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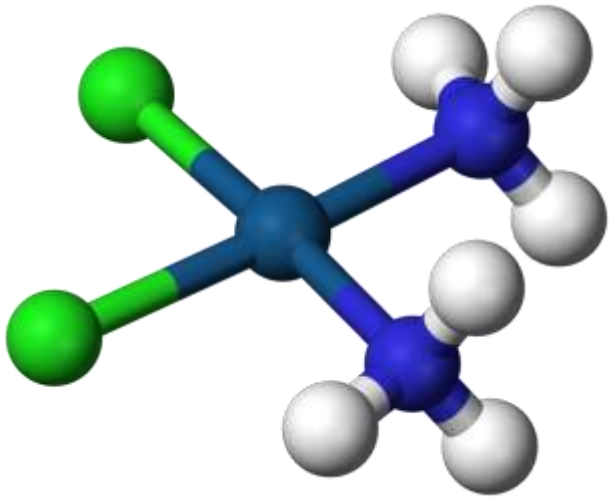
Chemistry of Molecular Systems



Cisplatin, $PtCl_2(NH_3)_2$
First discovered class of platinum-containing anti-cancer drugs

Fundamental Reactivity of Transition metal complexes – Lecture 11

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Intended learning outcomes

After the next four lectures you will be able to…

- classify the primary types of organometallic reactions.
- define what is meant by inert and labile TM complexes.
- explain the features that dictate inertness or lability of a complex.
- understand the effects of catalyst on reaction pathways.
- define key terms in catalysis.
- rationalise the effectiveness of TM complexes in catalysis.
- analyse catalytic cycles and their respective data to infer key steps in the cycles.
- understand key aspects of catalyst design to optimise performance.
- understand the importance of TM complexes in small molecule activation.
- recognise, explain and rationalise key catalytic cycles
- propose catalytic cycles for a given transformation.

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Organometallic Reaction Types: Association

Property	Starting Material	Product
d-electron count	X	X
Total VE count	N	N+2
Oxidation state	Y	Y[(1)]
Coordination number	Z	Z+1
Other notes	Requires metal to have free coordination site	

[(1)]Though oxidation state doesn't change, overall charge on complex can change if L charged (e.g. if L is an X-type: Cl^-)

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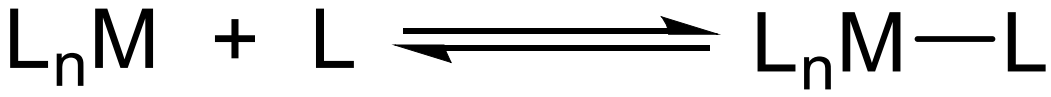
Organometallic Reaction Types: Dissociation

Property	Starting Material	Product
d-electron count	X	X
Total VE count	N	N-2
Oxidation state	Y	Y
Coordination number	Z	Z–1
Other notes	Reverse of association	

Organometallic Reaction Types: Association



$$K = \frac{[LnM - L]}{[L_nM][L]}$$

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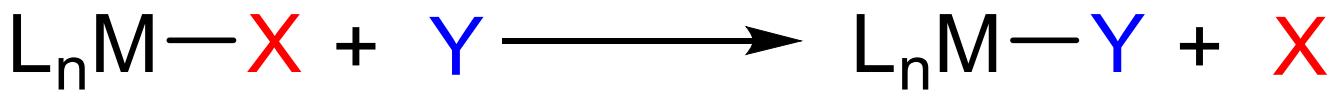
Organometallic Reaction Types: Substitution



Property	Starting Material	Product
d-electron count	X	X
Total VE count	N	N
Oxidation state	Y	Y
Coordination number	Z	Z
Other notes		

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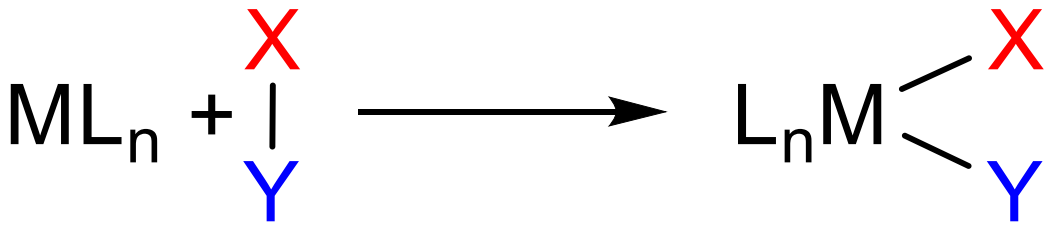
Organometallic Reaction Types: Oxidative Addition



Property	Starting Material	Product
d-electron count	X	X-2
Total VE count	N	N+2[(1)]
Oxidation state	Y	Y+2
Coordination number	Z	Z+1
Other notes	[(1)]Assuming that the molecule isn't already bound (e.g. σ-H_2)	

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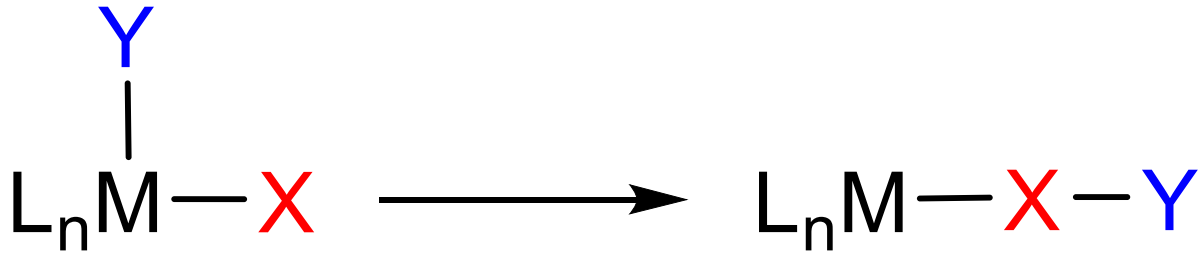
Organometallic Reaction Types: Migration



Property	Starting Material	Product
d-electron count	X	X
Total VE count	N	N-2
Oxidation state	Y	Y
Coordination number	Z	Z-1
Other notes	Can be 1,1-insertion (e.g. CO) or 1,2-insertion (e.g. Ethylene)	

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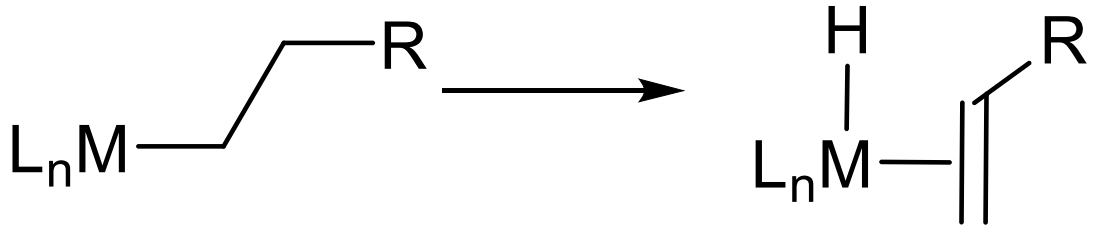
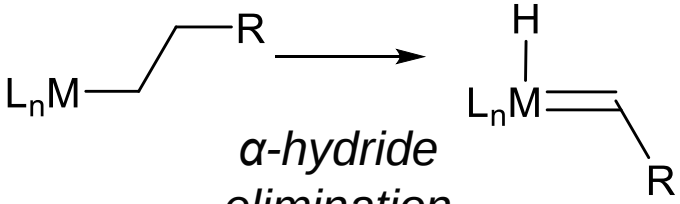
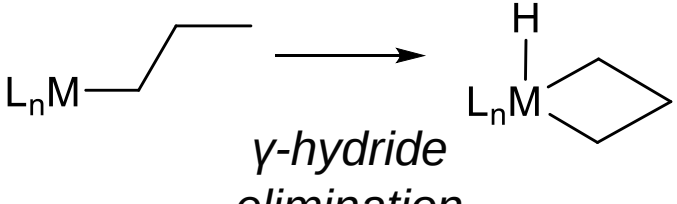
Organometallic Reaction Types: Elimination (1) - Hydride



