

## Open Shell:

Chemical species containing an unpaired valence electron. In the context of organic compounds this will describe radicals, but also includes transition metal complexes that have nonzero spin.

## What will be covered:

- Radical clocks, CW-EPR, Pulsed-EPR, CIDNP
- Key physical interactions that lead to observed phenomenon
- Examples in recent literature using these techniques and how they provided mechanistic information.

## What will not be covered:

- Methods useful for studying these species/reactions that are already broadly applied in other contexts (e.g. UV-Vis, KIEs, etc.)
- Detailed mechanisms for every reaction covered
- How to interpret spectra
- The gory details behind this math (you're welcome):

$$E(\tau, T) = \left( \frac{V_{decay}}{2} \right) \left[ \prod_{i=1}^N E_{\alpha}^i(\tau, T) + \prod_{j=1}^N E_{\beta}^j(\tau, T) \right]$$

$$t = t_0: \rho_{\sigma\sigma, \sigma\sigma}^E(t_0) = \rho_{\sigma\sigma, \sigma\sigma}^R(t_0) = \delta_{\sigma\sigma} \delta_{\sigma\sigma} \rho_{\sigma} Z_R^{-1}; \quad \rho_{\pm} = \rho_{\mp}$$

$$t = t_1: \rho_{\sigma\sigma, \sigma\sigma}^E(t_1) = (1 - \lambda) \rho_S Z_R^{-1}; \quad \rho_{\sigma\sigma, \sigma\sigma}^D(t_1) = \rho_{\sigma\sigma, \sigma\sigma}^E(t_1); \quad \rho_{\sigma\sigma, \sigma\sigma}^C(t_1) = \lambda \rho_S Z_R^{-1};$$

$$\rho_{Tn, Tn}^E(t_1) = \rho_T Z_R^{-1}$$

$$t = t_2: \rho_{\sigma\sigma, \sigma\sigma}^D(t_2) = Z_R^{-1} e^{-(t_2 - t_1)/\tau_S} \{ (1 - \lambda) \rho_{\sigma\sigma, \sigma\sigma}^E(t_1) + \lambda \rho_{\sigma\sigma, \sigma\sigma}^C(t_1) \}$$

$$\sum_{\sigma} \rho_{\sigma\sigma, \sigma\sigma}^{SD}(t_2) = Z_R^{-1} (1 - e^{-(t_2 - t_1)/\tau_S}) [ \rho_{\sigma\sigma, \sigma\sigma}^E(t_1) + \lambda \rho_{\sigma\sigma, \sigma\sigma}^C(t_1) ]$$

$$\hat{H}_{dipolar} = -g\beta g_N \beta_N \left\{ \left[ \frac{r^2 - 3x^2}{r^5} \right] \hat{S}_x \hat{I}_x + \left[ \frac{r^2 - 3y^2}{r^5} \right] \hat{S}_y \hat{I}_y + \left[ \frac{r^2 - 3z^2}{r^5} \right] \hat{S}_z \hat{I}_z - \left[ \frac{3xy}{r^5} \right] (\hat{S}_x \hat{I}_y + \hat{S}_y \hat{I}_x) - \left[ \frac{3xz}{r^5} \right] (\hat{S}_x \hat{I}_z + \hat{S}_z \hat{I}_x) - \left[ \frac{3yz}{r^5} \right] (\hat{S}_y \hat{I}_z + \hat{S}_z \hat{I}_y) \right\}$$

where

$$\delta_n = 1/2(\omega_1 - \omega_n)$$

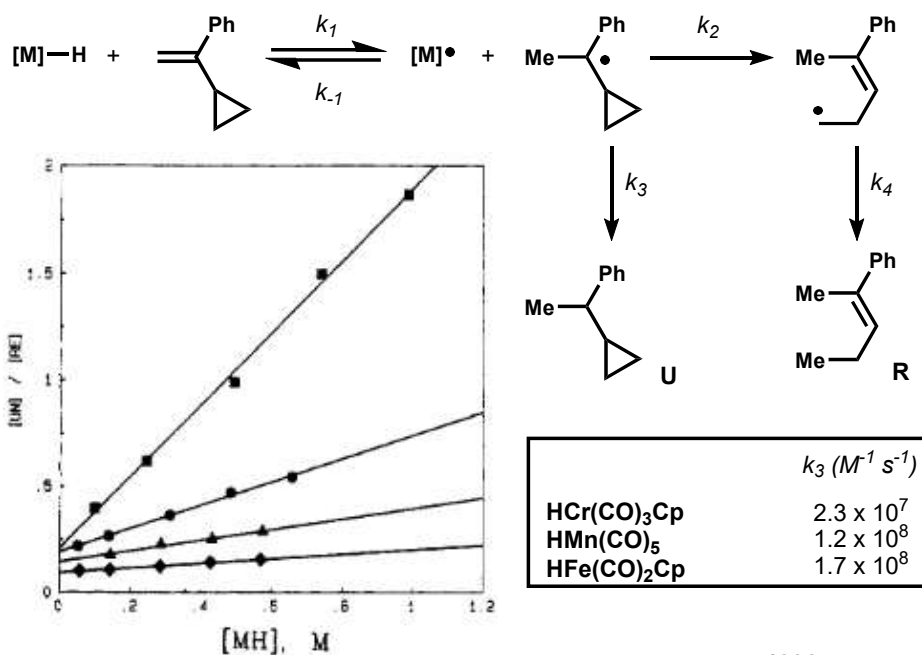
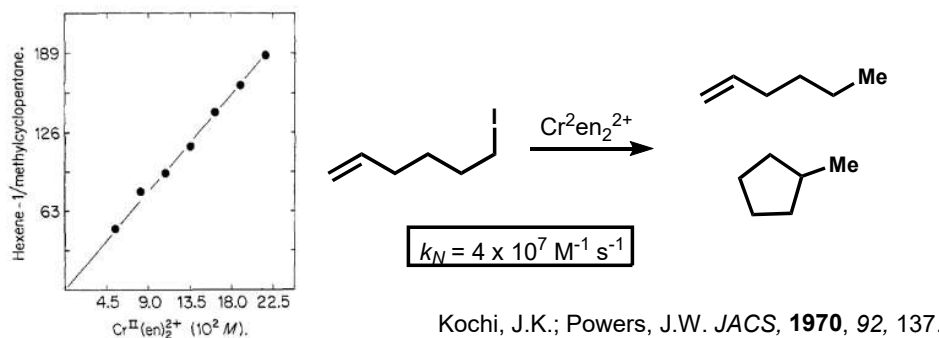
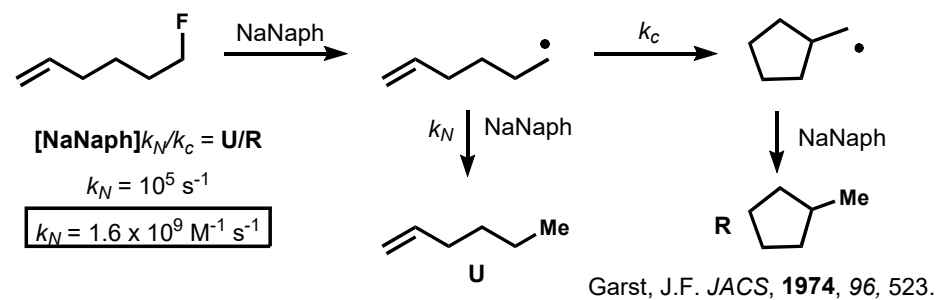
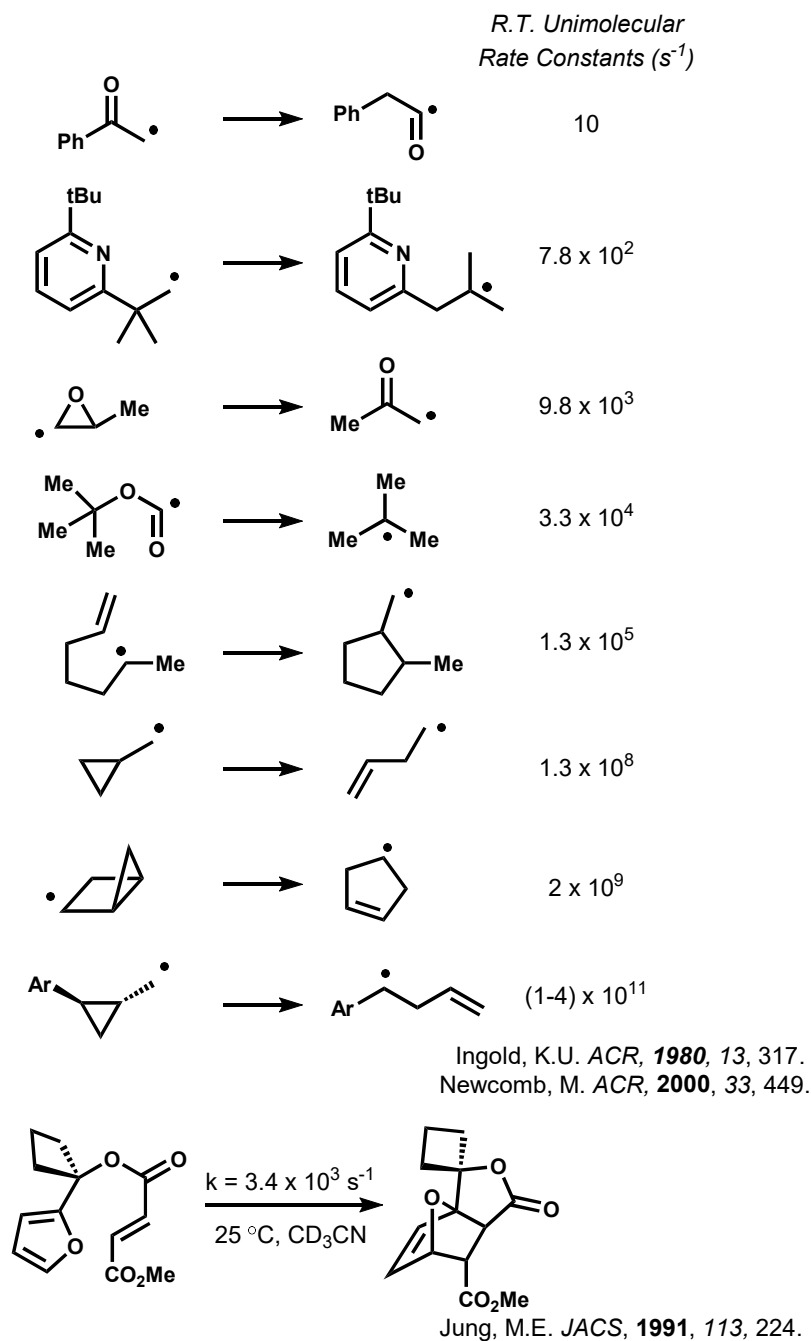
$$= \text{singlet-triplet splitting}$$

