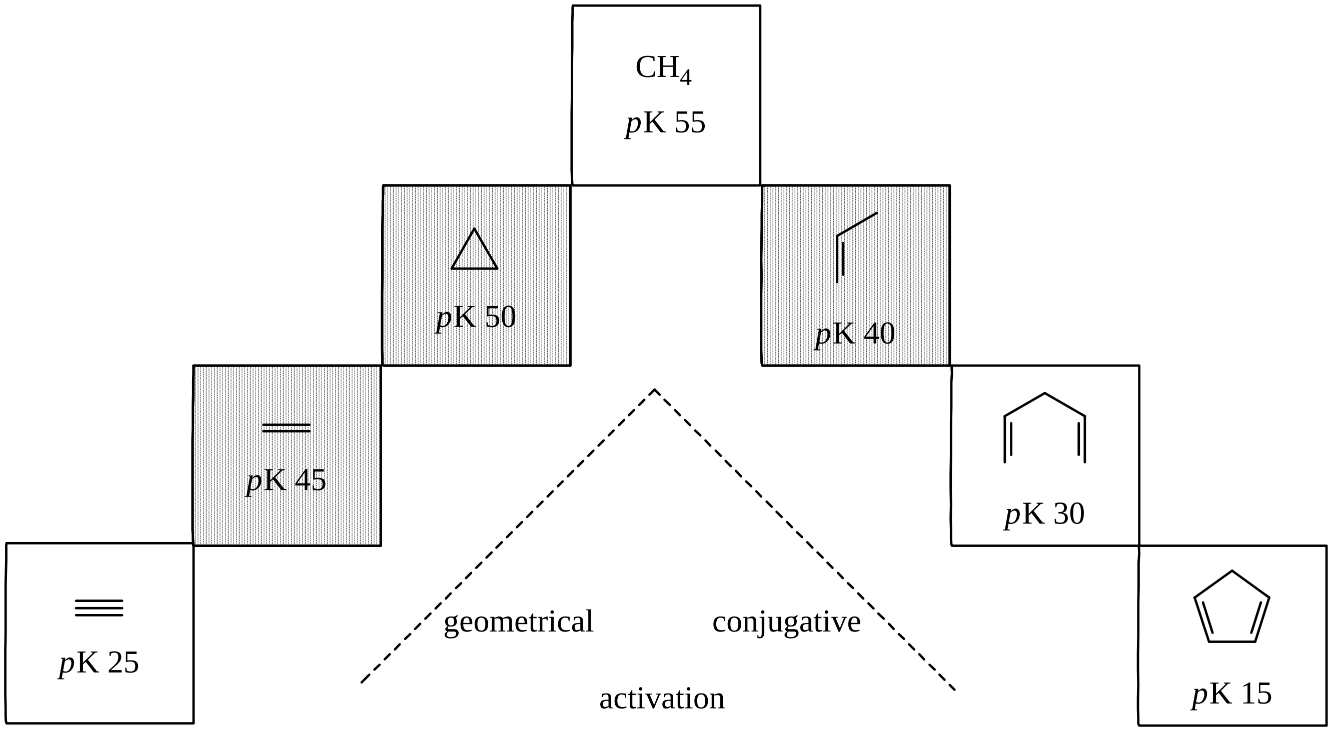
Table of Elements

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
H 1 Hydrogen																	**He** 2 Helium
Li 3 Lithium	**Be** 4 Beryllium											**B** 5 Boron	**C** 6 Carbon	**N** 7 Nitrogen	**O** 8 Oxygen	**F** 9 Fluorine	**Ne** 10 Neon
Na 11 Sodium	**Mg** 12 Magnesium											**Al** 13 Aluminum	**Si** 14 Silicon	**P** 15 Phosphorous	**S** 16 Sulfur	**Cl** 17 Chlorine	**Ar** 18 Argon
K 19 Potassium	**Ca** 20 Calcium	**Sc** 21 Scandium	**Ti** 22 Titanium	**V** 23 Vanadium	**Cr** 24 Chromium	**Mn** 87 Manganese	**Fe** 26 Iron	**Co** 27 Cobalt	**Ni** 28 Nickel	**Cu** 29 Copper	**Zn** 30 Zinc	**Ga** 31 Gallium	**Ge** 32 Germanium	**As** 33 Arsenic	**Se** 34 Selenium	**Br** 35 Bromine	**Kr** 36 ypton
Rb 37 Rubidium	**Sr** 38 Strontium	**Y** 39 Yttrium	**Zr** 40 Zirconium	**Nb** 41 Niobium	**Mo** 42 Molybdenum	**Tc** 43 Technectium	**Ru** 44 Ruthenium	**Rh** 45 Rhodium	**Pd** 46 Palladium	**Ag** 47 Silver	**Cd** 48 Cadmium	**In** 49 Indium	**Sn** 50 Tin	**Sb** 51 Antimony	**Te** 52 Tellurium	**I** 53 Iodine	**Xe** 54 Xenon
Cs 55 Caesium	**Ba** 56 Barium	**La** 57 Lanthanum	**Hf** 72 Hafnium	**Ta** 73 Tantalum	**W** Tungsten	**Re** 75 Rhenium	**Os** 76 Osmium	**Ir** 77 Iridium	**Pt** 78 Platinum	**Au** 79 Gold	**Hg** 80 Mercury	**Ti** 81 Thallium	**Pb** 82 Lead	**Bi** 83 Bismuth	**Po** 84 Polonium	**At** 85 Astatine	**Rn** 86 Radon
Fr 87 Francium	**Ra** 88 Radium	**Ac** 89 Actinium															

La	**Ce**	**Pr**	**Nd**	**Pm**	**Sm**	**Eu**	**Gd**	**Tb**	**Dy**	**Ho**	**Er**	**Tm**	**Yb**	**Lu**
Ac	**Th**	**Pa**	**U**	**Np**	**Pu**	**Am**	**Cm**	**Bk**	**Cf**	**Es**	**Fm**	**Md**	**No**	**Lr**

