EU FT-ICR MS

SC3- Roma, 25-27 June 2019

Ion Chemistry in FT-ICR MS

SAPIENZA
UNIVERSITÀ DI ROMA

Simonetta Fornarini

Dipartimento di Chimica e Tecnologie del Farmaco,
Sapienza Università di Roma, P.le A. Moro 5, I-00185, Roma (Italy)

EU FT-ICR MS

FT-ICR mass spectrometry

Operation		Performance
Unmatched mass accuracy and resolution	→	Elemental composition of analytes
Ion-molecule reactions	→	- Structural characterization of analytes - Mechanisms of ionic reactions - Identification of elusive intermediates
Ion-molecule equilibria	→	Thermodynamic parameters, e. g. gas phase basicities, ligand binding energetics, non covalent interactions
IRMPD spectroscopy	→	IR spectroscopy of trapped ions (isomeric and conformational assignment)
Thermal and non-thermal MS^n	→	Dissociation paths and dynamics

Ions are highly reactive.
They have a role in (in)organic reaction chemistry as:

- reactants
- intermediates
- Catalysts

Very large solvation energies;
masked differences in intrinsic reactivity between similar species.

Gas phase ion chemistry, in the absence of solvent and counterions, allows to elucidate the intrinsic behavior in ionic reactions and expose the role of the environment.

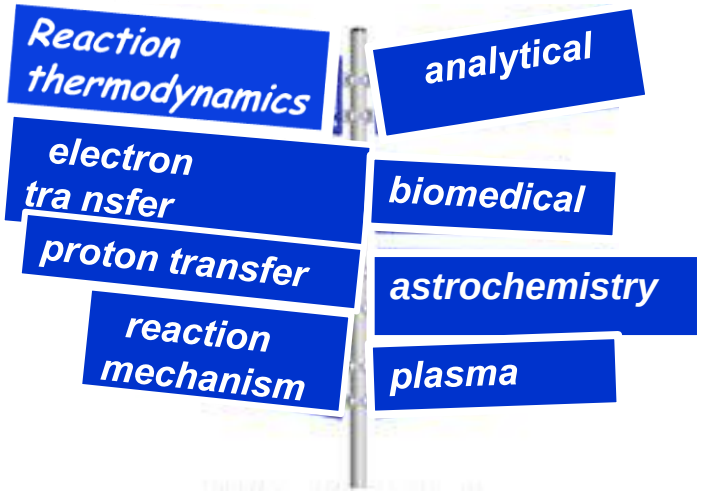
ion-molecule reactions ⟺ mass spectrometry

Gas phase ion chemistry

mass spectrometry ⟷ solvent free environment

IMPACT

fundamentals



applied areas

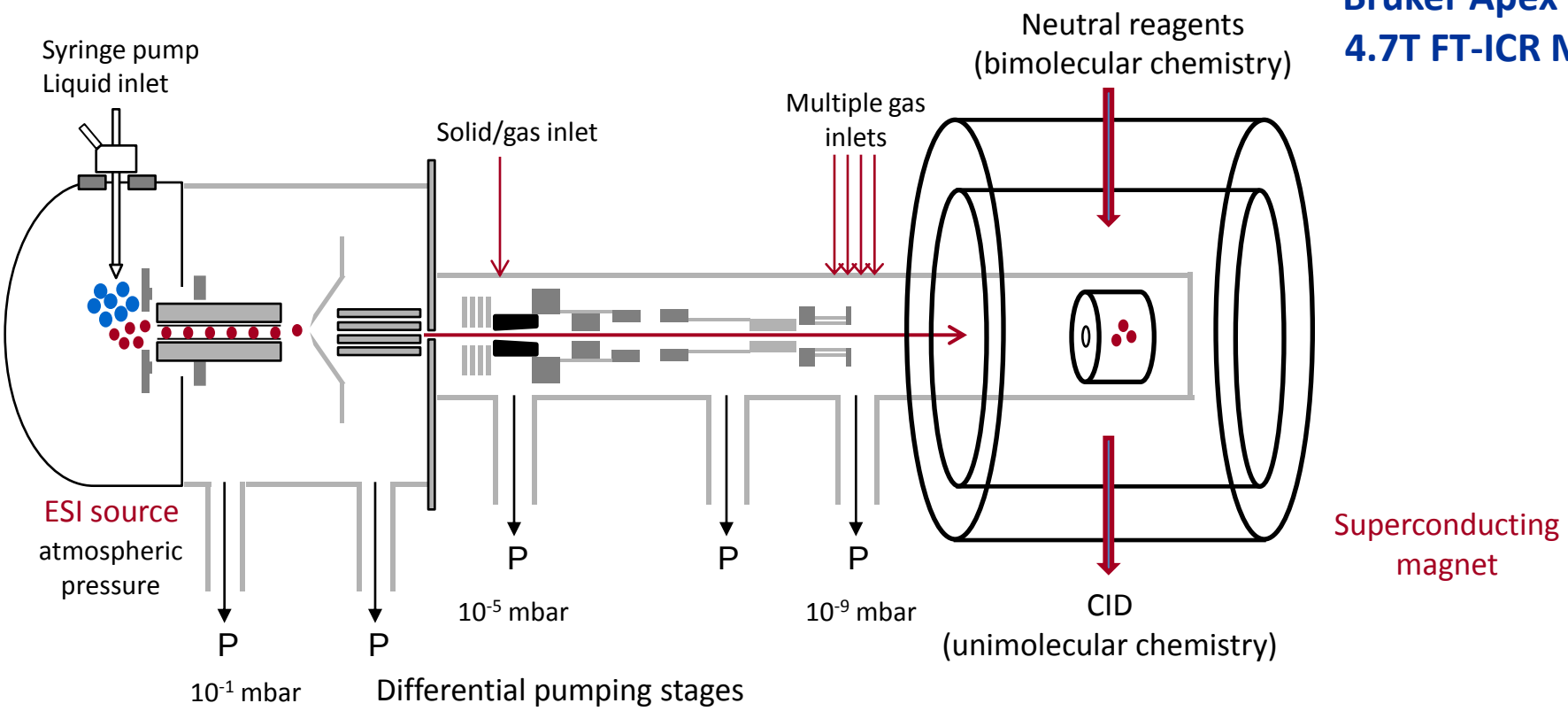
J. S. Brodbelt, Mass Spectrom. Rev. 1997; S. Gronert, Chem. Rev. 2001; V. Ryzhov, Anal. Chem. 2013

Gas phase ion chemistry

- Measuring rate constants
- Determining reaction efficiency
- Theory of ion-molecule capture/collision
- Slow/fast reactions: double minimum PES
- Examples of Ion Molecule Reactions (IMR)

FT-ICR mass spectrometer

Bruker Apex II, 4.7T FT-ICR MS



Equipment for TNA in Roma

Reaction Rates

$$R^+ + N \longrightarrow P^+ + \text{neutral products}$$

$$-\frac{dR(t)}{dt} = k\, n\, R(t)$$

the reaction is bimolecular

n = number density of neutral N

In a conventional bimolecular process the number density of neutral reactant would decrease with time. Here, it does not.

$$I_{(t)} = I_0\, e^{-nkt}$$

pseudo-first order reaction

$$\ln \frac{I_{(t)}}{I_0} = -\, n\, k\, t \qquad k = k_{exp}$$

- The semilog plot of the decrease of the parent ion abundance with time is linearly interpolated and the **pseudo-first order rate constant** is obtained.
- The bimolecular rate constant (k_{exp}) at 300 K is gained from the ratio between the negative slope and ***n***, the number density of the neutral.
- ***n*** is calculated from the ideal gas equation and allows to convert the measured value of the neutral pressure (mbar) in molecule cm^{-3} at 300 K.