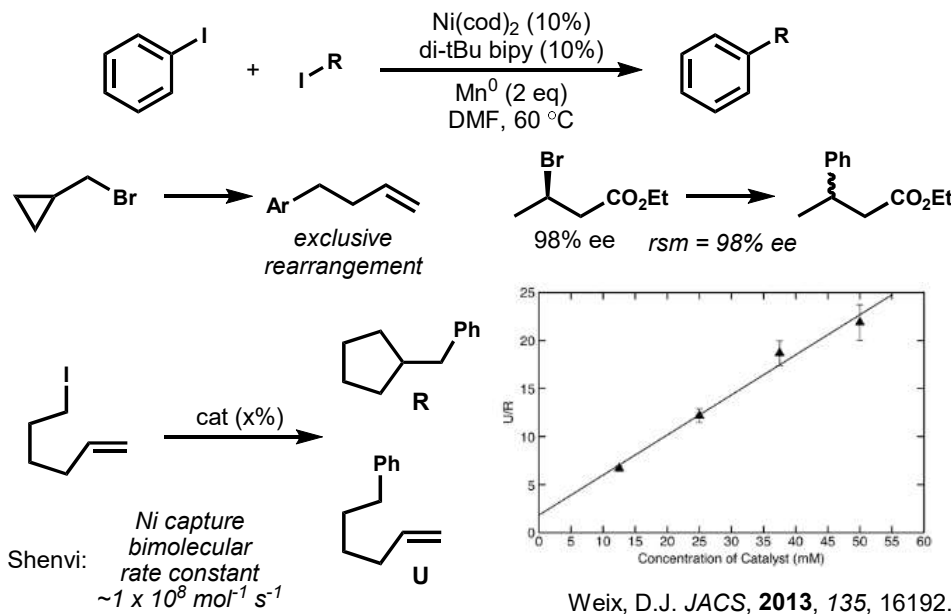
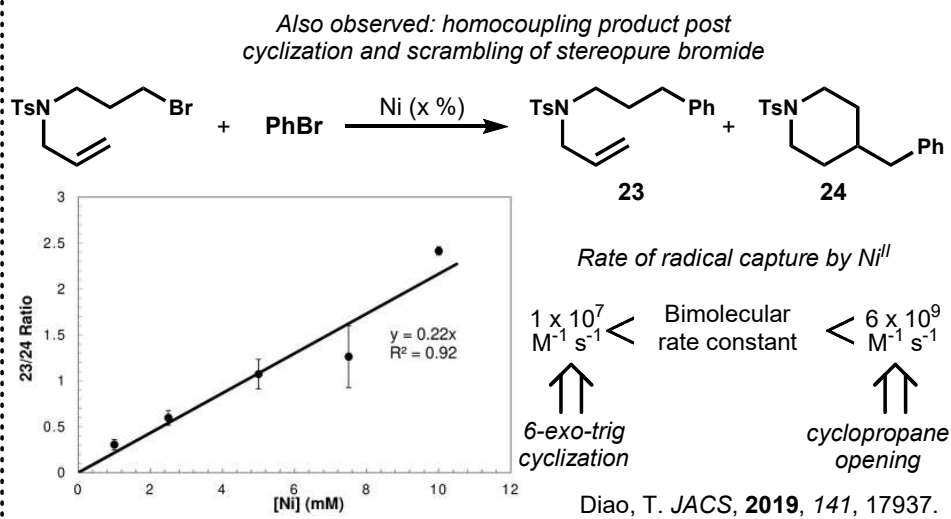
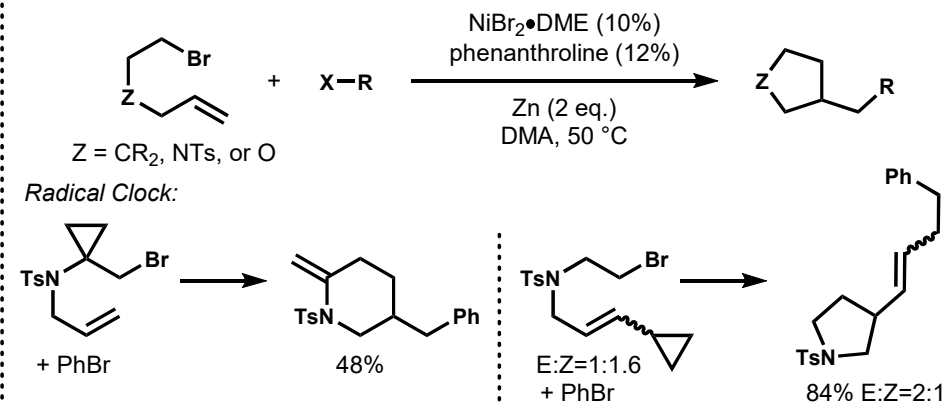
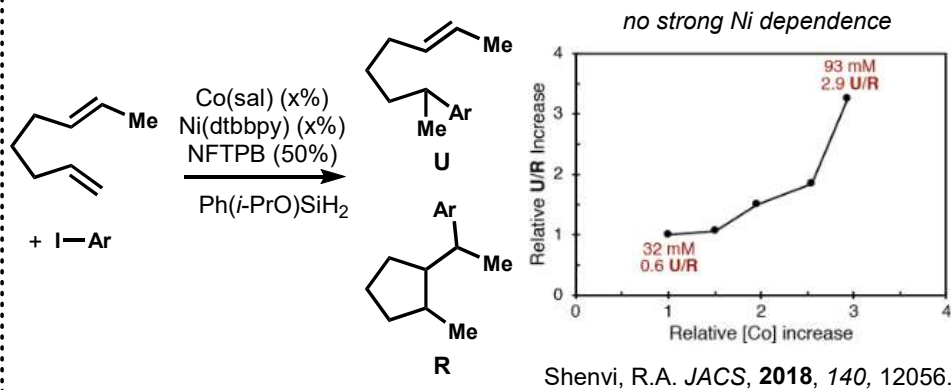
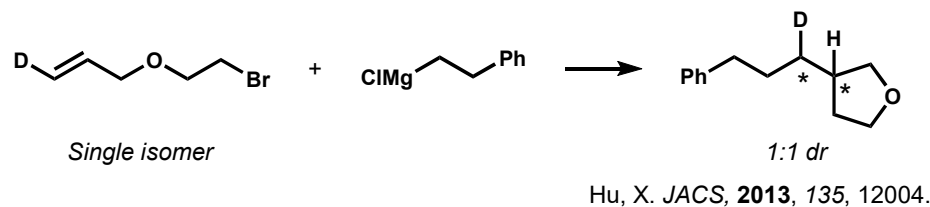
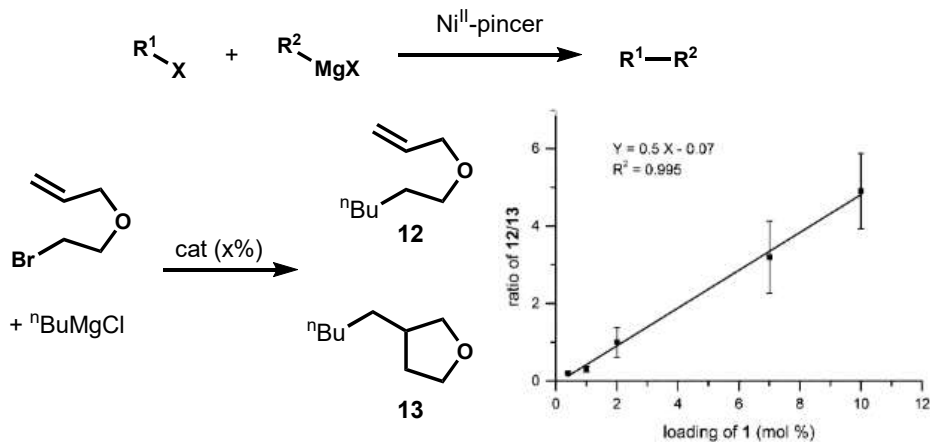
$$t = t_3: \phi_n^C = Z_R \rho_{\sigma\sigma, \sigma\sigma}^C(\infty) = \lambda \rho_S [1 + (1 - \lambda) e^{-(t_2 - t_1)/\tau_S}] + \lambda e^{-t_2/\tau_S}$$

