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N-heterocyclic carbenes: from laboratory curiosities to workhorse ligands in homogeneous catalysis: History, general trends, and modern applications

Trieste-Venice PhD School,

12 May 2022

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University of Bern, Switzerland

Frontier orbitals of carbenes

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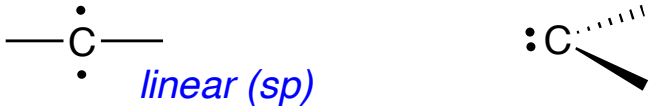
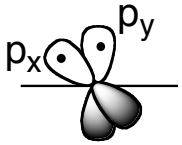
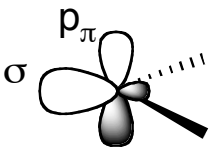
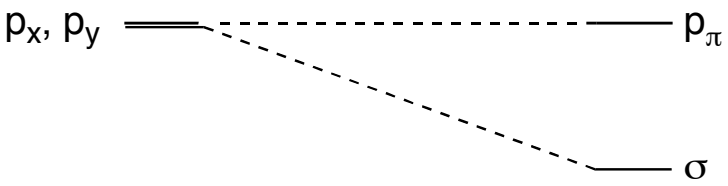
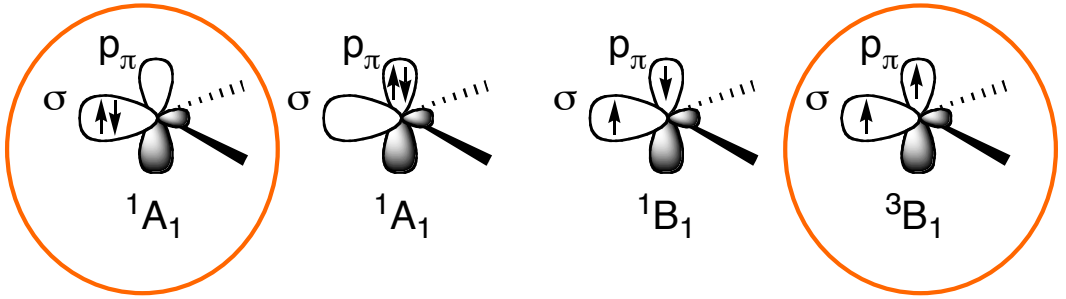
geometrical considerations





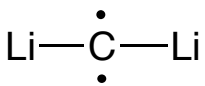




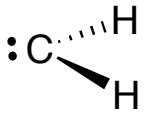


π donor substituents raise p_π (stability)

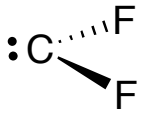
examples



180°



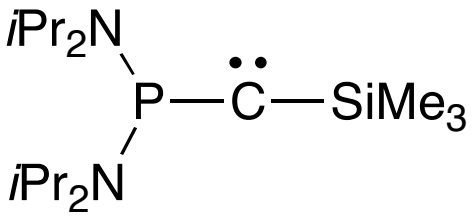
129°



104°

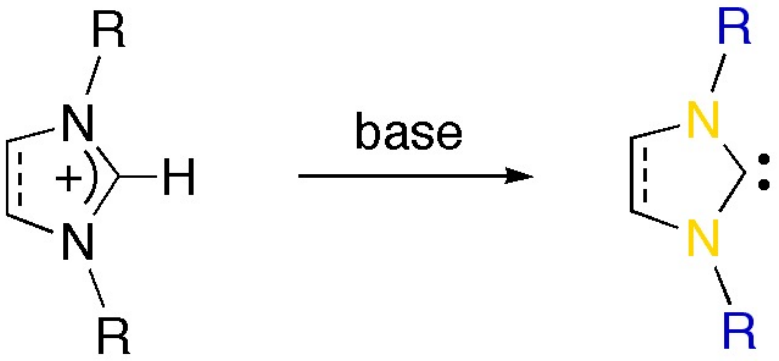
Bertrand, *Chem Rev* **2000**, *100*, 39;

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



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

Trick 1 : extensive
π–donor stabilization



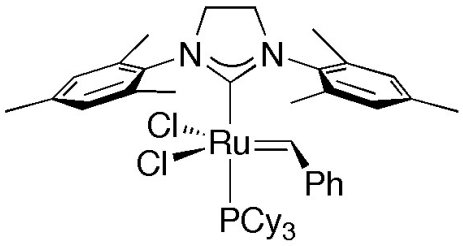
Arduengo, *JACS* **1991**, *113*, 361

Trick 2 : very bulky
substituents R (wingtip groups)

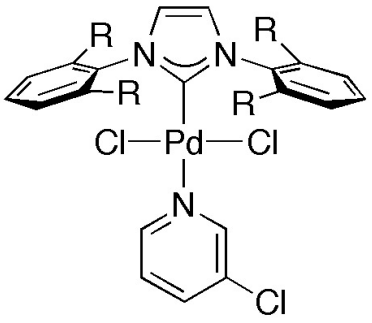
Potential as ligand:

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

N-heterocyclic carbenes as catalyst promotors

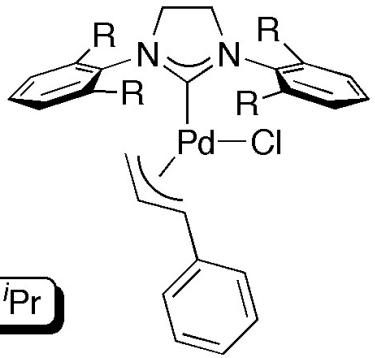


Grubbs 1999



Organ, 2006

R = ^{i}Pr



Nolan, 2006

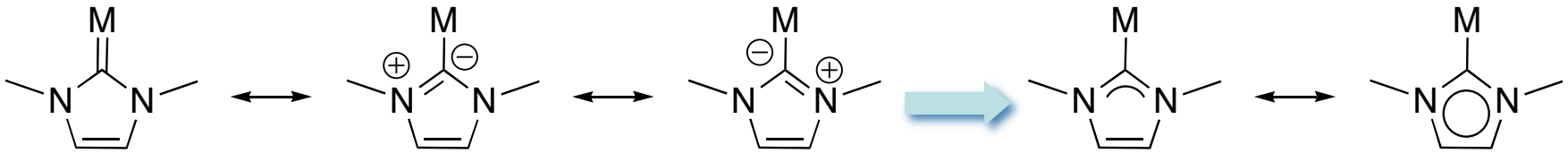
Variations:

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

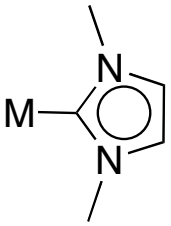
covalent M–carbene bond & strong donor ability of NHCs

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

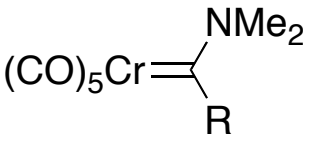
L-type donor or X-type ligand ?



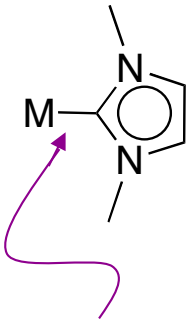
Metal coordination -- dichotomy to Fischer



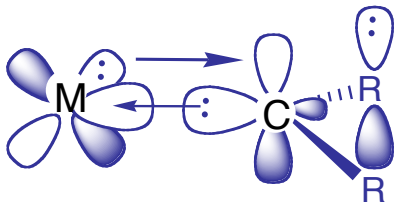
single bond *vs* representations



double bond



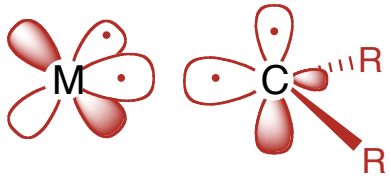
X-ray:
typically single bond lengths



Fischer carbene complexes

ACIE **1964**, *3*, 580

Nobel laureate 1973

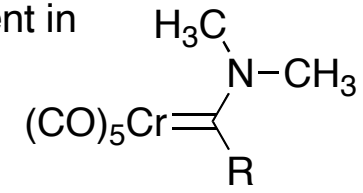


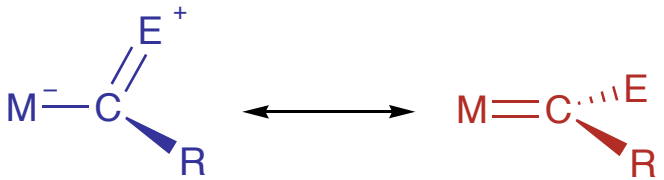
Schrock carbene complexes

JACS **1974**, *96*, 6796

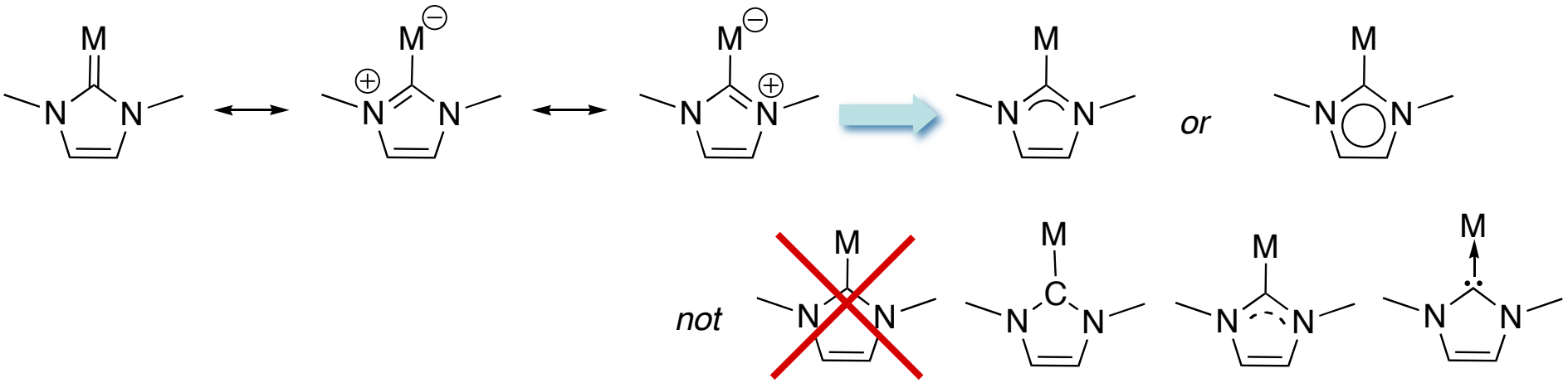
Nobel laureate 2005

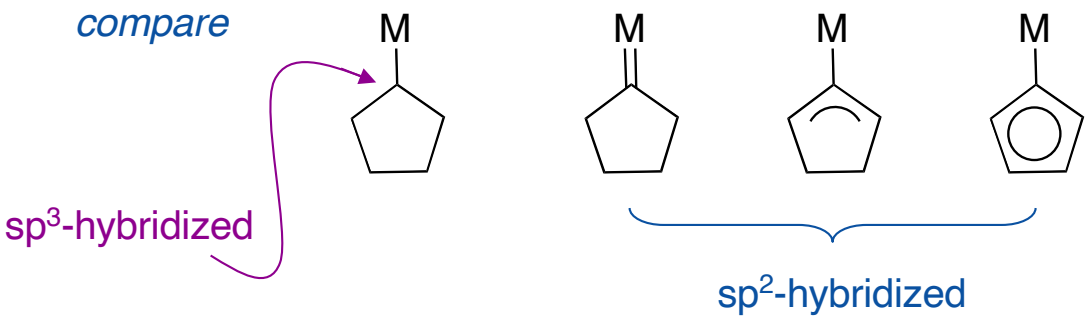
But: CH_3 groups magnetically inequivalent in





