Master de Chimie Moléculaire et Supramoléculaire

Introduction à la chimie supramoléculaire

Des atomes aux molécules : Chimie et synthèse moléculaires

Des molécules aux complexes : Chimie et synthèse supramoléculaire

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Chimie Supramoléculaire

Ouvrages

1) Supramolecular Chemistry

Concepts and perspectives

J.-M. Lehn

VCH, Weinheim

2) Aspects de la chimie des composés macrocycliques

B. Dietrich, P. Viout, J.-M. Lehn

InterEditions/Editions du CNRS, Chichester

3) Supramolecular Chemistry

F. Vögtle

Wiley, Chichester

4) Supramolecular Chemistry

J. W. Steed, J. L. Atwood

Wiley, Chichester

Introduction à la chimie supramoléculaire

Les objectifs de cours est d'initier à la chimie supramoléculaire des étudiants en première année de Master. Etant donné le nombre d'heures consacré à cette tache, nous ne pouvons pas être exhaustifs. Pour cette raison, nous présentons essentiellement les concepts généraux que nous ponctuons d'exemples réels.

Le plan suivi est :

1) Interactions et reconnaissance moléculaire
- Type d'interactions
- Reconnaissance et stabilité
- Stoichiométrie des complexes
- Reconnaissance et sélectivité

2) Préorganisation et récepteurs moléculaires
- Topologie et géométrie de récepteurs
- Les podants
- Les coronands
- Les cryptands

3) Reconnaissance de substrats cationiques
- Effets de l'organisation
- Les éthers couronnes
- Les cryptands

4) Reconnaissance de substrats neutres
- Reconnaissance par liaisons hydrogène
- Polynucléotides et ADN

5) Quelques classes de particulières de récepteurs
- Les cyclodextrines
- Les métallamacrocycles

6) Reconnaissance de substrats anioniques
- Récepteurs d'anion
- Reconnaissance d'anions sphérique
- Reconnaissance d'anions linéaire
- Reconnaissance de nucléotides

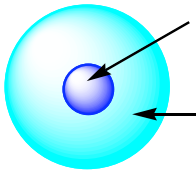
7) Extraction
- Extraction et solubilisation de sels en milieu organique

8) Transport
- Transport passif et
- Sélectivité de transport
- Transport actif

9) Réactivité et catalyse supramoléculaire
- Catalyse par transfert de phase
- Catalyse d'yhdrolyse d'esters sur substrats cationiques
- Catalyse de rupture de liaisons sur substrats anioniques
- Cocatalyse de formation de liaisons

10) Quelques classes de molécules particulières
- Les rotaxanes et caténanes
- Les calixarènes
- Les porphyrines
- Les dendrmères

Atomes : un monde petit et vaste

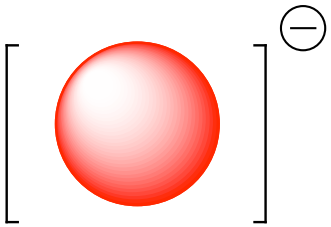


Noyau (Neutrons + Protons)
Chargé positivement

Nuage Electronique
Chargé négativement

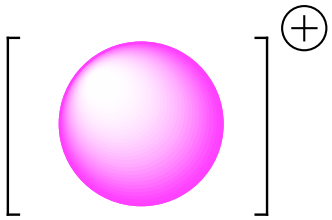
Neutre

Ions



Anion

Charge

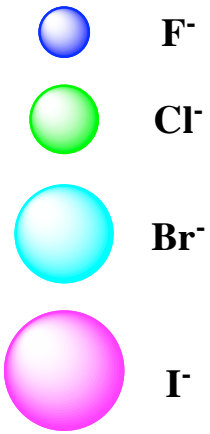


Cation

Dimension
- Noyau : 10^{-14} m
- 1Å = 10^{-10} m
- Atome : 10^{-10} m

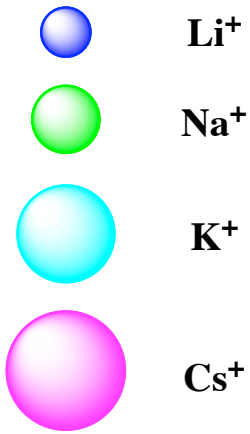
Géométrie : Sphérique

Taille



F^-
Cl^-
Br^-
I^-

Halogenures



Li^+
Na^+
K^+
Cs^+

Alcalins

Molécule = des **atomes** connectés par des liaisons (*interactions*) fortes ou liaisons covalentes.
Le lien ou ciment qui relie les atomes est une densité électronique

Alors que l'atome est sphérique, les molécules peuvent avoir des géométries simples ou complexes très variées

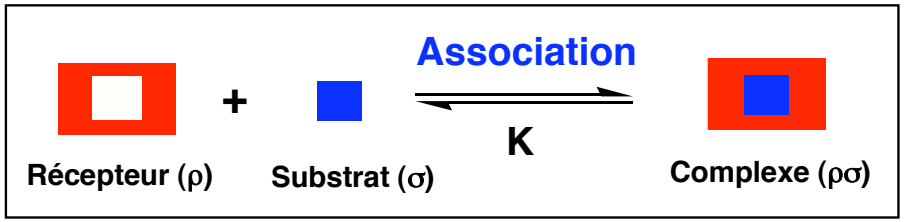
103 Eléments chimiques "utilisables"
Ceci conduit à une infinité de combinaisons possibles

Interactions Intermoléculres et la Reconnaisance Moléculaire

***Au delà de la chimie moléculaire*,**
fondée sur la liaison covalente, s'étend ainsi un domaine qu'on peut nommer *supramoléculaire* : la chimie des *interactions moléculaires*, des associations de deux ou plusieurs espèces chimiques, les complexes, et de la liaison intermoléculaire.

Jean-Marie Lehn, Leçon Inaugurale au Collège de France, 7 mars 1980

La reconnaissance moléculaire implique une complémentarité de formes, de charges et de tailles entre le récepteur et le substrat.



$$K = \frac{[\rho\sigma]}{[\rho] \times [\sigma]}$$

$$\Delta G = -RT\ln K$$

$$\Delta G = \Delta H - T\Delta S$$

$$K = \frac{k_f}{k_d}$$

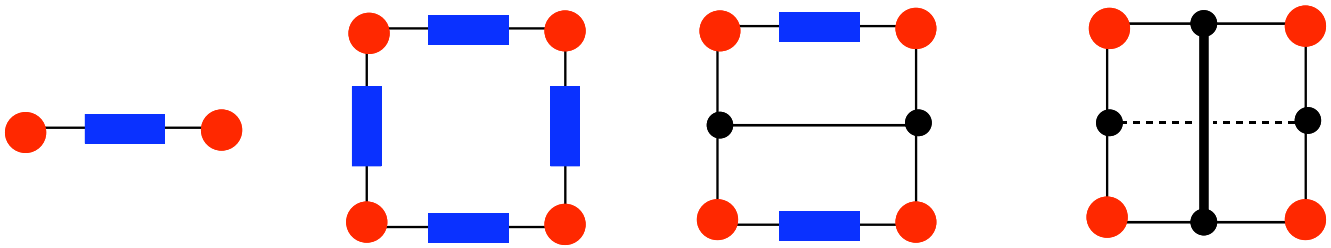
K_f = Constante de formation
K_d = Constante de dissociation

La reconnaissance moléculaire résulte d'une association entre un récepteur ou molécule hôte (ρ) et un substrat ou molécule invitée (σ) conduisant à un complexe moléculaire.
Cette association se fait par des processus réversibles conduisant à un équilibre caractérisé par une constante K.

Récepteurs moléculaires

Un récepteur est composé de deux parties
- **une squelette (partie permettant d'organiser des sites d'interaction dans l'espace**
- **Des sites d'interaction capables d'interagir avec le substrat**

Topologie

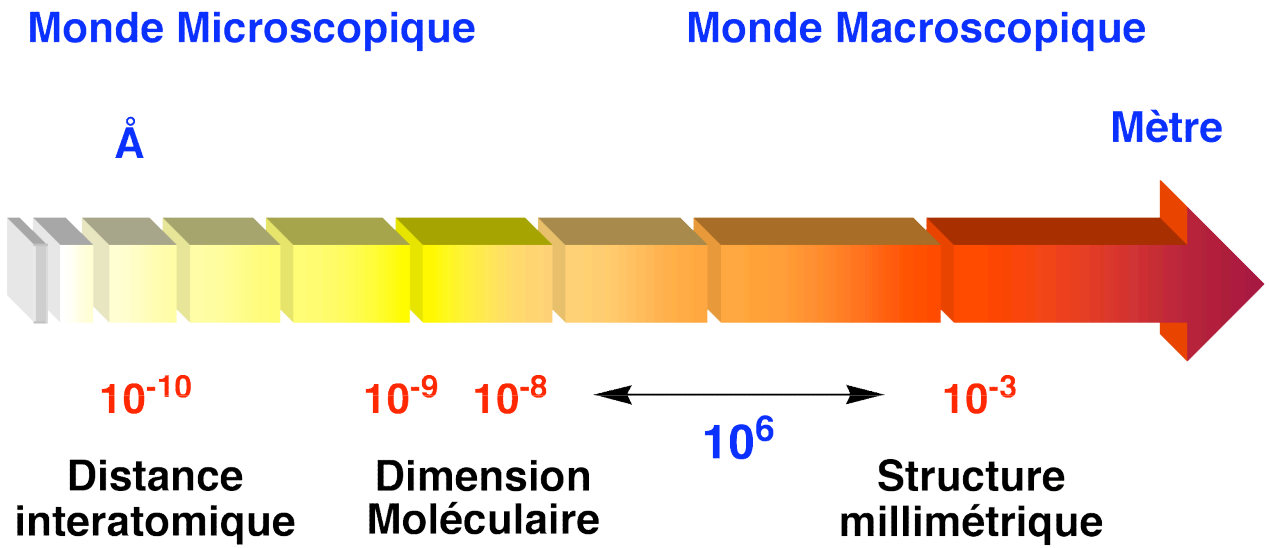


Linéaire **Macrocyclique** **Macrobicyclique** **Macrotricyclique**

Site d'interaction,chargés ou neutres, riches ou pauvre en densité électronique

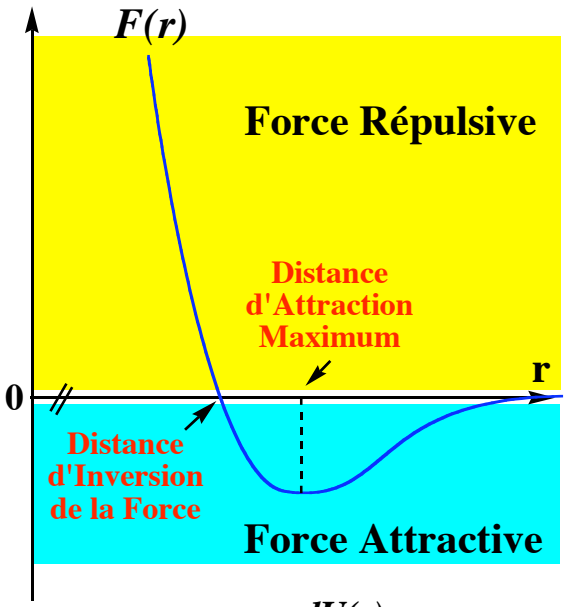
Espaceur (flexible ou rigide) contrôlant l'espacement (distance) entre les sites d'interaction

Echelle des Dimensions



Energie et Force d'Interaction

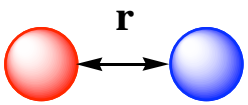
Force



$$F(r) = -\frac{dU(r)}{dr}$$

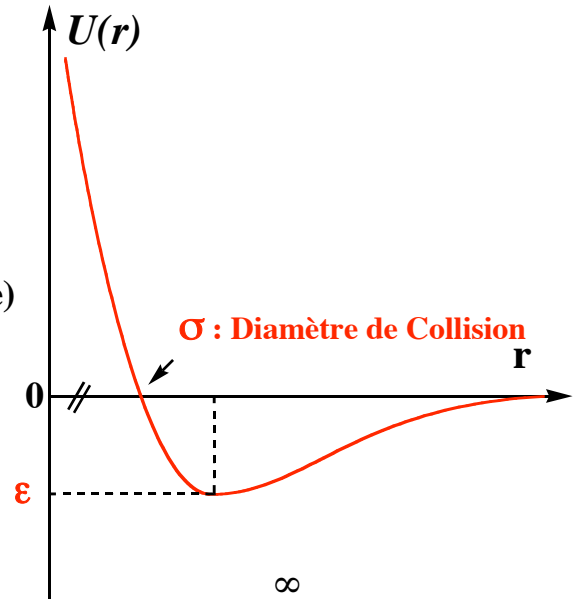
A l'infini, il n'y a pas d'interaction

Simplification:



Deux Molécules Sphériques (Isotropie)
Pas de dépendance Angulaire

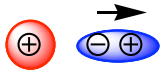
Energie ou Potentiel



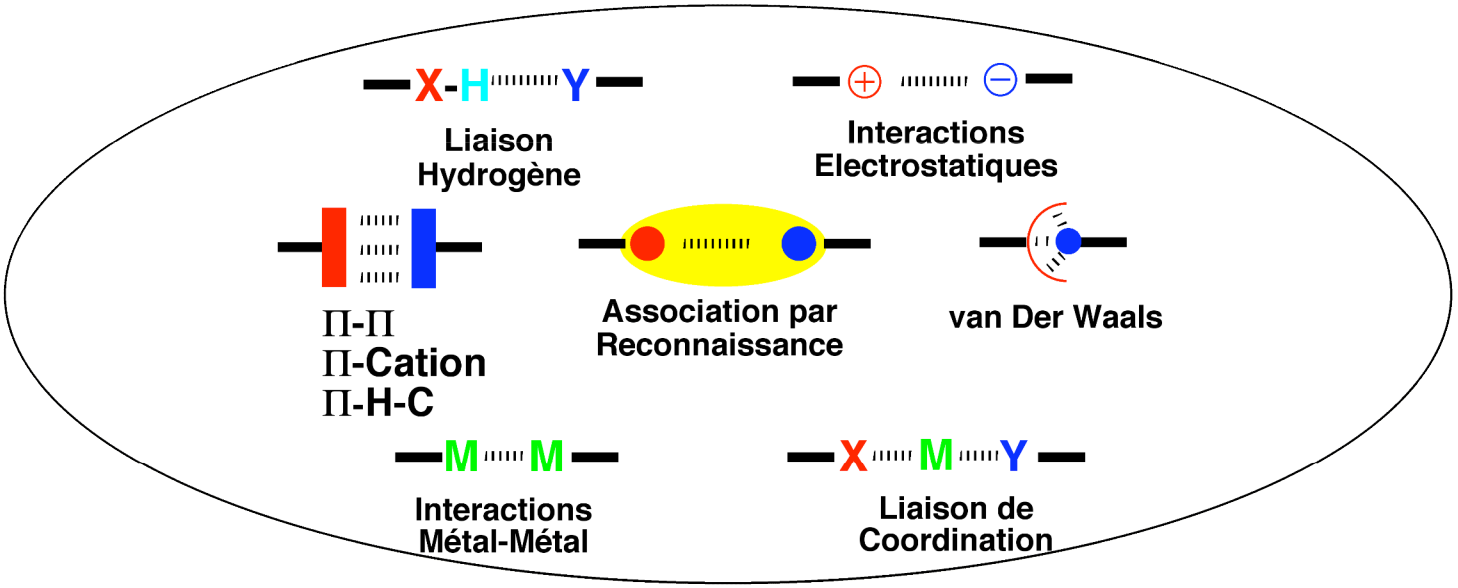
$$U(r) = \int_{r}^{\infty} F(r)dr$$

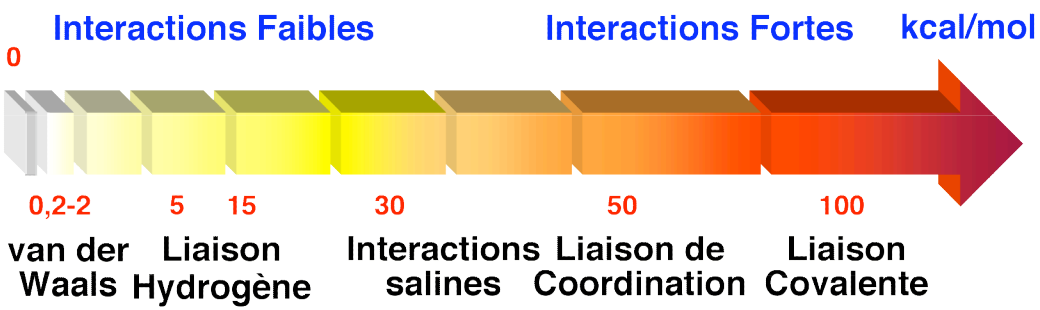
Travail effectué pour amener les deux molécules à la distance r

Les interactions : nature, force et portée

	Origine	*Intensité*	*Dépendance*	*Porté*
REPULSIVE		**Très Intense**	$\frac{1}{r^9}$ à $\frac{1}{r^{16}}$	**Très Courte**
ATTRACTIVE	***Coulombienne*** **Ion-Ion**	**Très Intense**	$\frac{1}{r}$	**Très Longue**
	 **Ion-Dipôle fixe**	**Intense**	$\frac{1}{r^2}$	**Longue**
	Dipolaire **Dipôle-Dipôle fixes**	**Moyenne**	$\frac{1}{r^3}$	**Longue**
	Polarisation **Ion-Molécule**	**Faible**	$\frac{1}{r^4}$	**Moyenne**
	Dispersion **Molécule-Molécule**	**Moyenne**	$\frac{1}{r^6}$	**Courte**

La Boite à outils de la chimie supramoléculaire

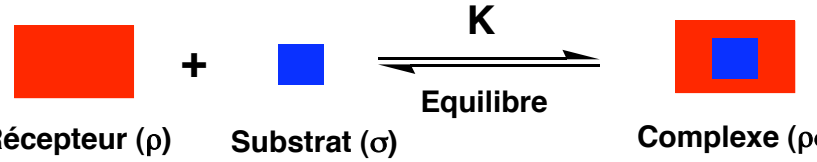




Reconnaissance Moléculaire

La reconnaissance moléculaire résulte d'une association entre un récepteur (ρ : ou molécule hôte) et un substrat (σ : molécule invitée).
Cette association se fait par des processus réversibles qui conduisent à un équilibre chimique entre le récepteur et le substrat libres et le complexe. A cette équilibre correspond une constante d'équilibre K (paramétre thermodynamique). Parfois on utilise K_s (constante de stabilité) ou K_{ass} (constante d'association)

Association



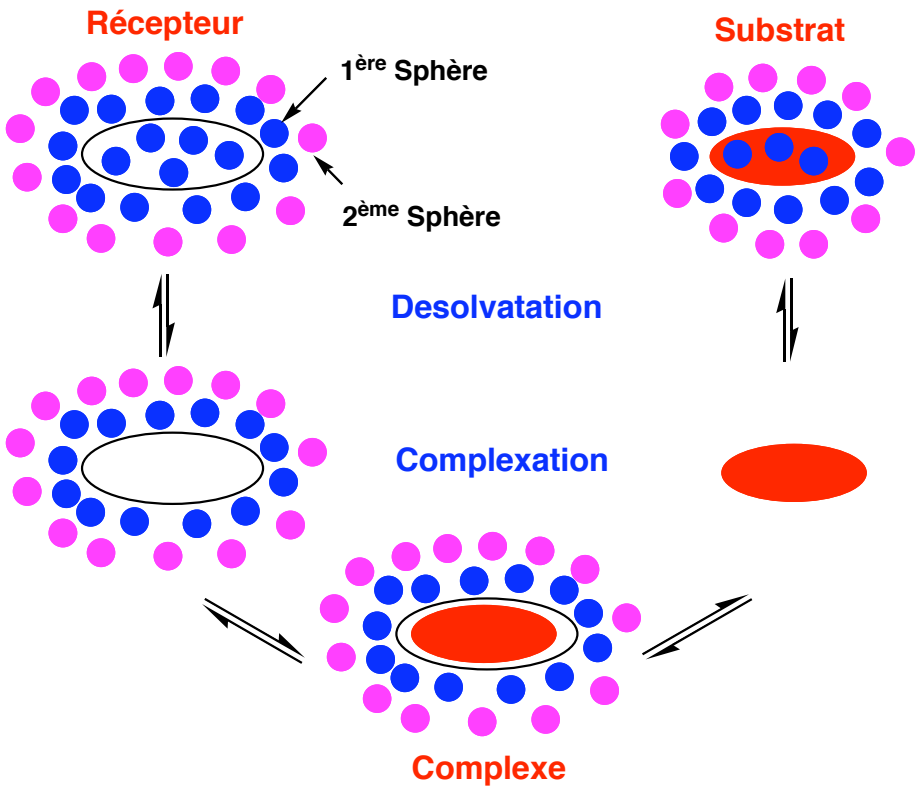
$$K = \frac{[\rho\sigma]}{[\rho] \times [\sigma]}$$

K = Constante d'équilibre

Une association forte correspond à une constante d'équilibre élevée.
Pour des concentrations de récepteur et de substrat données, plus la valeur de K est élevée, plus la concentration du complexe est élevée et par conséquent les concentrations du récepteur et du substrat libres sont faibles.

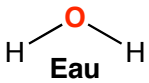
Association Moléculaire

En réalité, souvent le processus de reconnaissance a lieu en phase liquide (cependant, on ne peut pas exclure la formation de complexe en phase gaz). Or, en solution à la fois le récepteur et le substrat sont solvatés. Pour que le substrat et le récepteur puissent former un complexe, il faut que les deux soient au moins en partie desolvatés et le complexe solvaté. Par conséquent la complexation du substrat par le récepteur est en compétition avec la desolvatation au moins partielle des deux entités. Cette desolvation néccecite une certaine énergie (l'énergie de solvation).



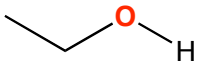
Les Solvants

Protique

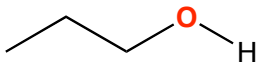


Eau

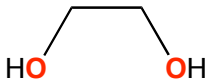
Méthanol



Ethanol

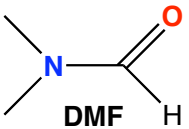


Propanol



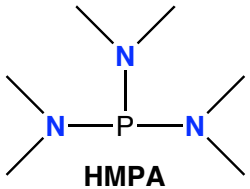
Glycol

Diéthylènglycol

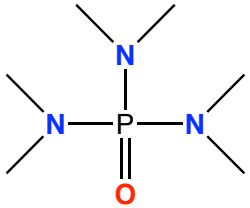


DMF

DMSO

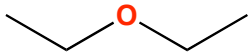


HMPA



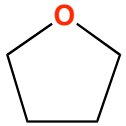
HMPT

Aprotique



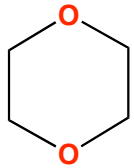
Ether

Dichlorométhane

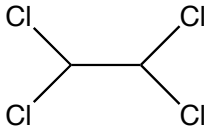


THF

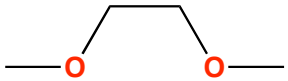
Chloroforme



Dioxane



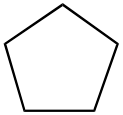
Tétrachloroéthane



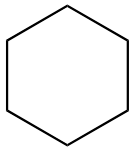
Diméthoxyéthane

Pentane

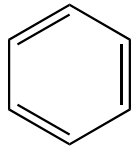
Hexane



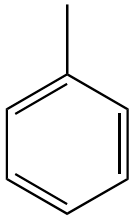
Cyclopentane



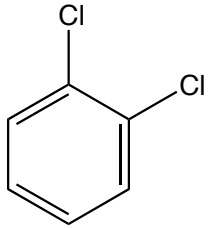
Cyclohexane



Benzène

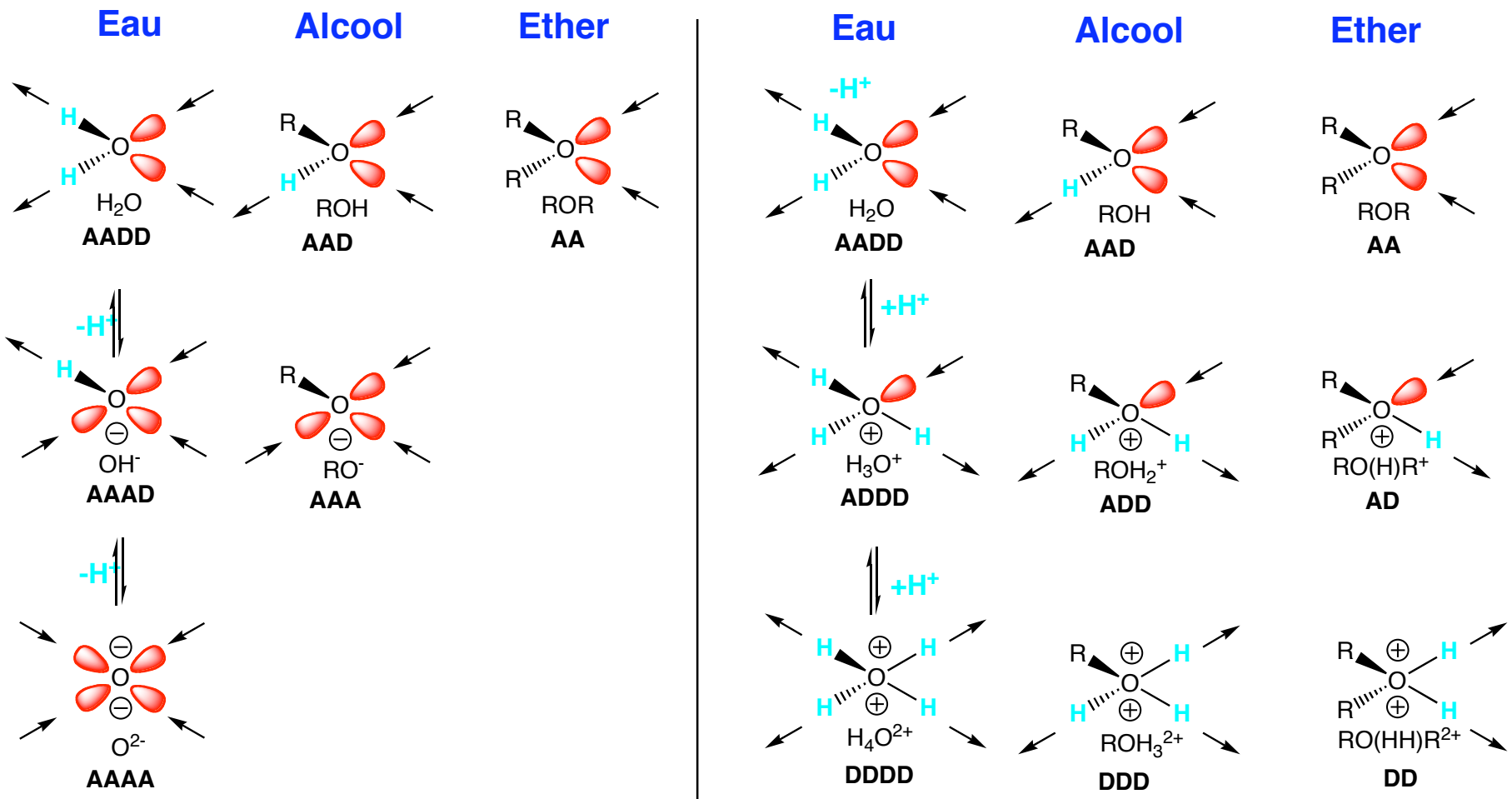


Toluène



1,2-Dichlorobenzène

Eau, Alcool et Ether



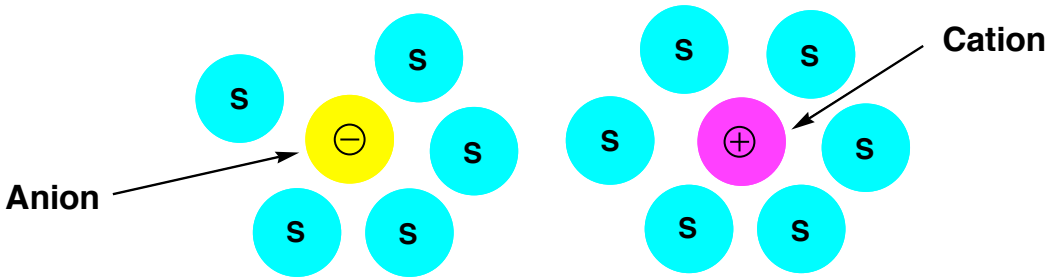
Déprotonation (caractère acide)

Protonation (caractère basique)

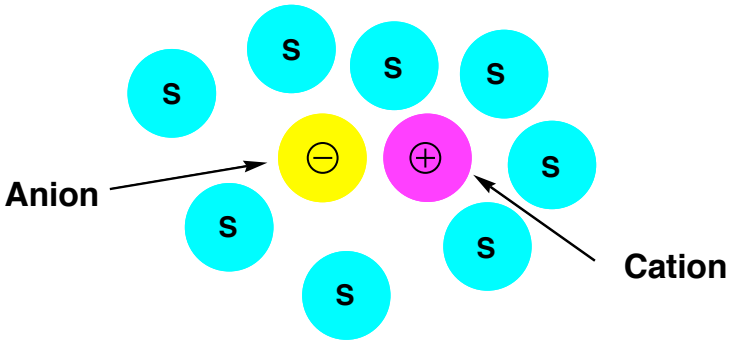
La solvatation

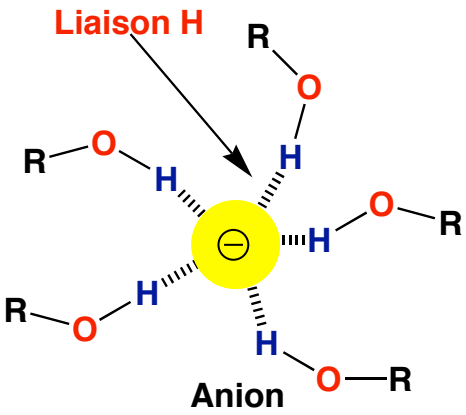
*Plus un composé est polaire, plus il sera insoluble dans les solvants apolaires (ε faible: alcane, benzène toluène etc...) et plus il sera soluble dans les solvants polaires.

*Plus un solvant est polaire plus il possède un pouvoir dissociant. En solvatant les espèces chargées, il conduit à une séparation des charges (paire d'ions séparés)

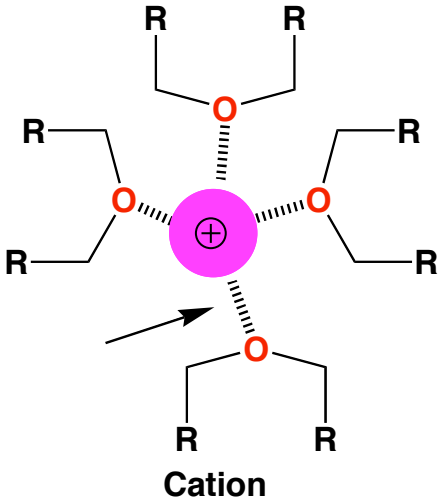


*Plus un solvant est apolaire moins il possède un pouvoir dissociant (pas de séparation des charges). Les espèces chargées forment une paire d'ions intimes (associée).



