

The Power of Ligand Design in Homogeneous Catalysis: Spotlight on N-heterocyclic Carbenes and Related Ligands

University of Trieste

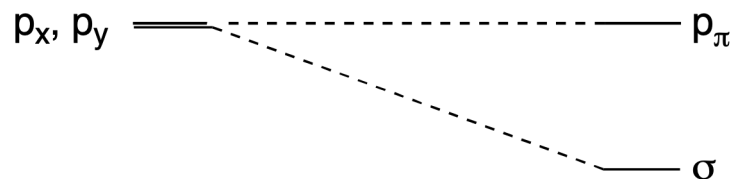
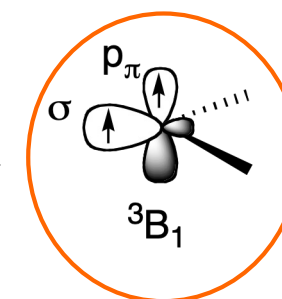
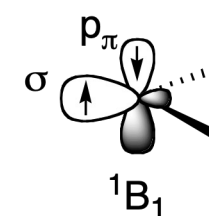
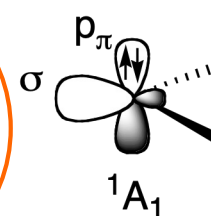
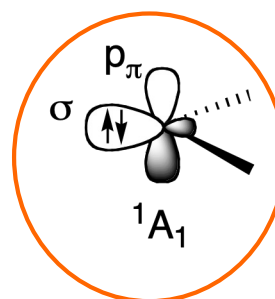
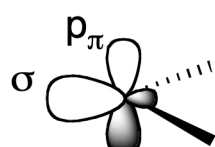
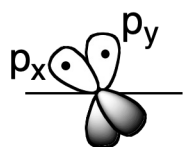
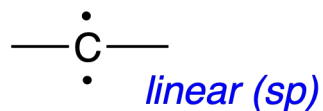
May 2026

Martin Albrecht



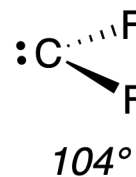
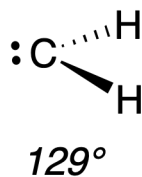
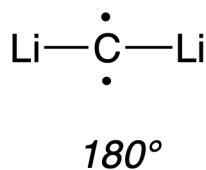
Carbenes: disubstituted C with 6 valence e⁻

geometrical considerations

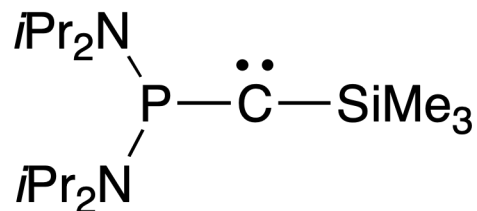


π donor substituents raise p_π (stability)

examples

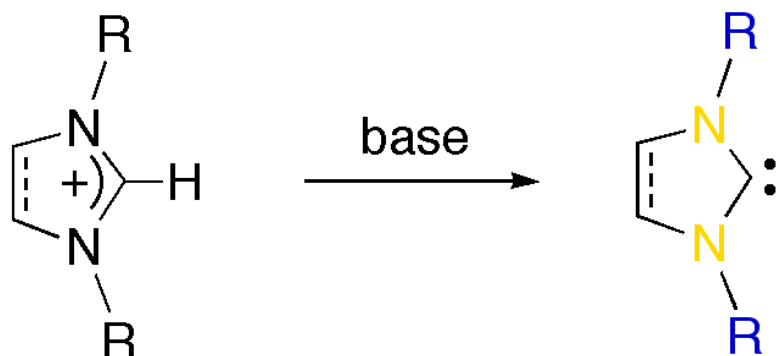


First bulk-stable (*N*-heterocyclic) carbenes



Bertrand, *JACS* **1988**, *110*, 6463

Trick 1 : extensive
 π -donor stabilization



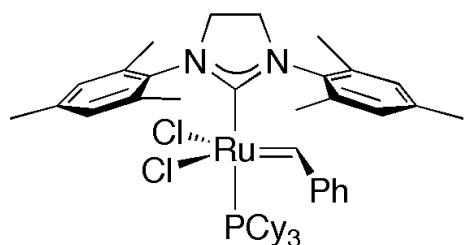
Arduengo, *JACS* **1991**, *113*, 361

Trick 2 : very bulky
substituents R (wingtip groups)

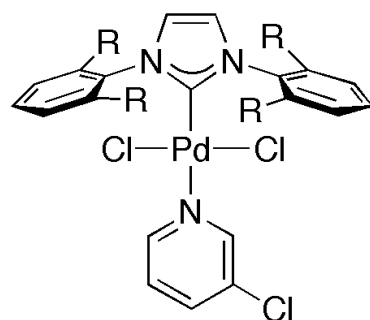
Potential as ligand:

- formally neutral $2e^-$ donor
- strong σ -donation
- high *trans* effect
- fan-like sterics
- tunable through R

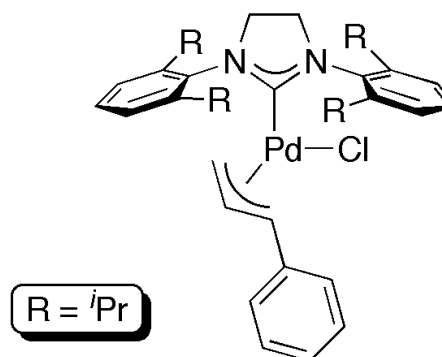
N-heterocyclic carbenes as catalyst promoters



Grubbs 1999



Organ, 2006



Nolan, 2006

R = ⁱPr

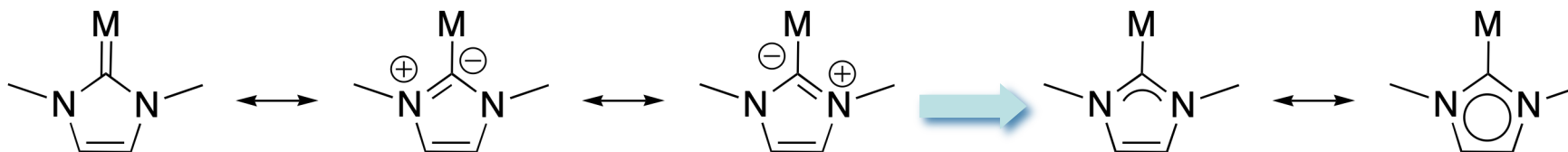
Variations:

- ring expansion
- heteroatom
(type/number/location)
- hybrid structures
(peptides, solids...)
- asymmetric version

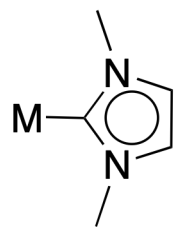
covalent M-carbene bond & strong donor ability of NHCs

Materials and biological activity: *Chem. Soc. Rev.* **2010**, 39, 1903

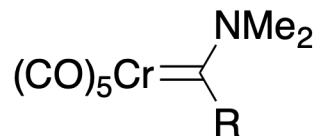
L-type donor or X-type ligand ?



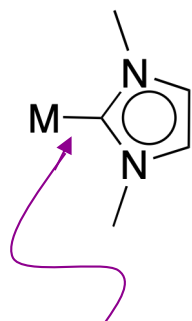
Metal coordination -- dichotomy to Fischer



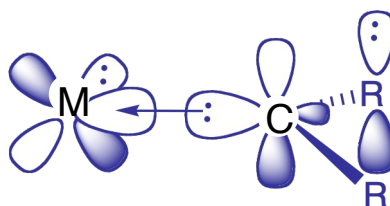
single bond vs
representations



double bond



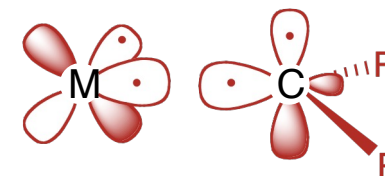
X-ray:
typically single bond lengths



Fischer carbene complexes

ACIE **1964**, 3, 580

Nobel laureate 1973

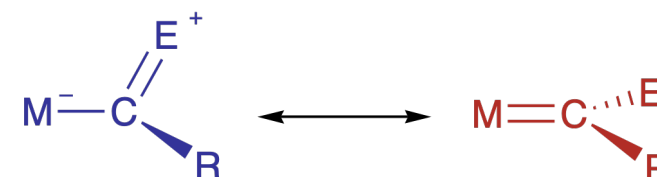
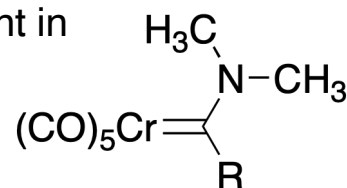


Schrock carbene complexes

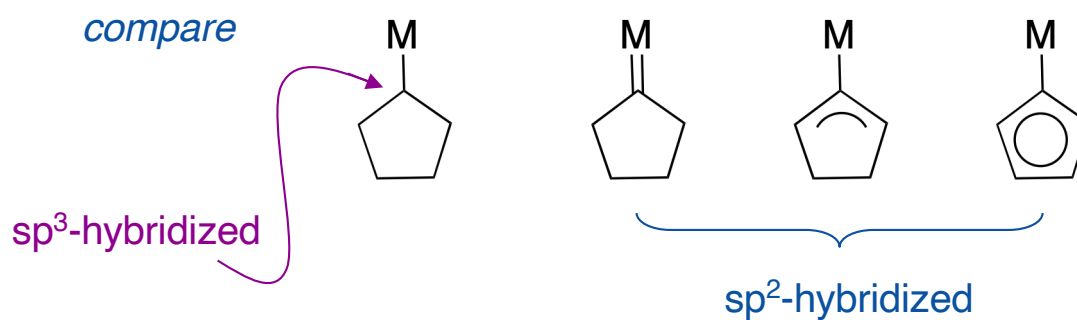
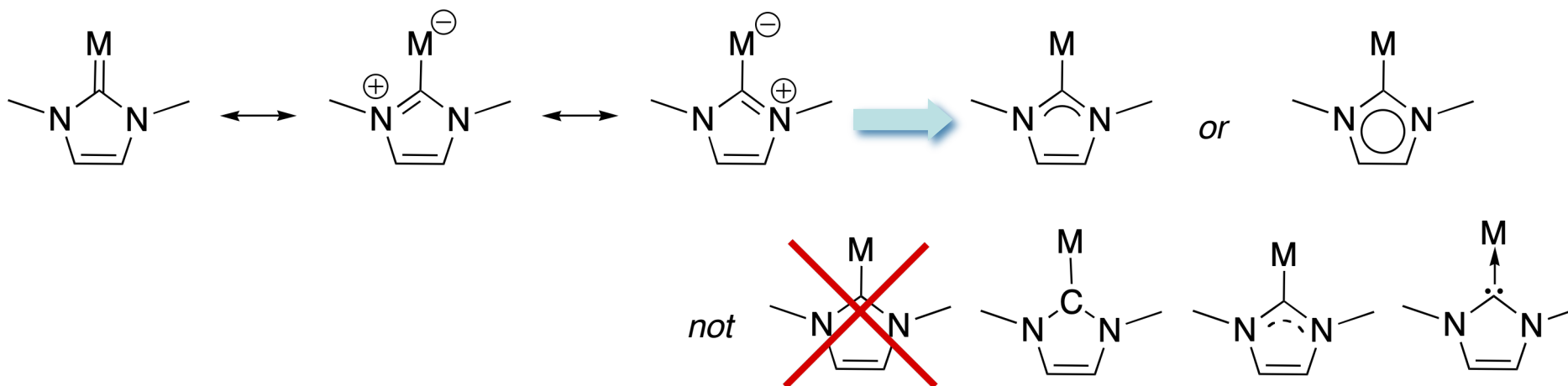
JACS **1974**, 96, 6796

Nobel laureate 2005

But: CH₃ groups magnetically inequivalent in

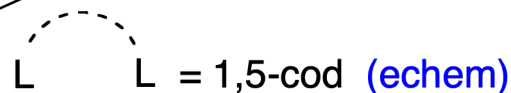
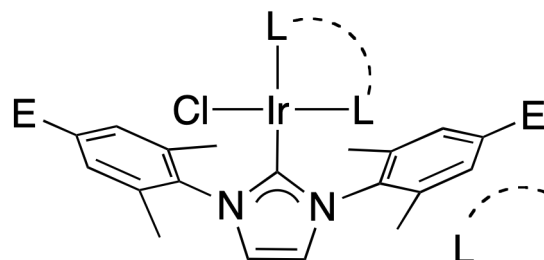
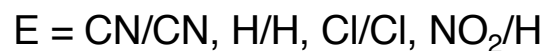
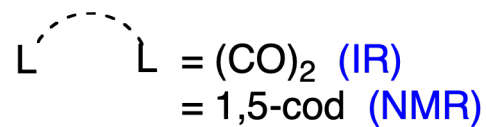
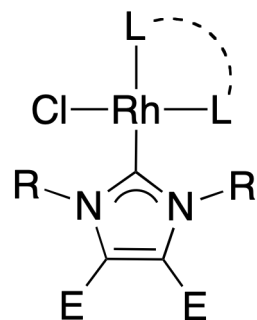