$$\hat{H}_{dipolar} = - (g\beta g_N \beta_N) [ \hat{S}_x \hat{S}_y \hat{S}_z ] \begin{bmatrix} \left\langle \frac{r^2 - 3x^2}{r^5} \right\rangle & \left\langle \frac{-3xy}{r^5} \right\rangle & \left\langle \frac{-3xz}{r^5} \right\rangle \\ \left\langle \frac{-3xy}{r^5} \right\rangle & \left\langle \frac{r^2 - 3y^2}{r^5} \right\rangle & \left\langle \frac{-3yz}{r^5} \right\rangle \\ \left\langle \frac{-3xz}{r^5} \right\rangle & \left\langle \frac{-3yz}{r^5} \right\rangle & \left\langle \frac{r^2 - 3z^2}{r^5} \right\rangle \end{bmatrix} \begin{bmatrix} \hat{I}_x \\ \hat{I}_y \\ \hat{I}_z \end{bmatrix}$$

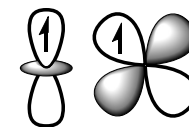
and the normalization condition from equation (11) requires that

$$\phi_n^S = Z_R \sum_{\sigma} \rho_{\sigma\sigma, \sigma\sigma}^{SD}(\infty) = 1 - \phi_n^C = 1 - \lambda \rho_S [1 + (1 - \lambda) e^{-(t_2 - t_1)/\tau_S}] - \lambda e^{-(t_2 - t_1)/\tau_S} [ \rho_T - (1 - \lambda) \rho_S ] \sin^2 \delta_n(t_2 - t_1)$$





$$\hat{H} = \frac{\beta_e \vec{B}_0 g \mathbf{S}}{h} + \tilde{S} \mathbf{D} \mathbf{S} + \sum_k \left( \tilde{S} \mathbf{A}_k \mathbf{I}_k - \frac{\beta_n g_{n,k} \vec{B}_0 \mathbf{I}_k}{h} \right) + \sum_{k, I_k > 1/2} \tilde{I}_k \mathbf{P}_k \mathbf{I}_k$$

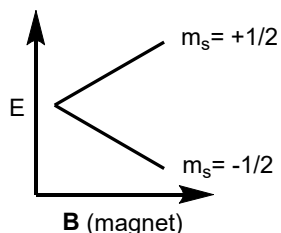


Energy = **Electronic Zeeman** + **Zero Field Splitting** + **Hyperfine Coupling** + **Nuclear Zeeman** + **Nuclear Quadrupole Interactions**

The electron equivalent of what causes NMR

In a magnetic field  $\mathbf{B}$ , the electron spin quantum number  $m_s$  will energetically split in proportion to the g-factor. Transitions between these energy levels in the microwave spectrum give the EPR signal.

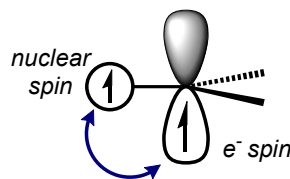
Key Parameter: **g**, analogous to  $\delta$ ,



Electron-Proton coupling akin to proton-proton J-coupling in NMR

Similar to how protons will couple each other in NMR, any nuclear spins in close proximity to an unpaired electron spin will engage in so-called **hyperfine coupling**.

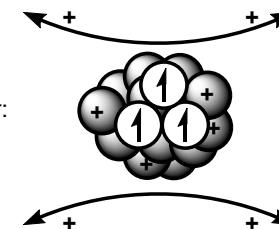
Key Parameter: **A**, analogous to J,



Higher order interactions for high spin nuclei

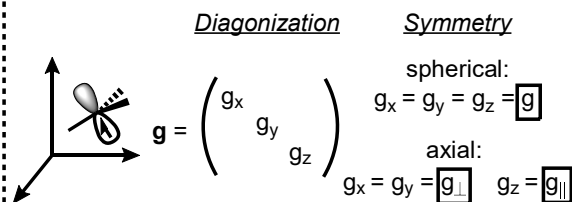
Nuclei with spin  $\geq 1$  (e.g.  $^2\text{D}$ ,  $^{14}\text{N}$ , ) have distorted nuclei that generate electric quadrupoles which can couple with spins.

Key Parameter: **Q** or  $\mathbf{P}_k$



What's with those bolded g's, D's, A's, etc.?

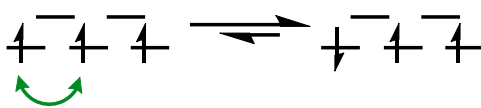
Many of the key parameters are actually second order tensors (tensor:vector is like vector:scalar). This complexity contains info on **geometry** and **distances**, and depends on molecular **symmetry**.



Background electronic interactions

Multiple unpaired electrons (e.g. in high spin transition metals) will engage in dipole and spin-orbit coupling. Additional couplings also manifest in weakly coupled spins (i.e. biradicals)

Key Parameter: **D**



Exactly what you know from NMR, but inside an EPR magnet

Much lower energy transitions than with  $e^-$  Zeeman effect, so mostly occupy the background akin to vibrational transitions in a condensed phase UV-Vis spectra. Come into play in more advanced EPR experiments (**ENDOR, ESEEM, HYSCORE**)

## Instrumentation:



Images from [www.Bruker.com](http://www.Bruker.com)  
accessed 03/14/2020

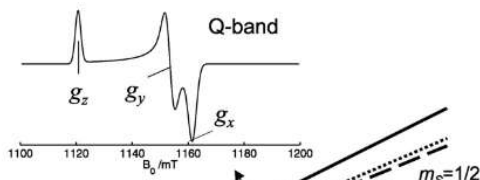


Band:	X-Band	Q-Band	W-Band	.....	<sup>1</sup> H NMR
Frequency:	10 GHz	35 GHz	95 GHz	.....	400 MHz
Field:	0.33 T	1.25 T	3.5 T	.....	9.4 T
	} standard electromagnet		} superconducting electromagnet		

for  
reference:

## Sample Prep:

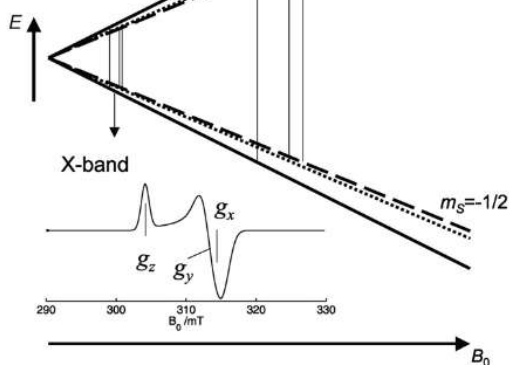
Samples usually frozen to form glasses (liquid nitrogen @ 77K or colder). Solid state means dipolar couplings and anisotropy observable



## Experiments:

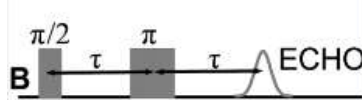
### Continuous Wave (CW-EPR):

Constant irradiation with microwave radiation. Magnetic field is varied, and the **change** in absorbance w/ respect to field is recorded (1st derivative spectrum).