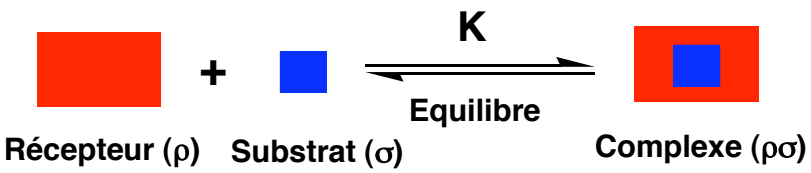


Interactions Electrostatiques charge/dipôles



Reconnaissance Moléculaire

Thermodynamique

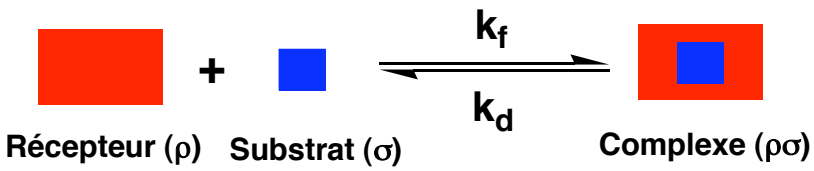


$$K = \frac{[\rho\sigma]}{[\rho] \times [\sigma]}$$

$\Delta G = -RT\ln K$
$\Delta G = -2.3RT\mathrm{Log}K$
$\Delta G = \Delta H - T\Delta S$

Une constante d'équilibre élevée correspond à une énergie d'association élevée (valeur absolue de ΔG grande).
Une association peut être favorisée (ΔG négatif) par le facteur enthalpique (ΔH) et/ou entropique (ΔS).

Cinétique



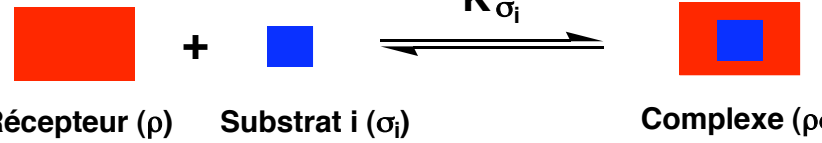
$$K = \frac{k_f}{k_d}$$

K_f = Constante de formation
K_d = Constante de dissociation

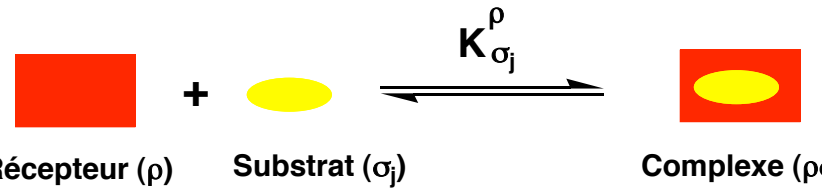
La constante d'équilibre K (paramètre thermodynamique) correspond au rapport des constantes cinétiques de formation (k_f) et de dissociation (k_d).
Une constante d'association K forte correspond à une constante de formation k_f élevée et une constante de dissociation k_f faible.

Sélectivité de Reconnaissance

Sélectivité de Substrat

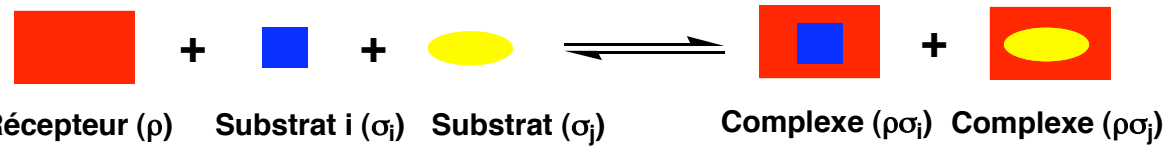


$$K^{\rho}_{\sigma_i} = \frac{[\rho\sigma_i]}{[\rho] \times [\sigma_j]}$$



$$K^{\rho}_{\sigma_j} = \frac{[\rho\sigma_j]}{[\rho] \times [\sigma_j]}$$

Compétition

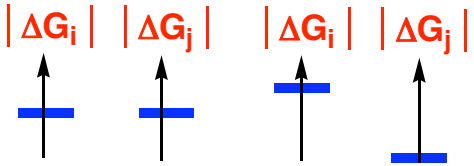


Lorsque le récepetrur ρ est mis en présence des substrats σ_i et σ_j, les deux équilibres de complexation se mettent en place, en d'autres termes, les deux complexes $\rho\sigma_i$ et $\rho\sigma_j$ se forment. Il s'agit d'une compétition entre les deux substrats σ_i et σ_j pour le récepteur ρ. Plus l'affinité du récepteur pour l'un des substrats est élevée plus la concentration du complexe correspondant sera élevée.

$$S^{\rho}_{\sigma_i\sigma_j} = \frac{K^{\rho}_{\sigma_i}}{K^{\rho}_{\sigma_i}}$$

Sélectivité de complexation ou de reconnaissance du récepteur ρ entre les substrats σ_i et σ_j.

$$\Delta G_i = -RT\ln K_i$$



$\Delta(\Delta G) = 0$

$K^{\rho}_{\sigma_i} = K^{\rho}_{\sigma_i}$

$[\rho\sigma_i] = [\rho\sigma_j]$

$\Delta G_i >>>>> \Delta G_j$

$K^{\rho}_{\sigma_i} >>>>>> K^{\rho}_{\sigma_i}$

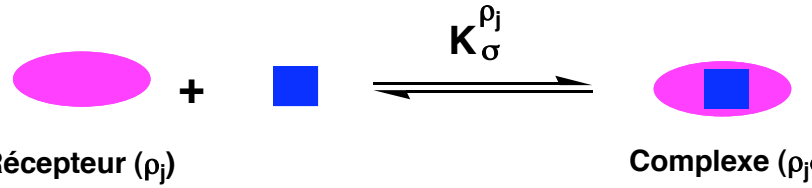
$[\rho\sigma_i] >>>>> [\rho\sigma_j]$

La qualité d'un processus de reconnaissance moléculaire se traduit par la préférence pour l'un des substrats. En d'autres termes, par la différence des constantes d'association.

Sélectivité de Reconnaissance

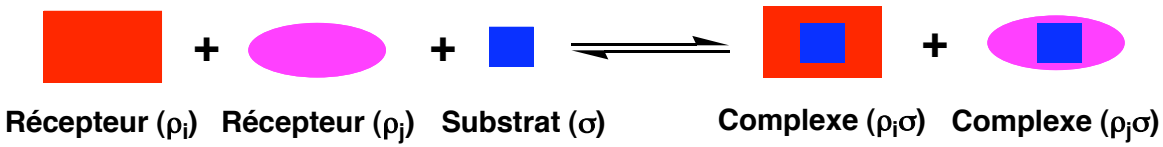
Sélectivité de Récepteur

$$K_\sigma^{\rho_i} = \frac{[\rho_i\sigma]}{[\rho_i] \times [\sigma]}$$



$$K_\sigma^{\rho_j} = \frac{[\rho_j\sigma]}{[\rho_j] \times [\sigma]}$$

Compétition

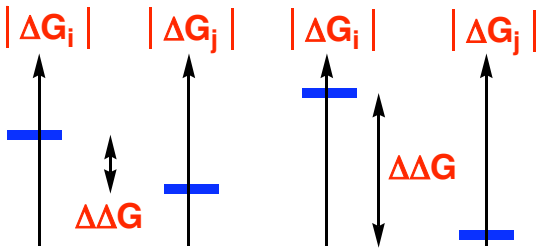


Lorsque le substrat σ est mis en présence des récepteurs ρ_i et ρ_j, les deux équilibres de complexation se mettent en place, en d'autres termes, les deux complexes $\rho_i\sigma$ et $\rho_j\sigma$ se forment. Il s'agit d'une compétition entre les deux récepteurs ρ_i et ρ_j pour le substrat σ. Plus l'affinité d'un des deux récepteurs pour le substrat est élevée plus la concentration du complexe correspondant sera élevée.

$$S^{\rho}_{\rho_i\rho_j} = \frac{K_\sigma^{\rho_i}}{K_\sigma^{\rho_j}}$$

sélectivité de complexation ou de reconnaissance du substrat σ entre les récepteurs ρ_i et ρ_j.

$$\Delta G_i = -RT\ln K_i$$



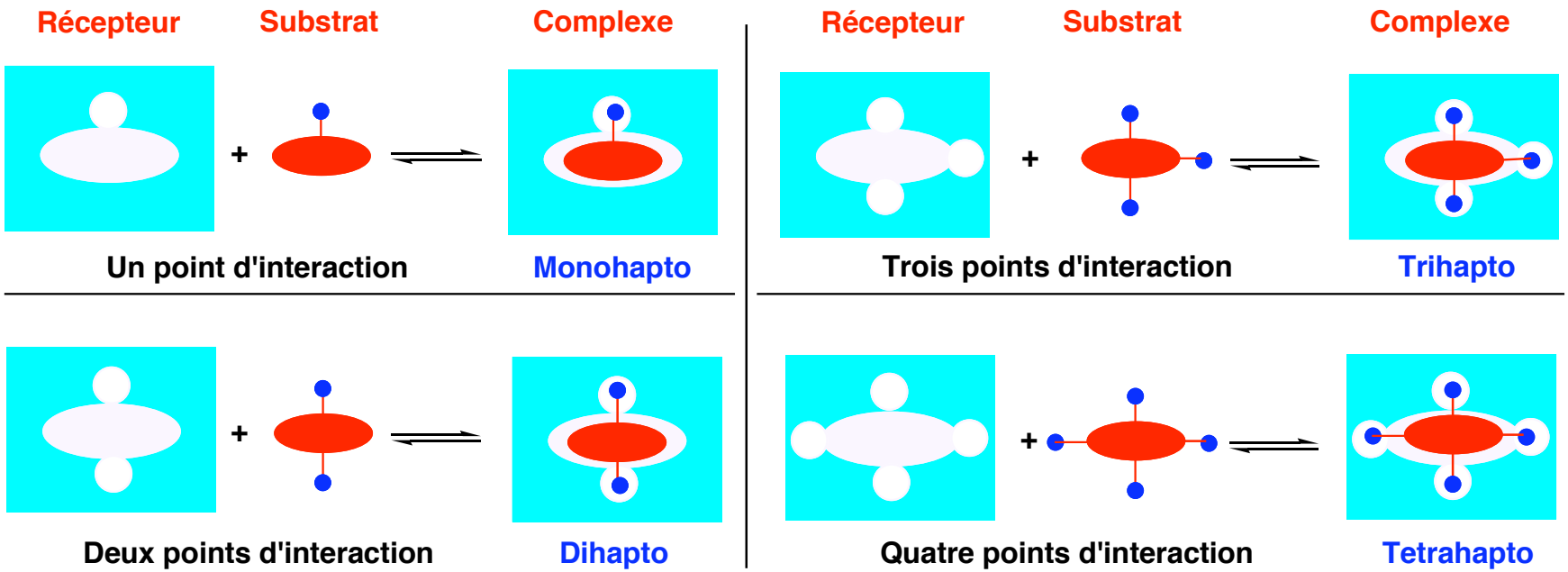
$\Delta G_i > \Delta G_j$ $\quad$ $\Delta G_i >>>>> \Delta G_j$

$K_{\sigma_i}^{\rho} > K_{\sigma_i}^{\rho}$ $\quad$ $K_{\sigma_i}^{\rho} >>>>>> K_{\sigma_i}^{\rho}$

$[\rho\sigma_i] > [\rho\sigma_j]$ $\quad$ $[\rho\sigma_i] >>>>> [\rho\sigma_j]$

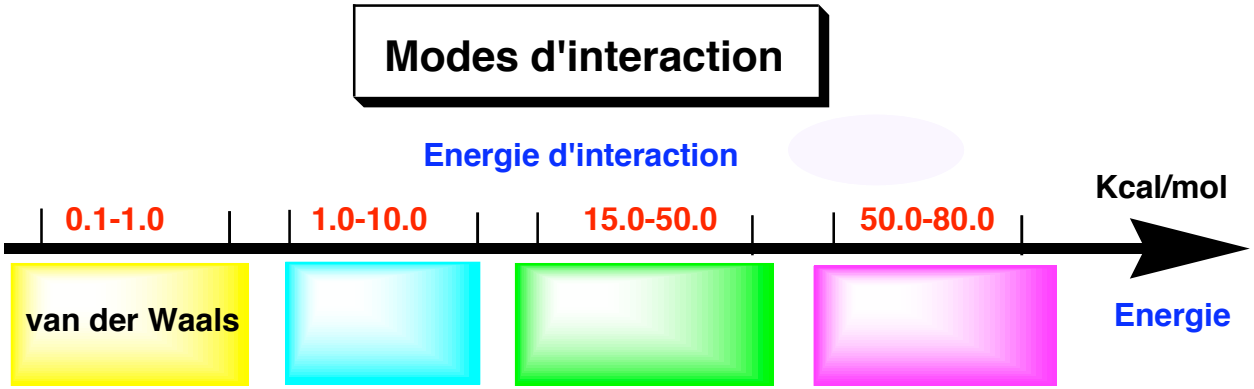
Plus la différence d'énergie libre d'association ($\Delta\Delta G$) entre les deux complexes est grande, plus la compétition est en faveur du complexe qui possède le ΔG la plus élevée.

Modes de complexation

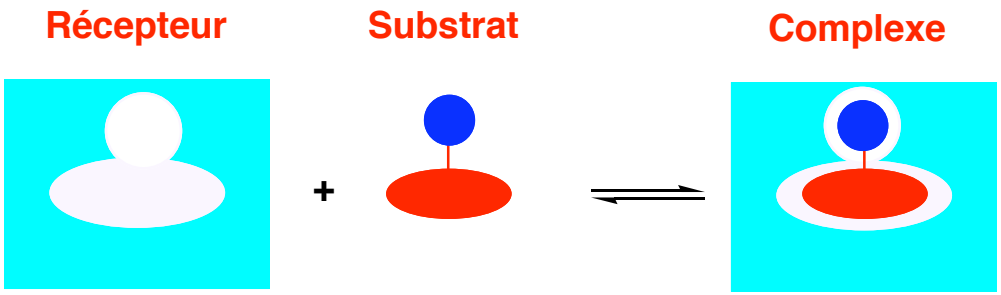


La reconnaissance moléculaire a lieu lorsqu'un ou plusieurs sites d'interaction au niveau du récepteur et du substrat entrent en contact et définissent ainsi un motif de reconnaissance.

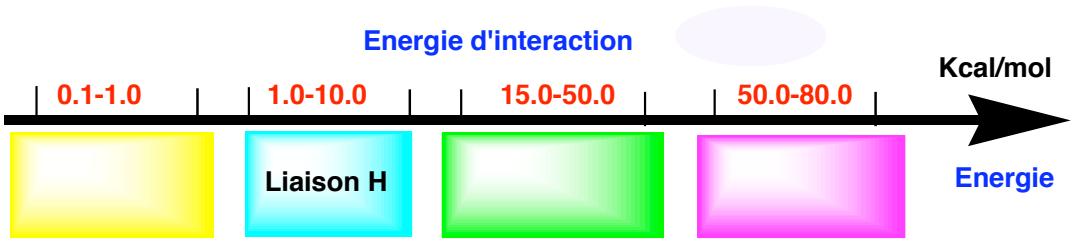
Quand le nombre de points d'interaction entre le récepteur et le substrat augmente, l'énergie d'interaction augmente (la constante d'équilibre aumente). Une disposition adéquate des sites d'interaction au niveau du récepteur par rapport aux sites d'interaction situés sur le substrat conduit à processus de reconnaisance efficace.



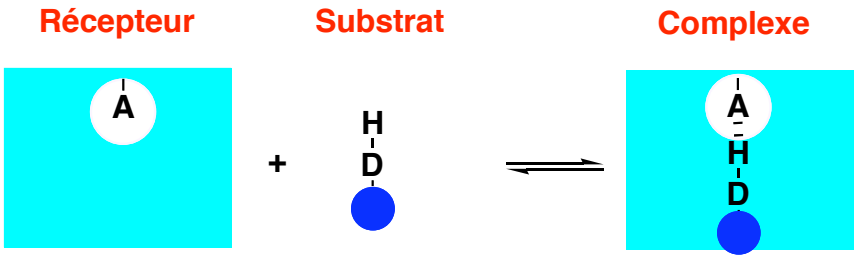
van der Waals : Les interactions de van der Waals sont non directionnelles. Elles augmentent avec la surface de contact.



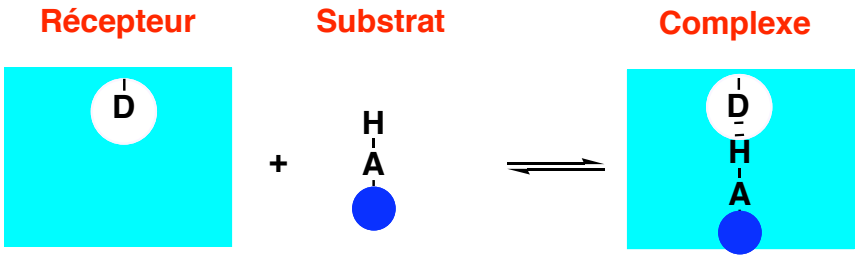
Modes d'interaction

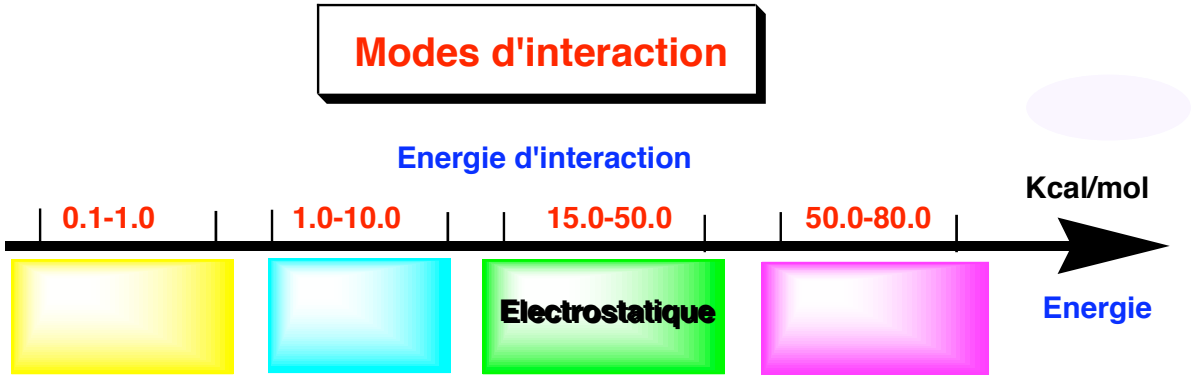


Liaison Hydrgène : La liaison s'établie lorsqu'un atome d'hydrogène est lié à un atome électronégatif (donneur)et à une distance d'interaction d'un atome électronégatif (accepteur). La liaison H est directionnelle (dépendence angulaire). Sa force dépend de la distance séparant le site donneur (D) et le site accepteur (A) de liaison H ainsi que de l'angle DHA .

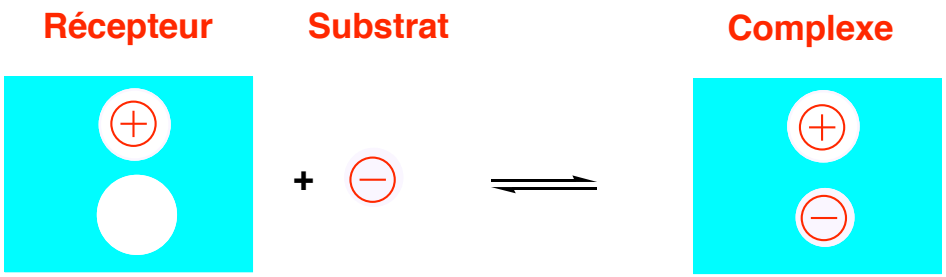


Afin que la liaison H puisse s'établir, il faut que le récepteur et le substrat soient complémentaires.
Les sites donneurs et accepteurs peuvent être portés par le récepteur ou par le substrat.



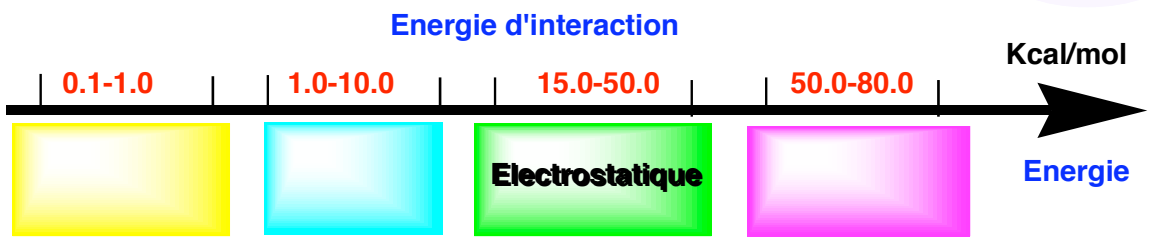


Interactions électrostatiques charge/charge : L'interaction électrostatique charge/charge s'établie lorsque deux entités portant des charges opposées sont en présence et à une distance d'interaction. Cette interaction n'est pas directionnelle. Sa force dépend de la distance séparant le site cationique (C^+) et le site anionique (A^-).

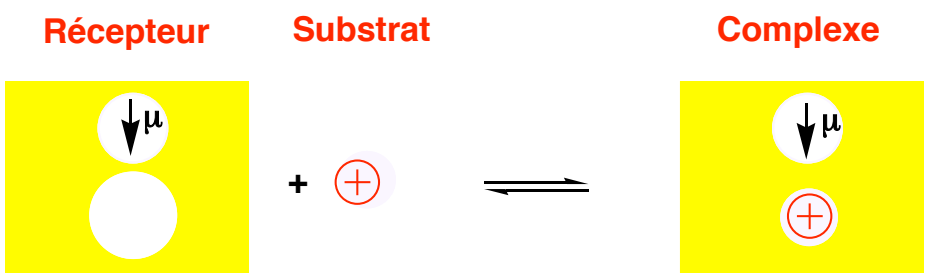


Afin que la liaison électrostatique puisse s'établir, il faut que le récepteur et le substrat portent des charges complémentaires. Les sites cationiques et anioniques peuvent être portés par le récepteur ou par le substrat.

Modes d'interaction

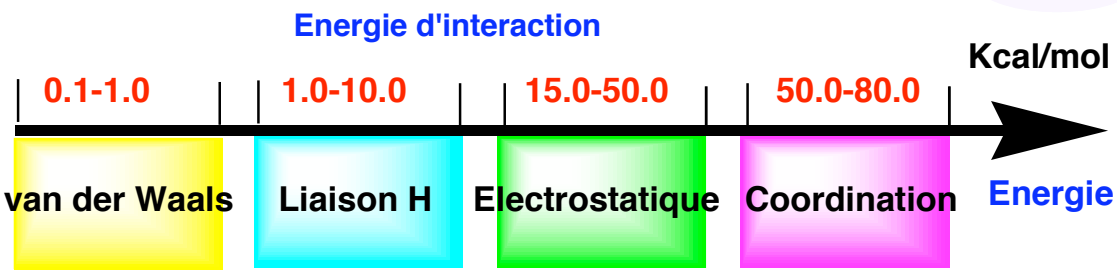


Interactions électrostatiques charge/dipôle : L'interaction électrostatique charge/dipôle s'établie lorsqu'une charge se trouve à proximité d'un dipôle orienté de façon adéquate.

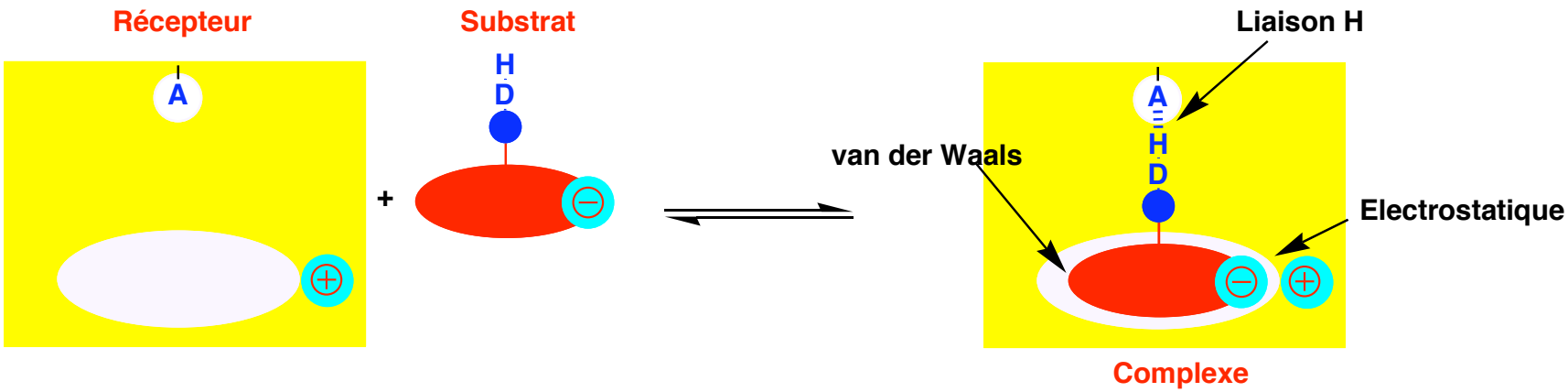


Afin que l'interaction charge/dipôle puisse s'établir, il faut que soit le récepteur porte la charge et le substrat le dipôle soit l'inverse. Desc interactions de type dipôle/dipôle ou dipôle/quadrupôle ou encore quadrupôle/quadrupôle peuvent être également utilisées.

Modes de complexation

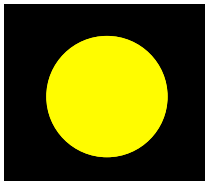


Combinaison d'interactions : le phénomène de reconnaissance souvent combine plusieurs interactions. En particulier, les interactions de van der Walls avec la liaison H et les interactions électrostatiques.



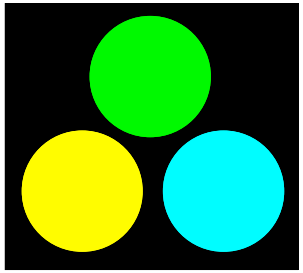
Topologie des Récepteurs

La topicité d'un récepteur est définie par le nombre de pôles qu'il possède. Les pôles peuvent être identiques (récepteur homopolytopique) ou différents (récepteur hétéropolytopique).



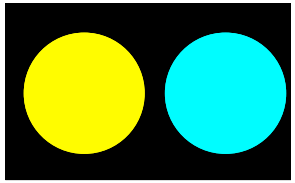
Monotopique

Un récepteur monotopique possède un seul pôle de reconnaissance



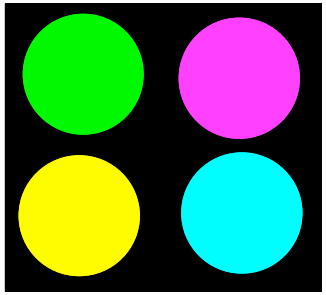
Tritopique

Un récepteur tritopique possède trois pôles de reconnaissance



Ditopique

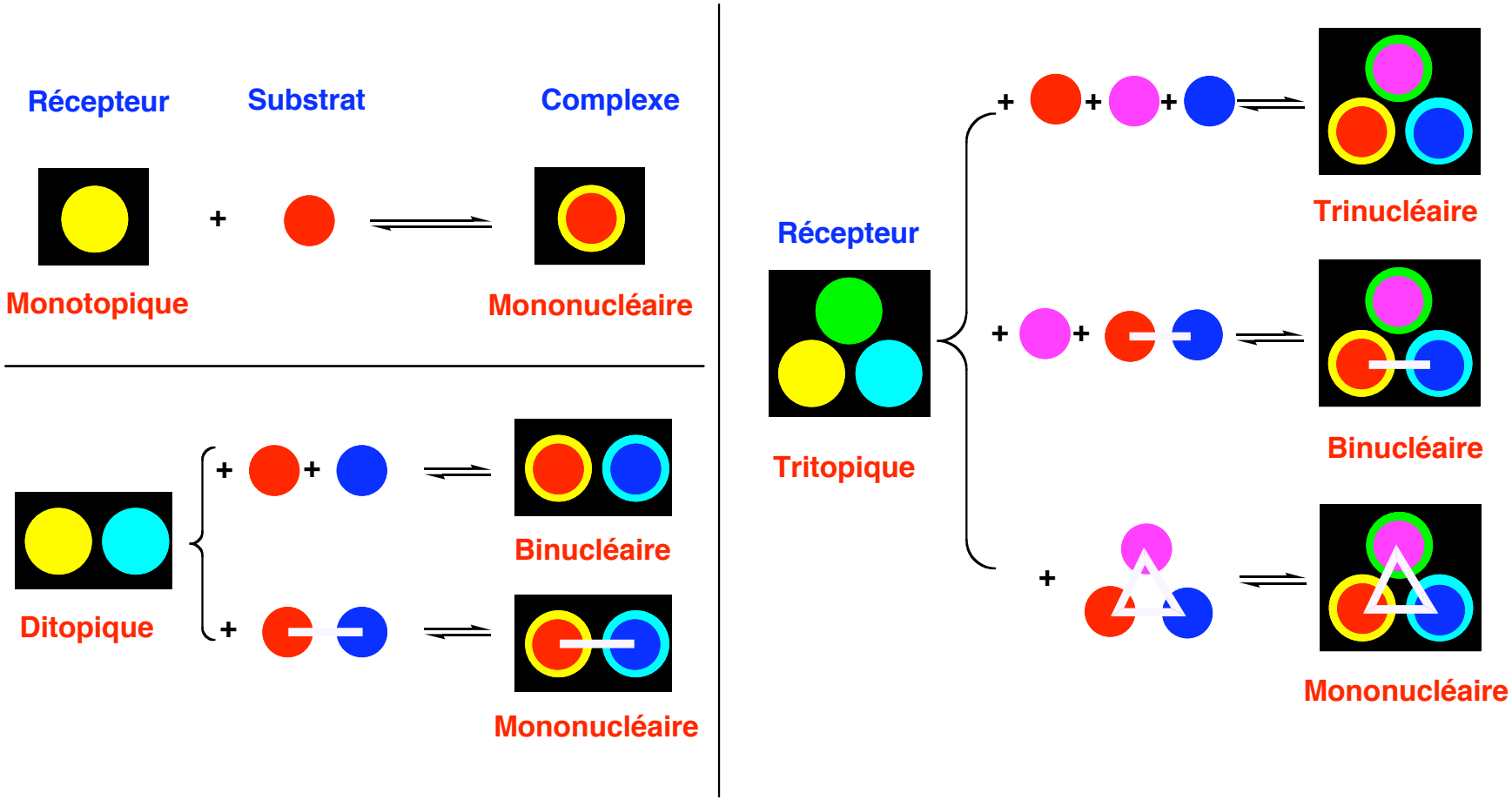
Un récepteur ditopique possède deux pôles de reconnaissance



Tétratopique

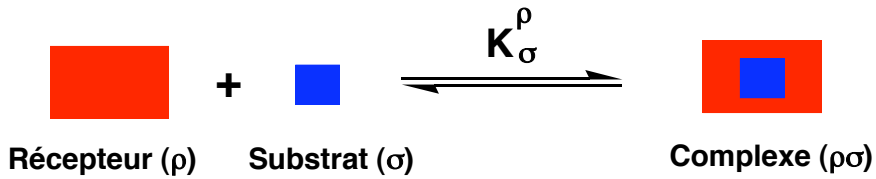
Un récepteur tétratopique possède quatre pôles de reconnaissance

Topologie des Récepteurs et stéchiométrie des complexes

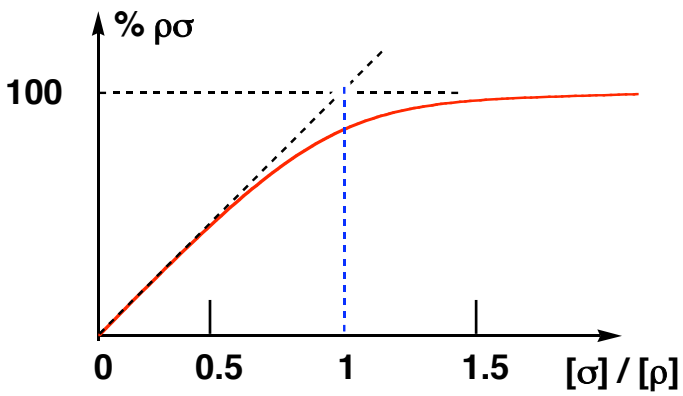


La stoechiométrie ou nucléarité

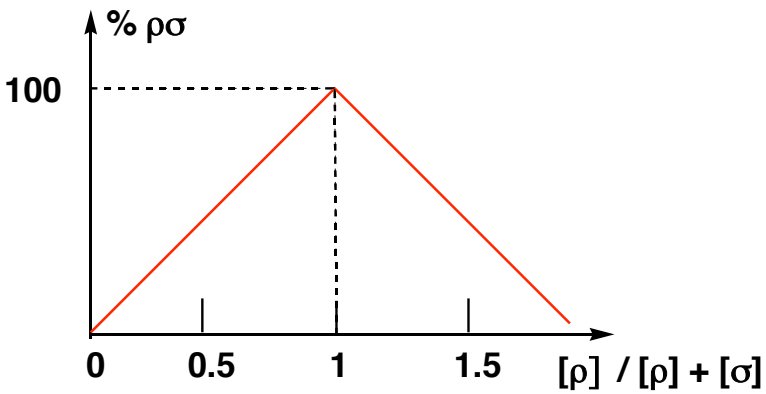
Complexe mononucléaire : un récepteur s'associe avec un seul substrat pour former un complexe mononucléaire. La nucléarité est de 1:1.



$$K_\sigma^\rho = \frac{[\rho\sigma]}{[\rho] \times [\sigma]}$$



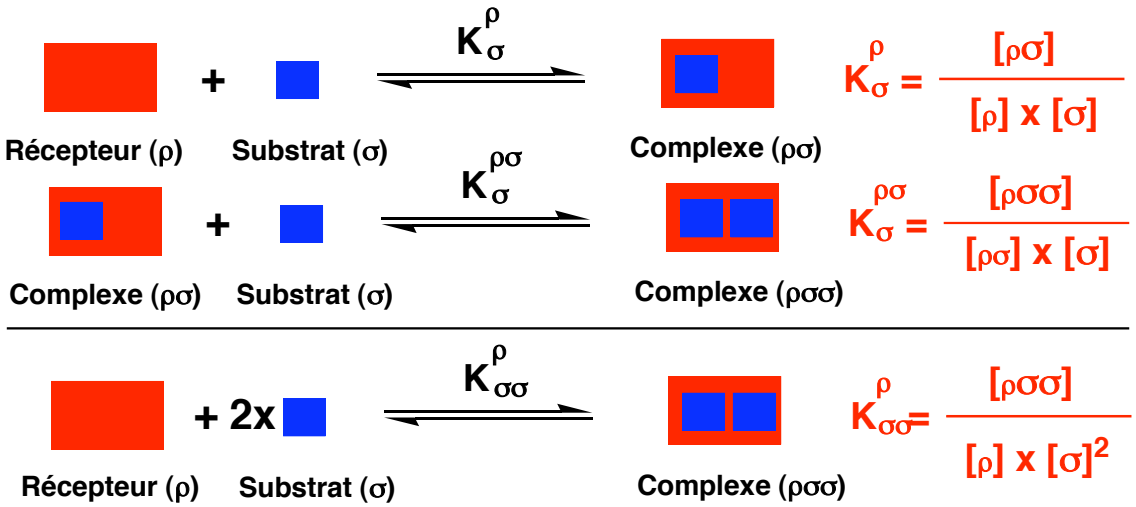
Plus la valeur de K est élevée plus l'écart à la linéarité est faible



Méthode de Job (Job plot)

La stoechiométrie ou nucléarité

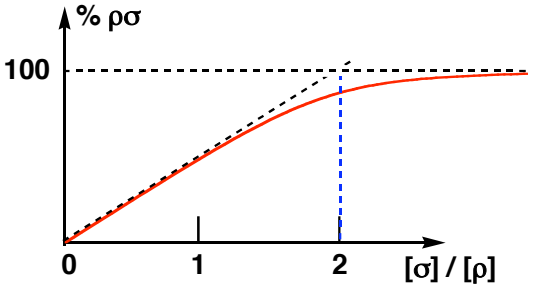
Complexe binucléaire : un récepteur s'associe avec deux substrats pour former un complexe binucléaire. La nucléarité est de 1:2.