Complex resonance structures

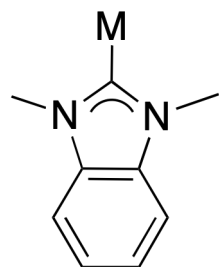


care is needed, some popular notions are wrong

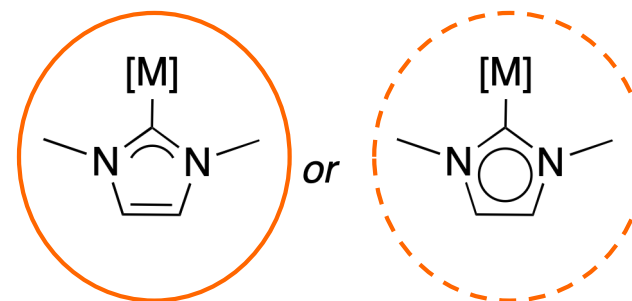
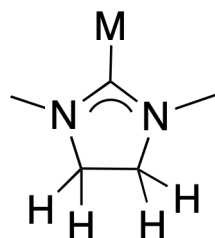
Probing π (de)localization



X-ray: CC bond typically around 1.33 Å



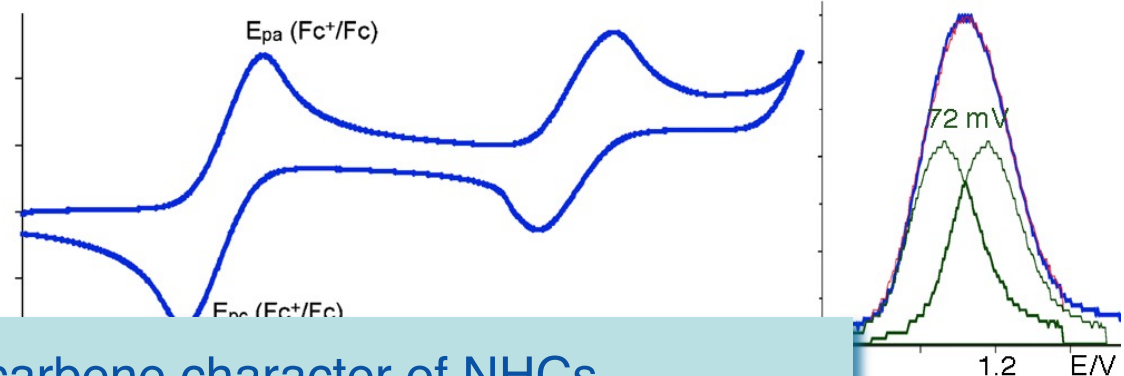
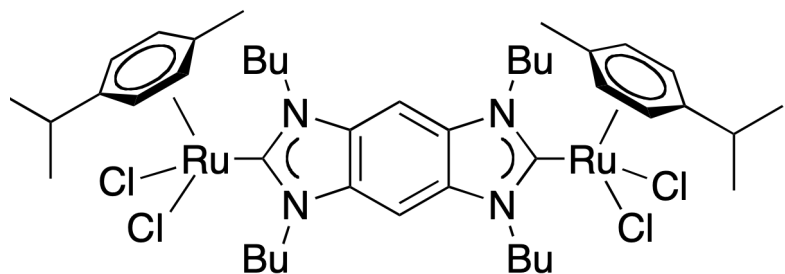
similar to



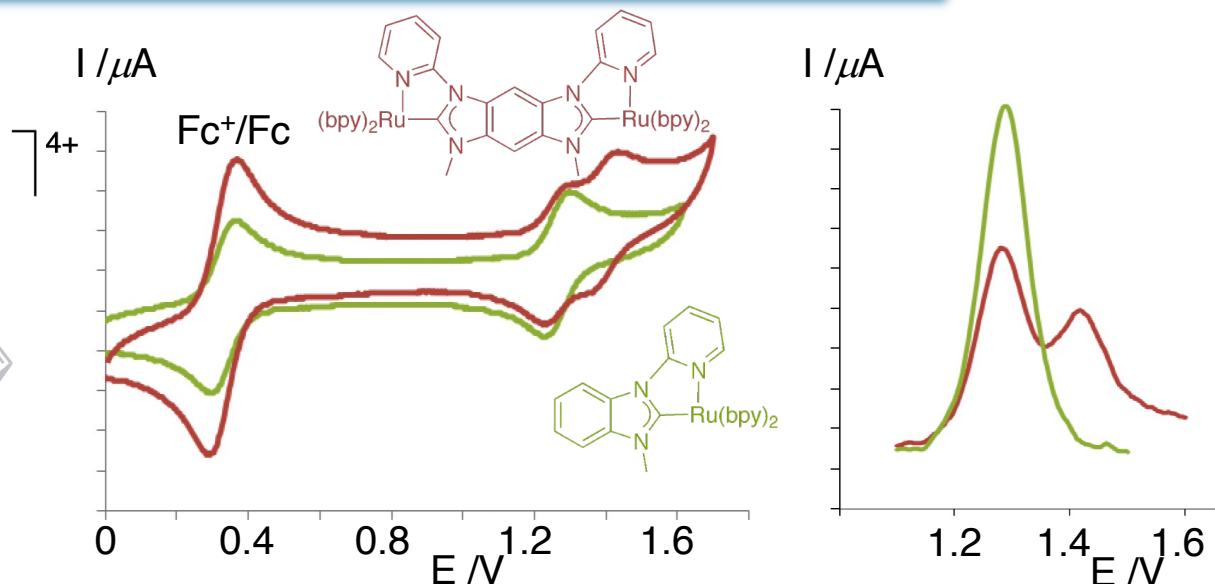
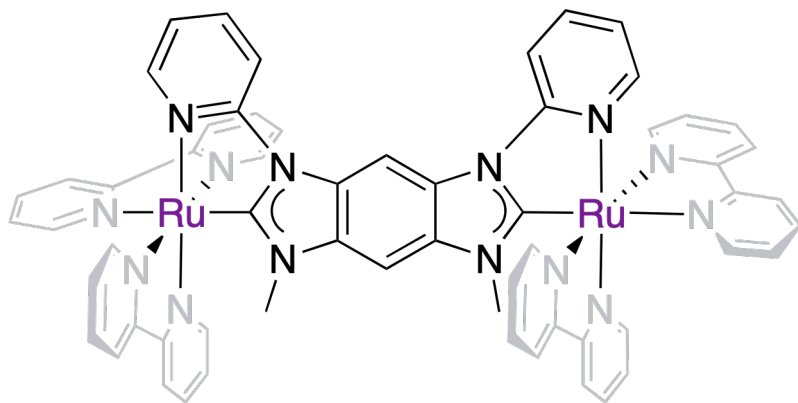
Electronical coupling through Ru=C unit

cyclic voltammetry

diff pulse volt.

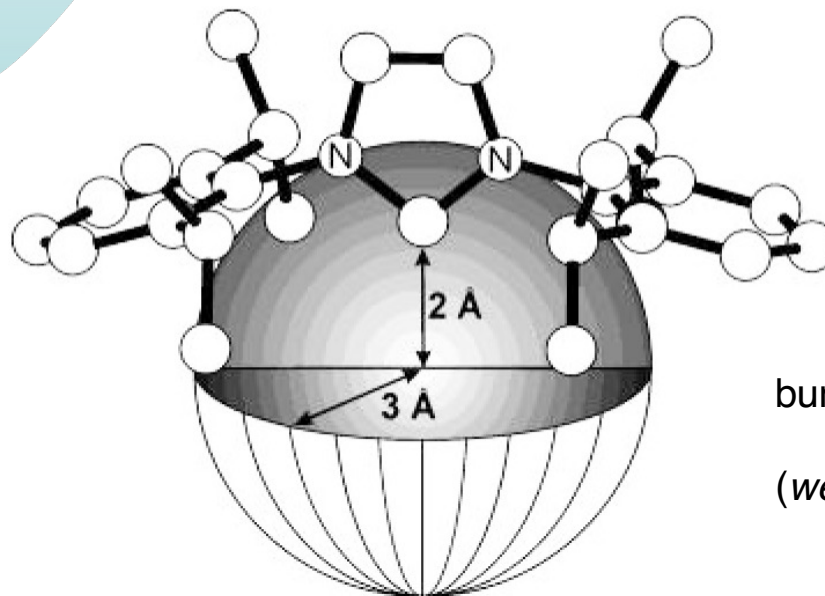
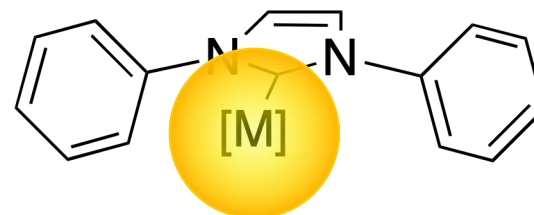
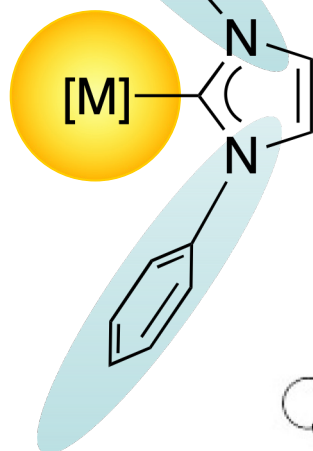


Generally very little carbene character of NHCs — a better terminology needed, such as N-heterocyclic C-ylide



Steric and stereoelectronic impact of carbenes

fan-like sterics

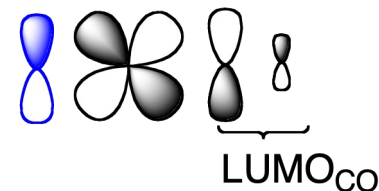
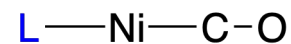
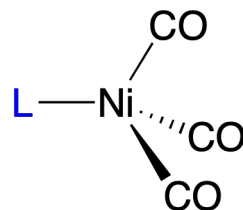


buried volume (% V_{Bur}) of NHC ligands

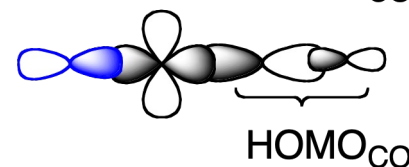
(web application)

Quantifying NHC donor ability

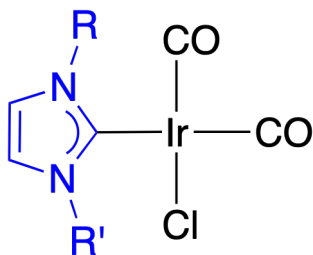
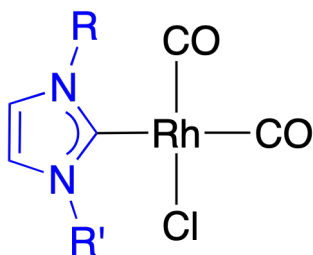
Tolman electronic parameters (TEP)



π donor/acceptor



σ donor

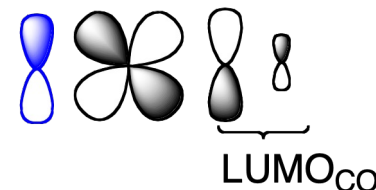
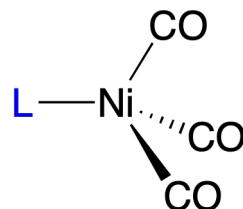


~~two bands, ν_{cis} + ν_{trans}~~

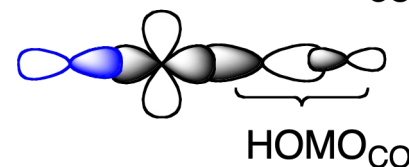
a myth....