Acidities of Carbon Acids



CH_4

pK 55

pK 50

pK 40

pK 45

pK 30

pK 25

pK 15

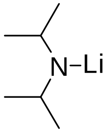
geometrical

conjugative

activation

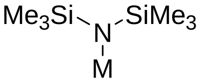
Non-nucleophilic Bases

- Non-nucleophilic bases are used to effect deprotonation and elimination in cases where direct addition of the nucleophile (*e.g. n*.butyl lithium) could cause problems. These reagents were called ‘harpoon bases’ at one time, because of their ability to effect kinetic deprotonation very efficiently.
- LDA (lithium di-*iso*-propylamide is the most common one of these. It is formed by treating a cooled (-78 °C) THF solution of dried and distilled di-*iso*-propylamine with 100 mol-% *n*-butyllithium (typically a hexane solution) and allowing the reaction temperature then reach either 0 °C or room temperature. LDA is also commercially available as a *non-pyrophoric* solid. LDA has a *p*K value of *ca*. 34, and is thus suitable for the deprotonation of most common carbon acids.
- The silicon based amides (KHMDS, NaHMDS and LiHMDS) are often used in cases where one for some reason cannot use LDA. The *p*K values of these reagents are lower (KHMDS, *p*K ≈ 26), and deprotonation is possible for rather acidic C-acids.
- LiTMP is a more sterically crowded analoogue of LDA, and therefore also slightly more basic. It is often a good choice in cases where LDA does not affect complete deprotonation.



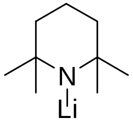
LDA

Lithium di-isopropylamide



M-HMDS

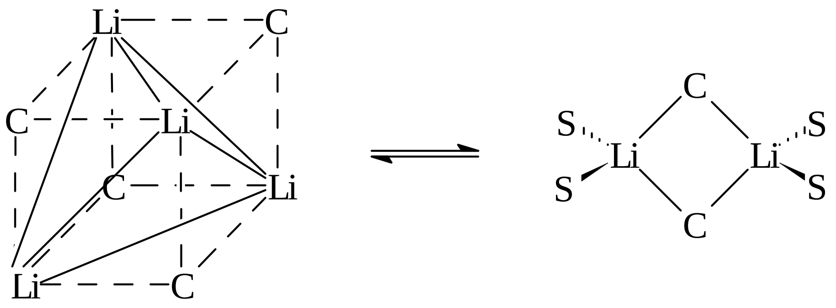
metal-hexamethyldisilazide



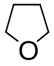
LiTMP

Lithium tetramethylpiperidide

Lithium reagents

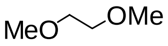


- Alkyl lithium reagents are typically oligomeric in the crystalline state and in solution. The most common form is the tetramer, which is also relatively non-reactive. The reactivity can be enhanced by decomposing the oligomer into dimeric and monomeric species. Good coordinating solvents and cosolvents are used for this purpose.



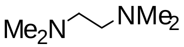
THF

Tetrahydrofuran



DME

Dimethoxyethane



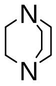
TMEDA

Tetramethylethylenediamine

$(Me_2N)_3P{=}O$

HMPA

Hexamethyl phosphoric triamide

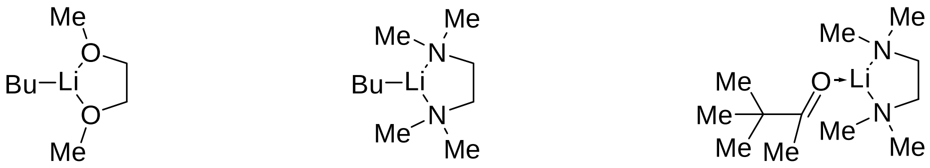


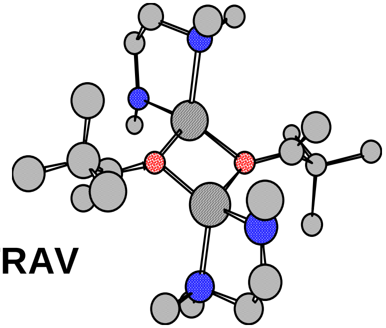
DABCO

Diazabicycloctane

Lithium Reagents

- **Particularly useful for deaggregation are bidentate ligands, such as DME and TMEDA, the latter of which is very often used in difficult metallation reactions.**

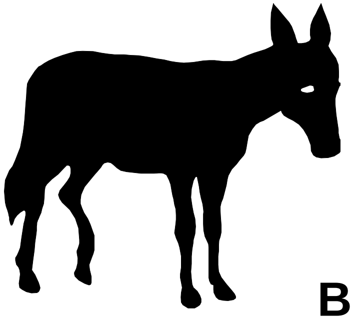




CCDC: DETRAV

- **The reactivity can be enhanced even more, if one uses activation by metal-metal change; the use of potassium *tert*-butoxide in conjunction with butyllithium has proven to be a particularly powerful and reliable superbasic system, known as the 'Schlosser base' or LICKOR.**

BuLi/TMEDA



BuLi/tBuOK

Metal Catalyzed Reactions

- Allow you to perform reactions otherwise impossible or too slow to be practical
- Regio-, stereo- and chemoselectivity often different from uncatalyzed processes
- Traces of metal catalyst used to give:
  - pure products
  - easy isolation
  - little pollution
  - cost effective
- Capable of asymmetric catalysis

Metal Catalysts Take Over Enzymes

- New Reactions
  - metals can promote reactions which do not occur in nature
- Catalyst modifiable
  - ligand modification: chirality inversion
- Unnatural substrates
- High concentrations
- Downstream processing
  - organic solvents accepted
- Stability of catalysts
  - heat, oxidation, pH

Commercial Applications of Metal-catalyzed Asymmetric Processes

Company	*Metal*	*Reaction type*	*Product*
Monsanto	Rh	Hydrogenation	L-Dopa
Sumitomo	Cu	Cyclopropanation	Cilastatin
Anic, Enichem	Rh	Hydrogenation	L-Phenylalanine
J.T.Baker	Ti	Epoxidation	Disparlure
ARCO	Ti	Epoxidation	Glycidols
Takasago	Rh	Rearrangement	L-Menthol
Merck	B	C=O reduction	MK-417 (ophthalmic)
E. Merck	Mn	Epoxidation	Antihypretensive
Takasago	Ru	Hydrogenation	Carbapenem