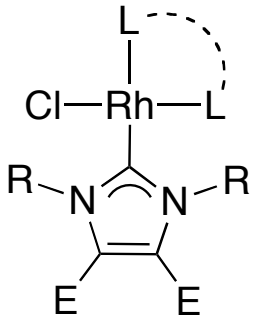
Complex resonance structures





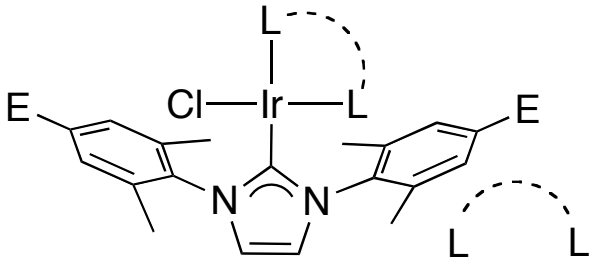
care is needed, some popular notions are wrong

Probing π (de)localization



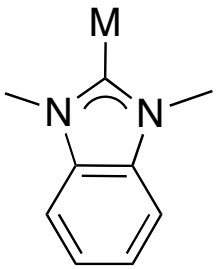
L L = $(CO)_2$ (IR)
= 1,5-cod (NMR)

E = CN/CN, H/H, Cl/Cl, NO_2/H

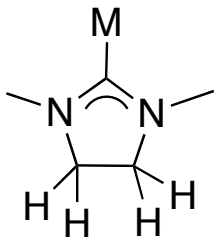


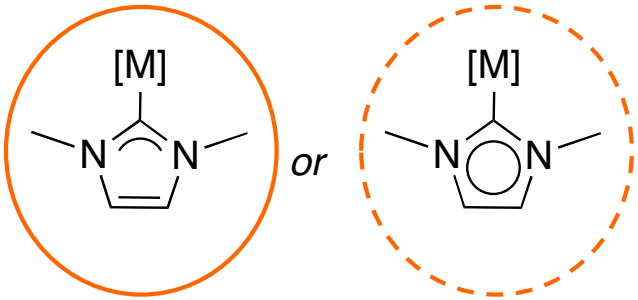
= 1,5-cod (echem)

X-ray: CC bond typically around 1.33 Å

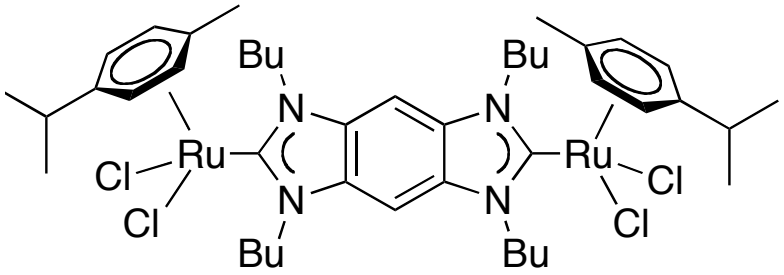


similar to



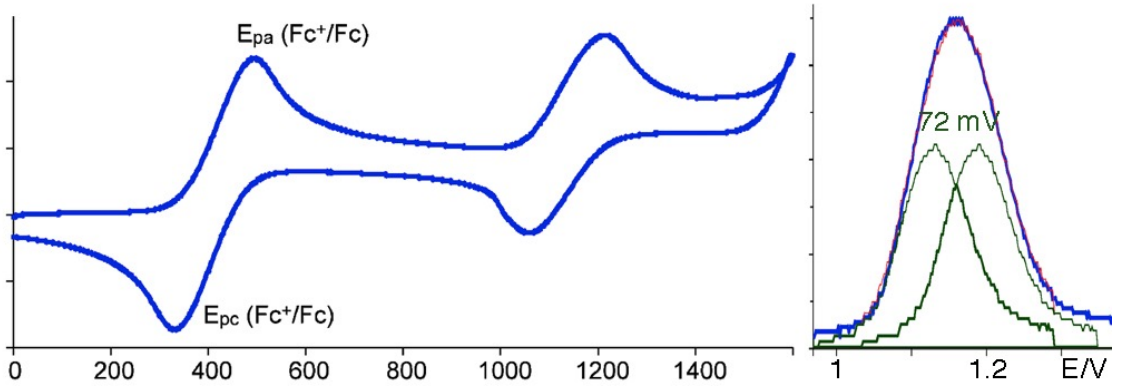


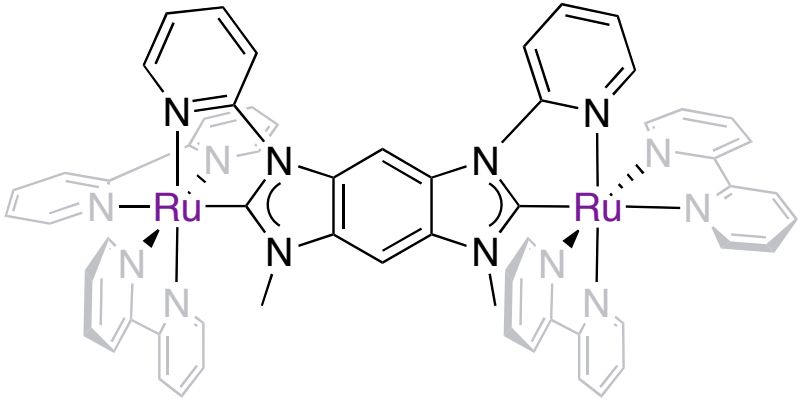
Electronically coupling via carbenes

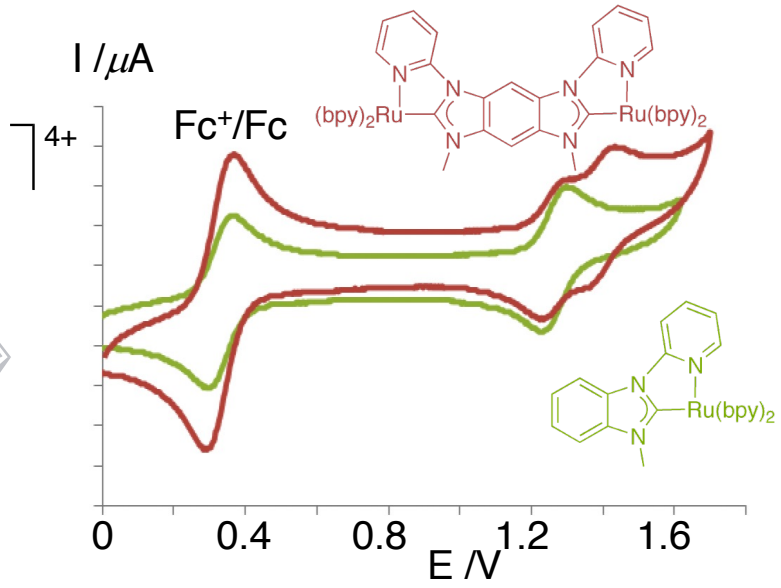


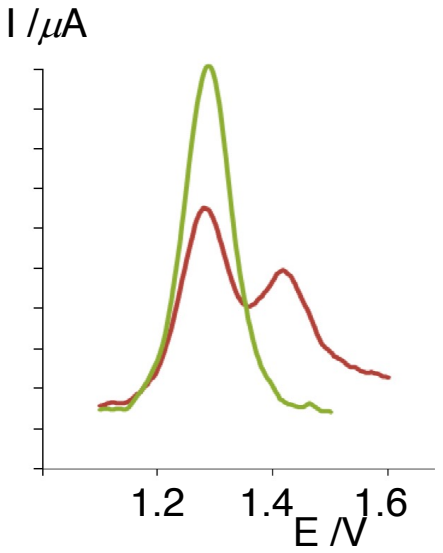
ChemEurJ **2013**, *19*, 17517

cyclic voltammetry *diff pulse volt.*









with Oliver Schuster, *Chem Eur J* **2013**, *19*, 17517

Steric and stereoelectronic impact of carbenes

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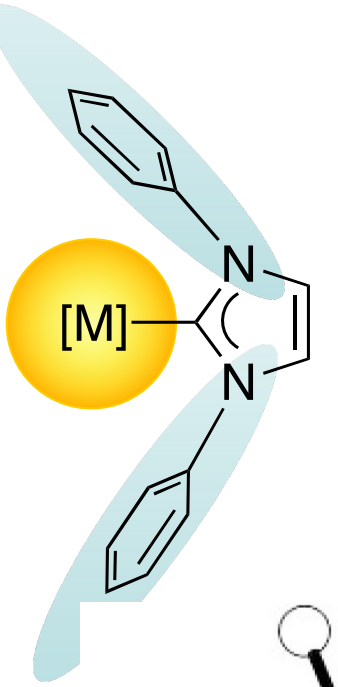
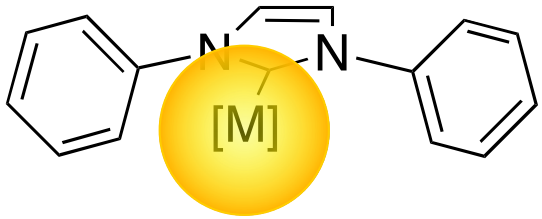
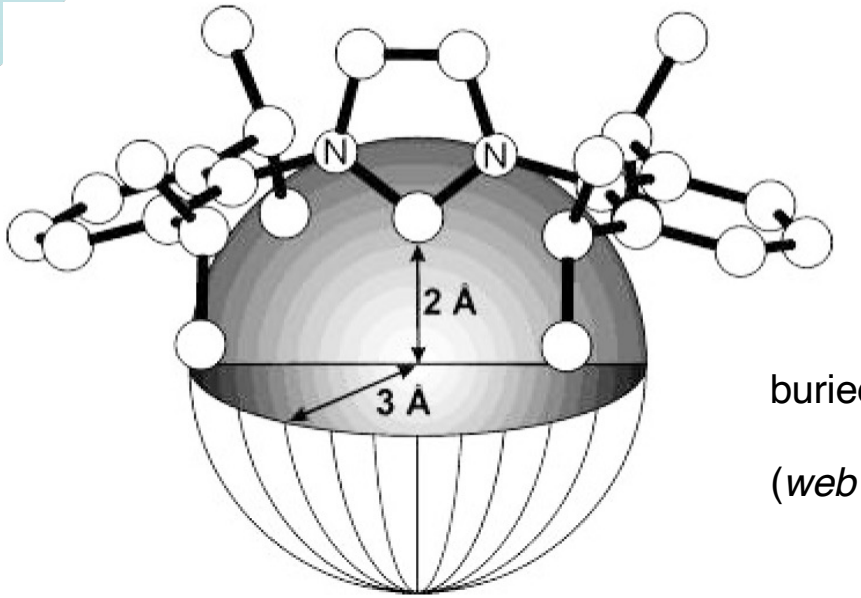
fan-like sterics







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

(*web application*)

Quantifying NHC donor ability

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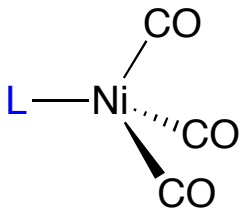
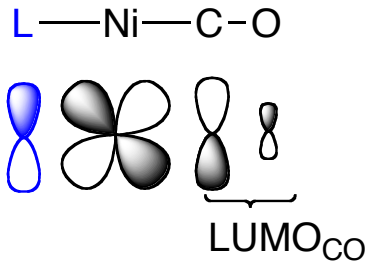
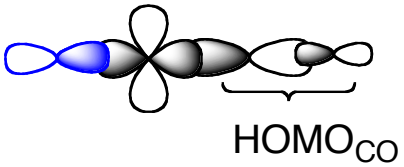
Tolman electronic parameters (TEP)