- $$k_{exp} = \frac{\text{- slope } (s^{-1})}{n \text{ (molecule cm}^{-3})} = \ldots. \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$$

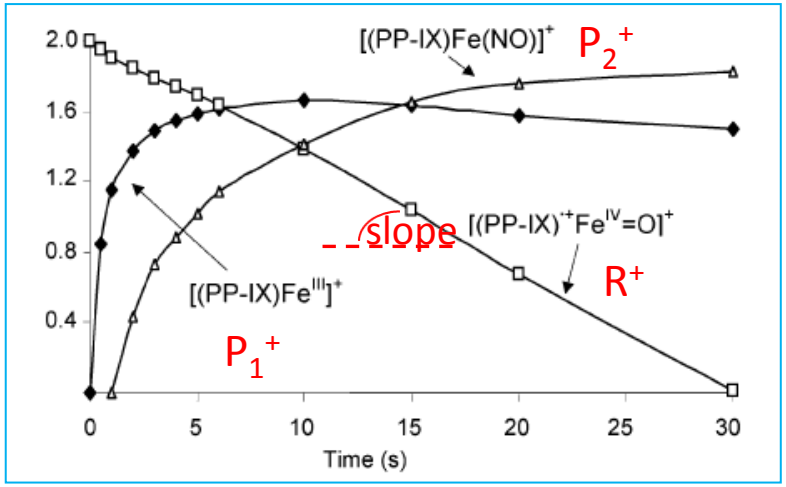


Figure 2. Plot of the logarithm of the relative ion abundances (%) versus time for the reaction of $(PP\text{-}IX)^{\bullet+}Fe^{IV}{=}O$ with NO at 3.0×10^{-8} mbar.

$$R^+ + NO \xrightarrow{OAT} P_1^+ + NO_2$$

$$P_1^+ + NO \xrightarrow{Add} P_2^+$$

Two consecutive reactions

Typically, the reproducibility of k_{exp} values is within 10%;

while the error in the absolute rate constants is estimated to be ± 30%.

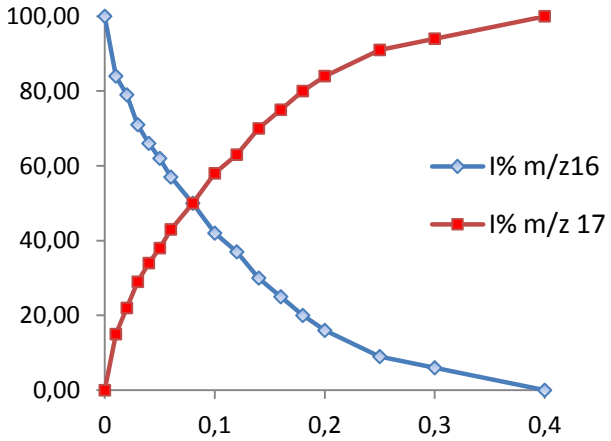
It is mainly due to uncertainty in pressure measurements.

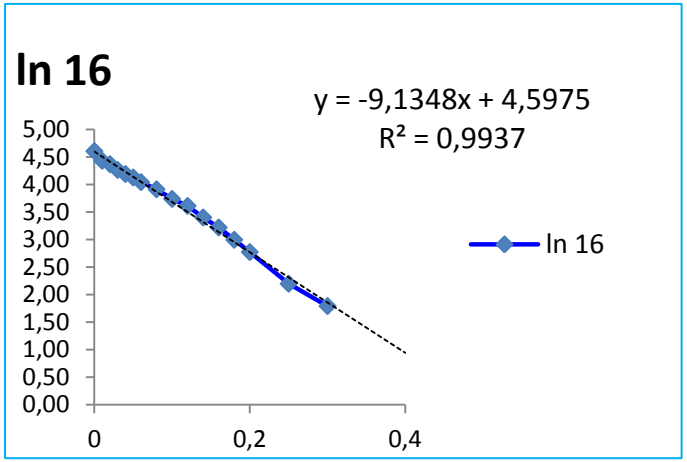
calibration of cold cathode gauge

$CH_4^{+\cdot} + CH_4 \longrightarrow CH_5^+ + CH_3$

$k_{CH4} = 1{,}1 \times 10^{-9}\ cm^3\ molecule\ s^{-1}$

time	I% m/z 16	I% m/z 17	ln 16
0	100.00	0.00	4.605
0.01	84.00	15.00	4.431
0.02	79.00	22.00	4.369
0.03	71.00	29.00	4.263
0.04	66.00	34.00	4.190
0.05	62.00	38.00	4.127
0.06	57.00	43.00	4.043
0.08	50.00	50.00	3.912
0.1	42.00	58.00	3.738
0.12	37.00	63.00	3.611
0.14	30.00	70.00	3.401
0.16	25.00	75.00	3.219
0.18	20.00	80.00	2.996
0.2	16.00	84.00	2.773
0.25	9.00	91.00	2.197
0.3	6.00	94.00	1.792
0.4	0.00	100.00	





-slope

$$k_{exp} = \frac{9{,}13}{2{,}4 \times 10^{16} \times 1{,}1 \times 10^{-7}}\ cm^3\ molecule^{-1}\ s^{-1}$$

number density at 1.1×10^{-7} mbar

$K_{exp} / k_{CH4} = f$ (calibration factor)

The efficiency (Φ) of an ion molecule reaction can be determined by comparing the experimental rate constant (k_{exp}) with a theoretical estimate of the capture rate constant (k_{coll}).

$$\Phi = \frac{k_{exp}}{k_{coll}}$$

reaction probability per collision
(number of events that bring to reaction)

Many exothermic reactions exhibit unit reaction probability at room T;

others proceed with reaction efficiency much less than unity.

1) how do we calculate k_{coll}

2) how do we explain the evidence that many exothermic reactions have unit efficiency whereas others present (very) low reaction efficiency

Theoretical aspects of ion-molecule reactions

$$A^+ + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [AB]^+ \xrightarrow{k_2} C^+ + D$$

collision complex

Capture/collision rate : $k_{coll} \sim 1 \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}

One or two orders of magnitude larger than molecule-molecule reactions

Calculation of collision rate constant

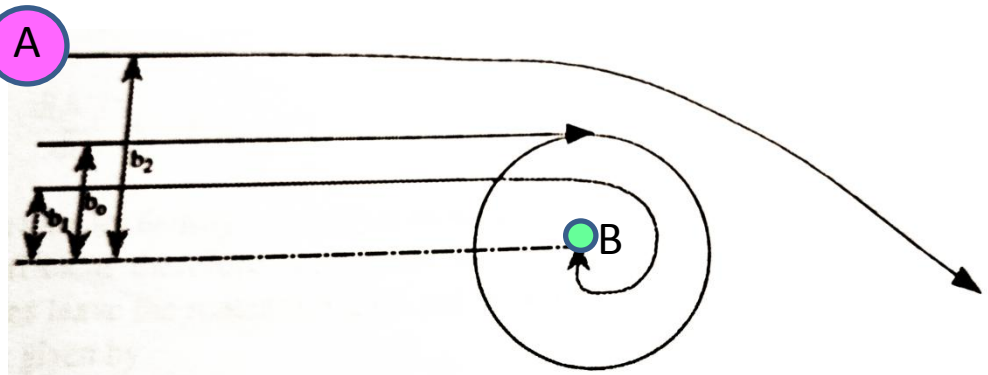
- Ion/induced dipole potential: Langevin (and Gioumousis-Stevenson) theory
- Average dipole orientation (ADO) : Su & Bowers
- Angular momentum conserved ADO : Su & Chesnavich

Langevin Theory

the ion is a point charge;
the neutral molecule has a polarizability α.

$$V = \frac{-\alpha e^2}{2r^4}$$

potential energy of attraction



the two spheres will collide for $0 \le b \le b_C$

$$k_L = 2\pi e\left(\frac{\alpha}{\mu}\right)^{1/2}$$

capture rate coefficient

equation of Giomousis and Stevenson

μ is the reduced mass of the pair

The Langevin model does not deal with the case of molecules that have a permanent dipole moment: it underestimates k_{coll} by a factor of 2.

