Activation of $H_2$ and C-H Bonds

by Non-Redox Processes

slide credits go to JEB. Thanks, John!
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

oxidative addition/reductive elimination

\[
[L_nM^q] + R-H \rightleftharpoons L_nM^{q+2}
\]

\[
\begin{bmatrix}
L_nM^q \\
\sigma \text{ complex}
\end{bmatrix}
\]

- L's good σ donors; M^q very reduced, often d^8 → M^{q+2} d^6
- mediated by σ complex:
  1. small, normal \( k_H / k_D \) for oxidative addition
  2. inverse \( k_H / k_D \) for reductive elimination, if right favored
  3. normal \( k_H / k_D \) for reductive elimination, if left favored
- generally observe low kinetic selectivity for various types of C-H bonds, primary often favored for sp^3 C-H
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

oxidative addition/reductive elimination

\[ [\text{LnM}^q] + \text{R-H} \rightleftharpoons \text{LnM}^{q+2}\]

sigma bond metathesis (R, R' = H, sp\(^3\), sp\(^2\), sp C)

\[ \text{LnM}^q \rightleftharpoons \text{R'} + \text{LnM}^q \rightleftharpoons \text{R'} + \text{R-H} \]

"1,2 addition/elimination" (X = NR, possibly O)

\[ \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \rightleftharpoons \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \]

homolytic cleavage by two metals

\[ 2\text{LnM}^q \rightleftharpoons \text{LnM}^q \rightleftharpoons \text{M}^q\text{Ln} + \text{LnM}^{q+1} \rightleftharpoons \text{R} + \text{LnM}^{q+1} \rightleftharpoons \text{H} \]

"electrophilic displacement" of H\(^+\) (X = halide, aquo, etc.)

\[ \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \rightleftharpoons \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \]
C-H bond activation without redox: σ bond metathesis

\[ \text{M}^q - \text{R} \ + \ \text{R'} - \text{H} \quad \Leftrightarrow \quad \text{M}^q - \text{R'} \ + \ \text{R} - \text{H} \]

- \( \text{Cp}^\ast_2 \text{M}^q \leq 16 \) electron; 14 electron common
- \( \text{R}, \text{R'} = \text{H}, \text{alkyl}, \text{alkenyl}, \text{aryl}, \text{alkynyl} \)
- rate: \( \text{R}, \text{R'} = \text{H} > \text{sp} \text{C} > \text{sp}^2 \text{C} > \text{sp}^3 \text{C} \)

unfortunately, opposite metathetical process does not occur:

\[ \text{M}^q - \text{R} \ + \ \text{R'} - \text{H} \quad \Leftrightarrow \quad \text{M}^q - \text{H} \ + \ \text{R} - \text{R'} \]

"Selective Hydrocarbopn Activation: Principles and Progress" VCH 1990, Chapters 3
(Rothwell) and 4 (Watson).
Watson, JACS 1983, 6491.
Thompson, et al. JACS 1987, 203
Marks, et al. JACS 1985, 8091
Use of pentamethylcyclopentadienyl ligands simplifies metallocene chemistry by disfavoring oligomers and adducts of these highly coordinatively unsaturated group 3 and lanthanide metallocene complexes:

\[
\begin{align*}
\text{Sc}^{\text{III}} & \text{Cl} \quad \text{Sc}^{\text{III}} \\
\text{Cl} & \quad \text{Sc}^{\text{III}} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

(L = py, THF, etc.)

\[
\begin{align*}
\text{Sc}_{2}\text{O}_{3} \quad & \xrightarrow{1. \text{ 12 } M \text{ HCl}_{\text{aq}}} \\
& \xrightarrow{2. \text{ SOCl}_{2}} \\
& \xrightarrow{3. \text{ THF}} \\
\text{ScCl}_{3}(\text{THF})_{3}
\end{align*}
\]

\[
\begin{align*}
\text{2 eq LiCp}^* & \text{ refluxing xylenes} \\
\text{sublime residue} \\
\text{yellow crystals}
\end{align*}
\]

\[
\begin{align*}
\text{Sc} & \xrightarrow{\text{alkene or alkyne}} \\
\text{Sc} & \xrightarrow{\text{H}_2 \quad - \text{ R-H}} \\
\text{Sc} & \xleftarrow{\text{R} = \text{higher alkyl, alkenyl}} \\
\text{Sc} & \xrightarrow{\text{R} = \text{CH}_3, \text{C}_6\text{H}_5, \text{CH}_2\text{C}_6\text{H}_5}
\end{align*}
\]
Cp*: a life-long obsession:

\[
\text{Cp}^* = [\eta^5-C_5(CH_3)_5] =
\]