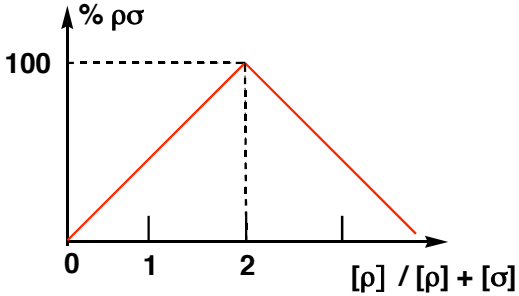
$$K_{\sigma}^{\rho} = \frac{[\rho\sigma]}{[\rho] \times [\sigma]}$$

$$K_{\sigma}^{\rho\sigma} = \frac{[\rho\sigma\sigma]}{[\rho\sigma] \times [\sigma]}$$

$$K_{\sigma\sigma}^{\rho} = \frac{[\rho\sigma\sigma]}{[\rho] \times [\sigma]^2}$$

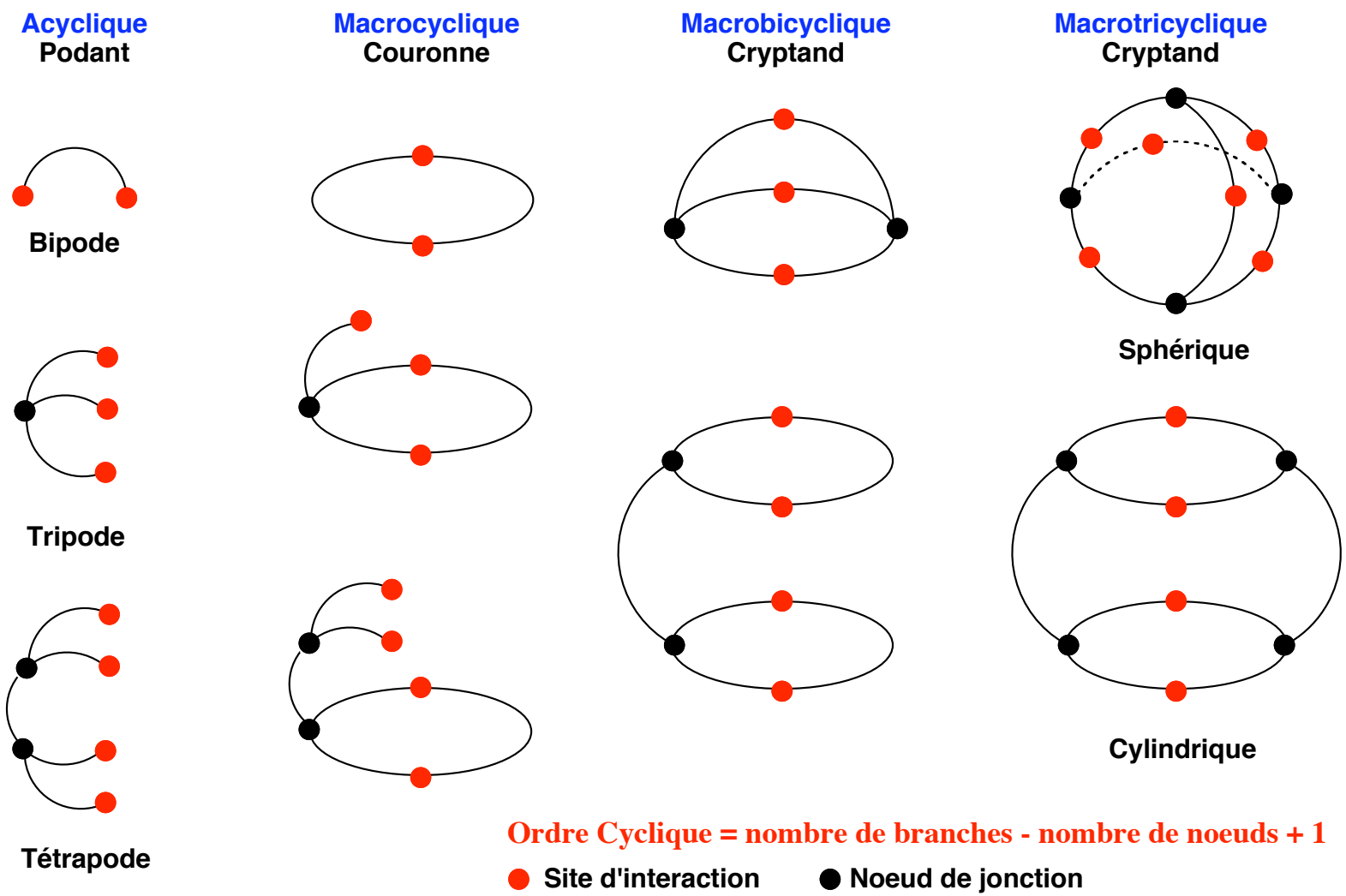


Plus la valeur de K est élevée plus l'écart à la linéarité est faible



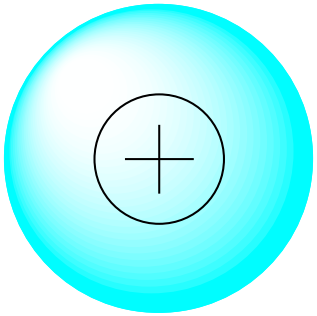
Méthode de Job (Job plot)

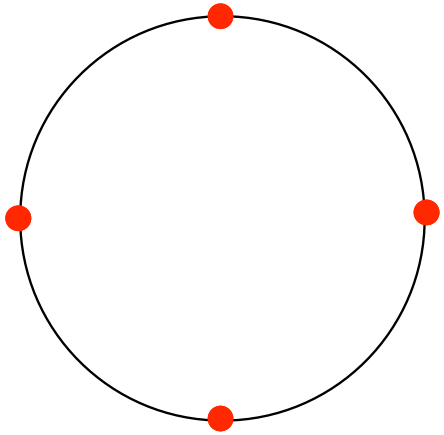
Topologie des ligands



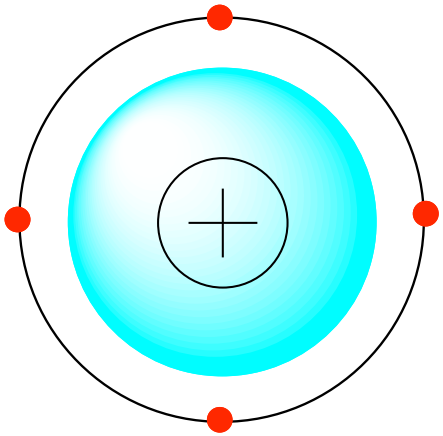
Ordre Cyclique = nombre de branches - nombre de noeuds + 1

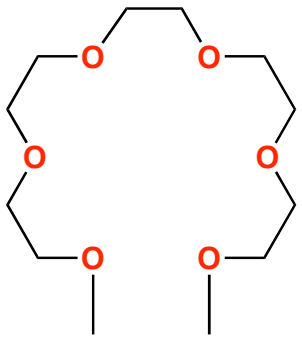
● Site d'interaction ● Noeud de jonction

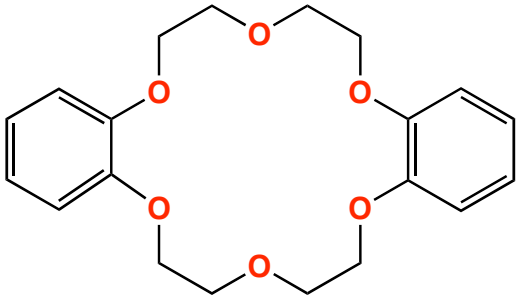




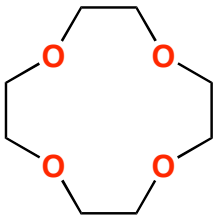
Complexation et reconnaissance de cations par des récepteurs synthétiques

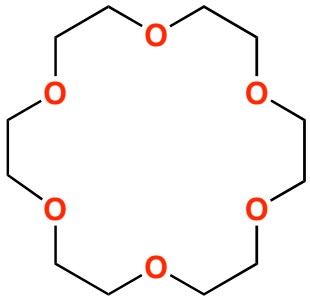




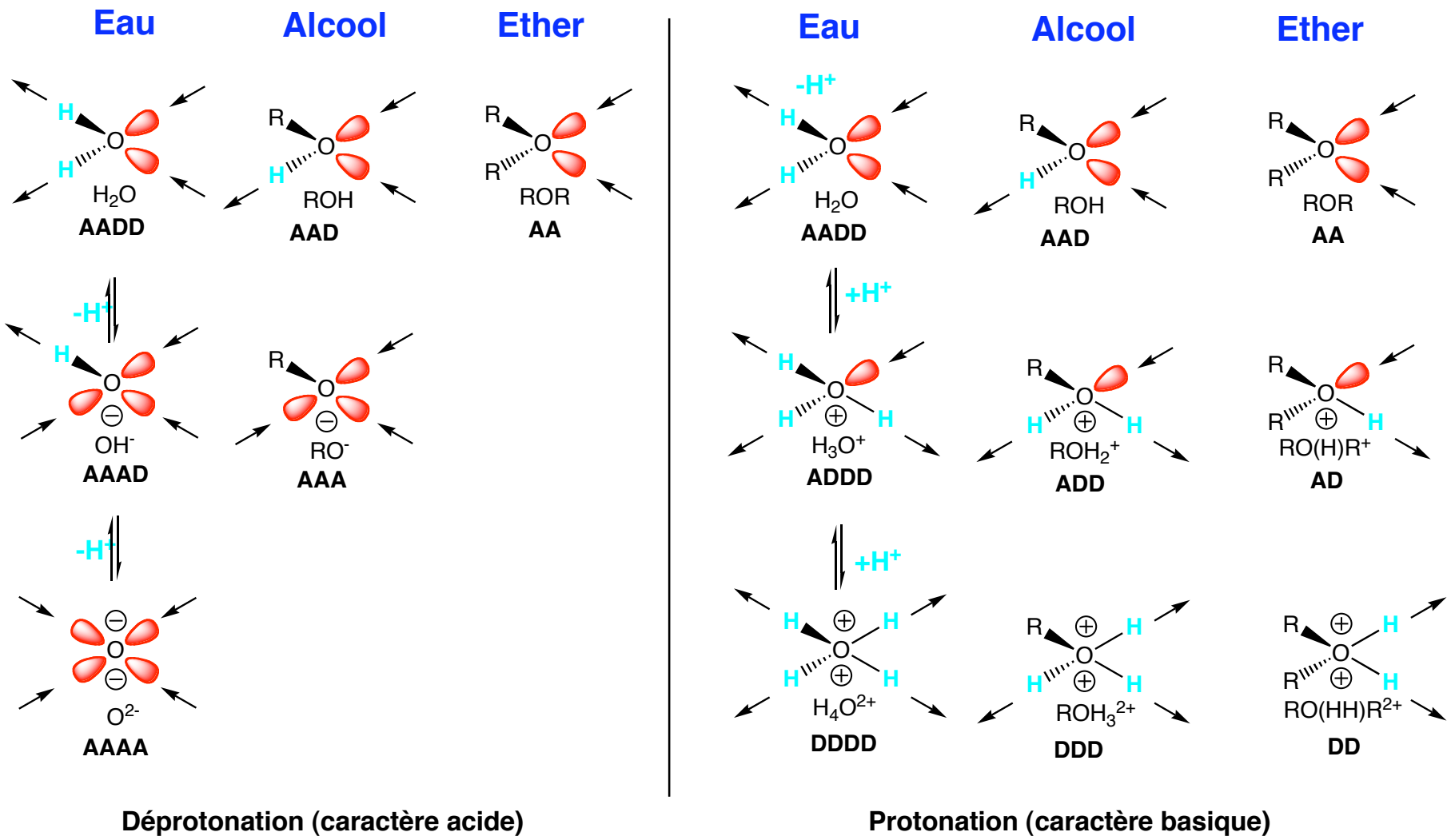


Polyéthers : podants et coronands





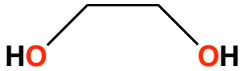
Eau, Alcool et Ether



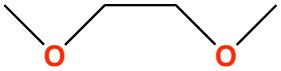
Déprotonation (caractère acide)

Protonation (caractère basique)

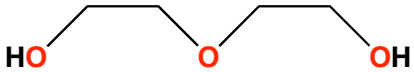
Les polyéthers acycliques



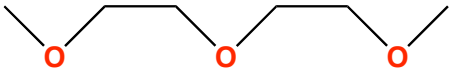
Ethylèneglycol

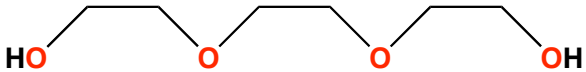


Diméthoxyéthane (DME)

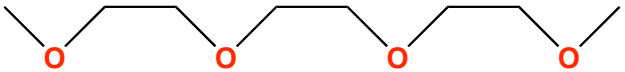


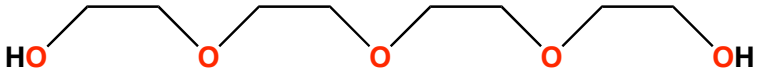
Diéthylèneglycol



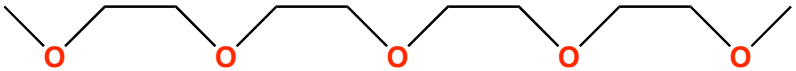


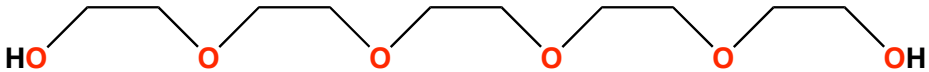
Triéthylèneglycol





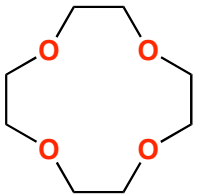
Tétraiéthylèneglycol



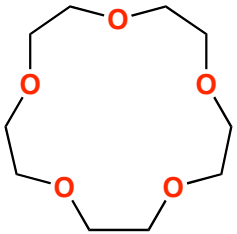


Pentaéthylèneglycol

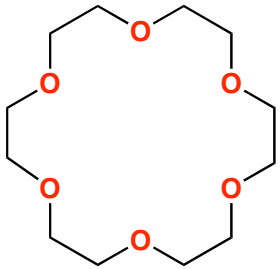
Les polyéthers cycliques (Ethers Couronnes)



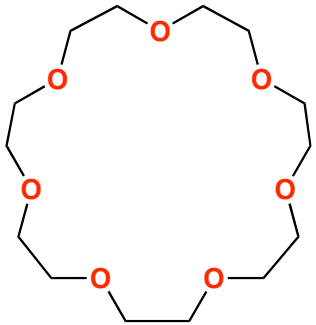
[12]O_4



[15]O_5



[18]O_6



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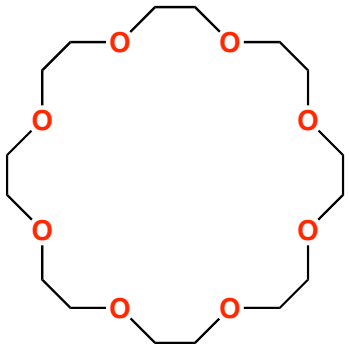
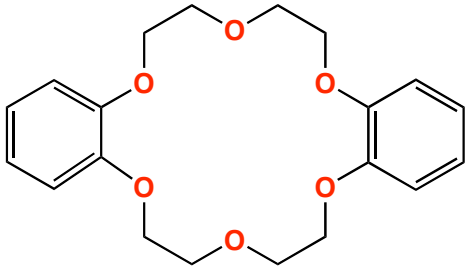
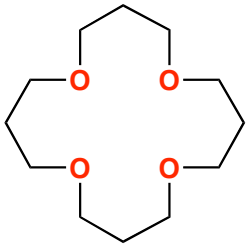


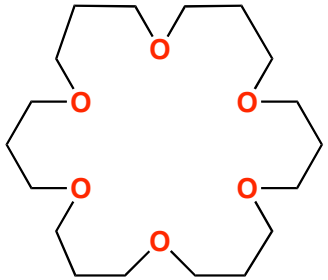
[24]O_8



Dibenzo[18]O_6



[16]O_4



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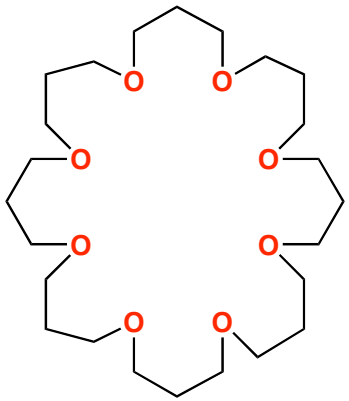
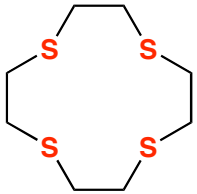
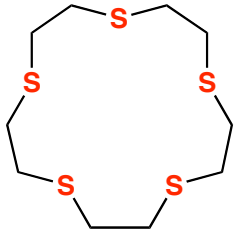


[32]O_8

Les polythioéthers cycliques (Thioéthers Couronnes)



[12]S_4



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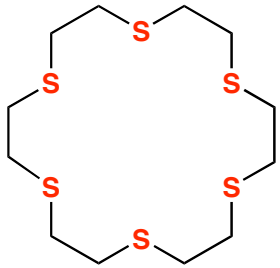
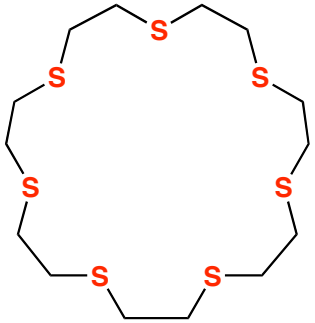


[18]S_6



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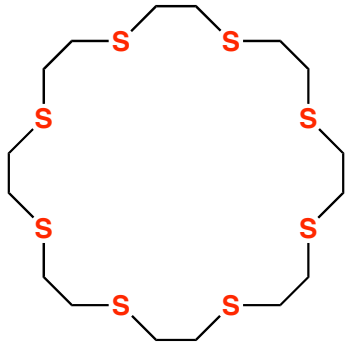

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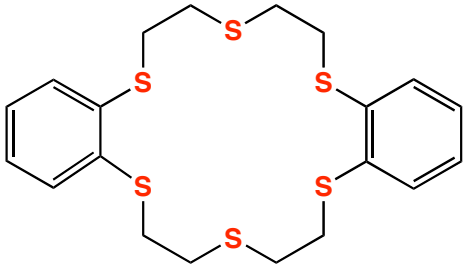
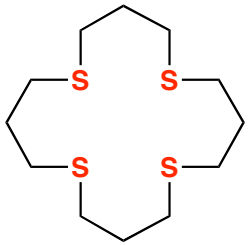


Dibenzo[18]S_6



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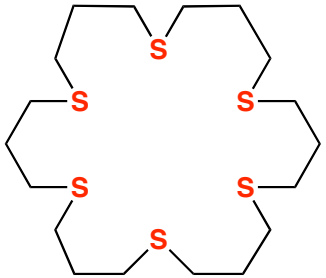
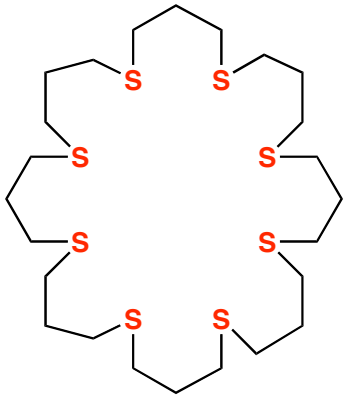
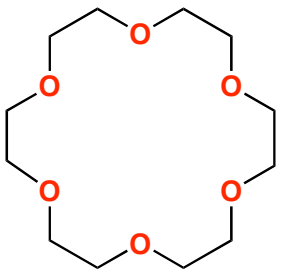


[24]S_6

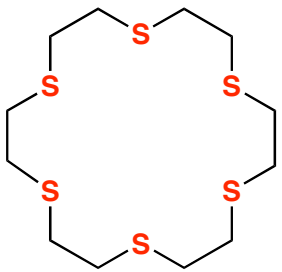


[32]S_8

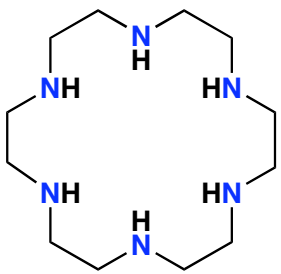
Les polyaaza-oxa-thia cycliques



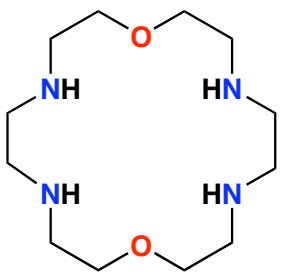
[18]O_6



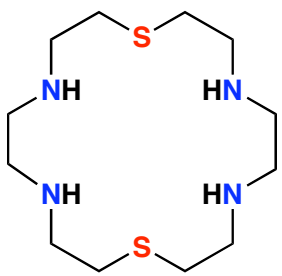
[18]S_6



[18]N_6



[18]O_2N_4



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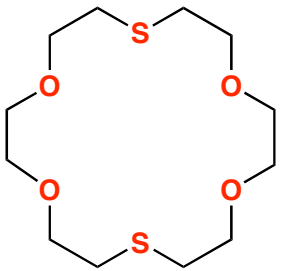

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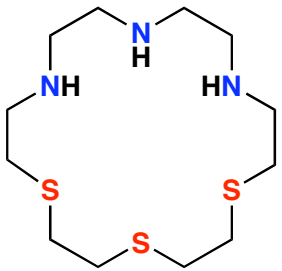

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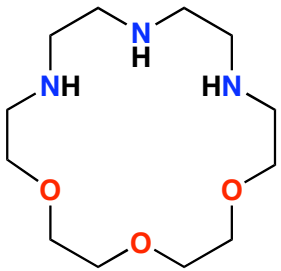

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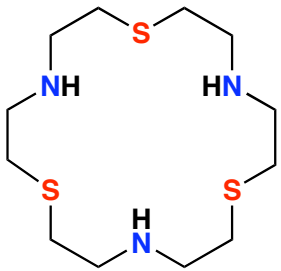

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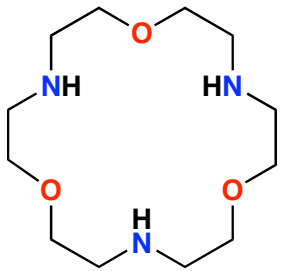

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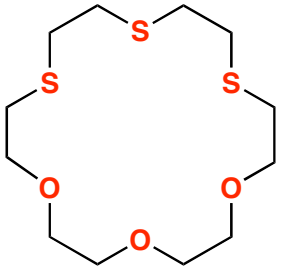

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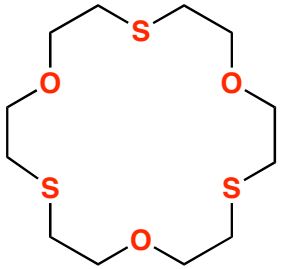

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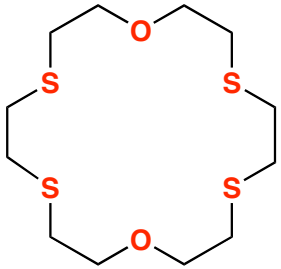

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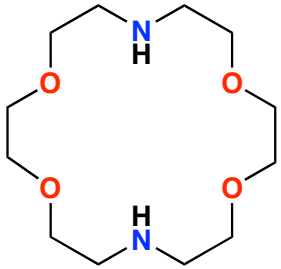
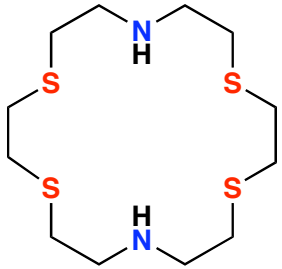


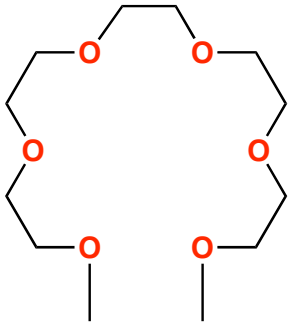
[18]O_4N_2

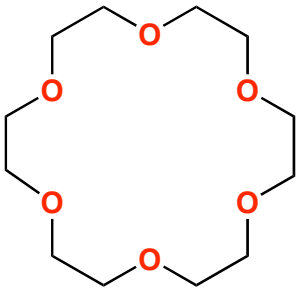


[18]S_4N_2

Organisation croissante

Diminution de l'organisation et augmentation de l'éspace conformationnel



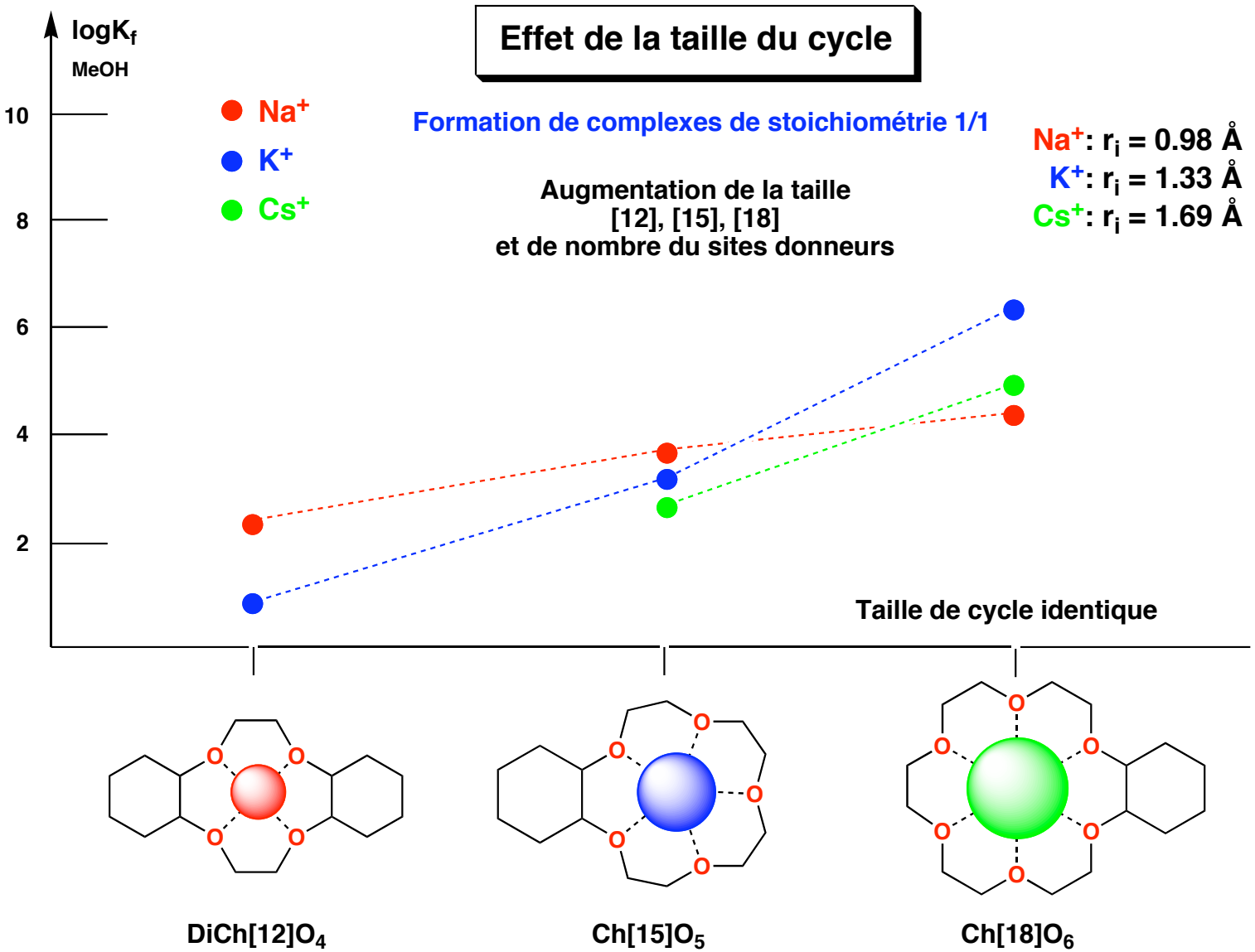


Podant	Coronand
Acyclique	Macrocyclique
File	Cavité
logKs = 2.0	logKs = 6.08

Stabilité pour le complexe au potassium dans le méthanol

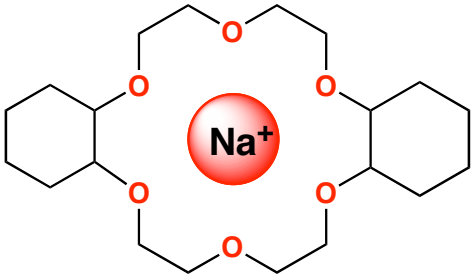
Augmentation de l'organisation et réduction de l'éspace conformationnel

