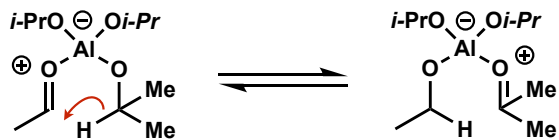


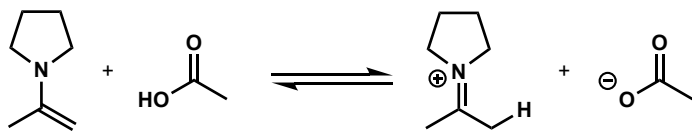
# Metal Hydride Atom Transfer

Eisenberg, D. C; Norton, J. R. *Isr. J. Chem.* **1991**, 31, 55–66.

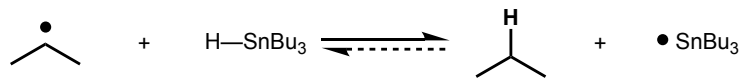
# Metal Hydride Atom Transfer



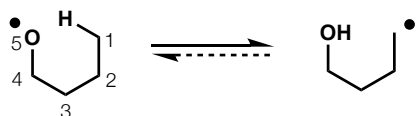
"hydride transfer" : H nucleus and 2 electrons  
**H<sup>-</sup>**



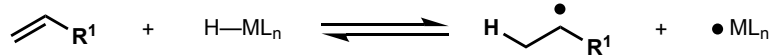
"proton transfer" : H nucleus and 0 electrons  
**H<sup>+</sup>**



"hydrogen atom transfer" HAT : H nucleus and 1 electron  
**H•**

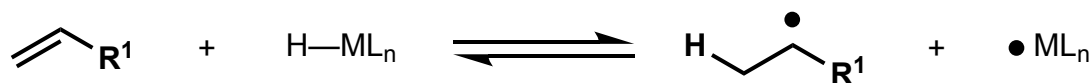


1,5-HAT (Barton nitrite ester, Suárez, HLF reactions etc.)



"metal hydride atom transfer" MHAT  
 (or metal hydride hydrogen atom transfer)

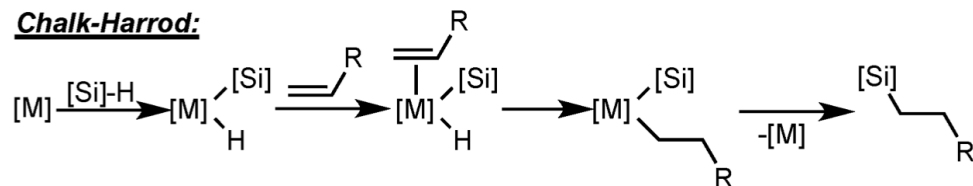
# Metal Hydride Atom Transfer



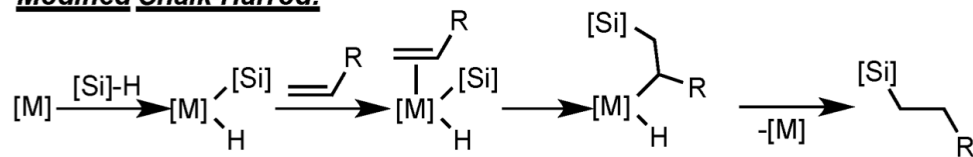
“outer-sphere”  
alkene is not part of the ligand sphere

see: Eisenberg, D. C; Norton, J. R. *Isr. J. Chem.* **1991**, *31*, 55–66.

## Chalk-Harrod:



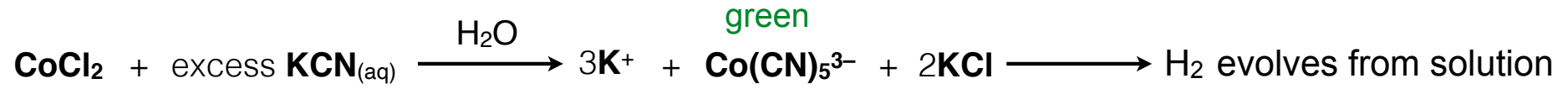
## Modified Chalk-Harrod:



“inner-sphere”  
alkene ligates the metal center

Chirik et al. *ACS Catal.* **2016**, *6*, 4105–4109.

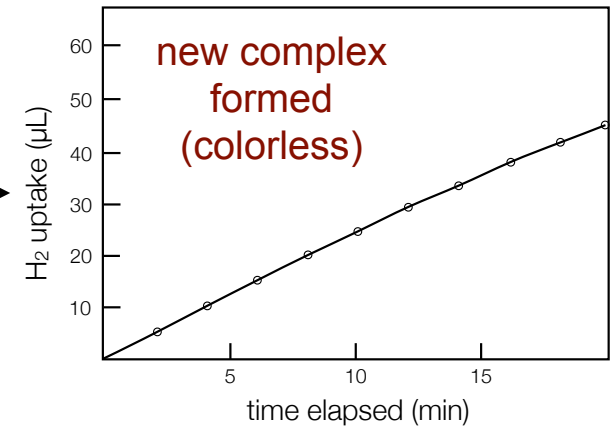
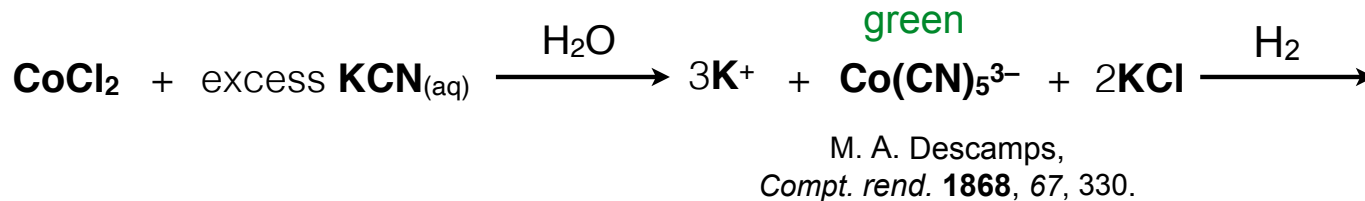
## Origin story



M. A. Descamps,  
*Compt. rend.* **1868**, 67, 330.



## Origin story



Iguchi, *J. Chem. Soc. Japan* **1942**, 63, 1752

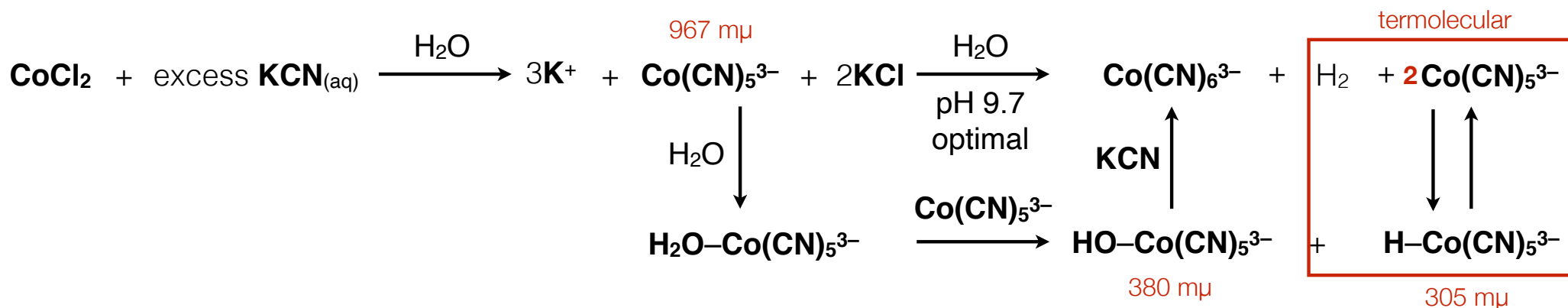
adapted from:

King and Winfield, *J. Am. Chem. Soc.* **1961**, 83, 3366

- Iguchi showed that solutions of  $\text{Co(CN)}_5^{3-}$  absorb hydrogen gas at ambient temperature
- why did this attract interest?
- what is the reduction product?
- the same complex is produced by electrolysis or by “self-reduction” (allowing aqueous solutions to age)

# Origin story

“For about a century, mention has been made from time to time of the liberation of hydrogen gas which occurs when aqueous solutions of cobalt chloride and potassium cyanide are mixed. The reaction was regarded as extraordinary but of little practical value. With the recent interest in the deuterium exchange reaction catalyzed by cobalt cyanide solutions (Ogg, Mills, Weller and Wheeler), and **the more general problems of hydrogenation in solution by metal complexes** and by hydrogenase (see Halpern or Winfield), it has become important to study the mechanism of H<sub>2</sub> evolution.”



- Griffith and Wilkinson observe new PMR signal at 695 cycles/sec (water at 40 Mc/sec); disappears if prepared in deuterium oxide
- High pressures of H<sub>2</sub> allow reduction at low [Co]
- Self-reduction (aging) is very slow to produce 305 mμ peak compared to H<sub>2</sub> reduction

see: King, N. K.; Winfield, M. E. “Reduction of Water to Hydrogen by a Complex Cyanide of Cobalt” *J. Am. Chem. Soc.* **1958**, 80, 2060.

Griffith, W. P.; Wilkinson, G. “The Pentacyanohydride Complexes of Cobalt(I) and Rhodium(I).” *J. Chem. Soc.* **1959**, 2757.

King, N. K.; Winfield, M. E. “The Liquid Phase Hydrogenation of Cyanocobaltate(II)” *J. Am. Chem. Soc.* **1961**, 83, 3366.

Halpern, J.; Pribanic, M. “Hydrogenation of pentacyanocobaltate(II) at high pressures” *Inorg. Chem.* **1970**, 9, 2616.



# Hydrogenation, $\sigma$ -complex, stereochemistry and mechanistic hypothesis

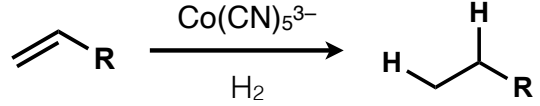
JACS **1962** 304.

**CATALYTIC HYDROGENATION OF ORGANIC COMPOUNDS BY PENTACYANOCOBALTATE(II)**

U. S. INDUSTRIAL CHEMICALS CO.  
DIVISION OF NATIONAL DISTILLERS  
AND CHEMICAL CORPORATION  
CINCINNATI 37, OHIO

JACK KWILATEK  
I. L. MADOR  
JAY K. SEYLER

“No other homogeneous hydrogenation system is known to reduce such a wide variety of substrates”



Substrate	Ratio, moles substrate/ $K_1[\text{Co(CN)}_5]$	Mole % $\text{H}_2$ absorbed <sup>a</sup>	Initial rate of $\text{H}_2$ absorp. (ml./min.)	Products
Isoprene	6.7	79	12	~85% 1,4-, ~15% 1,2-addition
1,3-Cyclohexadiene	7.0	96	60	Cyclohexene
Styrene	2.9	89	21	Ethylbenzene
Tiglic aldehyde	3.4	57	22	$\alpha$ -Methylbutyraldehyde
Methacrylic acid <sup>b</sup>	3.3	97	35	Isobutyric acid
Sorbic acid <sup>c</sup>	3.3	87	57	2-Hexenoic acid
Cinnamic acid <sup>c</sup>	3.3	49	8	$\beta$ -Phenylpropionic acid

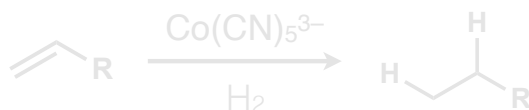
# Hydrogenation, $\sigma$ -complex, stereochemistry and mechanistic hypothesis

JACS 1968 1914.

## CATALYTIC HYDROGENATION OF ORGANIC COMPOUNDS BY PENTACYANOCOBALTATE(II)

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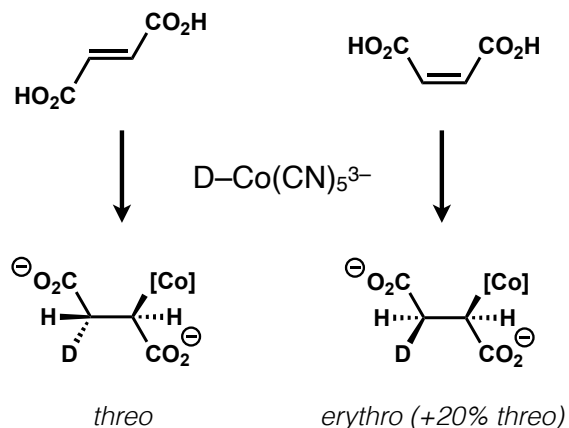
Substrate

Isoprene  
1,3-Cyclohexadiene  
Styrene  
Tiglic aldehyde  
Methacrylic acid<sup>b</sup>  
Sorbic acid<sup>c</sup>  
Cinnamic acid<sup>c</sup>

- rate unaffected by  $[\text{CN}^-]$
  - $[\text{HO}-\text{Co(CN)}_5]^{3-}$  ineffective under  $\text{H}_2$
- | Substrate                     | mole % | Mole % | rate of H <sub>2</sub> uptake | Notes                         |
|-------------------------------|--------|--------|-------------------------------|-------------------------------|
| Isoprene                      | 6.7    | 79     | 12                            | ~85% 1,4-, ~15% 1,2-addition  |
| 1,3-Cyclohexadiene            | 7.0    | 96     | 60                            | Cyclohexene                   |
| Styrene                       | 8.4    | 87     | 29                            | Ethylbenzene                  |
| Tiglic aldehyde               | 9.4    | 87     | 29                            | $\alpha$ -Methylbutyraldehyde |
| Methacrylic acid <sup>b</sup> | 3.3    | 87     | 57                            | Isobutyric acid               |
| Sorbic acid <sup>c</sup>      | 3.3    | 87     | 57                            | 2-Hexenoic acid               |
| Cinnamic acid <sup>c</sup>    | 8      | 8      | 8                             | $\beta$ -Phenylpropionic acid |
- non-coordinative
  - non-hydridic (not H<sup>-</sup>)
  - (protic unlikely)