Property	Starting Material	Product
d-electron count	X	X (for β)
Total VE count	N	N+2 (for β)
Oxidation state	Y	Y (for β)
Coordination number	Z	Z+1
Other notes		



α-hydride elimination



γ-hydride elimination

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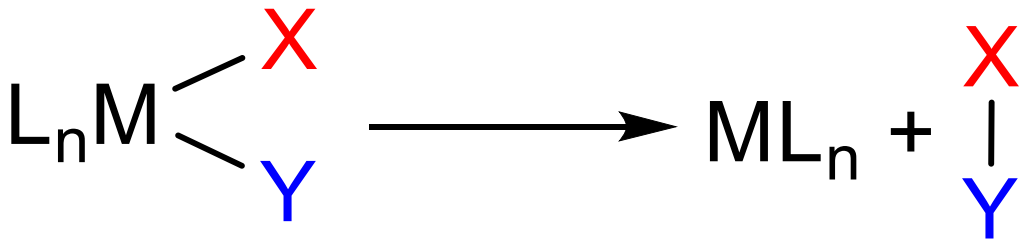
Organometallic Reaction Types: Elimination (2) Reductive



Property	Starting Material	Product
d-electron count	X	X+2
Total VE count	N	N-2
Oxidation state	Y	Y-2
Coordination number	Z	Z-1
Other notes	Reverse of Oxidative Addition Substituents must be cis	

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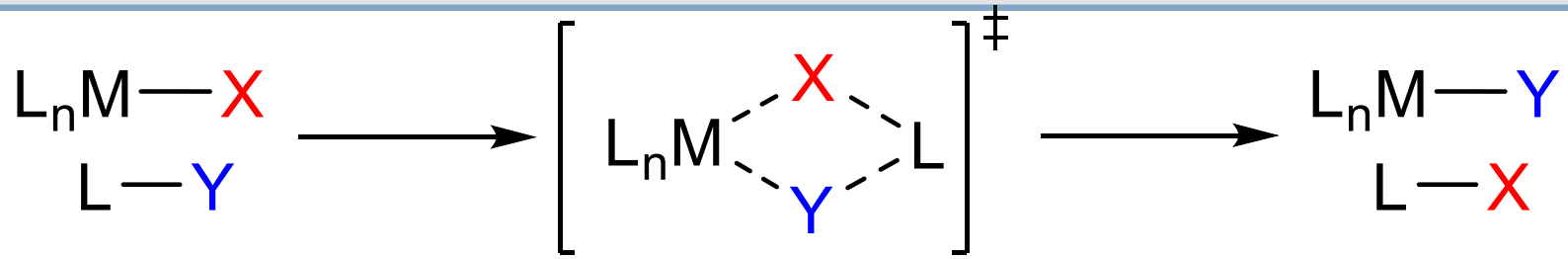
Organometallic Reaction Types: σ-bond metathesis



Property	Starting Material		Product
d-electron count	X		X
Oxidation state	Y		Y
Coordination number	Z		Z
Other notes		Concerted transition state	

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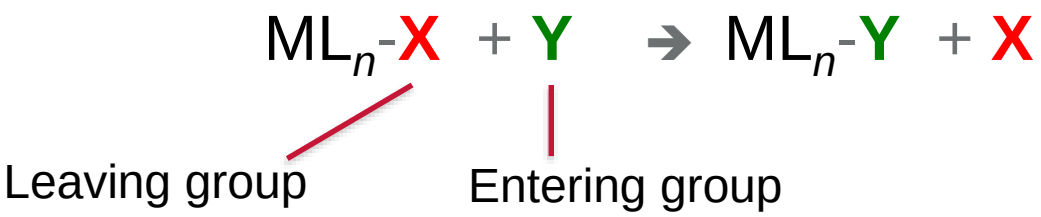
Reaction Mechanisms: Ligand substitution reactions



ML_n = metal, Lewis acid + other ligands
X and Y = ligands, Lewis bases

- Inorganic mechanisms have been less well studied: often fast and less predictable
- Mechanism: series of elementary steps by which the reaction takes place
- Mechanism can be investigated at two levels:

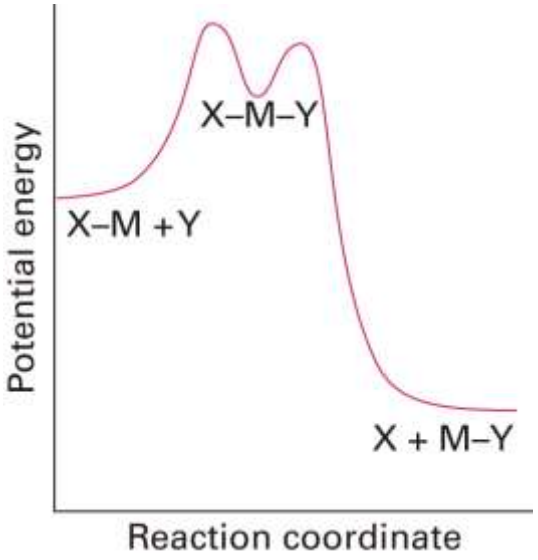
  (i) Stoichiometric mechanism: sequence of elementary steps

  (ii) Intimate mechanism: describes the transition state passed through during an elementary step
- Rates of reactions are used elucidate the mechanism
- Details of the activation process and rate determining step

Classification of Stoichiometric mechanisms

- **Associative (A)**
- ML_n-X + Y ➔ ML_n-Y + X
- M-Y bond forms before M-X bond breaks
- Intermediate with an increased coordination number is formed. Rate depends on both [MX] and [Y]

$$\text{Rate} = \frac{d[MX]}{dt} = k_a[MX][Y]$$



$[Ni(CN)_4]^{2-} + {}^{14}CN^- \rightarrow [Ni(CN)_4({}^{14}CN)]^{3-}$

$[Ni(CN)_4({}^{14}CN)]^{3-} \rightarrow [Ni(CN)_3({}^{14}CN)]^{2-} + CN^-$

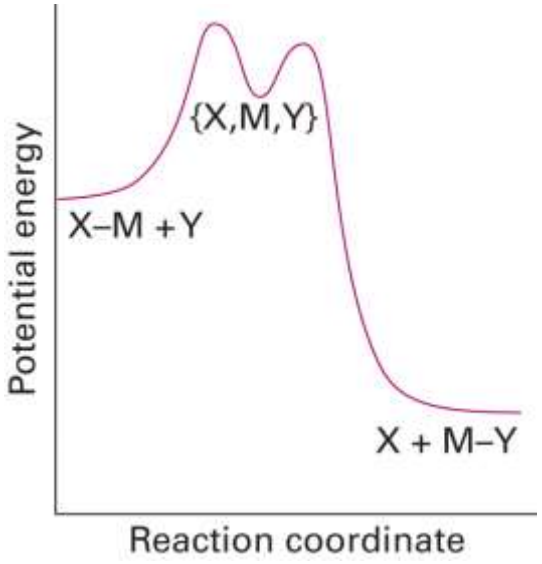
Reaction classed as associative if we can ‘see’ the intermediate nickel pentacyanide complex.

Classification of Stoichiometric mechanisms

- **Dissociative (D)**
- ML_n-X + Y ➔ ML_n-Y + X
- M-X bond breaks before M-Y bond forms
- Intermediate reduction in coordination number. Rate depends on [MX] not [Y]

$$\text{Rate} = \frac{d[MX]}{dt} = k_d[MX]$$

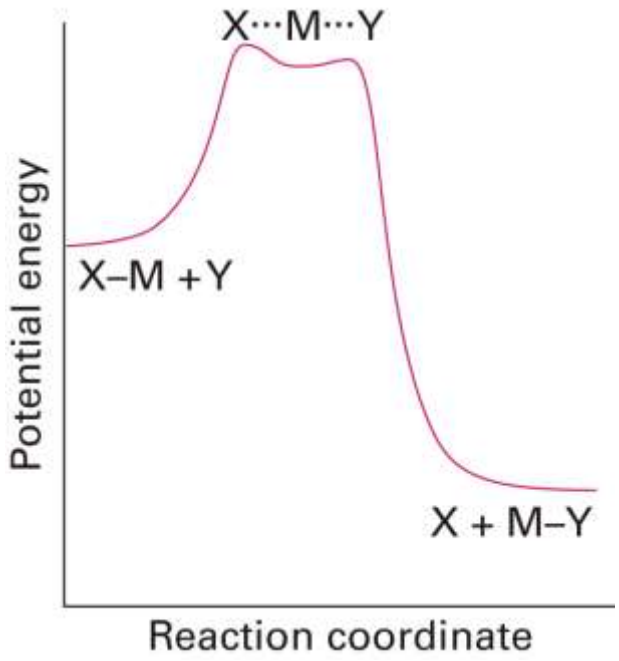
$W(CO)_6$ ➔ $W(CO)_5$ + CO
$W(CO)_5$ + PPh_3 ➔ $W(CO)_5PPh_3$



Reaction classified as dissociative if the intermediate tungsten pentacarbonyl can be '*seen*' (i.e. detected via spectroscopy, it must be long enough lived).