Effet de la taille du cycle

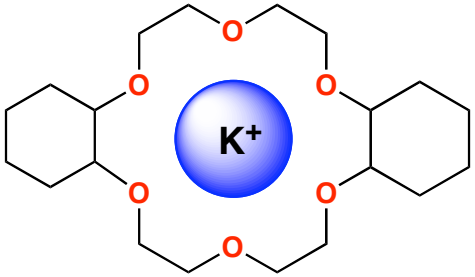


Effet des solvants

La complexation est en compétition avec la solvatation



DiCh[18]O_6



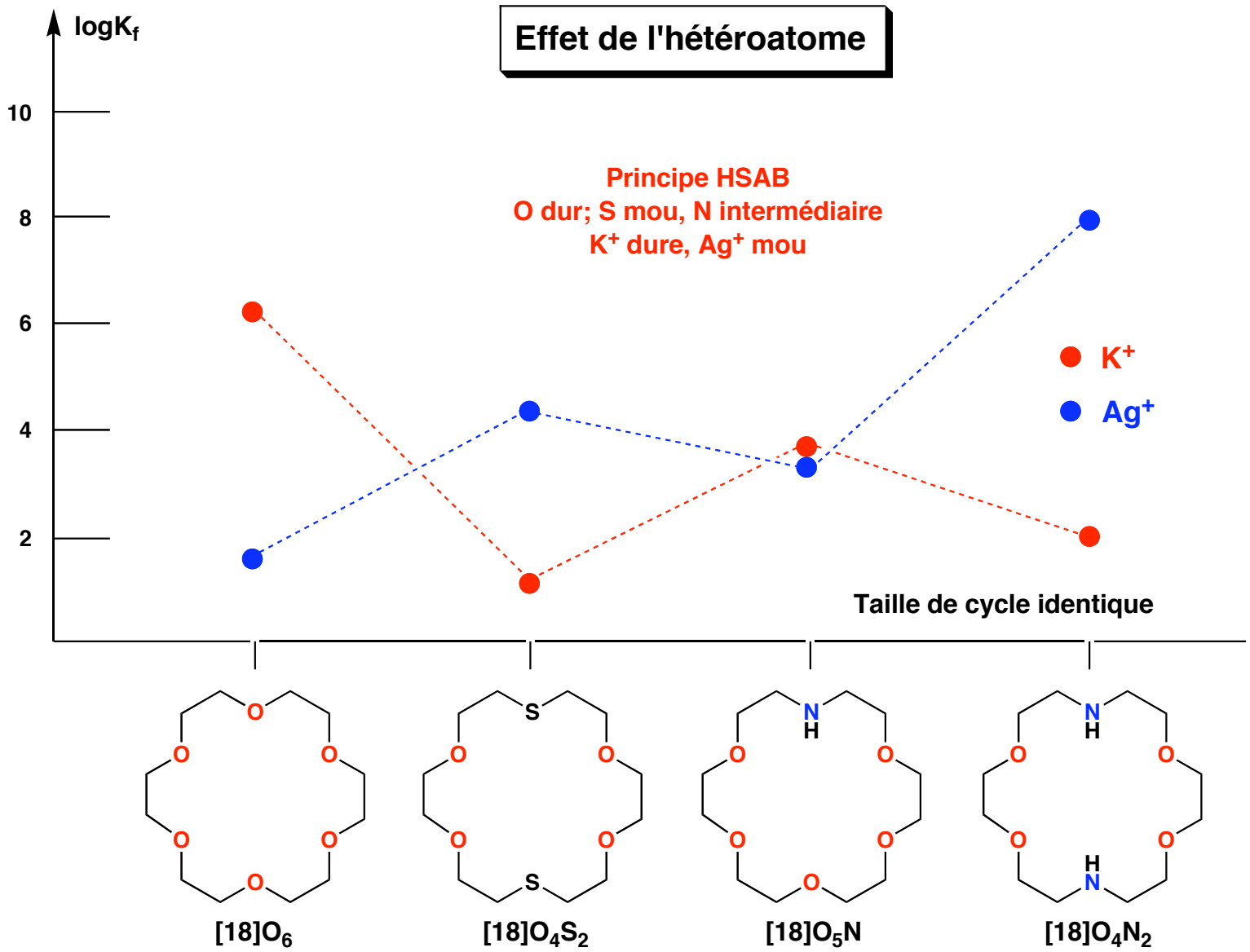
DiCh[18]O_6

	Na^+	logKf (25° C)	K^+
H_2O	1.21		2.02
MeOH	4.08		6.01

La complexation d'espèces chargées est nettement plus favorisée dans le méthanol. Habituellement un facteur mille d'augmentation de la constante d'association (K_f) est obtenue.. L'eau, très polaire, solvate très bien à la fois le cation (interactions charge/dipôle) et l'éthercouronne (interactions en partie par la formation de liasons hydrogène avec les oxygènes de la couronne.

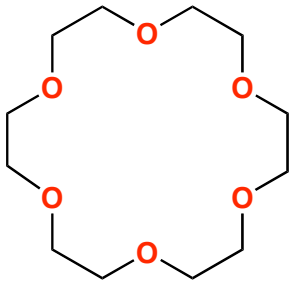
H_2O: Solvant très polaire Protique (ε = 78)
MeOH: Solvant polaire Protique (ε = 33)

Effet de l'hétéroatome

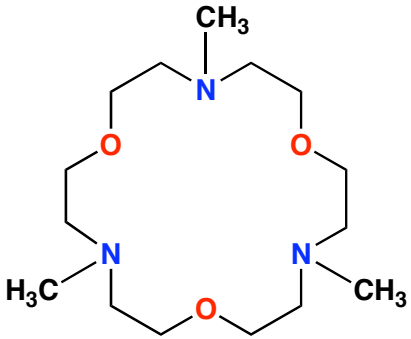


Complexation d'alkylammonium

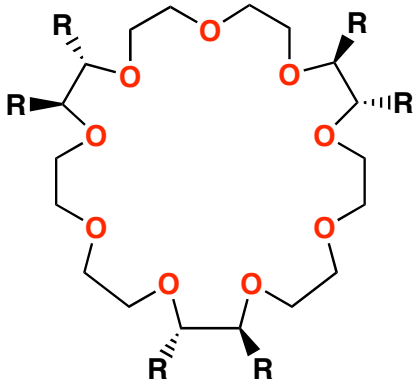
Etablissement de liaisons H avec les amines et les éthers

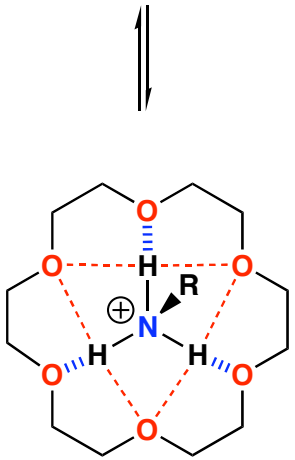


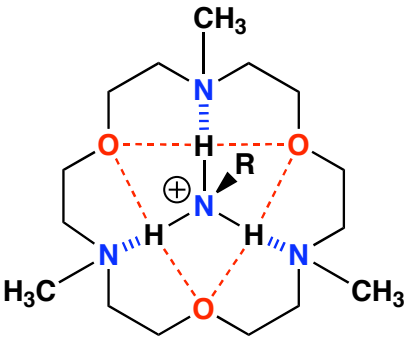
[18]O_6

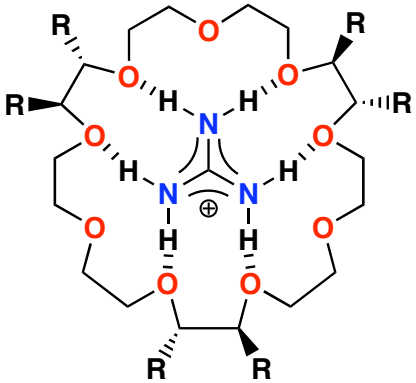


[18]O_3N_3

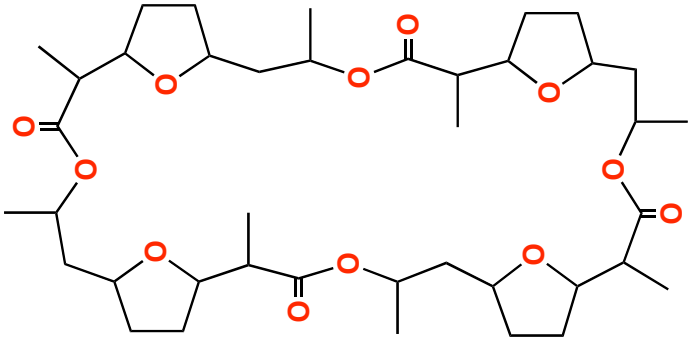




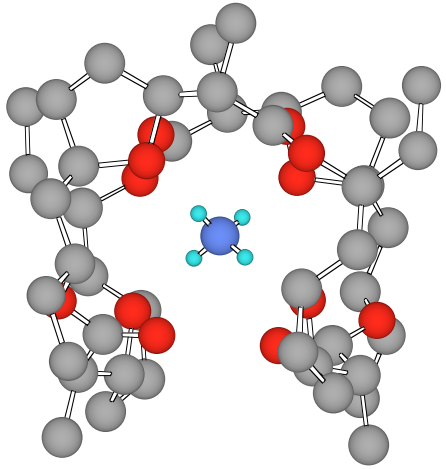


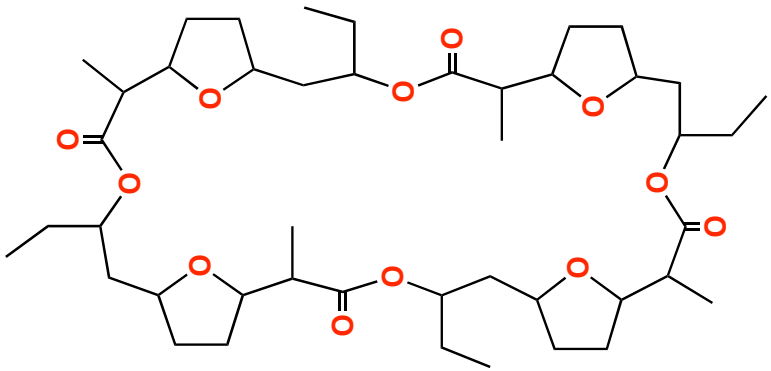


Complexation d'ammonium par desAntibiotics

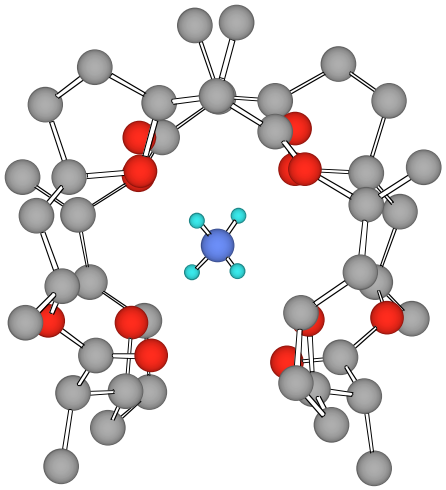


Nonactin

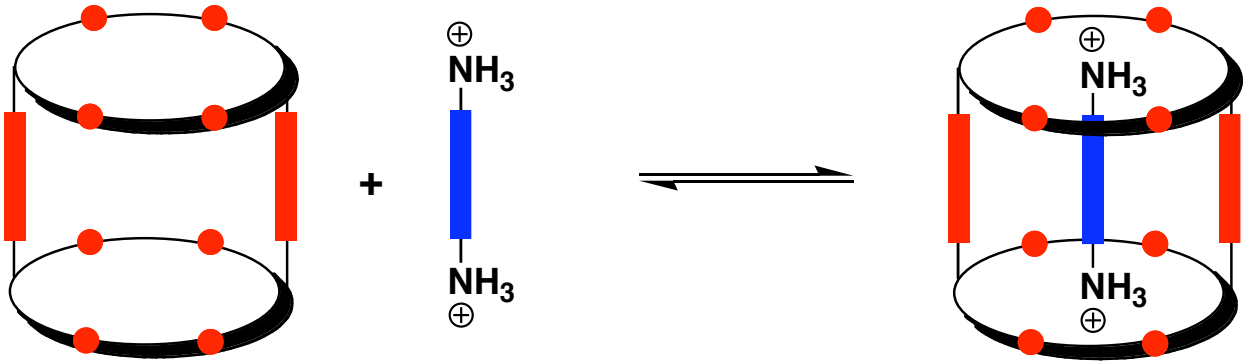


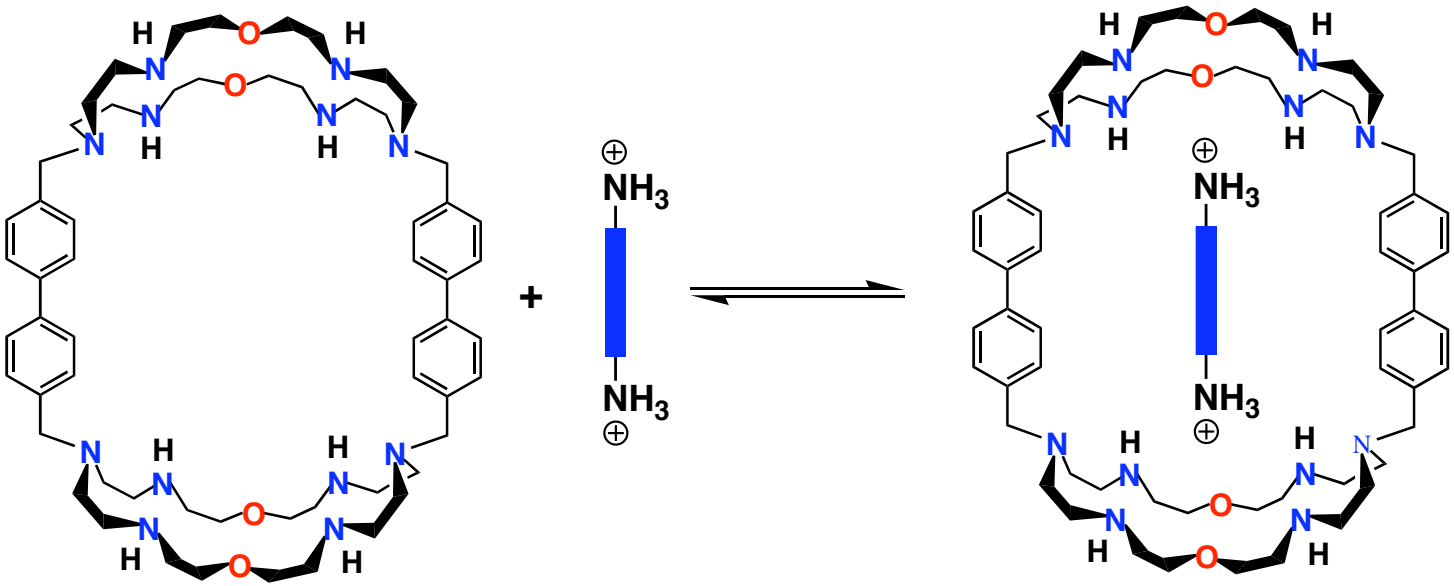


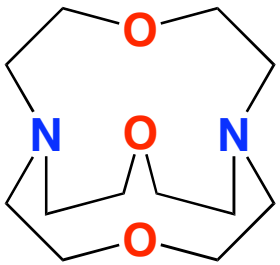
Tetranectin

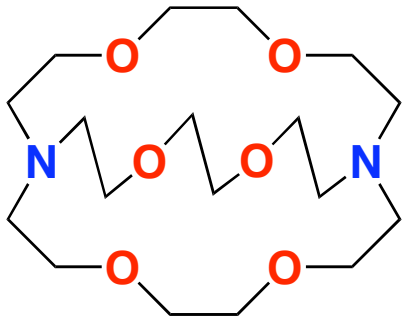


Reconnaissance linéaire de diammonium

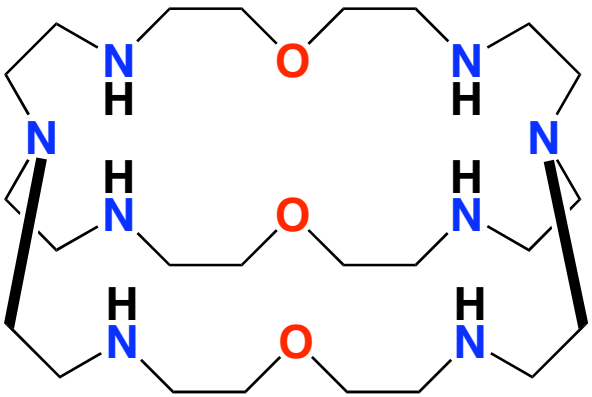


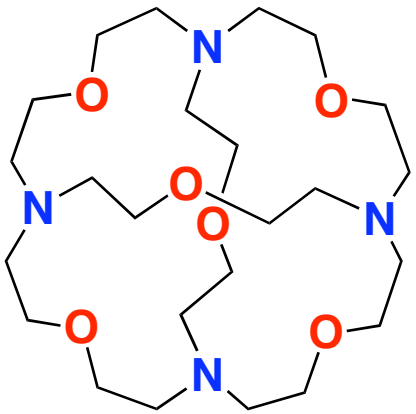




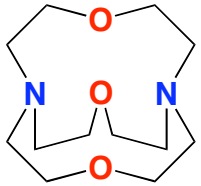


Les cages : Cryptands et cryptates

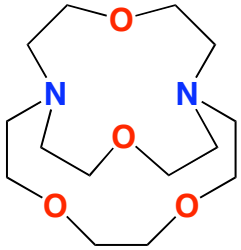




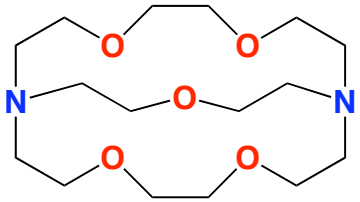
Les Cryptands



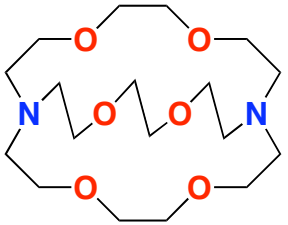
Macrobicycle
(111)Cryptand



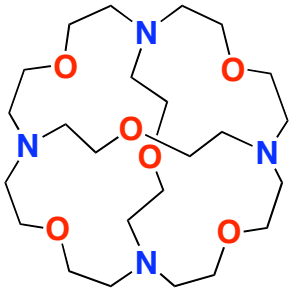
Macrobicycle
(211)Cryptand



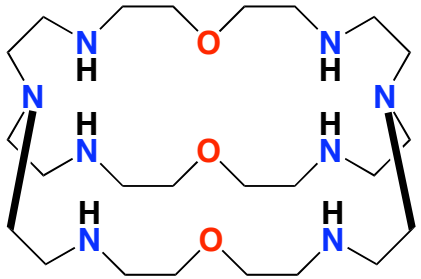
Macrobicycle
(221)Cryptand

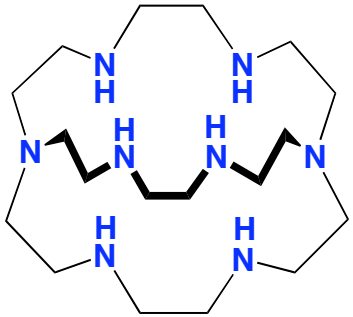


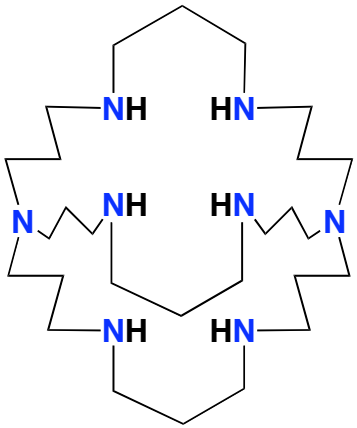
Macrobicycle
(222)Cryptand



Macrotricycle
(222)Cryptand

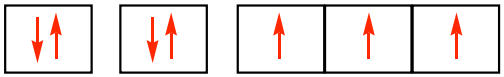




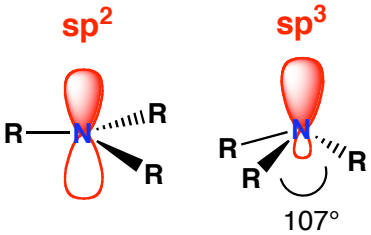


Azote : $^{7}N : 1s^2 2s^2 2p^3$

Electronégativité 3.0

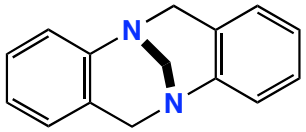


$1s^2$ $2s^2$ $2p^3$



Différence d'énergie entre l'hybridation sp^2 et sp^3 est faible (5-10 kcal/mol)

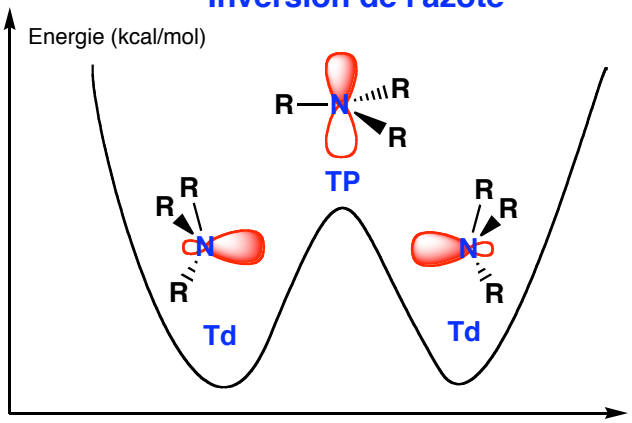
Les amines sinversent très rapidement (Inversion de Walden)
NH_3 : 210^{11} fois par seconde
R_3N : 10^4 - 10^5 fois par seconde

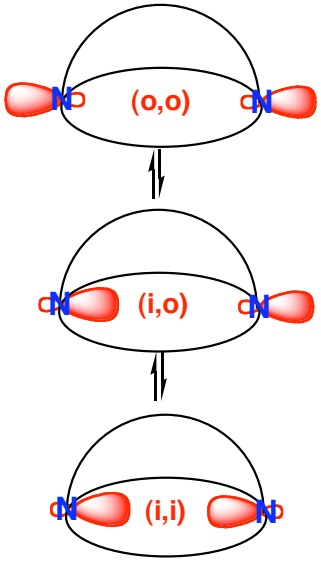


Inversion Bloquée
Base de Tröger

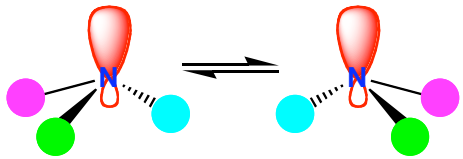
Facteurs controlant le processus:
Taille de cycle
Nature des substituants
Ordre cyclique (mono, bi, tri)

Inversion de l'azote

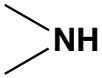
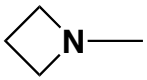
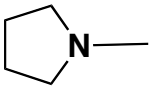
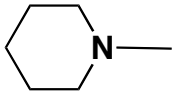




La chiralité (R ou S) portée par une amine tertiaire n'est pas conservable. La racémisation est très rapide

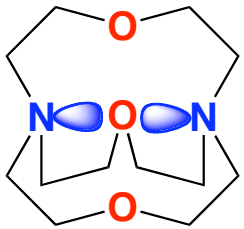


Pour le phosphore l'nversion de Walden est très nettement plus lente. On peut générer et conserver une chiralité sur le phosphore.

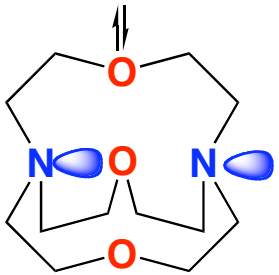
Amine	$\Delta G^{activation}$
 Diméthylamine	18.4
 Méthylpyrrolidine	42.7
 Méthylpiperidine	28.5
	35.2

A caude de la structure bicyclique et des connecteurs courts reliant les azotes, l'inversion des amines est ralentie.

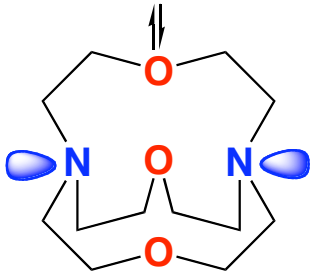
Isomères



(i,i)



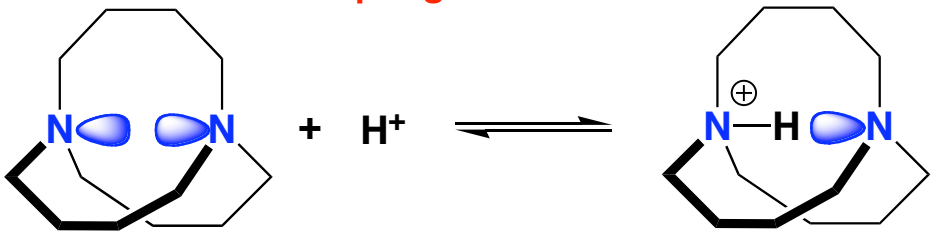
(i,e)



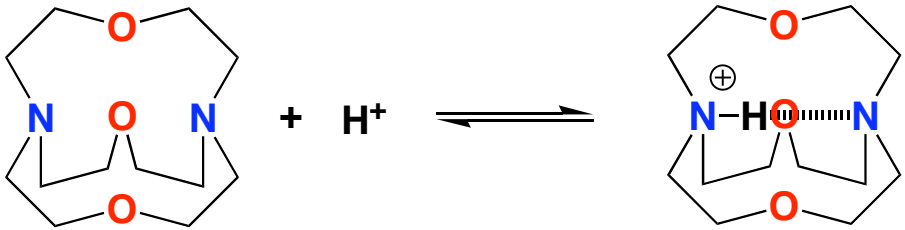
(e,e)

Complexation du proton

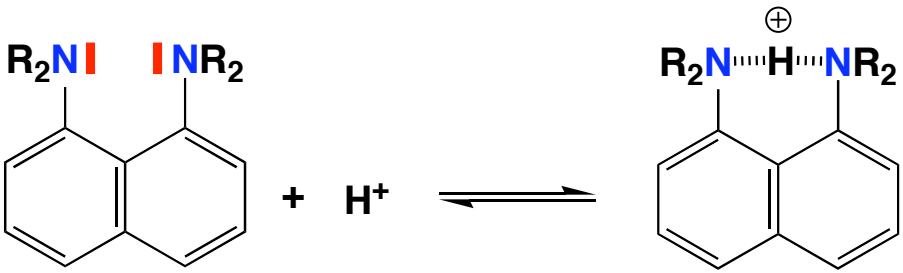
Eponge à Proton



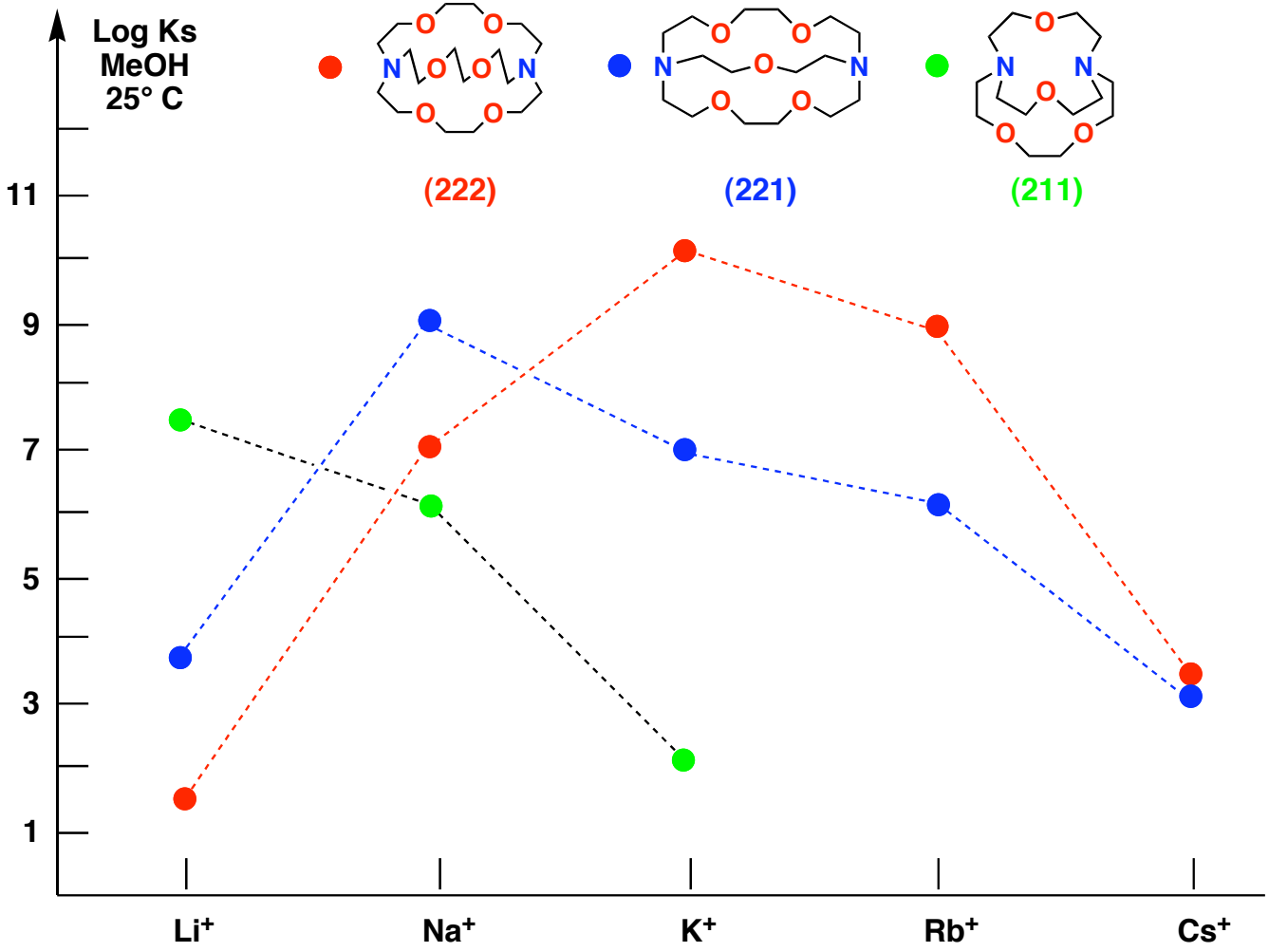
[444]Cryptand



(111)Cryptand

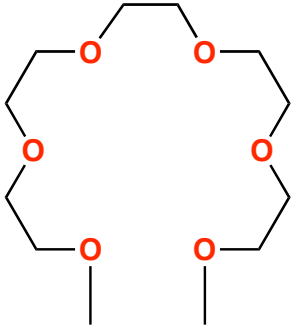


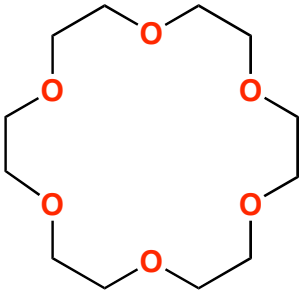
Complexation des alcalins par les cryptands