[Chemical structure diagrams and images of research group and vanity license plate presented by Bercaw research group, ca. 1983]
H/D exchange: the Cp*₂Sc-R system

H/D exchange between C-H bonds of many substrates and D₂/C₆D₆ is promoted by Cp*₂ScR:

\[
\begin{align*}
\text{Cp}^*\text{₂Sc} - \text{H} + \text{D}_2 & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{D} + \text{HD} & \text{very fast} \\
\text{Cp}^*\text{₂Sc} - \text{H} + \text{C}_6\text{D}_6 & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{C}_6\text{D}_5 + \text{HD} & \text{fast} \\
\text{Cp}^*\text{₂Sc} - \text{D} + \text{RH} & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{R} + \text{HD} & \text{slow} \\
\text{Cp}^*\text{₂Sc} - \text{C}_6\text{D}_5 + \text{RH} & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{R} + \text{C}_6\text{D}_5\text{H} & \text{very slow} \\
\text{Cp}^*\text{₂Sc} - \text{R} + \text{D}_2 & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{D} + \text{RD} & \text{fast} \\
\text{Cp}^*\text{₂Sc} - \text{R} + \text{C}_6\text{D}_6 & \rightleftharpoons \text{Cp}^*\text{₂Sc} - \text{C}_6\text{D}_5 + \text{RD} & \text{slow}
\end{align*}
\]

\[
net: \quad \text{RH} \rightarrow \text{RD}
\]

(benzylic C-H slightly slower than aromatic C-H) (CH₃D first product) (1ˢ C-H much faster than 2ⁿ C-H) (H/D exchange with no ring opening) (very slow)

\[\text{C}_5(\text{CH}_3)_5\text{H}, \text{P}(\text{CH}_3)_3, \text{Si}(\text{CH}_3)_4, \text{THF} (\alpha's \text{ faster})\]
Rates of $\sigma$ bond metathesis are relatively sensitive to hybridization of reacting bonds

- Rate of $\sigma$ bond metathesis reaction maps with...
  (a) steric factors
  (b) $s$ character of reacting bonds

\[
\begin{align*}
\text{s + s-s} & \quad \text{Cp}^*\text{Sc}-H + \text{H-H} \quad \text{\textcolor{red}{-80 °C}} \quad \text{Cp}^*\text{Sc}-H + \text{H-H} \quad k_2 > 10^3 \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{sp}^3 + s-s & \quad \text{Cp}^*\text{Sc}-\text{CH}_3 + \text{H-H} \quad \text{\textcolor{red}{-80 °C}} \quad \text{Cp}^*\text{Sc}-H + \text{CH}_3-H \quad k_2 \approx 10 \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{s + sp}^2-s & \quad \text{Cp}^*\text{Sc}-H + \text{C}_6\text{H}_5-H \quad \text{\textcolor{red}{25 °C}} \quad \text{Cp}^*\text{Sc}-\text{C}_6\text{H}_5 + \text{H-H} \quad k_2 > 10 \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{sp}^3 + \text{sp}^2-s & \quad \text{Cp}^*\text{Sc}-\text{CH}_3 + \text{C}_6\text{H}_5-H \quad \text{\textcolor{red}{80 °C}} \quad \text{Cp}^*\text{Sc}-\text{C}_6\text{H}_5 + \text{CH}_3-H \quad k_2 \approx 3 \times 10^{-5} \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{sp}^3 + \text{sp}^2-s & \quad \text{Cp}^*\text{Sc}-\text{CH}_3 + \text{C}_6\text{H}_5\text{CH}==\text{CH}-H \quad \text{\textcolor{red}{60 °C}} \quad \text{Cp}^*\text{Sc}-\text{CH}==\text{CHC}_6\text{H}_5 + \text{CH}_3-H \quad k_2 \approx 1 \times 10^{-3} \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{sp}^3 + \text{sp-s} & \quad \text{Cp}^*\text{Sc}-\text{CH}_3 + \text{CH}_3\text{C}==\text{C}-H \quad \text{\textcolor{red}{0 °C}} \quad \text{Cp}^*\text{Sc}-\text{C}==\text{CCH}_3 + \text{CH}_3-H \quad k_2 > 10 \ \text{M}^{-1}\cdot\text{s}^{-1} \\
\text{sp}^3 + \text{sp}^3-s & \quad \text{Cp}^*\text{Sc}-\text{CH}_3 + \text{^{13}CH}_3-H \quad \text{\textcolor{red}{80 °C}} \quad \text{Cp}^*\text{Sc}\text{^{13}CH}_3 + \text{CH}_3-H \quad k_2 \approx 1 \times 10^{-5} \ \text{M}^{-1}\cdot\text{s}^{-1}
\end{align*}
\]
Faster rates of $\sigma$ bond metathesis for sp$^2$ and sp hybridized C-H bonds might suggest electrophilic Cp*$_2$Sc-R attacks at $\pi$ bonds of substrate:

- HOMO of arene attacked by electrophilic Cp*$_2$ScR
- sterically worst approach and TS

- C-H $\sigma$ bond attacked (lower energy than $\pi$ orbitals) by Cp*$_2$ScR
  ...as for H$_2$, CH$_4$, etc.
- sterically best approach and TS
Experimental probes of rates and regioselectivity for reaction of \( \text{Cp}^*\text{ScCH}_3 \) with arenes provides convincing evidence for mechanism of \( \sigma \) bond metathesis.

\[
\begin{align*}
(C\text{p}^*-d_{15})_2\text{ScCH}_3 + \text{C}_6\text{H}_5X & \xrightarrow{k \quad 80 \, ^\circ\text{C}} (C\text{p}^*-d_{15})_2\text{Sc-C}_6\text{H}_4X + \text{CH}_4 \\
\text{X} & \quad k \ (M^{-1}\cdot\text{s}^{-1}) \\
\text{CF}_3 & \quad 1.4 \times 10^{-5} \\
\text{H} & \quad 3.3 \times 10^{-5} \quad (k_\text{H}/k_\text{D} = 2.9) \\
\text{CH}_3 & \quad 3.4 \times 10^{-5} \\
\text{NMe}_2 & \quad 3.2 \times 10^{-5}
\end{align*}
\]

- CH\(_4\) less than 5\% isomerization 7.5 hr at 80 \( ^\circ\)C

\( \text{Cp}^*_2\text{Sc-CH}_3 \) + \( \text{C}_6\text{H}_5\text{CH}_3 \) \( \xrightarrow{-\text{CH}_4} \) \( \text{Cp}^*_2\text{Sc-CH}_3 \) \( \xrightarrow{-\text{CH}_4} \) \( \text{Cp}^*_2\text{Sc-CH}_3 \) 23\% 26\% \( \xrightarrow{-\text{CH}_4} \) \( \text{Cp}^*_2\text{Sc-CH}_3 \) 57\% 61\% 6\% 13\%

- cf. nitration of toluene, which yields ca. 58\% ortho, 38\% para, \( \leq 4\% \) meta.

**conclusions:** \( \sigma \)-bond metathesis of arene C-H bonds is not "electrophilic aromatic substitution"-like; Sc attacks at C-H \( \sigma \) bond directly; normal \( k_\text{H}/k_\text{D} \)
Bonding interactions for $\sigma$ bond metathesis

Valence bond description:

$\text{C} - \text{H} + \text{M} - \text{C}$ →

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

$|\delta\delta| = ??$

Rate decreases $\rightarrow$

$C, C = \text{sp} C > \text{sp}^2 C > \text{sp}^3 C$

Orbital overlap in TS decreases $\rightarrow$

Molecular orbital description:

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{M} \\
\text{C} \\
\text{C} \\
\text{H}
\end{array}
\]

TS

$2a_1$

$1a_1$

$b_2$

$a_1$
Better total overlap leads to preferred metathetical direction for $\sigma$ bond metathesis:
Steric interactions with the Cp* ligands place constraints on C-H bond activation:

All three are sterically much preferred over...

one bad interaction

two bad interactions
Theoretical studies of σ bond metathesis confirm these pictures of the bonding interactions in the transition state.

- Goddard and Steigerwald *JACS* 1984, 308.
- Upton and Rappé *JACS* 1985, 1206.
- Ziegler *et. al.* *JACS* 1993, 636.