P. Langevin, *Ann. Chim. Phys. Ser.* 1905

G. Giomousis, D. P. Stevenson, *J. Chem. Phys.* 1958

Locked dipole Theory

- it is assumed that the dipole is oriented toward the ion with a zero degree angle.
- maximization of dipole contribution: **excessively large calculated rate constants**
- Langevin treatment and "locked dipole" served to **bracket** capture limit rate constants of ion-polar molecule collisions

k_{ADO} Theory

ADO: averaged dipole orientation

- it is assumed that there is no net angular momentum transfer between the rotating molecule and the ion-molecule orbital motion
- statistical methods are used to calculate the average orientation of the polar molecule in the ion field
- predicts accurately absolute proton transfer rate constants

G. Giomousis, D. P. Stevenson, *J. Chem. Phys.* 1958

k_{ADO} Theory

ADO: averaged dipole orientation

$$V(r) = -\frac{\alpha q^2}{2r^4} - \frac{\mu_D q}{r^2}\cos\Theta$$

Θ is the instantaneous angle between the dipole and the line of interaction with the ion (in the locked dipole approximation $\cos\Theta = 1$). It varies with r.

the first term is the Langevin or induced dipole contribution

the second term reduces the dipolar contribution to V (average dipole energy)

$$k_{ADO} = \frac{2\pi q}{\sqrt{\mu}}\left\{\sqrt{\alpha} + C\mu_D\left(\frac{2}{\pi k_B T}\right)^{1/2}\right\}$$

μ is the reduced mass; μ_D is the permanent dipole;
C is a correction factor that is function of $\mu_D/\alpha^{1/2}$;
k_B is Boltzmann's constant

T. Su, . T. Bowers, *J. Chem. Phys.* 1973; *Int. J. Mass Spectrom. Ion Phys.* 1973

The double-well model for IMRs

Many exothermic ion-molecule reactions proceed at collision rates :
- ion-dipole and ion-induced dipole attraction at long range;
- large interaction energy at short range

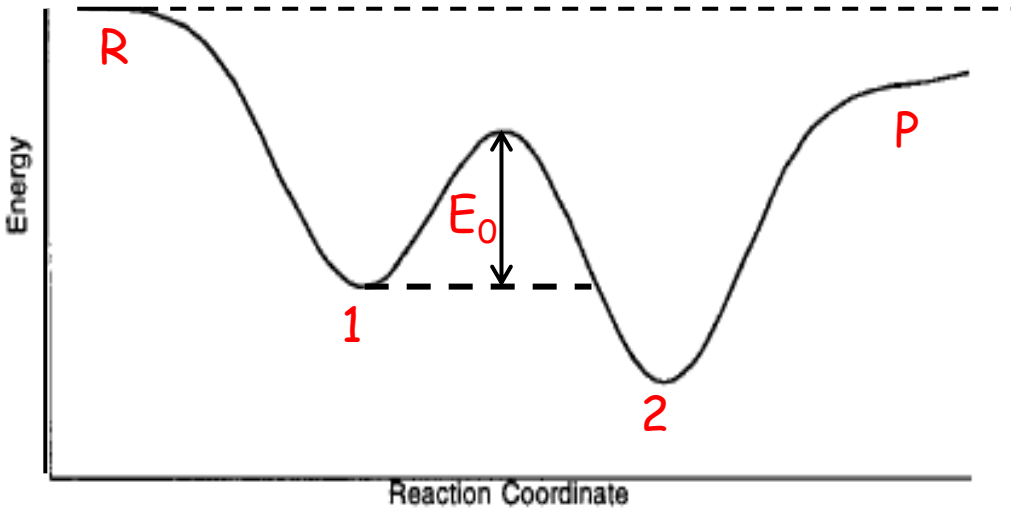
Though, many counter-examples (slow rates) are known.

slow means that most of the collisions simply return back to reactants

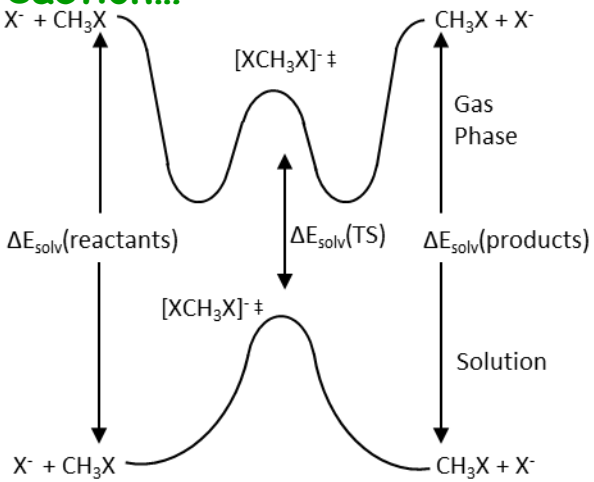
$$X^- + CH_3Y \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X^- \bullet CH_3Y \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} CH_3 X^{\bullet} Y^- \xrightarrow{k_3} CH_3X + Y^-$$

nucleophilic displacement (S_N2)

Capture is a necessary but not sufficient condition for reaction…



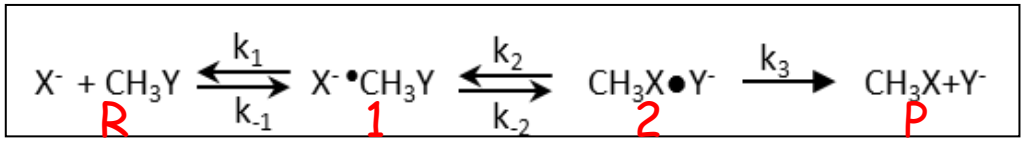
Gas-phase double-well potential energy surface.

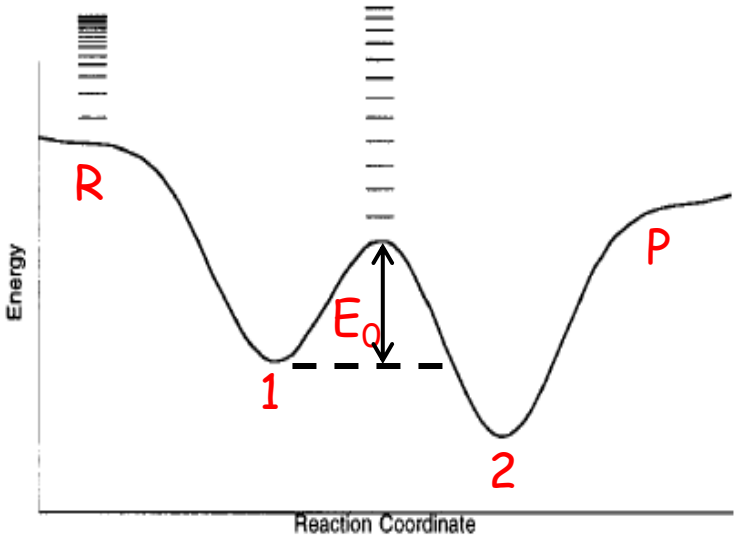


Gas-phase and solution PES for the S_N2 reaction.