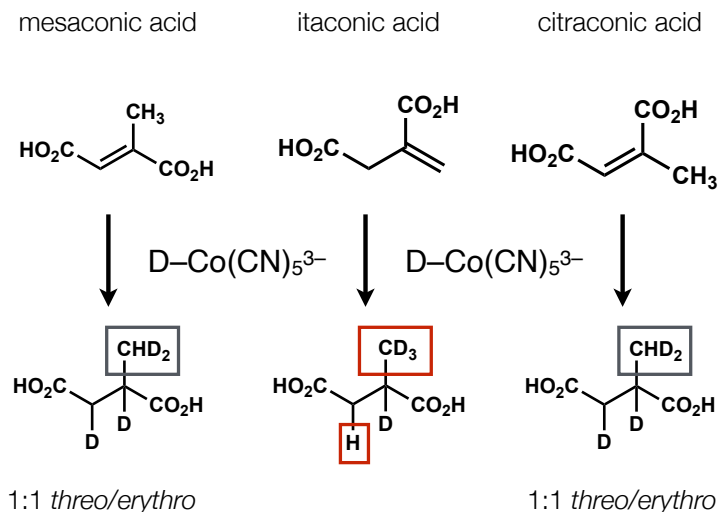
## Reactions of Hydridopentacyanocobaltate with the Anions of $\alpha,\beta$ -Unsaturated Acids

L. M. Jackman,<sup>9</sup> J. A. Hamilton, J. M. Lawlor  
Department of Organic Chemistry, University of Melbourne  
Melbourne, Victoria, Australia  
Received December 13, 1967



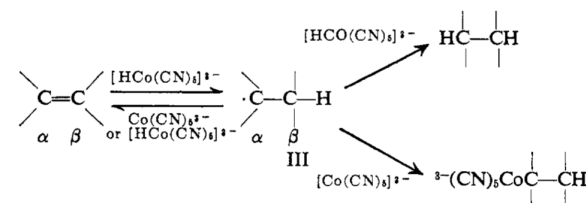
could exclude *syn*-addition,  
unless E/Z isomerization occurs!  
(spoiler alert: it does)

JACS 1968 1914; cf. Halpern JACS 1961 753)



Reduction is non-stereospecific,  
independent of isomerization,  
inconsistent with a coordinative *syn*-selective hydrogenation

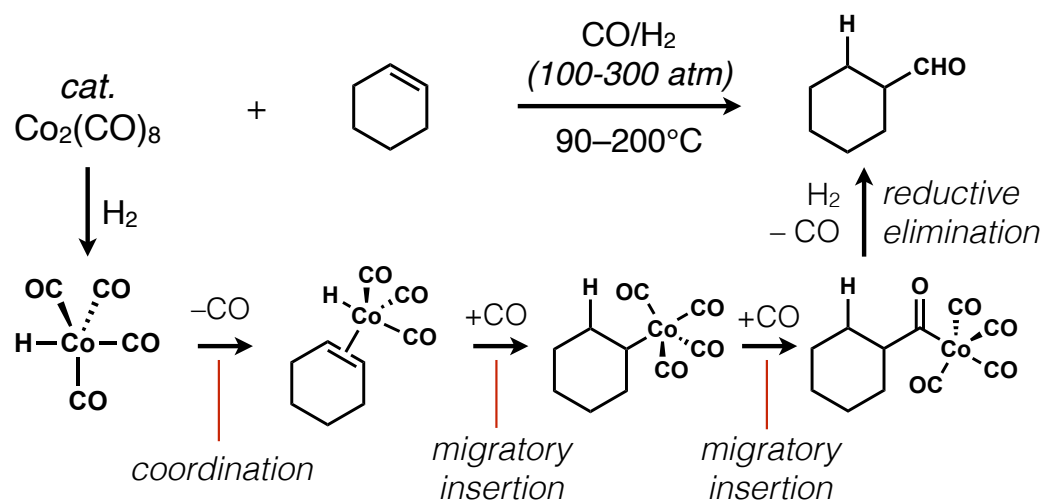
The results presented here lend support to the mechanism proposed by Simandi and Nagy,<sup>1h,i</sup> and considered by Kwiatek,<sup>1j</sup> in which the hydride is a hydrogen atom donor which generates the organic free-radical intermediate III. Reduction is completed by attack at the



$\alpha$  position by a second hydride molecule. Exchange and isomerization involve removal of a hydrogen atom from the  $\beta$  position by either  $[\text{Co(CN)}_5]^{3-}$  or  $[\text{HCo(CN)}_5]^{3-}$ , the latter giving molecular hydrogen which subsequently regenerates the hydride.  $\sigma$ -Complex formation, which is stereospecific, can be formulated either as a concerted addition<sup>1j</sup> or as collapse of a "cage" at a rate substantially greater than the rate of rotation about the  $\alpha,\beta$ -carbon-carbon single bond.

In accord with this mechanism, the rate of attack by hydride (cf. Table I) is facilitated by  $\alpha$ -alkyl groups as these will stabilize the radical III.  $\beta$  Substituents retard the reaction presumably by sterically hindering the approach of the hydride.<sup>8</sup>

## A related system: replacement of CN (X) by CO (L)

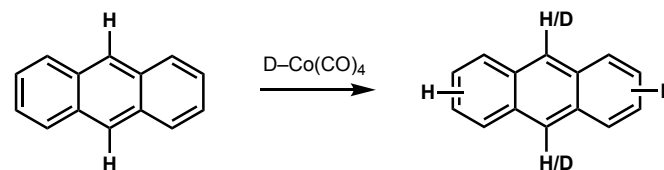


-196 °C trap, then warm with C<sub>6</sub>H<sub>10</sub> >15 °C: see Orchin *JACS* **1953** 3041

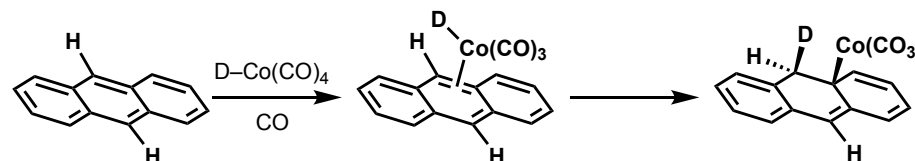
for early mechanistic work, see: Heck *JACS* **1961** 4023.

Do these coordinative pathways explain all the reactivity of HCo(CO)<sub>4</sub>?

1. Weil, Friedman, and Wender have observed that deuteration of anthracene or pyrene with DCo(CO)<sub>4</sub> results in rapid isotopic exchange at the positions of addition only.



Why is exchange unlikely to proceed through a coordination mechanism?



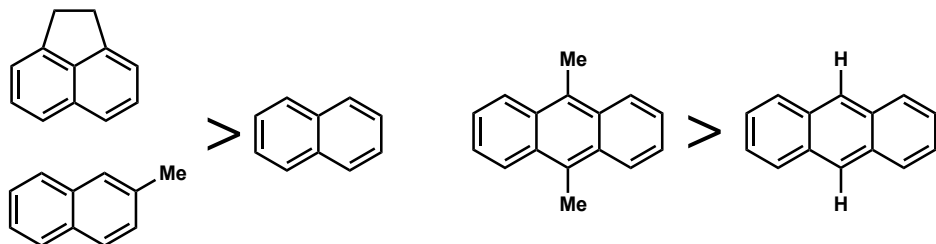
“Because of microscopic reversibility concerted *cis* addition and elimination of DCo(CO)<sub>4</sub> cannot lead to exchange since the nonequivalence of H and D is preserved by the cyclic structures.”

Poll:

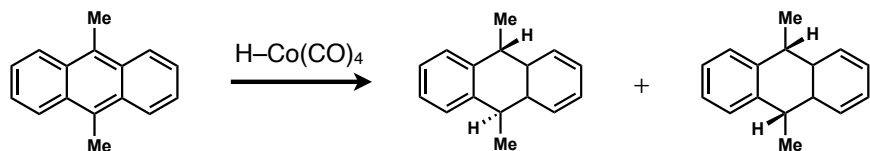
- A)** anthracene cannot coordinate metal centers
- B)** *syn*-addition prevents exchange
- C)** CO cannot dissociate from Co
- D)** coordination leads to hydroformylation

# Do these coordinative pathways explain all the reactivity of $\text{HCo}(\text{CO})_4$ ?

3. 2-Methylnaphthalene and acenaphthene are hydrogenated more readily than naphthalene and 9,10-dimethylantracene more readily than anthracene.



4. Taylor and Orchin observed nearly equal amounts of *cis*- and *trans*-dihydro products from the hydrogenation of 9,10-dimethylantracene, although only *cis*-9,10-dihydro-9,10-dimethylantracene was expected. The scheme they used to rationalize this observation was rather elaborate and only applicable to alkyl substituents which possess  $\alpha$ -hydrogens.

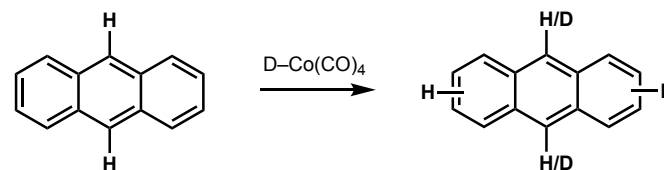


equimolar mixture of *cis*- and *trans*-

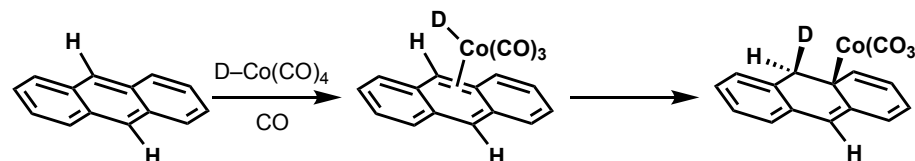
SHADE

SHADE

1. Weil, Friedman, and Wender have observed that deuteration of anthracene or pyrene with  $\text{DCo}(\text{CO})_4$  results in rapid isotopic exchange at the positions of addition only.



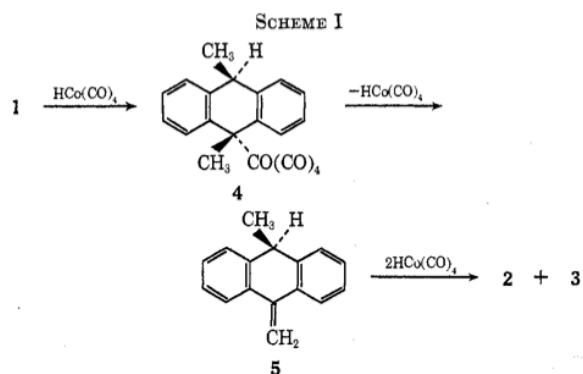
Why is exchange unlikely to proceed through a coordination mechanism?



“Because of microscopic reversibility concerted *cis* addition and elimination of  $\text{DCo}(\text{CO})_4$  cannot lead to exchange since the nonequivalence of H and D is preserved by the cyclic structures.”

2. Hydroxymethylated compounds are not found among the products of catalytic hydrogenation of PAH, although these are the usual products derived from olefins under oxo conditions above 180 °C.

## Two different hypotheses

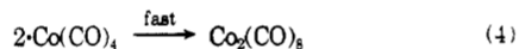
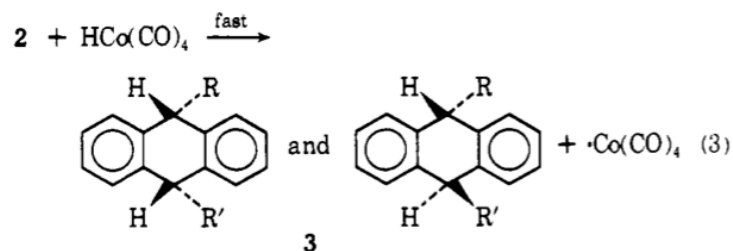
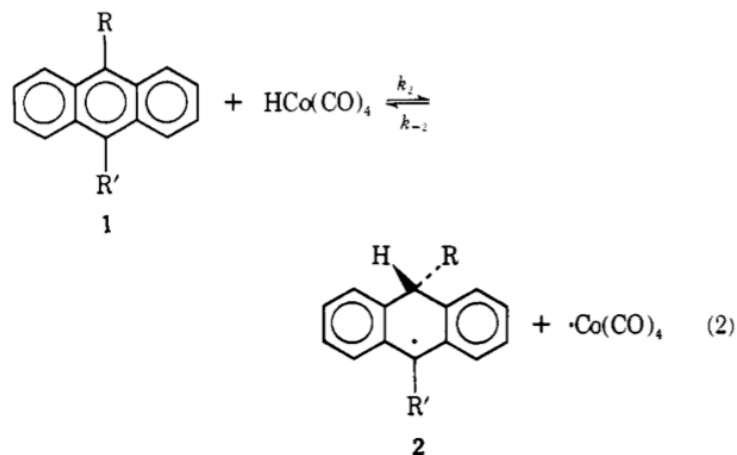
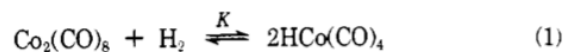


The failure to obtain cis product exclusively in the hydrogenation of **1** leads us to propose Scheme I. This scheme requires that compound **5** be present, at least at low concentration, as free olefin so that subsequent attack of  $\text{HCo(CO)}_4$  can occur at either face of the olefin and thus produce both cis and trans isomers. This scheme also requires that the hydrogenolysis of **4** proceed slowly enough to permit competitive elimination to **5**. It is, of course, not necessary that the reaction of **5** with  $\text{HCo(CO)}_4$  produce **4** again; anti-Markovnikov addition is also possible. In an experiment with the structurally related 1,1-diphenylethene, it was shown that the reaction proceeds smoothly and relatively rapidly with  $\text{HCo(CO)}_4$  to give 1,1-diphenylethane. It is likely that this reaction proceeds by anti-Markovnikov addition

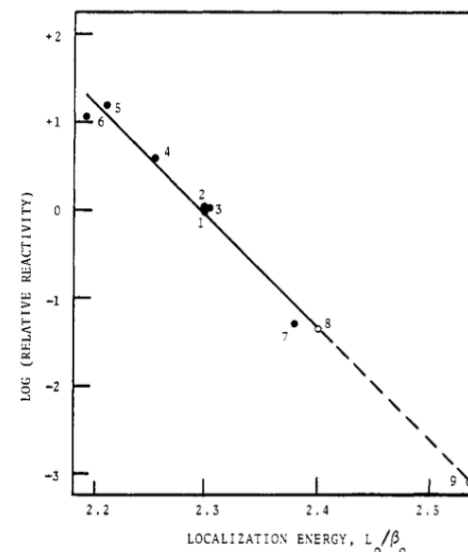


The reaction with **5** may proceed similarly. Pre-

Taylor, P. D.; Orchin, M. *JOC* **1972**, 37, 3913.