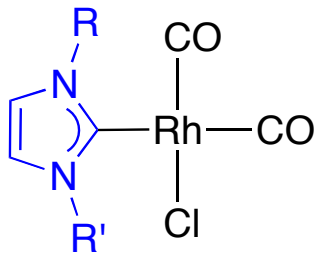


π donor/acceptor



σ donor

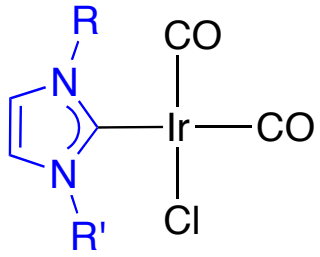
determine ν_{av} (CO) = (ν_{sym} + ν_{asym})/2 in



two bands, ν_{cis} + ν_{trans}

TEP = 1.308 [ν_{av}(CO)] – 612 cm^{-1} — *Organometallics* **2009**, *28*, 3901

ν_{av}(CO)Ir = 0.867 [ν_{av}(CO)] + 251 cm^{-1} — *JOM* **2009**, *694*, 1487



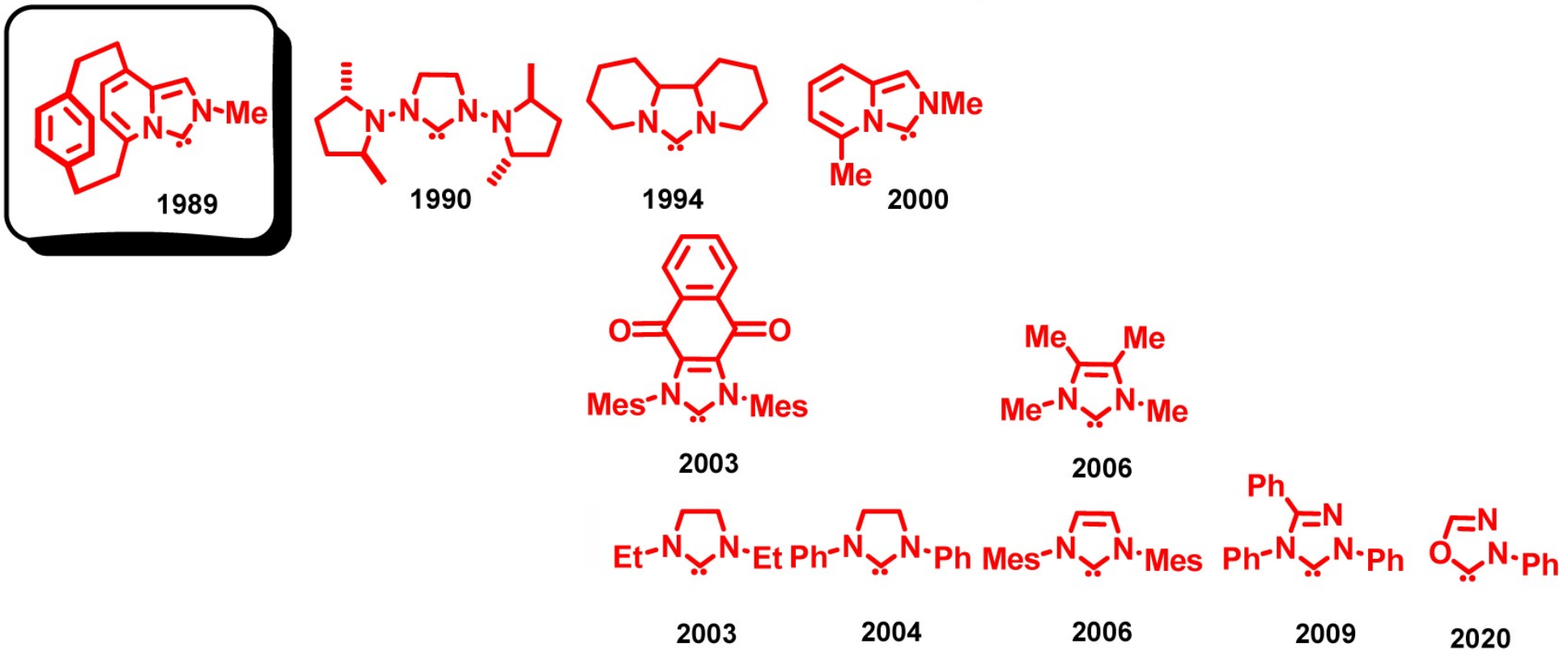
TEP = 0.722 [ν_{av}(CO)] + 593 cm^{-1} — *Organometallics* **2003**, *22*, 1663

TEP = 0.847 [ν_{av}(CO)] + 336 cm^{-1} — *Organometallics* **2008**, *27*, 202

significantly stronger donors than phosphines

Relevance of stereoelectronic parameters

ν_{av} (CO) in NHCRhCl(CO)$_2$)



TEP: stereoelectronic effects not considered -- caution required

Introduction of repulsiveness

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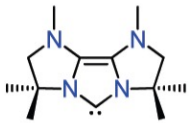
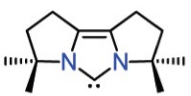
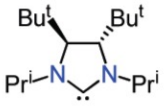
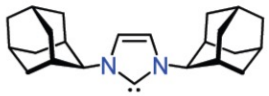
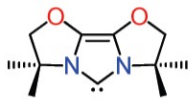
TEP values & repulsiveness factor R (ΔH values for CO dissociation from $LNi(CO)_3$)

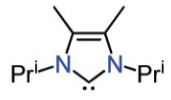

2046.4, 3.5 (16.2)

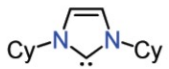

2046.5, 4.0 (15.1)

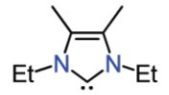

2047.1, 7.3 (7.7)

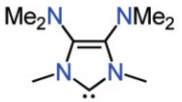

2048.9, 2.4 (18.6)

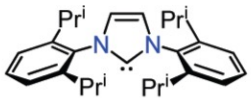

2049.5, 2.8 (17.7)

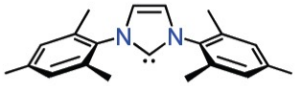

2049.6, 2.2 (18.9)

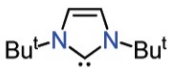

2049.7, 1.6 (20.2)

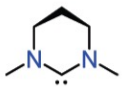

2050.1, 1.5 (20.4)

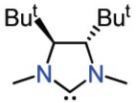

2050.2, 1.3 (21.0)

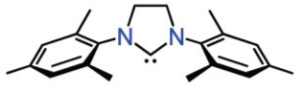

2050.5, 1.8 (19.7)

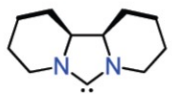

2050.5, 1.5 (20.6)


2050.6, 7.0 (8.2)


2051.0, 3.6 (15.7)

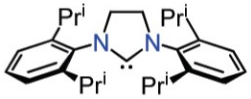

2051.0, 1.8 (19.9)

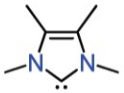

2051.2, 1.9 (19.5)

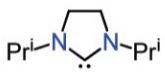

2051.3, 1.7 (19.9)

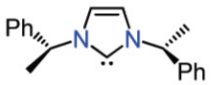

2051.4, 1.3 (20.9)

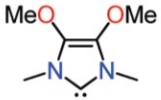

2051.5, 1.6 (20.2)

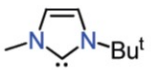

2051.5, 2.5 (18.1)


2051.7, 1.4 (20.7)


2051.9, 2.3 (18.6)

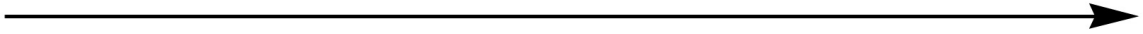

2052.0, 1.5 (20.3)


2052.1, 1.1 (21.2)


2052.5, 3.3 (16.4)

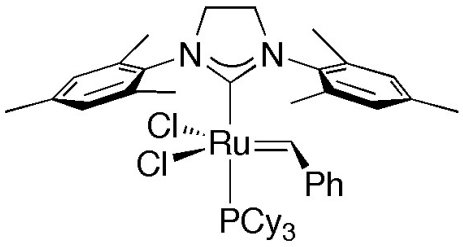
even small NHCs are relatively bulky

ligand donor strength

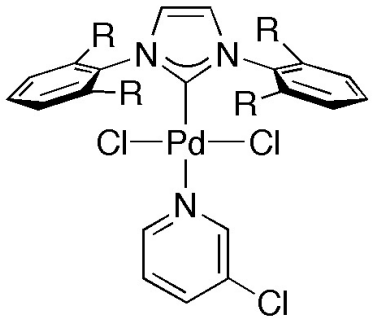


imines, etc. **phosphines** **carbenes**

N-heterocyclic carbenes as catalyst promotors

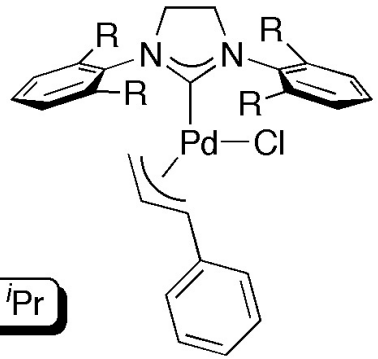


Grubbs 1999



Organ, 2006

R = ^{i}Pr

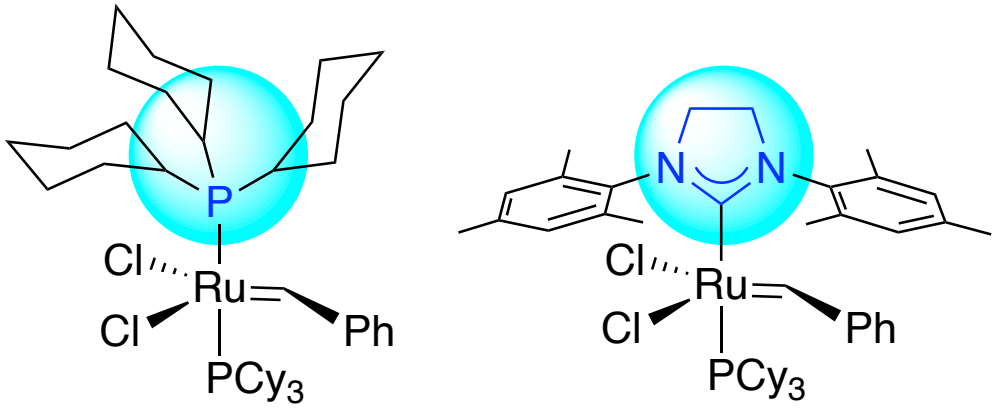


Nolan, 2006

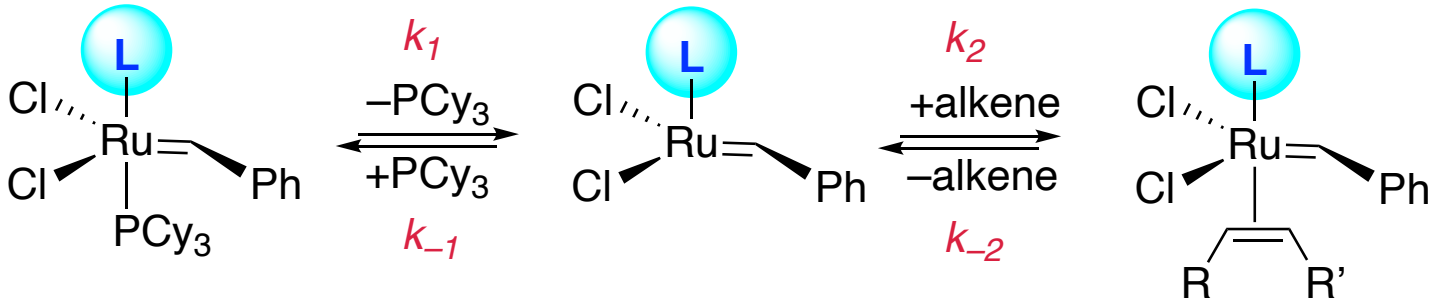
Variations:

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

Ruthenium olefin metathesis catalysis



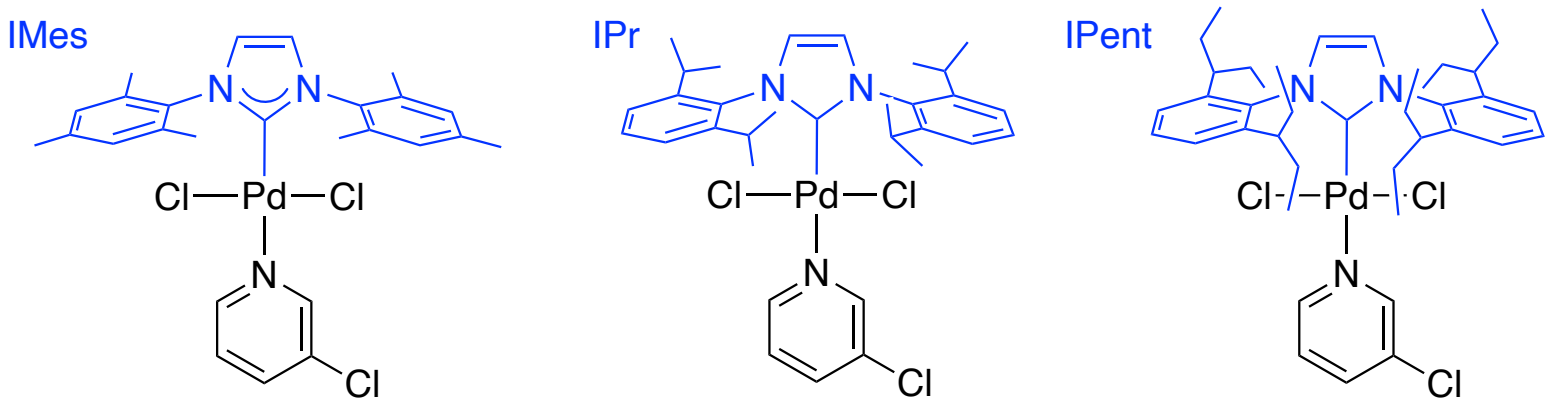
G-I **G-II**



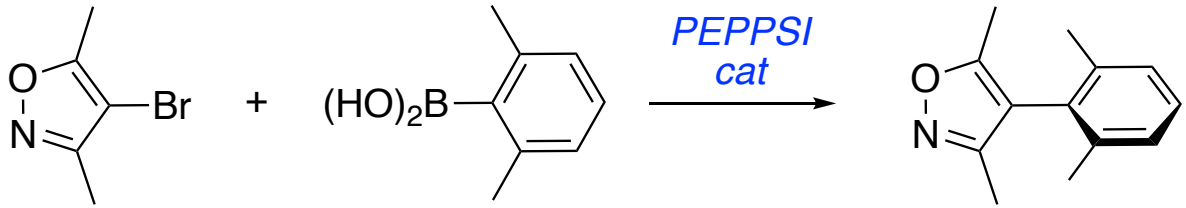
for L = PCy_3	$k_1 = 10^2$	$k_2/k_{-1} = 10^{-4}$
for L = SIMes	$k_1 = 1$	$k_2/k_{-1} = 1$

Grubbs, *JACS* **2001**, *123*, 749 & 6543; Chen, *Helv. Chim. Acta* **2003**, *86*, 941

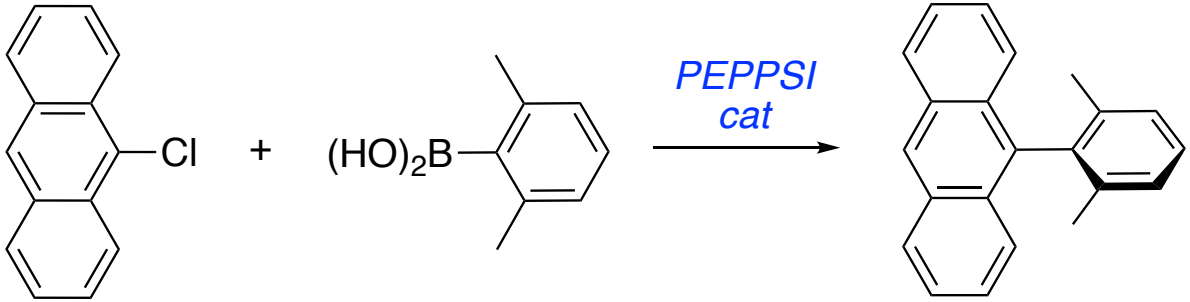
Palladium cross-coupling catalysis



PEPPSI : Pyridine-Enhanced Precatalyst Preparation Stabilization and Initiation



	IPr	IPent	
	87%	69%	65 °C, 24 h KOH, dioxane



	0%	95%	65 °C, 24 h KO*t*Bu, *t*BuOH

Organ, *Chem Eur J* **2006**, *12*, 4743; *Angew. Chem. Int. Ed.* **2009**, *48*, 2383

Catalytic processes beyond metathesis/x-coupling

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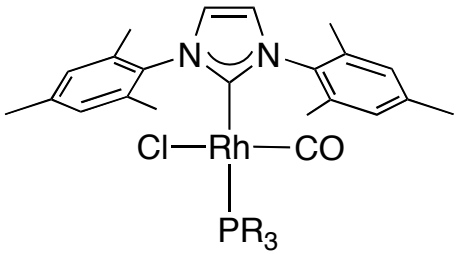
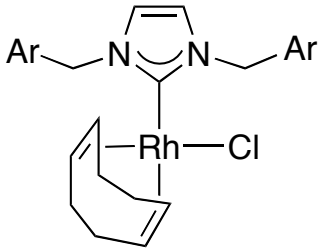
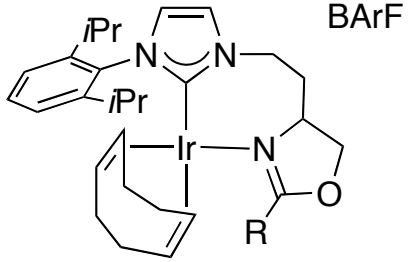
an incomplete listing of reactions with representative catalyst precursors



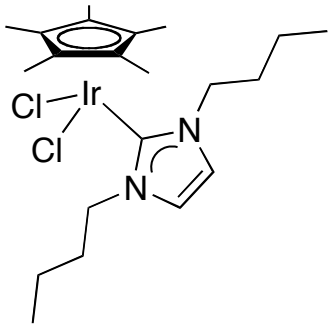
hydroformulation



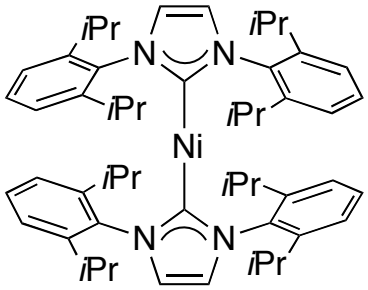
carbonyl arylation



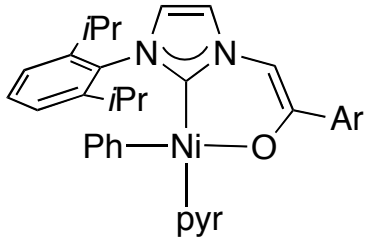
alkene hydrogenation



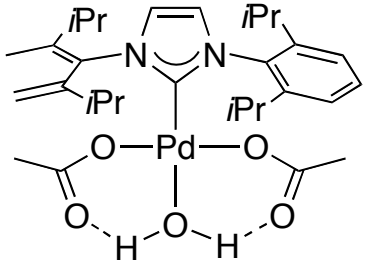
H_2O oxidation H/D exchange



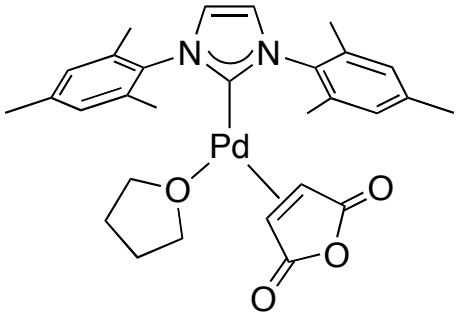
Kumada-Corriu coupling



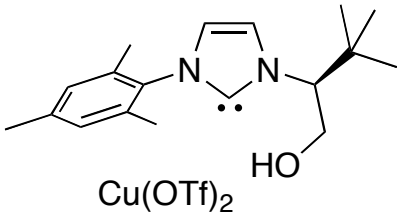
ethylene polymerization



alcohol oxidation



alkyne semihydrogenation



CO_2 reduction, Michael addition

Carbenes with Increased Donor Ability

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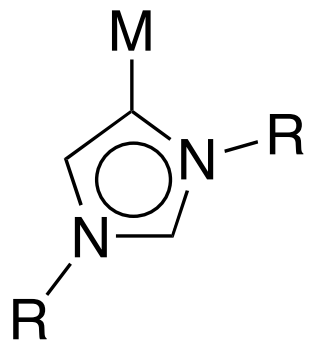
π–donor nitrogens
stabilize free carbene

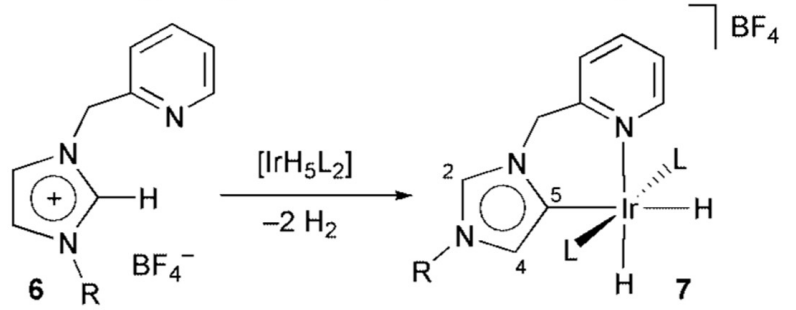


mesoionic/abnormal carbenes

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 $IrH_5(PPh_3)_2$ give an $[(N–C)IrH_2(PPh_3)_2]^+$ species with the imidazole ring bound in the 'wrong way': at C-5, not at the expected C-2.