W. N. Olmstead, J. I. Brauman, *J. Am. Chem. Soc.* 1977

Overall the efficiency depends on the height of the central barrier and the entropic constraints at the transition state.





under the collisionless conditions of FT-ICR, the intermediate complexes 1 and 2 are chemically activated

k_2: unimolecular isomerization with a *tight* (highy organized) TS (low A factor);
k_{-1} : fragmentation reaction with a *loose* (with many degrees of freedom) TS (high A factor)

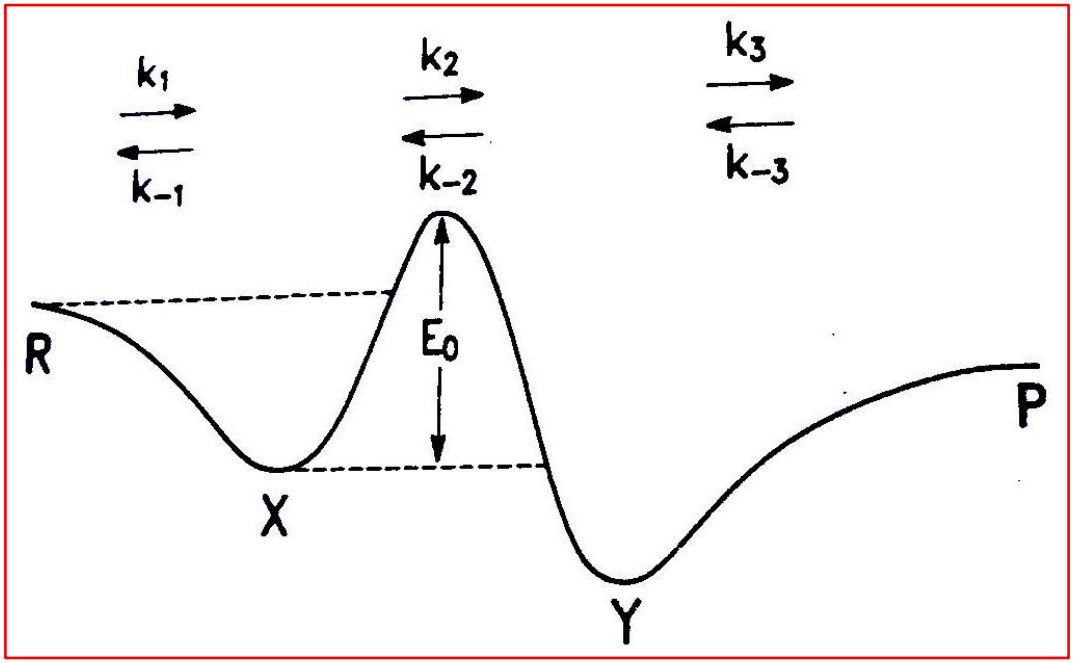
energy favors k_2; entropy favors k_{-1}

Negative temperature dependence

competition takes place between one pathway that is energetically favored and another that is entropically favored.

At low E_0 a fast reaction will occur

S. Gronert, Chem. Rev. 2001



Slow reactions

Double-minimum potential surface with a TS lying above the reactants in energy.

For **long-lived** initial complexes, the energy can be removed via photon emission (**radiative stabilization**)

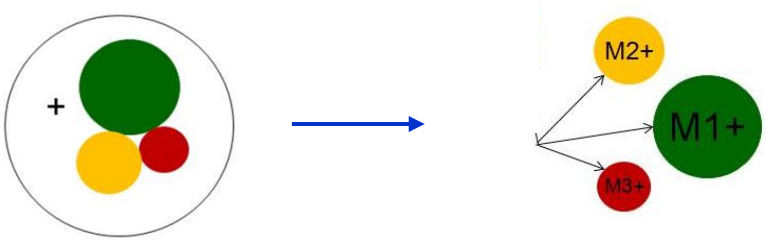
Types of Ion-Molecule Reactions

- Electron-Transfer
- Proton transfer
- H-atom/ O-atom transfer
- R^+ transfer
- H/D exchange
- Nucleophilic displacement
- Radiative association

Proton-Transfer Reactions

$$AH^+ + B \rightleftharpoons BH^+ + A$$

$$A^- + BH \rightleftharpoons AH + B^-$$

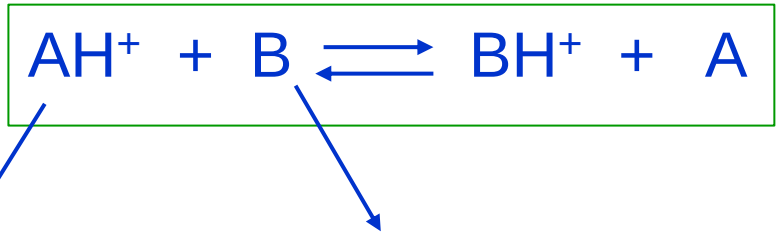


large exothermicity

$$BH^+ \longrightarrow M_1^+ + M_2^+ + M_3^+ + \text{neutrals}$$

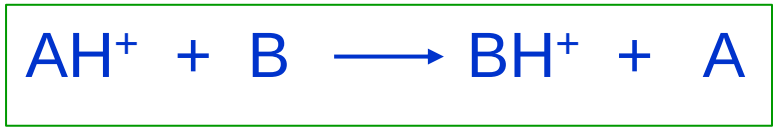
$$\mathbf{A + H^+ \rightarrow AH^+} \qquad \mathbf{GB(A) = -\Delta G°}$$

Proton-Transfer Reactions



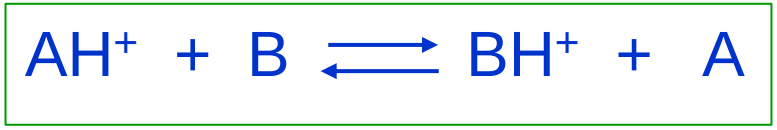
by using several reference bases B, the GB (PA) of A can be determined

Bracketing method: kinetics



- measurement of k_{exp}
- presence of gaseous B

Equilibrium method: equilibrium



- measurement of K_{eq}
- presence of gaseous A and B

$$K_{eq} = \frac{[BH]^+ [A]}{[AH]^+ [B]} \qquad \ln K_{eq} = \frac{-\Delta G^\circ}{RT}$$

Thermokinetic method

ELSEVIER

International Journal of Mass Spectrometry and Ion Processes 153 (1996) 37–48

International Journal of Mass Spectrometry and Ion Processes

A relationship between the kinetics and thermochemistry of proton transfer reactions in the gas phase

G. Bouchoux*, J.Y. Salpin, D. Leblanc

Département de Chimie, Laboratorie des Mécanismes Réctionnels, URA CNRS 1307, Ecole Polytechnique, 91128 Palaiseau, Cedex, France