History

1827	*Zeise's salt* discovered ($K^+[C_2H_4PtCl_3]^-$
1890	*Mond* discovers $Ni(CO)_4$
1891	*Mond and Berthelot* prepare $Fe(CO)_5$
1925	*Fischer-Tropsch* process
1938	*Roelen* discovers Co-catalyzed OXO-process
1948	*Reppe*: acetylene cyclotrimerization
1951	*Orgel, Pauling and Zeiss*: backbonding
1952	Ferrocene (*Wilkinson and Woodward*)
1955	*Ziegler-Natta* polymerisation
1959	*Shaw and Chatt*: oxidative addition
1962	*Vaska complex* discovered
1964	*Fischer*: metal carbene
1964	*Banks*: olefin metathesis
1965	*Wilkinson* Catalyst

History

1971	*Monsanto*: acetic acid process
1973	*Fisher*: first metal-carbyne complex
1974	*Monsanto*: L-DOPA by asymmetric hydrogenation
1978	*Tebbe* reagent
1980	*Brown and Halpern*: Mechanism for the Monsanto process
1980	*Sharpless* Asymmetric Epoxidation
1980	*Noyori* Rh-BINAP
1981	*Schrock*: acetylene metathesis
1983	Activation of methane by oxidative addition
1983	*Itsuno* asymmetric reduction of ketones
1985	Pd-catalysed asymmetric allylation
1986	*Hayashi* asymmetric transmetallation
1987	*Noyori* Rh-BINAP isomerisation
1988	*Sharpless* asymmetric dihydroxylation
1988	*Hayashi* Au-catalysed Aldol-reaction
1990	*Noyori* Ru-BINAP
1990	Asymmetric carboxylation

Recommended Reading

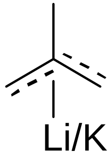
- **Bochmann, M.** *Organometallics 1. Complexes with Transition Metal-Carbon σ-Bonds*. **OUP, 1994, 91 pp.**
- **Bochmann, M.** *Organometallics 2. Complexes with Transition Metal-Carbon π-Bonds*. **OUP, 1994, 89 pp.**
- **Crabtree, R.H.** *The Organometallic Chemistry of the Transition Metals*. **John Wiley & Sons, 1988, 416 pp.**
- **Constable, E.C.** *Metals and Ligand Reactivity - An Introduction to the Organic Chemistry of Metal Complexes*. **VCH, 1996, 299 pp.**
- **Hegedus, L.S.** *Transition Metals in the Synthesis of Complex Organic Molecules*. **University Science Books, 1994, 333 pp.**

Recommended Reading

- **Davies, S.G.** *Organotransition Metal Chemistry: Applications to Organic Synthesis*. **Pergamon Press, 1982, 404 pp.**
- **Collman, J.P.; Hegedus, L.** *Principles and Applications of Organotransition Metal Chemistry*. **University Science Books, 1980, 703 pp.**
- **Schlosser, M. (Ed.)** *Organometallics in Synthesis - A Manual*. **John Wiley & Sons, 1994, 596 pp.**
- **Tsuji, J.** *Palladium Reagents and Catalysts - Innovations in Organic Synthesis*. **John Wiley & Sons, 1995, 549 pp.**
- **Cintas, P.** *Activated Metals in Organic Synthesis*. **CRC Press, 1993, 236 pp.**
- **Gibson, S.E. (Ed.)** *Transition Metals in Organic Synthesis - A Practival Approach*. **Oxford University Press, 1997, 234 pp.**

Organometallics in Solution

- ☞ Aggregation number often higher in hydrocarbon solvents than in ethereal solvents
  - EtLi, BuLi hexameric in hexane; tetrameric in Et_2O, THF
- ☞ Hybridization towards increasing s-character disfavors aggregation
  - *i*PrLi tetrameric in ethers, PhLi dimeric/tetrameric
- ☞ Charge delocalization disfavors aggregation



monomeric in THF

- ☞ Low temperatures cause deaggregation
  - BuLi in THF at < -100 °C dimeric

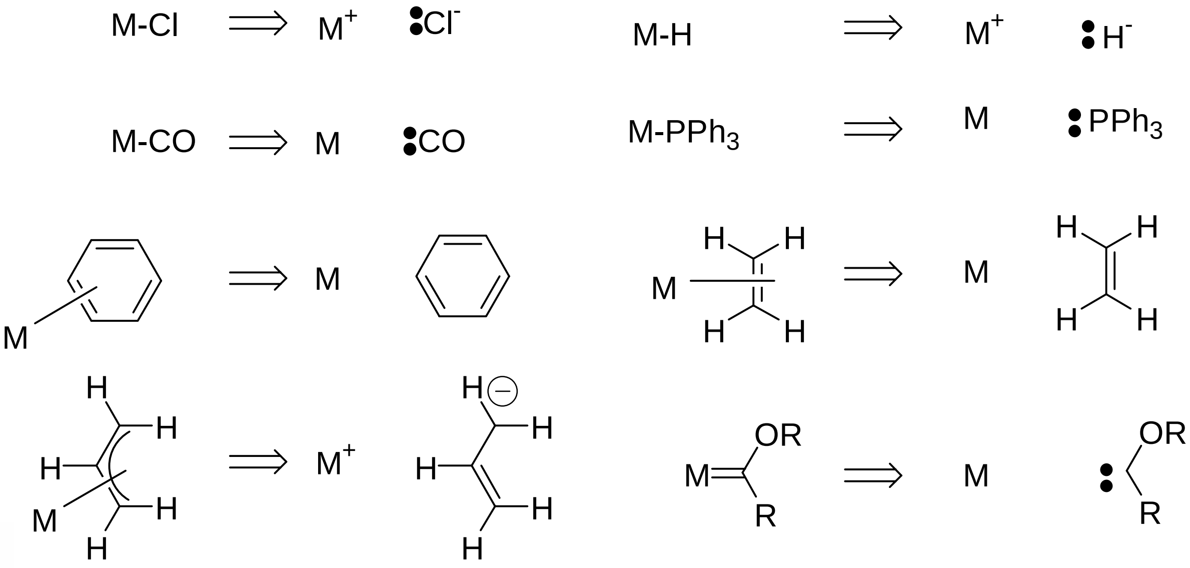
Transition metal organometallics

- Reactions proceed within the coordination sphere of the transition metal. Factors affecting formal mechanisms:

1. Oxidation state of the metal
2. Number of *d* electrons on the metal
3. Coordination number of the metal
4. Availability of vacant coordination sites

Oxidation state

- The oxidation state of a metal is defined as the charge left on the metal atom after *all* ligands have been removed *in their normal, closed shell configuration* – that is, *with their electron pairs*. (NB! Old European style removes anionic ligands as neutral species, *i.e.* homolytically!)



