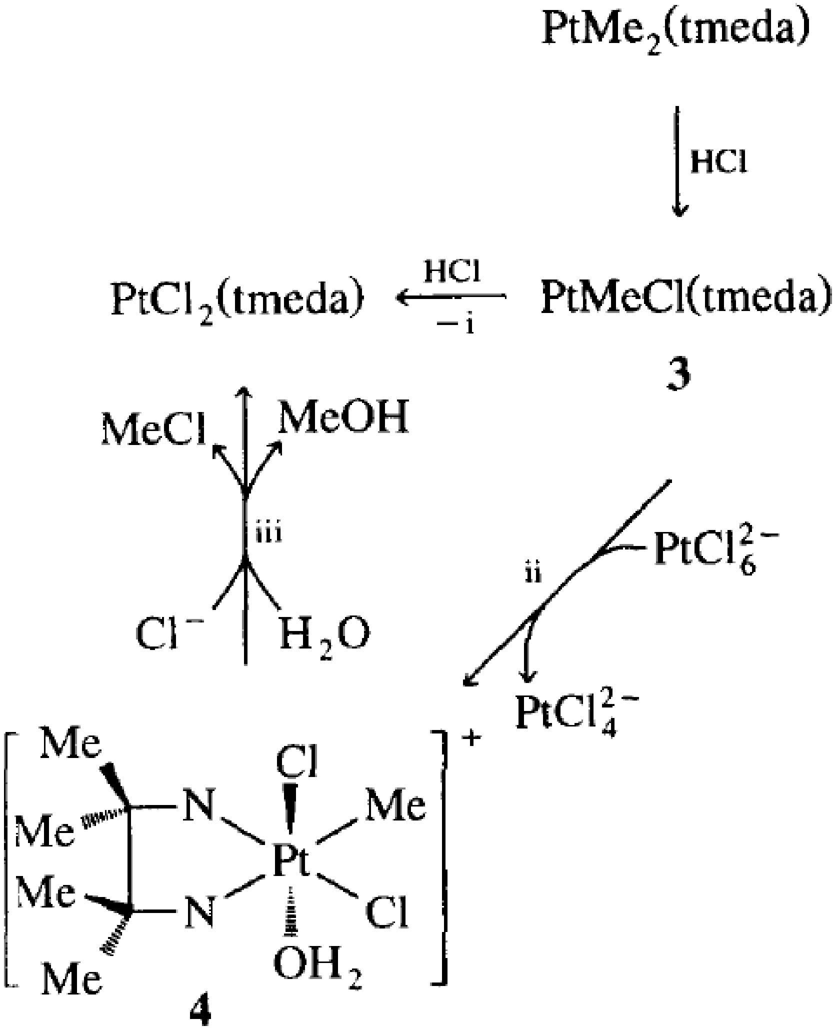
MECHANISTIC STUDY VIA A MODEL SYSTEM

- The formation of **4** rather than $[PtMeCl_5]^{2-}$ is consistent with $PtCl_6^{2-}$ oxidizing **3** via electron transfer rather than an alkyl transfer in step ii

- The actual alkane activating system does not contain a strongly bound ligand such as TMEDA and hence it's not safe to conclude that the same holds true



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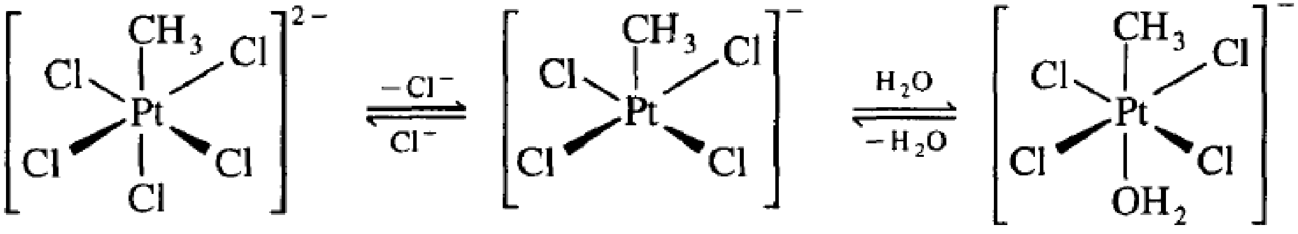
KINETICS