A way to deduce thermochemical information from kinetic data

$$[MH]^+ + B \underset{k_{-1}}{\overset{k_{coll}}{\rightleftharpoons}} [MHB]^+ \xrightarrow{k_1} M + [BH]^+$$

$$k_{exp} = \frac{k_{coll}\ k_1}{k_{-1} + k_1}$$

$$\Phi = \frac{k_{exp}}{k_{coll}} = \frac{1}{1 + (k_{-1} / k_1)}$$

the efficiency is high for highly exoergic reactions and decreases as the transfer approaches thermoneutrality

$$k_i(T) = \frac{k_B T}{h} \exp(-\Delta G_i^{\circ\ddagger}/RT)$$

free energy change for the formation of the activated complex

$$\frac{k_{-1}}{k_1} = \exp(\Delta G_1^{\circ\ddagger}/RT) \qquad \Delta G_1^{\circ\ddagger} = -(\Delta G_{-1}^{\circ\ddagger} - \Delta G_1^{\circ\ddagger})$$

$$\Phi = \frac{k_{exp}}{k_{coll}} = \frac{1}{1 + \exp(\Delta G_I^{0*}/RT)}$$

$$\Delta G_I^{0*} = \Delta G_I^{0} + \Delta G_a^{0}$$

Intrinsic barrier separating reactants and products

free energy for the formation of the activated complex

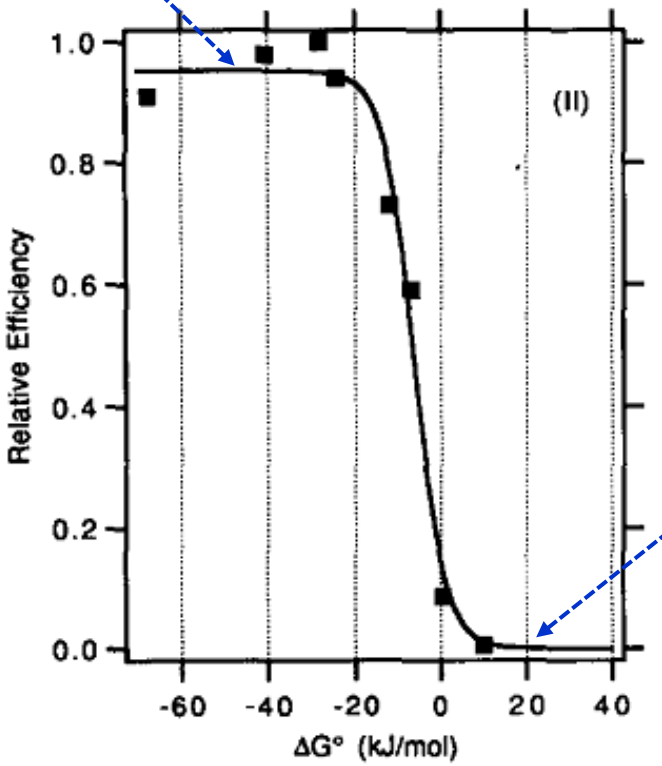
free energy for a given reaction: **GB(M)-GB(B)**

$$\Phi = \frac{1}{1 + \exp[(\Delta G_I^{0} + \Delta G_a^{0})/RT]}$$

provides a direct link between the kinetic and thermodynamic properties of a proton transfer reaction

G. Bouchoux, Int. J. Mass Spectrom. Ion Processes 1996

a high efficiency is observed for exoergic reactions ($\Delta G_l^0 \leq -20$ kJ mol^{-1})



an efficiency close to zero is associated with endoergic processes ($\Delta G_l^0 \geq 10$ kJ mol^{-1})

correlation of Eff with ΔG° allows to determine the unknown GB(M) from a series of experiments involving bases B of known GB

G. Bouchoux, Int. J. Mass Spectrom. Ion Processes 1996

$$H_3SO_3^+ + B_i \rightarrow B_iH^+ + H_2SO_3$$

$$\Delta G^\circ_1 = GB(H_2SO_3) - GB(B_i)$$

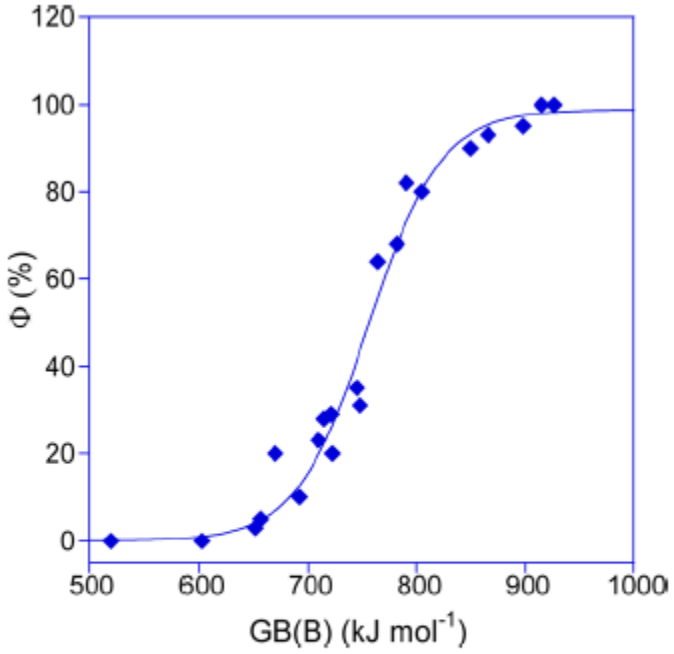
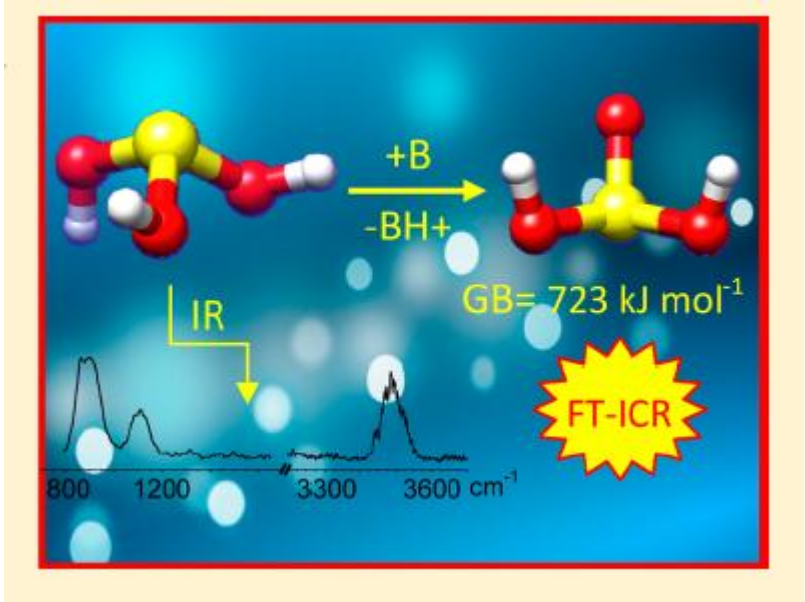