- Cl· and Cp· very similar in their demands for metal orbitals
- esssentially no barrier for sbm
- d character in Sc-H bond is an important feature
- isoelectronic [Cl₂TiH]⁺ even more reactive.
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

\[
\begin{align*}
\text{L}^n\text{M}^q & \text{ -- } \text{R}' \\
\text{+} & \\
\text{R} & \equiv \text{H} \\
\sigma \text{ complex} & \\
\text{[} & \\
\text{R'} & \equiv \text{H} \\
\text{L}^n\text{M}^q & \text{ -- } \text{R}' \\
\sigma \text{ complex} & \\
\end{align*}
\]

\[
\begin{align*}
\text{L}^n\text{M}^q & \text{ -- } \text{R}' \\
\text{+} & \\
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\sigma \text{ complex} & \\
\text{[} & \\
\text{R'} & \equiv \text{H} \\
\text{L}^n\text{M}^q & \text{ -- } \text{R}' \\
\sigma \text{ complex} & \\
\end{align*}
\]

**Sigma bond metathesis** \((R, R' = H, \text{sp}^3, \text{sp}^2, \text{sp} C)\)

- \(L^nM^q\) very electrophilic, coordinatively unsaturated
- proceeds via a \(\sigma\) complex, although weakly held as compared to oxidative/addition reductive elimination
- normal \(k_H / k_D\)
- kinetic selectivity for C-H bonds
  (i) primary strongly favored for sp\(^3\) C-H
  (ii) rate increases with increased s character of reacting bonds: Sc-H + H\(_2\) > sp > sp\(^2\) > sp\(^3\) C-H
- orbital overlap and very open R'-H-R angle in TS lead to strong preference for observed metathetical direction for \(\sigma\) bond metathesis
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

sigma bond metathesis (R, R' = H, sp³, sp², sp C)

\[
\begin{align*}
    L_n M^q & \rightarrow R' \\
    + & \\
    R & \rightarrow H \\
\end{align*}
\]

\[
\begin{align*}
    [L_n M^q \cdots R'] & \xrightarrow{\sigma \text{ complex}} [L_n M^q \cdots H] \\
    & \xrightarrow{\sigma \text{ complex}} [L_n M^q \cdots H] \\
    & \xrightarrow{\sigma \text{ complex}} [L_n M^q \cdots R'] \\
\end{align*}
\]

- \( L_n M^q \) very electrophilic, coordinatively unsaturated
- proceeds via a \( \sigma \) complex, although weakly held as compared to oxidative/addition reductive elimination
- normal \( k_H / k_D \)
- kinetic selectivity for C-H bonds
  
  \( (i) \) primary strongly favored for sp³ C-H
  
  \( (ii) \) rate increases with increased s character of reacting bonds: Sc-H \( + H_2 \) > sp \( > \) sp² \( > \) sp³ C-H

- orbital overlap and very open R'-H-R angle in TS lead to strong preference for observed metathetical direction for \( \sigma \) bond metathesis
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

oxidative addition/reductive elimination

\[ [\text{LnM}^q] + \text{R-H} \rightleftharpoons \text{LnM}^{q+2} \]

sigma bond metathesis \((\text{R}, \text{R}' = \text{H, sp}^3, \text{sp}^2, \text{sp C})\)

\[ \text{LnM}^q \rightleftharpoons \text{R}' + \text{R-H} \]

"1,2 addition/elimination" \((\text{X} = \text{NR, possibly O})\)

\[ \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \]

homolytic cleavage by two metals

\[ 2 \text{LnM}^q \rightleftharpoons \text{LnM}^q \rightleftharpoons \text{M}^q \text{Ln} \rightleftharpoons \text{LnM}^q+1 \text{R} + \text{R-H} \]

"electrophilic displacement" of \(\text{H}^+\) \((\text{X} = \text{halide, aquo, etc.})\)

\[ \text{LnM}^q \rightleftharpoons \text{X} + \text{R-H} \rightleftharpoons \text{LnM}^q \rightleftharpoons \text{X} + \text{H}^+ \text{X}^- \]
Bergman and Wolczanski simultaneously discover 1,2-addition of C-H bonds to [Zr=NR]

Bergman, et al. JACS 1988, 8729

Wolczanski, et al. JACS 1988, 8731
Jordan Bennett and Peter Wolczanski take a careful and in-depth look at mechanism for 1,2 addition of C-H to [Ti=NR] (and by inference to his [Zr=NR], [V=NR] and [Ta=NR] systems): Wolczanski, et al. *JACS* 1997, 10696 - 10719 (yeah, 23 pages!)