- To study step iii of the catalytic cycle, complexes of type **2,** (alkyl)Pt^{IV}, were synthesized

$$3[PtCl_4]^{2-} + 2RI \longrightarrow 2[PtRCl_5]^{2-} + PtI_2 + 2Cl^-$$

$$R = Me, CH_2CH_2OH$$

- For $[PtMeCl_5]^{2-}$, the ^1H and ^{13}C NMR spectra show single peak for Pt-Me, which is not affected by the addition of excess Cl^-
- In contrast, the ^{195}Pt NMR spectrum show two signals whose relative intensities depend on $[Cl^-]$



5a **5b** **5c**

K = 0.9 M

- 822 ppm

- 780 ppm

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem*. **1995,** *504,* 75-91.

Kinetics

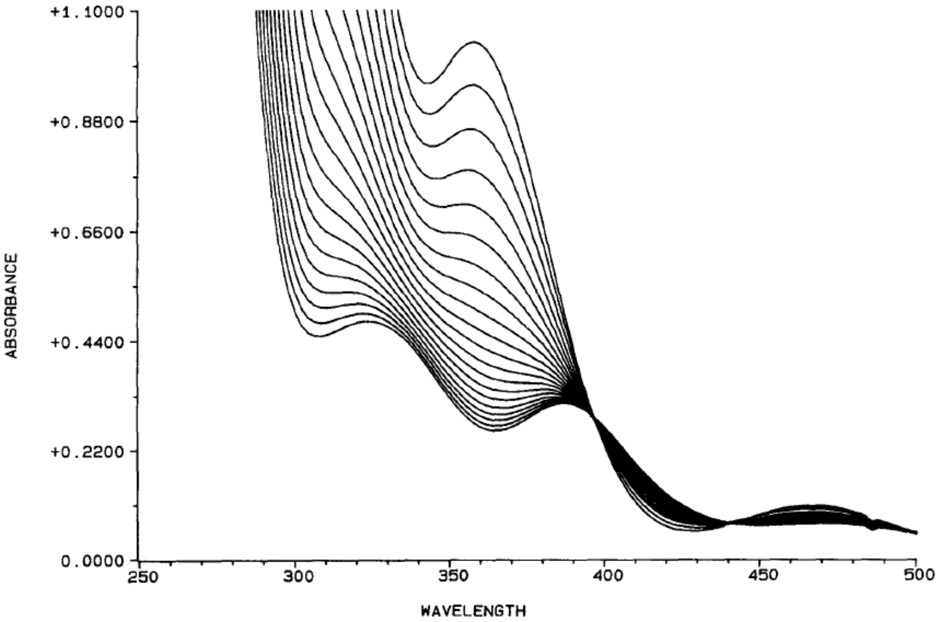
- The kinetics for the decomposition of **5** & **6** were followed by disappearance of the UV-vis absorption (364 nm & 366 nm, respectively) over a range of [Cl$^-$]

$$[PtCH_3Cl_5]^{2-} \xrightarrow{Cl^-/H_2O} CH_3Cl + CH_3OH + [PtCl_4]^{2-}$$

5

$$[Pt(CH_2CH_2OH)Cl_5]^{2-} \xrightarrow{Cl^-/H_2O} ClCH_2CH_2OH + HOCH_2CH_2OH + [PtCl_4]^{2-}$$