18 Electron Rule

- In mononuclear, diamagnetic complexes, the total number of electrons in the bonding shell (the sum of the metal *d* electrons plus those contributed by the ligands) never exceeds 18.

- Thus, for a d^n metal:

$$n + 2(CN)_{\max} = 18$$

- or, conversely:

$$(CN)_{\max} = \frac{18 - n}{2}$$

18 Electron Rule

Group number	3	4	5	6	7	8	9	10	11
First row	$3d$	Ti	V	Cr	Mn	Fe	Co	Ni	Cu
Second row	$4d$	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag
Third row	$5d$	Hf	Ta	W	Re	Os	Ir	Pt	Au

Oxidation State

									d^n
0	4	5	6	7	8	9	10	-	
I	3	4	5	6	7	8	9	10	
II	2	3	4	5	6	7	8	9	
III	1	2	3	4	5	6	7	8	
IV	0	1	2	3	4	5	6	7	

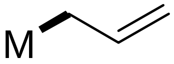
Saturated ligands

- 1e donated to the metal:
  - Cl^-, Br^-, CN^-, -OR, -H, alkyl
  - all formal oxidation state -1
- 2 e donated to the metal
  - PR_3, CO, RCN, RNC, NR_3, R_2O, R_2S
  - all formal oxidation state 0

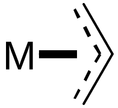
Unsaturated Ligands

Unsaturated ligands	*Electrons*	*Formal charge*	*Hapto number*
Alkyl, aryl, α-allyl	1	(-1)	η1
Olefins	2	(0)	η2
π-Allyl	3	(-1)	η3
Conjugated diene	4	(0)	η4
Dienyls, Cp's	5	(-1)	η5
Arenes, Trienes	6	(0)	η6
Trienyls	7	(-1)	η7
COT	8	(0)	η8
Carbene, NO, Oxo	2	(-2)	
Carbyne, Nitride	3	(-3)	

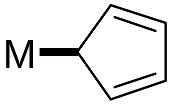
Types of Metal Ligands: hapto number η



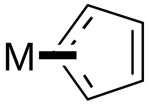
η^1



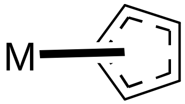
η^3



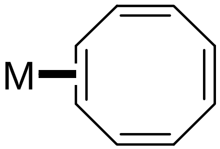
η^1



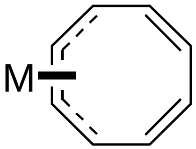
η^3



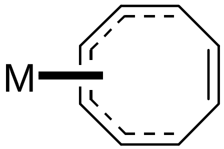
η^5



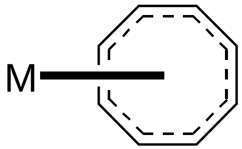
η^2



η^4



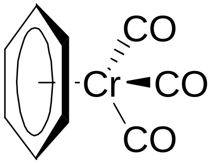
η^6



η^8

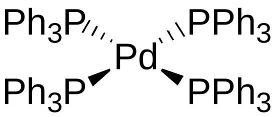
The 18-electron rule

In mononuclear, diamagnetic complexes, the total number of electrons in the bonding shell (the sum of the metal *d* electrons plus those contributed by the ligands) never exceeds 18.



Cr: 6 electrons
Benzene: 6 electrons
3 x CO: 3 x 2 electrons

Total: 18

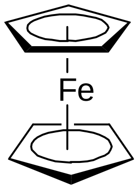


Pd: 10 electrons
4 x Ph_3P: 4 x 2 electrons

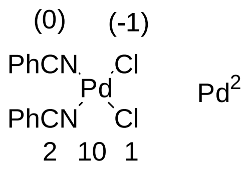
Total: 18

18-electron complexes are stable (i.e. unreactive!)

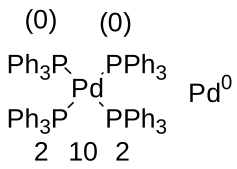
Electron Counting



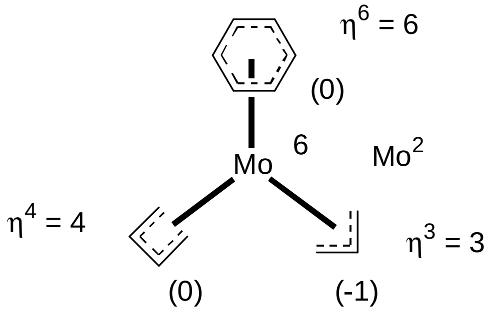
$C_5H_5^-$	6 e^-	$C_5H_5^\cdot$	5 e^-
Fe^{2+}	d^6	Fe^0	d^8
$C_5H_5^-$	6 e^-	$C_5H_5^\cdot$	5 e^-
	18 e^-		18 e^-
Ionic counting convention		Covalent counting convention	



Total: 16 e^-



Total: 18 e^-



Total: 19 e^- ⟹ 1 e^- removed

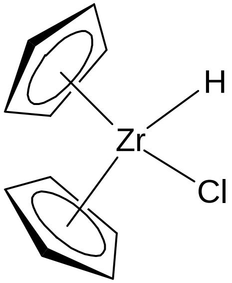
⇓

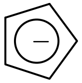
cationic complex

Total: 18 e^-

Stable 16-electron complexes usually adopt a square planar geometry (Ni, Pd, Pt), leaving one vacant orbital high in energy perpendicular to the plane.
The vacant orbital provides a site for further reactions!