Feder, H. M.; Halpern, J. *JACS* **1975**, 97, 7186.



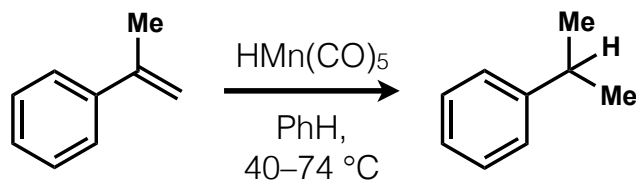
**Figure 1.** Correlation of relative hydrogenation reactivities at 200° with radical localization energies. The code is as follows: 1, naphthalene; 2, phenanthrene; 3, coronene; 4, chrysene; 5, fluoranthene; 6, pyrene; 7, triphenylene; 8, biphenyl; 9, benzene. (Reactivity of naphthalene = 1). The points for benzene and biphenyl correspond to the relative rates predicted for these substrates by extrapolation of the line drawn through the other points.

for a description of localization energy and correlation to relative rates of addition to aromatic rings, see:  
 Coullson, C. A. *J. Phys. Chem.* **1955**, 1435.

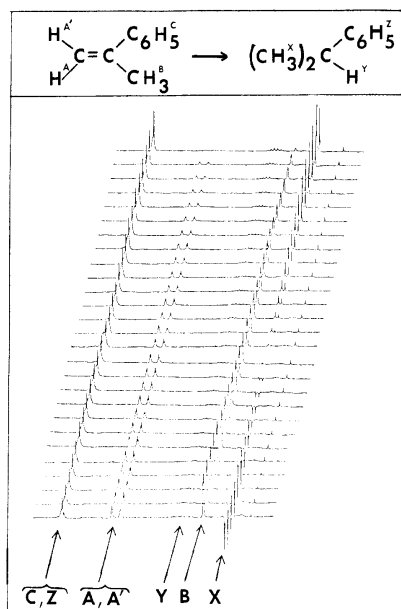


## Polar (hydride, proton) or radical (hydrogen)?

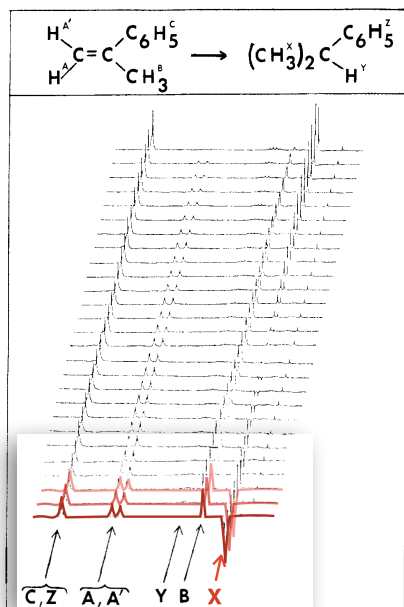
**Seminal paper:** Sweany, R. L.; Halpern, J. "Hydrogenation of  $\alpha$ -Methylstyrene by hydridopentacarbonylmanganese (I). Evidence for a Free-Radical Mechanism" *J. Am. Chem. Soc.* **1977**, *99*, 8335.



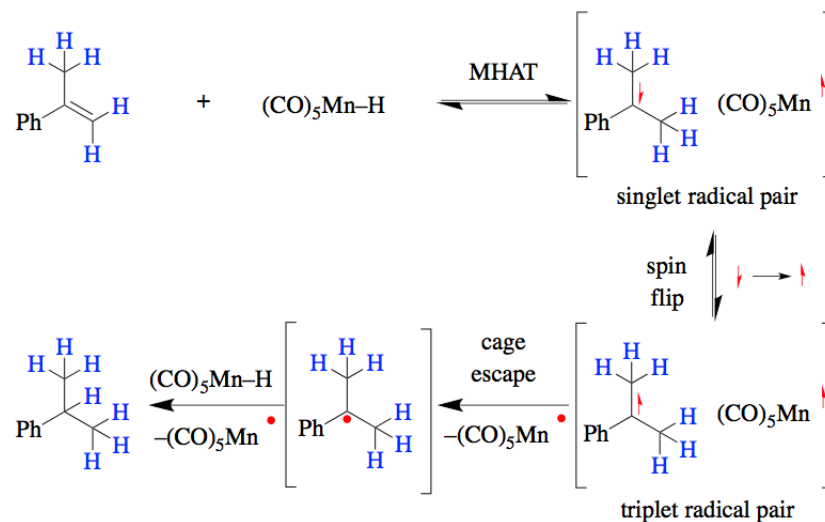
$$-d[\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2]/dt = k'[\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2][\text{HMn}(\text{CO})_5]$$



# Telltale sign: CIDNP

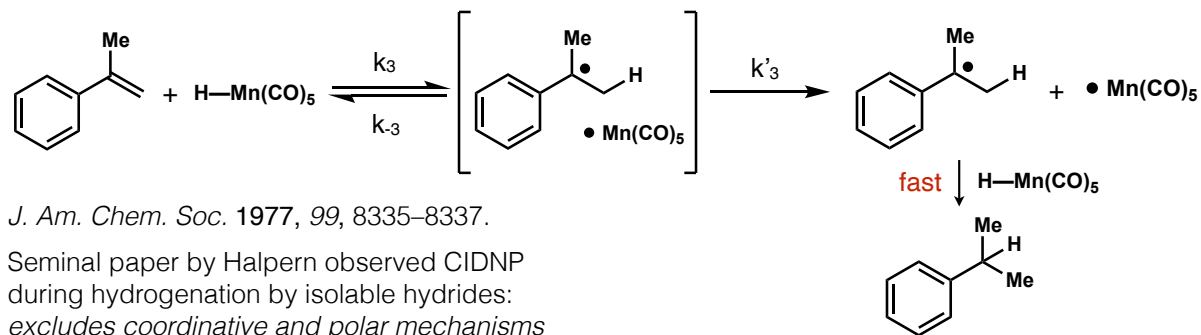
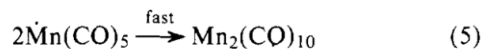
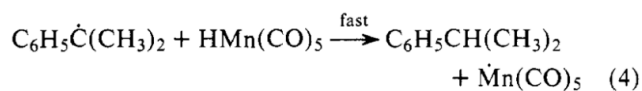
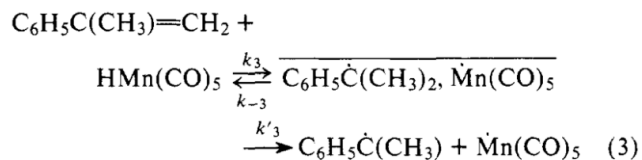
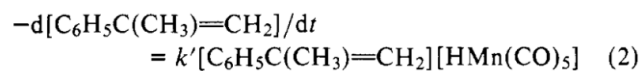


enhanced  
absorption  
of radiowaves



emission  
of radiowaves

Matos, J.; Green, S. A.; Shenvi, R. A. *Org. React.* **2019**, *100*, 383-470.



*J. Am. Chem. Soc.* **1977**, *99*, 8335–8337.

Seminal paper by Halpern observed CIDNP during hydrogenation by isolable hydrides: excludes coordinative and polar mechanisms

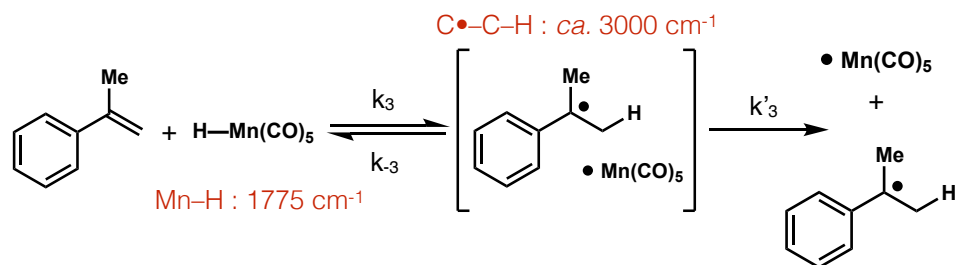
# Telltale sign: inverse KIE

the following observations. (1) When  $\text{DMn}(\text{CO})_5$  was reacted with  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$ , the formation of products was accompanied by isotopic exchange, reflected in the accumulation of  $\text{HMn}(\text{CO})_5$  and a decrease in the intensity of the  $\text{CH}_3$  signal of the unreacted  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$ , resulting from deuterium incorporation. This exchange is in accord with the requirement of reversibility of step 3 of the proposed mechanism.

The extent of the observed exchange suggests that  $k_{-3}/k_3' \geq 1$ . (2) The rate constant for the reaction of  $\text{DMn}(\text{CO})_5$  with  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$  was found to be larger than that for  $\text{HMn}(\text{CO})_5$  ( $k_{\text{H}}'/k_{\text{D}}' \sim 0.4$  at  $65^\circ\text{C}$ ). In view of the very low initial frequency of the Mn-H bond ( $\sim 1800\text{ cm}^{-1}$ ) relative to that of the C-H bond ( $\sim 3000\text{ cm}^{-1}$ ), such an inverse isotope effect is not unexpected and has indeed been anticipated.<sup>14</sup>

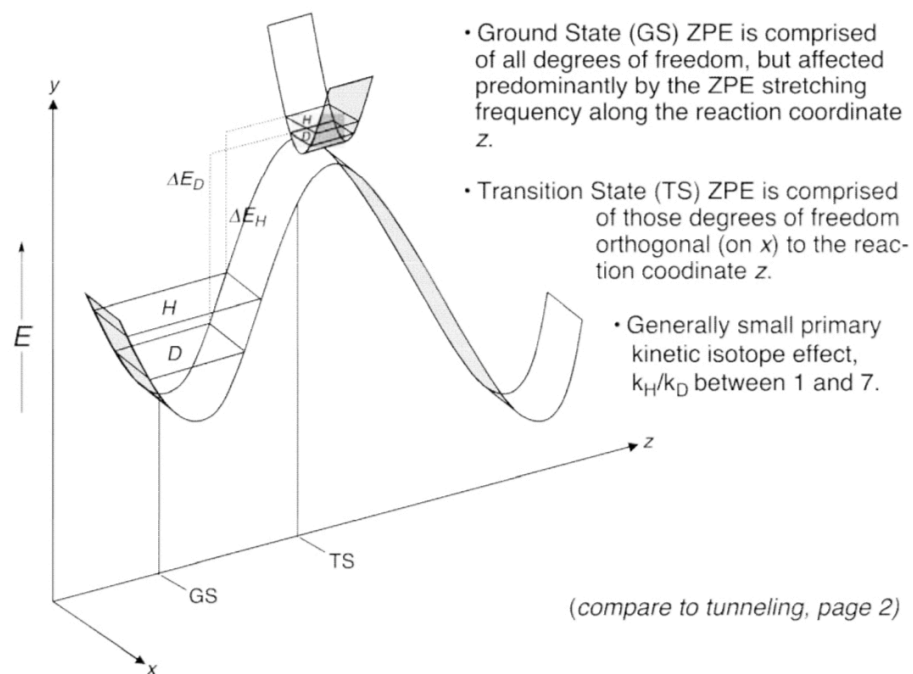
Similar inverse isotope effects also have been observed recently in related reactions of  $\text{HCo}(\text{CO})_4$ <sup>15</sup> and  $\text{HMn}(\text{CO})_5$ <sup>16</sup> with arenes.

(9) Attention is directed to the similarities between the reactions of  $\text{HMn}(\text{CO})_5$  and of  $\text{HCo}(\text{CN})_5^{3-}$  with styrenes and with  $\alpha,\beta$ -unsaturated compounds.<sup>8,10,11</sup>



Inverse KIE is unusual!

H/D kinetic isotope effect (KIE)



\*\*H/D ZPE differences smaller at TS: lower force constant\*\*

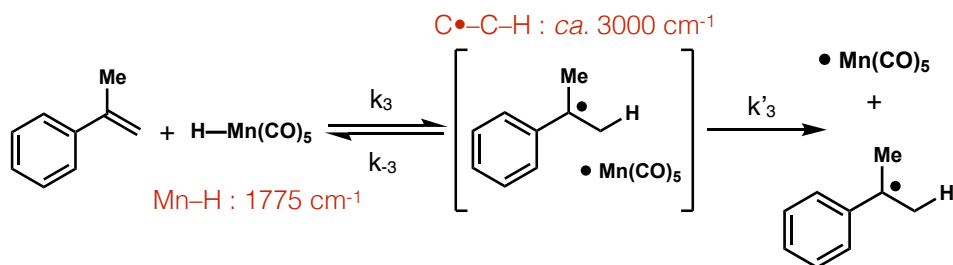
## Telltale sign: inverse KIE

the following observations. (1) When  $\text{DMn}(\text{CO})_5$  was reacted with  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$ , the formation of products was accompanied by isotopic exchange, reflected in the accumulation of  $\text{HMn}(\text{CO})_5$  and a decrease in the intensity of the  $\text{CH}_3$  signal of the unreacted  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$ , resulting from deuterium incorporation. This exchange is in accord with the requirement of reversibility of step 3 of the proposed mechanism.