6



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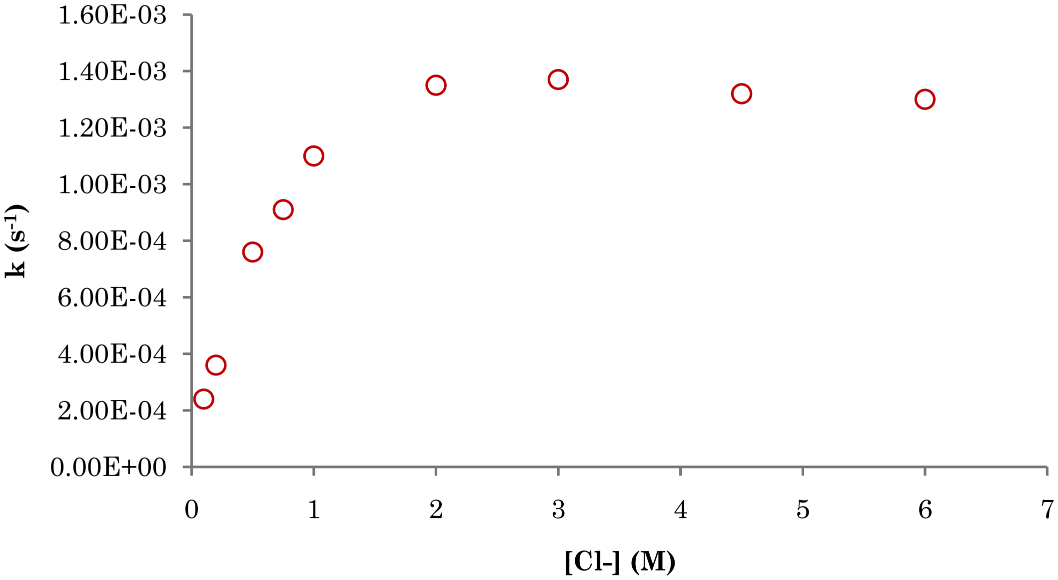
KINETICS

- Each run showed pseudo-first order kinetics in total [Pt^{IV}]
- As [Cl^-] increases, the rate increases, and the relative amount of RCl (vs. ROH) increases
- This is consistent with competitive nucleophilic attack by Cl^- and H_2O

First-order rate constant for decomposition of **5** at 45 C as a function of [Cl^-]



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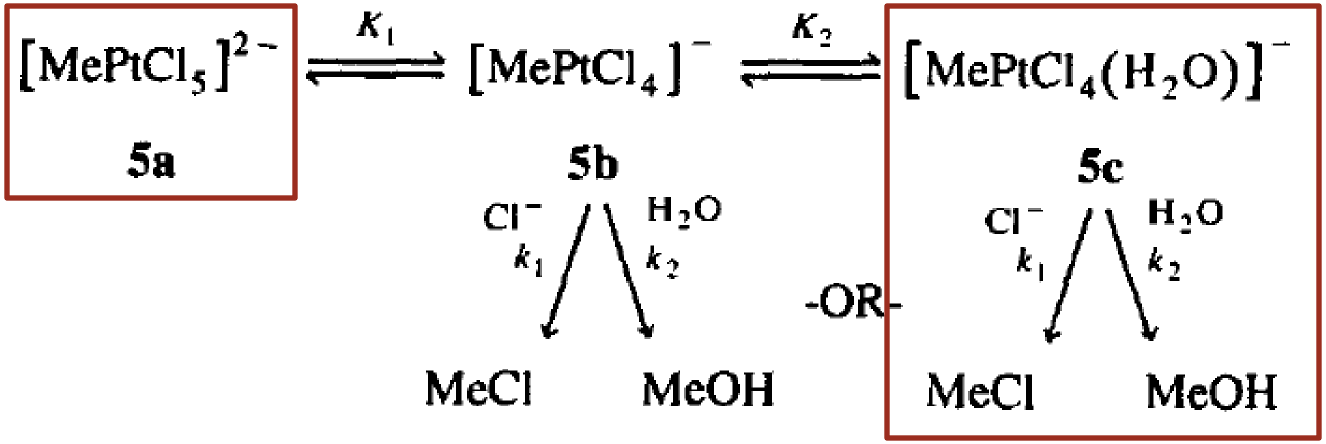
KINETICS



$$\mathbf{5c} + Cl^- \xrightarrow{k_1} RCl + Pt^{II}$$

$$\mathbf{5c} + H_2O \xrightarrow{k_2} ROH + Pt^{II}$$

$$d[Pt_{total}]/dt = -(k_1[Cl^-] + k_2)[\mathbf{5c}]$$

$$[\mathbf{5c}][Cl^-]/[\mathbf{5a}] = K_1K_2$$

$$[\mathbf{5a}] = [\mathbf{5c}][Cl^-]/K_1K_2$$

$$[Pt_{total}] = [\mathbf{5a}] + [\mathbf{5c}] = [\mathbf{5c}([Cl^-]/K_1K_2 + 1)$$

$$d[Pt_{total}]/dt = -\frac{(k_1[Cl^-] + k_2)[Pt_{total}]}{[Cl^-]/K_1K_2 + 1}$$

$$k_{obs} = \frac{k_1[Cl^-] + k_2[H_2O]}{1 + K^{-1}[Cl^-]}$$

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem*. **1995,** *504,* 75-91.