Electron Counting



2 x 	6 e$^-$, -1 charge	
H^-	2 e$^-$, -1 charge	
Cl^-	2 e$^-$, -1 charge	

complex is neutrals, 4 x -1 charged ligands

thus, Zr^{IV}, d^0

electron count 0 *d*'s; 12 e$^-$ from 2 Cp
2 e$^-$ from H$^-$, 2 e$^-$ from Cl$^-$

---

overall 16 e$^-$ unsaturated

Complex Stability and Reactivity

$$\begin{tikzcd}
\underset{\mathbf{1}}{RhCl_3.H_2O} + 3\,L \arrow[r, shift left] & \underset{\mathbf{2}}{L_3RhCl_3} \arrow[l, shift left] \arrow[r, shift left, "EtOH"] & \underset{\mathbf{3}}{L_3RhCl_2H} \arrow[l, shift left, "H_2O"] \arrow[d, "EtOH"', "\Delta"] \\
 & & \underset{\mathbf{4}}{L_3RhCl}
\end{tikzcd}$$

L = Et_2PPh ***2*** is isolated

No ***3*** or ***4*** can be isolated

L = $EtPPh_2$ ***2*** is isolated below 25 C

3 is isolated unpon heating

4 can not be produced

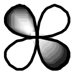
L = PPh_3 ***2*** cannot be isolated

3 can be isolated

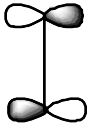
4 is obtained upon heating

Details of π-Bonding

Symmetry of d Orbitals and π* orbitals

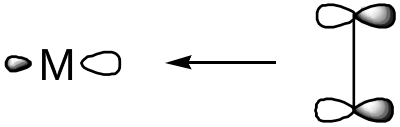


d



π*

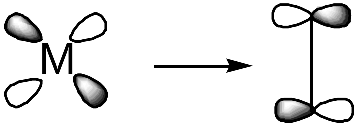
Organic π-bond as a σ-donor



vacant "*dsp*"

filled π

Organic π* orbital as π-acceptor



filled *d*

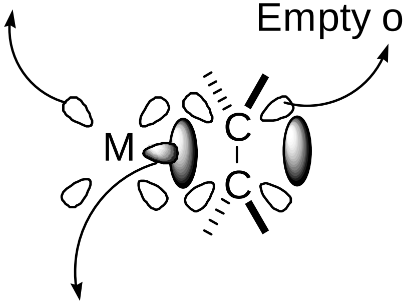
vacant π*

Bonding in Metal Complexes

Metal - Olefin

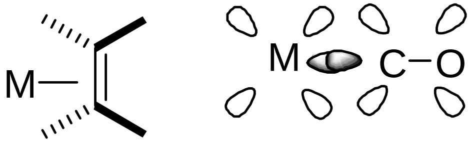
Filled metal d-orbital

Empty olefin π* orbitals



Antibonding metal orbital

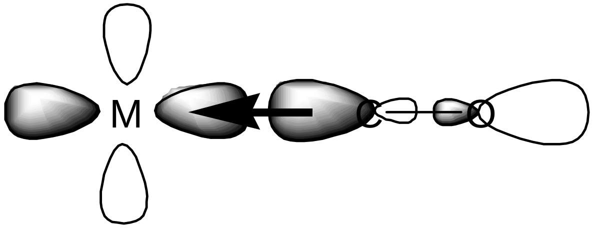
Metal - Carbonyl



$M-C\equiv O$

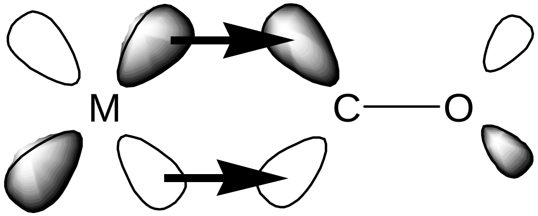
Bonding in Metal Carbonyls

Dative Bond



M-C bond is strenghened

M to CO(π) π bond*



M-C bond is strenghened
C-O bond weakened

Bonding in transition metal complexes 1

1) **Ligand lone pairs and metal orbitals (“dsp hybrid orbitals”) can form a σ-type bond:**

vacant metal orbital

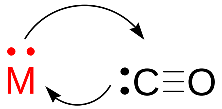
filled ligand orbital (e.g. lone pair)

σ complex

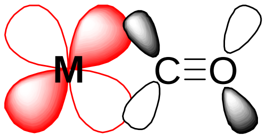
Bonding in transition metal complexes 2

2) **π-Type bonds are possible with CO and alkenes. The filled metal d orbitals can also interact with the p* orbitals of CO or alkenes (back-bonding):**

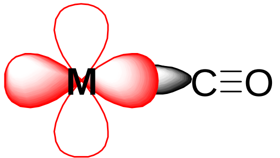
π donation from M to ligand



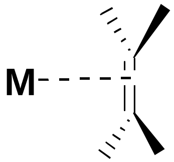
σ donation from ligand to M



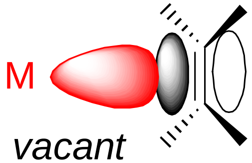
filled d orbital *empty π* orbital*



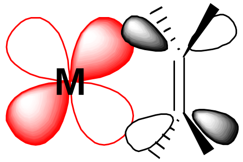
empty d orbital *filled sp orbital*



π complex



vacant metal orbital *filled alkene π orbital*

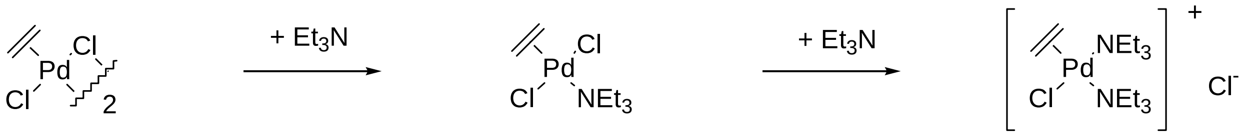


filled d orbital *empty π* orbital*

Ligand Substitution (Exchange)

- For catalytic processes, stable catalyst precursor must lose a ligand, coordinate a substrate, promote the desired reaction, and release the product.