\[ \Delta G^\ddagger, \Delta G^\circ, \Delta \Delta G^\ddagger \text{'s} \]

\[ R = \text{methyl, ethyl, cyclopentyl, cyclopropyl, aryl, benzyl, vinyl, etc.} \]

\[ (L = \text{OEt}_2, \text{THF}, \text{NMe}_3, \text{py}, \text{PMe}_3) \]

\[ \Delta G^\ddagger \text{ increases} \rightarrow H-H < H-\text{CH}=\text{CH}_2 < H-\text{cyclopropyl} < H-\text{phenyl} < H-\text{CH}_3 < H-\text{cyclobutyl} \sim H-\text{ethyl} < H-n-\text{butyl} < H-\text{cyclopentyl} \]

rate of 1,2-C-H-addition decreases \[ \rightarrow \]
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

- TS for 1,2-R-H addition and 1,2-R-H elimination is 4-centered with nearly linear C-H-N angle
- Activation parameters, large $k_H / k_D$, and relative thermodynamics indicate a concerted process with balanced Ti-C, C-H, N-H, and Ti=N bonding making/breaking and little charge build up
- $[(\text{Me}_3\text{C})_3\text{SiO}]_2\text{Ti} = \text{NSi(CMe}_3)_3$ is a potent electrophile that attacks C-H $\sigma$ bond
- $\Delta\Delta G^\ddagger$'s for 1,2-R-H addition roughly follow $H < \text{sp}^2$ C-H < $1^\circ \text{sp}^3 < 2^\circ \text{sp}^3$ C-H and span > 9 kcal/mol

"1,2 addition/elimination" (X = NR, possibly O)
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

- TS for 1,2-R-H addition and 1,2-R-H elimination is 4-centered with nearly linear C-H-N angle
- activation parameters, large $k_H / k_D$, and relative thermodynamics indicate a concerted process with balanced Ti-C, C-H, N-H, and Ti=N bonding making/breaking and little charge build up
- $[(\text{Me}_3\text{C})_3\text{SiO}]_2\text{Ti} = \text{NSi(CH}_3)_3$ is a potent electrophile that attacks C-H $\sigma$ bond
- $\Delta\Delta G^\ddagger$'s for 1,2-R-H addition roughly follow H < sp$^2$ C-H < 1$^\circ$ sp$^3$ < 2$^\circ$ sp$^3$ C-H and span > 9 kcal/mol

"1,2 addition/elimination" (X = NR, possibly O)
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

oxidative addition/reductive elimination

\[ [L_nM^q] + R-H \rightleftharpoons L_nM^{q+2} \]

sigma bond metathesis \((R, R' = H, sp^3, sp^2, sp C)\)

\[ L_nM^q - R' + R-H \rightleftharpoons L_nM^q + R' + R-H \]

"1,2 addition/elimination" \((X = NR, possibly O)\)

\[ L_nM^q - X + R-H \rightleftharpoons L_nM^q - X + R-H \]

homolytic cleavage by two metals

\[ 2 L_nM^q \rightleftharpoons L_nM^q - M^q L_n + L_nM^{q+1} - R + R-H \rightarrow L_nM^{q+1} - H \]

"electrophilic displacement" of \(H^+\) \((X = \text{halide, aquo, etc.})\)

\[ L_nM^q - X + R-H \rightleftharpoons L_nM^q + R + H^+ X^- \]
Brad Wayland developed the cleanest and most generally reactive metalloradical system based on (porphyrin)Rh$^{	ext{II}}$, a stable, low spin d$^7$, 15-electron complex:
(porphyrin)Rh\textsuperscript{II} radicals are remarkably reactive for methane cleavage:

\[
\begin{align*}
[(\text{TXP})\text{Rh}]_2 + \text{CH}_4 & \xrightleftharpoons[k_{-1}]^{k_1} (\text{TXP})\text{Rh-CH}_3 + (\text{TXP})\text{Rh-H} \\
\Delta H^0 & \approx 0 \text{ kcal/mol} \\
\Delta S^0 & = -7(3) \text{ e.u.} \\
\text{rate forward} & = k_1[\text{CH}_4][(\text{TXP})\text{Rh}]_2 \\
\Delta H^\ddagger & = 17(3) \text{ kcal/mol} \\
\Delta S^\ddagger & = -25(7) \text{ e.u.} \\
\text{solvent, benzene, unreactive for weeks at 80 °C} & \\
(\text{mixtures of } (\text{TXP})\text{RhH} & \text{ and } (\text{TXP})\text{RhC}_6\text{H}_5 \text{ fail to} \\
\text{eliminate benzene over months at 80 °C})
\end{align*}
\]