Quantifying NHC donor ability

Tolman electronic parameters (TEP)

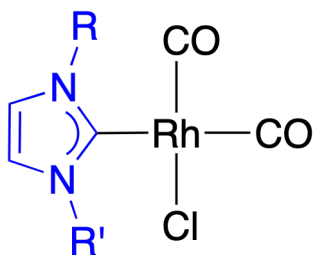


π donor/acceptor



σ donor

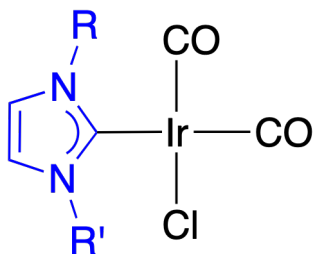
determine $\nu_{av}(\text{CO}) = (\nu_{sym} + \nu_{asym})/2$ in



$$\text{TEP} = 1.308 [\nu_{av}(\text{CO})] - 612 \text{ cm}^{-1}$$
$$\nu_{av}(\text{CO})_{\text{Ir}} = 0.867 [\nu_{av}(\text{CO})] + 251 \text{ cm}^{-1}$$

Organometallics **2009**, 28, 3901

JOM **2009**, 694, 1487



$$\text{TEP} = 0.722 [\nu_{av}(\text{CO})] + 593 \text{ cm}^{-1}$$
$$\text{TEP} = 0.847 [\nu_{av}(\text{CO})] + 336 \text{ cm}^{-1}$$

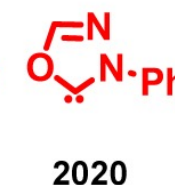
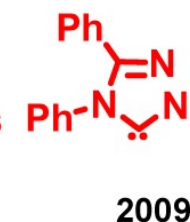
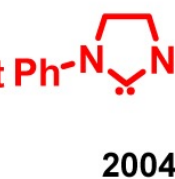
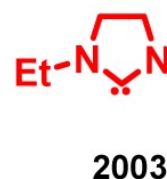
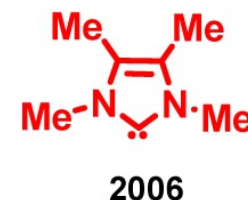
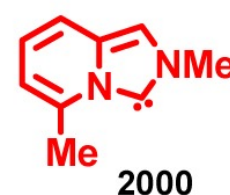
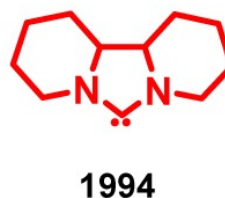
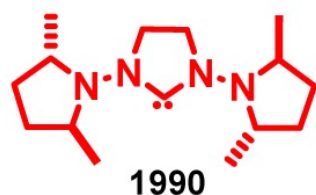
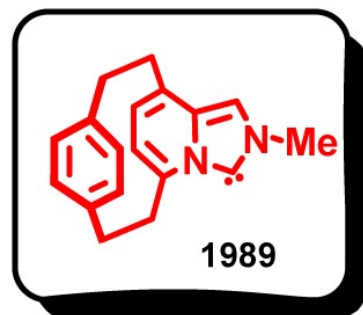
Organometallics **2003**, 22, 1663

Organometallics **2008**, 27, 202

significantly stronger donors than phosphines

Relevance of stereoelectronic parameters

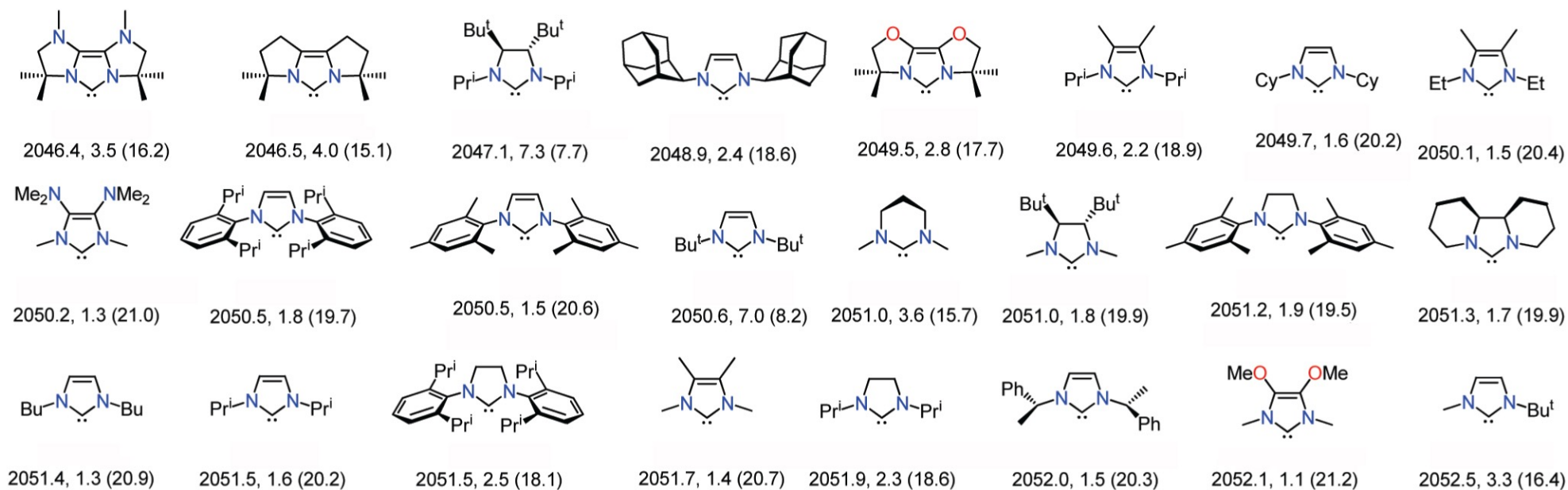
$\nu_{\text{av}}(\text{CO})$ in $\text{NHCRhCl}(\text{CO})_2$



TEP: stereoelectronic effects not considered -- caution required

Introduction of repulsiveness

TEP values & repulsiveness factor R (ΔH values for CO dissociation from $\text{LNi}(\text{CO})_3$)



even small NHCs are relatively bulky

Organometallics **2009**, 28, 6458

ligand donor strength

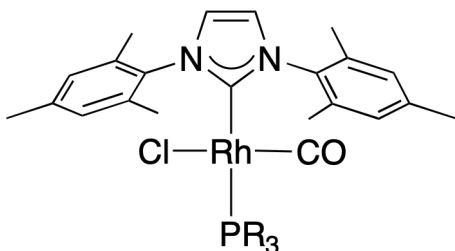
imines, etc.

phosphines

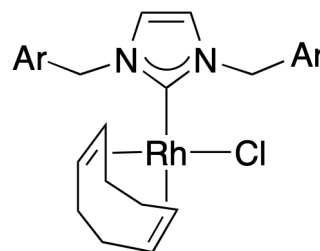
carbenes

Catalytic processes beyond metathesis/x-coupling

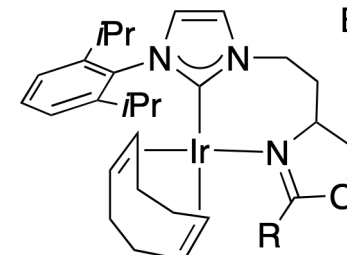
an incomplete listing of reactions with representative catalyst precursors



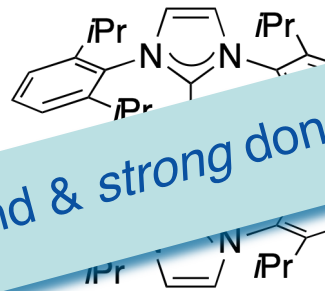
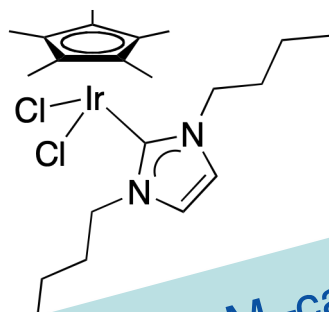
hydroformylation



carbonyl arylation

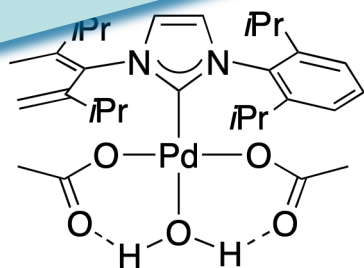


alkene hydrogenation

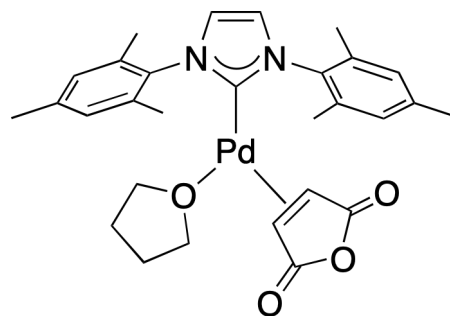


Kumada-Corriu coupling

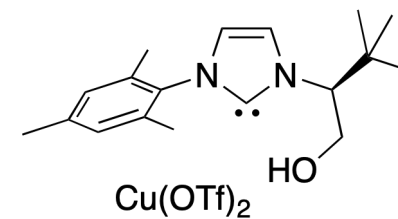
ethylene polymerization



alcohol oxidation



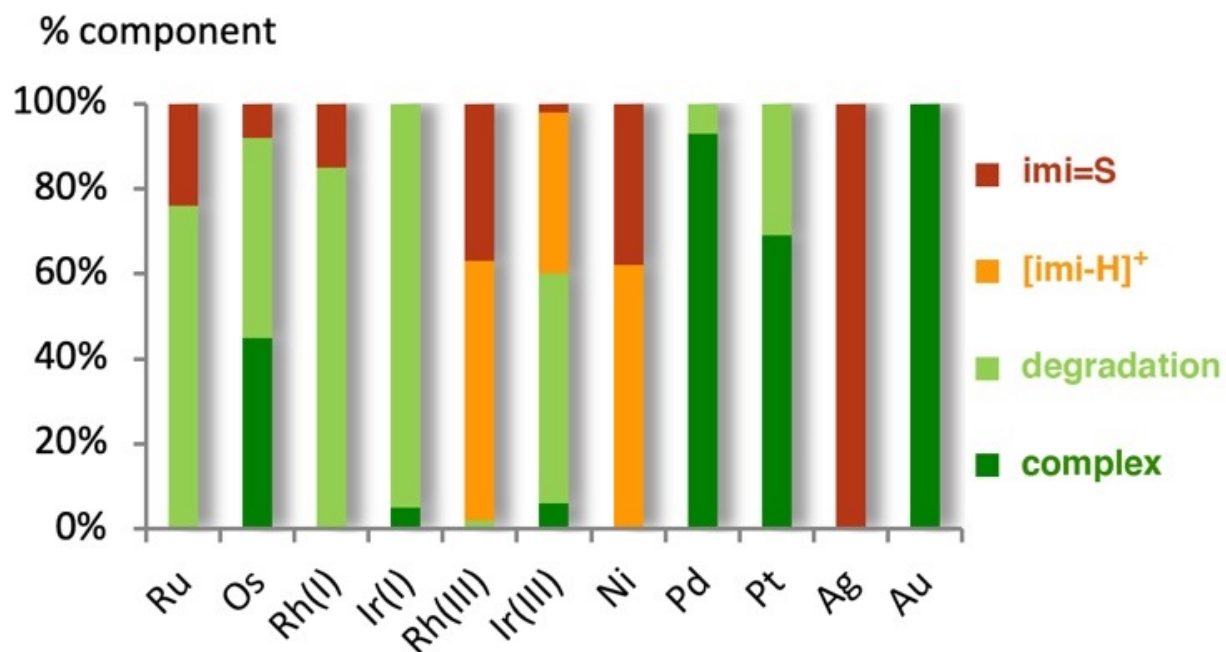
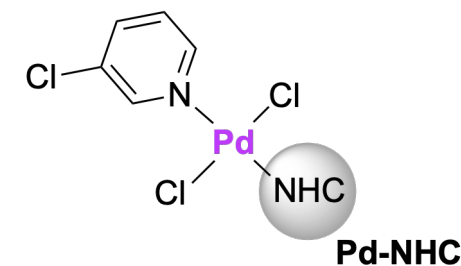
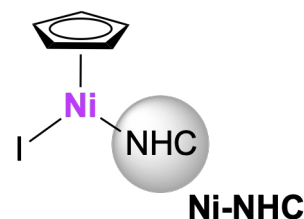
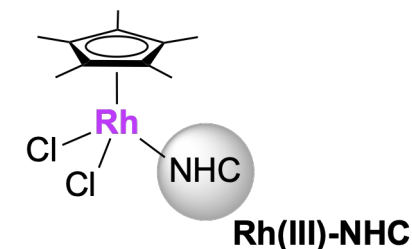
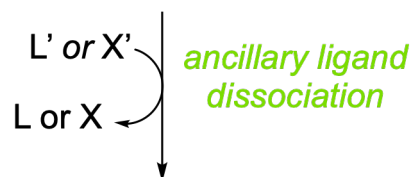
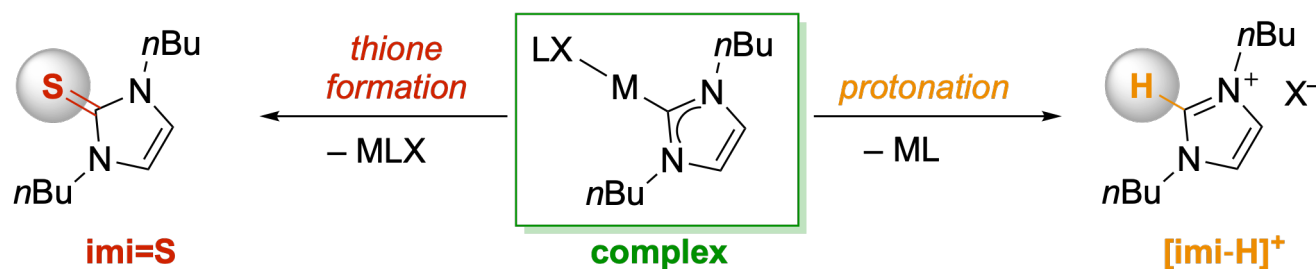
alkyne semihydrogenation



CO₂ reduction, Michael addition

covalent M-carbene bond & strong donor ability of NHCs

Robust Metal Bonding? Caution....