The extent of the observed exchange suggests that  $k_{-3}/k_3' \geq 1$ . (2) The rate constant for the reaction of  $\text{DMn}(\text{CO})_5$  with  $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)=\text{CH}_2$  was found to be larger than that for  $\text{HMn}(\text{CO})_5$  ( $k_{\text{H}}'/k_{\text{D}}' \sim 0.4$  at  $65^\circ\text{C}$ ). In view of the very low initial frequency of the  $\text{Mn}-\text{H}$  bond ( $\sim 1800\text{ cm}^{-1}$ ) relative to that of the  $\text{C}-\text{H}$  bond ( $\sim 3000\text{ cm}^{-1}$ ), such an inverse isotope effect is not unexpected and has indeed been anticipated.<sup>14</sup>

Similar inverse isotope effects also have been observed recently in related reactions of  $\text{HCo}(\text{CO})_4$ <sup>15</sup> and  $\text{HMn}(\text{CO})_5$ <sup>16</sup> with arenes.

(9) Attention is directed to the similarities between the reactions of  $\text{HMn}(\text{CO})_5$  and of  $\text{HCo}(\text{CN})_5^{3-}$  with styrenes and with  $\alpha,\beta$ -unsaturated compounds.<sup>8,10,11</sup>



Leusink, A. J.; Budding, H. A.; Drenth, W. J. *Organomet. Chem.* **1967**, *9*, 295.

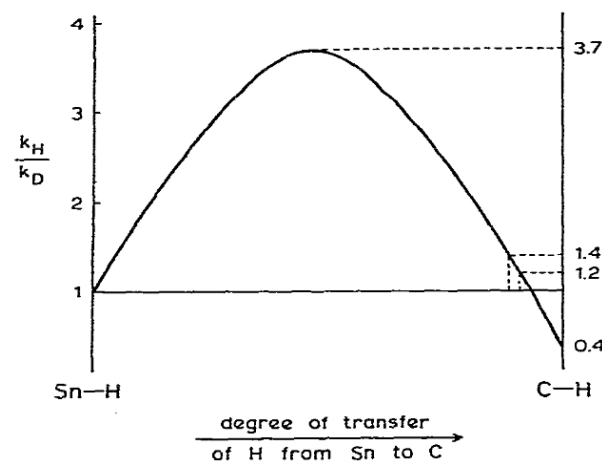


Fig. 5. Isotope effect for a hydride transfer reaction as a function of the degree of transfer of hydrogen from tin to carbon in the transition state.

Three cases will be distinguished, corresponding with the left hand, the middle and the right hand regions of this figure, respectively:

- the hydrogen is still almost completely attached to tin: the isotope effect will be slightly more than unity;
- the hydrogen-tin bond is broken but the hydrogen-carbon interaction is still weak: the isotope effect will be larger than unity (theoretical value at room temperature: approximately 3.7);
- the hydrogen is completely or almost completely attached to carbon: the isotope effect will be smaller than unity as a result of the large difference between the zero-point energies of the tin-hydrogen and the carbon-hydrogen bonds.

This may be depicted schematically as in Fig. 6.

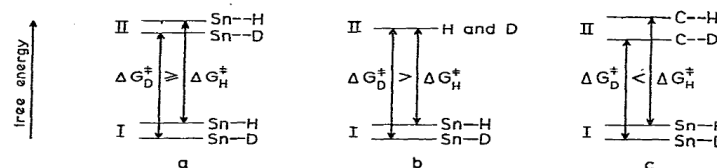


Fig. 6. Free energies of activation for the transfer of hydrogen and deuterium from tin to carbon (see text). I: initial state; II: transition state.  $G$  = Gibbs' free energy; in the Lewis-Randall notation called  $F$ .

# Could MHAT (low $\nu$ M-H/D to high $\nu$ C-H/D) yield a normal KIE?

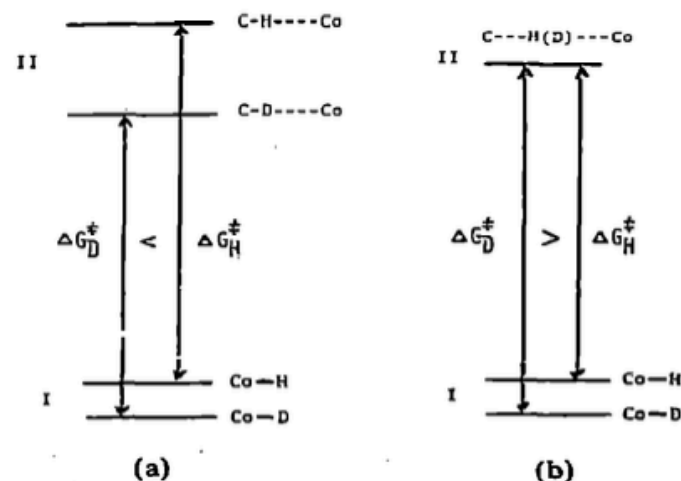
Poll:

- A)** No, ZPEs would be reversed
- B)** No, inverse KIE is diagnostic of MHAT
- C)** Yes, if TS is not too late
- D)** Yes, if rxn is irreversible

**TABLE 1**  
Isotope effects with  $\text{H(D)Co(CO)}_4$

Olefin	Temp. (°C)	$k_{\text{H}}/k_{\text{D}}$	$\Delta H^\ddagger$		$\Delta S^\ddagger(\text{H,D})$		$\Delta G_D^\ddagger(\text{H,D})$	
			H-Co	D-Co	H-Co	D-Co	H-Co	D-Co
$\text{Ph}_2\text{C}=\text{CH}_2$	0	0.58	17.0	16.5	-10	-4.8	19.7	17.8
$\text{Fl}=\text{CHCH}_3^a$	-10	0.43	15.7	13.3	-6	-13	17.3	16.8
$\text{Fl}=\text{CHPh}$	0	1.22	12.2	12.6	-21	-20	17.9	18.1
$\text{Fl}=\text{Fl}$	-12	2.02	12.1	11.9	-20	-23	17.5	18.2
	0	2.01						
	24	1.96						

Nalesnik, T. E.; Freudenberger, J. H.; Orchin, M. *J. Mol. Catal.* **1982**, *16*: 43.



**Fig. 3.** Effect of extent H and D transfer from Co to C on free energy of inverse isotope effect with  $\text{Ph}_2\text{C}=\text{CH}_2$ ; (b) normal isotope effect with bifluorenylidene

So, theory allows inverse KIE with a sufficiently late TS or a normal KIE with anything earlier, but there is an alternative interpretation

## Telltale sign: inverse KIE

the following observations. (1) When  $\text{DMn(CO)}_5$  was reacted with  $\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2$ , the formation of products was accompanied by isotopic exchange, reflected in the accumulation of  $\text{HMn(CO)}_5$  and a decrease in the intensity of the  $\text{CH}_3$  signal of the unreacted  $\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2$ , resulting from deuterium incorporation. This exchange is in accord with the requirement of reversibility of step 3 of the proposed mechanism.

The extent of the observed exchange suggests that  $k_{-3}/k'_3 \geq 1$ . (2) The rate constant for the reaction of  $\text{DMn(CO)}_5$  with  $\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2$  was found to be larger than that for  $\text{HMn(CO)}_5$  ( $k_{\text{H}}'/k_{\text{D}}' \sim 0.4$  at  $65^\circ\text{C}$ ). In view of the very low initial frequency of the Mn-H bond ( $\sim 1800\text{ cm}^{-1}$ ) relative to that of the C-H bond ( $\sim 3000\text{ cm}^{-1}$ ), such an inverse isotope effect is not unexpected and has indeed been anticipated.<sup>14</sup>

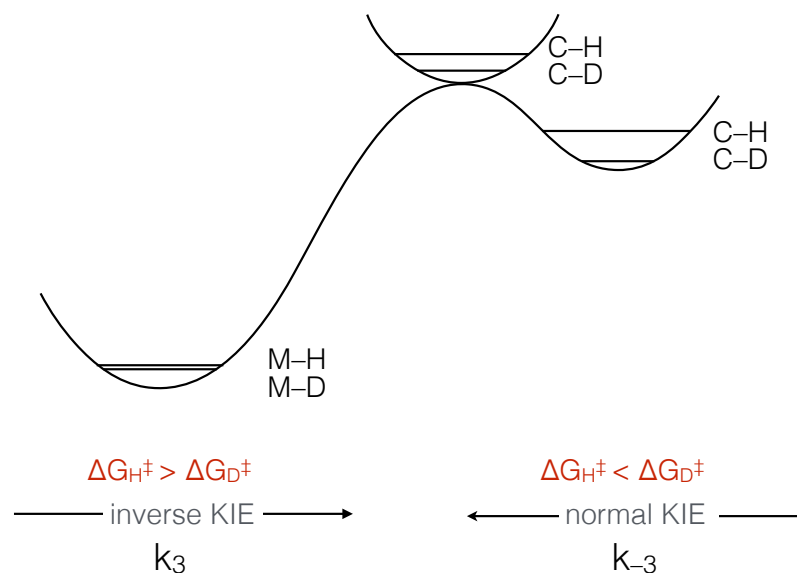
Similar inverse isotope effects also have been observed recently in related reactions of  $\text{HCo(CO)}_4$ <sup>15</sup> and  $\text{HMn(CO)}_5$ <sup>16</sup> with arenes.

$$-\text{d}[\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2]/\text{d}t = k'[\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2][\text{HMn(CO)}_5]$$

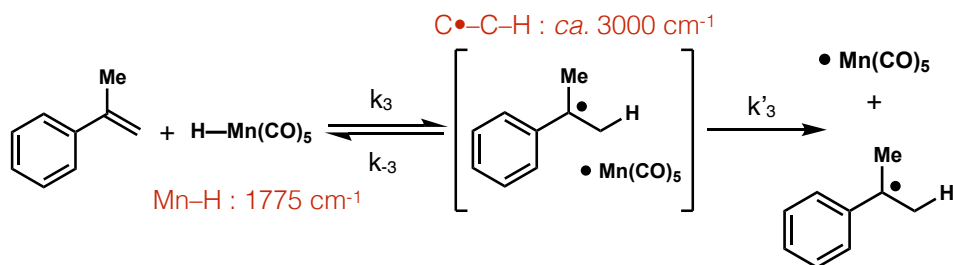
$$= k_3k'_3/(k_{-3} + k'_3)[\text{C}_6\text{H}_5\text{C(CH}_3)=\text{CH}_2][\text{HMn(CO)}_5]$$

$$\text{dP}/\text{d}t = k'_3 [\text{radical pair}]$$

“equilibrium isotope effect”  
larger  $k_{-3}$  for H

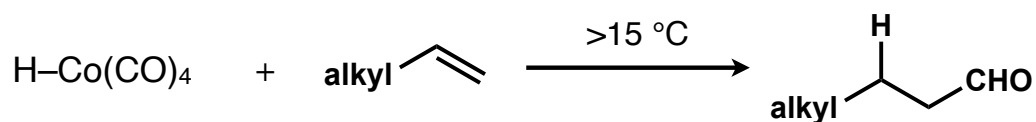


(9) Attention is directed to the similarities between the reactions of  $\text{HMn(CO)}_5$  and of  $\text{HCo(CN)}_5^{3-}$  with styrenes and with  $\alpha,\beta$ -unsaturated compounds.<sup>8,10,11</sup>



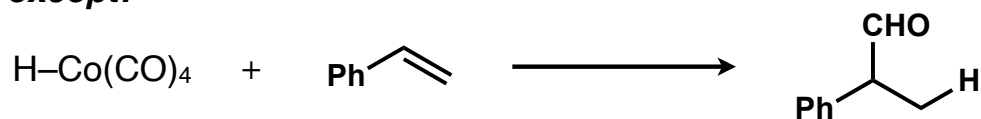
# MHAT allows specific predictions to be made: branched hydroformylation

*recall:*



- linear aldehydes predominate
- inhibited by CO pressure

*except:*



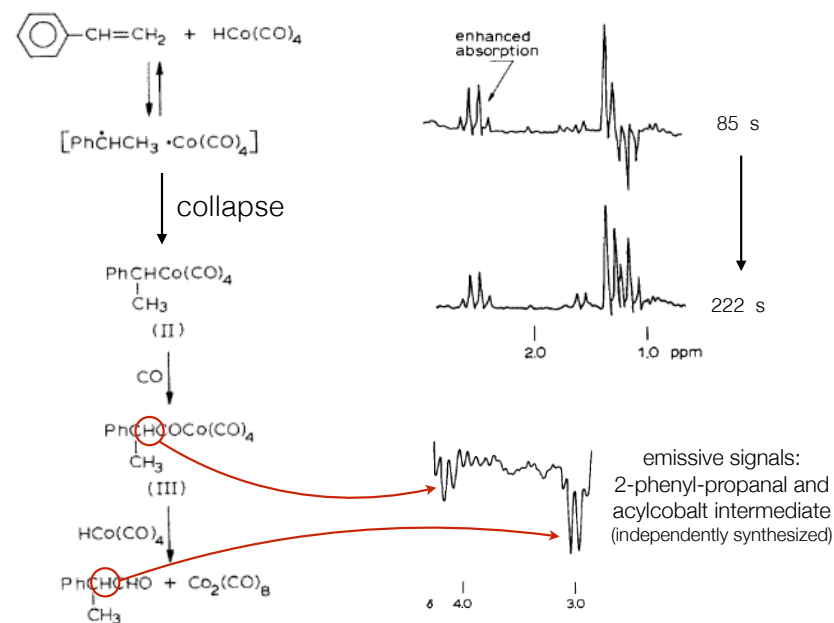
- *branched* aldehydes predominate
- *uninhibited* by CO pressure

*J. Organomet. Chem.* **1985**; 279, 165.

CO pressure: H-Mn(CO)<sub>5</sub> hydrometallation of dienes: *JACS* **1987**, 1995.