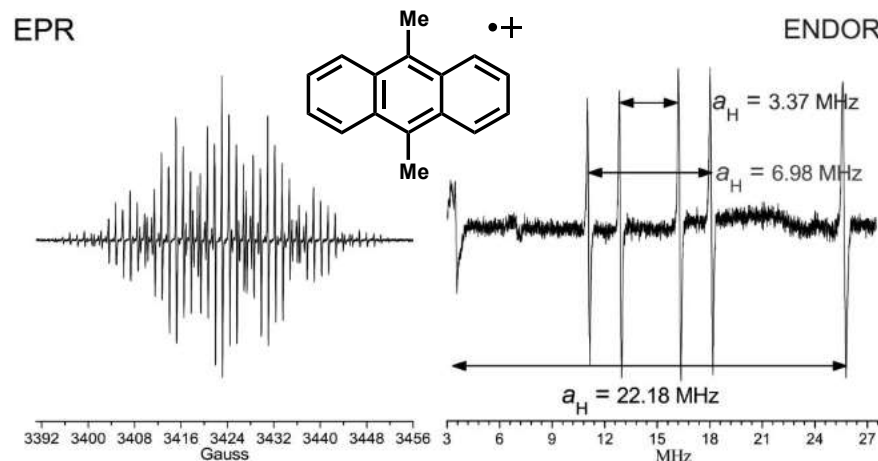
### Pulsed-EPR:

Observation of **spin echo** intensity vs. field. Requires freezing to increase relaxation time.



## Electron Nuclear DOuble Resonance (ENDOR):

Stimulate a single EPR transition (fixed wavelength, fixed magnetic field), and then sweep a second radiofrequency radiation and observe changes in EPR signal. Gives **nuclear** transitions coupled to the spin.



Murphy, D.M. *Chem. Soc. Rev.* **2006**, 35, 249.

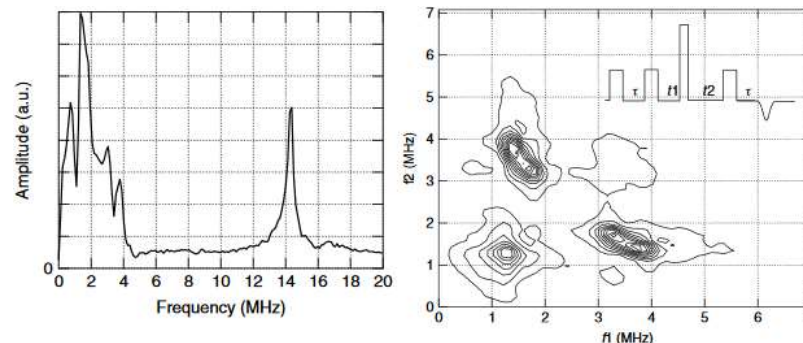
## Electron Spin Echo Envelope Modulation (ESEEM):

Similar info to ENDOR, but better for weakly coupled spins. Pulsed method that observes the change in the spin echo intensity with varying delays.

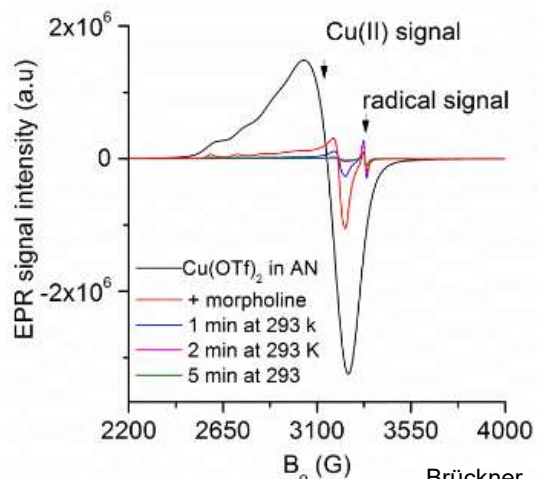
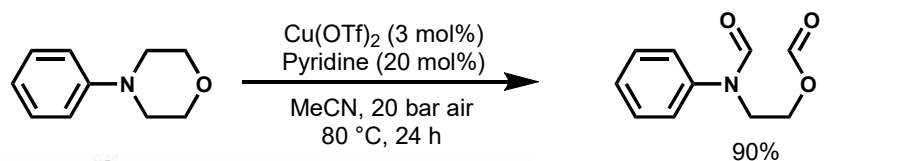
## HYperfine Sublevel CORrelation spectroscopy (HYSCORE):

2-D analogue of ESEEM experiments. Good for assigning complex resonances to single nuclei for determining hyperfine couplings

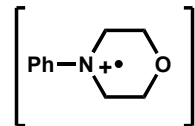
### ESEEM and HYSCORE of protein Cu(II) site w/ 2 nonequivalent N<sup>14</sup> His ligands



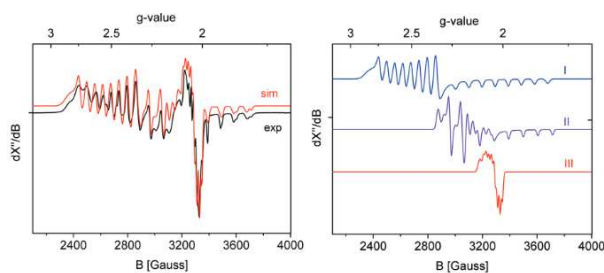
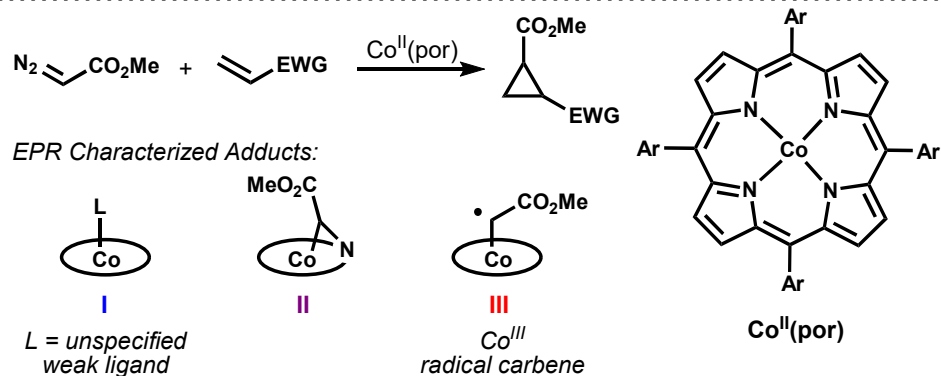
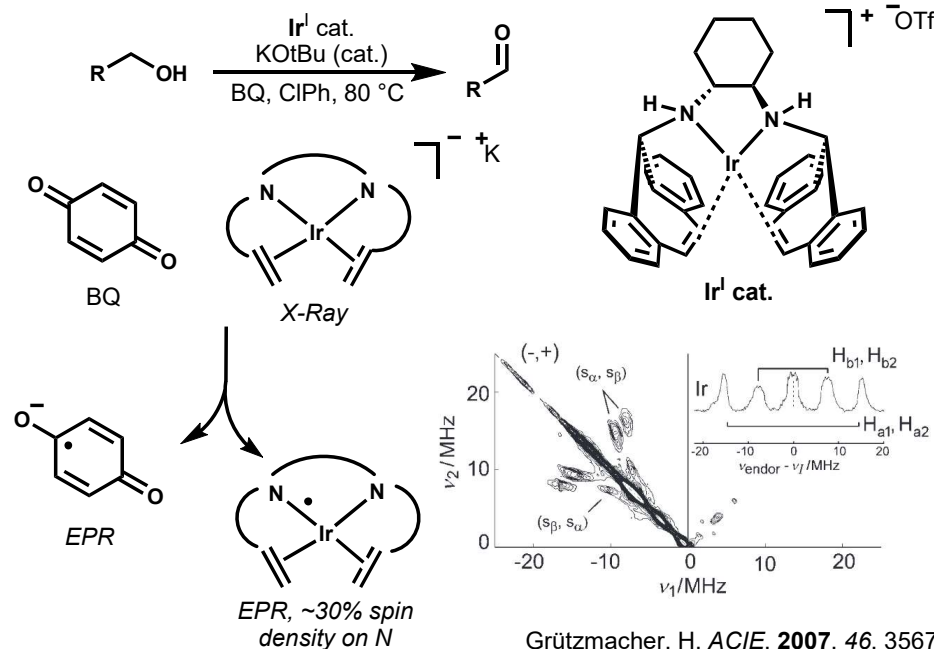
McCracken, J. "Electron Spin Echo Envelope Modulation (ESEEM) Spectroscopy" *Encyclopedia of Inorganic and Bioinorganic Chemistry*, **2011**.