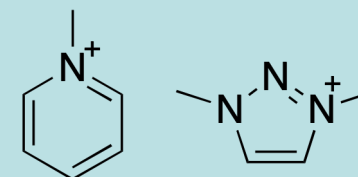


1,2-Cl₂C₆H₄, 120 °C, 24 h

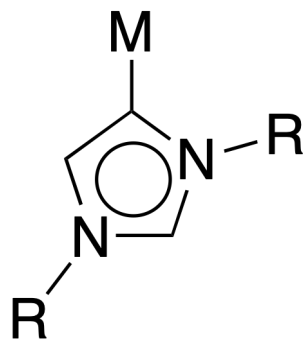
Carbenes with Increased Donor Ability

π -donor nitrogens
stabilize free carbene

What is normal/abnormal in



UNIVERSITÄT
BERN

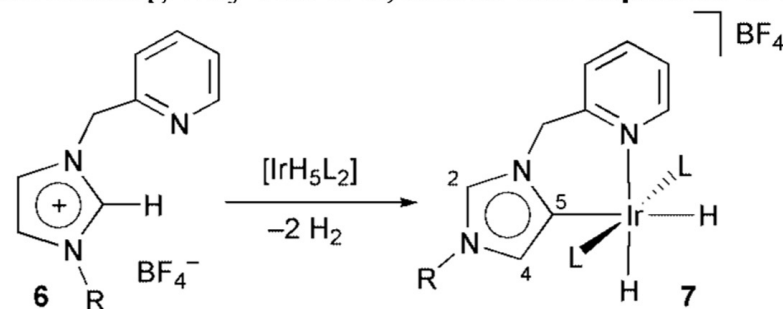


mesoionic/abnormal carbenes

Abnormal binding in a carbene complex formed from an imidazolium salt and a metal hydride complex

Stephan Gründemann, Anes Kovacevic, Martin Albrecht, Jack W. Faller* and Robert H. Crabtree*

2-Pyridylmethylimidazolium salts and $\text{IrH}_5(\text{PPh}_3)_2$ give an $[(\text{N}-\text{C})\text{IrH}_2(\text{PPh}_3)_2]^+$ species with the imidazole ring bound in the 'wrong way': at C-5, not at the expected C-2.

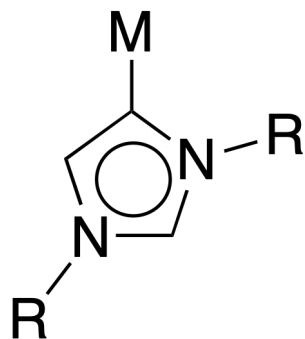


[a R = Prⁱ, b R = Buⁿ; L = PPh₃]

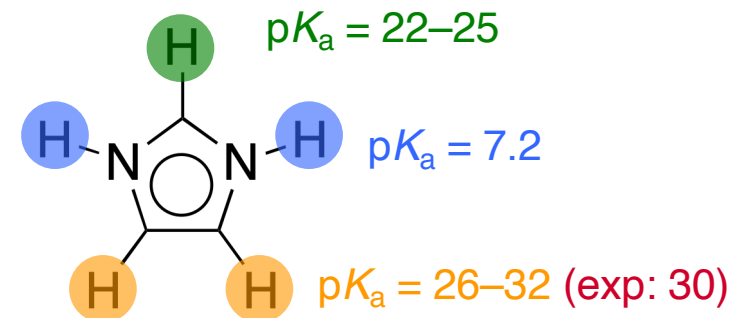
2274 *Chem. Commun.*, 2001, 2274–2275

Carbenes with Increased Donor Ability

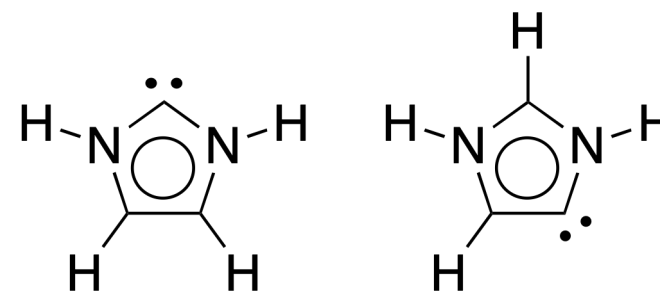
π -donor nitrogens
stabilize free carbene



mesoionic/abnormal carbenes
(no neutral resonance form)



Yates, *Aust. J. Chem.* **2004**, *51*, 1205
Cavell & Yates, *JACS* **2004**, *126*, 8717

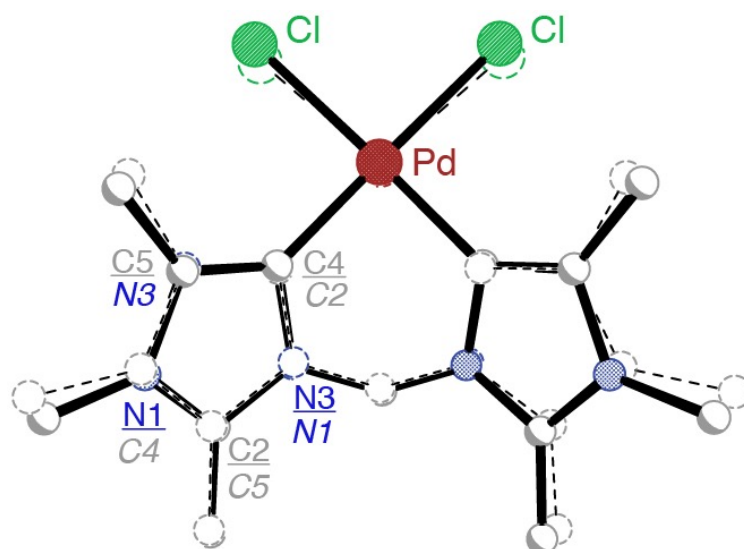
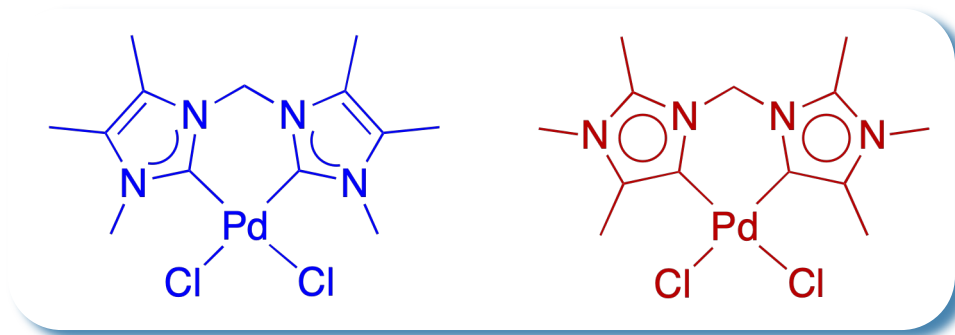


$\Delta E \sim +80 \text{ kJ mol}^{-1}$

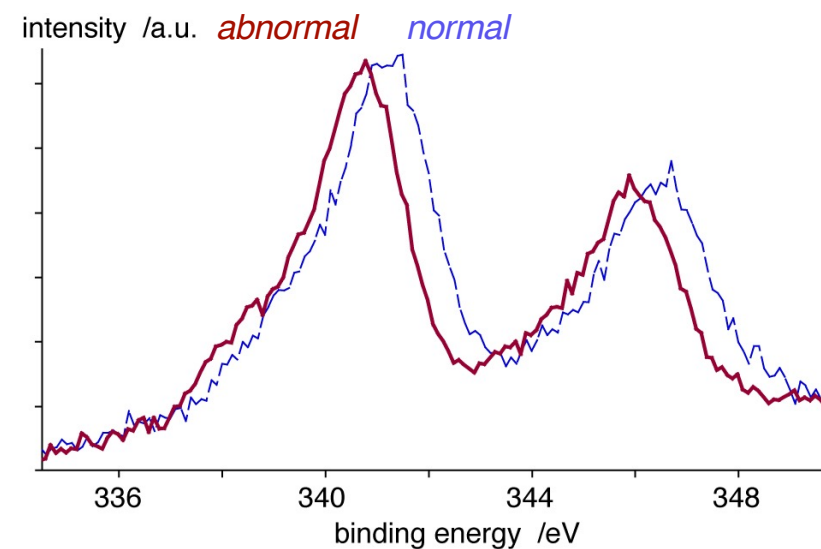
Frenking, *Chem. Asian J.* **2007**, *2*, 1555

suggests: stronger donor ability
better charge relais

Isostructural Dicarbene Palladium Complexes



Pd-C	1.979(4), 1.976(5)	1.976(9), 1.981(9)
Pd-Cl	2.359(1), 2.356(1)	2.400(2), 2.407(2)

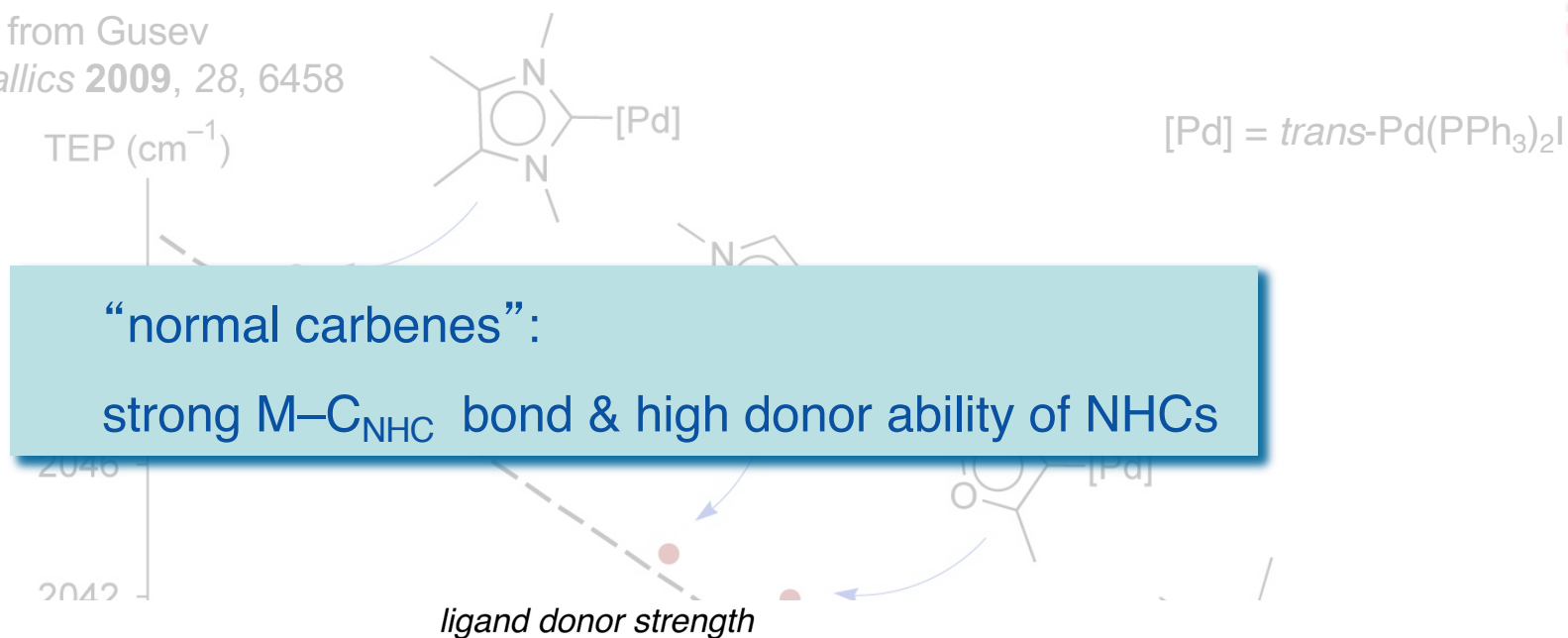


X-ray photoelectron spectroscopy

Tunability of abnormal carbenes

calculations from Gusev
Organometallics **2009**, 28, 6458

TEP (cm⁻¹)

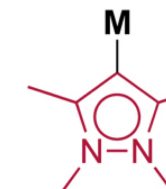
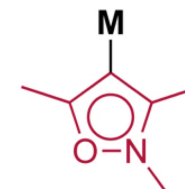
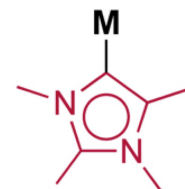
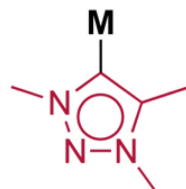
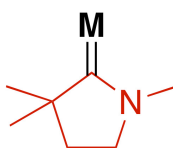
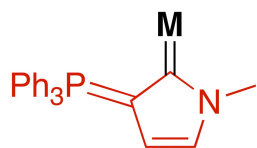


imines, etc.