“In addition, after more than one minute, some runs in C<sub>6</sub>D<sub>6</sub>, show the kind of line-broadened deterioration of the NMR spectra that would be expected if paramagnetic species were present. Paramagnetic species greatly enhance proton spin-lattice relaxation times, causing polarization to disappear rapidly. In view of these factors, it might be considered remarkable that any CIDNP can be detected from HCo(CO)-styrene reactions.”

Other implication is that polarization is carried through multiple steps, which then must be fast. These could be radical steps, but the presence of polarization in ethylbenzene (reduction path) indicates CIDNP from the first step, consistent with Halpern's experiments.



“no alternative explanation for CIDNP is considered to be viable”  
not entirely true: see para-hydrogen and the “monday morning effect”

Bockman, T.M.; Garst, J. F.; King, R.B.; Marko, L.; Ungvary, F.  
*J. Organomet. Chem.* **1985**; 279, 165.



# BDEs (we are not invoking $H^{\bullet}_{(sol)}$ )

Tilset, M.; Parker, V. D. "Solution Homolytic Bond Dissociation Energies of Organotransition-Metal Hydrides"  
*J. Am. Chem. Soc.* **1989**, *111*, 6711–6717.

**Table I.** Metal Anion Oxidation Potentials, Metal Radical Recombination Rate Constants, and Calculated Kinetic Potential Shifts

	$\Delta G^{\circ}$		compound	$E_{ox}(M^{\bullet})^a$	$k_{dim}^b$	$E_{corr}^c$
$M-H(sol) \rightarrow M^{\bullet}(sol) + H^{\bullet}(sol)$	$2.301RTpK_a$	(4)	$(\eta^5-C_5H_5)Cr(CO)_3^-$	-0.688 <sup>d</sup>		0.000
$M^{\bullet}(sol) \rightarrow M^+(sol) + e^-$	$FE^{\circ}_{ox}(M^{\bullet})$	(5)	$(\eta^5-C_5H_5)Mo(CO)_3^-$	-0.501	$3 \times 10^9^e$	0.116
$H^{\bullet}(sol) \rightarrow H^+(aq)$	$-\Delta G^{\circ}_{tr}(H^{\bullet})$	(6)	$(\eta^5-C_5Me_5)Mo(CO)_3^-$	-0.709 <sup>f</sup>	$1 \times 10^9^g$	0.106
$H^+(aq) + e^- \rightarrow 0.5H_2(g)$	0	(7)	$(\eta^5-C_5H_5)W(CO)_3^-$	-0.491	$1.9 \times 10^9^h$	0.112
$0.5H_2(g) \rightarrow H^{\bullet}(g)$	$\Delta G^{\circ}_f(H^{\bullet})_g$	(8)	$(\eta^5-C_5H_5)W(CO)_2PMe_3^-$	-1.225	$1 \times 10^9^g$	0.106
$H^{\bullet}(g) \rightarrow H^{\bullet}(sol)$	$\Delta G^{\circ}_{sol}(H^{\bullet})$	(9)	$(\eta^5-C_5H_5)Fe(CO)_2^-$	-1.352	$3.2 \times 10^9^i$	0.117
$M-H(sol) \rightarrow M^{\bullet}(sol) + H^{\bullet}(sol)$	BDE	(10)	$(\eta^5-C_5H_5)Ru(CO)_2^-$	-1.057	$3 \times 10^9^j$	0.116
			$Mn(CO)_5^-$	-0.555	$9.5 \times 10^8^k$	0.106
			$Mn(CO)_4PPh_3^-$	-0.870	$1 \times 10^7^l$	0.067
			$Re(CO)_5^-$	-0.690	$3.7 \times 10^9^k$	0.118
			$Co(CO)_4^-$	-0.271	$4.2 \times 10^8^m$	0.099
			$Co(CO)_3P(OPh)_3^-$	-0.489	$9 \times 10^7^n$	0.086
			$Co(CO)_3PPh_3^-$	-0.723	$1 \times 10^7^o$	0.067
			$HFe(CO)_4^-$	-0.403	$4 \times 10^8^p$	0.099

$$BDE = 2.301RTpK_a + FE^{\circ}_{ox}(M^{\bullet}) - \Delta G^{\circ}_{tr}(H^{\bullet}) + \Delta G^{\circ}_f(H^{\bullet})_g + \Delta G^{\circ}_{sol}(H^{\bullet}) \quad (11)$$

**Table II.** Metal Hydride Brønsted Acidity and Bond Dissociation Data in Acetonitrile

entry	compd	$E_{ox}(M^{\bullet})$ vs $(H^+/H_2)_{AN}$	M-H $pK_a^a$	M-H BDE, kcal/mol	
				$b$	lit. data
1	$(\eta^5-C_5H_5)Cr(CO)_3H$	-0.639	13.3	54	
2	$(\eta^5-C_5H_5)Mo(CO)_3H$	-0.336	13.9	62	$65 \pm 6^9$ $66 \pm 8^{37}$ $66 \pm 1.5^{38}$
3	$(\eta^5-C_5Me_5)Mo(CO)_3H$	-0.554 <sup>d</sup>	17.1	61	
4	$(\eta^5-C_5H_5)W(CO)_3H$	-0.330	16.1	65	$80.7^9$
5	$(\eta^5-C_5H_5)W(CO)_2PMe_3H$	-1.070 <sup>d</sup>	26.6	62	
6	$Mn(CO)_5H$	-0.400	14.1 <sup>c</sup>	60	$65^{2a}$ , $51^{11}$ $63^{21}$
7	$Mn(CO)_4PPh_3H$	-0.754	20.4	61	
8	$Re(CO)_5H$	-0.523	21.1	67	
9	$(\eta^5-C_5H_5)Fe(CO)_2H$	-1.186	19.4	50	
10	$(\eta^5-C_5H_5)Ru(CO)_2H$	-0.892	20.2	57	
11	$Fe(CO)_4H_2$	-0.255 <sup>d</sup>	11.4	60	$<65^{2a}$
12	$Co(CO)_4H$	-0.123 <sup>d</sup>	8.3	59	$58^{41}$
13	$Co(CO)_3P(OPh)_3H$	-0.354	11.3	58	
14	$Co(CO)_3PPh_3H$	-0.607 <sup>d</sup>	15.4	57	

cf. cyclohexane C–H: 96 kcal/mol;  $H_3CS$ –H: 88 kcal/mol;  $nBu_3Sn$ –H: 78 kcal/mol;  $Co(CO)_4H$ : 58 kcal/mol

Effects of neither phosphine or phosphite substitution nor permethylation of the cyclopentadienyl ring on the M–H bond energies could be detected within the error limits of the method. (*but these substitution reactions affect rate of MHAT*)

BDE is important because it influences rate of reaction with alkene, much like  $pK_a$  influences rate of reactivity with a base

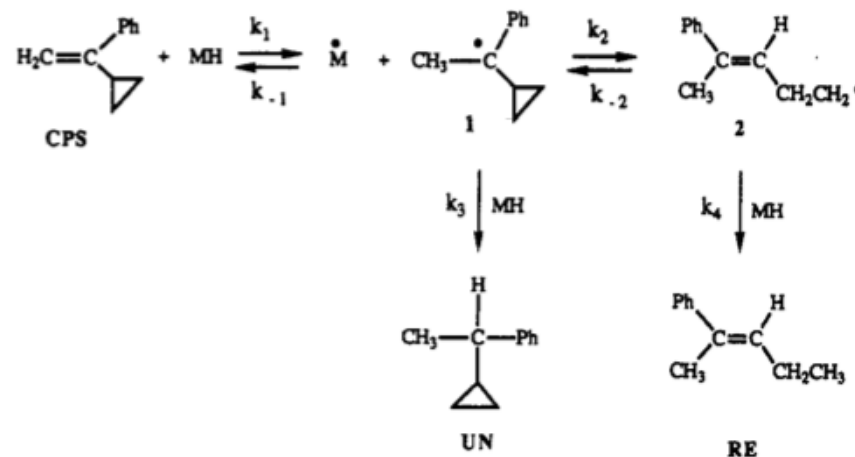


# Correlation of M–H BDE and rate: not the whole story!

Bullock, R. M.; Samsel, E. G. *J. Am. Chem. Soc.* **1990**, *112*, 6886–6898.

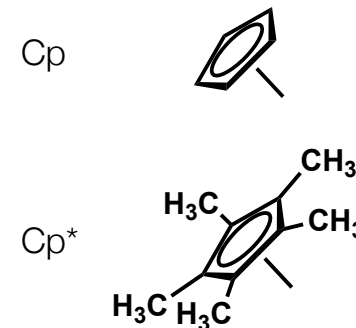
**Table I.** Second-Order Rate Constants for Reaction with CPS, Bond Dissociation Energies of the M–H Bond, and Relative  $k_3$  Values

metal hydride	temp, °C	$k_1,^a$ M <sup>-1</sup> s <sup>-1</sup>	BDE, <sup>b</sup> kcal/mol	$k_3^c$
HCr(CO) <sub>3</sub> Cp	22	$3.4(3) \times 10^{-3}$	62	1
HFe(CO) <sub>2</sub> Cp	22	$4.3(3) \times 10^{-4}$	58	5
HMn(CO) <sub>5</sub>	25	$7.4(5) \times 10^{-6}$ <sup>d</sup>	68	7
HFe(CO) <sub>2</sub> (C <sub>5</sub> Me <sub>5</sub> )	60	$9.6(5) \times 10^{-4}$		94
HMo(CO) <sub>3</sub> (C <sub>5</sub> Me <sub>5</sub> )	60	$6.3(4) \times 10^{-5}$	69	3.8
HMo(CO) <sub>3</sub> Cp	60	$8.3(1) \times 10^{-5}$	70	93
<i>cis</i> -HMn(CO) <sub>4</sub> PPh <sub>3</sub>	60	$9.0(2) \times 10^{-5}$	69	1
HMo(CO) <sub>3</sub> Cp	100	$2.6(1) \times 10^{-3}$	70	16
HMo(CO) <sub>2</sub> (PMe <sub>3</sub> )Cp	100	$1.2(1) \times 10^{-4}$		1
HW(CO) <sub>3</sub> Cp	100	$6.2(5) \times 10^{-5}$	73	5
HRu(CO) <sub>2</sub> Cp	100	<i>e</i>	65	
HRe(CO) <sub>5</sub>	105	<i>f</i>	75	



**Table II.** H• Transfer Rate Constants  $k_H$  (to Tris(*p*-*tert*-butylphenyl)methyl Radical (1) at 25 °C in Toluene) and Bond Dissociation Enthalpies for Transition-Metal Hydrides

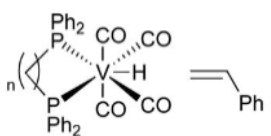
hydride	temp range of rate measurement, °C	wavelength monitored, nm	$k_H,$ M <sup>-1</sup> s <sup>-1</sup>	$\Delta H^\ddagger,$ kcal/mol	$\Delta S^\ddagger,$ eu	BDE, <sup>a</sup> kcal/mol
HFe(CO) <sub>2</sub> Cp	-35/-5	525	12000 (400)	5.7 (1)	-20.8 (5)	58
HFe(CO) <sub>2</sub> Cp*	0/45	558	300 (8)	7.3 (3)	-23 (1)	
HCr(CO) <sub>3</sub> Cp	0/50	523	335 (2)	5.75 (5)	-27.7 (2)	62
HRu(CO) <sub>2</sub> Cp	25/65	523	1030 (30)	7.1 (2)	-21 (1)	65
HCo(CO) <sub>4</sub>	-35	525	1600 (900) <sup>b</sup>			67
HMn(CO) <sub>5</sub> <sup>c</sup>	-40/50	523	741 (8)	7.00 (5)	-22.0 (2)	68
HMo(CO) <sub>3</sub> Cp*	30/60	540	13.9 (5)	7.7 (3)	-27.4 (8)	69
HMo(CO) <sub>3</sub> Cp	0/50	542	514 (2)	5.76 (5)	-26.8 (2)	70
HMn(PEtPh <sub>2</sub> )(CO) <sub>4</sub>	50	530	<3			71 <sup>d</sup>
HW(CO) <sub>3</sub> Cp	20/60	500	91 (1)	6.66 (8)	-27.2 (2)	73
H <sub>2</sub> Os(CO) <sub>4</sub>	30/70	530	15.7 (7)	8.7 (3)	-24 (1)	78 <sup>e</sup>



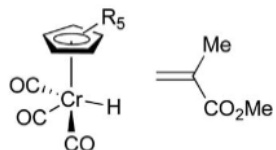
# Correlation of M-H BDE and rate: exceptions!