Classification of Stoichiometric mechanisms

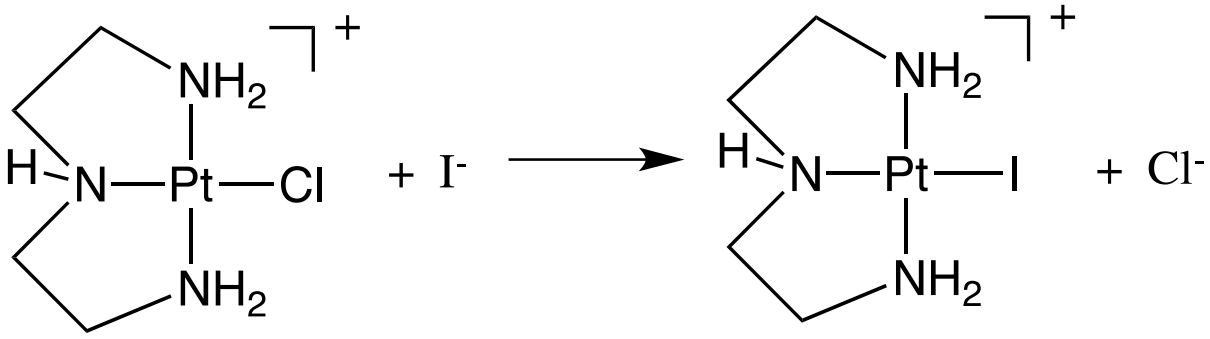
- **Interchange (I)**
- ML_n-X + Y ➔ ML_n-Y + X
- M-X bond breaking and M-Y bond formation is at the same time
- An activated complex is formed but no detectable intermediate
- Expect rate to depend on both [MX] and [Y]
- Interchange mechanisms are very common
- Distinction between **A** or **D** and **I** depends if the intermediate can be detected



$$[Ni(OH_2)_6]^{2+} + NH_3 \rightarrow [Ni(OH_2)_5(NH_3)]^{2+} + H_2O$$

Intimate Mechanisms

- Describes the formation of the activated complex (transition state)
- Focuses on what happens in an individual step at the highest point on the reaction coordinate (transition state)
- It is usually the RDS and can be classified as either associative or dissociative
- **Associative activation**: rate of formation of activated complex depends on the ***nature*** of the incoming ligand
- Activated complex must involve significant bonding to incoming ligand
- $\Delta S^{\neq}$ will decrease (increased order of activated complex)



Use of I^- instead of Br^- results in a 10-fold rate increase, thus strong dependence on incoming group

Intimate Mechanisms

- **Dissociative activation**: rate of formation of activated complex ***does not*** depend on the ***nature*** of the incoming ligand
- Controlled by the M-X bond breaking process
- $\Delta S^{\neq} \sim 0$

$$[Ni(OH_2)_6]^{2+} + NH_3 \rightarrow [Ni(OH_2)_5(NH_3)]^{2+} + H_2O$$

- For example, the use of pyridine instead of NH_3 does not significantly change the rate

Intimate Mechanisms

	Associative mechanism (increased coord. no.)	Interchange mechanism (no observed change in coord. no.)	Dissociative mechanism (decrease coord. no.)
Associative activation	A	I_a	-
Dissociative activation	-	I_d	D
	Detectable intermediate	No detectable intermediate	Detectable intermediate

A-------I_a-------I_d-------D

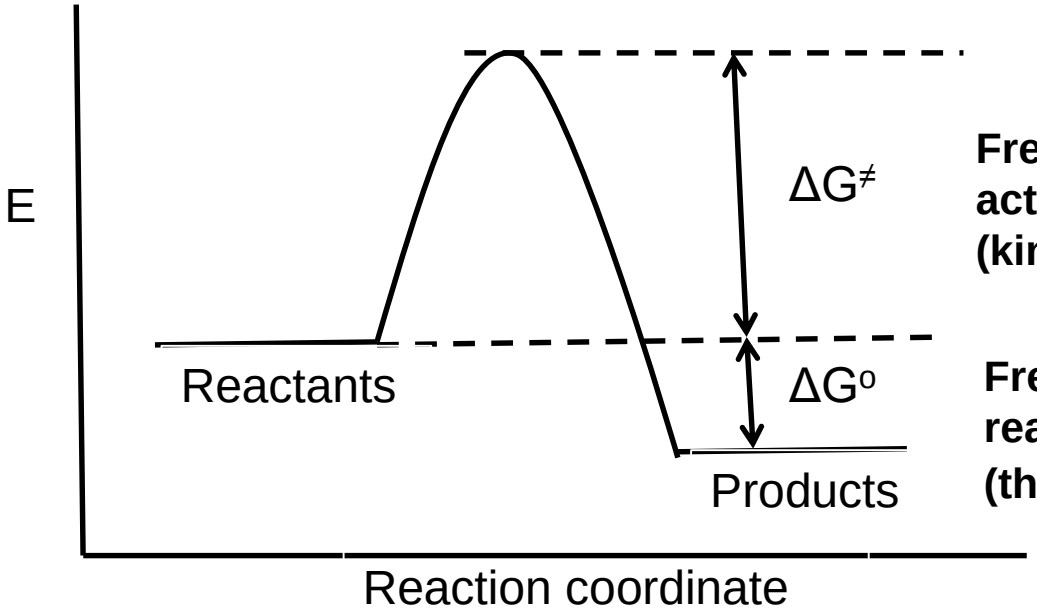
- Reaction designation A: If the mechanism is associative, the complex activation must also be associative
- Reaction designation D: If the mechanism is dissociative, the complex activation must also be dissociative
- Reaction designation I_a or I_d: If the mechanism is Interchange, the complex activation can be either associative or dissociative

Substitutionally Inert (non-labile) vs Labile

- Year 1 coordination chemistry – HSAB, stability constants and thermodynamic data, such as ΔH and ΔS. Likelihood of reaction from these data, but not length.
- The terms 'inert and 'labile' relate to the length of time a thermodynamically unstable complex will 'survive', and time taken to reach the equilibrium position, $t_{1/2}$.
- What factors control whether a complex is inert or labile? i.e. will convert into another complex
- Small ions are less labile, stronger M-L bonds and sterically 'restricted' at metal centre.
- Complexes with no CFSE or chelate effects tend to be most labile.

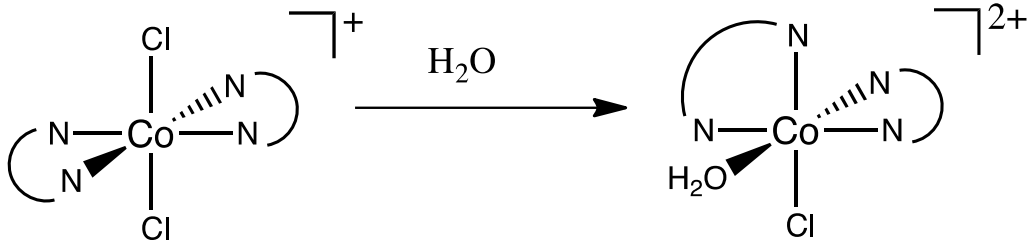
Inert: $t_{1/2}$ > 1 min
Labile: $t_{1/2}$ < 1 min

Rate is governed by height of activation energy barrier $\Delta G^{\neq}$



If reaction is slow, activation energy for the process must be high

Kinetically stable (but thermodynamically unstable)



Thermodynamically stable product

Slow conversion of complex as activation barrier prevents its rapid conversion. Solutions can be stored for days, decomposition rate slow, thus termed 'inert'.