KINETICS

- Kinetic parameters for nucleophilic attack on $[PtRCl_5]^{2-}$ obtained from the rate expression

R	k_1 ($M^{-1}s^{-1}$)	k_2 ($M^{-1}s^{-1}$)	K^{-1} (M^{-1})
Me	2.0(1) E -3	2(1) E -6	1.0(1)
CH_2CH_2OH	1.0(1) E -4	2(1) E -7	0.8(1)

- Thermodynamic activation parameters obtained by following the decomposition of **5** over varying temperatures

Nucleophile	$\Delta H^{\neq}$ (kJ/mol)	$\Delta S^{\neq}$ (J/mol/K)
Cl^-	101	29
H_2O	102	0

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem.* **1995,** *504,* 75-91.

OXIDATION OF ZEISE’S SALT

- Key step in the oxidation of ethanol to ethylene glycol
- Can be used as a model for studying step ii & iii

$$[PtCl_3(C_2H_4)]^- + [PtCl_6]^{2-} + H_2O \longrightarrow [Pt(CH_2CH_2OH)Cl_5]^{2-} + [PtCl_4]^{2-} + H^+$$

7 **6**

Two possible mechanisms

- Oxidation followed by hydration

$$[PtCl_3(C_2H_4)]^- + [PtCl_6]^{2-} \longrightarrow [PtCl_5(C_2H_4)]^- + [PtCl_4]^{2-}$$

$$[PtCl_5(C_2H_4)]^- + H_2O \longrightarrow [Pt(CH_2CH_2OH)Cl_5]^{2-} + H^+$$

^1H NMR spectrum of $[Pt(CH_2CD_2OH)Cl_5]^{2-}$ shows only 1 signal even after 8 h in solution at 45 °C

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem.* **1995,** *504,* 75-91.

OXIDATION OF ZEISE'S SALT

- Addition of water followed by oxidation

$$[PtCl_3(C_2H_4)]^- + H_2O \longrightarrow [Pt(CH_2CH_2OH)Cl_3]^{2-} + H^+$$

$$[Pt(CH_2CH_2OH)Cl_3]^{2-} + [PtCl_6]^{2-} \longrightarrow [Pt(CH_2CH_2OH)Cl_5]^{2-} + [PtCl_4]^{2-}$$

$[PtCl_6]^{2-}$ (M)	$[D^+]$ (M)	K_{obs} (s^{-1})
0.4	0.13	1.9 E -4
0.4	0.27	8.8 E -5