BDE is important because it influences rate of reaction with alkene, much like pKa influences rate of reactivity with a base

a. Influence of M-H Sterics on MHAT rate

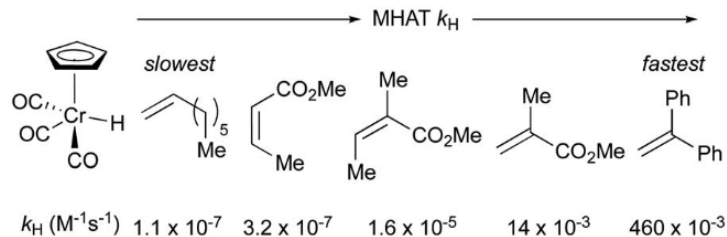


$n$	$k_H$ ( $M^{-1}s^{-1}$ )	M-H BDE (kcal/mol)
1	$17 \times 10^{-3}$	57.9
2	$9.0 \times 10^{-3}$	57.5
3	$7.5 \times 10^{-3}$	56.0
4	$5.0 \times 10^{-3}$	54.9



$R$	$k_H$ ( $M^{-1}s^{-1}$ )	M-H BDE (kcal/mol)
H	$4.0 \times 10^{-3}$	61.5
Me	$0.6 \times 10^{-3}$	62.3
Ph	$0.5 \times 10^{-3}$	59.6

b. Influence of Olefin Sterics and Electronics on MHAT rate



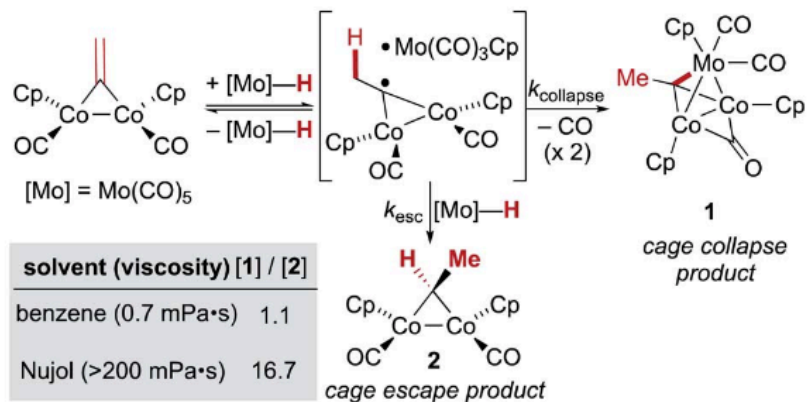
opposite correlation: as BDE decreases, rate decreases

not BDE for either: sterics

alkene electronics also affect MHAT rate

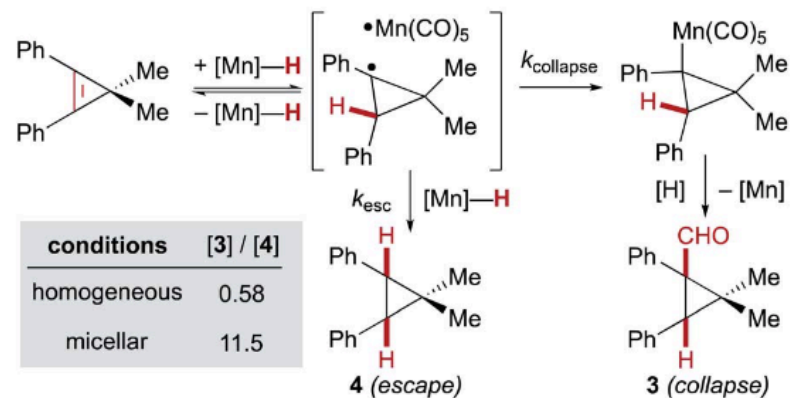
# Correlation of viscosity and product distribution

## a. Hydrogenation of bridging vinylidencobalt with [Mo]-H



E. N. Jacobsen and R. G. Bergman, *J. Am. Chem. Soc.*, **1985**, *107*, 2023–2032.

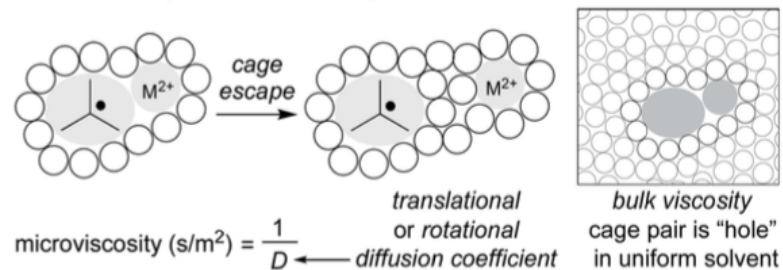
## b. Hydrogenation and hydroformylation of cyclopropenes with [Mn]-H



F. Ungvary and L. Markó, *J. Organomet. Chem.*, **1983**, *249*, 411–414.

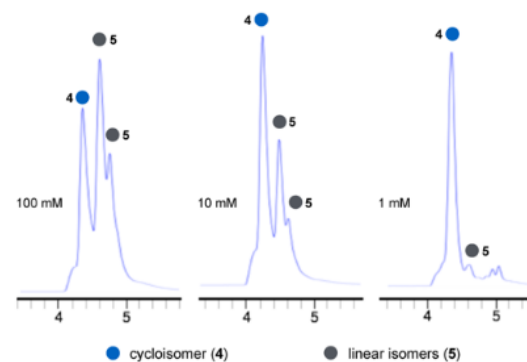
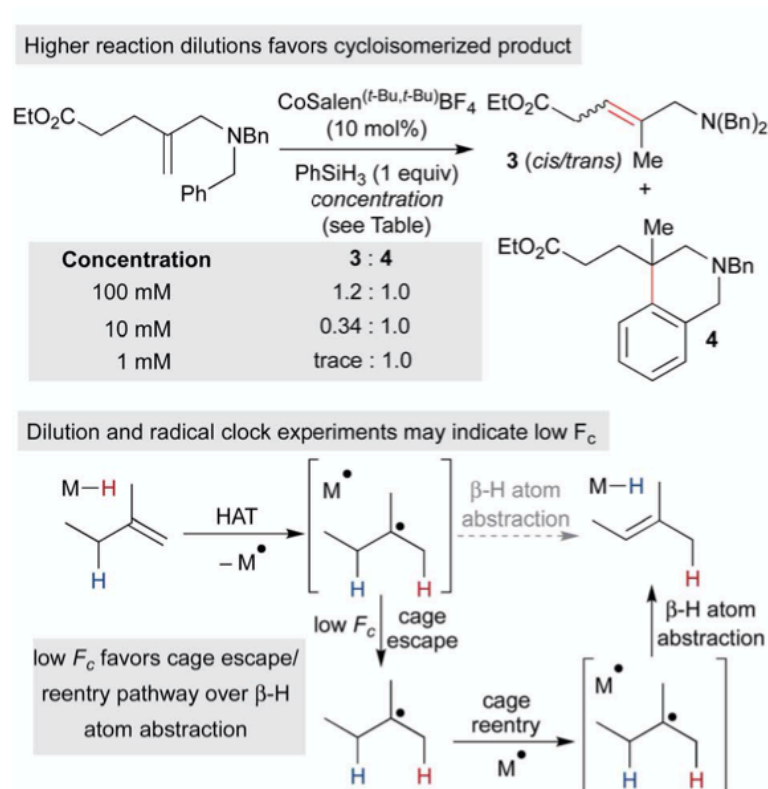
Y. Matsui and M. Orchin, *J. Organomet. Chem.*, **1983**, *244*, 369–373.

microviscosity better predicts cage effects than bulk solvent parameters



Tyler et al. *J. Am. Chem. Soc.*, **2016**, *138*, 9389–9392.

# Correlation of concentration and product distribution



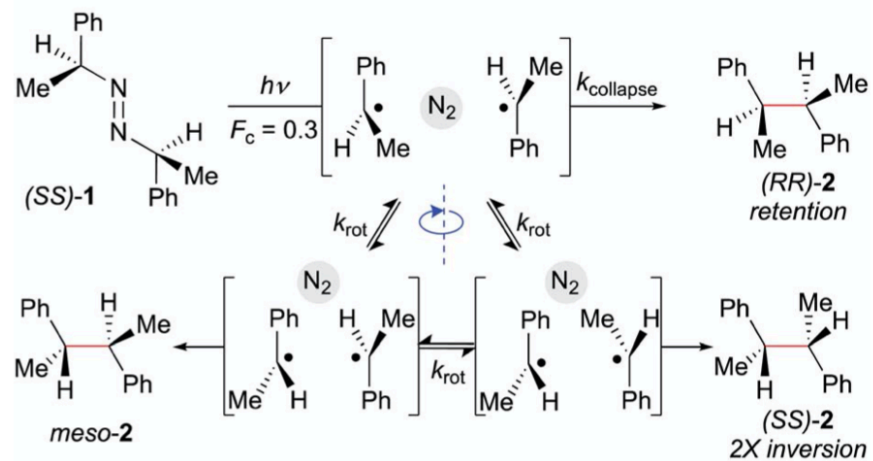
**Figure 5.** Effect of reaction concentration on the yield of the cyclic isomer vs. linear isomer. [a] Yield determined by  $^1\text{H}$  NMR analysis of the crude reaction mixture. ND = not determined.

$$F_c = k_{\text{collapse}} / (k_{\text{collapse}} + k_{\text{diffusion}})$$

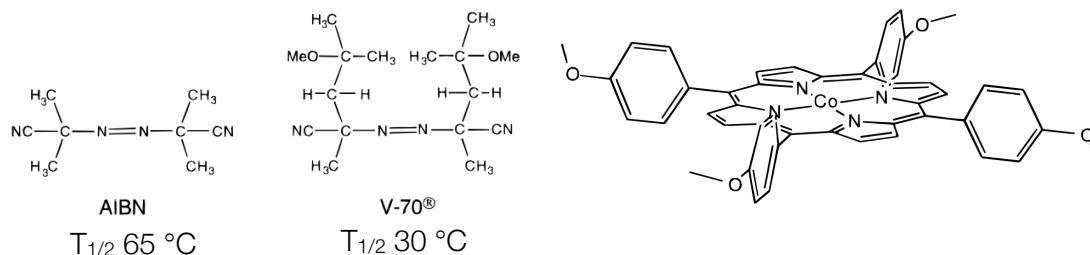
$$k_{\text{obs}} = [1 - F_c] \times k_1$$

# Rates of movement within cage

a. molecular rotation within the solvent cage before cage collapse

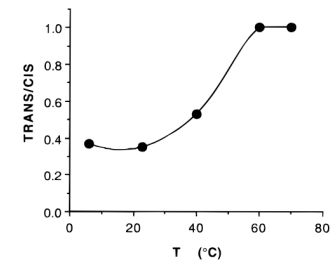
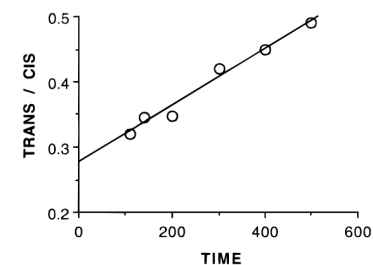
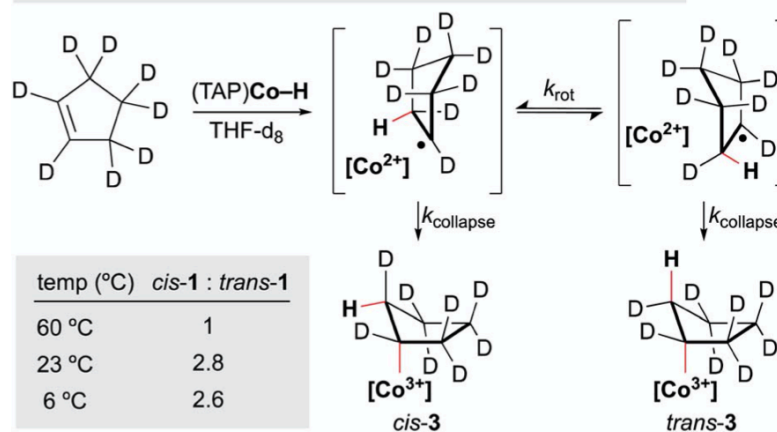


# Rates of movement within cage



The temperatures at which their half lives are 10 h are indicated by  $T_{1/2}$

## b. molecular rotation in the solvent cage before Co-C collapse



**Scheme 17** Molecular rotation occurs on the same timescale as cage collapse.

A. Gridnev, S. D. Ittel, B. B. Wayland and M. Fryd, *Organometallics*, **1996**, 15, 5116.

no regioisomeric scrambling!!  
 $\beta$ -H abstraction is not competitive

# Low energy hydrometalation with no M–H *cis*-vacant site

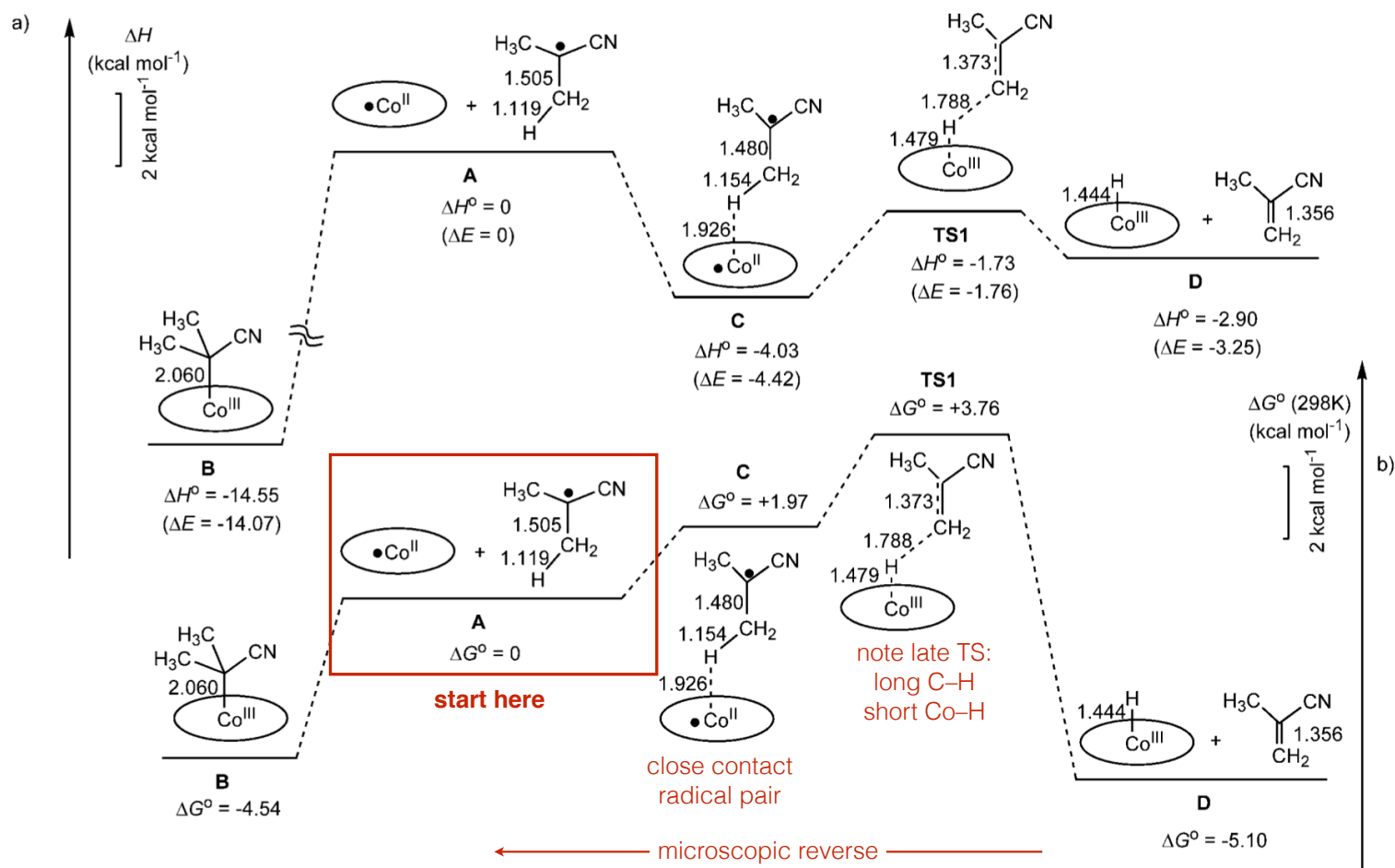
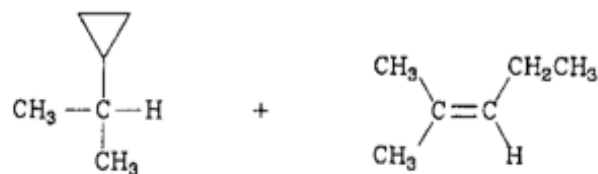
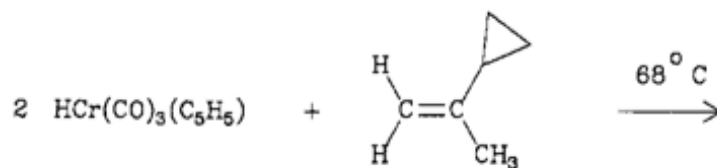