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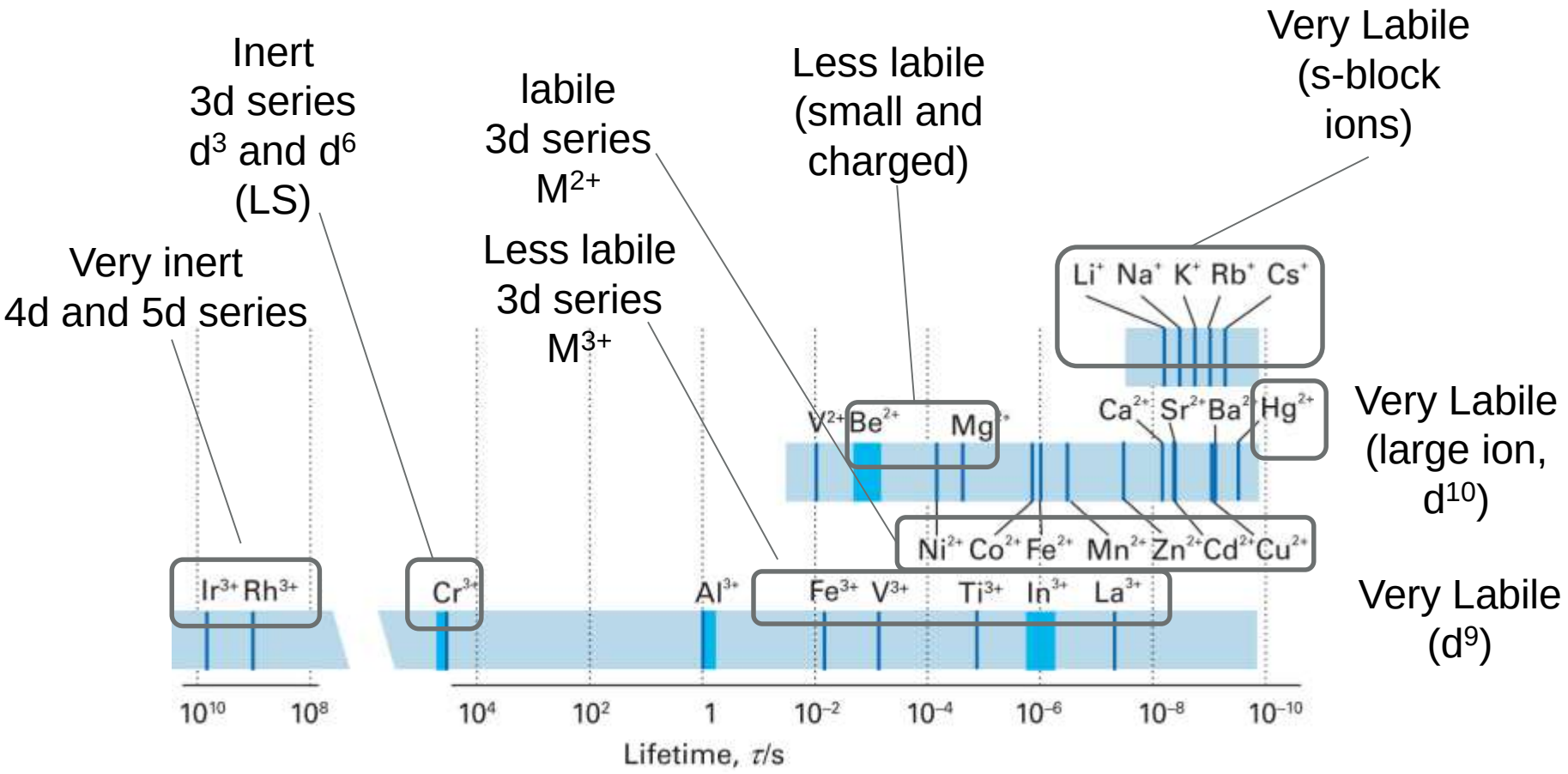
Survey of labile and inert complexes (exchange of water molecules)



If no additional 'special' factors to provide extra stability (i.e. CFSE, chelate effects) most reactions at transition metals complexes will be fast – labile
If additional stability factors present, result will be in an increase in activation energy

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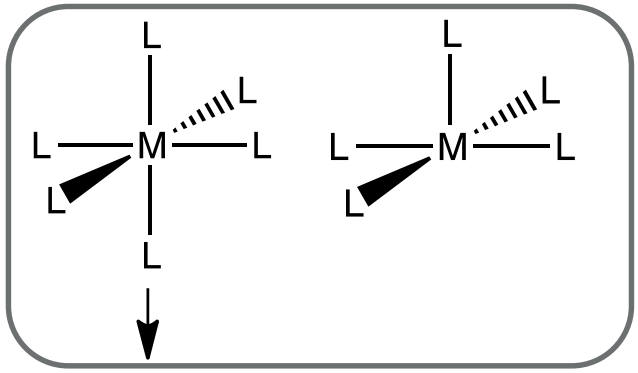
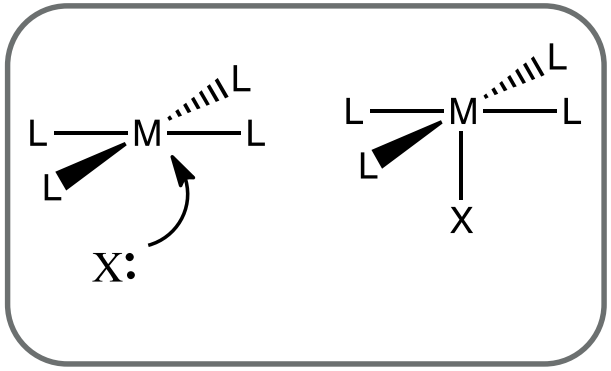
Inert complexes

Ion	Geometry	Spin	CFSE
Co^{3+}	Oh	d^6, LS	$2.4\ \Delta_o$
Cr^{3+}	Oh	d^3	$1.2\Delta_o$
Pt^{2+}	Sq pl	d^8 LS	Max sq pl Δ_{sp}

- Inert to ligand substitution
- For substitution at these complexes: coord. no. must initially either increase or decrease by one





For O_h d^6 Co^{3+}, on going from 6 to 5 coordinate, CFSE will decrease on going to a square-based pyramidal structure. This will result in a high spin configuration and a loss in the CFSE. For Sq. Pl., extra CFSE is lost on going to a 5-coord. complex.