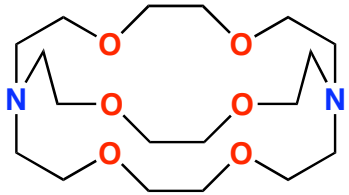


Organisation croissante

Diminution de l'organisation et augmentation de l'éspace conformationnel





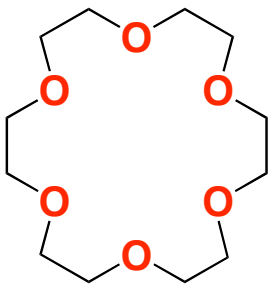


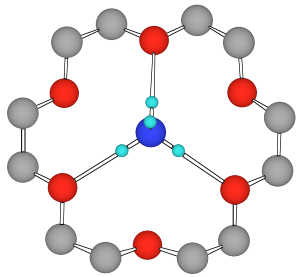
Podant	Coronand	Cryptand
Acyclique	Macrocyclique	Macrobicyclique
File	Cavité	Aage
logKs = 2.0	logKs = 6.08	logKs = 10.0

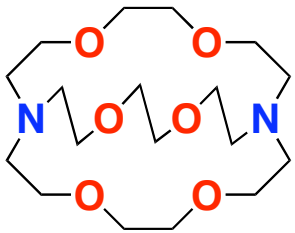
Stabilité pour le complexe au potassium dans le méthanol

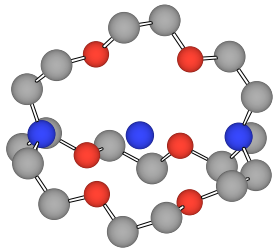
Augmentation de l'organisation et réduction de l'éspace conformationnel

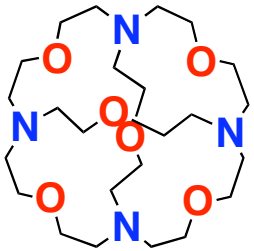
Reconnaissance de NH_4^+

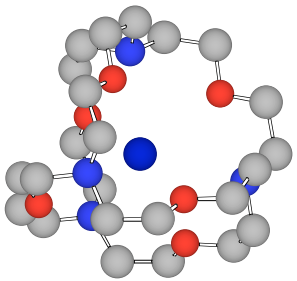


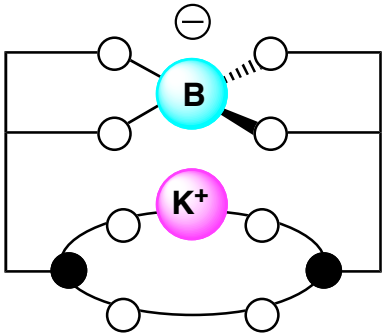




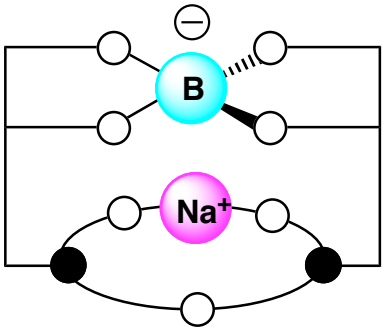


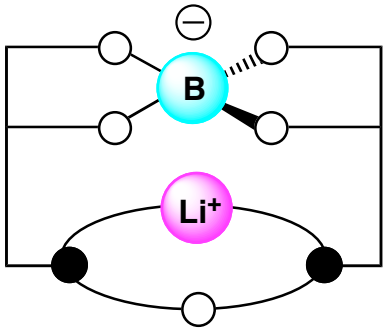




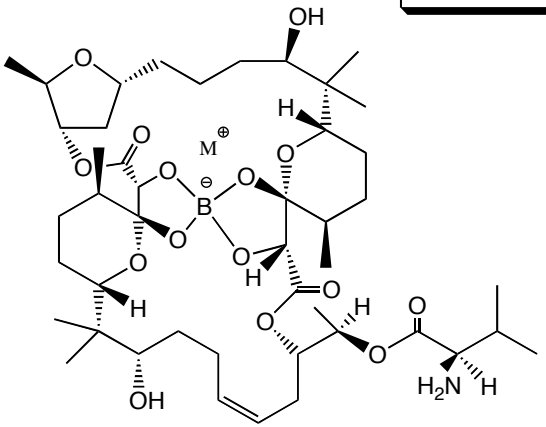


Les borocryptands et borocryptates

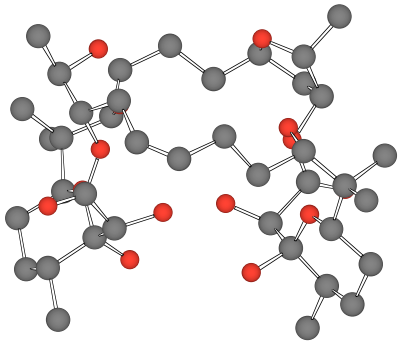


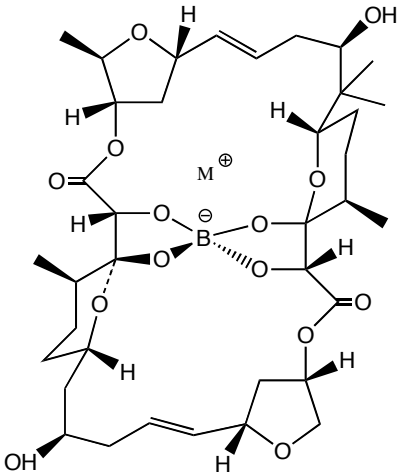


Des antibiotiques naturels

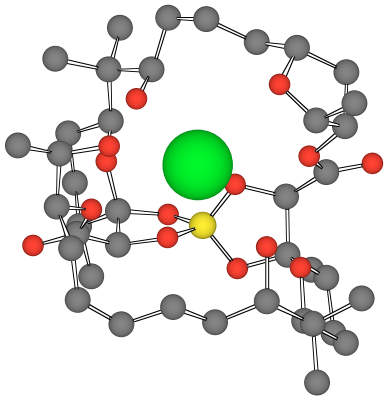


Boromycine

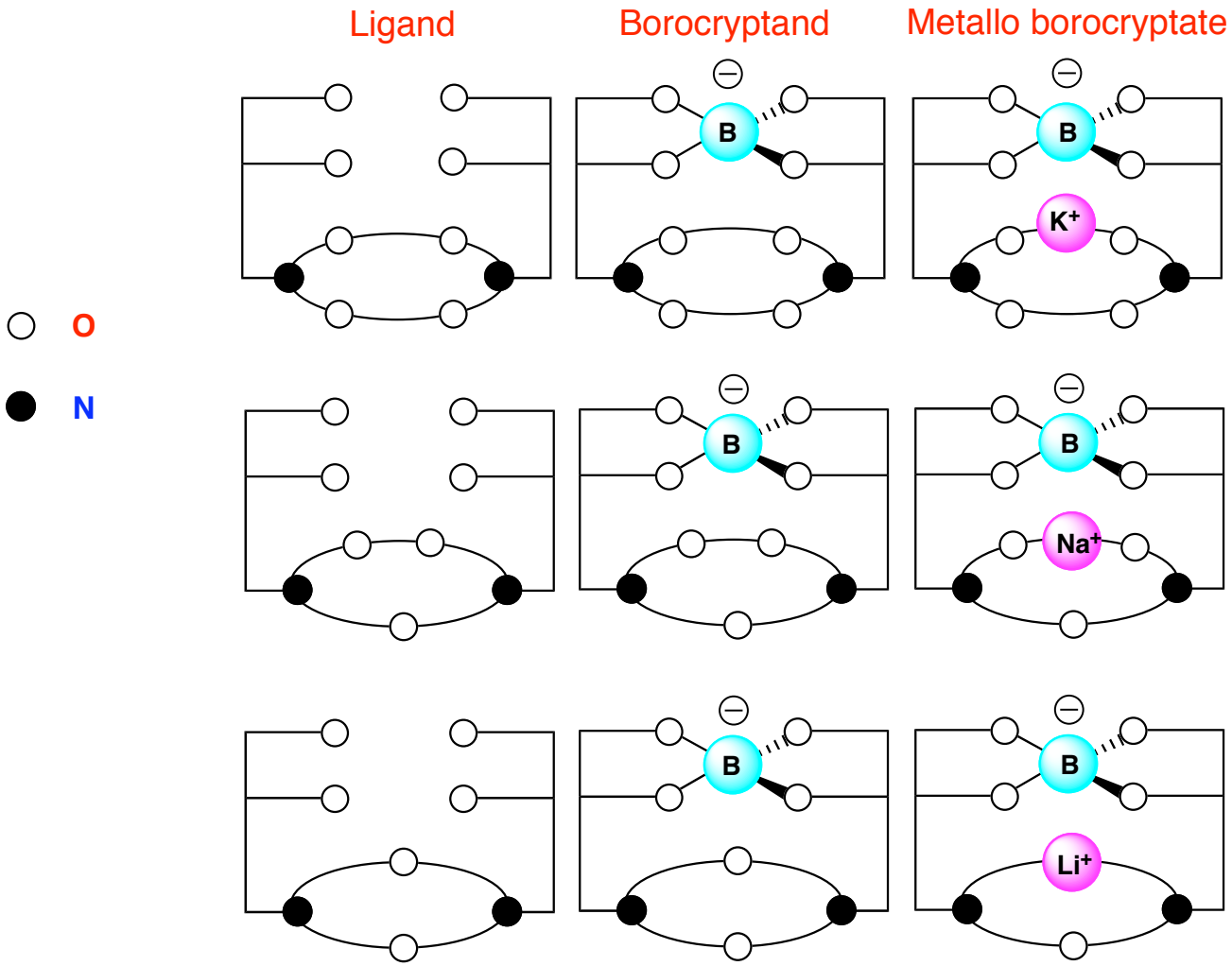




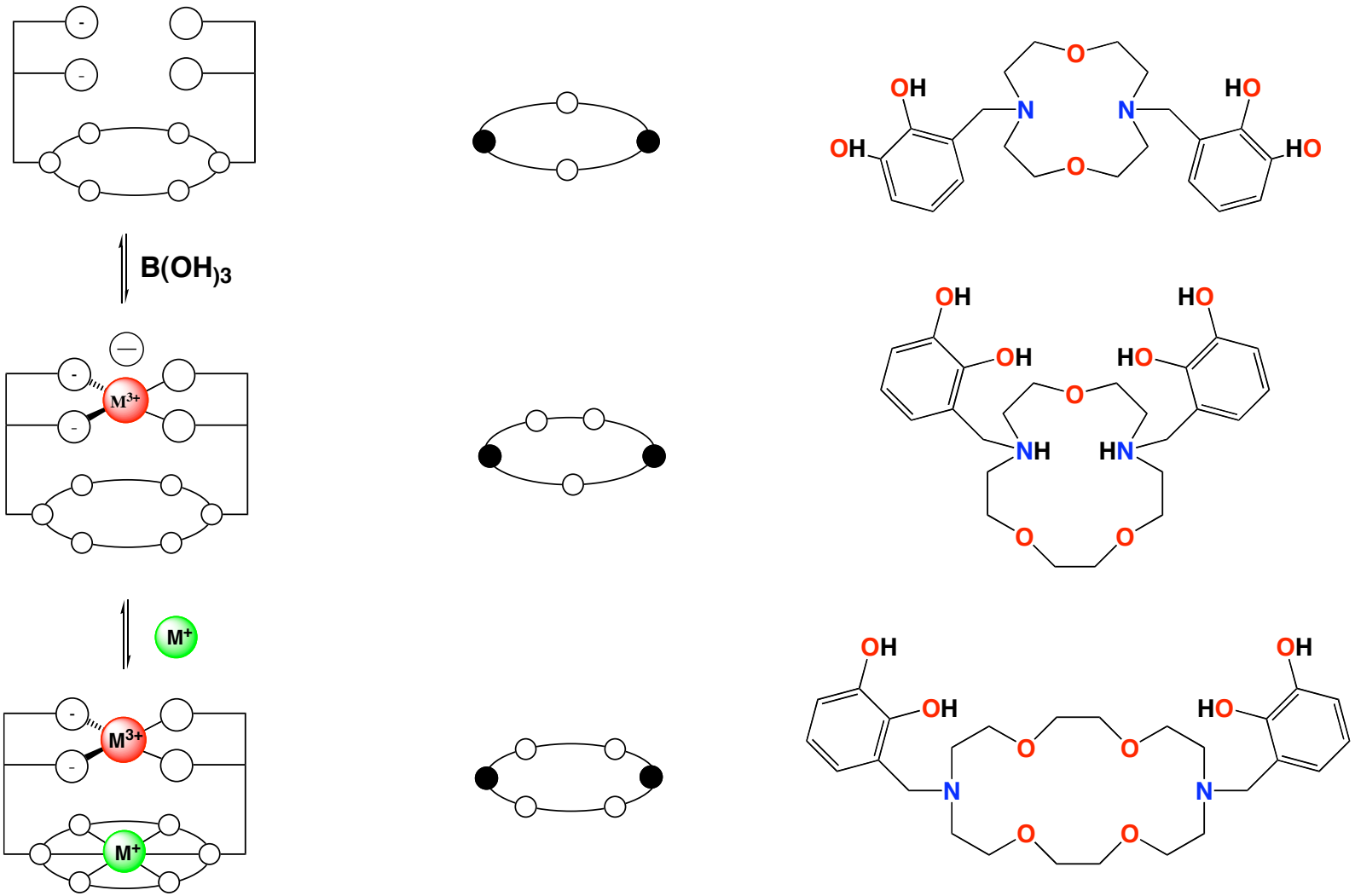
Aplasomycine



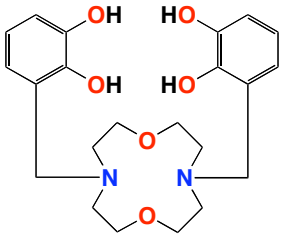
Les borocryptands

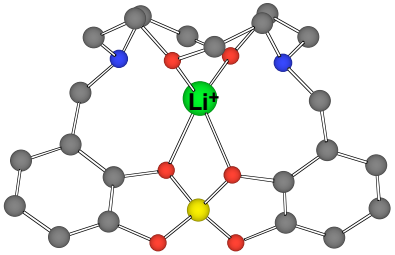


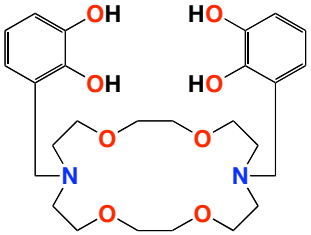
Borocryptands : conception

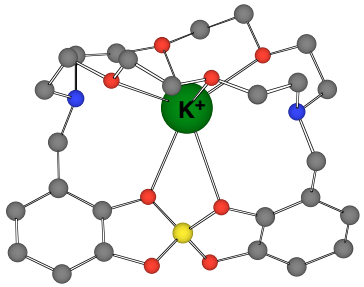


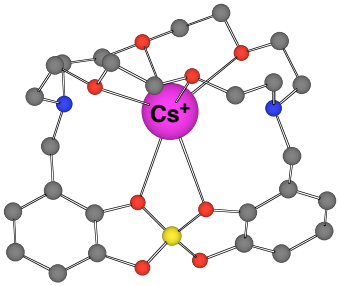
Les borocryptates : étude structurale

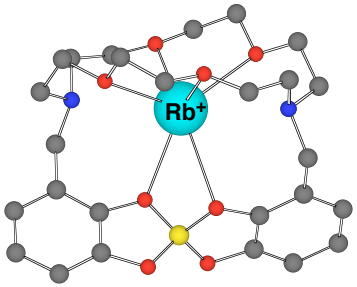


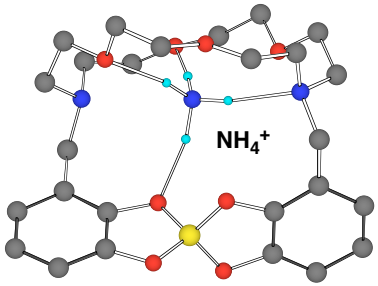


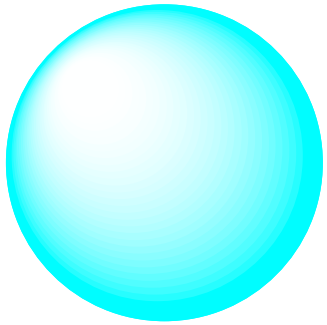


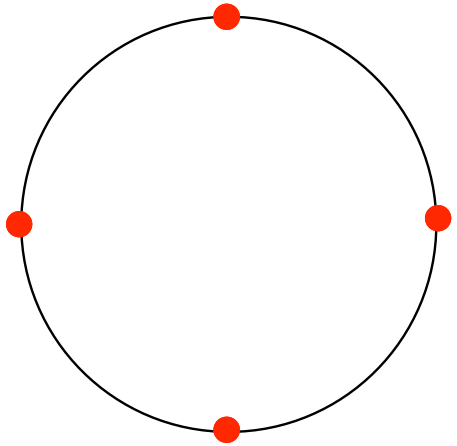




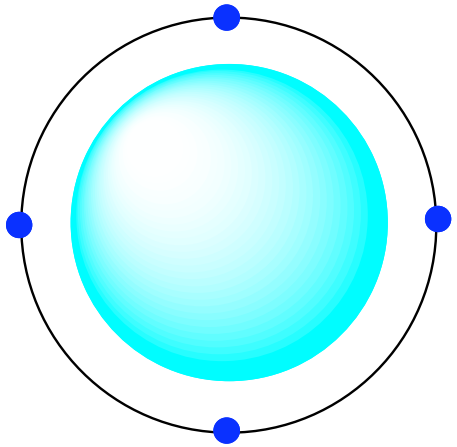




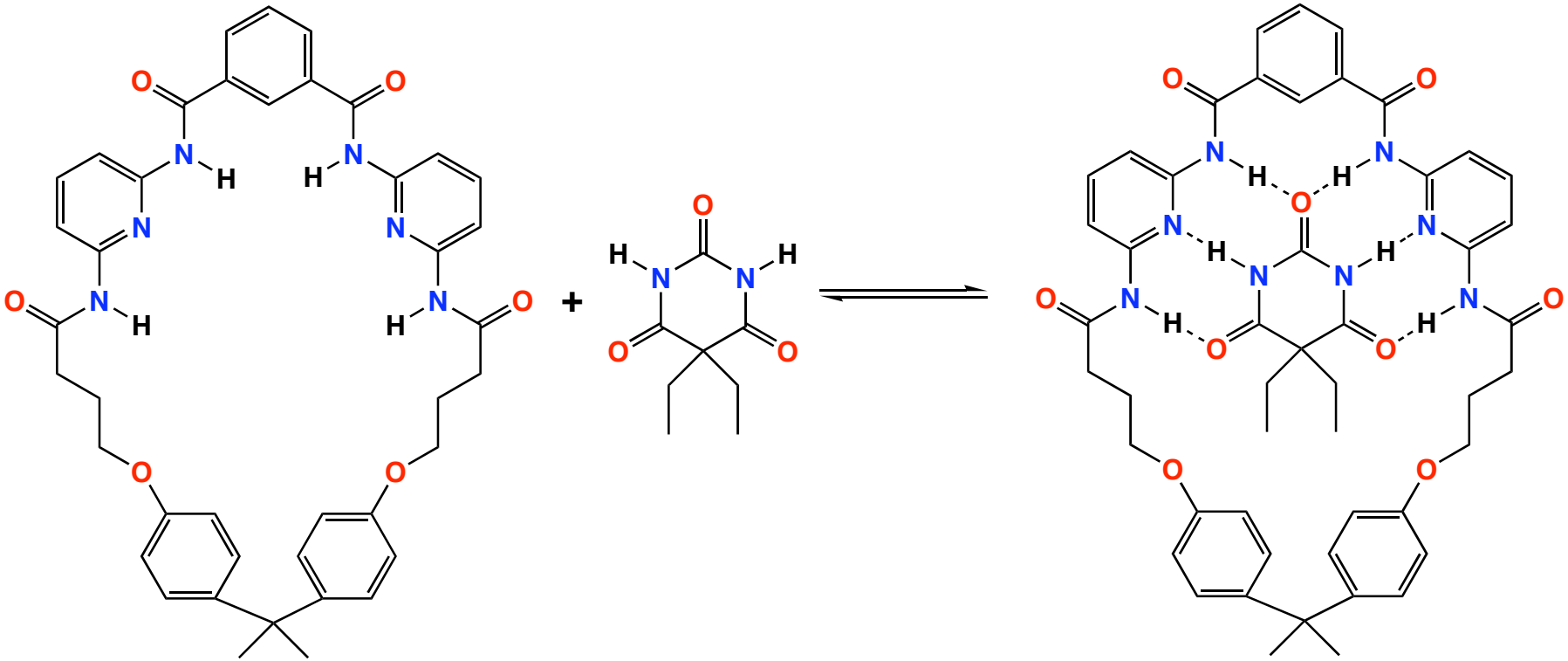




Complexation et reconnaissance de molécules neutres par des récepteurs synthétiques

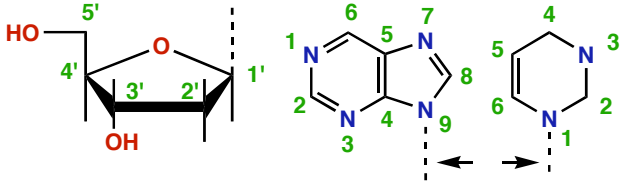


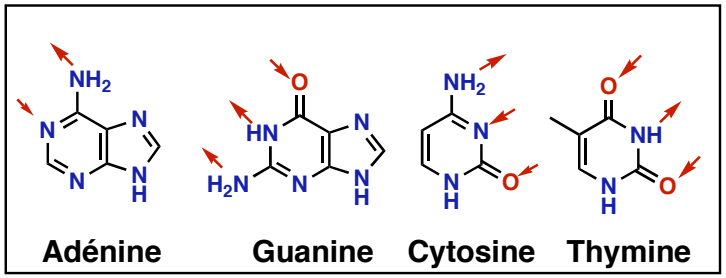
Reconnaissance de molécule neutre

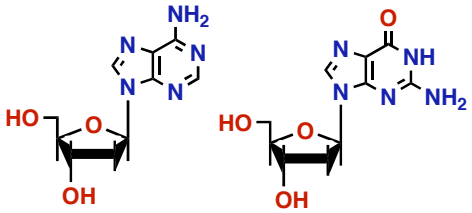


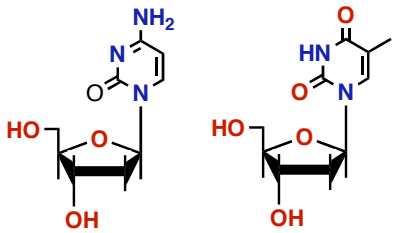
Nature et le Code Génétique

Deux familles d'hétérocycles

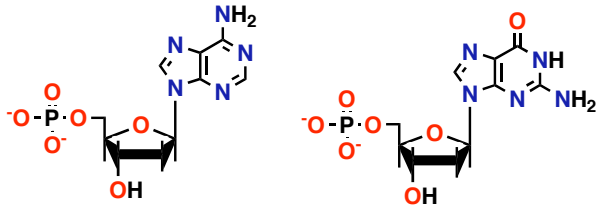


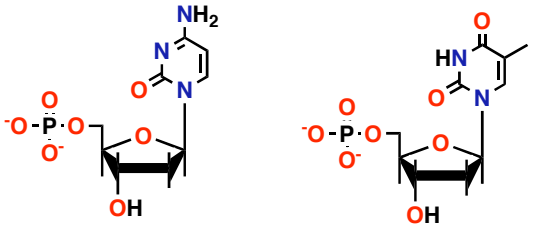






Phosphate

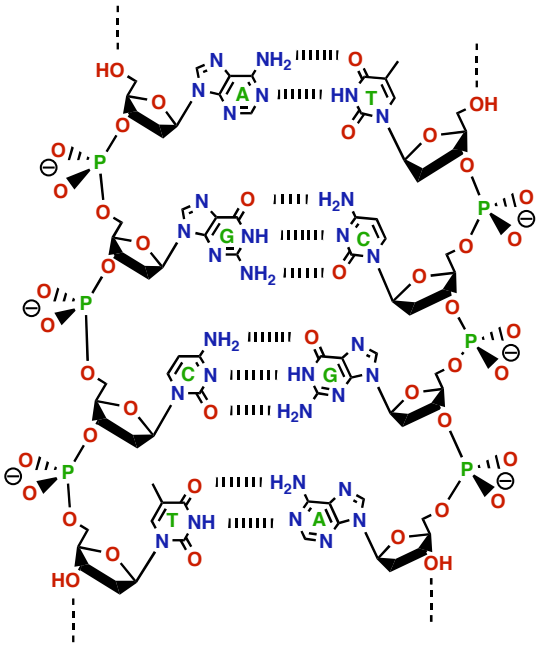


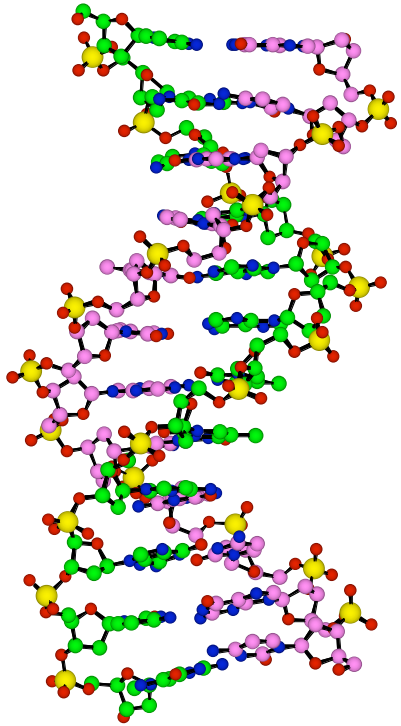


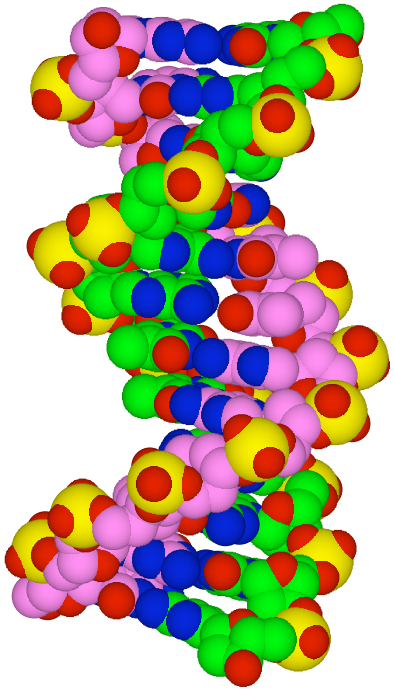
Nucléosides = acides nucléiques + D-ribose

Nucléotides = acides nucléiques + D-ribose + phosphate

ADN : Organisation et Reconnaissance

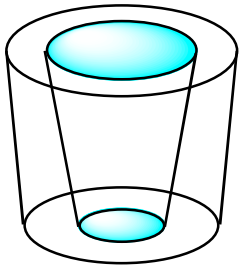




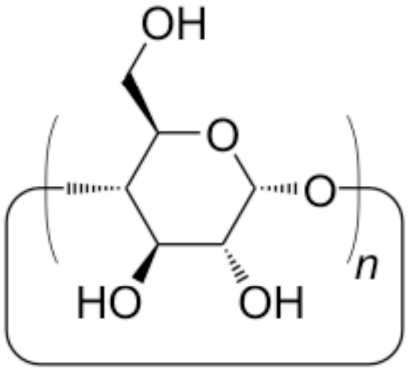


Association de deux brins par liaisons Hydrogène (Reconnaissance entre couples complémentaires A-T et G-C) pour former un duplex qui adopte une structure de double hélice.

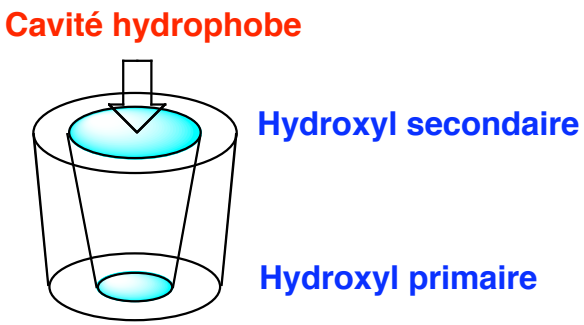
La pas de l'hélice est de 34 Å (une dizaine de paires de bases). La distance en tre les phosphates est de 7 Å. 45% de la surface externe est occupé par les phophates (négativement chargé).