Figure 2. Energy changes ( $\text{kcal mol}^{-1}$ ) for hydrogen-atom transfer from  $\cdot\text{C}(\text{CH}_3)_2\text{CN}$  to  $[\text{Co}^{\text{II}}(\text{por})]$  along with diagnostic Co–H, Co–C, C–C, and C–H internuclear distances (results taken from Table 2). a) Enthalpy change ( $\Delta H^\circ$ ) and internal energy change ( $\Delta E_{ZPE}$ ); b) free-energy change ( $\Delta G^\circ_{298K}$ ).

## MHAT to non-conjugated alkenes?



$k = 2.2 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$  (68°C)

$k_{\text{H}}/k_{\text{D}} \sim 0.5$

$\text{DCr}(\text{CO})_3\text{Cp}$

also H/D exchange  
in substrate

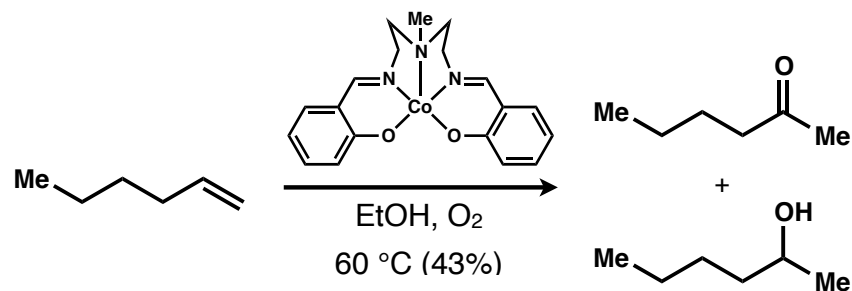
Bullock, R. M.; Samsel, E. G. *J. Am. Chem. Soc.* **1987**, 109, 6542.

“To our knowledge this is the first direct experimental evidence for hydrogen atom transfer from a metal hydride to an alkene which cannot form a stabilized benzylic or allylic intermediate”

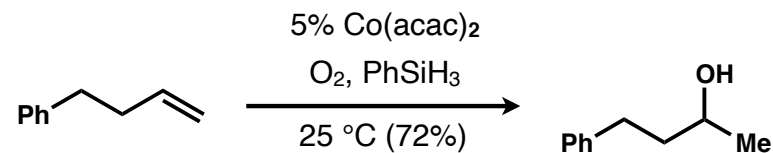
Slow, but general?



# MHAT to non-conjugated alkenes?

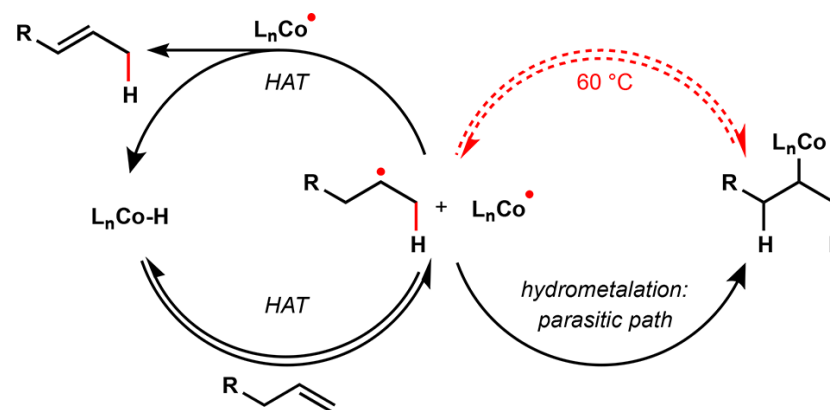
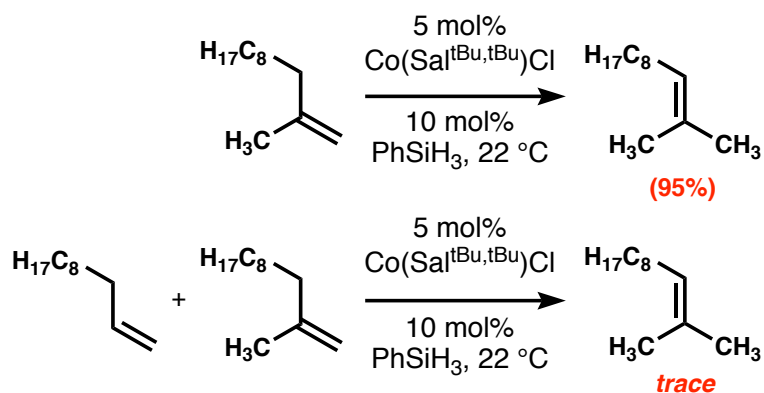


Drago *et al.* *J. Am. Chem. Soc.* **1982**, *104*, 6782



Mukaiyama *et al.* *Chem. Lett.* **1989**, 449 & 1071

See: *J. Am. Chem. Soc.* **2014**, *136*, 1300; *J. Am. Chem. Soc.* **2014**, *136*, 16788.

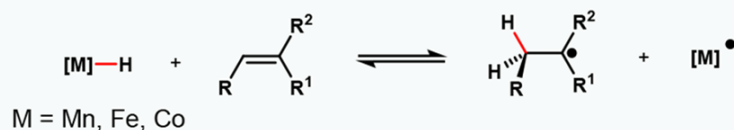


Organometallic is not an "intermediate" but rather lies off-cycle (!!). Contrast to *J. Am. Chem. Soc.* **2006**, *128*, 11693.

# Implications of MHAT to unconjugated alkenes

**Proposal:** A MHAT elementary step, not coordinative hydrometalation, underlies Drago-Mukaiyama hydrofunctionalization reactions

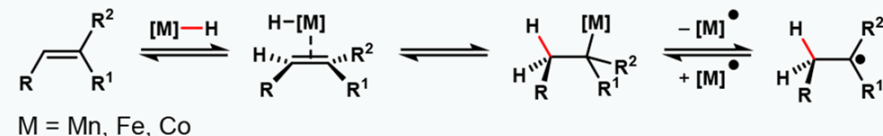
## a) MHAT to alkenes



MHAT mechanism explains:

- 1) exclusive Markovnikov selectivity
- 2) intermediacy of carbon-centered radicals
- 3) low sensitivity to Lewis basic functional groups
- 4) low sensitivity to alkene substitution

## b) Coordinative hydrometalation followed by M-C bond homolysis



Coordinative mechanism fails to explain:

- 1) exclusive Markovnikov selectivity (contra-steric)
- 2) reactivity of complexes without an open coordination site cis to M-H (cf. Ref. 33)
- 3) low sensitivity to Lewis basic functional groups

**Implications:** MHAT elementary step requires weak M-H bonds, which would be thermodynamically unstable to bimolecular H<sub>2</sub> evolution.

## a) Thermochemistry of MHAT to alkenes



$$\Delta G^{\circ}_{MH} < 50 \text{ kcal/mol}$$

$$BDE_{CH} = 35-40 \text{ kcal/mol}$$

- MHAT operates in equilibrium;  $K_{MHAT} = e^{-[(BDE_{CH} - \Delta G^{\circ}_{MH})/RT]}$  (see Ref. 2, 27, 58)
- Weakest stable metal hydride, H-V(CO)<sub>4</sub>(dppb):  $\Delta G^{\circ}_{MH} = 50.3 \text{ kcal/mol}$  no MHAT to unactivated alkenes because  $\Delta \Delta G^{\circ} \sim 10-15 \text{ kcal/mol}$  (see Ref. 58)
- Therefore, MHAT to unactivated alkenes may require  $\Delta G^{\circ}_{MH} < 50 \text{ kcal/mol}$

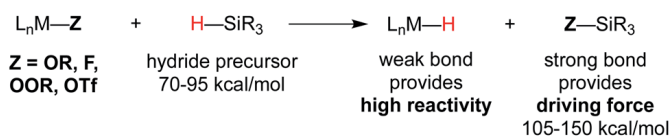
## b) Thermochemistry of bimolecular H<sub>2</sub> evolution



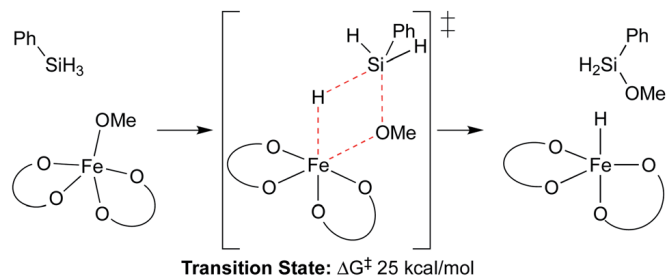
$$\Delta G^{\circ}_{MH} < 56 \text{ kcal/mol} \quad BDE_{H_2} = 104 \text{ kcal/mol}$$

- H<sub>2</sub> evolution is spontaneous when  $\Delta G^{\circ}_{MH} < 56 \text{ kcal/mol}$  (see Ref. 60)
- H<sub>2</sub> evolution becomes increasingly favorable as  $\Delta G^{\circ}_{MH}$  decreases
- For a productive reaction, MHAT to alkenes must outcompete H<sub>2</sub> evolution

# Why would MHAT occur to form an unstabilized radical?



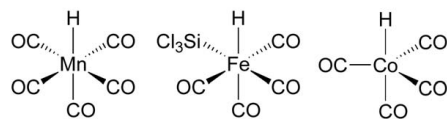
**Scheme 3** Top: use of O or F groups (indicated as Z) provides a strong Si-Z bond that drives uphill M-H formation. Bottom: potential mechanisms of metal-hydride formation.



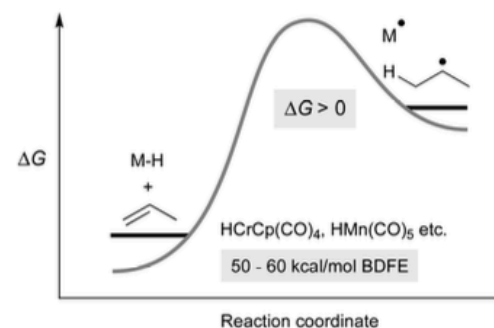
**Scheme 4** Potential mechanisms of metal-hydride formation.