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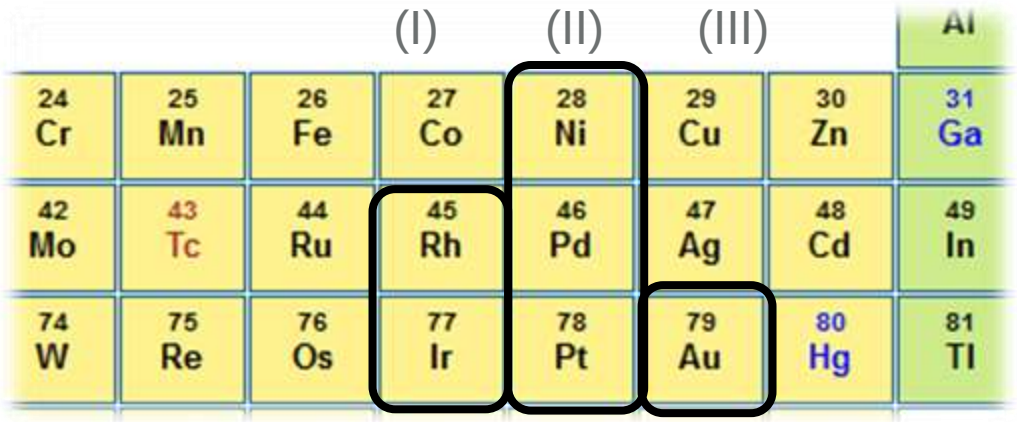
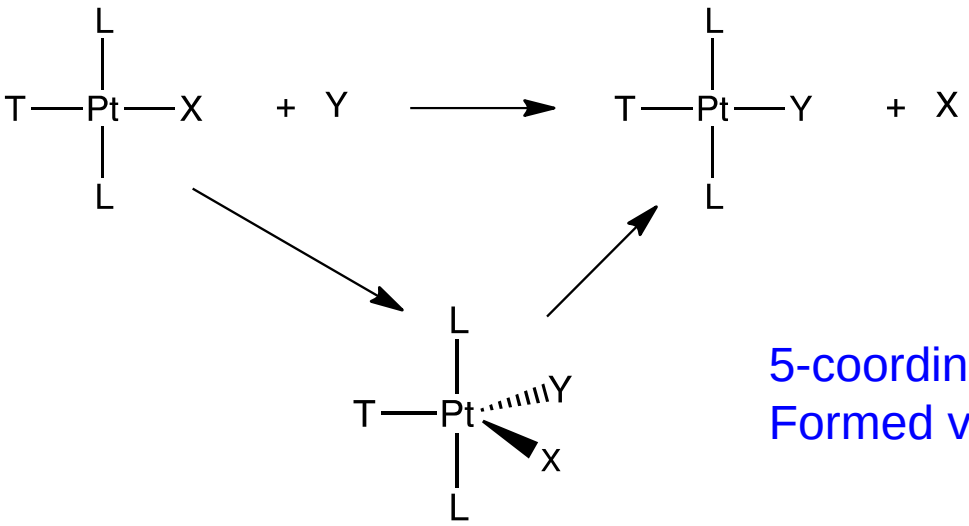
Substitution in Square Planar Complexes





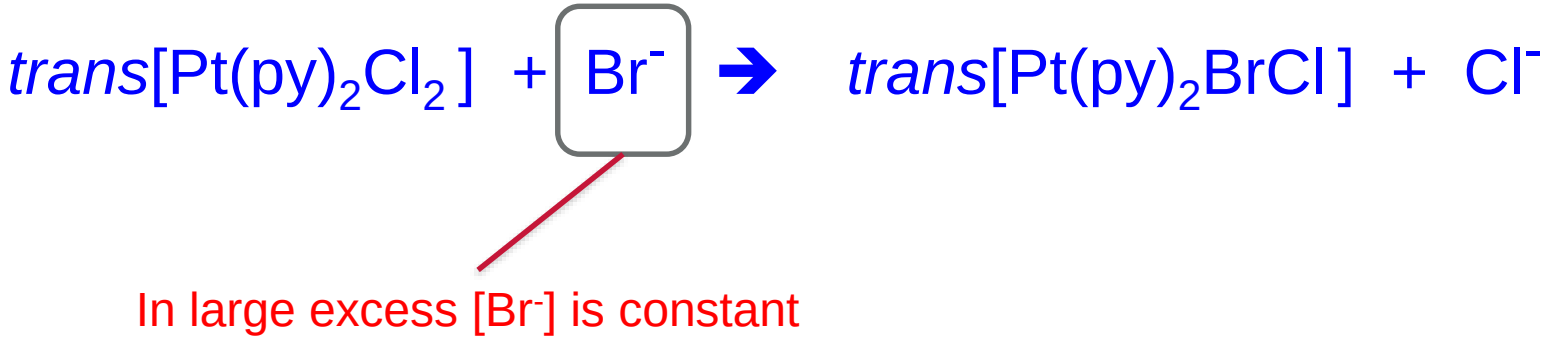
Ion	Rel. subs. rate
Ni(II)	10^7-10^8
Pd(II)	10^5-10^6
Pt(II)	1

5-coordinate sq. py. or trig. bipy.
Formed via A or I_a mechanism

T = *trans* ligand, *trans* to leaving/entering group

Rate law

- For most sq. pl. complexes rate depends on both concentration of complex and incoming ligand
- The data is not simple first or second order kinetics



- Rate = k_{obs} [$Pt(py)_2Cl_2$]
- Reaction is first order wrt to complex
- A pseudo rate constant as unknown dependence on [Br^-]
- To find the order of reaction wrt Br we need to measure the observed rate constant at various different concentrations but always keeping [Br] in excess of the complex

To determine order wrt Br^-, measure k_{obs} at various values of $[Br^-]$ ([Br-]>>[complex]

$y = a + bx$

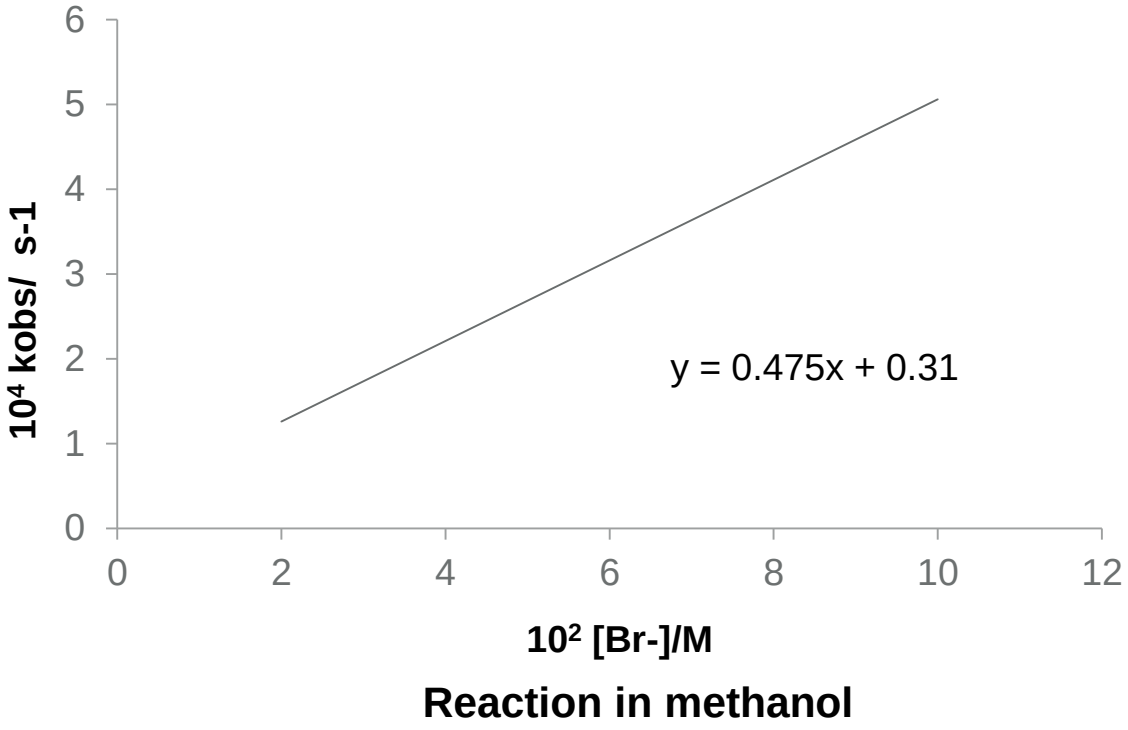
$k_{obs} = k_1 + k_2 [Br^-]$

k_1 = intercept, k_2 = slope

Substituting for k_{obs} :