phosphines

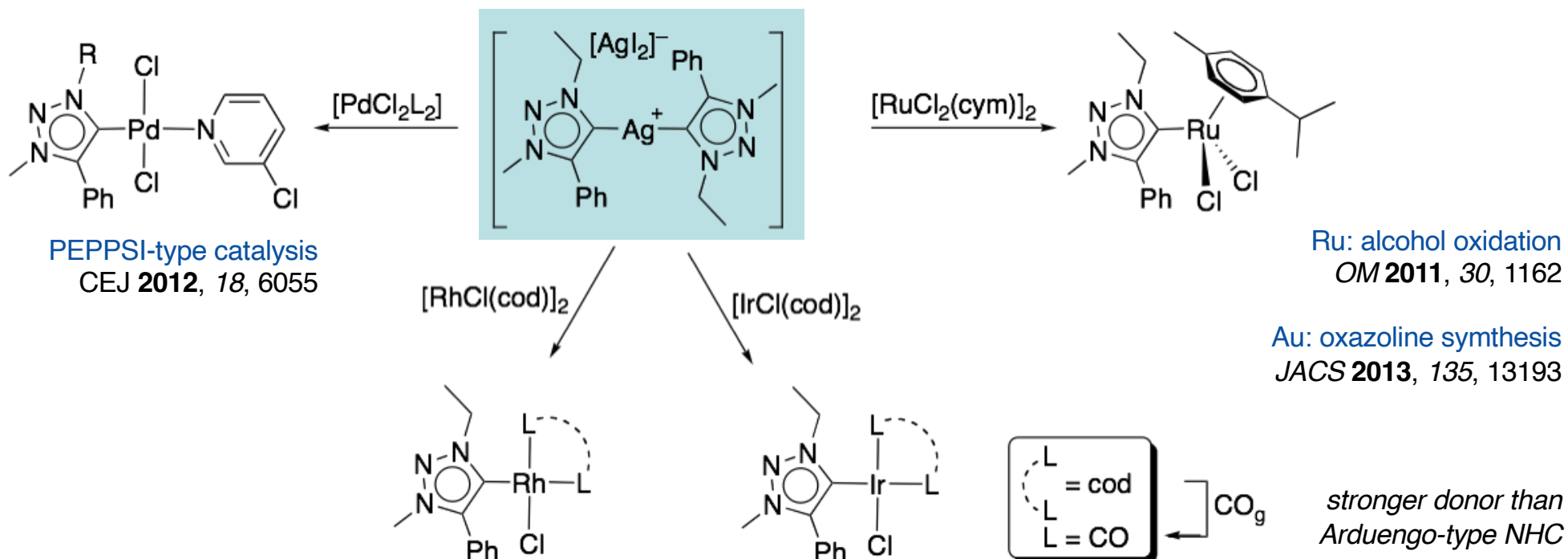
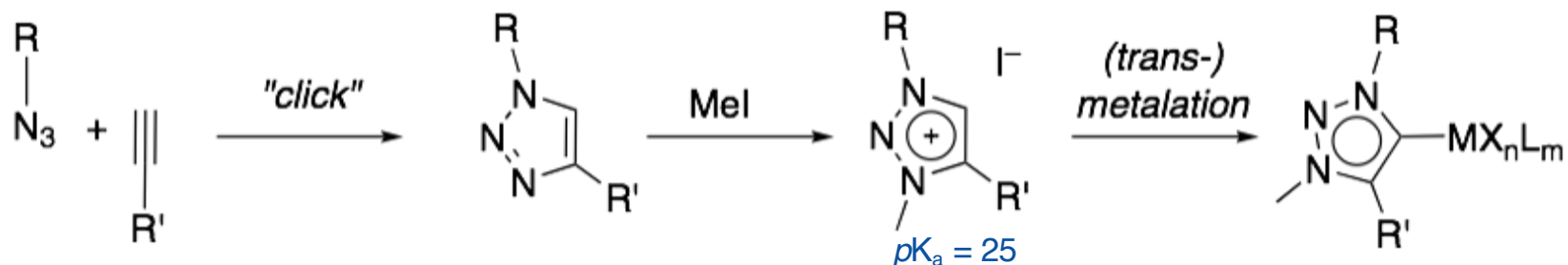
normal carbenes

abnormal carbenes



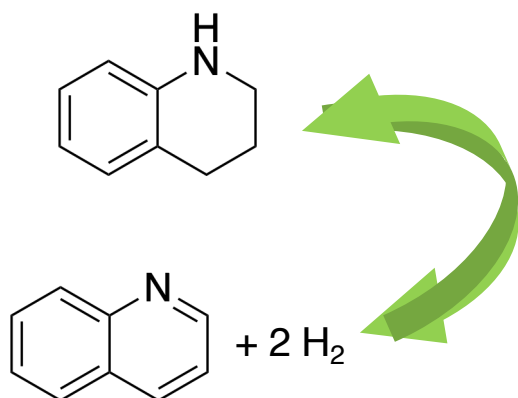
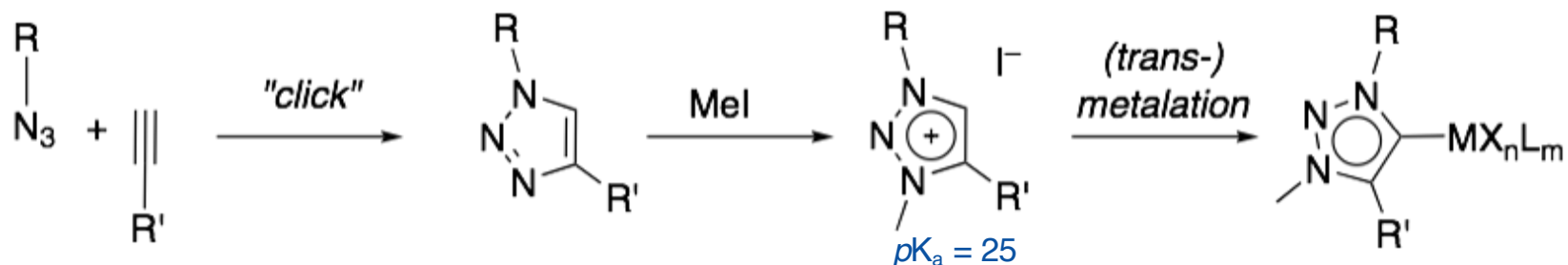
Triazole-derived click carbene complexes

Ligand synthesis:

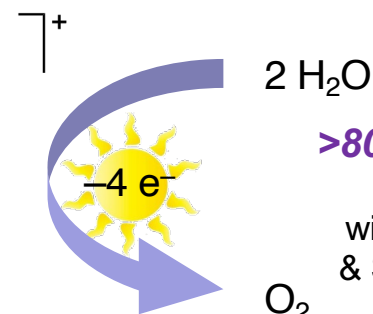
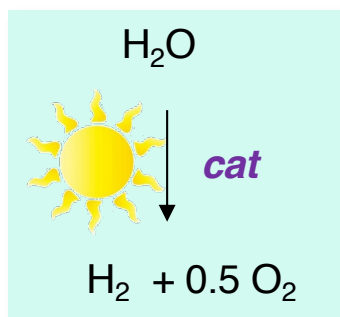
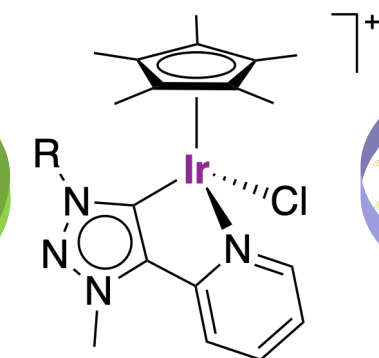


Click carbenes for artificial photosynthesis

Ligand synthesis:

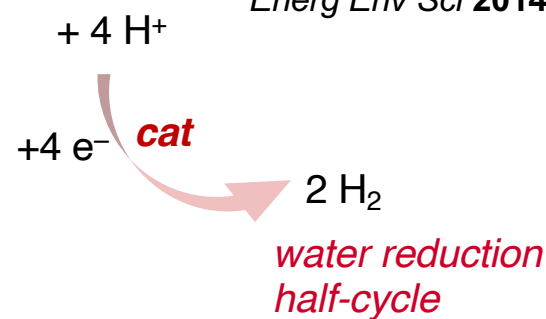


with Angela Vivancos & Matthias Beller
ACS Catal **2018**, 8, 17



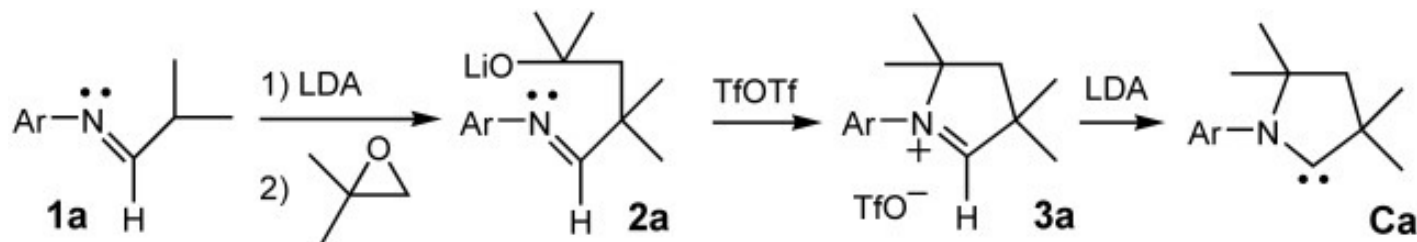
>80,000 TON

with Ana Petronilho, Marta Olivares
& Stefan Bernhard, Alceo Macchioni
ACS Catal **2015**, 5, 2714
Energ Env Sci **2014**, 7, 2316

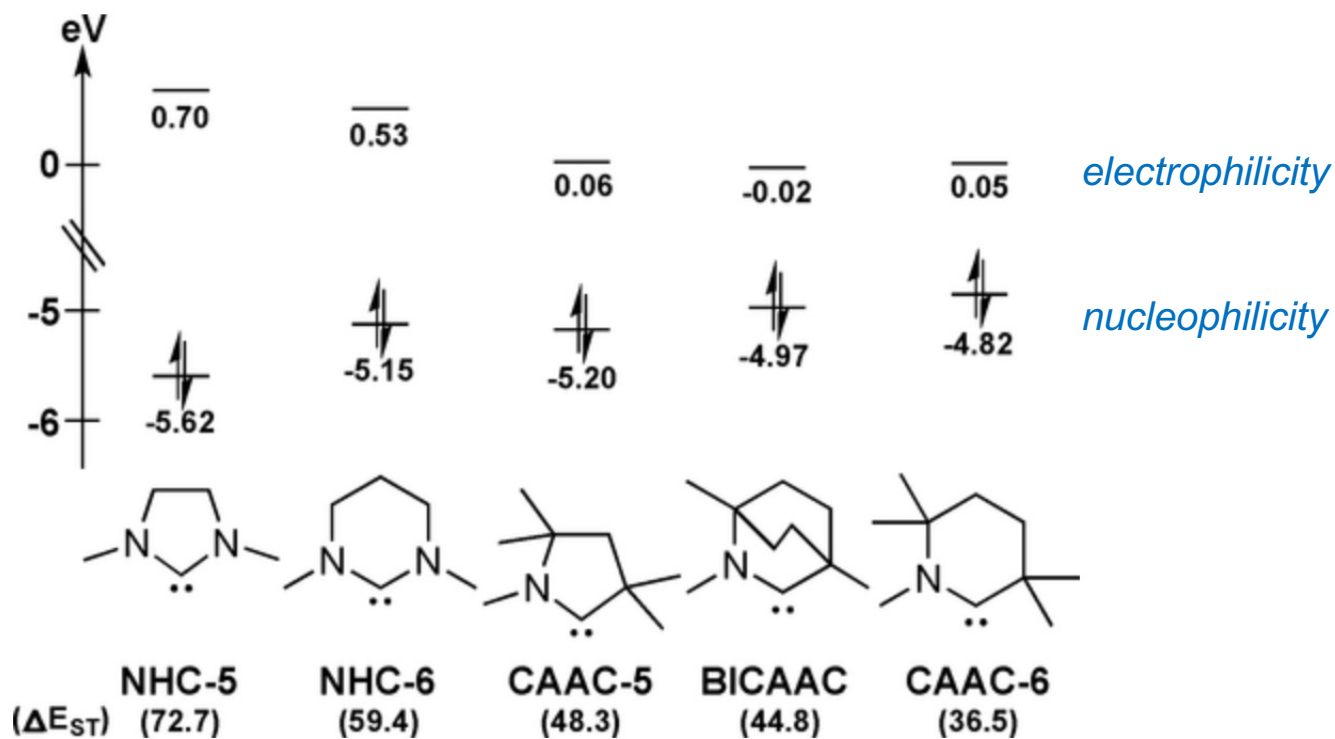


Cyclic Alkyl Amino Carbenes (CAACs)