## SF Systems

Isolable  
 Strong Field (SF) ligands  
 Low-spin electronic configurations  
 1+ and 2+ oxidation states  
 Stronger M-H bonds

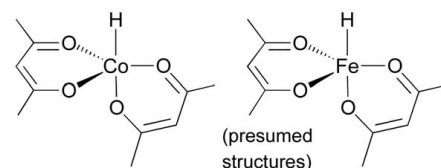


## Strong field (SF) MHAT

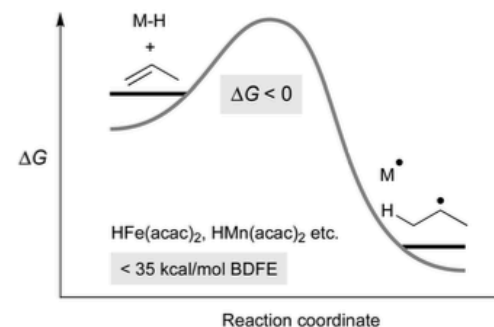


## WF Systems

Not isolable  
 Weak Field (WF) ligands  
 Intermediate- or high-spin configurations  
 3+ oxidation states  
 Weaker M-H bonds

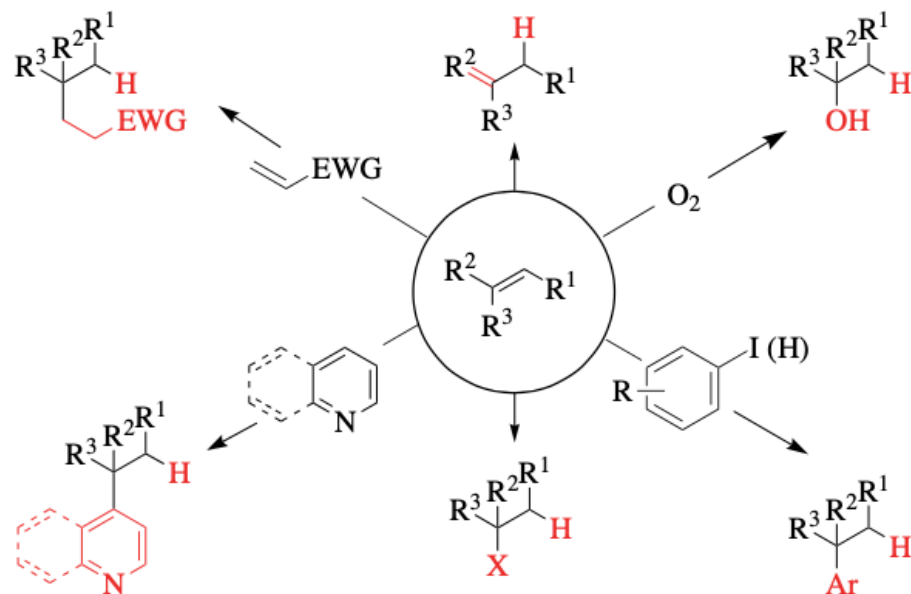


## Weak field (WF) MHAT



# Why do we care?

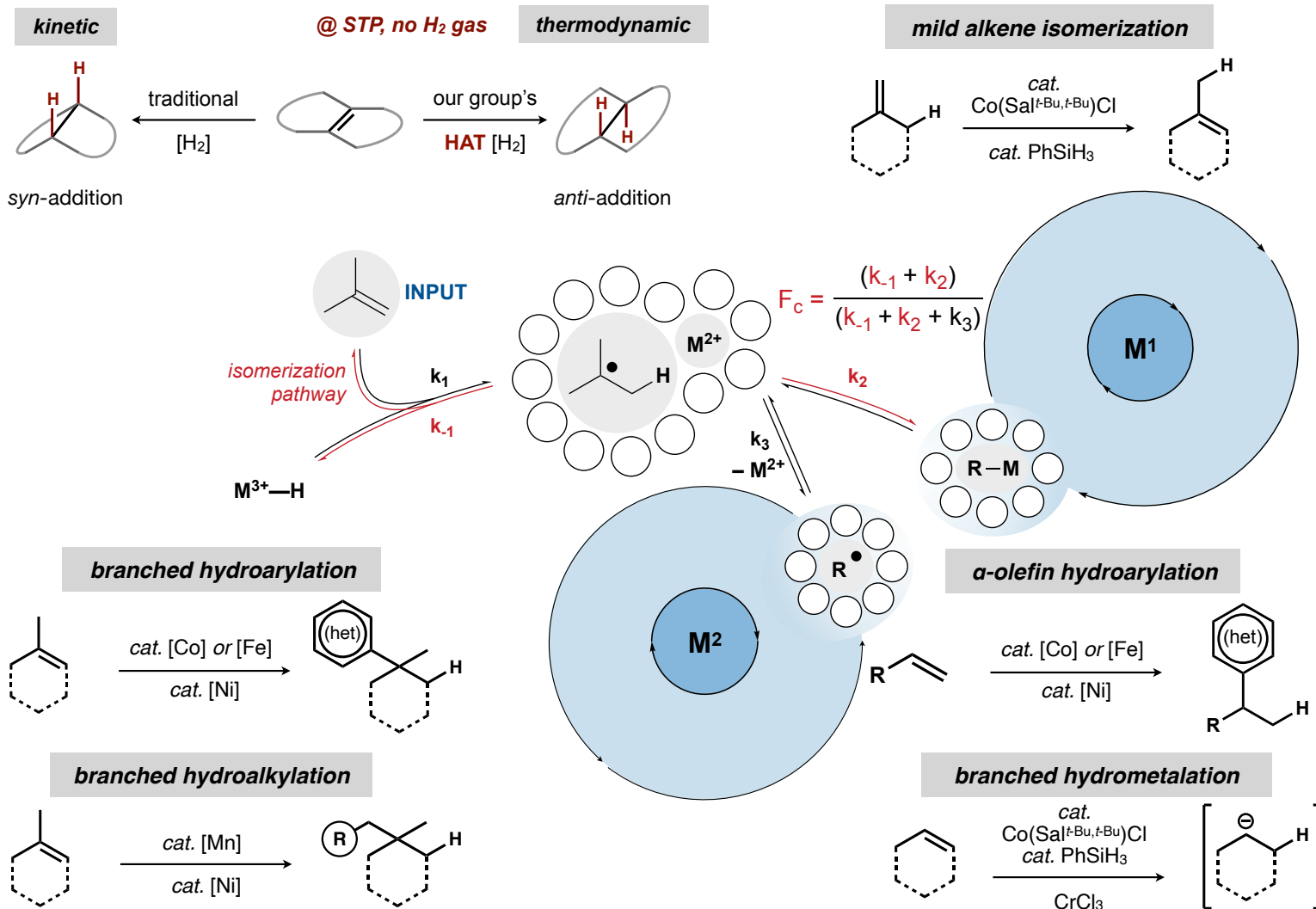
Markovnikov Functionalization by Hydrogen Atom Transfer" *Organic Reactions* **2019**, 100, 383. (already outdated)



**X** = H, F, Cl, Br, RO, RNH, N<sub>3</sub>, ON<sup>-</sup>,  
(H<sub>2</sub>NCO)HN, (Boc)HN(Boc)N,  
(BnO)N=CH, (BnO)N=C(CN), NC<sup>-</sup>,  
Me, TEMPO, NCS<sup>-</sup>

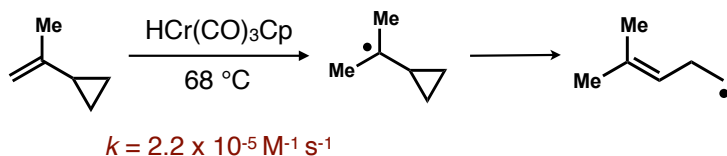
Direct generation of radical from alkene (!! ) and capture

# Why do we care?



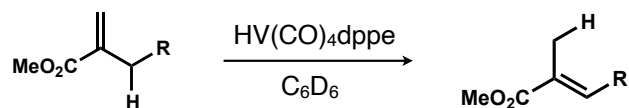
# Strong Field vs. Weak Field MHAT Similarities

Markovnikov selectivity/ radical



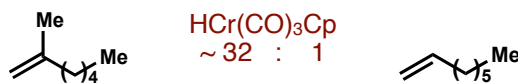
Bullock *et al.* *J. Am. Chem. Soc.* 1987, 109, 6544.

Reversible (in some cases)



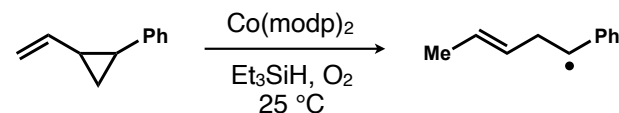
Norton *et al.* *J. Am. Chem. Soc.* 2008, 130, 4250.

Relative rates: radical stability, contrasteric



Norton *et al.* *J. Am. Chem. Soc.* 2007, 129, 234.

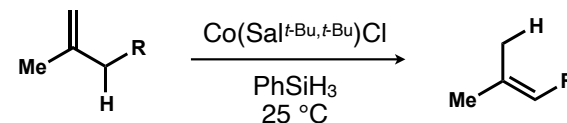
Markovnikov selectivity/ radical



Nojima *et al.* *Org. Lett.* 2002, 4, 3595.

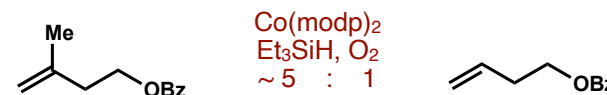
*estimate based on [Mn] hydrogenation: 60 M<sup>-1</sup>s<sup>-1</sup>*

Reversible (in some cases)



Crossley *et al.* *J. Am. Chem. Soc.* 2014, 136, 16788.

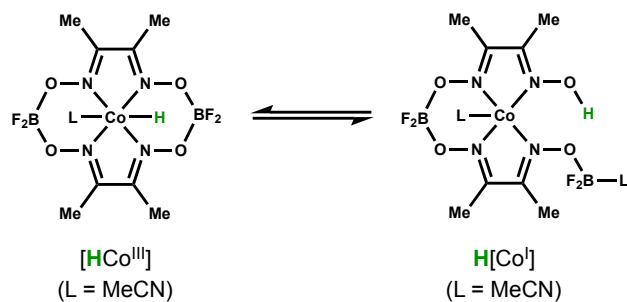
Relative rates: radical stability, contrasteric



Nojima *et al.* *J. Org. Chem.* 2005, 70, 251.

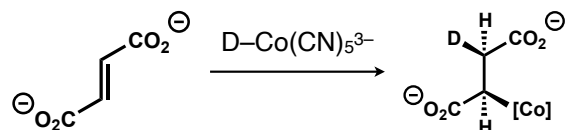
# Strong Field vs. Weak Field MHAT Similarities

## Metal-H vs. ligand-H



Norton *et al.* *J. Am. Chem. Soc.* 2014, 136, 17362

## Stereospecific collapse to organometallic

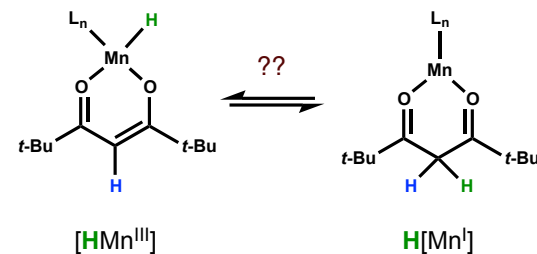


Jackman *et al.* *J. Am. Chem. Soc.* 1968, 90, 1914.

## Reductant

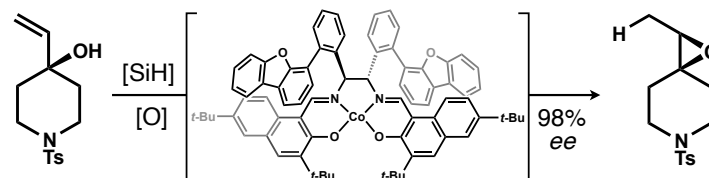
isolable M-H or H<sub>2</sub>

## No evidence of ligand-H transfer



Obradors *et al.* *J. Am. Chem. Soc.* 2016, 138, 4962.

## Only *sec*-alkyl-Co(Sa|*t*-Bu,*t*-Bu) [NMR]



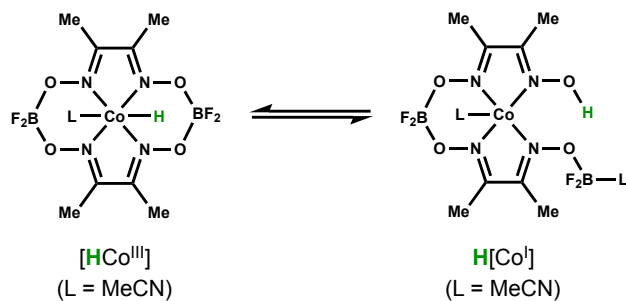
Pronin *et al.* *J. Am. Chem. Soc.* 2019, 141, 17527.

## Reductant

*i*-PrOH, NaBH<sub>4</sub>, NaBH<sub>3</sub>CN, PhSiH<sub>3</sub>, AIBN

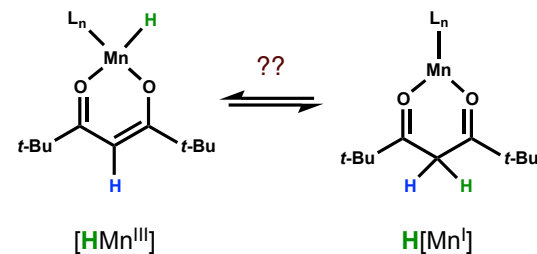
# Strong Field vs. Weak Field MHAT Similarities

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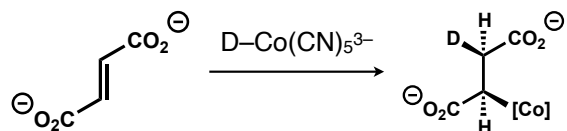
Norton *et al.* *J. Am. Chem. Soc.* 2014, 136, 17362

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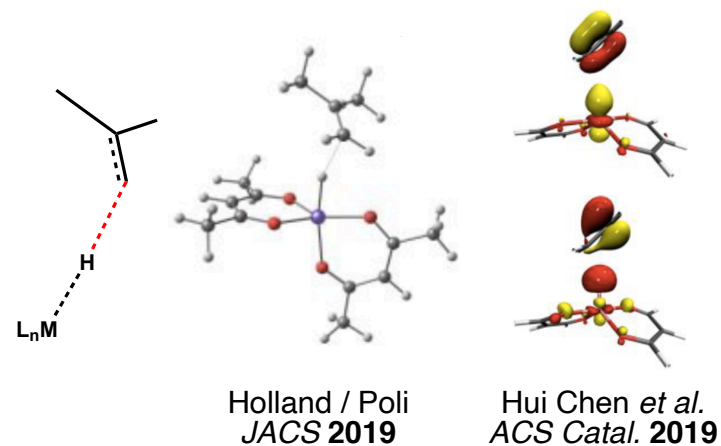


Jackman *et al.* *J. Am. Chem. Soc.* 1968, 90, 1914.

## Reductant

isolable M-H or H<sub>2</sub>

## Consistent with theory





# Summary

1. Definition and differentiation
2. Early work, hypotheses and development of understanding (Iguchi, Burnett, King/Winfield, Kwiatek, Jackman)
3. Halpern experiments: equilibrium outer-sphere exchange vs. 1,4-coordination
4. Inverse KIE
5. CIDNP
6. Relative rates
7. Cage pair implications: viscosity
8. Cage pair implications: stereoselectivity can be imperfect
9. Can HAT occur on non-conjugated alkenes? Bullock precedent; Drago-Mukaiyama reactions: elementary steps?
10. Crossley isomerization and AIBN use as hydride source (prior studies invoked organometallic as intermediate)
11. Implications of the generality of this rxn: Si-H, energetics, hydrogen evolution, Norton L-H
12. Examples of reactions/ differences