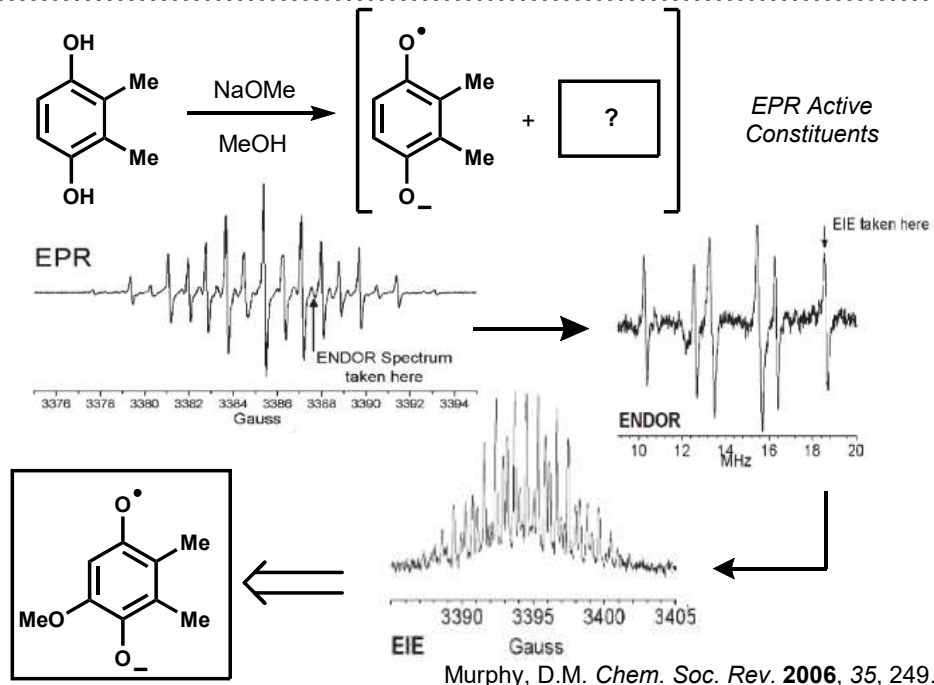
Addition of substrate to  $\text{Cu(OTf)}_2$  in MeCN resulted in rapid reduction of  $\text{Cu(II)}$  to  $\text{Cu(I)}$  characterized by EPR (left) and UV-Vis (not shown), along with generation of a  $g=2.004$  signal consistent with the proposed organic radical.

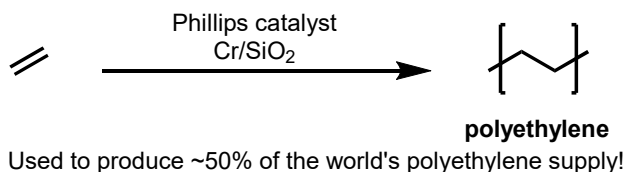


Brückner, A; Beller, M. *ACIE*, **2019**, *58*, 10693.

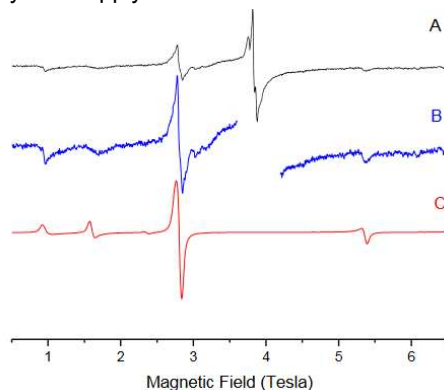
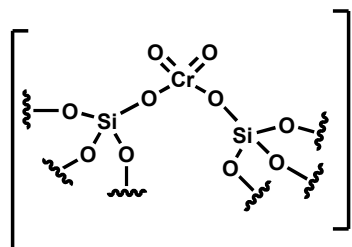


de Bruin, B. *JACS*, **2010**, *132*, 10891.

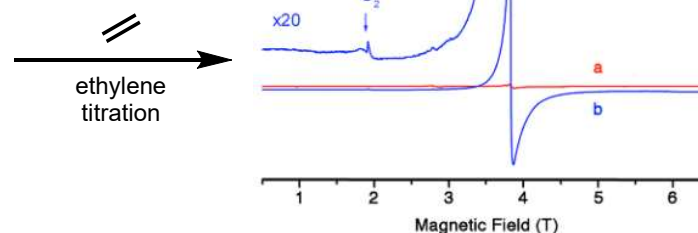




- The Problem: Integer spin oxidation states ("non-Kramers" e.g. high-spin  $\text{Cr}^{\text{II}}$ ,  $\text{Mn}^{\text{III}}$ , and  $\text{V}^{\text{III}}$ ) have high **zero-field splitting** and are rendered "EPR Silent" at traditional X and Q-bands.
- The Solution: Take EPR measurements at high fields strengths (**W-band, ~3.5 T**)



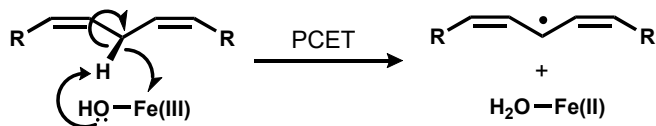
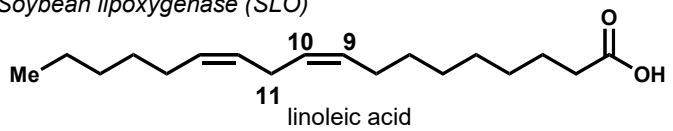
$\text{Cr}^{\text{IV}}$ ,  $\text{Cr}^{\text{III}}$ , and  $\text{Cr}^{\text{II}}$   
 $S = 1/2, 3/2, \text{ and } 2$  (Large ZFS)



**Organo- $\text{Cr}^{\text{III}}$**

Stigman, A. E.; Scott, S. L. *ACS Catal.* **2015**, 5, 5574.

Soybean lipoxygenase (SLO)



Temperature independent KIE ~80  $\implies$  Quantum tunneling

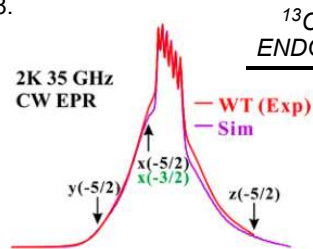
Klinman, J.P. *Biochemistry*, **1999**, 38, 12218.

$\text{Fe}^{\text{III}}$  has rapid  $e^-$ -spin relaxation

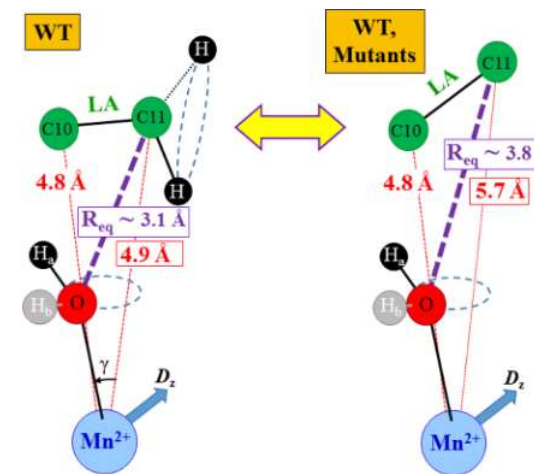
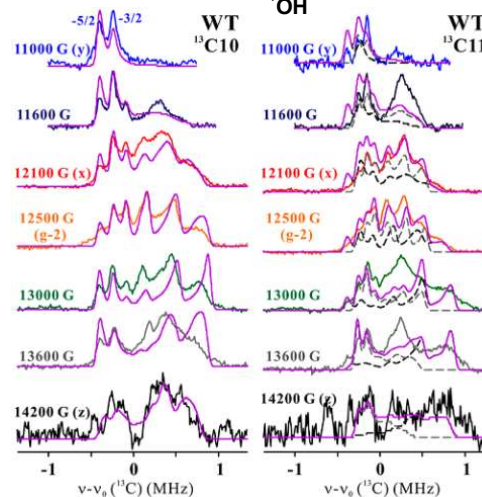
Substitution