\[
2 (\text{TMP})\text{Rh} \cdot + \text{CH}_4 \xrightleftharpoons[k_{-1}]^{k_1} (\text{TMP})\text{Rh-CH}_3 + (\text{TMP})\text{Rh-H} \\
\Delta H^0 & = -13.0(1.5) \text{ kcal/mol} \\
\Delta S^0 & = -19(5) \text{ e.u.} \\
\text{rate forward} & = k_1[\text{CH}_4][(\text{TMP})\text{Rh}]^2 \\
\Delta H^\ddagger & = 7.1(1.0) \text{ kcal/mol} \\
\Delta S^\ddagger & = -39(5) \text{ e.u.} \\
k_\mu / k_D & = 8.6 \text{ at 25 °C}; \text{ } = 5.1 \text{ at 80 °C} \\
\text{again, solvent, benzene is totally unreactive!}
\]

\[
\begin{align*}
\Rightarrow \text{-13 kcal/mol} & = \text{BDE(Rh-Rh)} + \text{BDE(H-CH}_3\text{)} - \text{BDE(Rh-H)} - \text{BDE(Rh-CH}_3\text{)} \\
& \approx 0 \quad 105 \quad 60 \quad 58 \text{ kcal/mol} \\
\text{from reaction w/H}_2
\end{align*}
\]
Mechanism deduced from rate laws, $k_H/k_D$, small $\Delta H^\ddagger$, and $\Delta H^0$:

\[
\begin{align*}
[(\text{porphyrin})\text{Rh}^{III}]_2 & \quad \xleftrightarrow{} \quad 2 \quad (\text{porphyrin})\text{Rh}^{II}. \\
(\text{porphyrin})\text{Rh}^{II}. \ + \ CH_4 & \quad \xleftrightarrow{} \quad [(\text{porphyrin})\text{Rh}^{II}(CH_4)] \\
\text{or} & \\
2 \ + \ (\text{porphyrin})\text{Rh}^{II}. + \ CH_4 & \quad \xrightarrow{\text{concerted}} \\
\end{align*}
\]

(not detectable by epr at 90 K)

\[
\begin{align*}
2 \quad (\text{porphyrin})\text{Rh}^{II}. \ + \ CH_4 & \quad \xrightarrow{\text{concerted}} \\
\end{align*}
\]

\[
\begin{align*}
H & \quad \xrightarrow{(105)} \quad C \xrightarrow{\text{H}} \quad \text{H} \xrightarrow{\text{Rh}^{II}(\text{porphyrin})} \\
\end{align*}
\]

Termolecular TS with backside attack restricts substrates to $H_2$ and unhindered $sp^3$ C-H bonds
Tethered binuclear (porphyrin)Rh\textsuperscript{II} expands substrate scope:


\[
\text{\cdot Rh}^{\text{II}}(m\text{-xylyl})\text{Rh}^{\text{II}} + \text{R-H} \underset{k}{\xrightarrow{\text{\textbullet}}} \text{R-Rh}^{\text{III}}(m\text{-xylyl})\text{Rh}^{\text{III}}-\text{H}
\]

\[\Delta G^\ddagger, \Delta G^o, \Delta\Delta G^\ddagger, k_H/k_D's\]

<table>
<thead>
<tr>
<th></th>
<th>(k (M^{-1}s^{-1})) at 296 K</th>
<th>BDE(R-H)</th>
<th>(k_H/k_D) (296 K)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{H}_2)</td>
<td>40</td>
<td>104</td>
<td>1.6 (TMP system)</td>
</tr>
<tr>
<td>(\text{CH}_4)</td>
<td>(8.3 \times 10^{-2})</td>
<td>105</td>
<td>10.8</td>
</tr>
<tr>
<td>(\text{CH}_3\text{CH}_3)</td>
<td>(3.3 \times 10^{-4})</td>
<td>100*</td>
<td>5.0</td>
</tr>
<tr>
<td>(\text{C}_6\text{H}_5\text{CH}_2\text{-H})</td>
<td>(2.0 \times 10^{-4})</td>
<td>90</td>
<td>5.0</td>
</tr>
<tr>
<td>(\text{CH}_3\text{OH})</td>
<td>(1.0 \times 10^{-2})</td>
<td>96</td>
<td>9.7</td>
</tr>
</tbody>
</table>