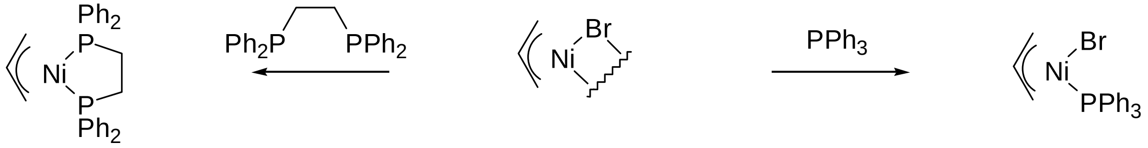
- Sometimes, a spectator ligand must be lost in order to adjust the reactivity of the coordinated ligand.



unreactive toward nucleophiles

reactive toward nucleophiles

- Ligand substitution can also render the complex stable for e.g. isolation for mechanistic studies.

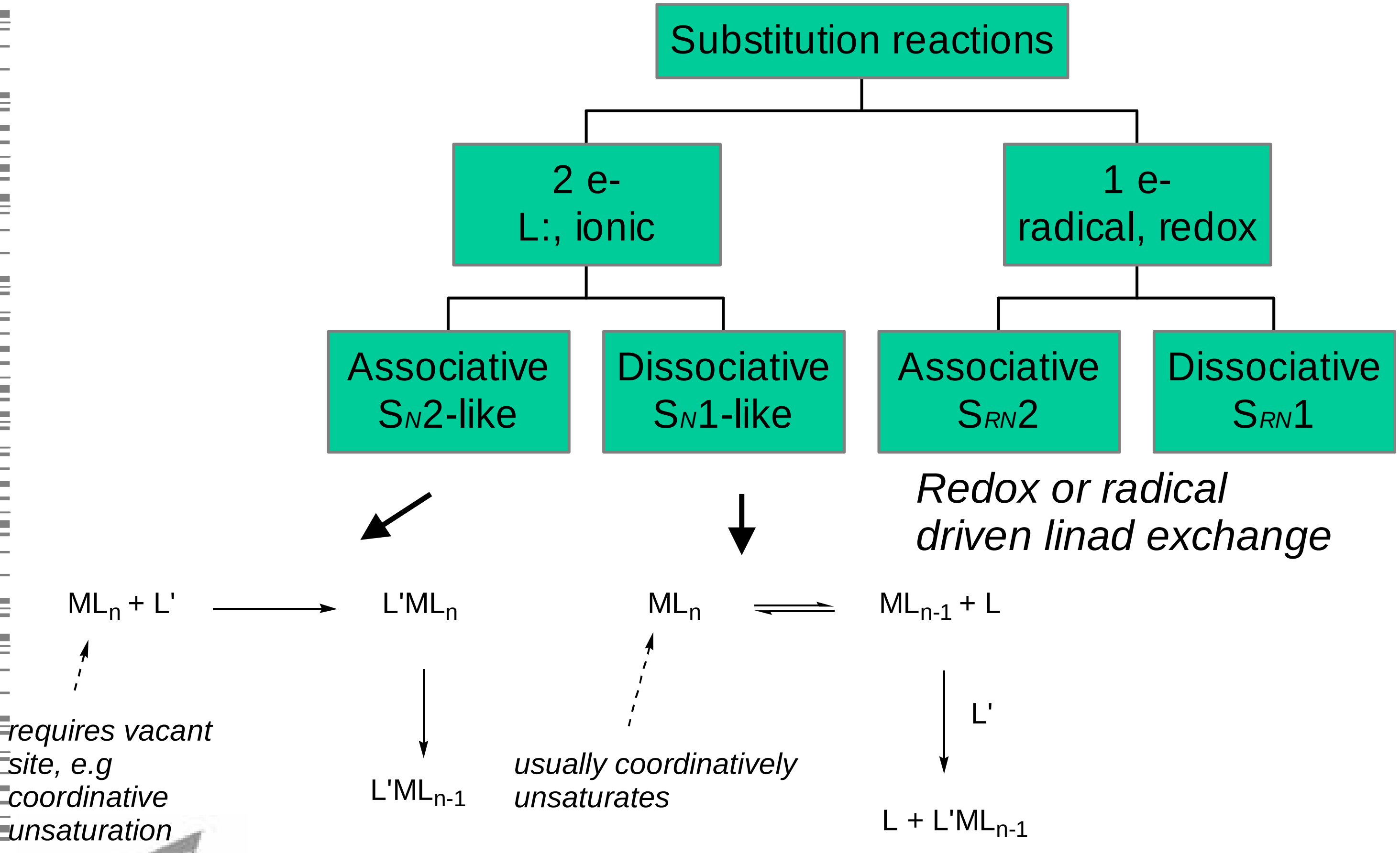


requires HCl/HNO_3 for activation

unstable to air

requires HNO_3 for activation

Classification of Ligand Substitution Processes



Substitution reactions

2 e-
L:, ionic

1 e-
radical, redox

Associative
S_N2-like

Dissociative
S_N1-like

Associative
$S_{RN}2$

Dissociative
$S_{RN}1$

Redox or radical driven linad exchange

$$ML_n + L' \longrightarrow L'ML_n \longrightarrow L'ML_{n-1}$$

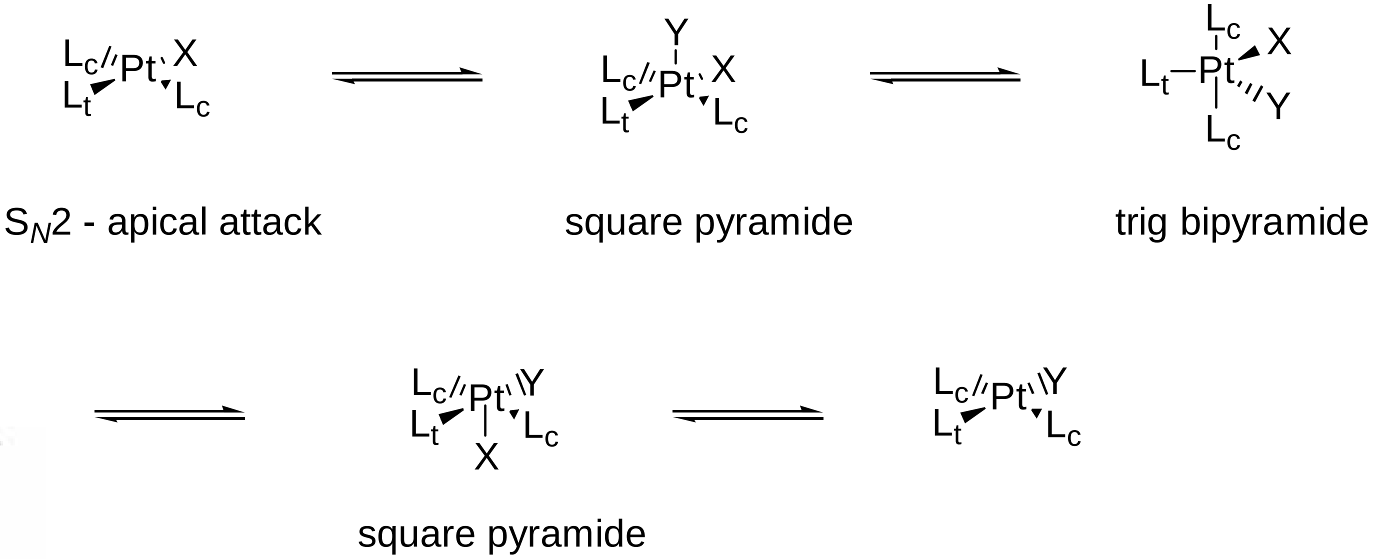
requires vacant site, e.g coordinative unsaturation

$$ML_n \rightleftharpoons ML_{n-1} + L \xrightarrow{L'} L + L'ML_{n-1}$$

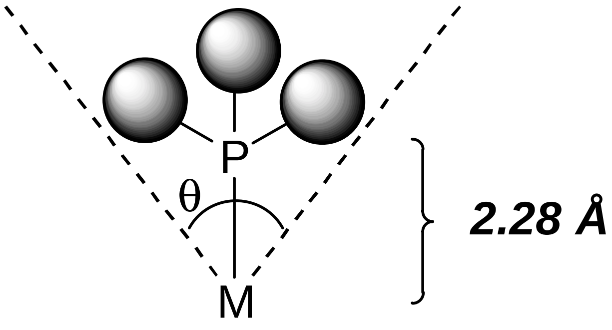
usually coordinatively unsaturates

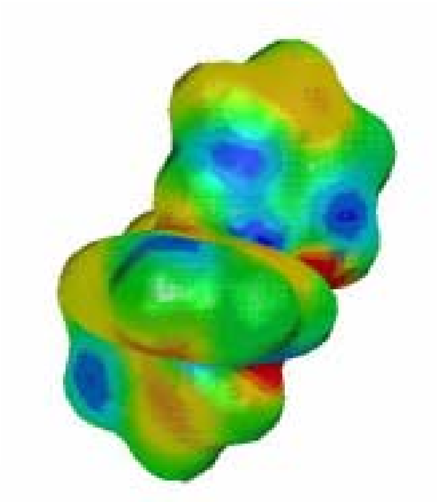
Typical Ligand Exchange

- coordinatively unsaturated, 16 e-, d8, square planar complexes of Ni(II), Pd(II), Pt(II), Rh(I) and Ir(I) are most studied.