$\text{Mn}^{\text{II}}$  used as a spin probe

EPR

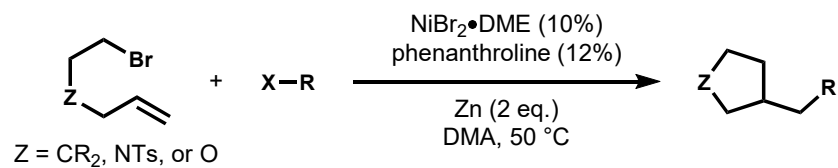


$^{13}\text{C}$   
ENDOR



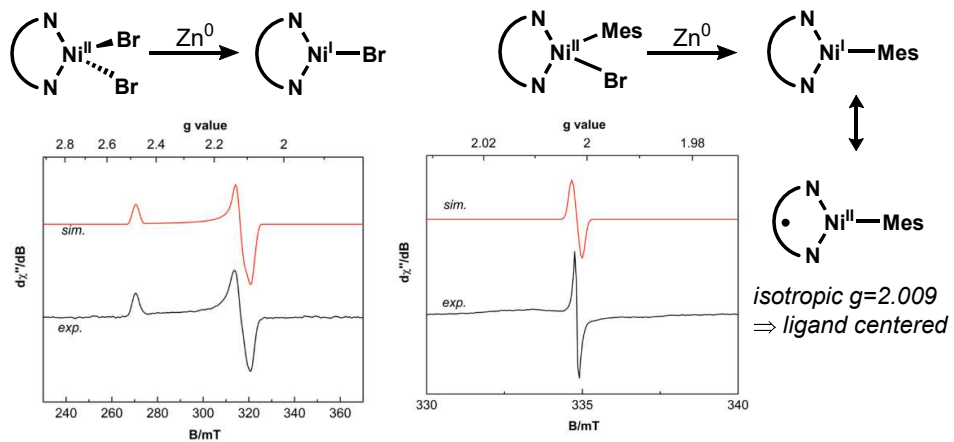
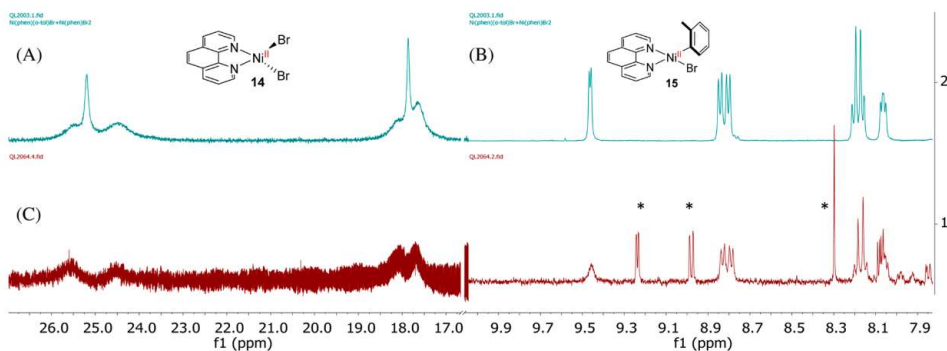
MD  $\implies$  Calculated bond lengths/angles

Klinman, J. P.; Hoffman, B. M. *JACS*, **2017**, 139, 1984.



**Freeze quench of reaction mixture = EPR Silent (X-Band)**

NMR to the rescue:



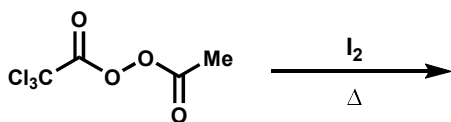


**Chemically Induced Dynamic Nuclear Polarization (CIDNP):**

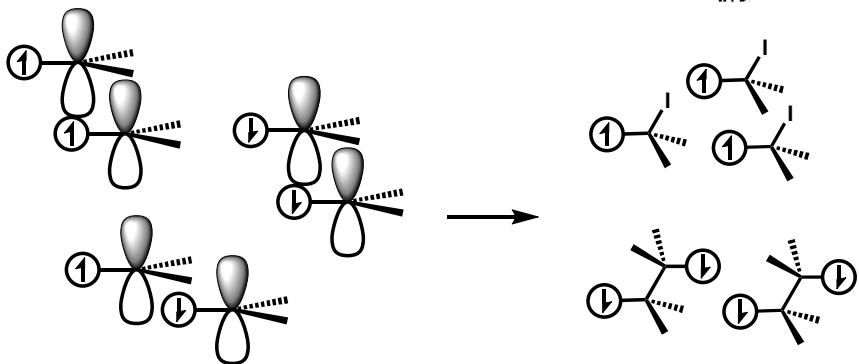
- Discovered independently in 1967 by Bargon and Fischer; Ward and Lawler
- CIDNP is a misnomer: dynamic nuclear polarization is not actually relevant
- The correct explanation of the phenomenon (Closs; Kaptein and Oosterhoff) has been **radical pair mechanisms**, for which CIDNP has become a probe.

**The Phenomenon:**

NMR of a reaction *in progress* shows unusual signal *intensities* in the product. The phenomenon is known exclusively in reactions that proceed via **radical intermediates**



**The Explanation: Radical Pairs and Nuclear Spin Sorting**

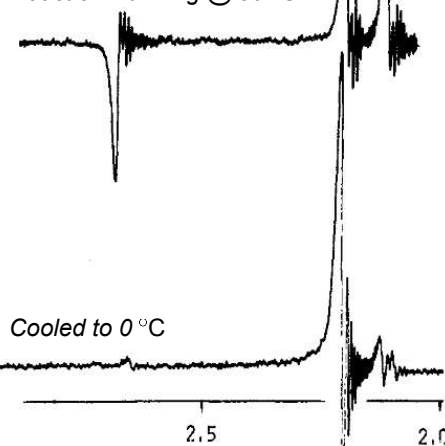


Boltzmann equilibrium of nuclear spins

Non-equilibrium in products: Large nuclear polarizations

"...such effects will arise if the **yield** of product is greater for some spin states of the nuclei than others; that is, if the **rate of formation of product depends on the nuclear spin states of the molecules undergoing reaction.**" -Lawler

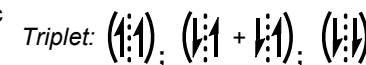
Reaction Running @ 50 °C



$$\text{Energy} = \boxed{\text{Electronic Zeeman}} + \boxed{\text{Hyperfine Coupling}} + \boxed{\text{Nuclear Zeeman}} + \boxed{e^-e^- \text{ Exchange Coupling}}$$

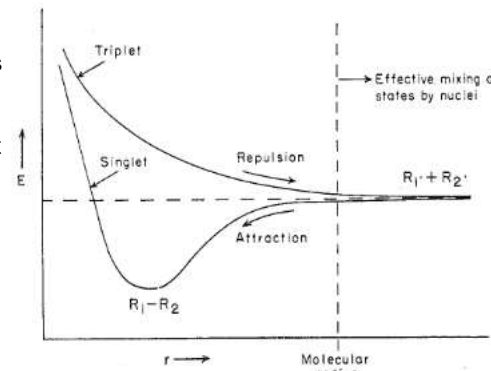
Weak coupling of distinct electron spins

Radical pairs will have a separate energetic term describing their mutual interaction, leading to energy differences between the singlet and triplet states.



**Spin Evolution:**

"In general, the pure spin states are not eigenfunctions of the Hamiltonian... and will consequently undergo coherent evolution in time." -Steiner

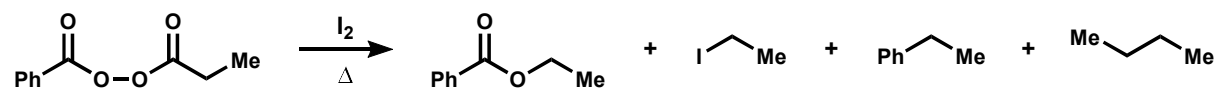


The spin evolution will be impacted by the differences in **g**-factors and hyperfine couplings **A** to nearby nuclei. Thus the probability of accessing a triplet state from a singlet and vice versa depends on the spin of nearby nuclei.