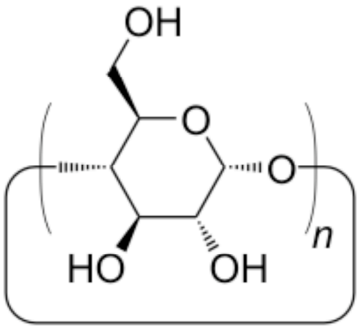


Les cyclodextrines



Les Cyclodextrines



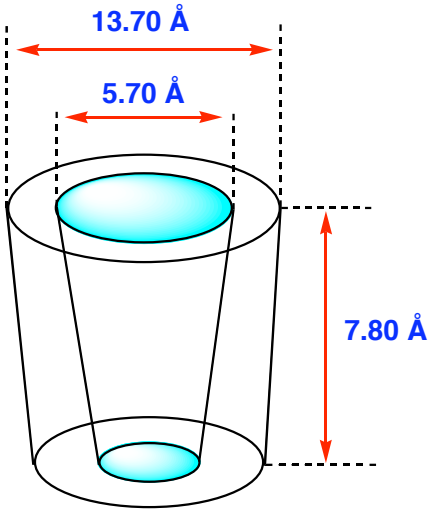


n = 6 : α-cyclodextrine

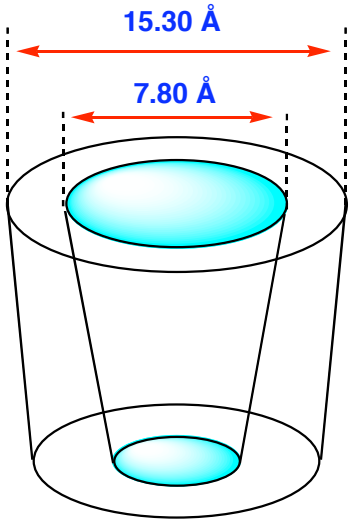
n = 7 : β-cyclodextrine

n = 8 : γ-cyclodextrine

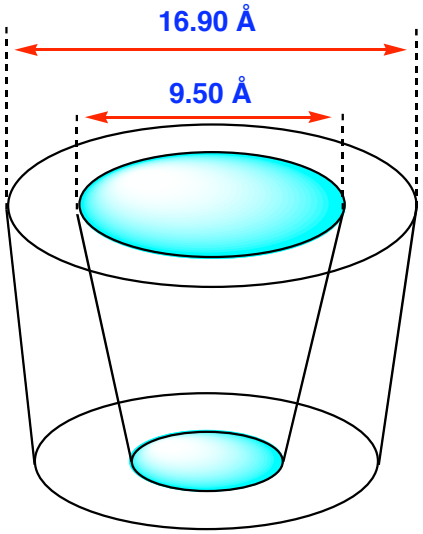
n = 9 : δ-cyclodextrine



α-cyclodextrine

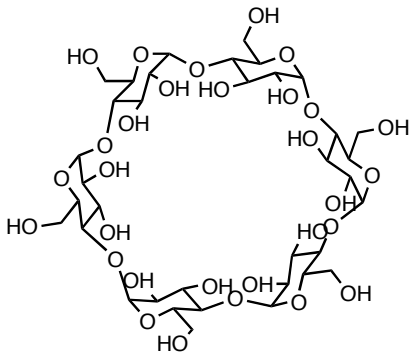


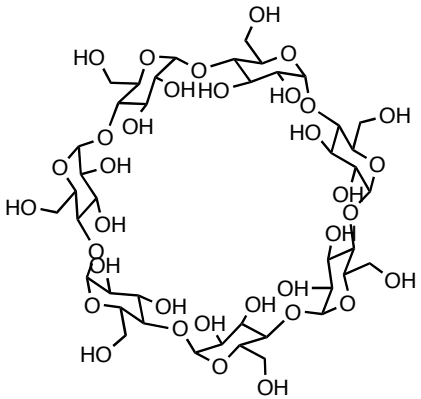
β-cyclodextrine

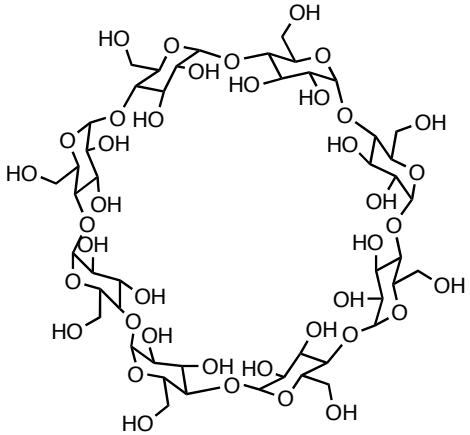


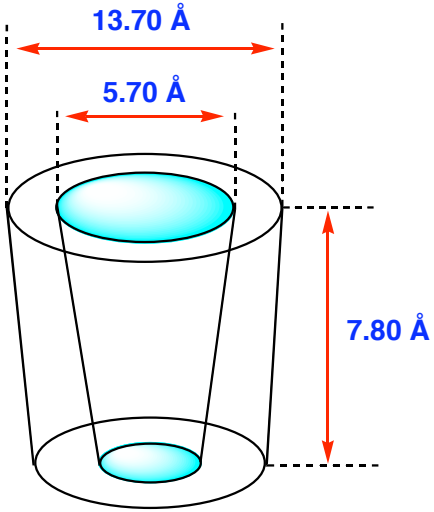
γ-cyclodextrine

Les Cyclodextrines

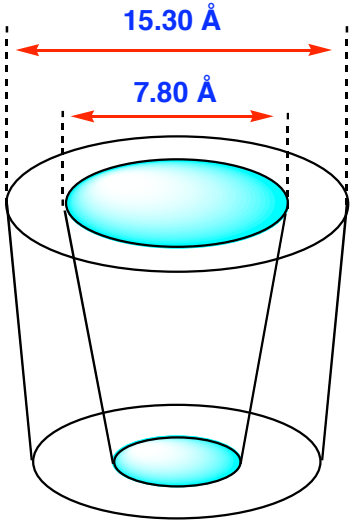




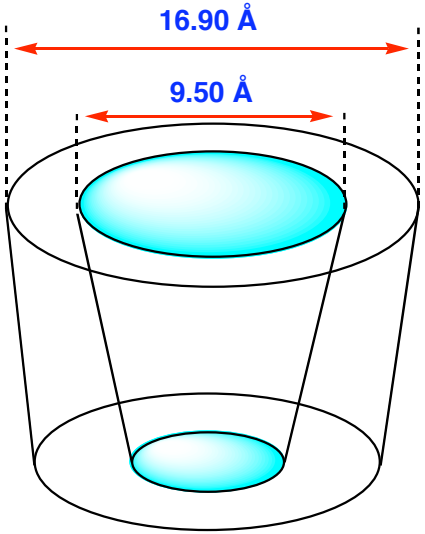




α-cyclodextrine

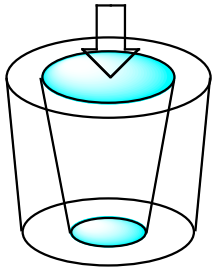


β-cyclodextrine



γ-cyclodextrine

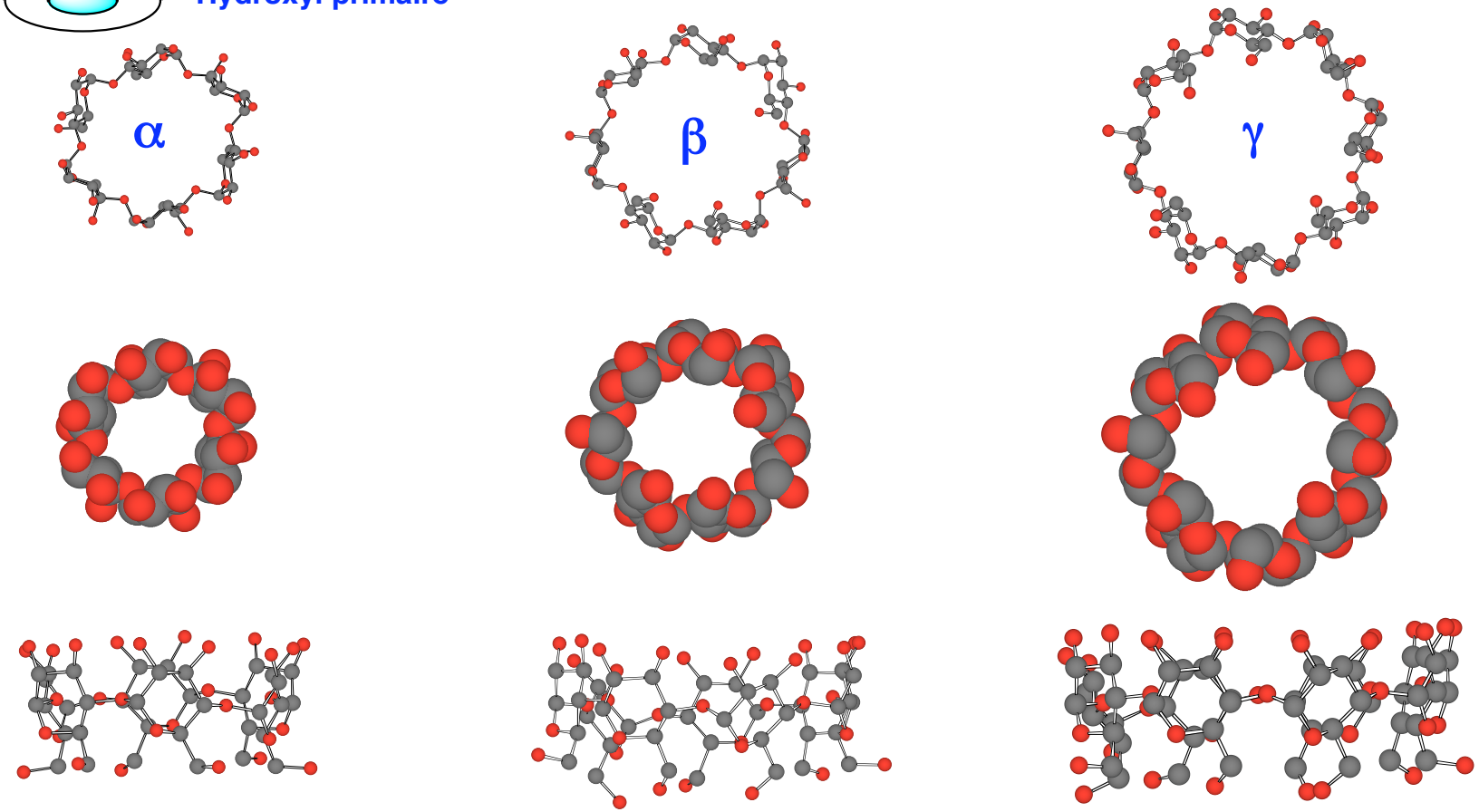
Les Cyclodextrines



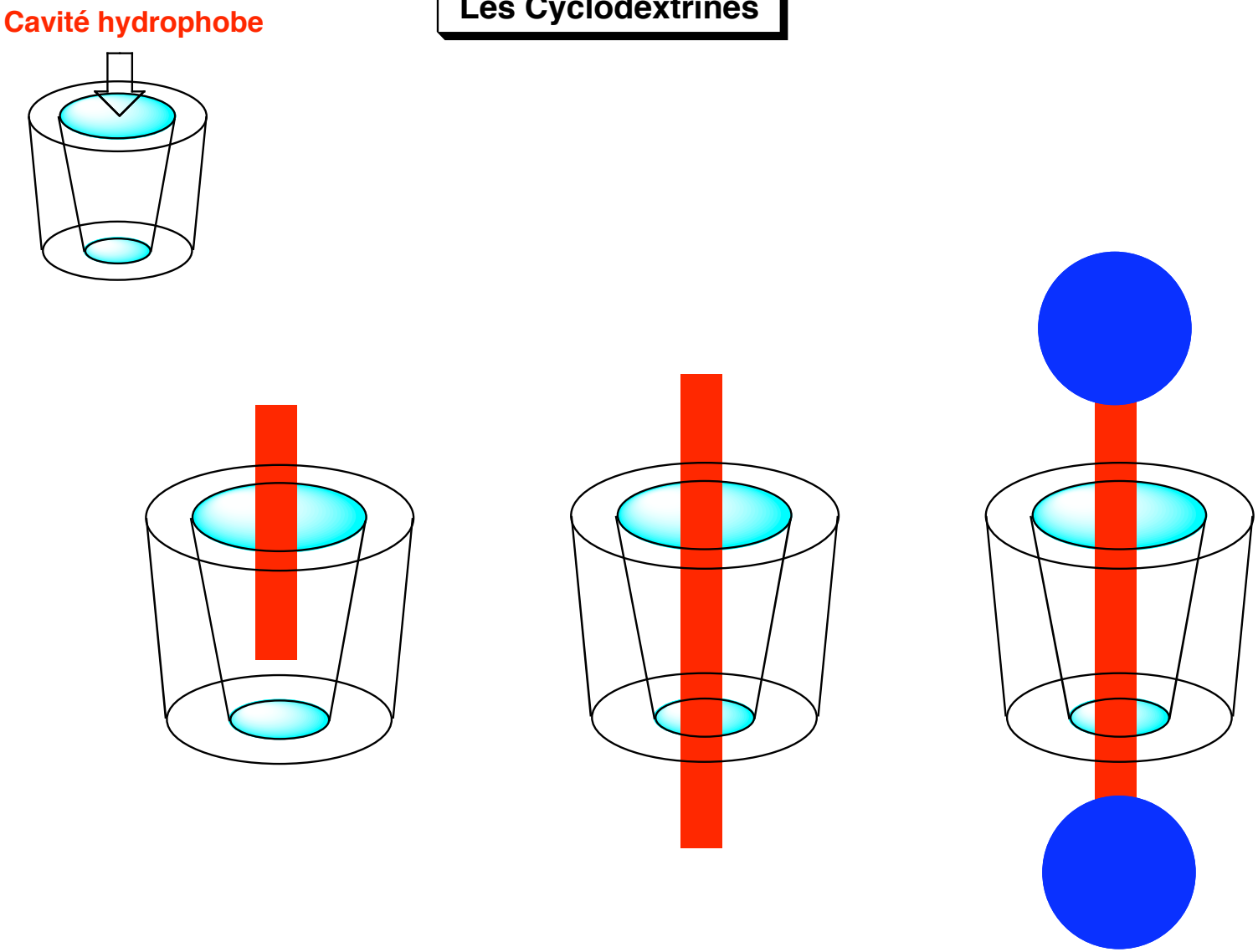
6 α-Cyclodextrine

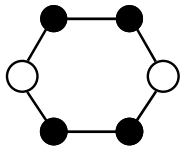
7 β-Cyclodextrine

8 γ-Cyclodextrine



Les Cyclodextrines





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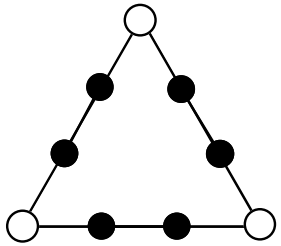

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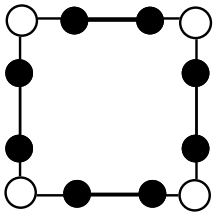
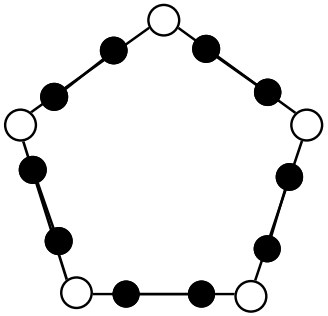
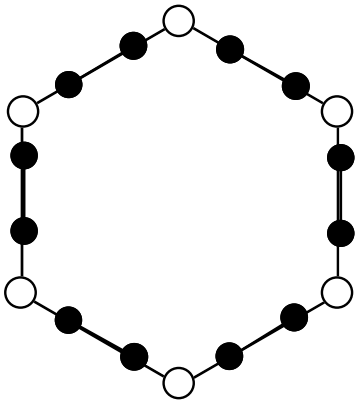


[4,4]

Les métallamacrocycles : métal en tant que jonction



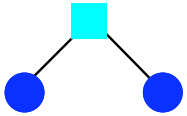
[5,5]



[6,6]

Métallamacrocycles

Un métallamacrocycle est une architecture cyclique contenant des fragments organiques (ligands) et des centres métalliques. Le métal est contenu dans la structure cyclique (endocyclique)



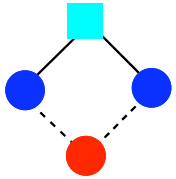
Ligand

Site coordinand

Elément structurant

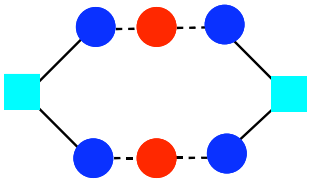
Métal

[1,1]



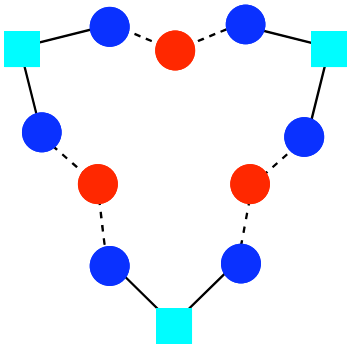
I

[2,2]



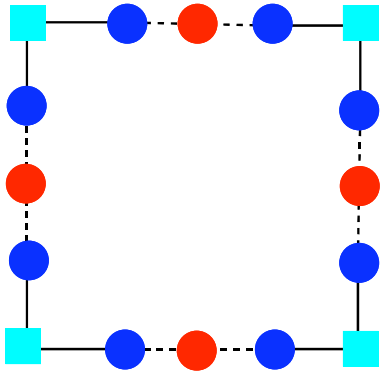
II

[3,3]



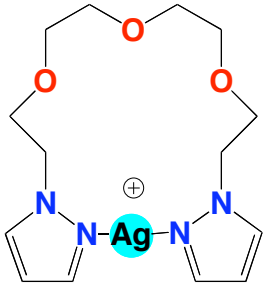
III

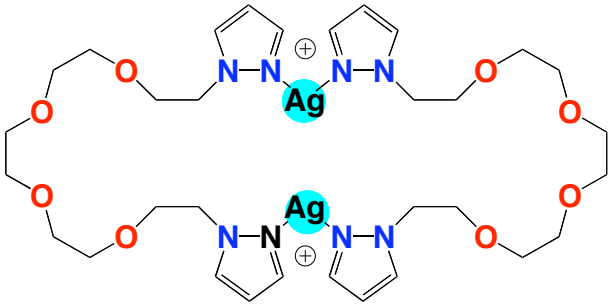
[4,4]

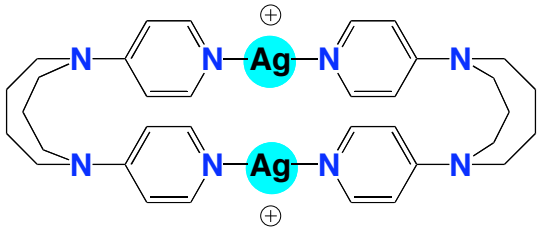


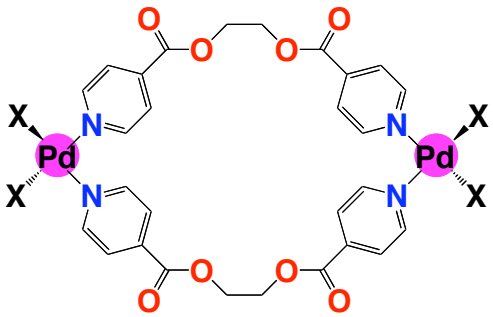
IV

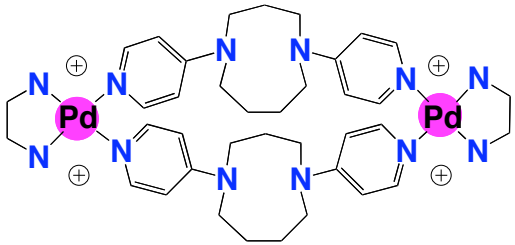
Des exemples de métallamacrocycles

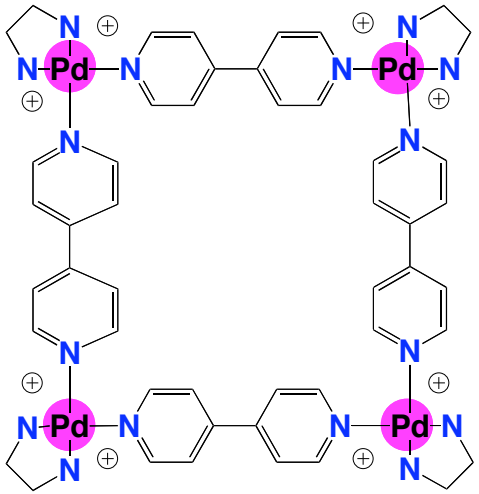


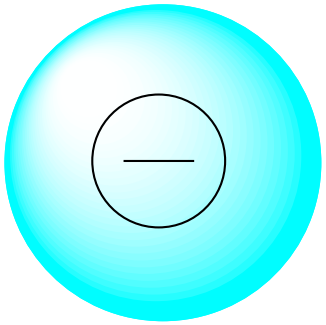


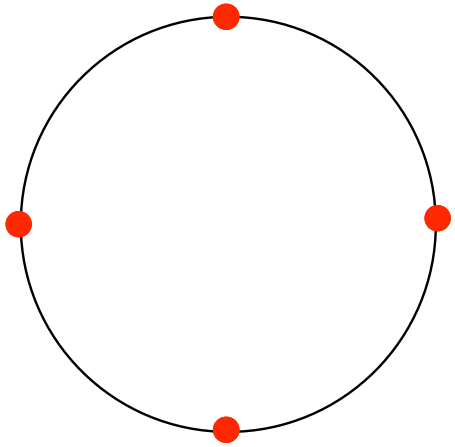




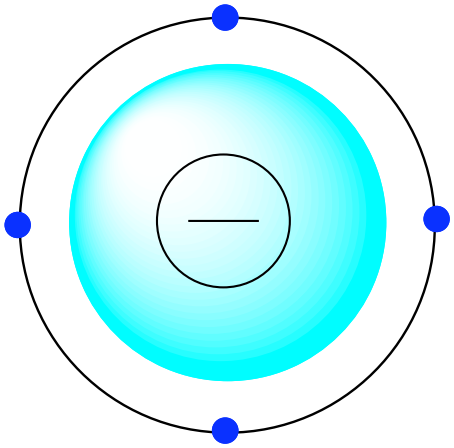








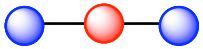
Complexation et reconnaissance d'anions par des récepteurs synthétiques



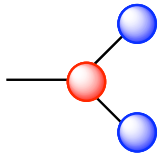
Anions : Diversité de charges, formes et tailles

Dans le monde vivant 70 % des substrats et cofacteurs sont chargés négativement

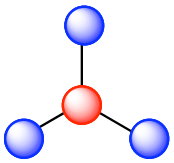
Sphérique : F^-, Cl^-, Br^-, I^-



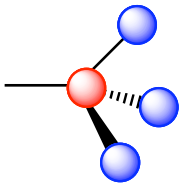
Linéaire : N_3^-, O_2^{--}, $M(CN)_2^-$



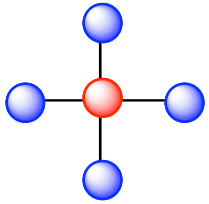
Coudé : RCO_2^-



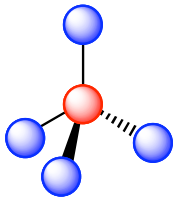
Trigonal Plan : NO_3^-, CO_3^{--}



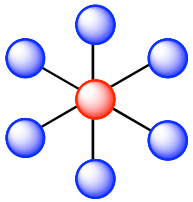
Trigonal : RSO_3^-



Carré : MX_4^{--}, $(M(CN)_4^{--})$

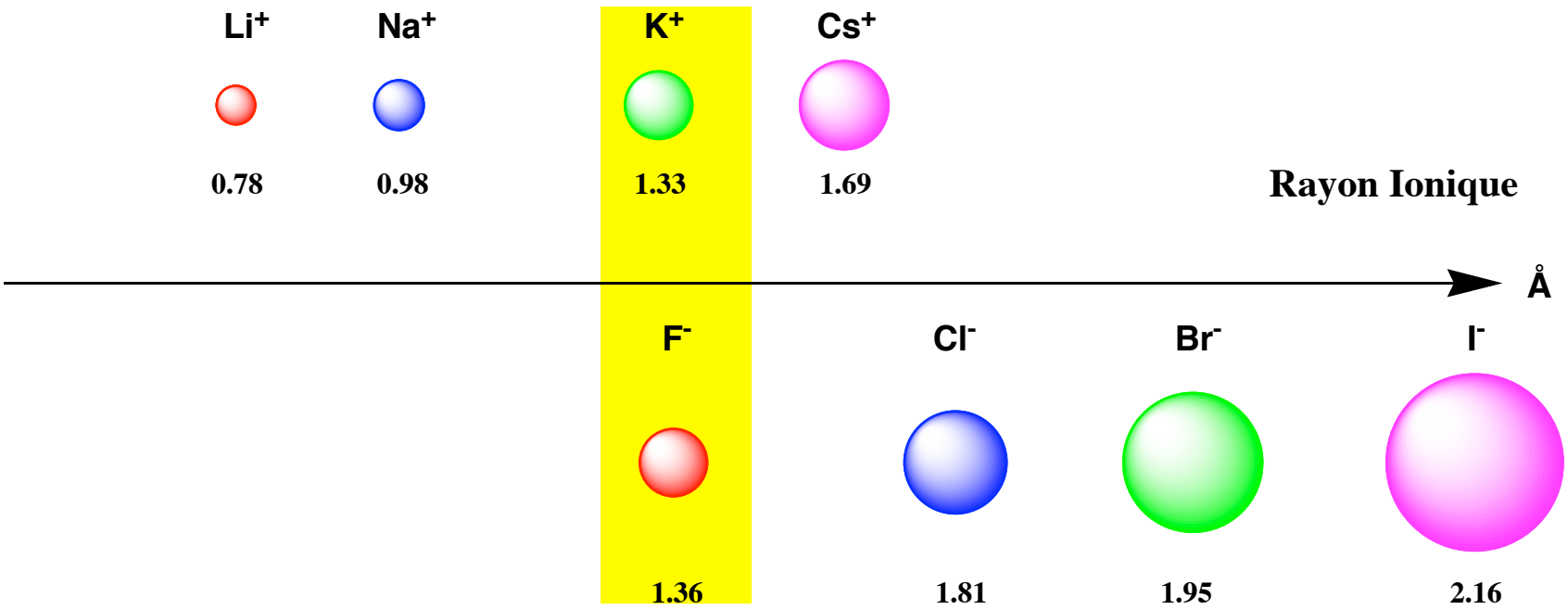


Tétraèdrique : XO_4^{n-} (BF_4^-, SO_4^{--} , PO_4^{---})

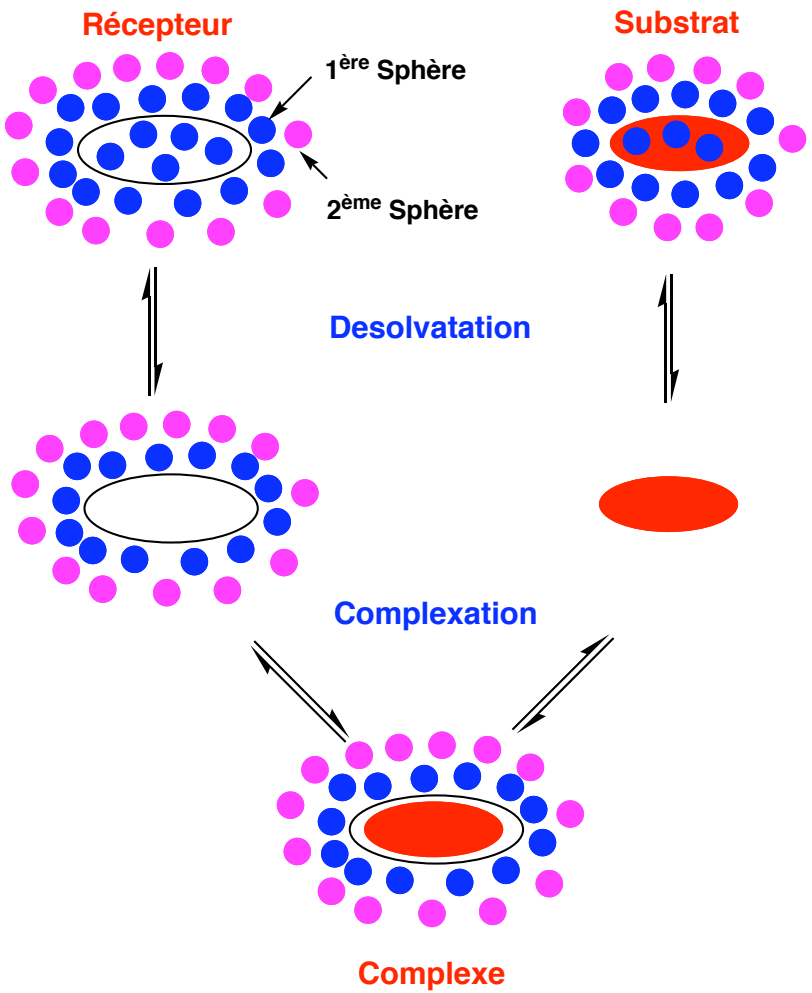


Octaèdrique : MX_6^{n-} (PF_6^-, $M(CN)_6^{3-}$, PO_4^-)

Les anions sont "gros"



La complexation est en compétition avec la solvatation

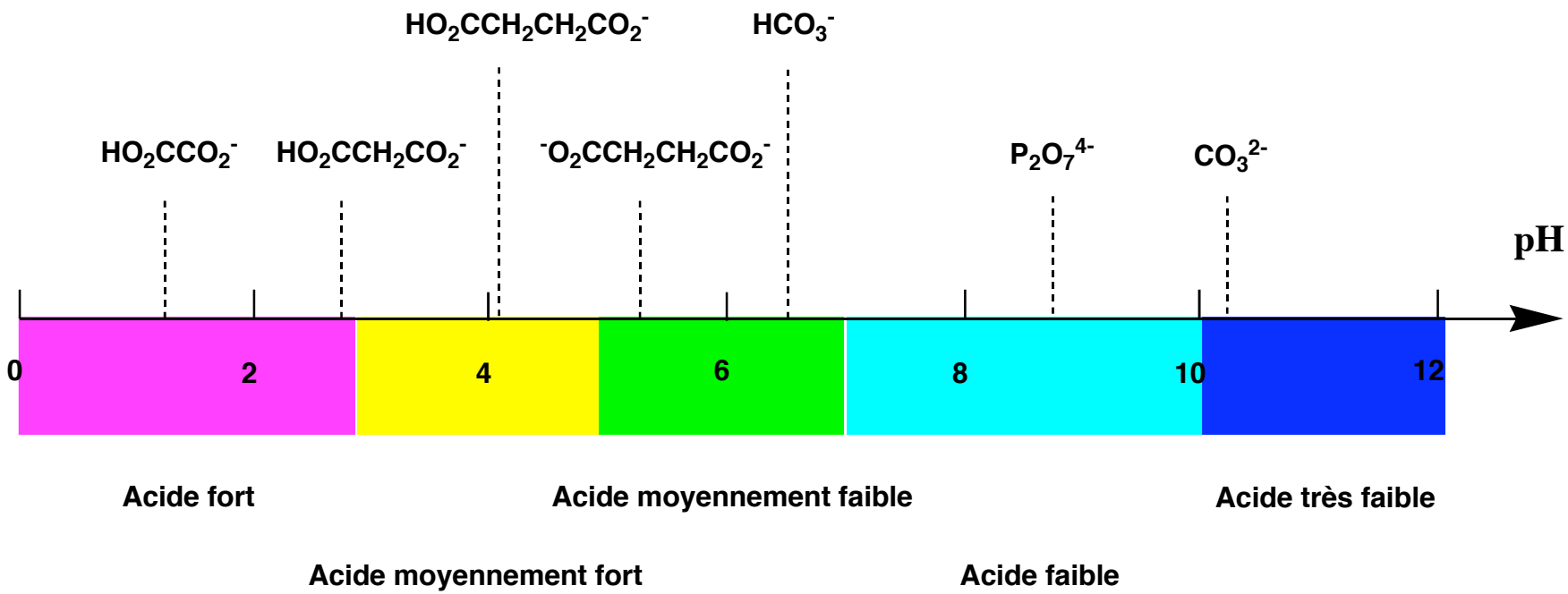


Cations	ΔG^0	ΔH^0	$T\Delta S^0$
Li^+	122.1	132.1	10.0
Na^+	98.2	106.0	7.8
K^+	80.6	85.8	5.8
Cs^+	67.8	72.0	4.2

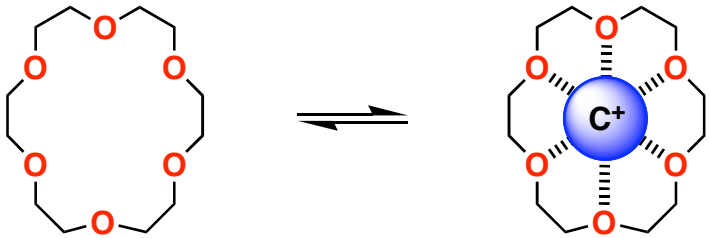
Anions	ΔG^0	ΔH^0	$T\Delta S^0$
F^-	103.8	113.3	9.5
Cl^-	75.8	81.3	5.5
Br^-	72.5	77.9	5.4
I^-	61.4	64.1	2.7