[**a** R = Pr^i, **b** R = Bu^n; L = PPh_3]

Carbenes with Increased Donor Ability

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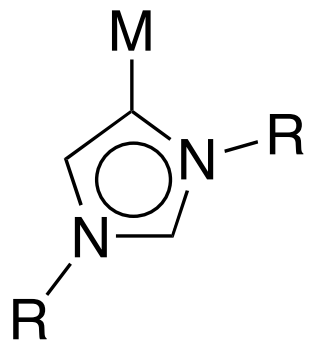
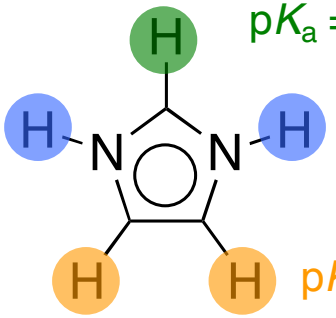
π–donor nitrogens
stabilize free carbene



mesoionic/abnormal carbenes
(no neutral resonance form)

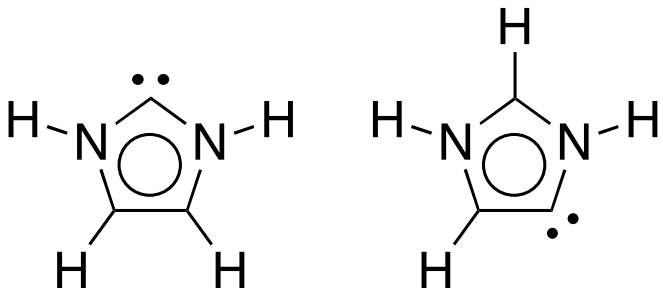


pK_a = 22–25

pK_a = 7.2

pK_a = 26–32 (exp: 30)

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



ΔE ~ +80 kJ mol^{-1}

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

suggests: stronger donor ability

Carbenes with Increased Donor Ability

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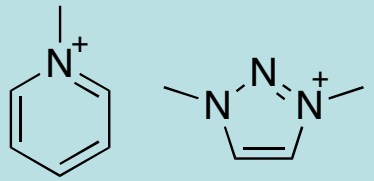
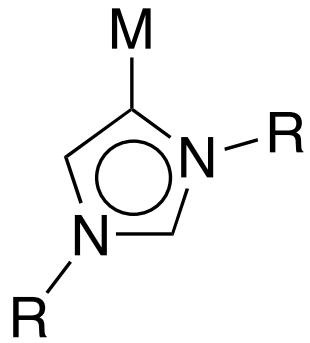
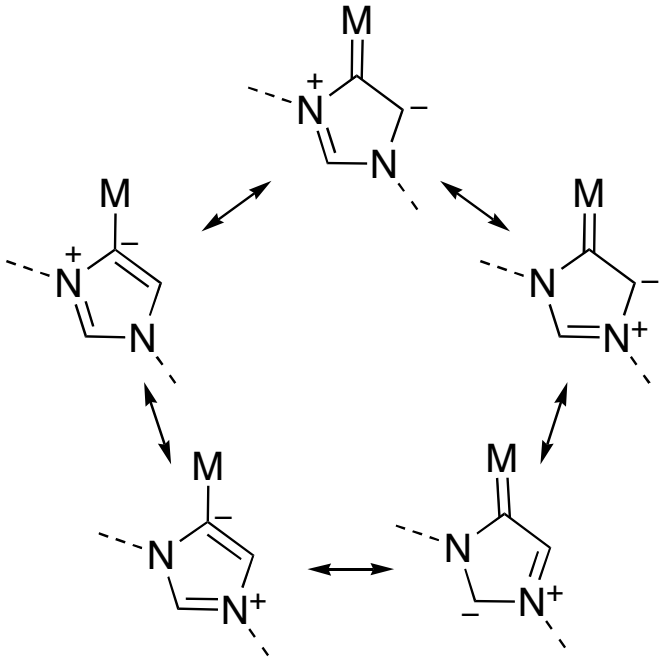
π–donor nitrogens
stabilize free carbene

What is normal/abnormal in





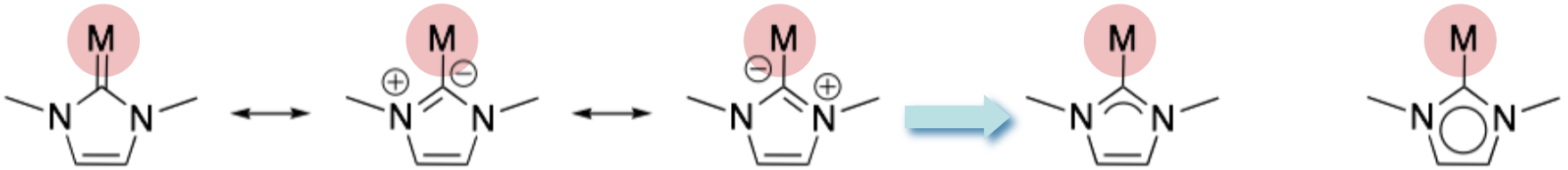
mesoionic/abnormal carbenes
(no neutral resonance form)



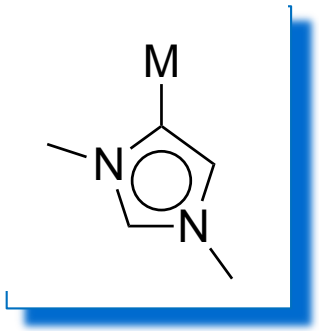
suggests: stronger donor ability
better charge relais

Chem. Commun. **2008**, 3601; *Chem. Rev.* **2009**, *109*, 3445; *Science* **2009**, *326*, 532

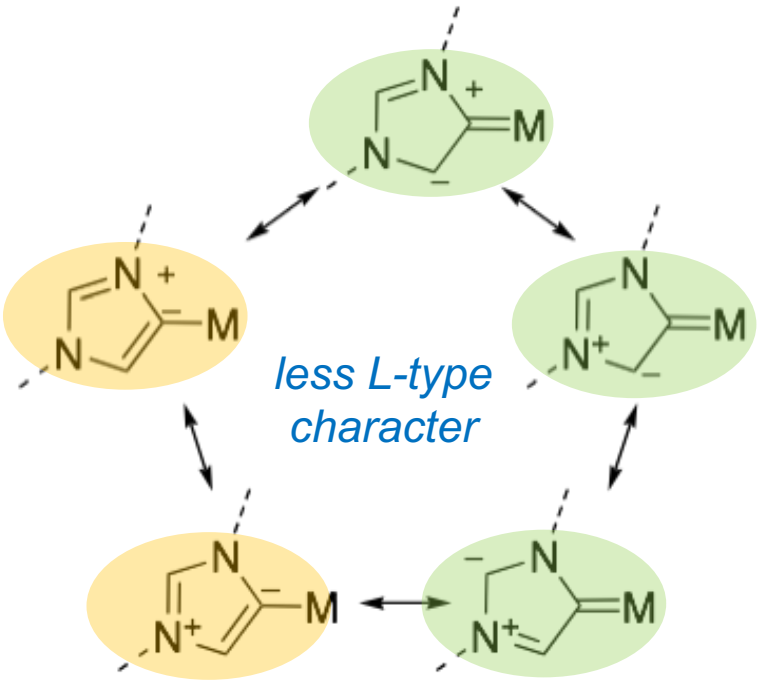
Stronger donor mesoionic carbenes



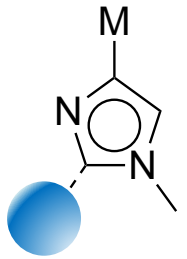
L-type donor (neutral) or **X-type ligand ? (anionic)**



mesoionic/abnormal carbenes



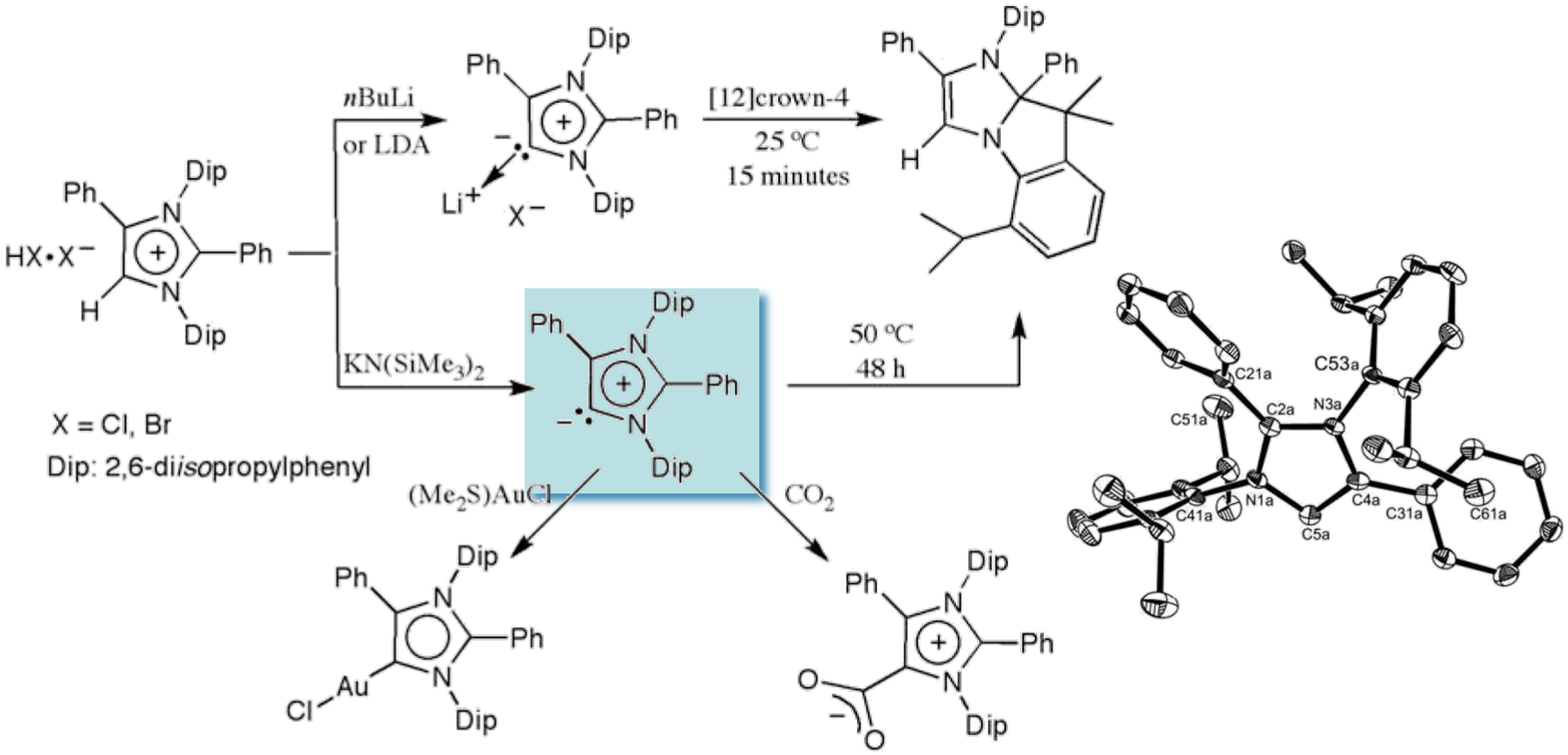
less L-type character



deactivation required

Stable abnormal carbenes

the free carbene route



Isostructural Dicarbene Palladium Complexes

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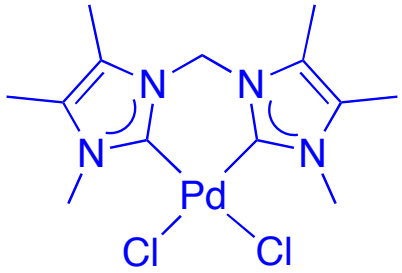
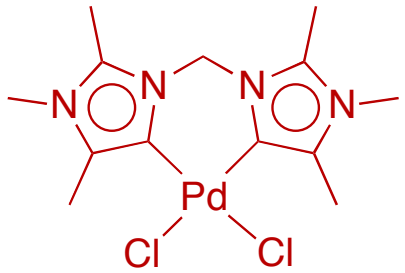
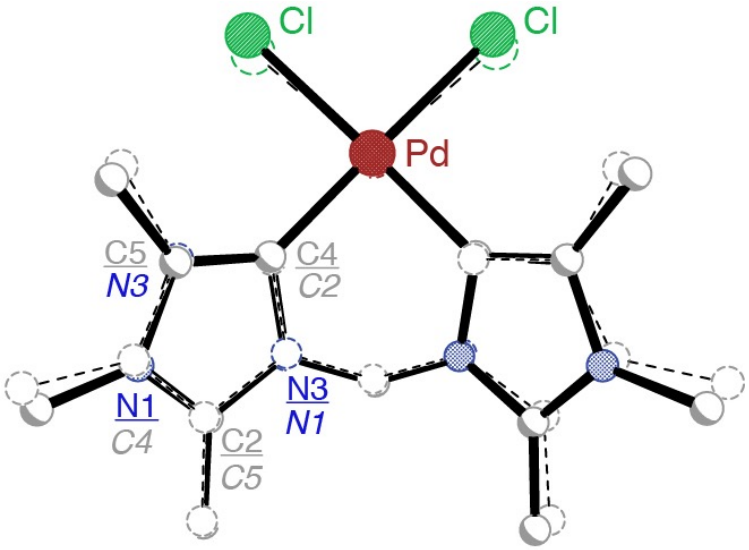
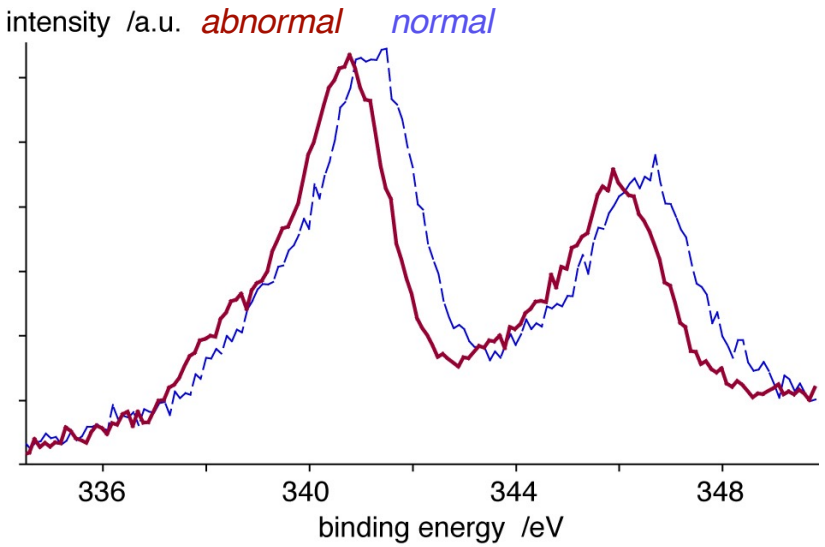
inert towards acids
catalytically **inactive**