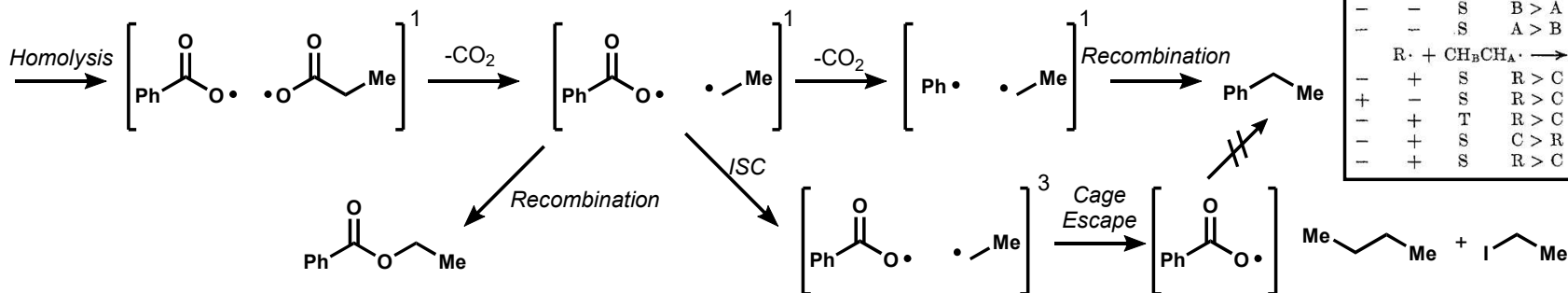
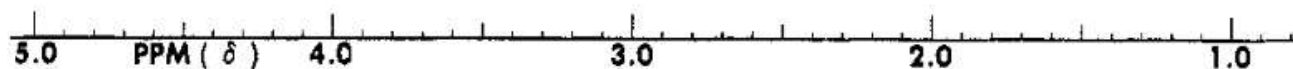
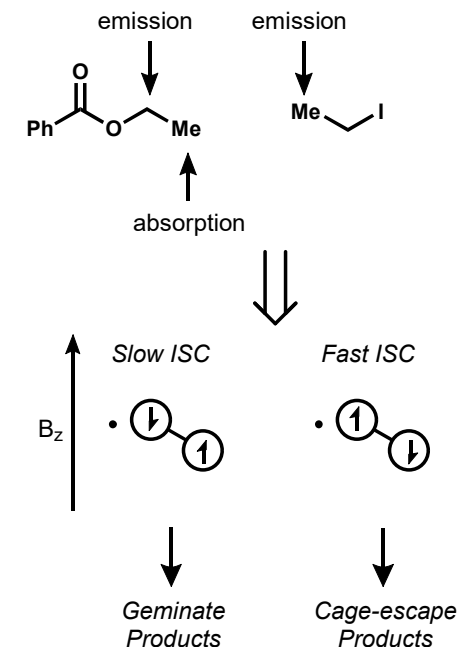
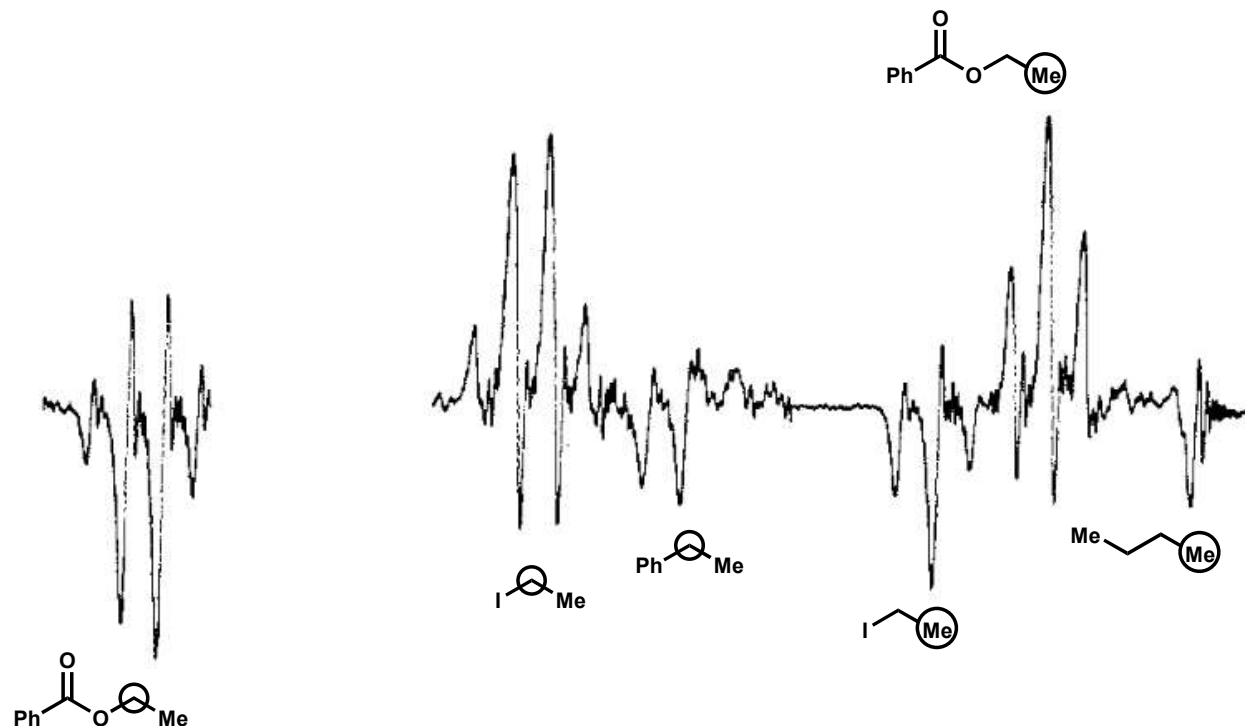
**Chemically Induced Dynamic Electron Polarization (CIDEP):**

- A sister phenomenon is known in EPR spectroscopy driven by the same processes.
- Due to very rapid relaxation times in EPR, observation is typically restricted to photochemical systems.

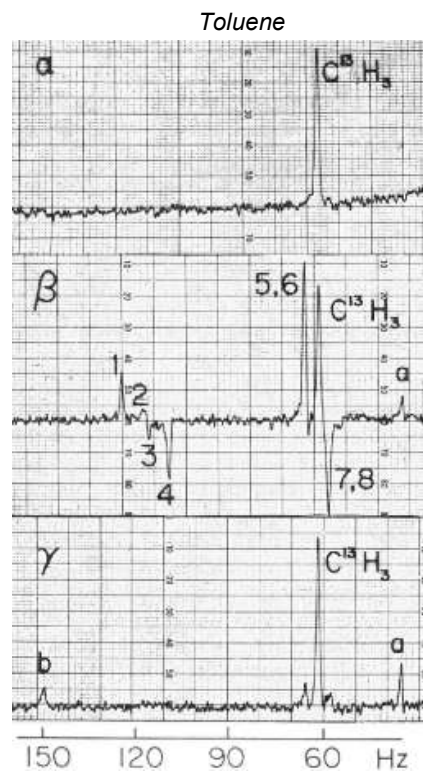
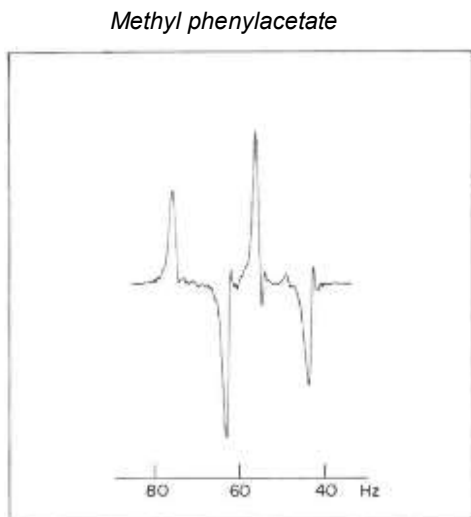
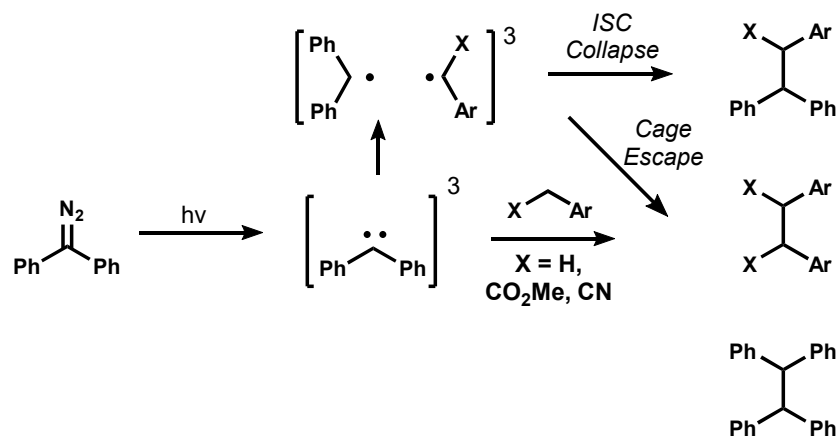
Buckley, C. D. *Molecular Physics*, **1985**, 54, 1.



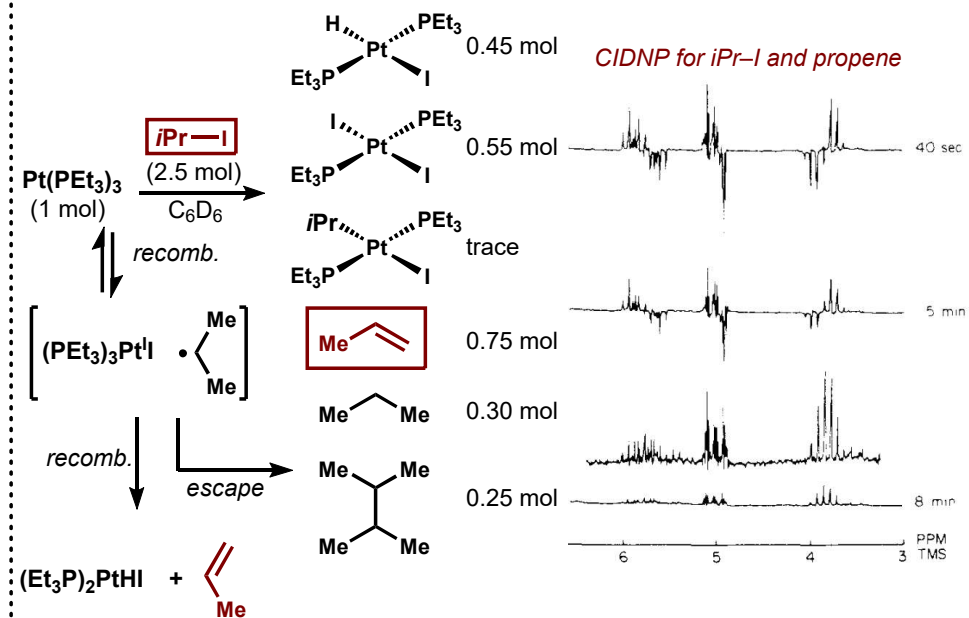
The parity of **A** is different for the  $\alpha$  and  $\beta$  protons