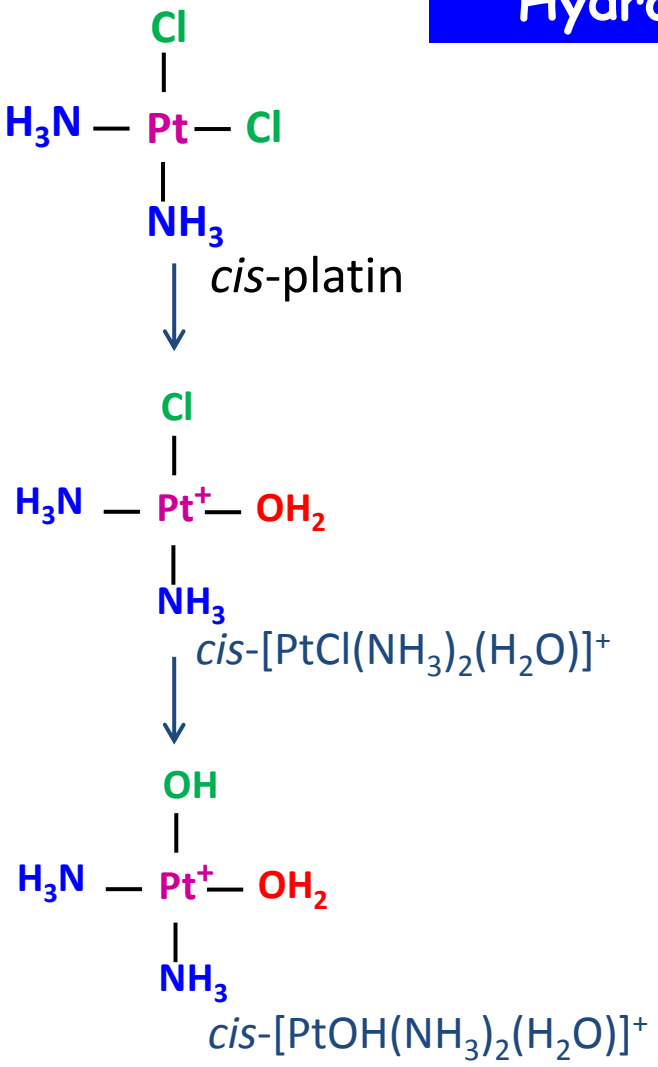
Figure 1. Reaction efficiency (Φ) for the $H_3SO_3^+ + B_i \rightarrow B_iH^+ + H_2SO_3$ proton-transfer reaction plotted versus the GB of the reference bases B_i. The solid curve fits the experimental data based on the parametric function $\Phi = a/\{1 + \exp[(c - GB_{298}(B_i))b]\}$.

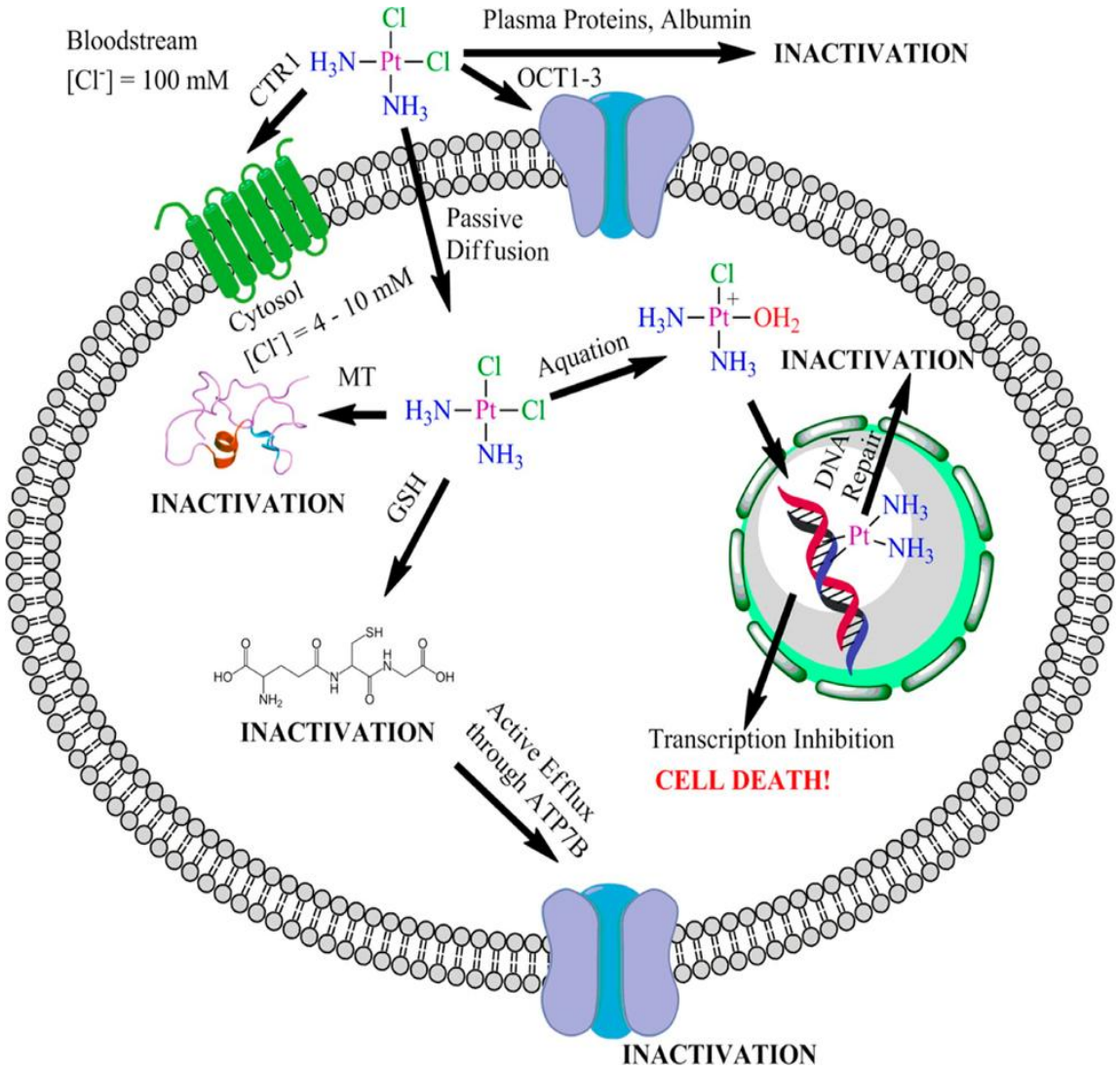
H_2SO_3
highly elusive molecule



M. E. Crestoni, S. Fornarini et al., J. Phys. Chem. Letters 2015

Hydrolysis of cis and transplatin





S. Fornarini et al., RSC Adv. 2017

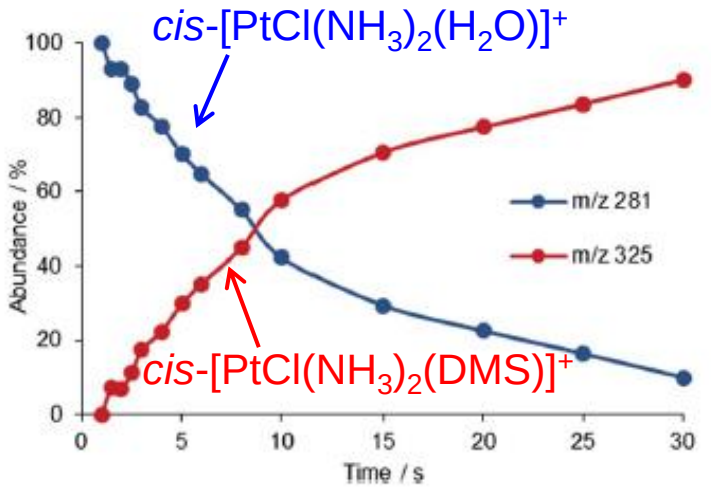
cis/trans-$[PtX(NH_3)_2(H_2O)]^+$ + L ⟶ *cis/trans*-$[PtX(NH_3)_2(L)]^+$ + H_2O