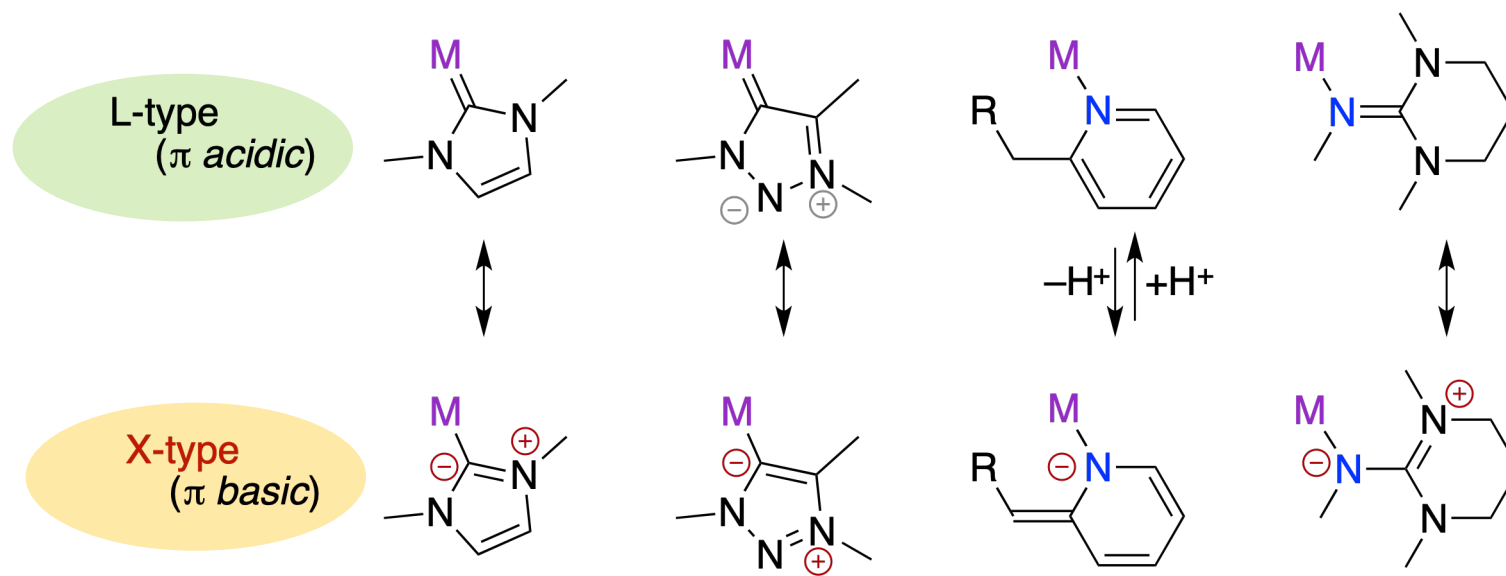
Ligand synthesis:



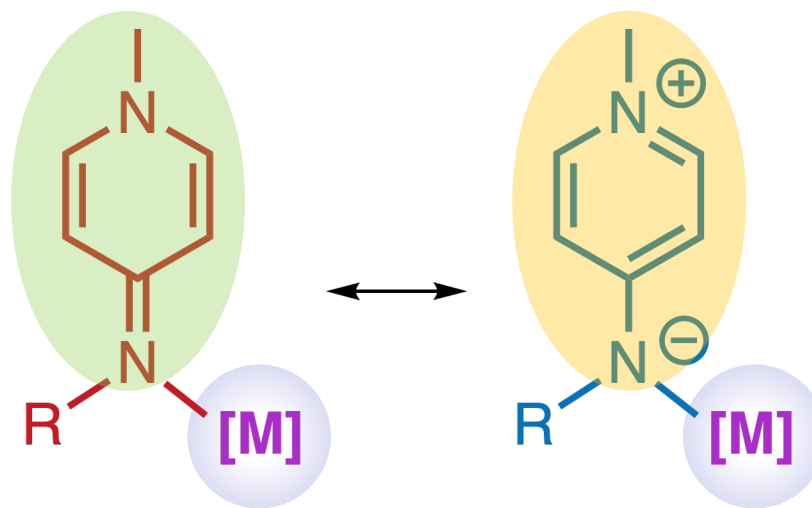
singlet-triplet gap:



Donor-flexible ligands



Donor-flexible *N*-ligands



neutral imine
 π acidic

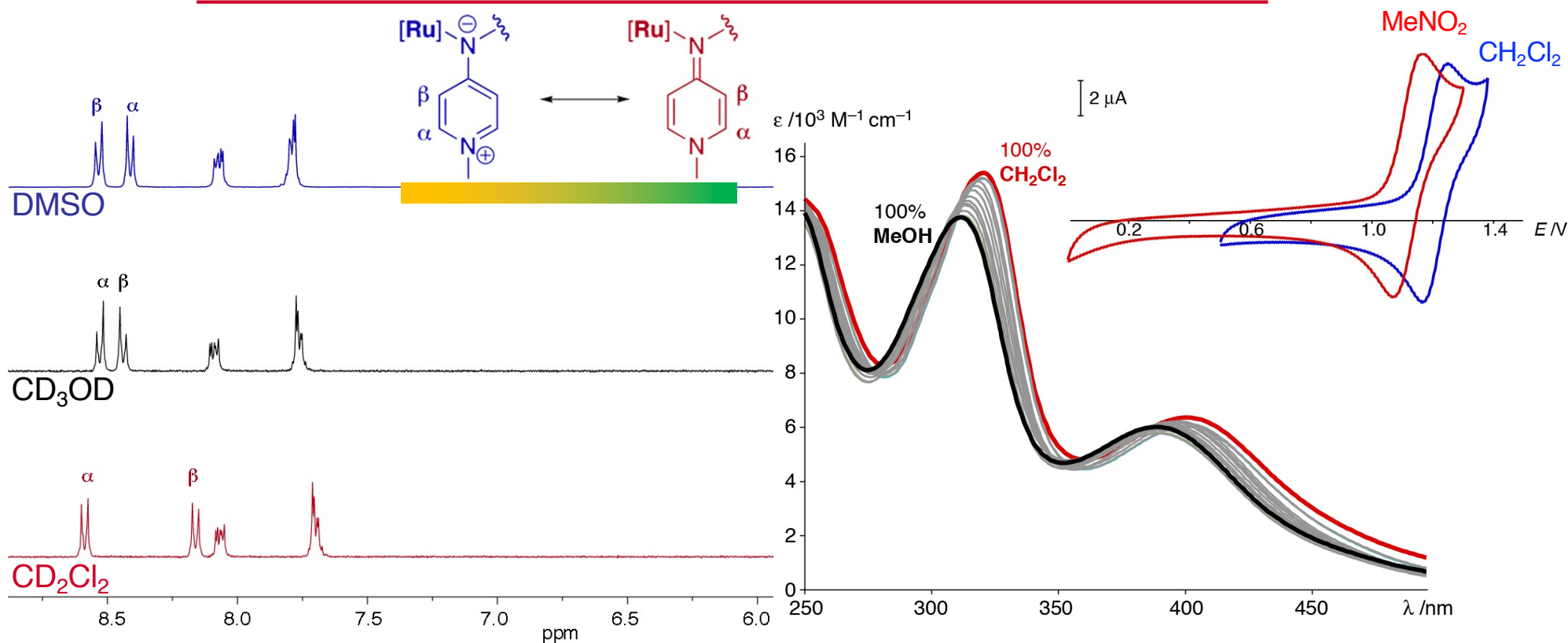
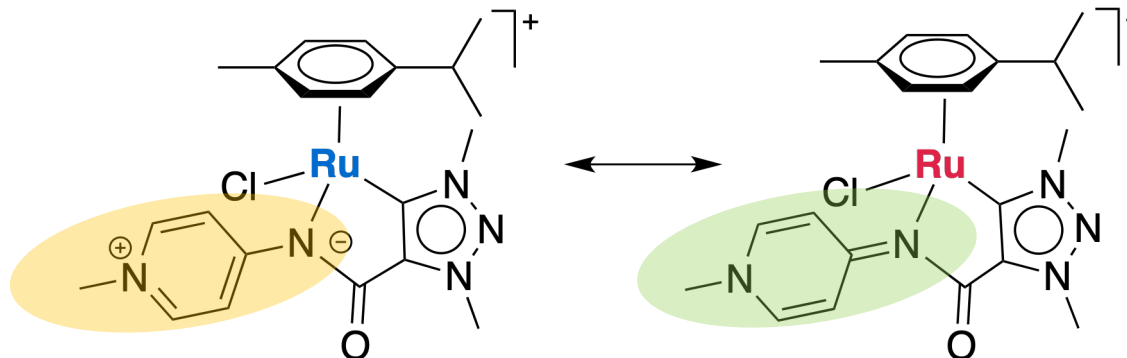
zwitterionic amide
 π basic

low valent M

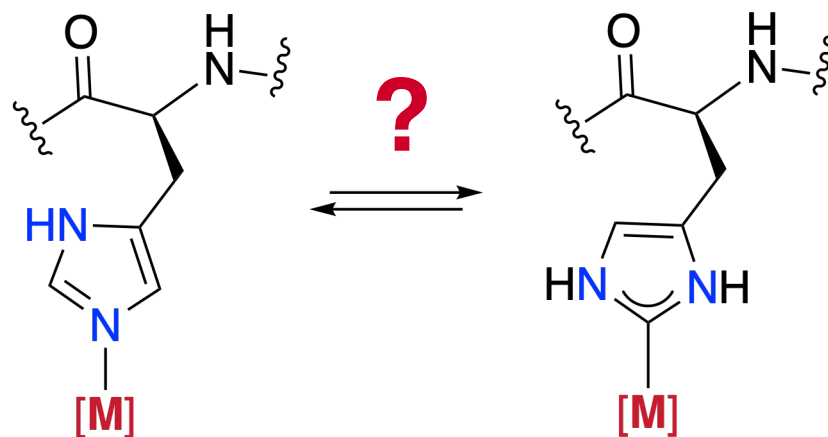
high valent M

- PYE (pyridylidene amine): R = alkyl, aryl *Johnson (2009), Douthwaite (2009)*
- PYA (pyridylidene amide): R = C(O)R' *Wright (2011)*

Solvent-dependent donor properties of PYAs

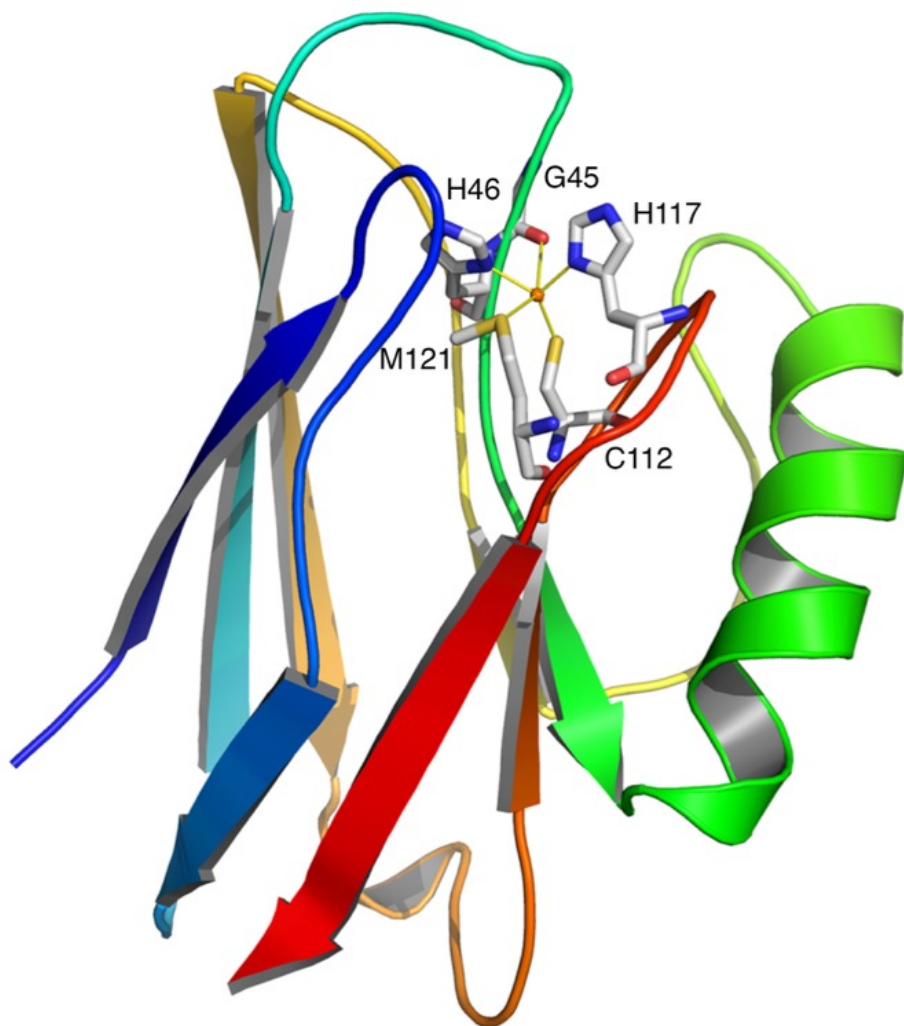


Is C-bonding of His plausible?