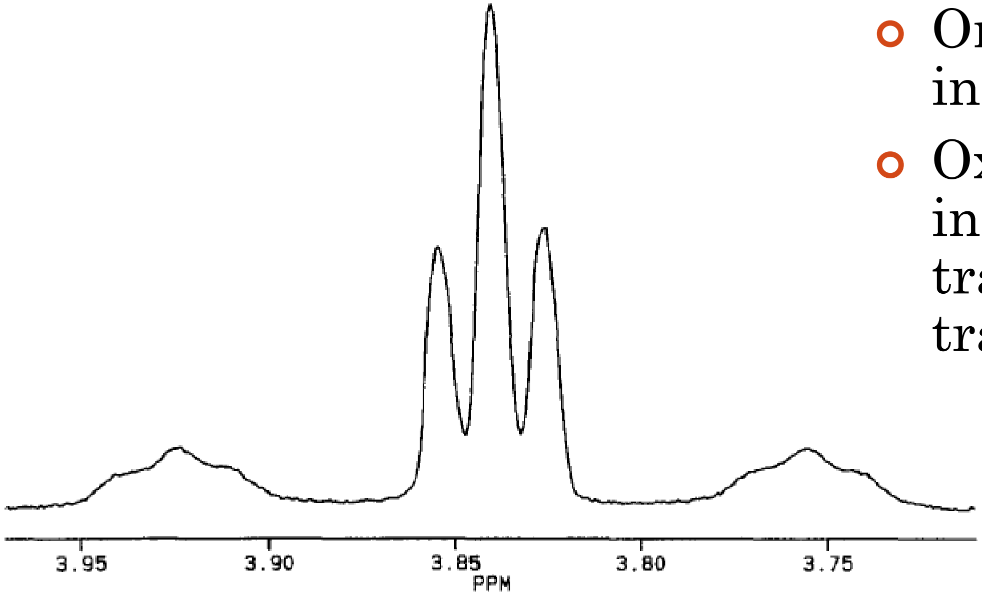
- Zeise's salt is not directly oxidized due to the stabilization of Pt^{II} by ethylene, a π-acceptor ligand.
- The (hydroxyethyl)Pt^{II} intermediate formed is rapidly oxidized

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem.* **1995,** *504,* 75-91.

ALKYL VS. ELECTRON TRANSFER

- Oxidation of Zeise's salt with a isotopically enriched $[^{195}PtCl_6]^{2-}$
- If the (alkyl)Pt^{II} intermediate undergoes transfer to $^{195}Pt^{IV}$ center, then the ^1H NMR signal of $PtC\mathit{H}_2CH_2OH$ will give enhanced satellite intensities

$$[PtCl_3(C_2H_4)]^- + [^{195}PtCl_6]^{2-} \xrightarrow{H_2O} [Pt(CH_2CH_2OH)Cl_5]^{2-} + [^{195}PtCl_4]^{2-}$$