(X=Cl, OH)

Table 2 Reactivity of $[PtX(NH_3)_2(H_2O)]^+$ (X = Cl, OH; *cis* and *trans* isomers) with simple molecules in the gas-phase

Reagent ion	Neutral	k_{exp} [a]	Eff [b] (%)
cis-$[PtCl(NH_3)_2(H_2O)]^+$	TMP	3.7	2.5 [b]
	Pyridine	0.6	0.41 [b,c]
	Thioanisole	1.4	1.1 [b]
	Dimethylsulfide	0.034	0.026
trans-$[PtCl(NH_3)_2(H_2O)]^+$	TMP	3.3	2.3
	Pyridine	1.4	0.93 [d]
	Thioanisole	7.7	6.3
	Dimethylsulfide	2.4	1.7
cis-$[Pt(OH)(NH_3)_2(H_2O)]^+$	TMP	0.96	0.66
	Pyridine	0.46	0.31 [e]
	Thioanisole	0.1	0.08
	Dimethylsulfide	n. r. [f]	
trans-$[Pt(OH)(NH_3)_2(H_2O)]^+$	TMP	1.1	0.78
	Pyridine	0.05	0.03 [g]
	Thioanisole	0.46	0.37
	Dimethylsulfide	n. r. [f]	

[a] Second order rate constant in units of 10^{-11} cm^3 s^{-1} at 298 K, estimated error ±30%. Other sampled compounds proved to be



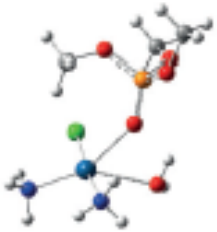
S. Fornarini et al., RSC Adv. 2017

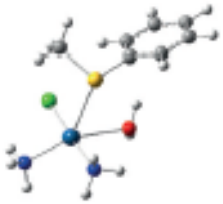
Ligand exchange is a stepwise process

$$[PtX(NH_3)_2(H_2O)]^+ + L \rightleftharpoons \underset{RC}{[PtX(NH_3)_2(H_2O)]^+ \bullet L} \overset{TS}{\rightleftharpoons}$$

$$\underset{PC}{[PtX(NH_3)_2(L)]^+ \bullet H_2O} \longrightarrow [PtX(NH_3)_2(L)]^+ + H_2O$$

Φ for the overall process depends on the branching of RC





cis-[PtCl(NH$_3$)$_2$(H$_2$O)]$^+$ + L

TMP
(143)

TA
(88)

TMP_TS

TA_TS

TMP_TS
(76)

TA_TS
(40)

0

cis-[PtCl(NH$_3$)$_2$(H$_2$O)](L)$^+$

cis-[PtCl(NH$_3$)$_2$(L)] $^+$ + (H$_2$O)

TMP_1
(41)

TMP_1
(-14)

TA_1
(-21)

TA_1
(-84)

cis-[PtCl(NH$_3$)$_2$(L)](H$_2$O)$^+$

higher Φ of TMP : high threshold energy for back dissociation vs activation energy for ligand exchange

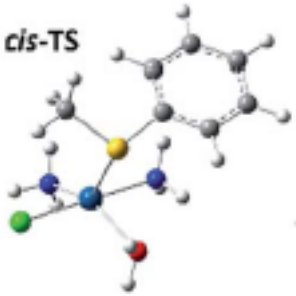
PES for the reaction of *cis*-[PtCl(NH$_3$)$_2$(H$_2$O)]$^+$ with L= TMP, TA. Relative enthalpies (kJ mol^{-1}) at 298 K are reported at the wB97X-D/6-311+G(d,p) level of theory.

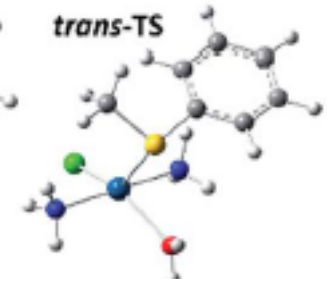
cis-$[PtCl(NH_3)_2(H_2O)]^+$ + TA

115

trans-$[PtCl(NH_3)_2(H_2O)]^+$ + TA

105





trans effect *operated by a resident ligand on the rate of substitution of the ligand trans to it.*

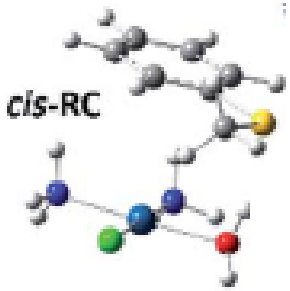
TS
69

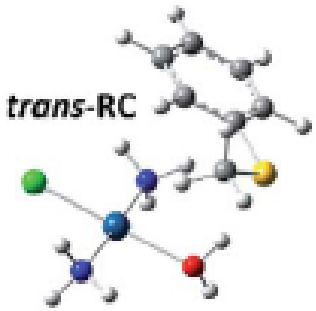
TS
51

trans*: higher energy difference between the separated reactants and the TS for the trans (54 kJ mol^{-1}) respect to the cis (46 kJ mol^{-1})*

0

RC





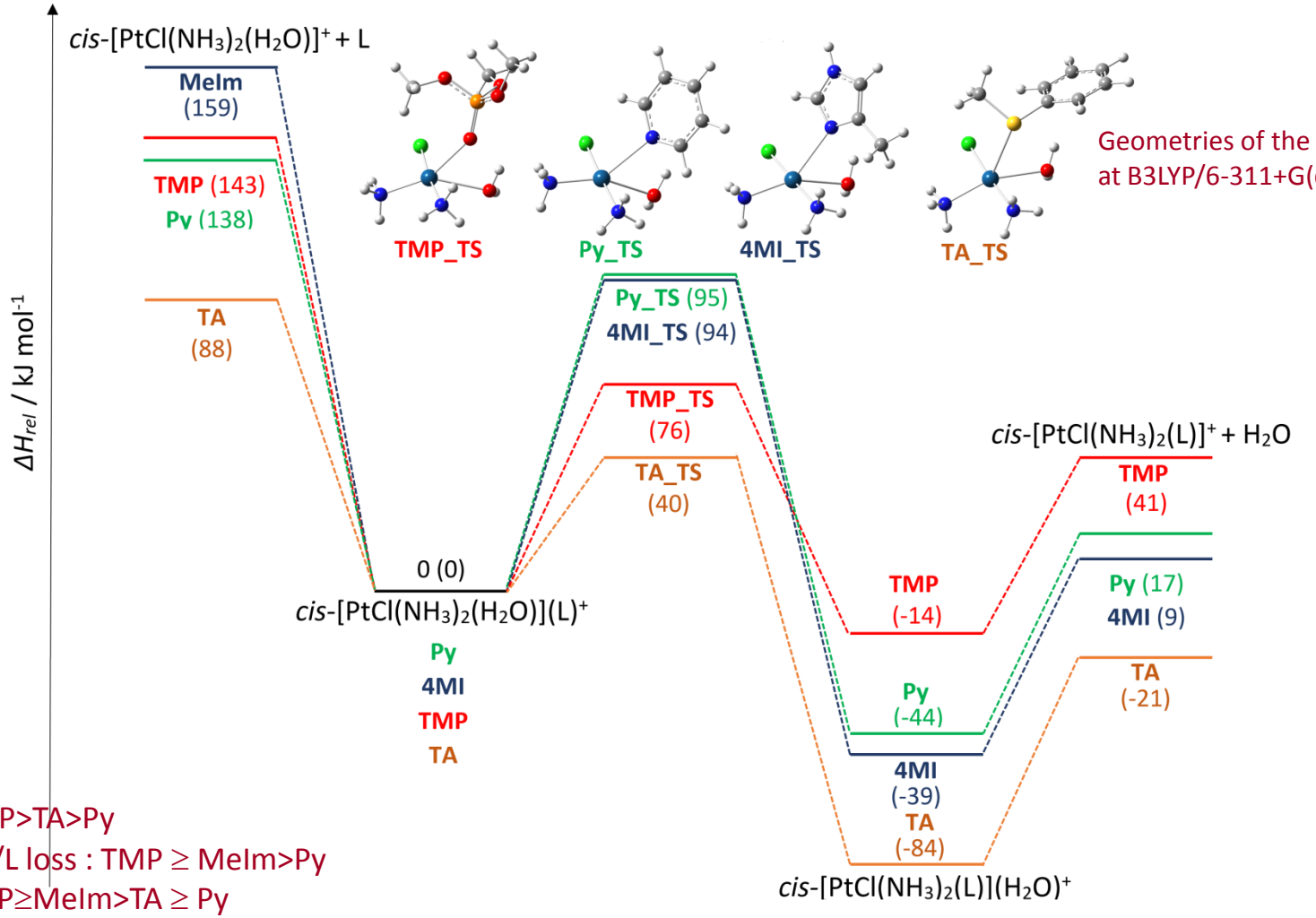
cis-$[PtCl(NH_3)_2(TA)]^+ + H_2O$
(6)