Rate = k_{obs} $[Pt(py)_2Cl_2]$

Rate = k_1 $[Pt(py)_2Cl_2]$ + k_2 $[Pt(py)_2Cl_2][Br]$



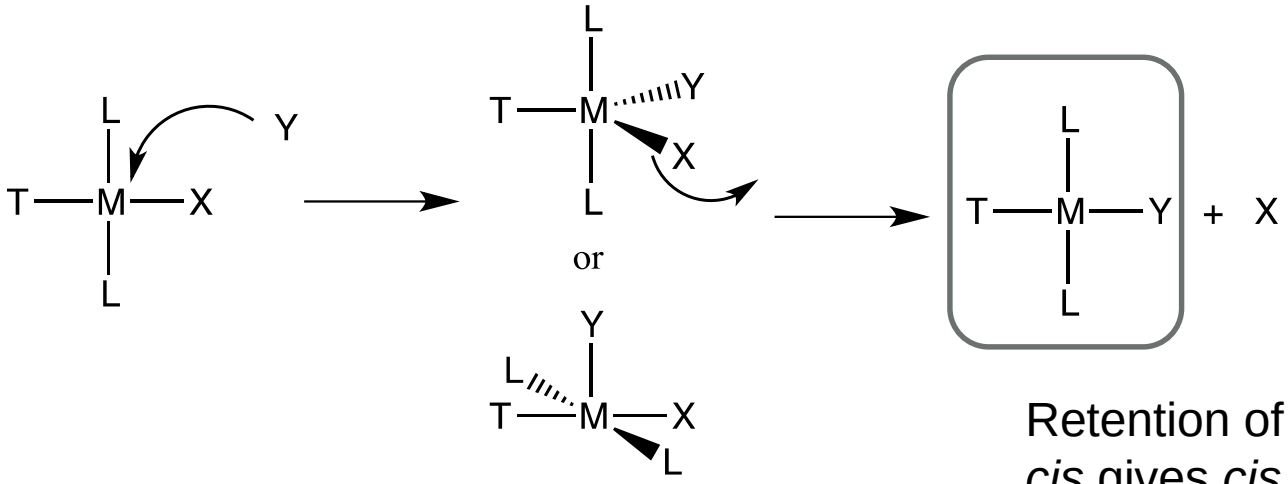
$$\text{Rate} = \frac{d[TL_2MX]}{dt} = \underbrace{k_1[TL_2MX]}_{K_1 \text{ path}} + \underbrace{k_2[TL_2MX][Y]}_{K_2 \text{ path}}$$

Two term rate law

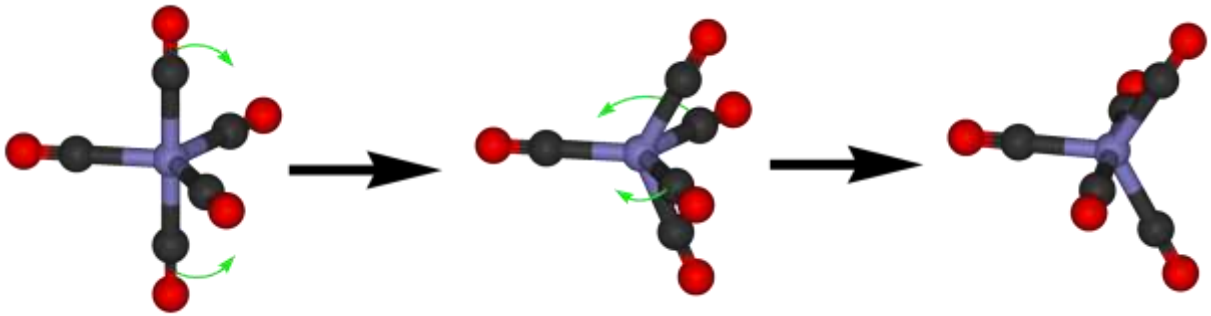
Depends only on [complex]

Depends on [complex] and [Y]

K_2 path, associative mechanism (A or I_a)



Retention of geometry
cis gives *cis*
trans gives *trans*



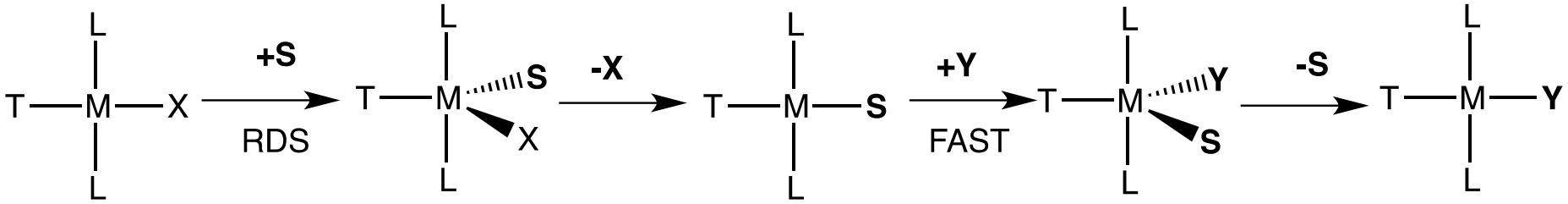
Scrambling of the geometric isomerism would indicate that either the mechanism is dissociative or a Berry pseudo rotation interconversion

K_1 path

$$k_{obs} = = k_1[TL_2MX] + k_2[TL_2MX][Y]$$

K_1 path K_2 path

- K_1 is independent of nature and conc. of incoming ligand [Y]
- K_1 path depends on the nature of the solvent, good nucleophiles best i.e. methanol (good), hexane (bad)
- **Suggests two successive associative substitution processes for K_1 path**



First substitution **Second substitution**

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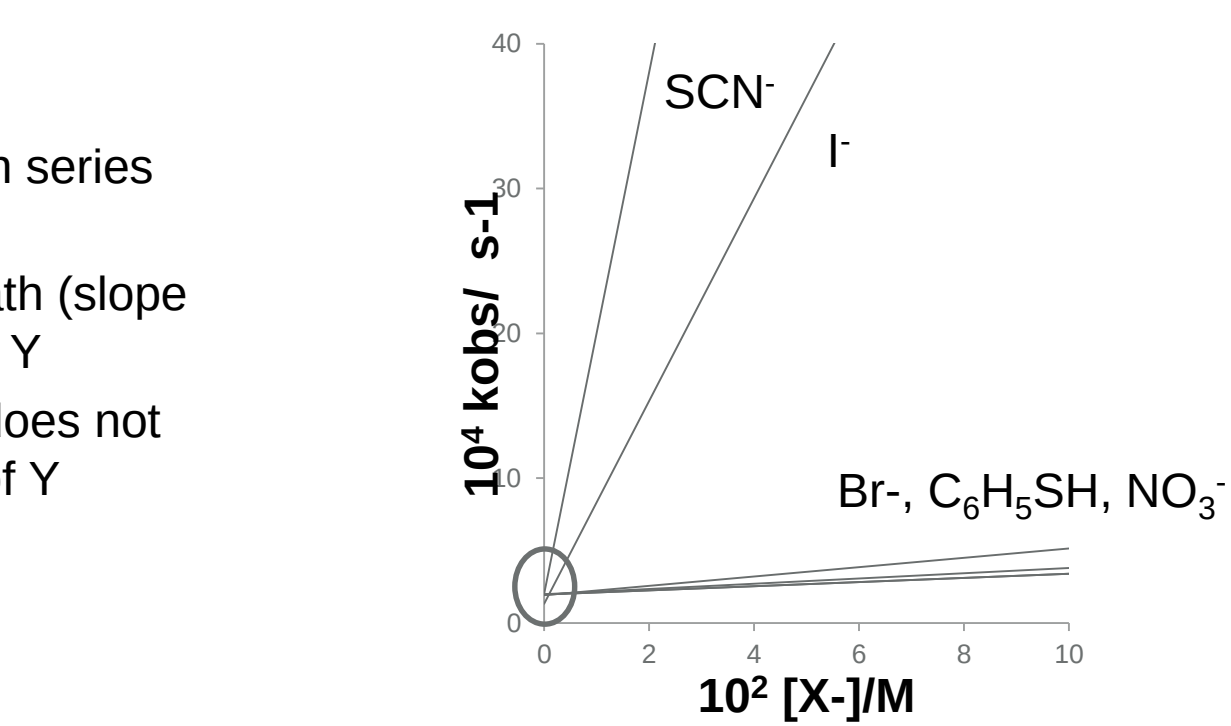
Variation of incoming group Y



- [Y]>>[complex] then series of k_{obs} v [Y]
- Rate constant k_2 path (slope of plot) depends on Y
- k_1 path (intercept) does not depend on nature of Y