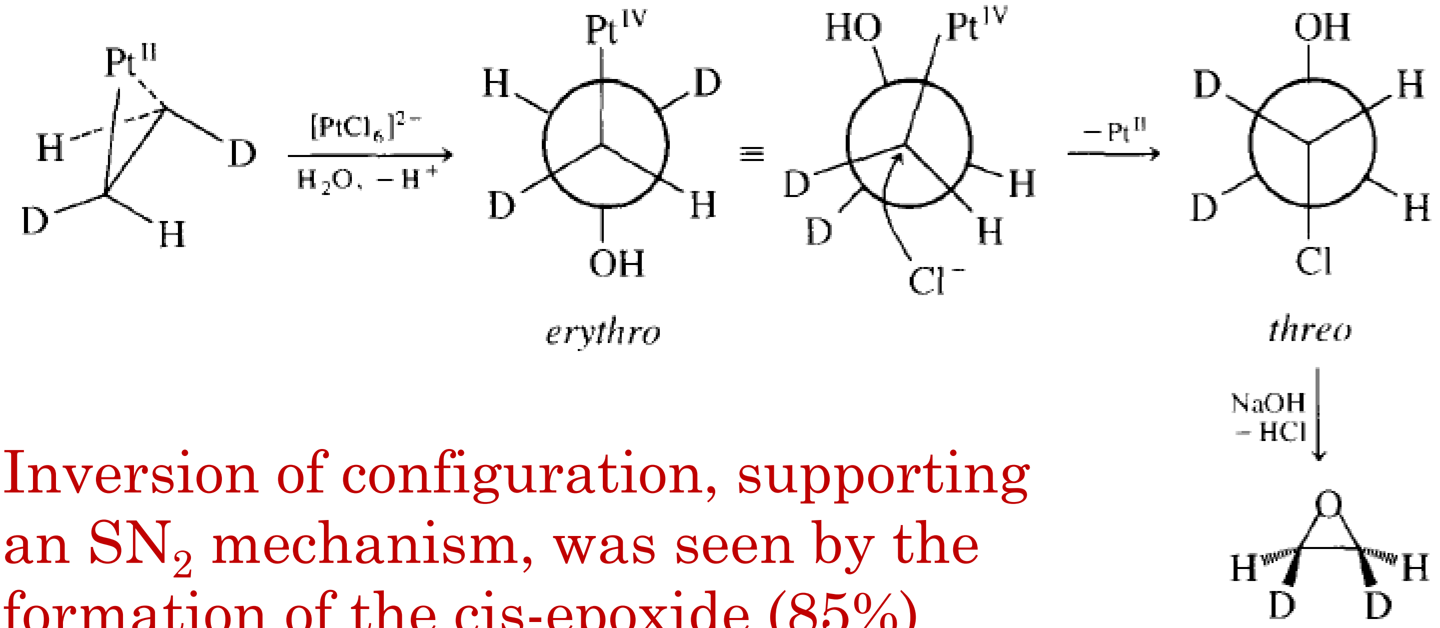


- Only satellites of normal intensity were observed.
- Oxidation proceeds via an inner-sphere two electron transfer accompanied by Cl transfer.

Luinstra, G. A., Wang, L., Stahl, S. S., Labinger, J. A. & Bercaw, J. E. *J. Organometall. Chem.* **1995,** *504,* 75-91.

REDUCTIVE ELIMINATION VS. NUCLEOPHILIC ATTACK

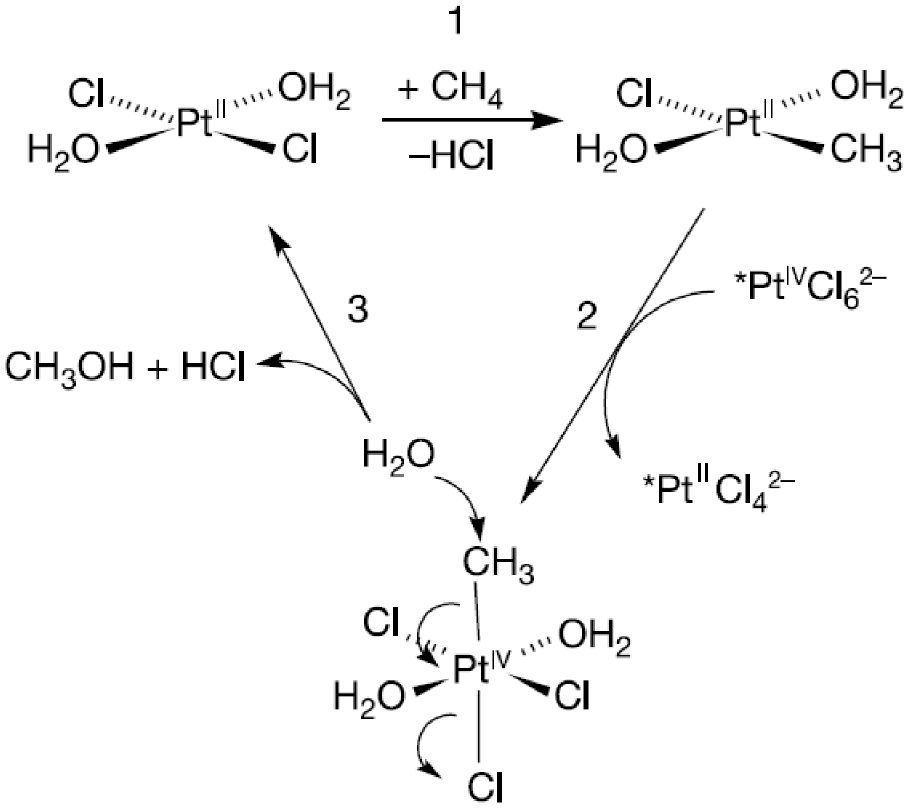
- Rate laws and reactivity trends cannot conclusively rule out reductive elimination
- Preparation of compounds to show change in stereochemistry



- Inversion of configuration, supporting an SN_2 mechanism, was seen by the formation of the cis-epoxide (85%) from an erythro-alkyl complex

Analyzed by IR

MECHANISM OF METHANE OXIDATION IN THE SHILOV SYSTEM



Practical Limitations

- Requires stoichiometric amounts of Pt^{IV}
- Catalytic species precipitates as metallic platinum
  - Pt^{II}-Pt^{0} redox potential lies close to Pt^{IV}-Pt^{II}

Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507