*oxidative addition to C-C bond thermodynamically favored by about 10 kcal/mol, but this alternative not observed.
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

homolytic cleavage by two metals

\[ 2 \text{LnM}^q \rightleftharpoons \text{LnM}^q \text{M}^q \text{Ln} \]
\[ + \text{R} \rightleftharpoons \text{LnM}^{q+1} \rightleftharpoons \text{R} \]
\[ + \text{L} \text{M}^q \text{C} \rightleftharpoons \text{H} \rightleftharpoons \text{M}^q \text{Ln} \]  

\[ \Delta G^\ddagger \text{s for homolytic cleavage of H}_2 \text{ and C-H bonds decrease regularly as the reactions become more favorable (}\Delta G^0\text{'s more negative)} \]
\[ \text{rates follow order H-H} > \text{H}_3\text{C-H} > \text{HOCH}_2\text{-H} > \text{CH}_3\text{CH}_2\text{-H} \sim \text{C}_6\text{H}_5\text{CH}_2\text{-H} \text{ and span about 5 orders of magnitude at 296 K} \]
Activation of Carbon-Hydrogen Bonds at Transition Metal Centers

- TS is 4-centered, termolecular with linear M-C-H-M angles
- Activation parameters, large $k_H / k_D$, and relative thermodynamics indicate a concerted process with balanced M-C, C-H, and M-H bonding making/breaking
- Substrate scope limited to H$_2$ and relatively unhindered sp$^3$ C-H bonds
- $\Delta G^\ddagger$'s for homolytic cleavage of H$_2$ and C-H bonds decrease regularly as the reactions become more favorable ($\Delta G^\circ$'s more negative)
- Rates follow order H-H > H$_3$C-H > HOCH$_2$-H > CH$_3$CH$_2$-H ~ C$_6$H$_5$CH$_2$-H and span about 5 orders of magnitude at 296 K
There are many examples of C-H bond "activation" of alkanes (including methane) by organometallic complexes under mild conditions.

Oxidative addition/reductive elimination:

$$[L_nM^q] + R-H \rightleftharpoons L_nM^{q+2} \mathrm{H}$$

Homolytic cleavage by two metals:

$$2L_nM^q \rightleftharpoons L_nM^q-M^qL_n \rightleftharpoons L_nM^{q+1} - R$$

Sigma bond metathesis (R, R' = H, sp^3, sp^2, sp C):

$$L_nM^q-R' \rightleftharpoons L_nM^q + R'$$

"Electrophilic displacement" of H^+ (X = halide, aquo, etc.):

$$L_nM^q-X \rightleftharpoons L_nM^q + H^+X^-$$

"1,2 addition/elimination" (X = NR, possibly O):

$$L_nM^q-X \rightleftharpoons L_nM^q-X$$

Unfortunately, thus far most of the organometallic complexes that react with C-H bonds of alkanes are decomposed by O_2 and/or ROH…

*with the exceptions of some of those complexes that react via "electrophilic displacement" of H^+…*
Similarities and differences among various C-H activation mechanisms: in some cases there are rather subtle differences that are often difficult to distinguish.

Sigma bond metathesis ($R, R' = H, sp^3, sp^2, sp C$), simplest in some ways:

\[
\begin{align*}
L_n M^q & \rightarrow R' \\
+ & \\
R & \rightarrow H \\
& \\
\end{align*} \quad \text{via} \quad \begin{array}{c}
\left[ \begin{array}{c}
R' \\
\cdots \\
R \\
\cdots \\
H \\
\end{array} \right] \\
\end{array}
\]

Oxidative addition/reductive elimination vs sigma bond metathesis:

\[
\begin{align*}
L_n \ddot{M}^q & \rightarrow R' \\
+ & \\
R & \rightarrow H \\
& \\
\end{align*} \quad \text{via} \quad \begin{array}{c}
\left[ \begin{array}{c}
R' \\
\cdots \\
R \\
\cdots \\
R \\
\cdots \\
H \\
\end{array} \right] \\
\end{array}
\]