- Two electron, associative processes.



Tolman: Cone Angle θ





Phosphine	θ	Phosphine	θ
PH_3	87	PPh_3	145
PF_3	104	$P(OPh)_3$	128
$P(OMe)_3$	107	PPr_3^{i}	160
PMe_3	118	PBu_3^{t}	182
PMe_2Ph	122	$P(o\text{-Tol})_3$	194
$PMePh_2$	136		

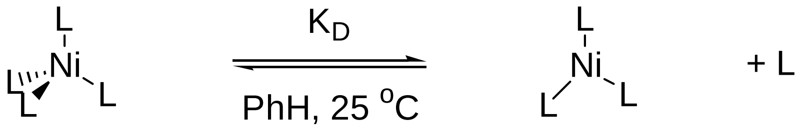
Tolman C.A. *Chem. Soc. Rev.* **1972**, *1*, 337.
Tolman, C.A. *Chem. Rev.* **1977**, *77*, 313.

Ligand Dissociation vs Cone Angles

$$\mathrm{Ni(CO)_4} \xrightleftharpoons{\text{slow}} \mathrm{Ni(CO)_3 + CO} \xrightleftharpoons[\text{fast}]{\mathrm{L}} \mathrm{LNi(CO)_3}$$

tetrahedral
labile

Rate proportional to [$Ni(CO)_4$] - 1st order



L	$P(OEt)_3$	$P(O\text{-}p\text{-tolyl})_3$	$P(O\text{-}i\mathrm{Pr})_3$	$P(O\text{-}o\text{-tolyl})_3$	PPh_3
cone angle	109	128	130	141	145
K_D	$<10^{-10}$	6×10^{-10}	2.7×10^{-5}	4×10^{-2}	No NiL_4

Electron Density in Phosphine Ligands

$L\text{-}Ni(CO)_3$

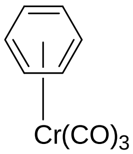
IR: ν_{CO} frequencies

Note: $E = h\nu$

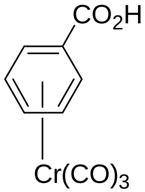
L	ν_{CO}
$^{t}Bu_3P$	2056.1
Me_3P	2064.1
Ph_3P	2068.9
$(MeO)_3P$	2079.5
$(PhO)_3P$	2085.0
PF_3	2110.8

Tolman C.A. *Chem. Soc. Rev.* **1972**, *1*, 337.
Tolman, C.A. *Chem. Rev.* **1977**, *77*, 313.