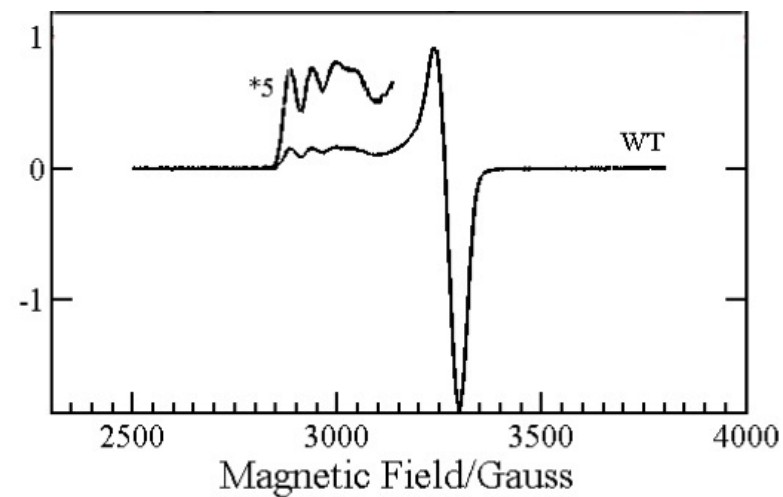
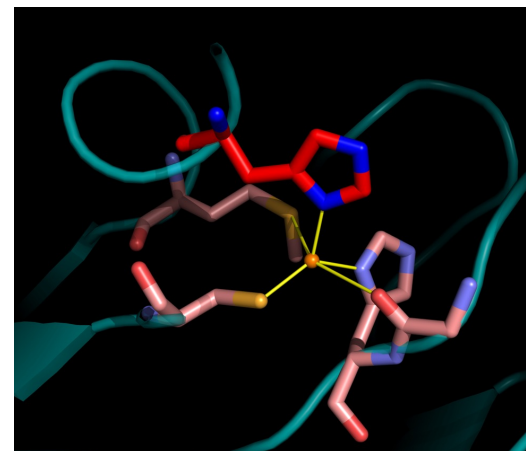


- Calculations indicate feasibility
(Eisenstein, *Inorg Chem* **2002**, 41, 602; Macgregor, *EurJIC* **2009**, 2000)
- Protic NHCs known
(Hahn *Chem Rev* **2018**, 118, 9642)
- Synthetic tautomerization (irreversible) known
(Riera, *J.Am.Chem.Soc.* **2008**, 130, 13530; Ruiz, *J.Am.Chem.Soc.* **2007**, 130, 7558; Li, *Organometallics* **2007**, 26, 4684)

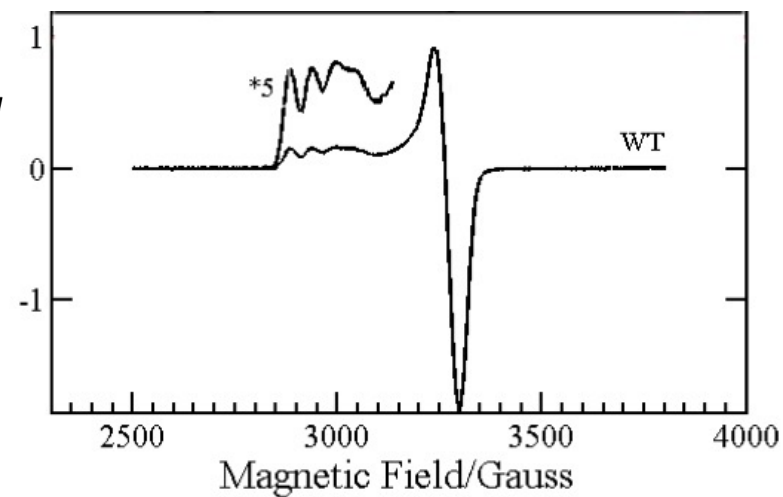
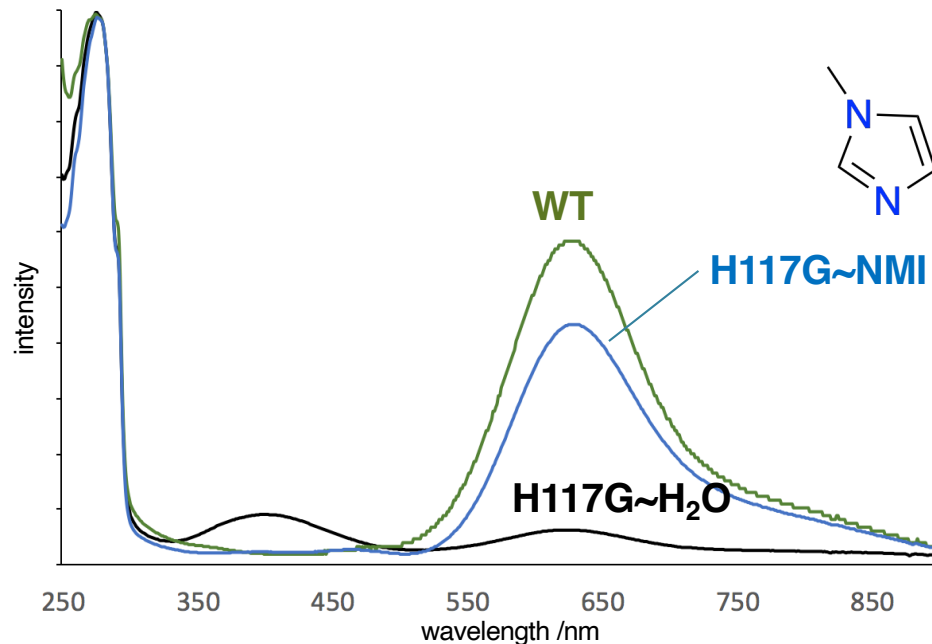
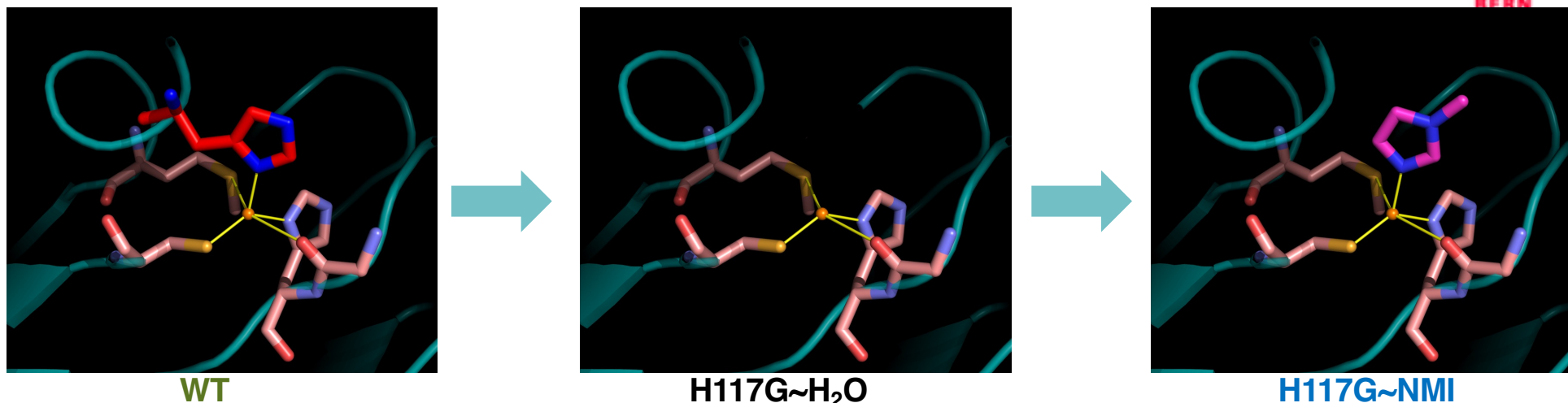
Evaluation of C-bonding: which enzyme?



Azurin (Azu) from *P. aeruginosa*
(3U25)

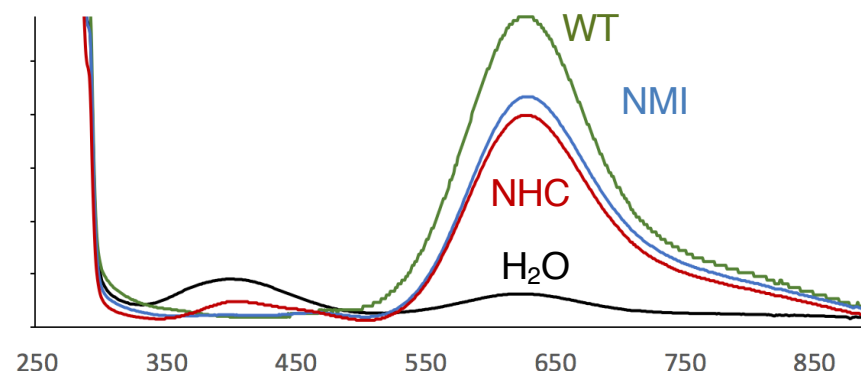
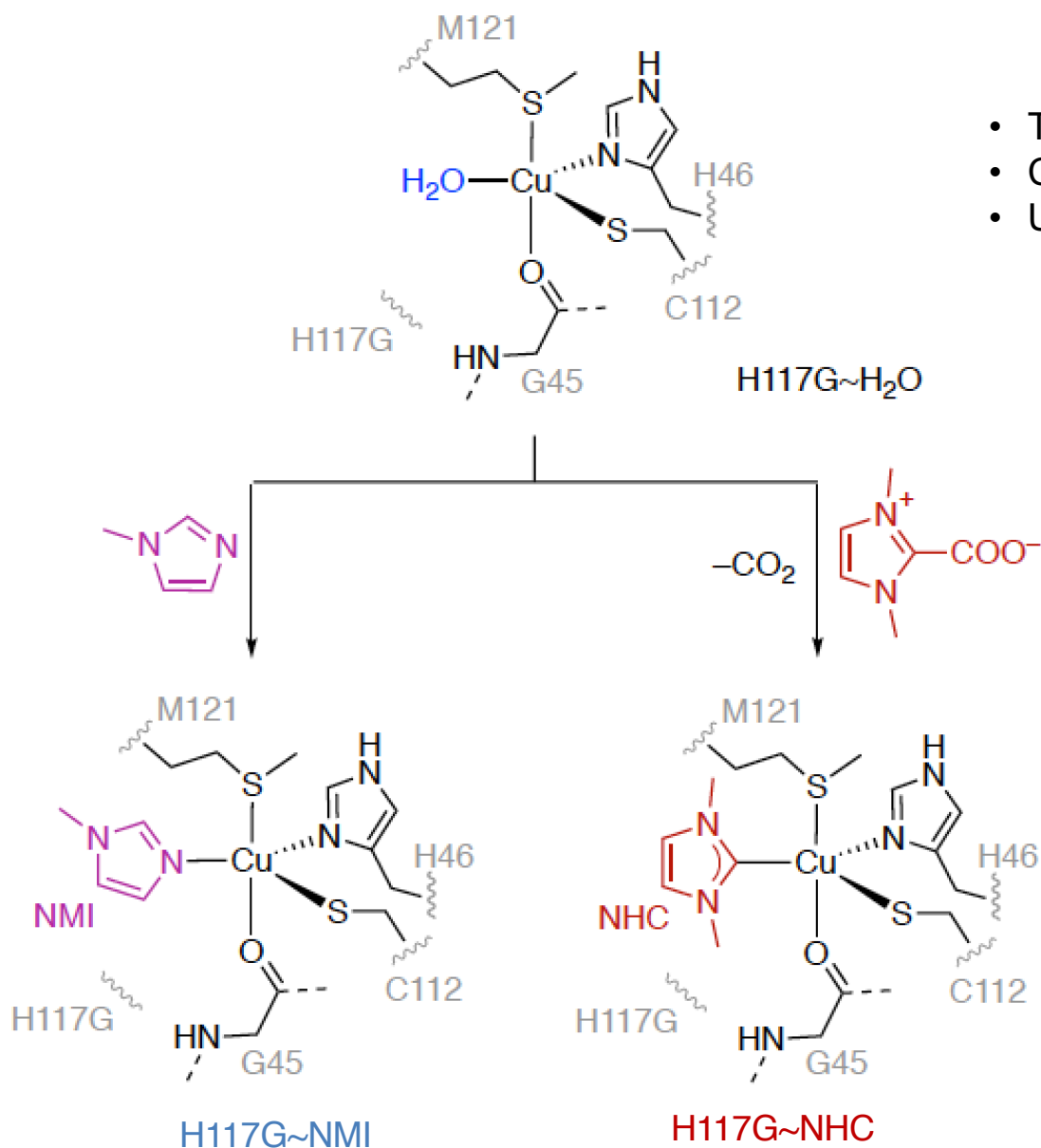