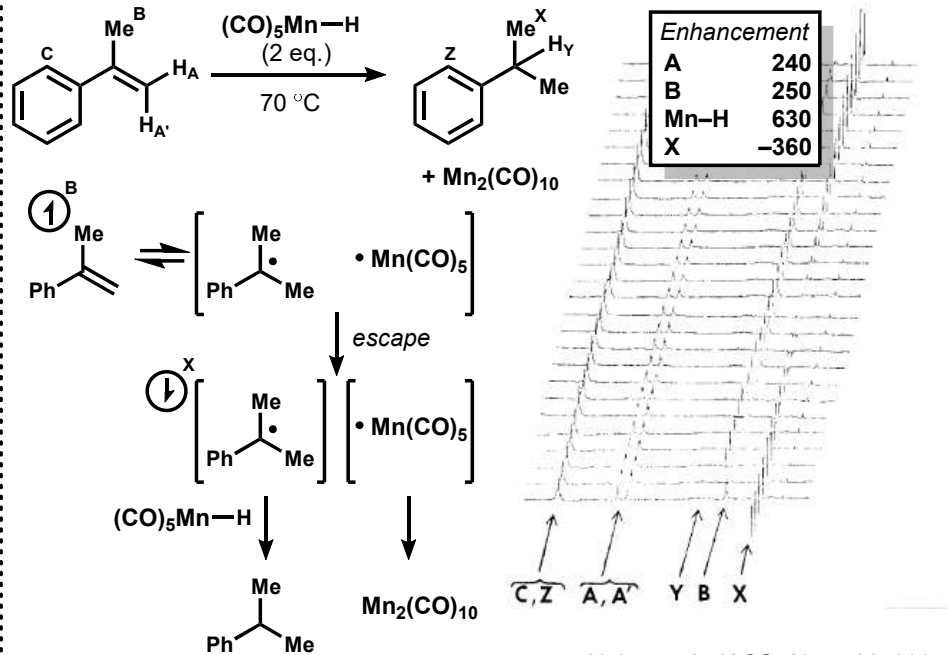
$\alpha_A$	$\alpha_B$	Birth	$\sigma$	$J_{AB}$	$H_A$	$H_B$
HA + $\cdot$ BH $\rightarrow$ HABH						
-	-	S	A > B	+	A, EA	E, EA
-	+	S	A > B	+	A, AE	A, AE
-	-	T	A > B	+	E, AE	A, AE
-	-	S	B > A	+	E, EA	A, EA
-	-	S	A > B	-	A, AE	E, AE
R $\cdot$ + CH <sub>B</sub> CH <sub>A</sub> $\cdot$ $\rightarrow$ RCH <sub>A</sub> CH <sub>B</sub>						
-	+	S	R > C	+	E, EA	A, EA
+	-	S	R > C	+	A, EA	E, EA
-	+	T	R > C	+	A, AE	E, AE
-	+	S	C > R	+	A, EA	E, EA
-	+	S	R > C	-	E, AE	A, AE



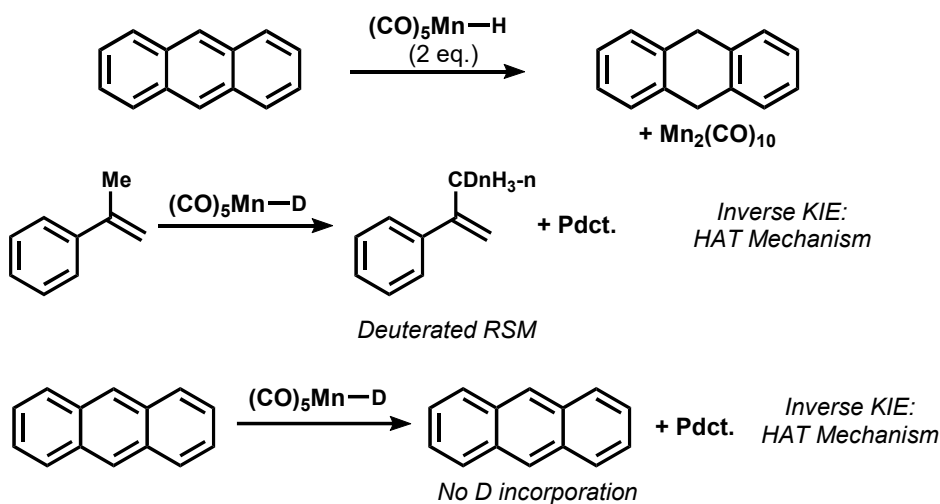
Closs, G.L. *JACS*, **1969**, *91*, 4549.



Osborn, J.A. *JACS*, **1974**, *96*, 7832.

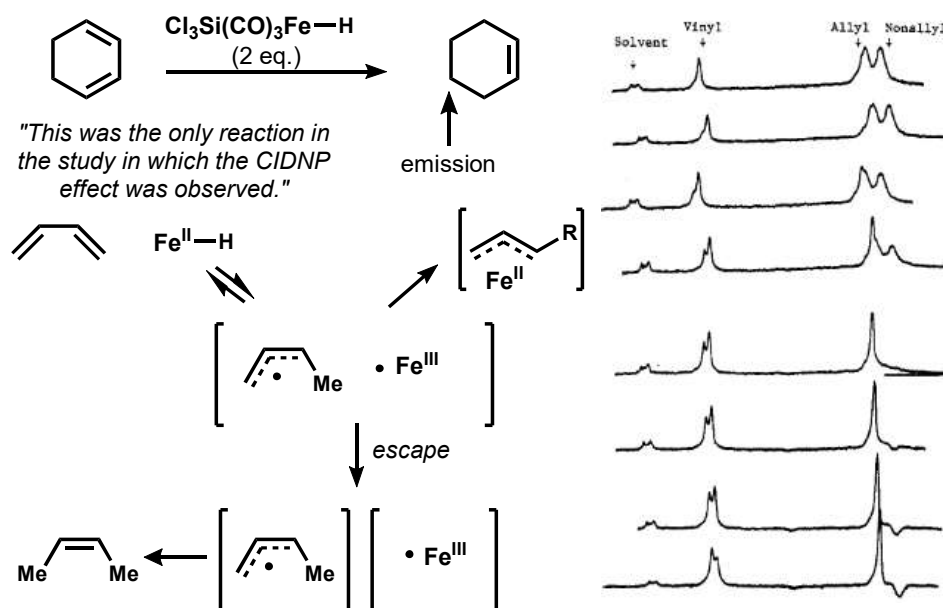


Halpern, J. *JACS*, **1977**, *99*, 8335.

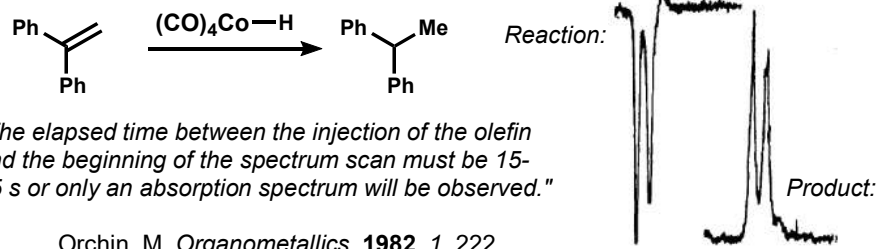


Even with radical pair mechanism, need to have cage escape AND recombination possibilities to get spin sorting and CIDNP.

Halpern, J. J. *Organomet. Chem.* **1981**, 213, 487.

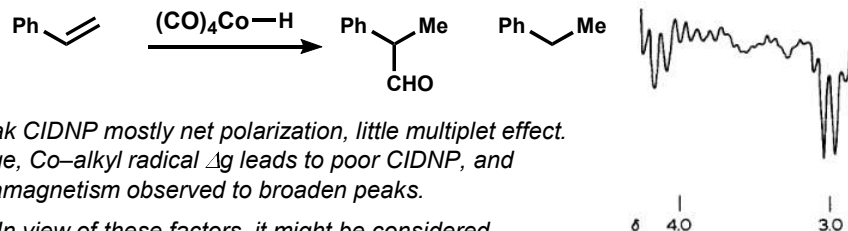


Connolly, J.W. *Organometallics*, **1984**, 3, 1333.



"The elapsed time between the injection of the olefin and the beginning of the spectrum scan must be 15-25 s or only an absorption spectrum will be observed."

Orchin, M. *Organometallics*, **1982**, 1, 222.



Weak CIDNP mostly net polarization, little multiplet effect. Large, Co-alkyl radical  $\Delta g$  leads to poor CIDNP, and paramagnetism observed to broaden peaks.

"In view of these factors, it might be considered remarkable that any CIDNP can be detected from  $\text{HCo}(\text{CO})_4$ -styrene reactions."

Garst, J. F.; Ungvary, F. J. *Organomet. Chem.* **1985**, 279, 165.