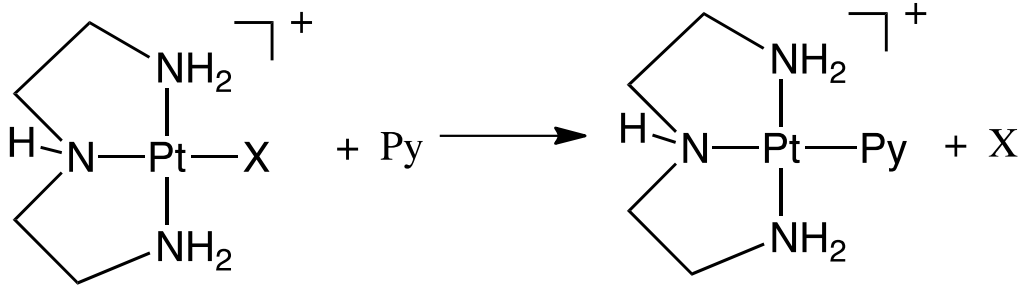
For Pt(II) and Pd(II) complexes, k_2 values in approximate order:

$PPh_3 > CN^- > I^- > Br^- > N_3 > Cl^- > NH_3 > F^- > CH_3O^-$

rate will be faster for nucleophilic entering groups i.e. soft, polarisable ligands that bind more strongly to the soft Pt(II) (HSAB) have the largest rate constants

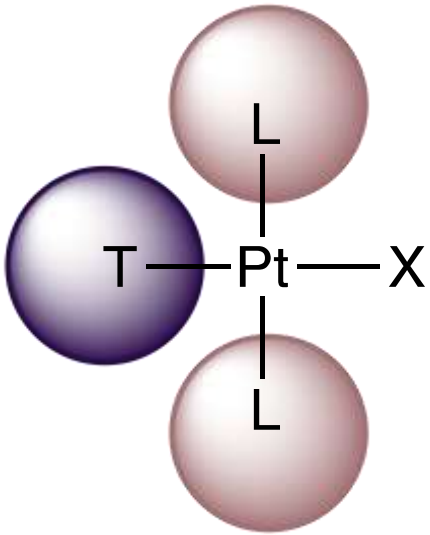
Variation of leaving group X

- Provides information on the extent of bond formation in a complex intermediate.
- Generally, order of leaving group is reverse of the entering group.
- The effect of leaving group suggests that dissociation is important.

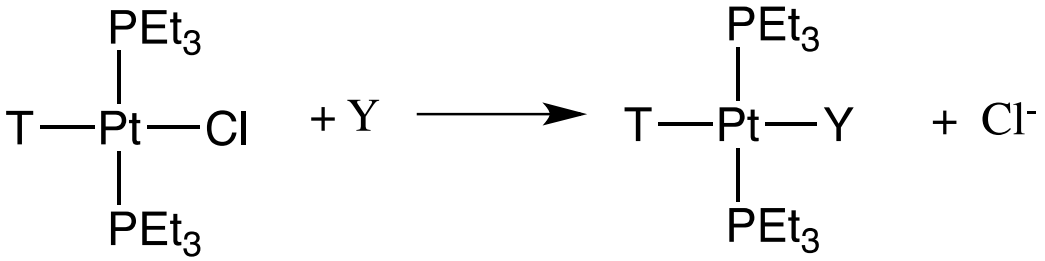


X	k_2 (M^{-1} s^{-1})
NO_3^-	Very fast
Cl^-	5.3×10^{-3}
Br^-	3.5×10^{-3}
I^-	1.5×10^{-3}
N_3^-	1.3×10^{-4}
SCN^-	4.8×10^{-6}
CN^-	2.8×10^{-6}

Other ligands

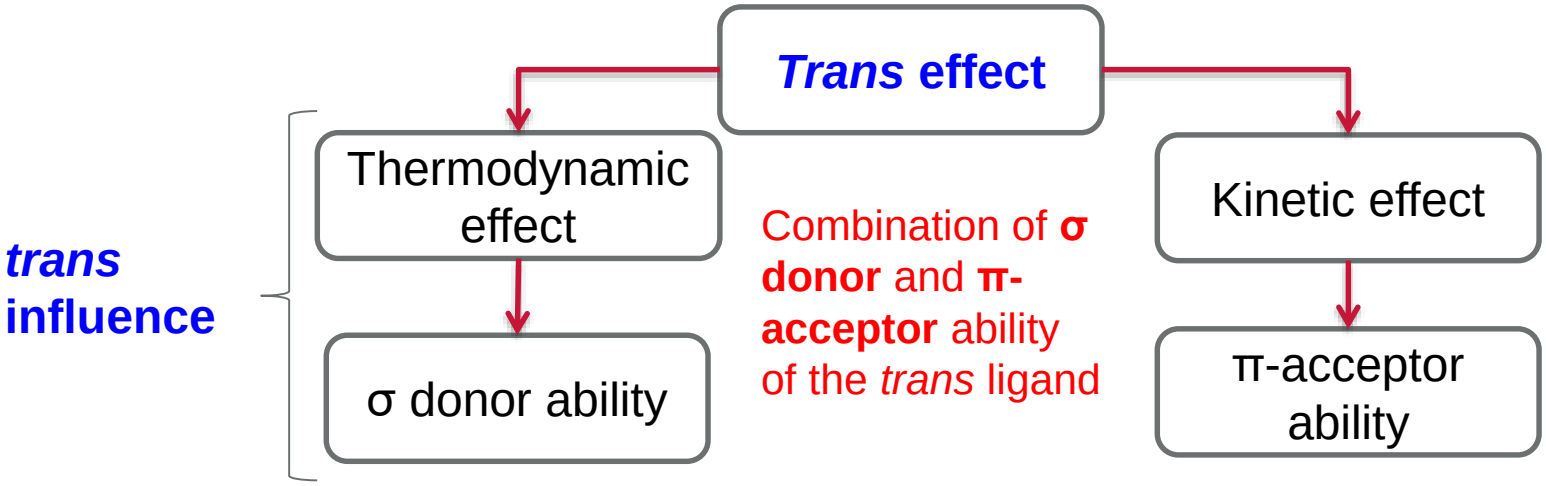


- *cis* ligands have limited effect
- *trans* ligands have a pronounced effect: ***trans effect***
- certain ligands *trans* to the leaving group will promote substitution *trans* to themselves



T	k_2 (M^{-1} s^{-1})
Cl^-	4.0×10^{-4}
$C_6H_5^-$	1.6×10^{-2}
CH_3^-	6.7×10^{-2}
PEt_3	3.8
H^-	4.2

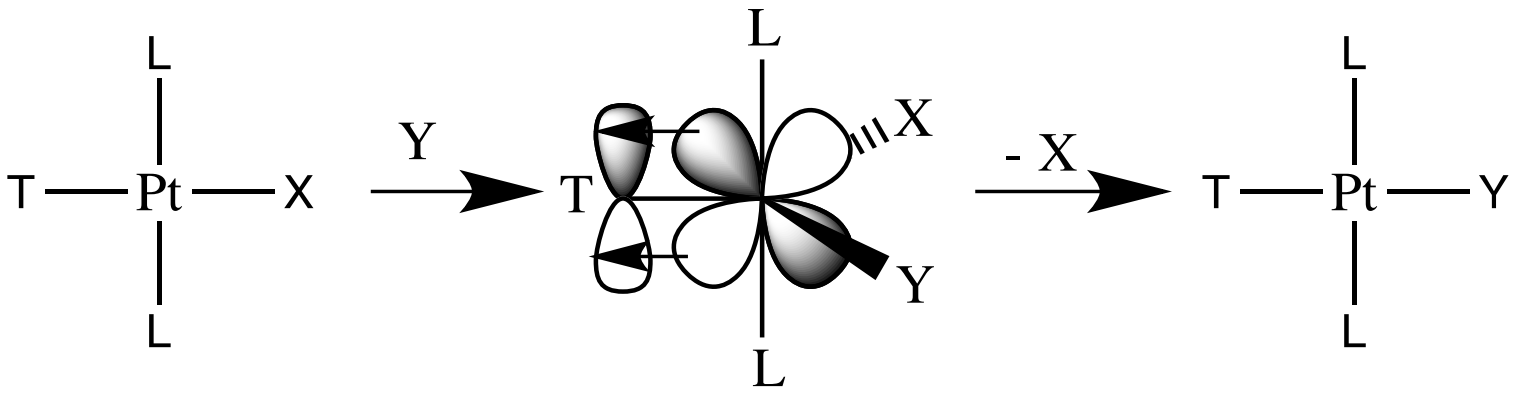
What causes the '*trans* effect'?