"Electrophilic displacement" of $H^+$ ($X = \text{halide, aquo, etc.}$) vs oxidative addition (or even sbm!)

\[
\begin{align*}
L_n M^q & \rightarrow X \\
+ & \\
R & \rightarrow H \\
& \\
\end{align*} \quad \text{via} \quad \begin{array}{c}
\left[ \begin{array}{c}
X \\
\cdots \\
R \\
\cdots \\
H \\
\end{array} \right] \\
\end{array}
\]

Note: all mechanisms have C-H sigma interaction with metal center in TS.
Olefin Metathesis Catalysts (there are many others)

\[
\begin{align*}
\text{Ar} &= 2,6-(i-\text{Pr})_2\text{C}_6\text{H}_3 \\
R &= (\text{F}_3\text{C})_2(\text{CH}_3)\text{C}
\end{align*}
\]

**Schrock (1990)**
- Highly reactive, hence poor tolerance of functional groups in the substrate.
- The catalytic activity increases with increasing electron-withdrawing nature of \( R \).
- Metathesis of tri- and tetrasubstituted olefins is possible.

**Grubbs (1995)**
- Tolerance of functional groups (CO, OH, NH\(_2\)).
- Selectivity towards sterically unhindered olefins and strained olefins.
- Tri- and tetrasubstituted olefins are not attacked.
1\textsuperscript{st} unimolecular metal-alkylidene
metathesis catalyst (\textit{cis}-pentene)

Kress-Welosek-Osborn
catalyst, 1983

Basset's catalyst, 1985

General formula of the family of Schrock's
metathesis catalysts (M = Mo or W; R and Ar
are bulky substituents, 1990) For an example of
more recent variations, see formula on the right

Commercial prototype of the family
of Schrock's metathesis catalysts
(can achieve RCM of tri- and
tetrasubstituted olefins)

From, "Organometallic chemistry and catalysis", \textit{Didier Astruc} (Springer, 2007)
RuCl$_3$, x H$_2$O

Natta, 1965  
Grubbs, 1988

Grubbs, 1988

Grubbs, 1992

Grubbs, 1995  
commercial, 1st generation  
most used catalyst

Grubbs, Nolan, Hermann, Fürstner, 1999  
2nd generation, commercial  
second most used catalyst

Hoveyda, 1999  
commercial

Hoveyda, 1999  
commercial

Hofmann, 1999

(also meta nitro isomer)

Grela, 2000

(also binaphthyl derivative)

Blechert, 2002

Chauvin Mechanism of Alkene Metathesis
Pairwise Mechanism:

Carbene "stepwise" mechanism:

Distinguished by an experiment with 1:1 mixture of:

Metathesis products: from 100% protio substrate

These olefins do not back-react with catalyst (i.e. are not metathesised) due to
A: low concentration of ethylene in reaction mixture
B: stabilization of phenanthene

D₂C=CD₂ is the product from the deuterated substrate, only.
From 1:1 substrate mixture, you get 1:2:1 mixture of ethylenes
By Pairwise Mechanism (after initiation)

Predicts 1:1 product distribution

A metathesis carried out with these starting materials

leads to the observed product distribution:

$1:2:1$

$H_2C=CH_2 : H_2C=CD_2 : D_2C=CD_2$
ROMP Examples

Schrock asymmetric catalyst (based on BINOL)

First ROMP commercial catalyst

\[ \begin{align*}
\text{RuCl}_3/\text{HCl} & \quad \text{BuOH} \\
\text{norsores}^\circledR \quad \text{(Elf-Atochem), an elastomer for special applications} \\
90\% \text{ trans}
\end{align*} \]
ROMP & RCM

ROMP processes are unique in that the C=C double bond of the monomer is conserved in the polymer. The catalytically active species is fixed to the end of the growing chain ("living polymer"). As soon as a certain monomer is consumed, the chain reaction can be continued with a different monomer (block polymerization). A [M]=CR₂ unit can be deactivated by reaction with a carbonyl group to yield [M]=O (Wittig reaction). In this manner, narrow molar-mass distributions can be achieved (Schrock, 1990).

ROMP incredibly useful/practical in materials/polymer syntheses
Ring closing metathesis (RCM) incredibly useful in natural product and pharmaceutical syntheses.

Hepatitis B protease inhibitor

[Chemical structures and reactions]