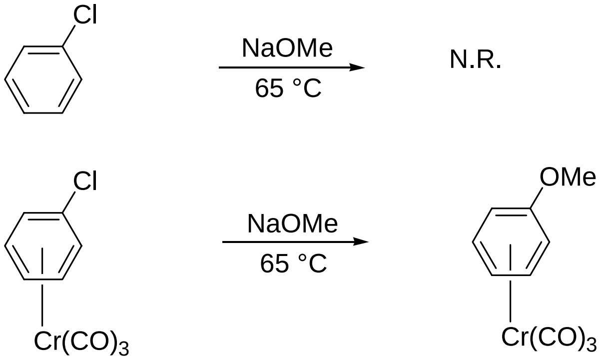
Effect of Ligand: Inductive

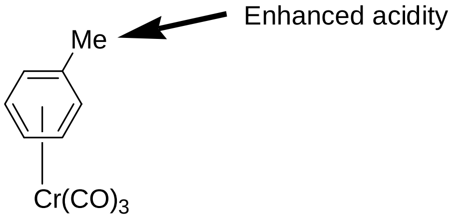


Strong electron withdrawing inductive effect
Not susceptible to Fr-Cr acylation
Suscpetible to anionic alkylation

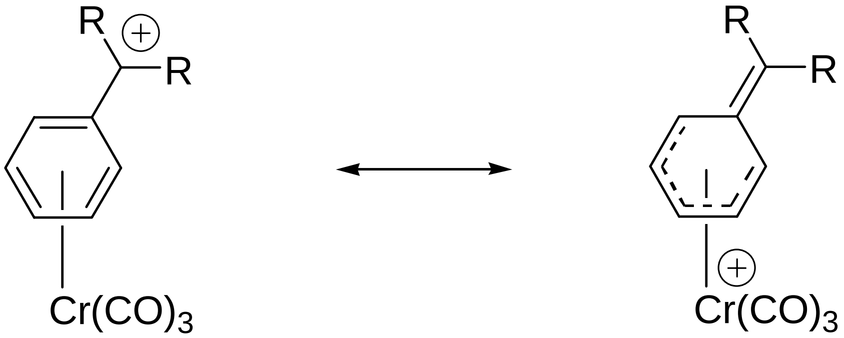


pK$_a$ = *4.77*
$PhCO_2H$: 5.68
p$NO_2C_6H_4CO_2H$: 4.48

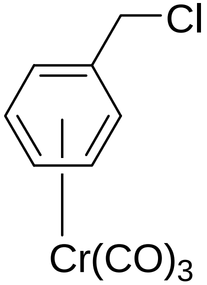




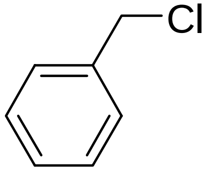
Effect of Ligand: Resonance



Solvolysis of

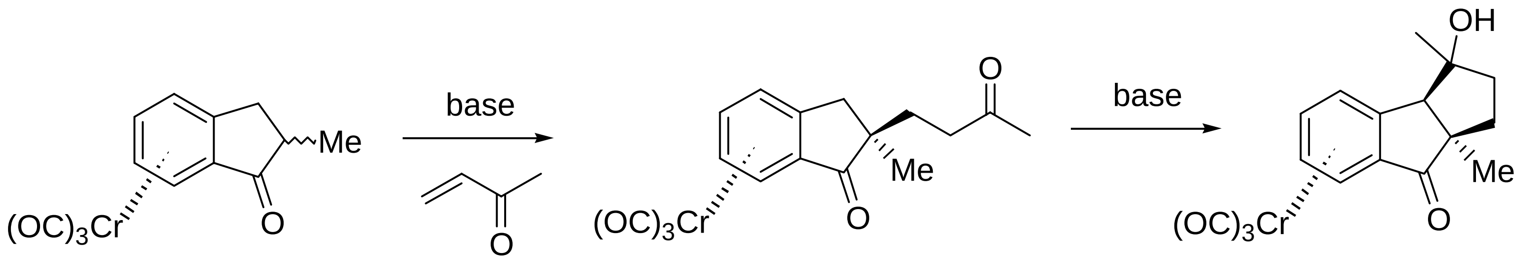


10^5 x Faster than

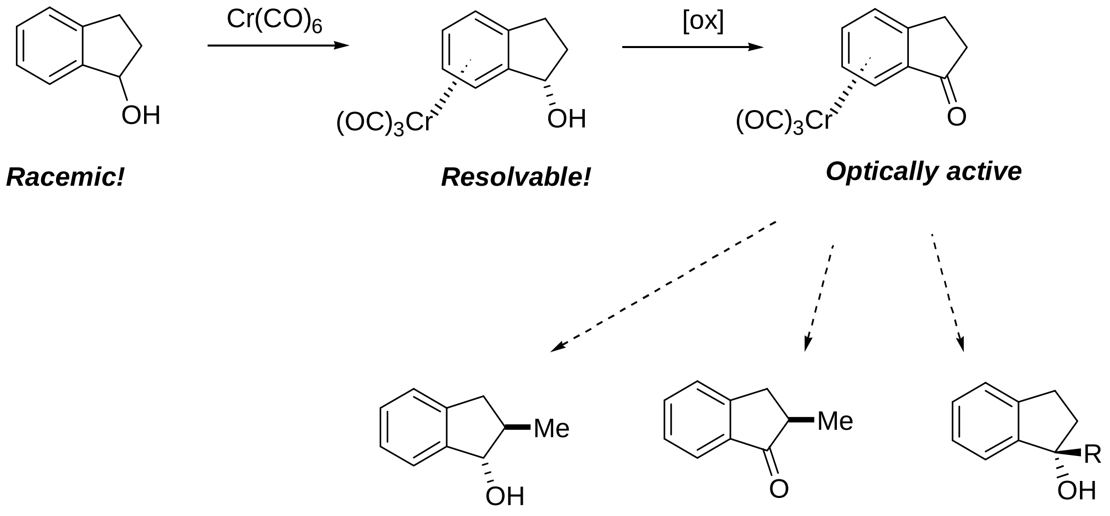


Applications:
Uemura, M.; Minami, T.; Hayshi, Y. *J. Organomet. Chem.***1986**, *102*, 119.
Davies, S.G.; Donohoe, D.J.; Williams, J.M.J. *Pure Appl. Chem.* **1992**, *64*, 379.

Effect of Ligand: Steric



Also for enantioselective synthesis!



Racemic!

Resolvable!

Optically active

Single enantiomers!

Jaouen, G.; Meyer, A. *Tetrahedron Lett.* **1976**, 3547.
Meyer, A.; Jaouen, G. *Chem. Comm.* **1974**, 787.
Schmalz, H.G. *et al. Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 631.