trans-$[PtCl(NH_3)_2(TA)]^+ + H_2O$
(-5)

PC
(-54)
(-57)

trans-directing sequence $Cl^- > NH_3$

PES for the reaction of *cis*-$[PtCl(NH_3)_2(H_2O)]^+$ with L (L= Py, 4-MeIm, TMP, TA)



Geometries of the transition states at B3LYP/6-311+G(d,p) level

Eff%: TMP>TA>Py

H_2O loss/L loss : TMP ≥ MeIm>Py

δΔH: TMP≥MeIm>TA ≥ Py

Corinti, Coletti, Re, Chiavarino, Crestoni, Fornarini *Chem. Eur. J.* **2016**, *22*, 3794

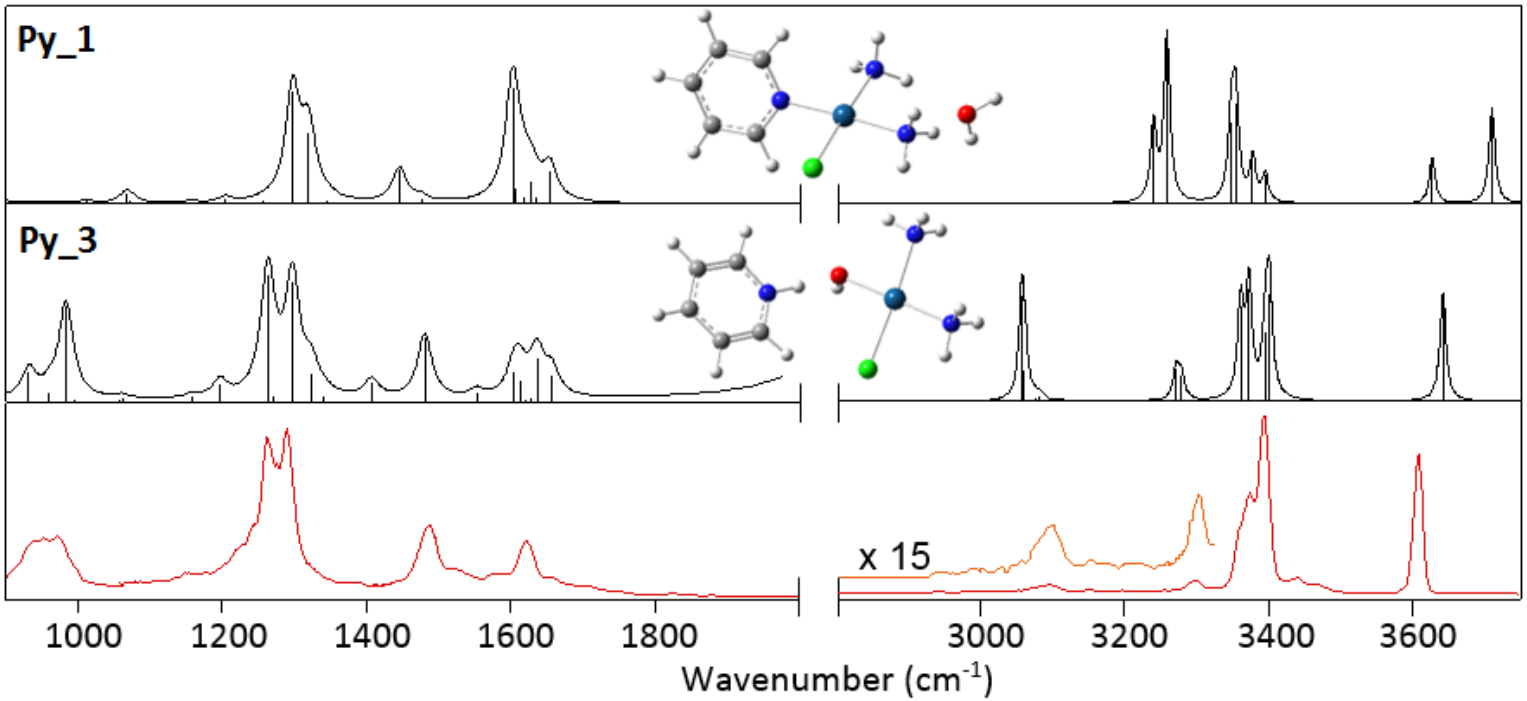
EU FT-ICR MS

SC3- Roma, 25-27 June 2019

"I just love it when they explode out of the water"

ESI can 'fish' reactants, intermediates and products, either ionic species or molecules in ionic form.

IR spectroscopy of $[PtCl(NH_3)_2(Py)(H_2O)]^+$



Corinti, Coletti, Re, Chiavarino, Crestoni, Fornarini *Chem. Eur. J.* **2016**, *22*, 3794

Ligand substitution at the encounter/collision complex level

ligand substitution in water

$$cis\text{-}[PtCl(NH_3)_2(H_2O)]^+ + L \rightleftharpoons cis\text{-}[PtCl(NH_3)_2(H_2O)](L)^+ \rightleftharpoons cis\text{-}[PtCl(NH_3)_2(L)]^+ + H_2O$$

encounter/collision complex

CID or IRMPD

CID or IRMPD

$$M(OH_2)^{m+} + L^{x-} \rightleftharpoons M\cdot(OH_2)\cdot L^{(m-x)+} \rightleftharpoons ML^{(m-x)+} + H_2O$$

Eigen-Wilkins reactant preassociation model

Corinti, Coletti, Re, Chiavarino, Crestoni, Fornarini *Chem. Eur. J.* **2016**, *22*, 3794