acid sensitive
catalytically competent (H_2 activation)





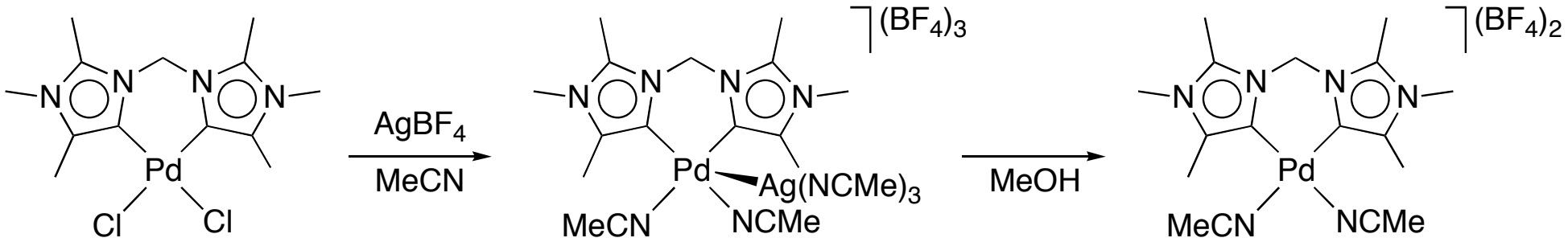


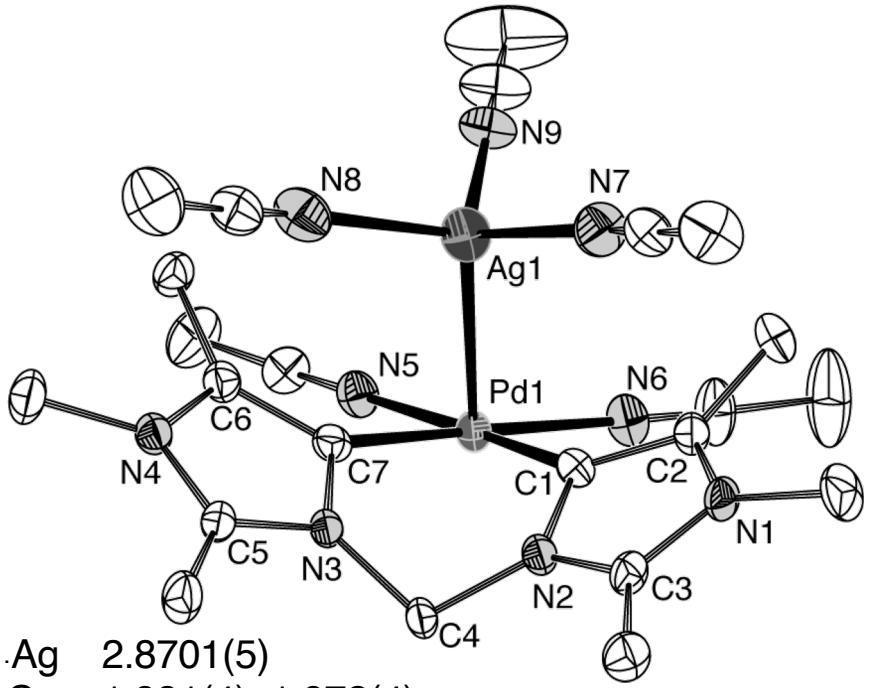


Pd–C	1.979(4), 1.976(5)	1.976(9), 1.981(9)
Pd–Cl	2.359(1), 2.356(1)	2.400(2), 2.407(2)

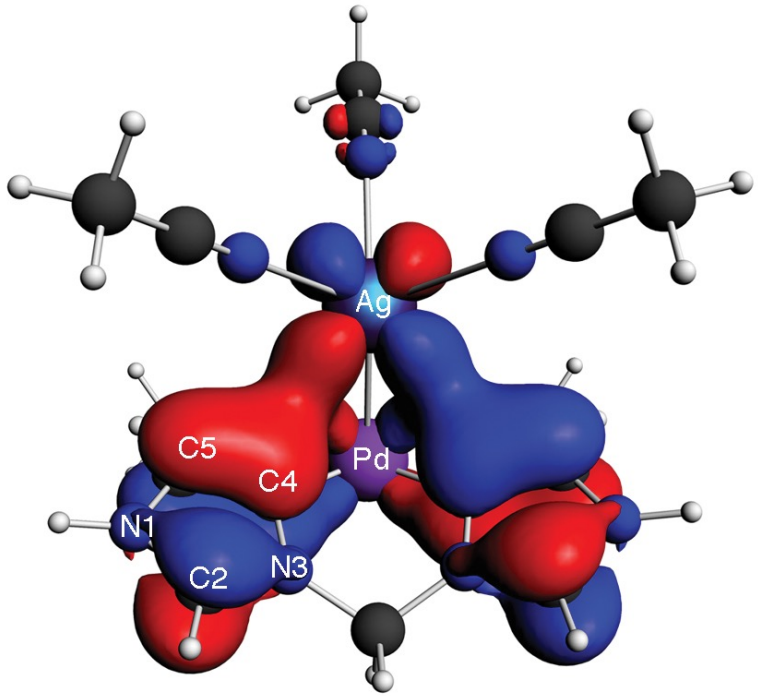
with Marion Heckenroth, *Angew Chem Int Ed* **2007**, *46*, 6293; *Chem Eur J* **2009**, *15*, 9375

Umpolung at the metal: Nucleophilic Palladium(II)



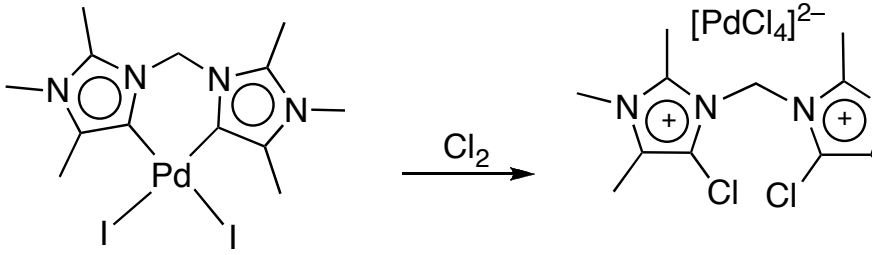


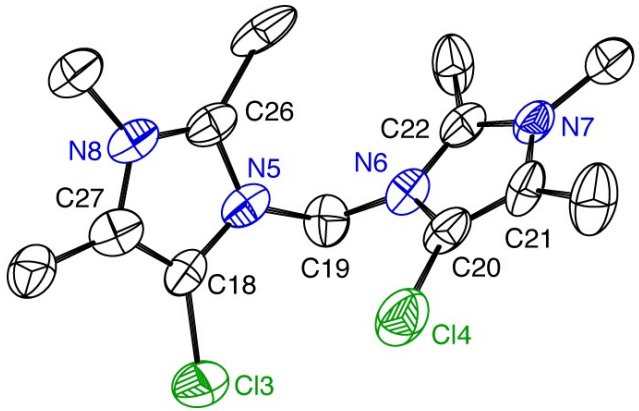
Pd···Ag 2.8701(5)
Pd–C 1.981(4), 1.972(4)

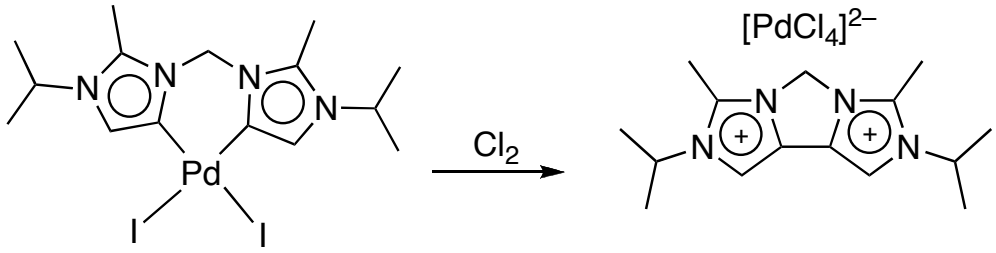


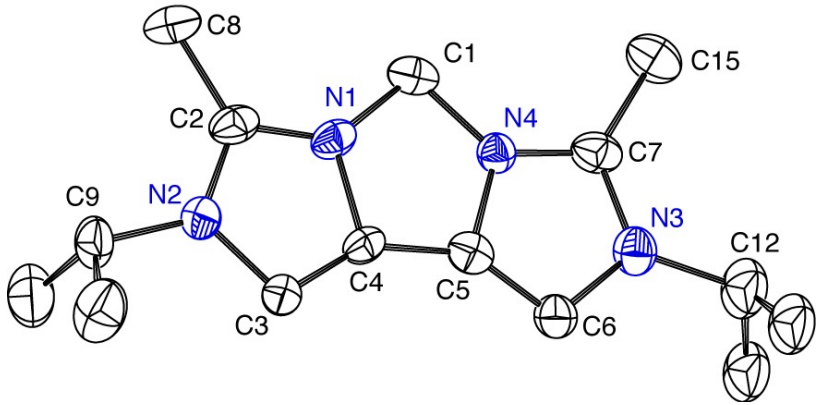
with Marion Heckenroth, *Chem Eur J* **2009**, *15*, 9375; calculations with Andreas Ehlers (VU)