- ***Trans* effect is the labilising effect a *trans* ligand has on the leaving group opposite, and rate of substitution of the ligand.**
- **Strong σ donors and/or strong π acceptors display strong *trans* effects**
- **(σ-donors) H^- > PPh_3 > SCN- > I^- > CH_3^- ~ CO ~ CN^- >Br^- > Cl^- > py ~ NH_3 > OH^-**
- **T and X donate electron density into the $6p_x$ and $5d_{x2-y2}$ orbitals of Pt.**
- **If a σ-donating *trans* ligand, and a weaker σ–donor opposite, then weaker ligand cannot donate electrons to metal as strongly so has a weaker interaction with metal.**
- **Good π-acceptors increase the rate of *trans* ligand substitution, via stabilisation of 5-coord transition state.**

π-acceptor order

- C_2H_4 ~ CO ~ CN^- > NO_2^- > NCS^-
- If T is a good π-acceptor it removes electron density from metal d_{xy} orbital
- Results in nucleophilic attack on the metal being easier
- This lowers the energy of the (5-coord) transition state/intermediate
- Combined order of the two effects which give the overall *trans* effect:
- CO ~ CN^- ~ C_2H_4 > PR_3 ~ H^- > CH_3^- > $C_6H_5^-$ > NO_2^- > SCN^- ~ I^- > Br^- > Cl^- > py ~ NH_3 ~ OH^- ~ H_2O



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Trans effects in NMR

In square planar complexes, sizes of coupling constants are often related to geometry. In Pt(II) complexes, J(Pt-P) is sensitive to the group *trans* to the phosphine ligand and increases in the order:

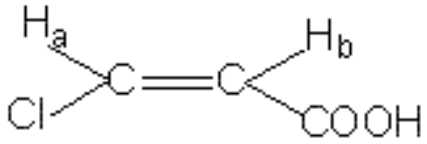
$$R^- < H^- < PR_3 < NH_3 < Br^- < Cl^-$$

A ligand that exerts a large *trans* influence substantially weakens the bond *trans* to itself, causing a reduction in the NMR coupling between the nuclei.

In general, *trans* coupling constants are larger than *cis*, due to more favourable orbital overlap, with bonds being 180 degrees with respect to each other.

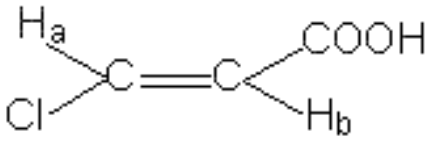
e.g. In $[Pt(H_2)(PMe_3)_2]$, $^2J_{P(cis)\text{-}H} = 24$ Hz, $^2J_{P(trans)\text{-}H} = 179$ Hz.

This is also observed in *cis/trans*-alkenes



$^3J_{HH} = 9$ Hz

Cis–



$^3J_{HH} = 14$ Hz

Trans–

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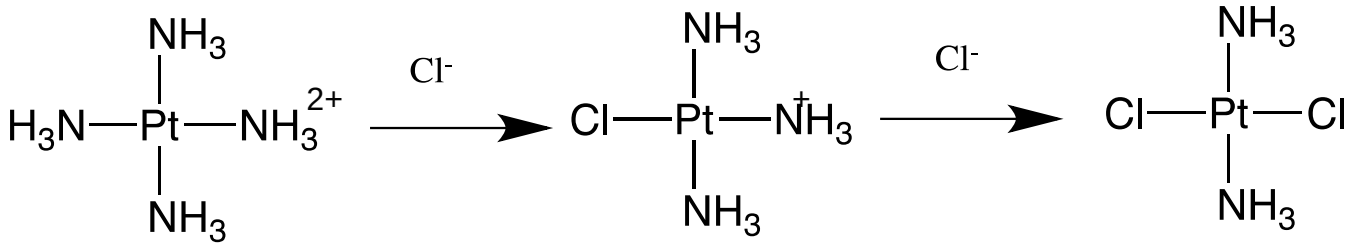
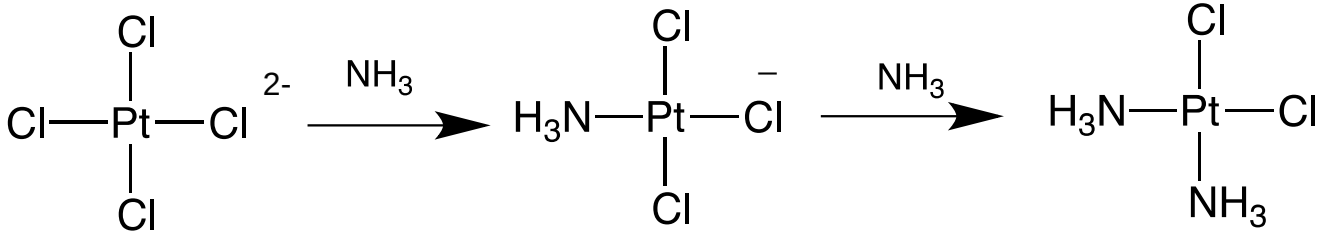
Synthetic utility of trans effect

$CH_3^- > C_6H_5^- > NO_2^- > SCN^- \sim I^- > Br^- > Cl^- > py \sim NH_3 \sim OH^- \sim H_2O$

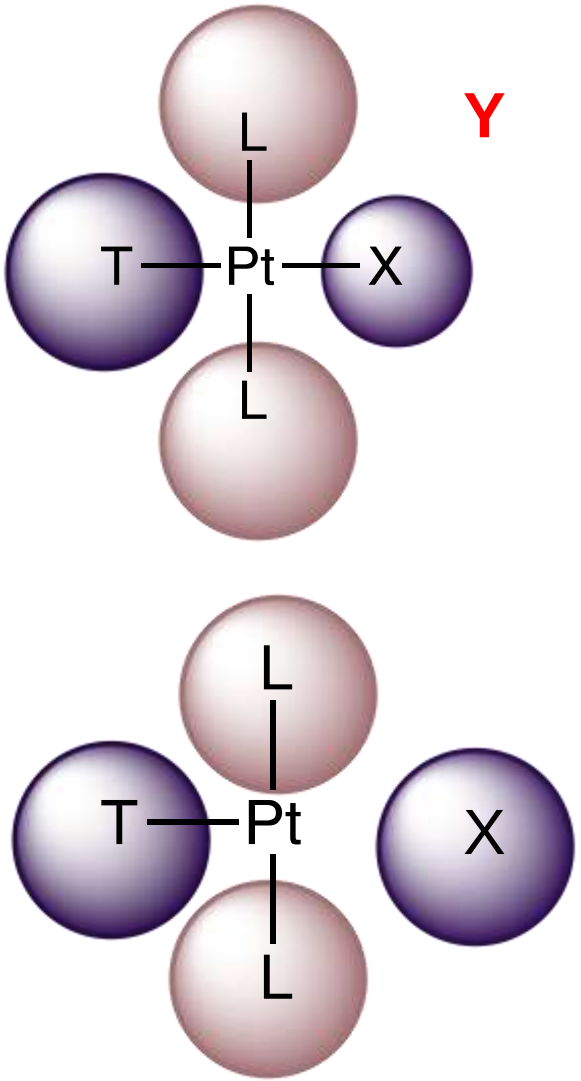




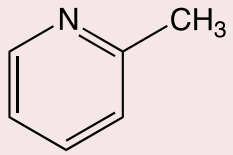
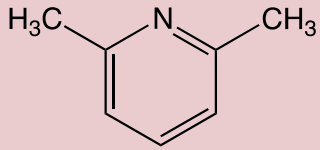
Classically observed in the formation of *cis*-platin. Starting from $PtCl_4^{2-}$, the first NH_3 ligand is added to any of the four equivalent positions – some stimulus is required. However, since Cl^- has the greater *trans* effect, the second NH_3 is added trans to Cl^-.

Starting from $Pt(NH_3)_4^{2+}$, only the *trans* product is obtained.

Steric effects



- Bulky ligands in complex inhibit an associative path by blocking approach of incoming ligand, Y.
- Dissociative pathway also favoured as loss of a large ligand will relieve steric congestion around metal.

L	k_{obs} (s^{-1})
py	8×10^{-1}
	2×10^{-4}
	1×10^{-6}