H_2O, 25 °C, en Kcal mol^{-1}

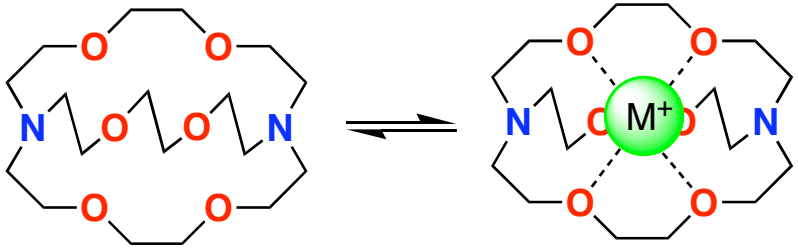
Les anions sont des bases : domaine d'existence



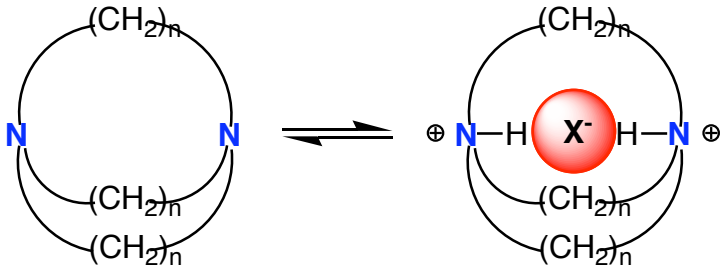
Reconnaissance d'Anion : un regard historique



crown ether

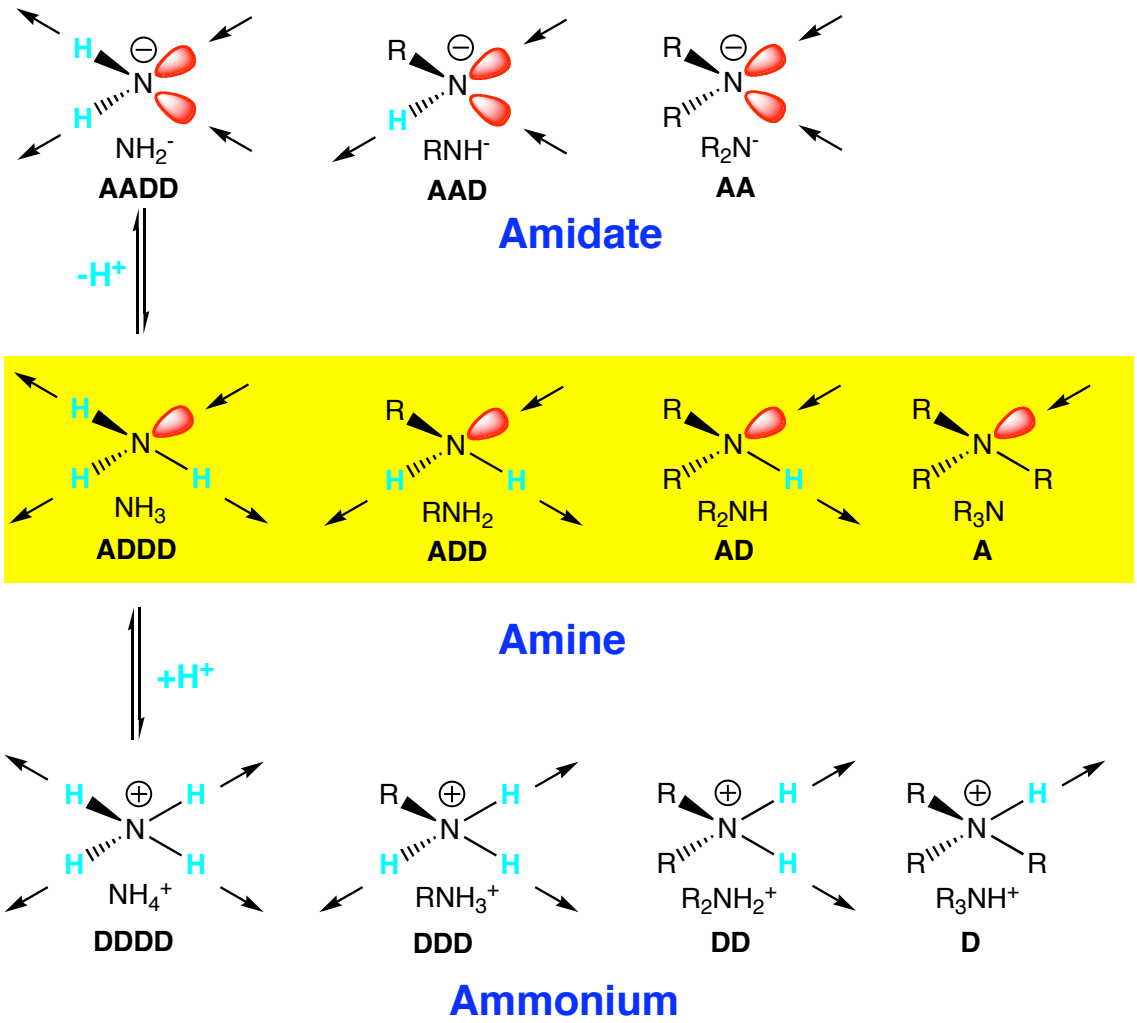


Cryptand



Katapinate

Amine, Amidate and Ammonium



Base

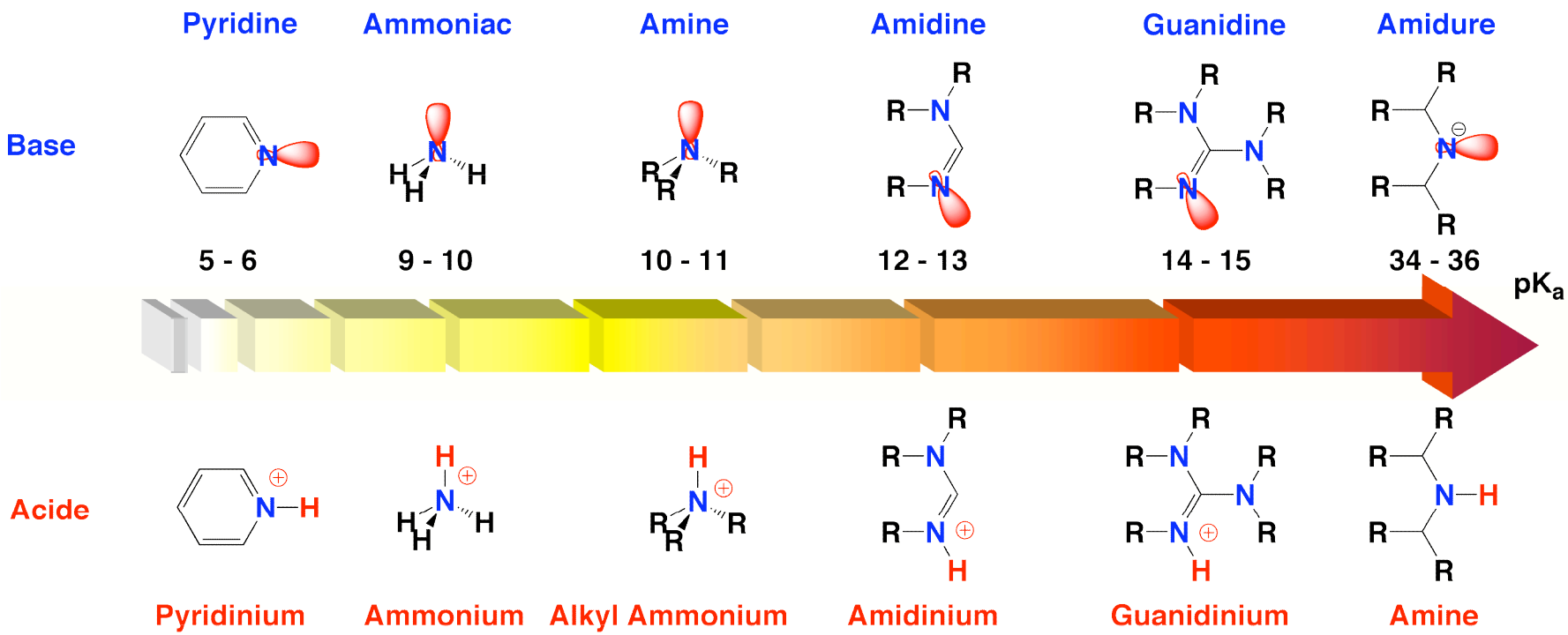
$$R_3N + HX \underset{pK_a = -\mathrm{Log}K_a}{\overset{K_a}{\rightleftharpoons}} R_3NH^{\oplus} + X^{\ominus}$$

Amine — Acide — Ammonium

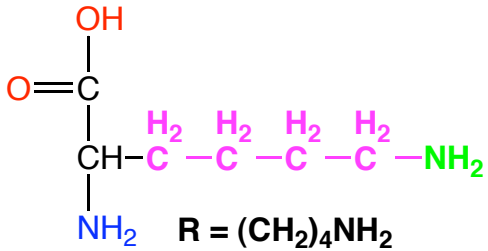
Acide

$$R_2NH + B^{\ominus} \rightleftharpoons R_2N^{\ominus} + BH$$

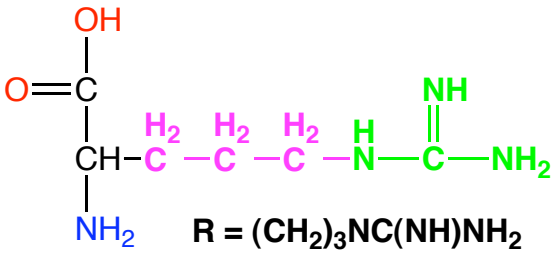
Amine — Base — Amidure



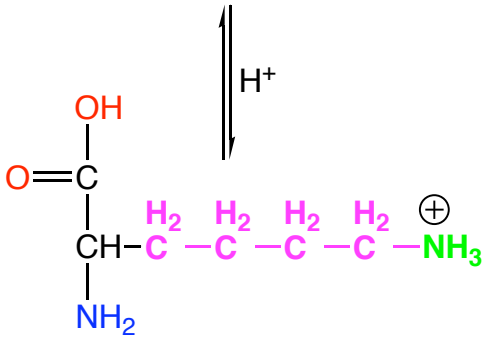
Amino-acids

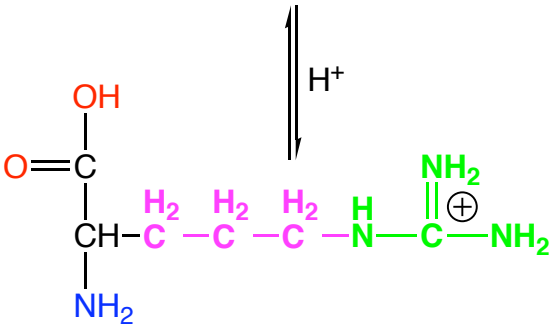


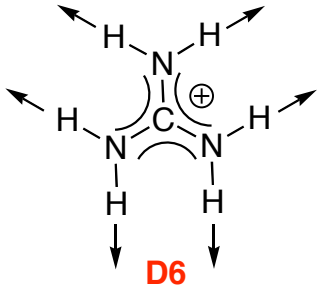
R = $(CH_2)_4NH_2$
Lysine (Lys)



R = $(CH_2)_3NC(NH)NH_2$
Arginine (Arg)

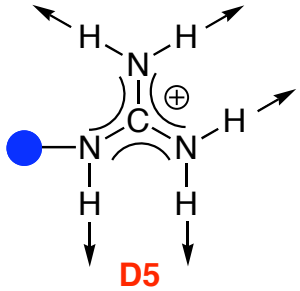






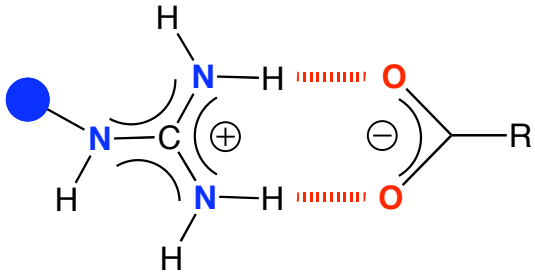
D6

Guanidinium

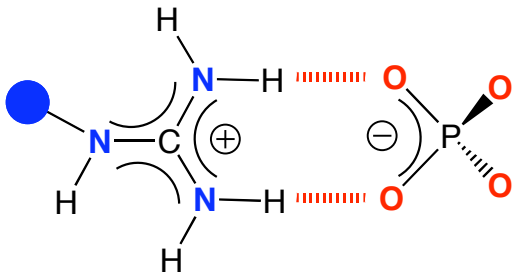


D5

iMode de reconnaissance



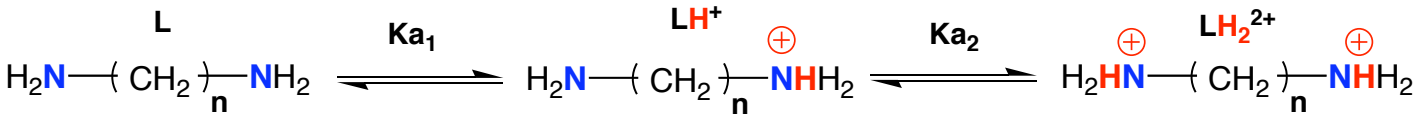
carboxylate



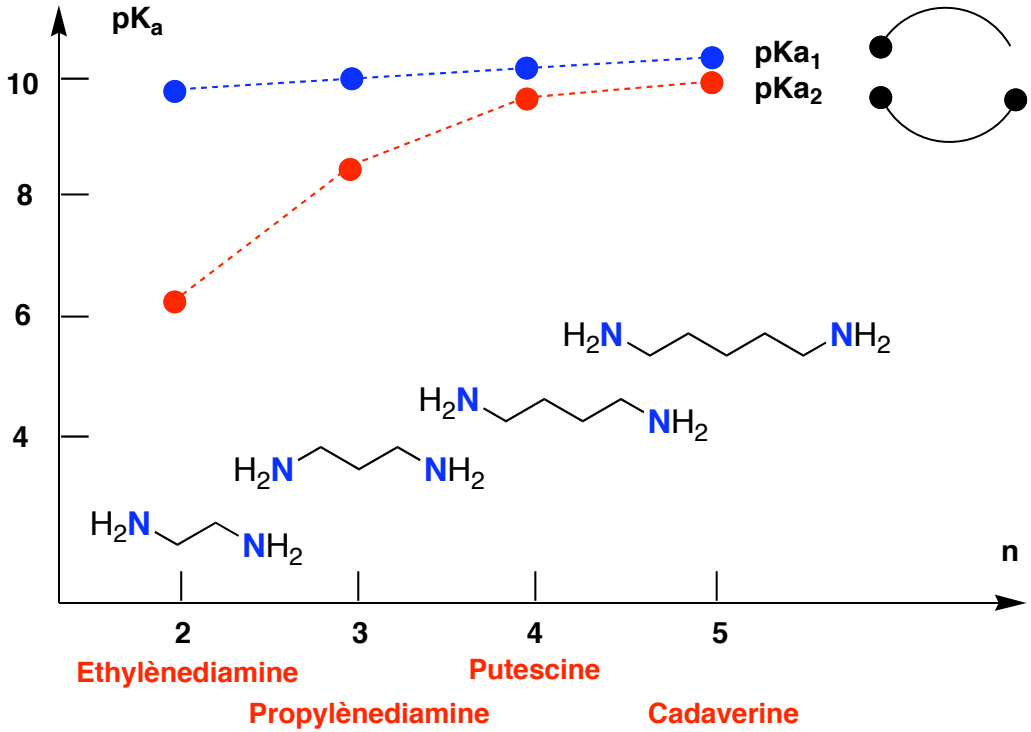
Phosphate

Dihapto mode of H-bonding

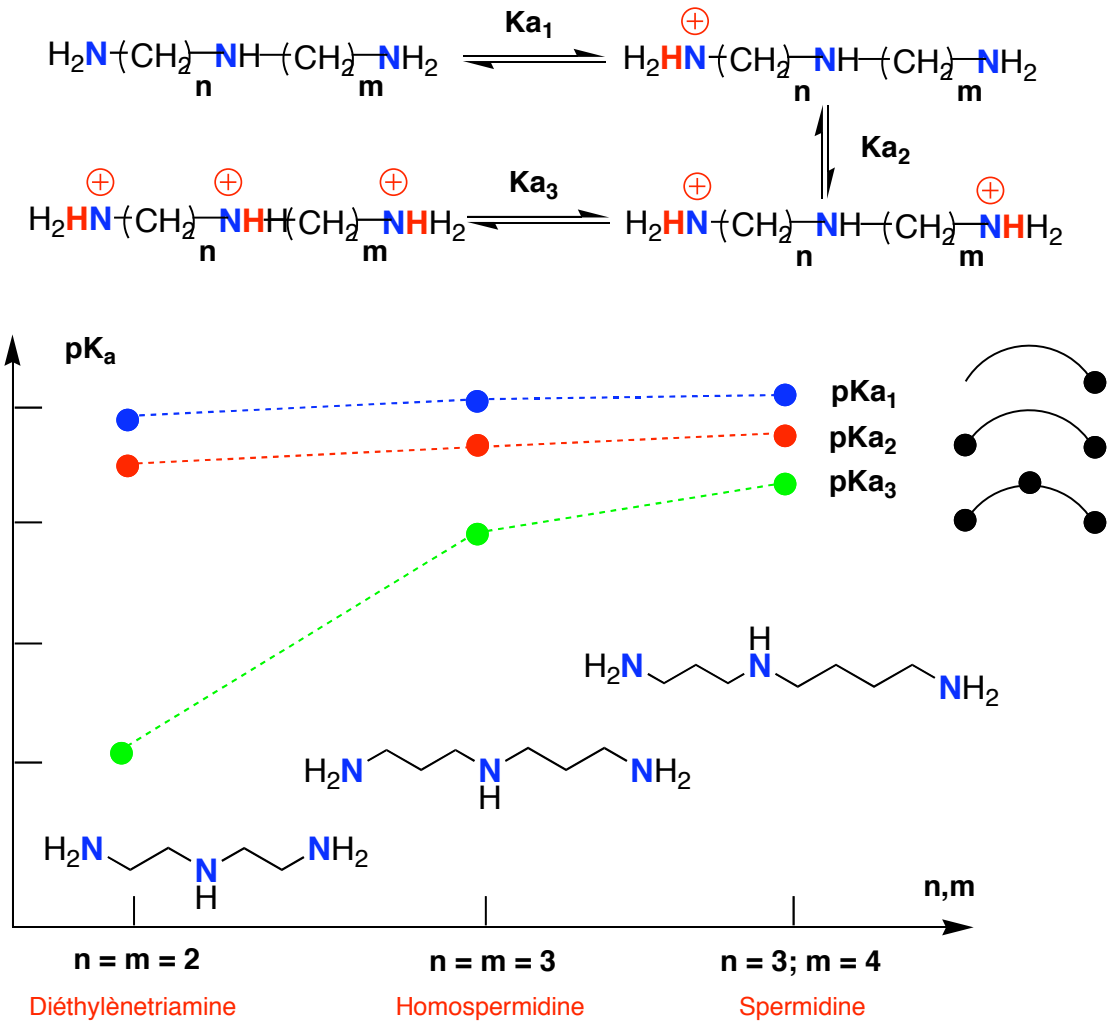
Protonation



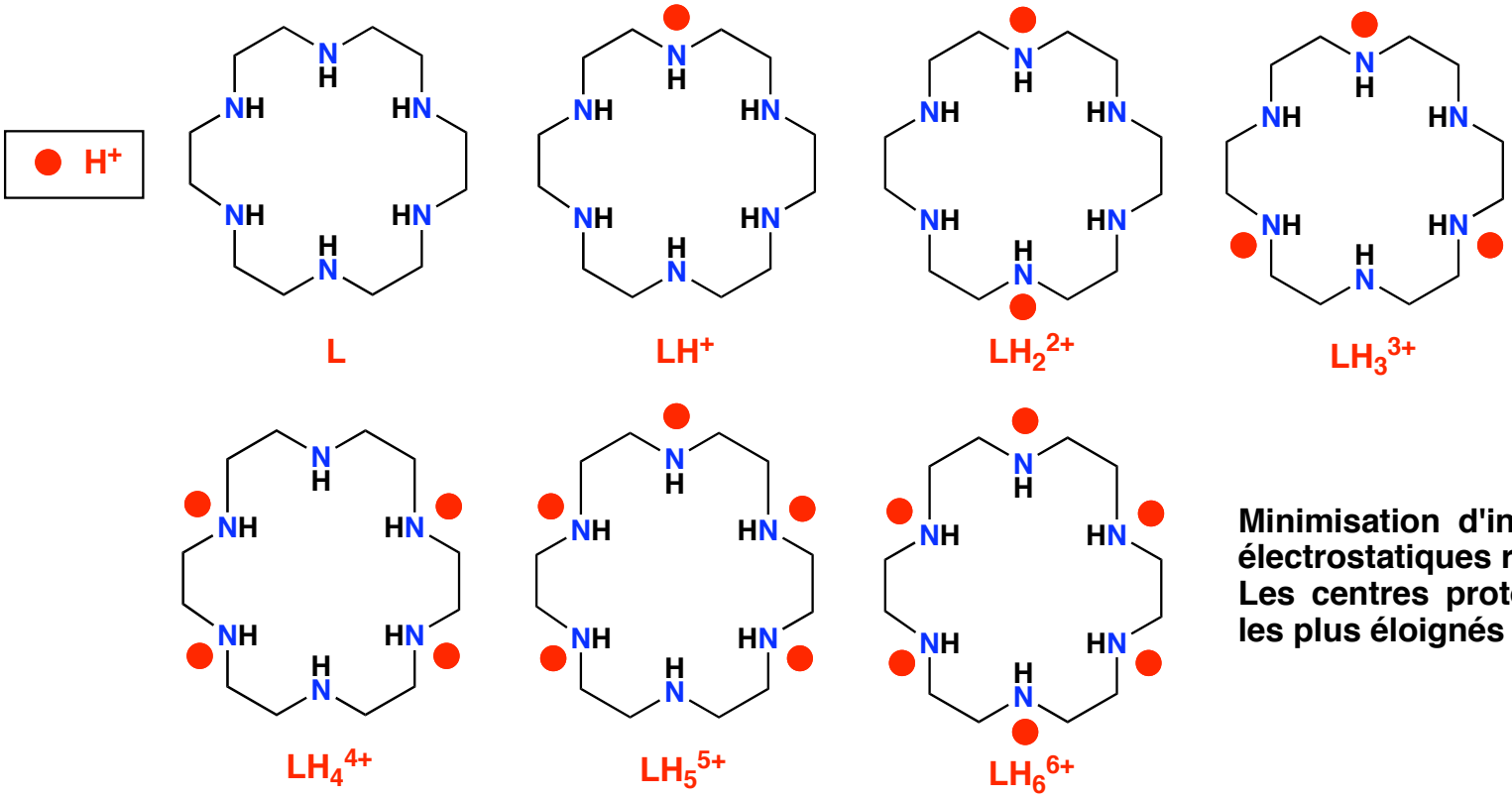
$$Ka_1 = \frac{[LH^+]}{[L] \times [H^+]} \qquad Ka_2 = \frac{[LH_2^{2+}]}{[LH^+] \times [H^+]}$$



Protonation



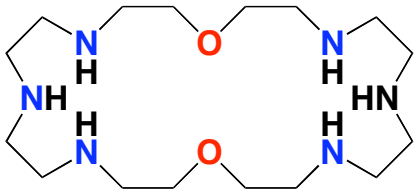
Séquence de protonation



Minimisation d'interactions électrostatiques répulsives. Les centres protonés sont les plus éloignés possibles

pK_1	pK_2	pK_3	pK_4	pK_5	pK_6
10.2	9.2	8.7	4.1	2	1

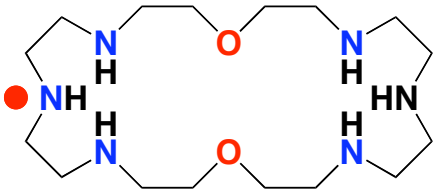
Séquence de protonation



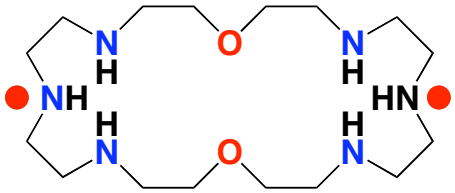
L

● H^+

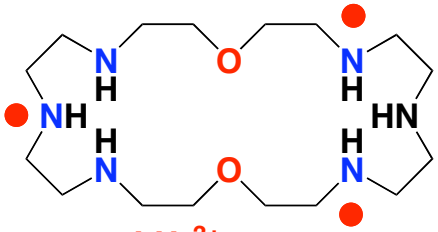
Minimisation d'interactions électrostatiques répulsives. Les centres protonés sont les plus éloignés possibles



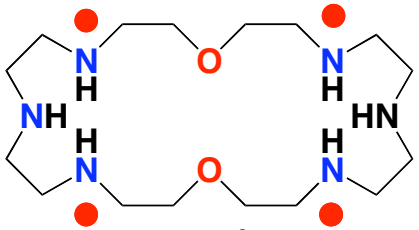
LH^+



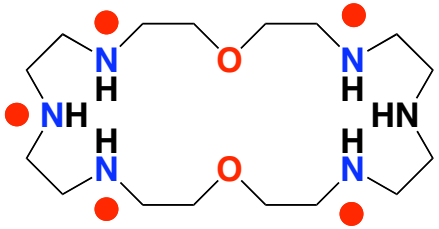
LH_2^{2+}



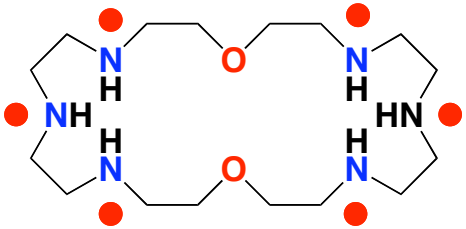
LH_3^{3+}



LH_4^{4+}



LH_5^{5+}



LH_6^{6+}

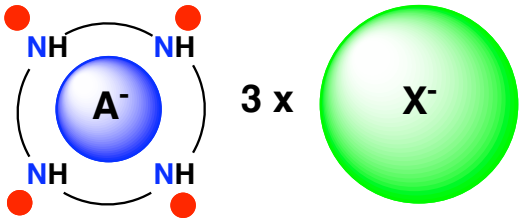
pK_1	pK_2	pK_3	pK_4	pK_5	pK_6
9.6	9.3	8.3	8.1	4.0	3.8

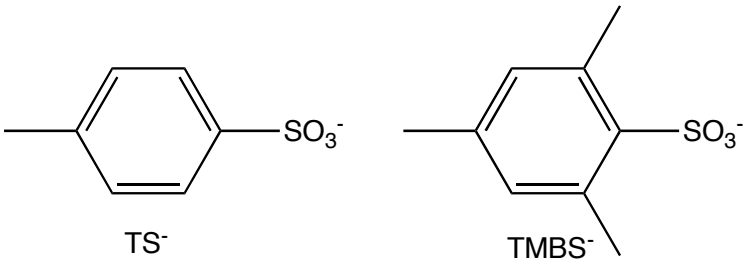
Reconnaissance d'anions par des polycations

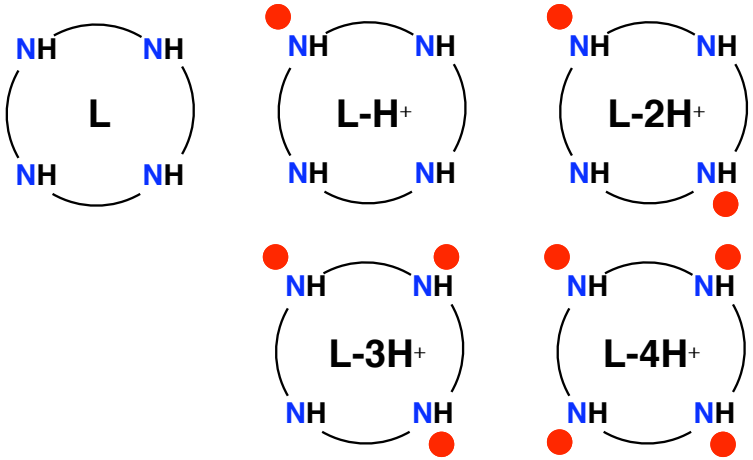
Complications :

$$L + nH^+ + nX^- \rightleftharpoons (L\text{-}nH^+ , nX^-)$$

La nature du contre ion est particulièrement importante.
Le contre ion doit être très faiblement associé au récepteur.