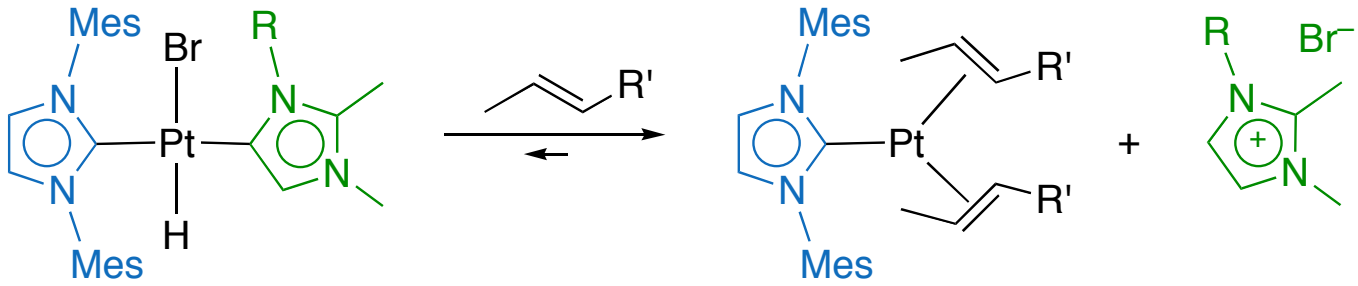
Facile redox reactions







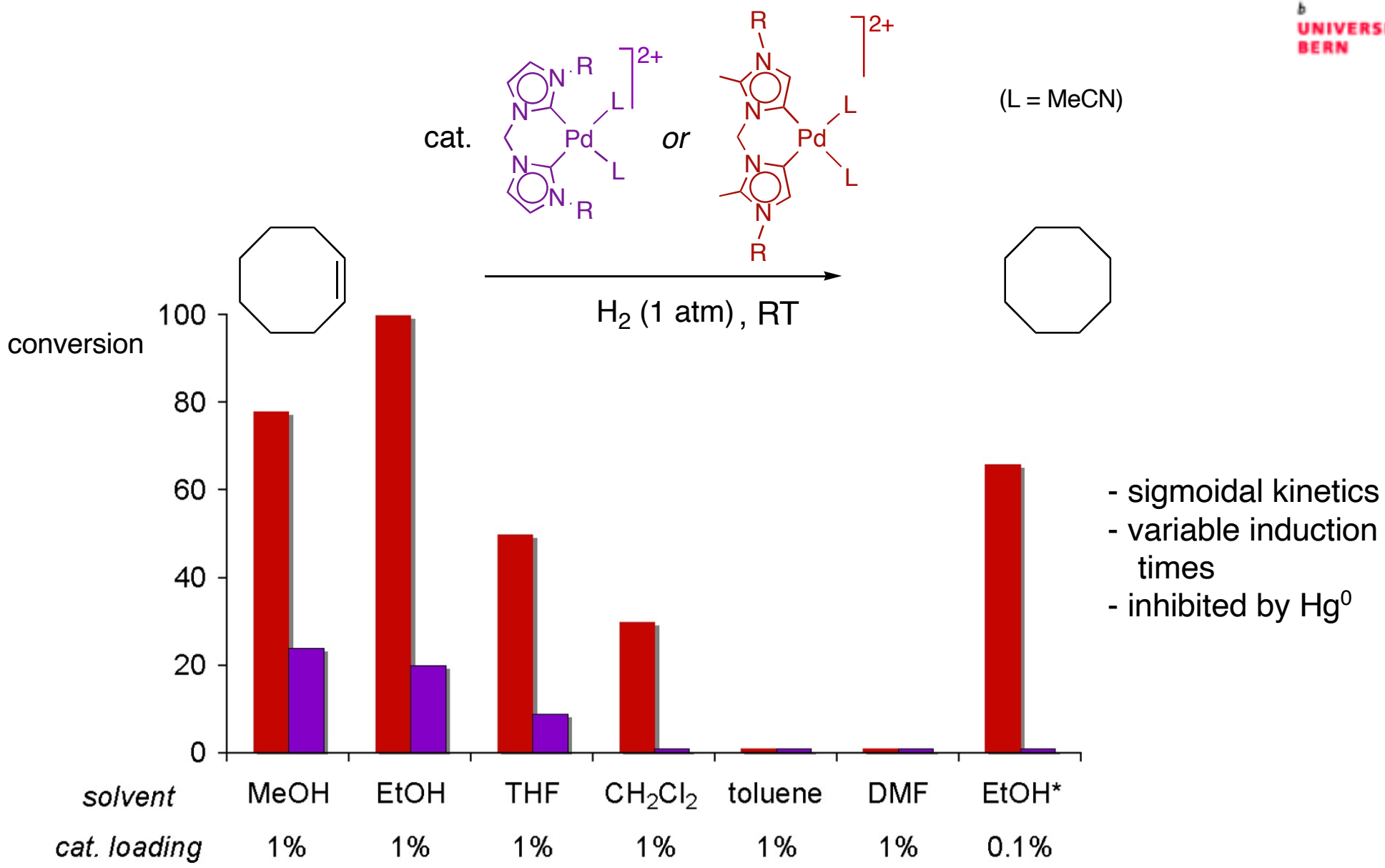




Cavell et al, *Angew. Chem. Int. Ed.*, **2005**, *44*, 5282.

with Marion Heckenroth *Chem Eur J* **2009**, *15*, 9375, Pt with Seva Khlebnikov *Dalton Trans.* **2013**, *41*, 4197

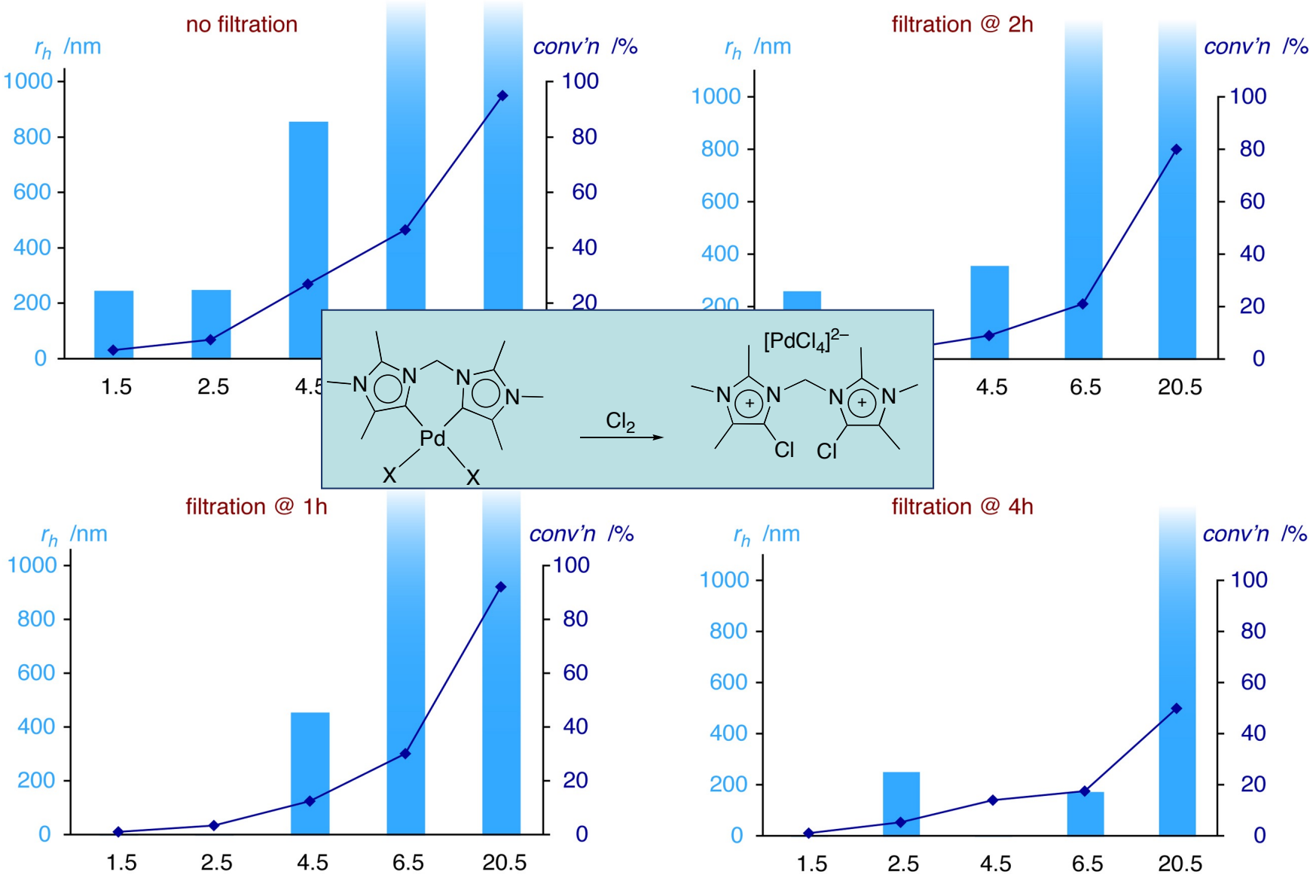
Nucleophilic Palladium: Catalytic H_2 Cleavage



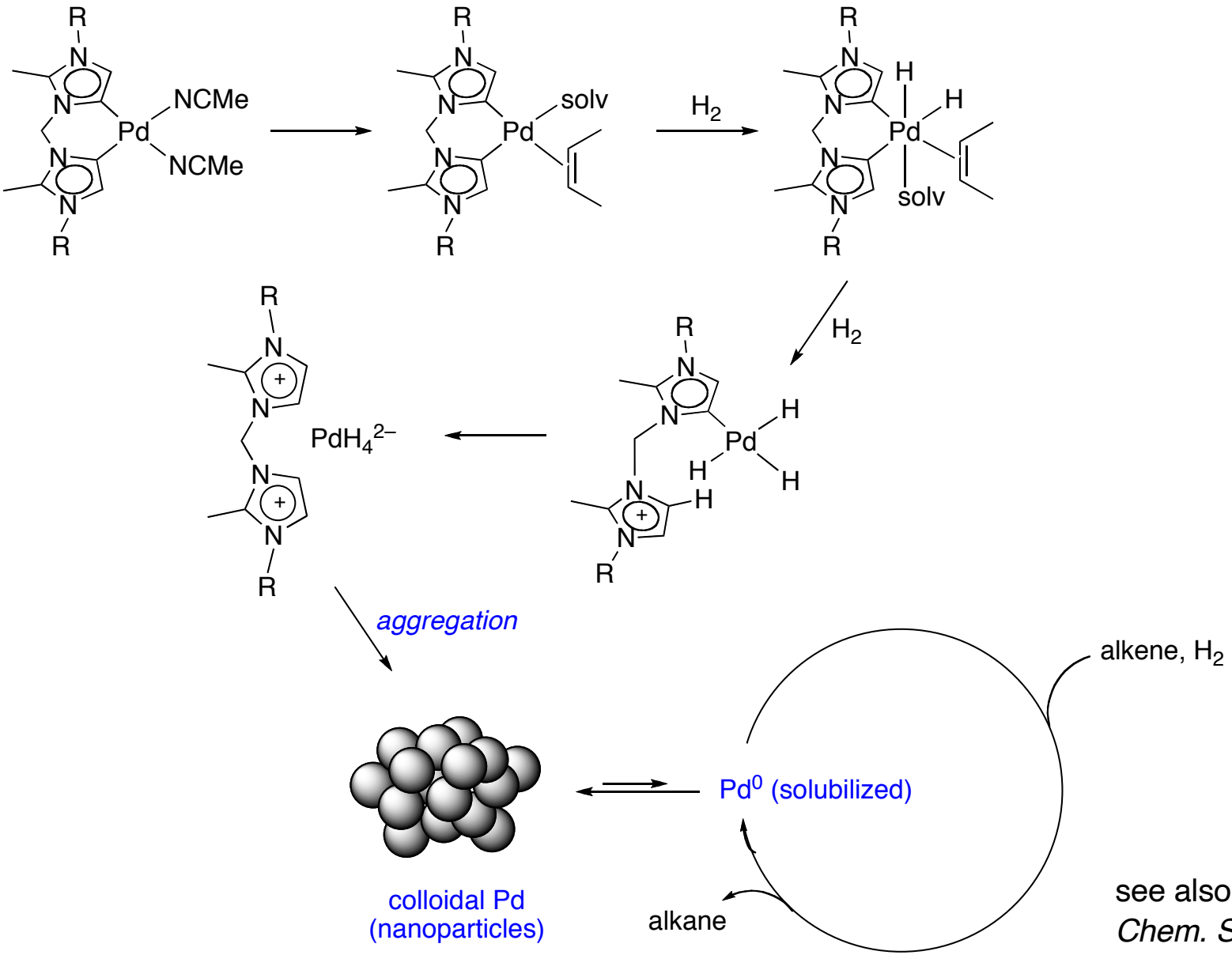
- sigmoidal kinetics
- variable induction times
- inhibited by Hg^0