Azurin H117G rescued by exogenous NMI



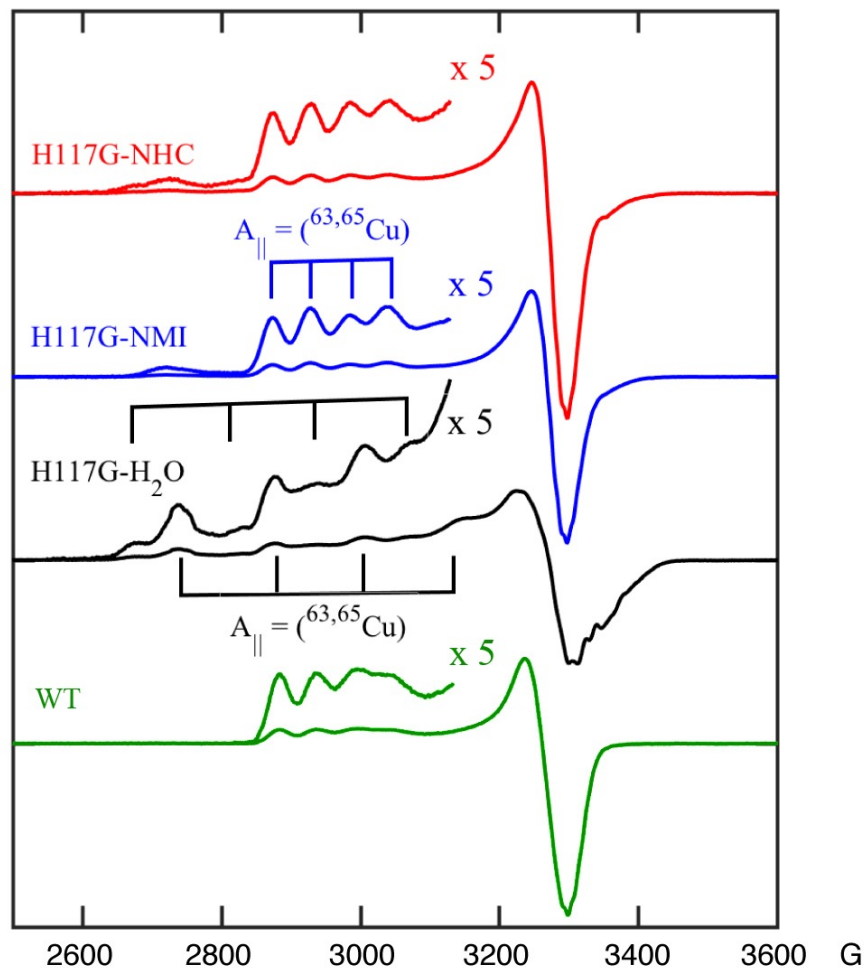
Installing the NHC at Azu H117G

- T1 copper center rescued with NHC bonding
- Controls (benzoate, imidazolium salt) yield T2 center
- UV-vis titration: larger excess of NHC needed



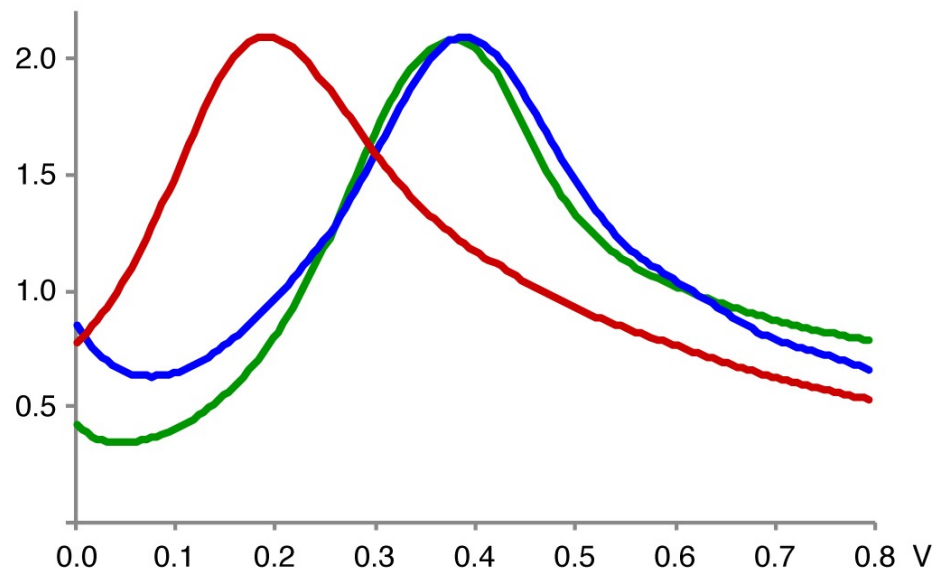
Impact of NHC bonding to Azu H117G

EPR



NHC: classic T1 EPR signature

Electrochemistry

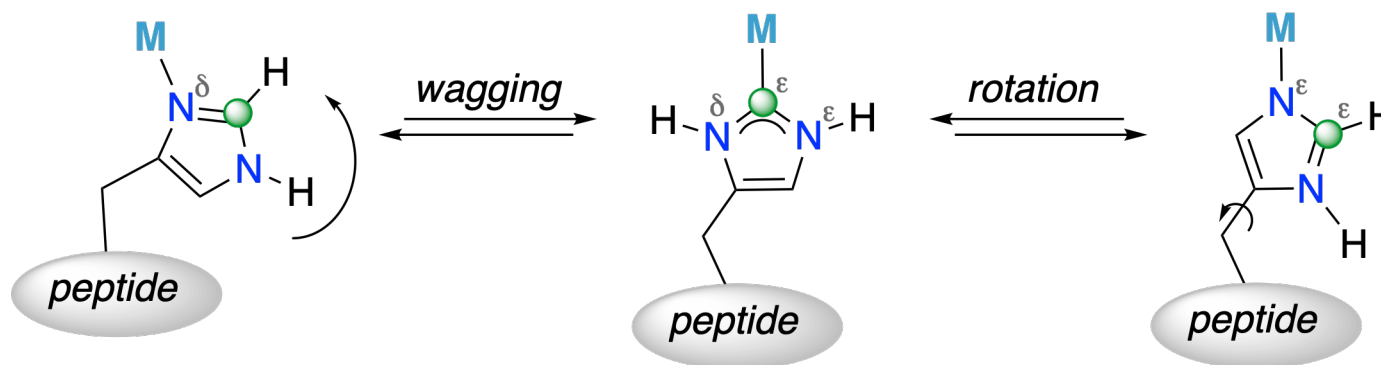


	WT	H117G~		
		~H ₂ O	~NMI	~NHC
g_{33}	2.2633	2.2813	2.2681	2.2673
$ A_{33} $	54.7	142.7	57.4	59.6
E_{pa}	+0.32	n.d.	+0.33	+0.15

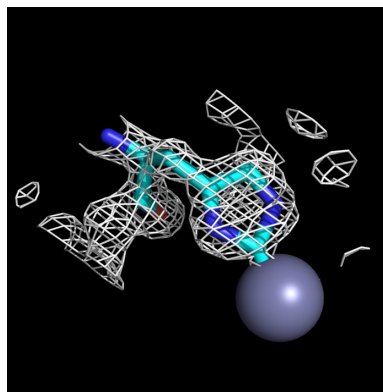
NHC stabilizes copper(I) (ΔE 0.18 V)

C- vs N-bonding spectroscopic features

Overlooked ground state? Transient tautomerization in active state of enzyme?

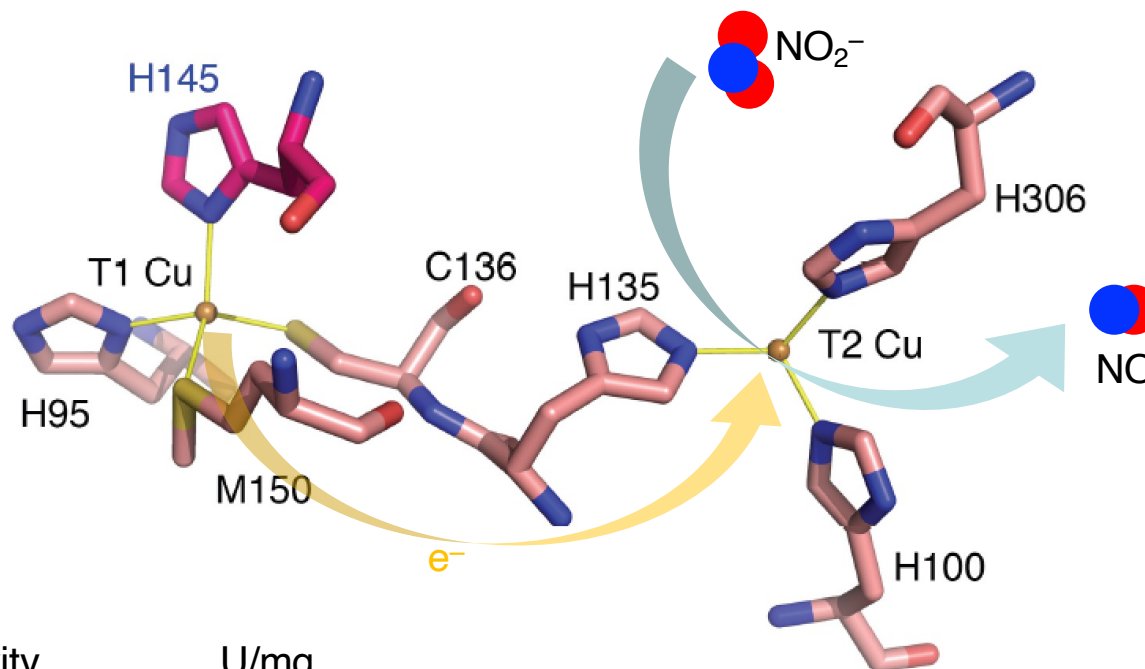


- structural barriers low
- synthetic evidence for both tautomerization process



Catalytic impact of carbene bonding

Nitrite Reductase (NiR) (*A. faecalis*)

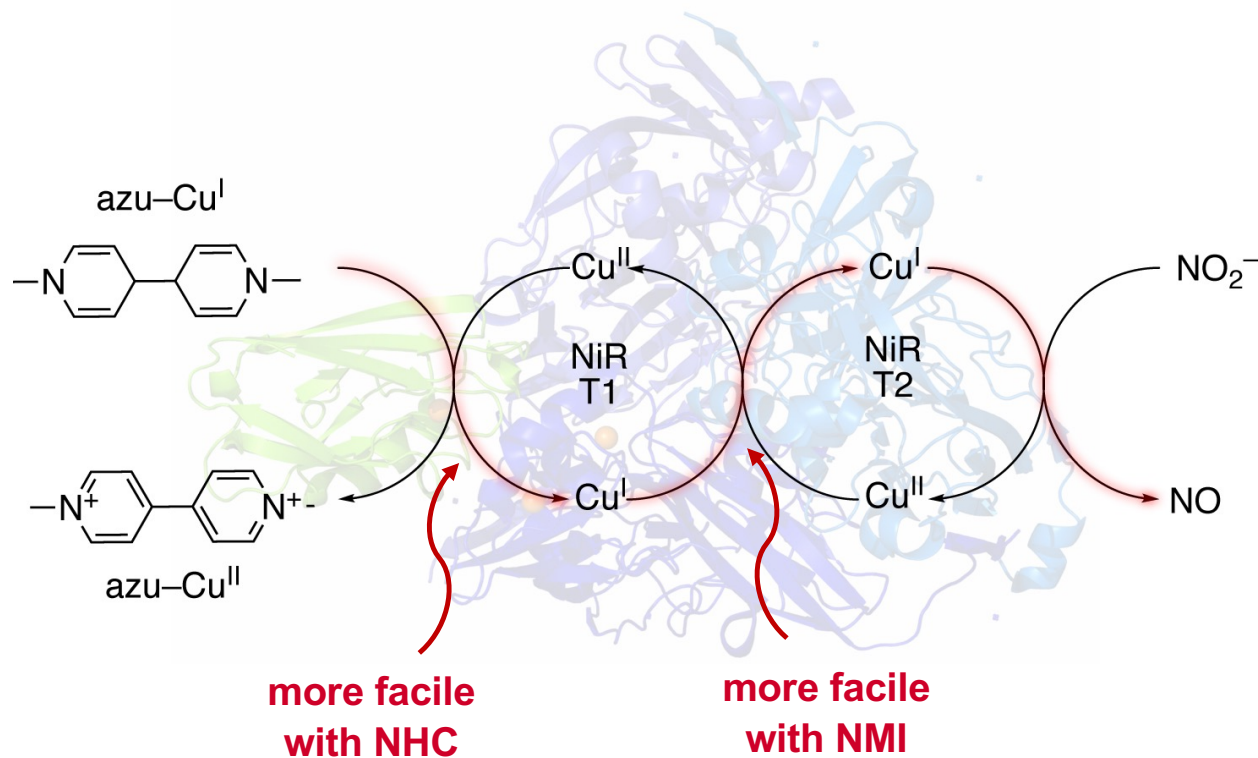


Activity	U/mg
WT	900 ± 140
H145G~H2O	31 ± 5
H145G~NMI	67 ± 14
H145G~NHC	111 ± 4

using in situ reduced methyl viologen as sacrificial reducing agent

Catalytic activity doubles – possible shift in rate-determining step?

Catalytic impact of C-bound ligand



swapping between both bonding modes may facilitate both redox steps

To summarize...

- ♦ N-heterocyclic carbenes: formally neutral, de facto mesoionic ligands with **remarkably strong donor** properties
- ♦ Mesoionic character is more pronounced in abnormal carbenes though **increased electron density at the metal center** is not per se providing a better catalyst
- ♦ **Carbene transfer** is a plausible process with relevance to catalytic transformations, and may become a desired property (e.g. in medicinal applications). Robust/covalent bonding needs to be validated!