with Marion Heckenroth *ACIE* **2007**, *46*, 6293

DLS-/GC-Monitoring of Catalytic Runs

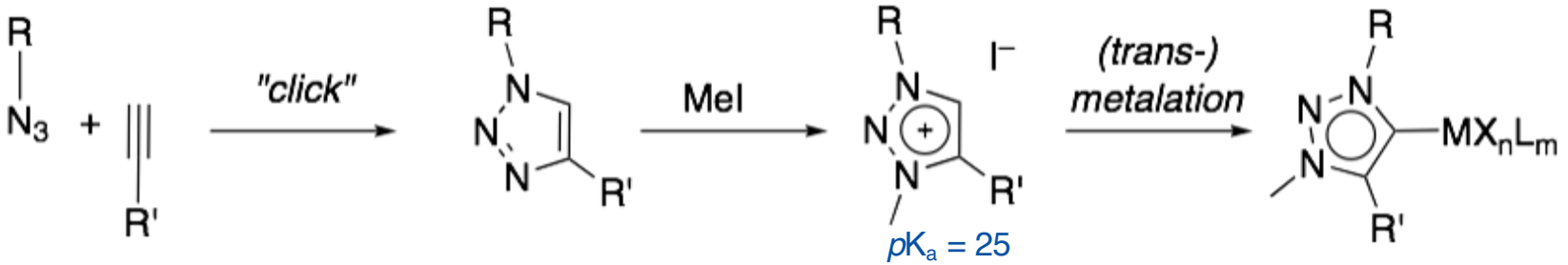


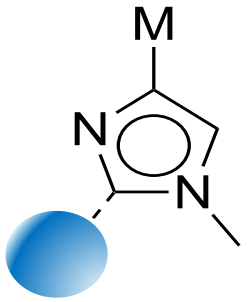
Apparently Homogeneous Olefin Hydrogenation



see also Ananikov,
Chem. Sci. **2020**, *11*, 6957

Facile access to abnormal carbene (complexes)





deactivation required

Triazole-derived click carbene complexes

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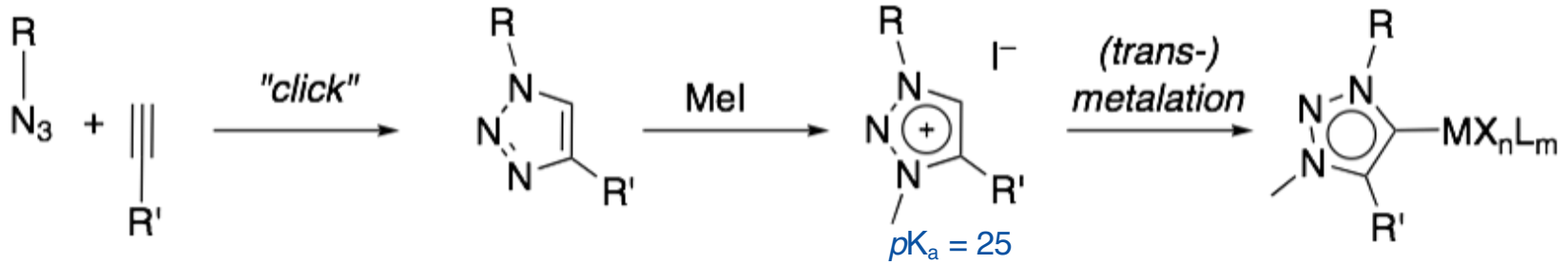
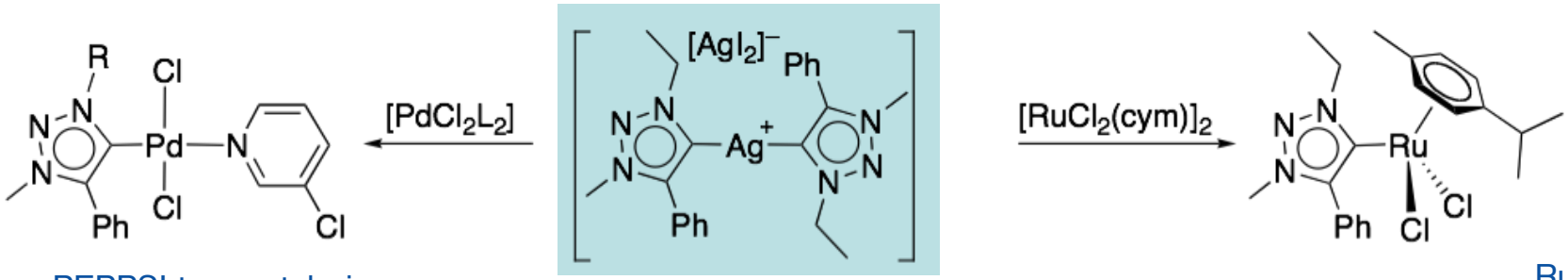
Ligand synthesis:





PEPPSI-type catalysis
CEJ **2012**, *18*, 6055

Ru: alcohol oxidation
OM **2011**, *30*, 1162

Au: oxazoline symthesis
JACS **2013**, *135*, 13193

stronger donor than Arduengo-type NHC

with Paulson Mathew *JACS* **2008**, *130*, 13534; Reviews: *Chem.Comm.* **2013**, *49*, 1145, *Chem. Rev.* **2018**, *118*, 9493

Click carbenes for artificial photosynthesis

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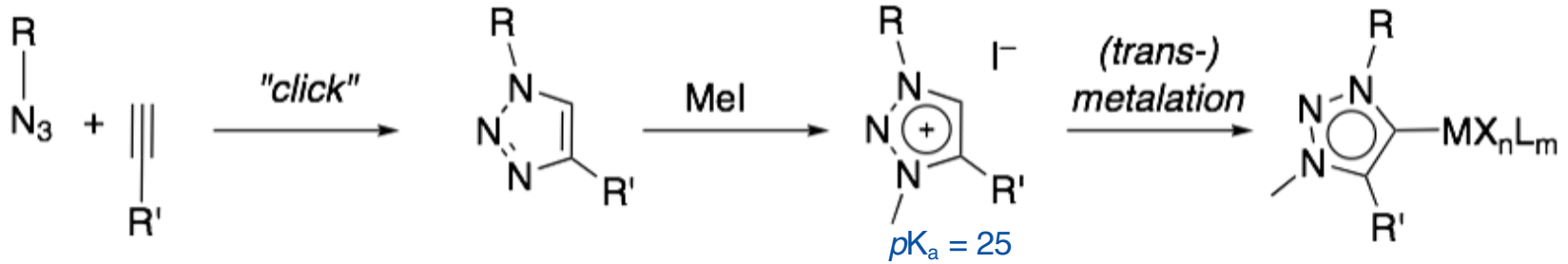
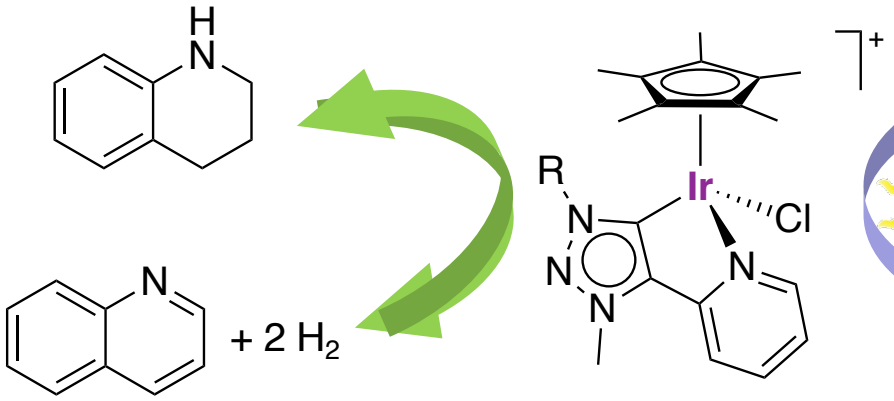
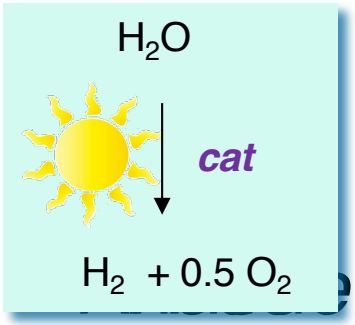
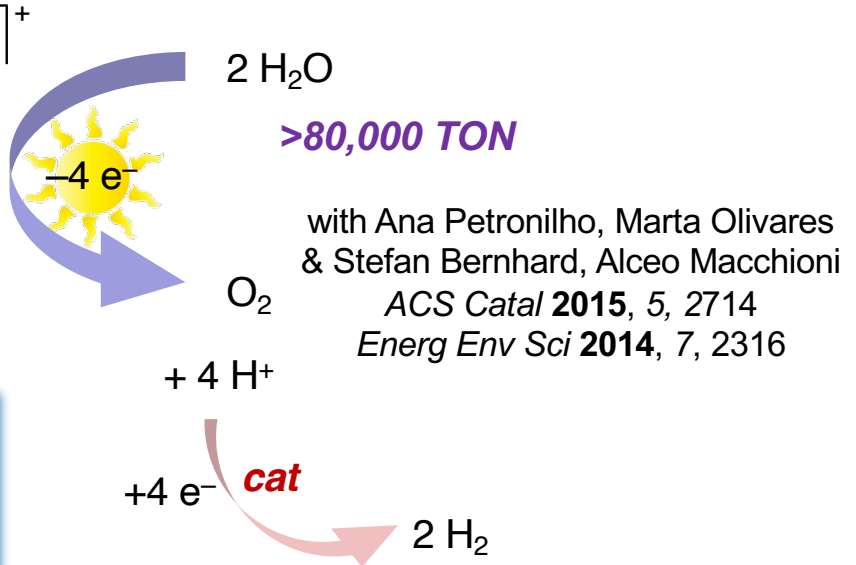
Ligand synthesis:





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





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

Tunability of abnormal carbenes

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

TEP (cm^{-1})

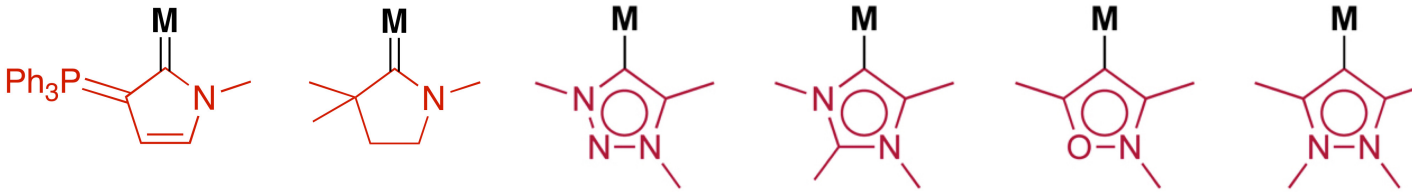
[Pd] = *trans*-$Pd(PPh_3)_2I$

"normal carbenes":

strong M–C_{NHC} bond & high donor ability of NHCs

ligand donor strength

imines, etc. **phosphines** **normal carbenes** **abnormal carbenes**



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!

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Prof. M. Beller (H_2 storage, LiKAT)

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ZUR FÖRDERUNG DER WISSENSCHAFTLICHEN FORSCHUNG

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Mn Fe Co Ni Cu

erc