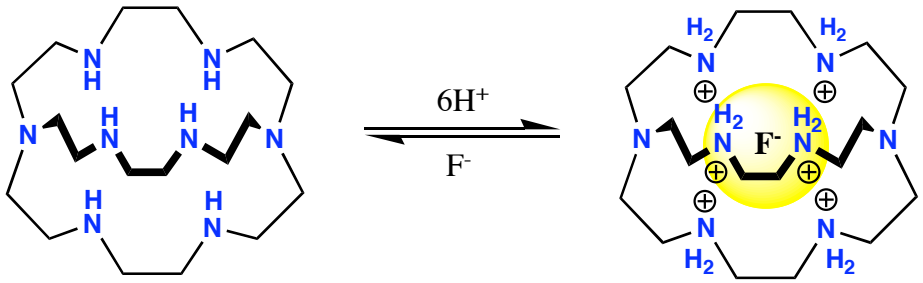




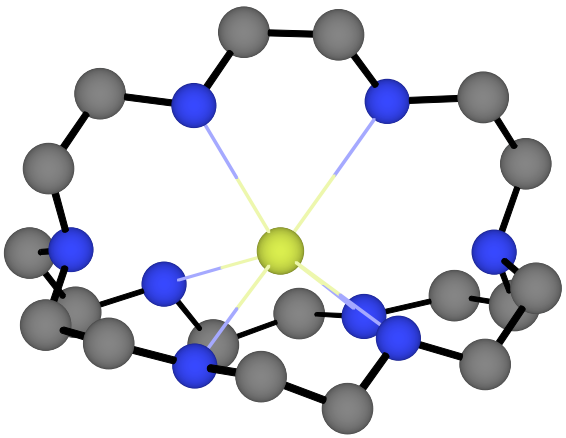


Existence de plusieurs formes protonées.
Existences de plusieurs complexes possibles.
Forte variation de nombre de charges nécessite la présence d'un sel de fond.
Les constantes de stabilités déterminées sont relatives au milieu

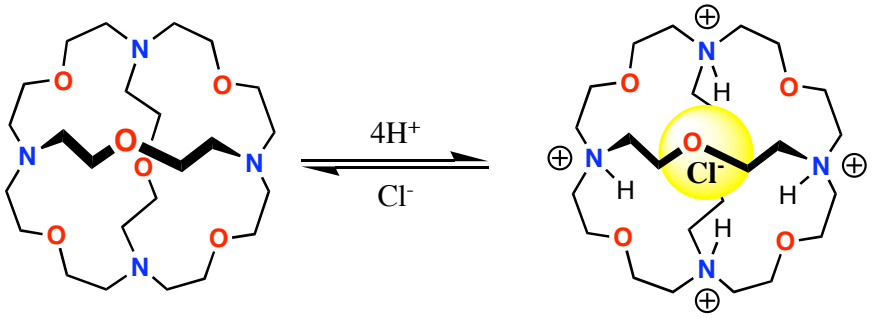
Reconnaissance de fluorure par un récepteur hexacationique

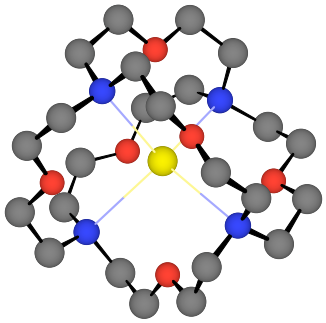


Macrobicycle

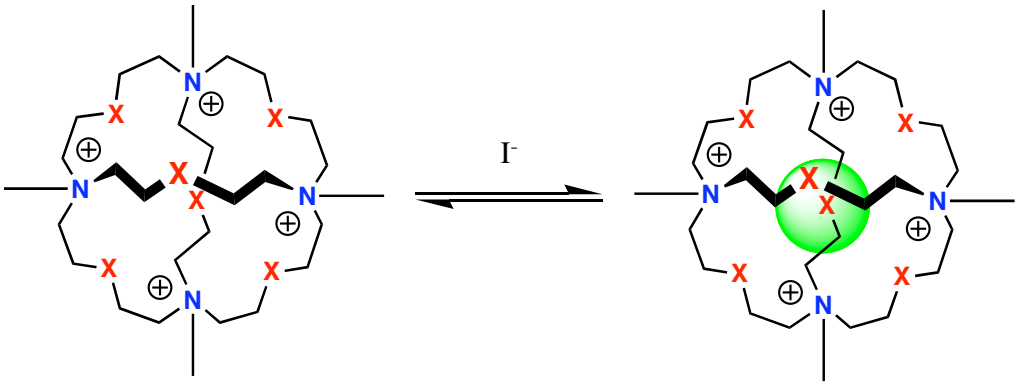


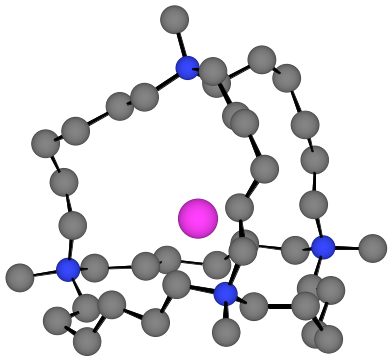
Reconnaissance de chorure par un récepteur tétracationique





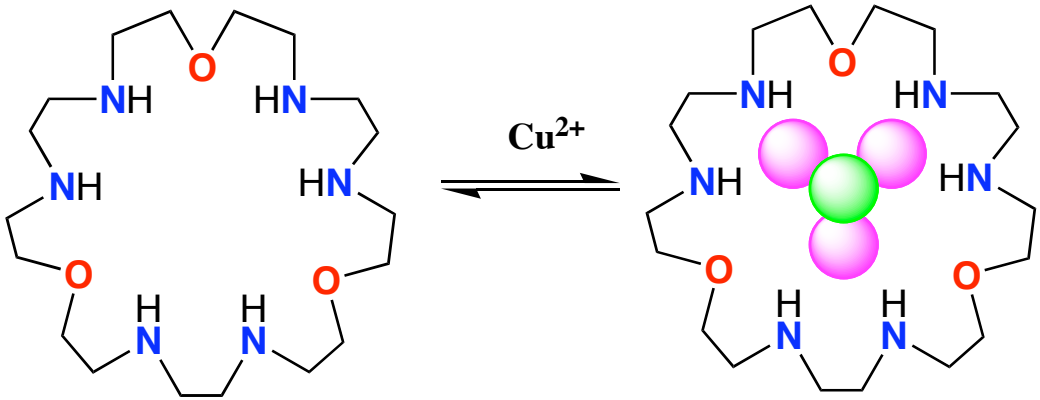
Macrotricycle

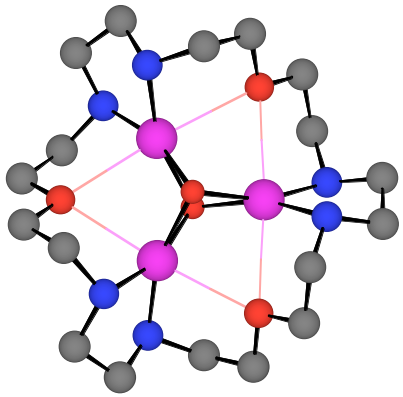




X = O
X = CH_2CH_2

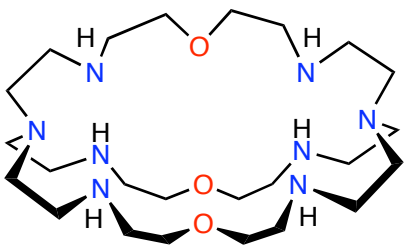
Reconnaissance de OH^- par un trinucléaire au cuivre





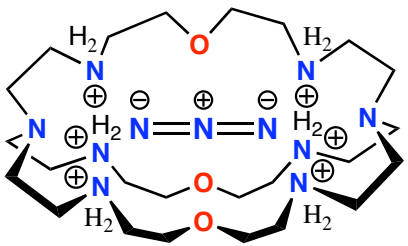
$d_{Cu\text{-}O}$ = 2.60Å
$d_{Cu\text{-}N}$ = 1.97Å
$d_{Cu\text{-}OH}$ = 2.05Å
$d_{Cu\text{-}Cu}$ = 2.80Å

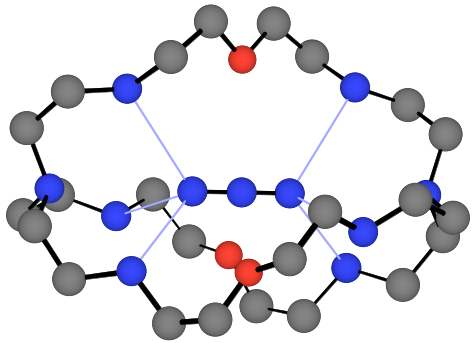
Reconnaissance d'azide par un récepteur hexacationique



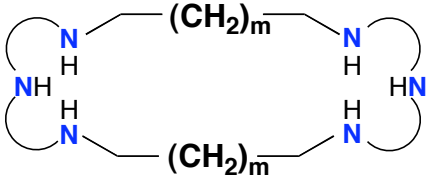
Macrobicycle

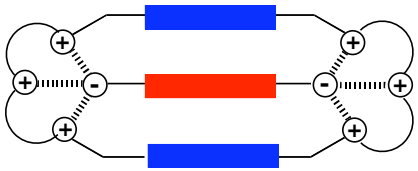
$$\rightleftharpoons \quad \begin{matrix} 6H^+ \\ N_3^- \end{matrix}$$

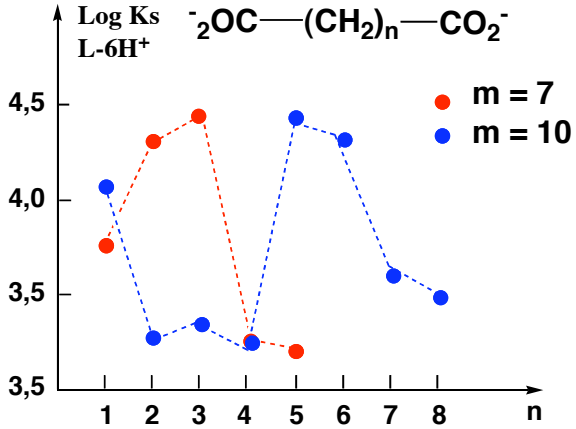


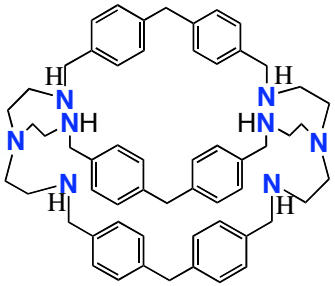


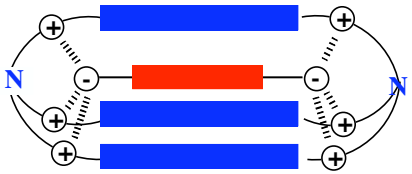
Reconnaissance de dianions ditopiques

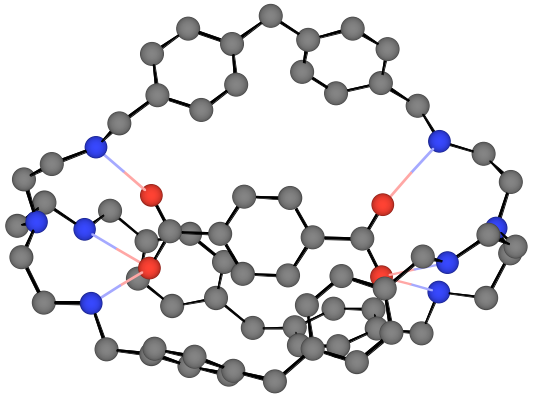




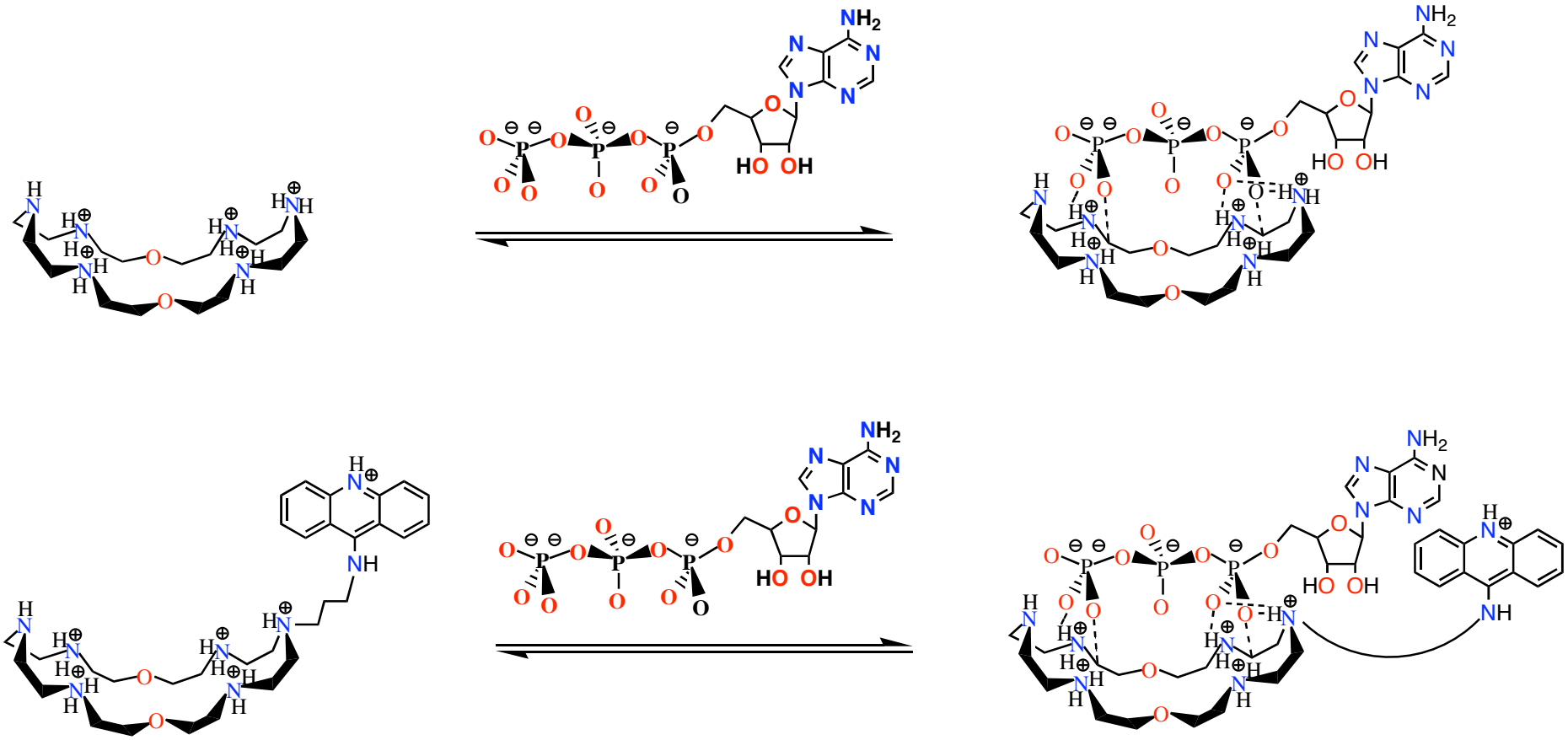




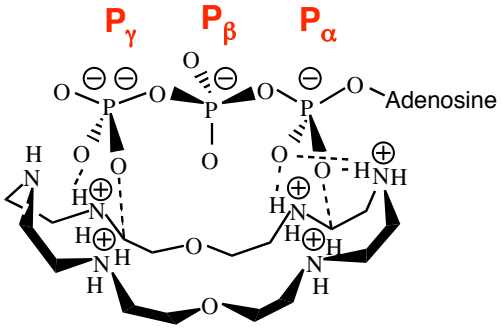


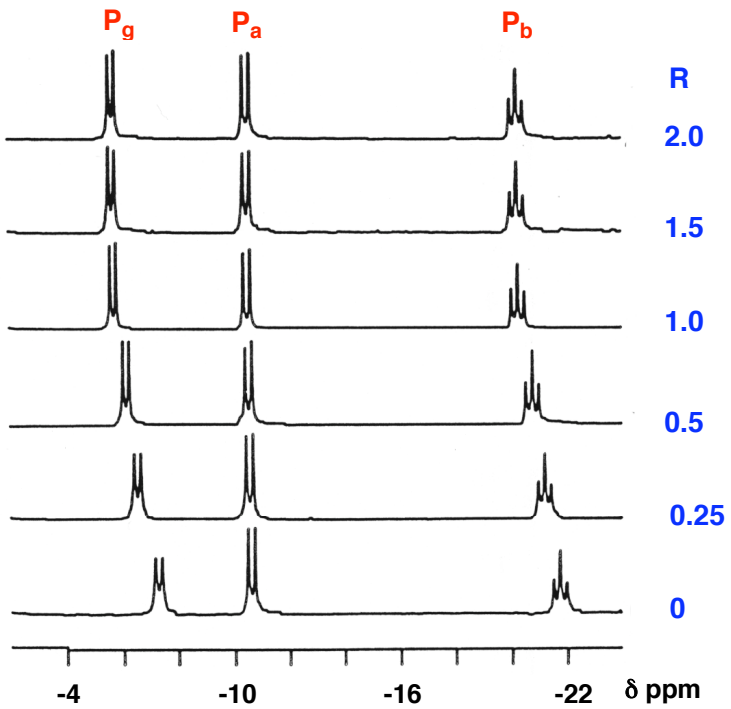


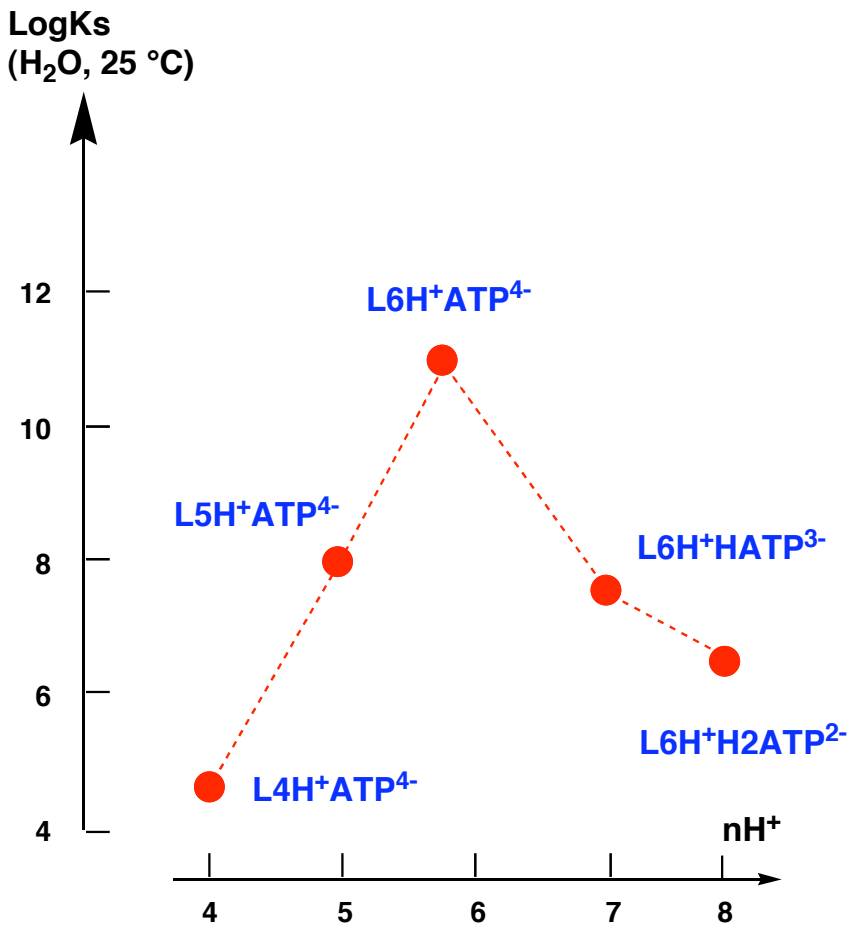
Reconnaissance d'ATP par des Récepteurs Cationiques



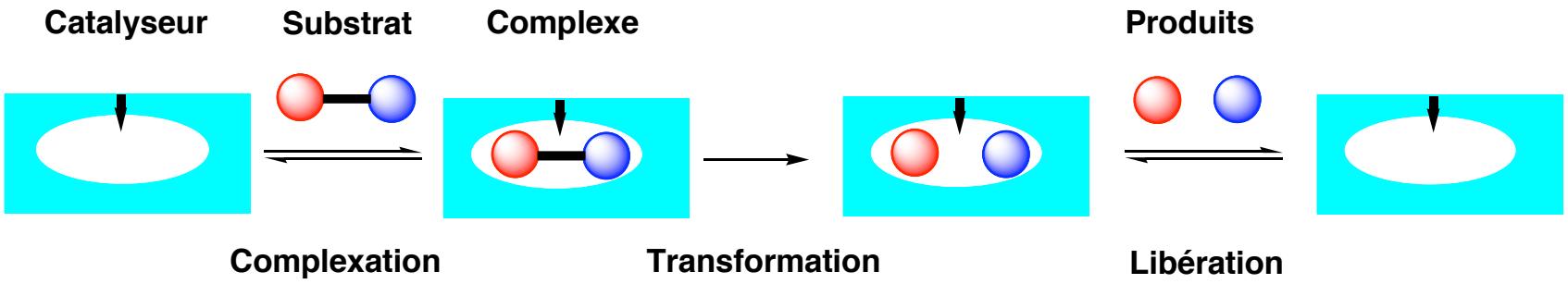
Complexation de l'ATP : Stoichiométrie et stabilité



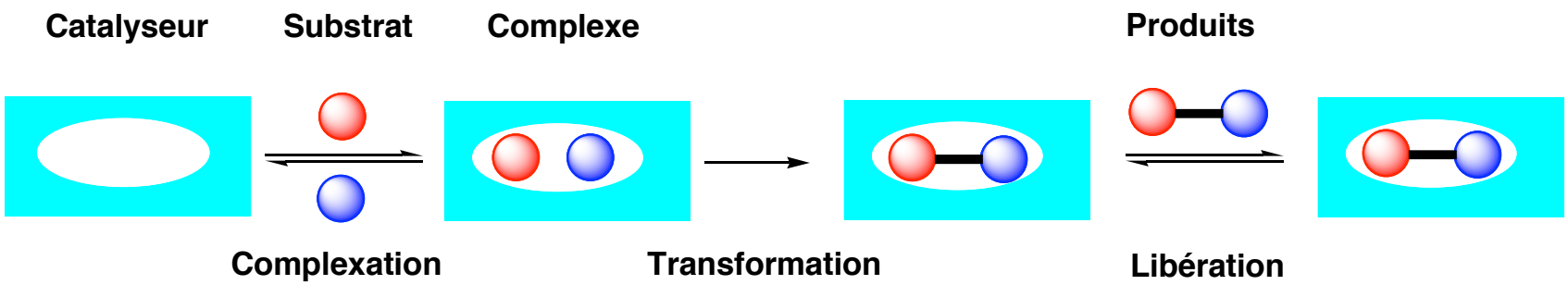




Rupture de liaison

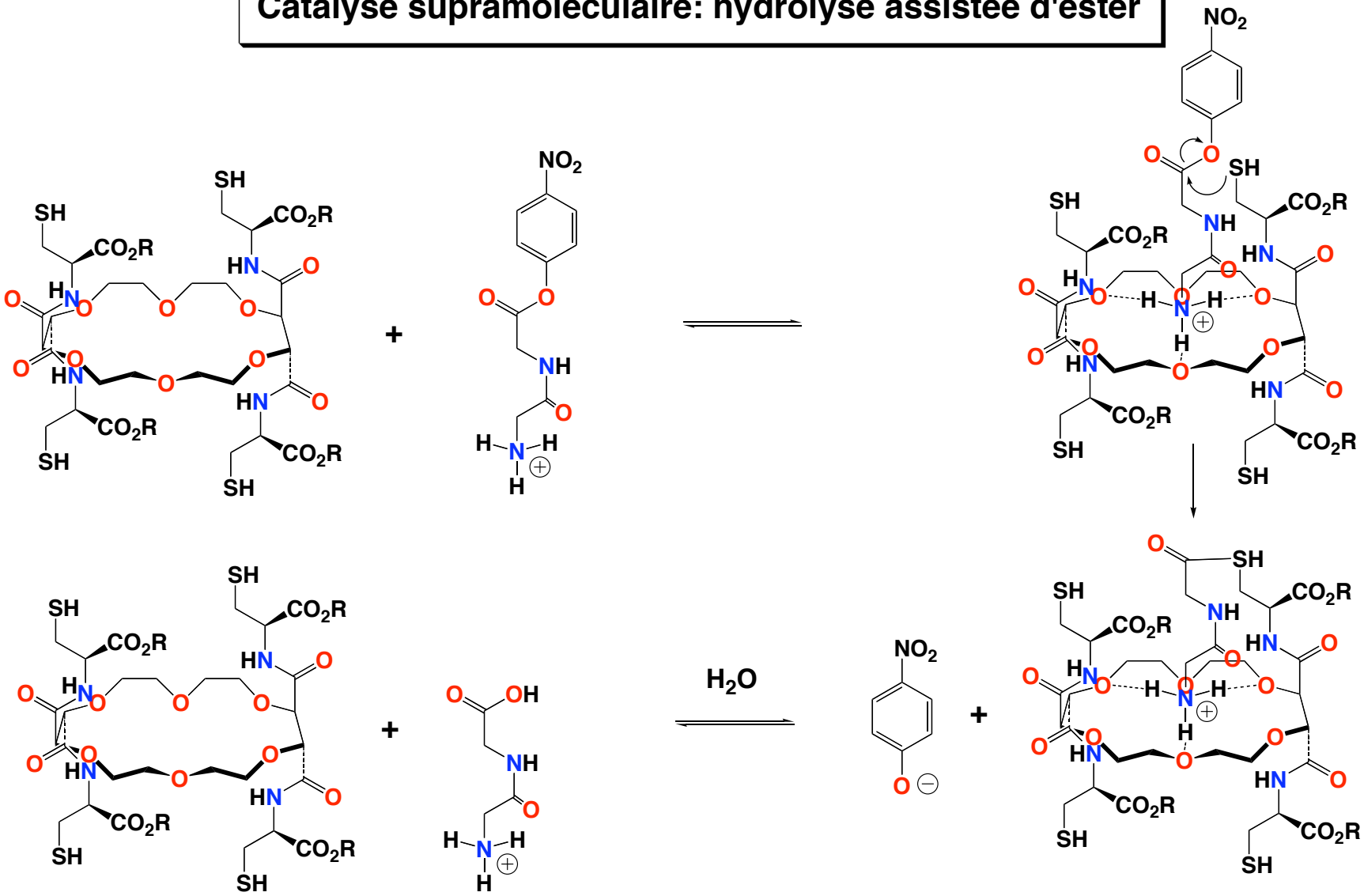


Ctalyse supramoléculaire : rupture (lyase) et formation (ligase) de liaisons

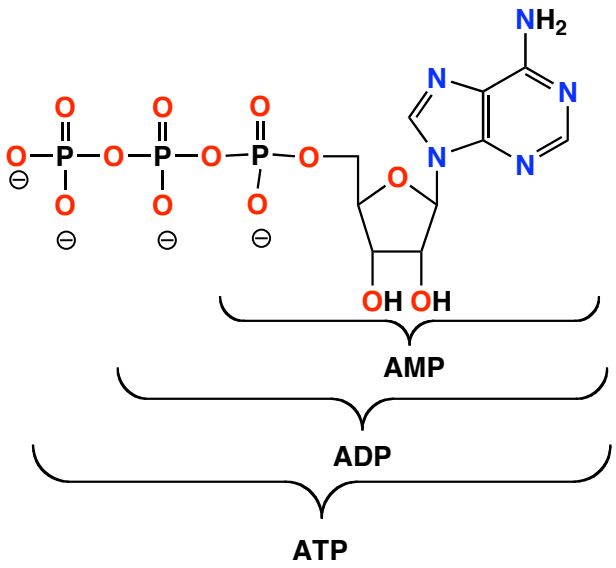


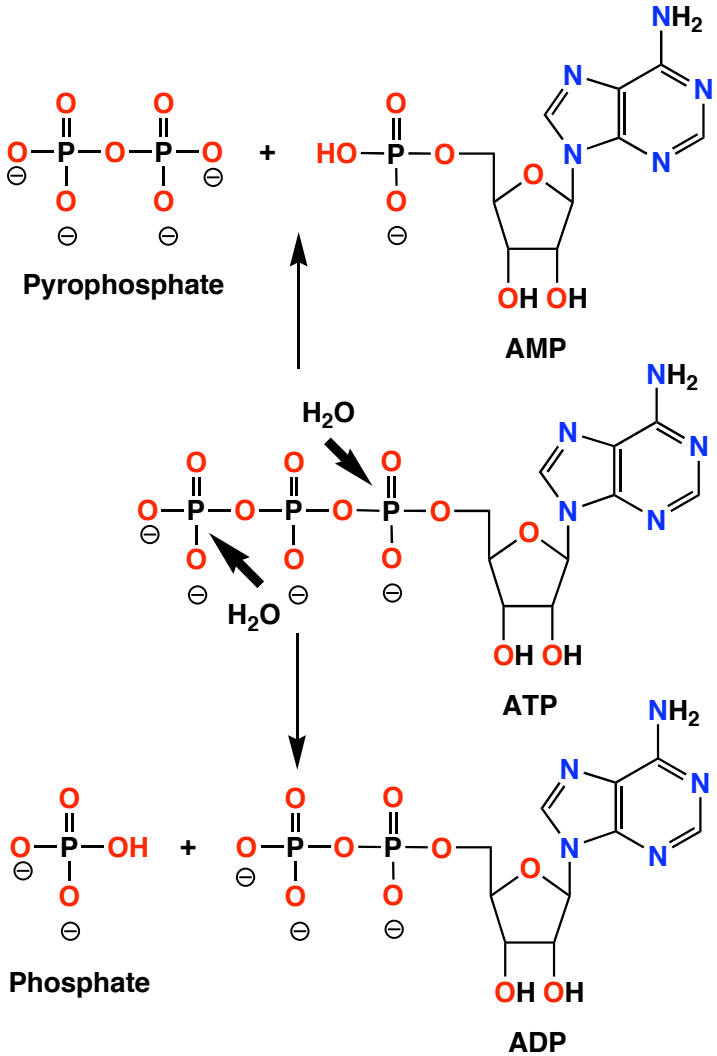
Formation de liaison

Catalyse supramoléculaire: hydrolyse assistée d'ester



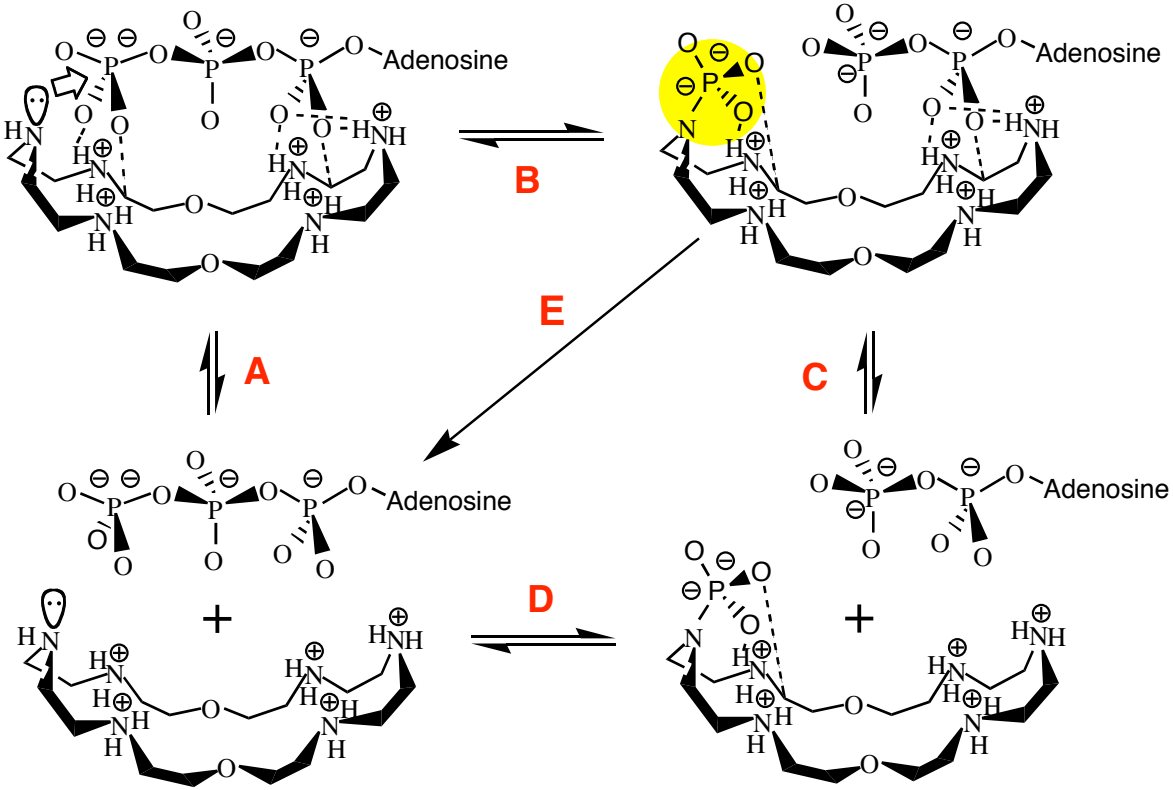
Hydrolyse non catalysée de l'ATP

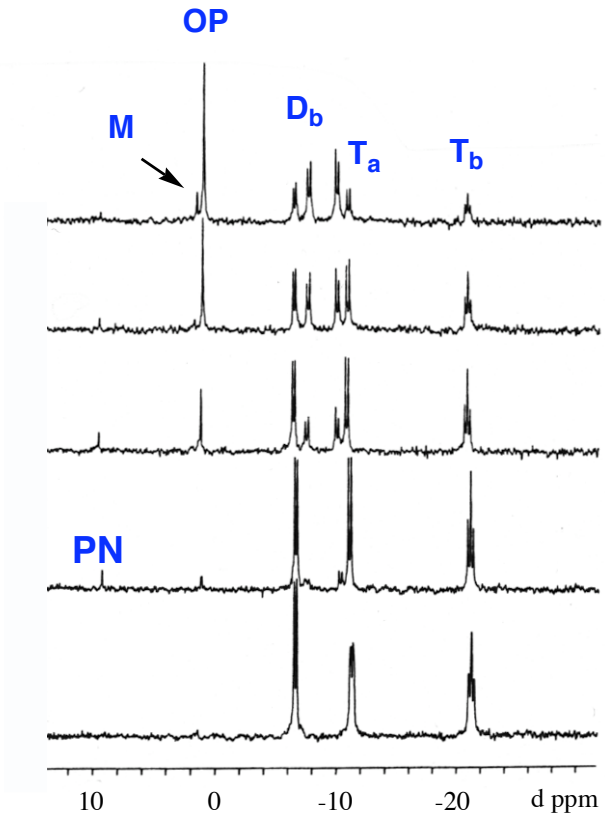




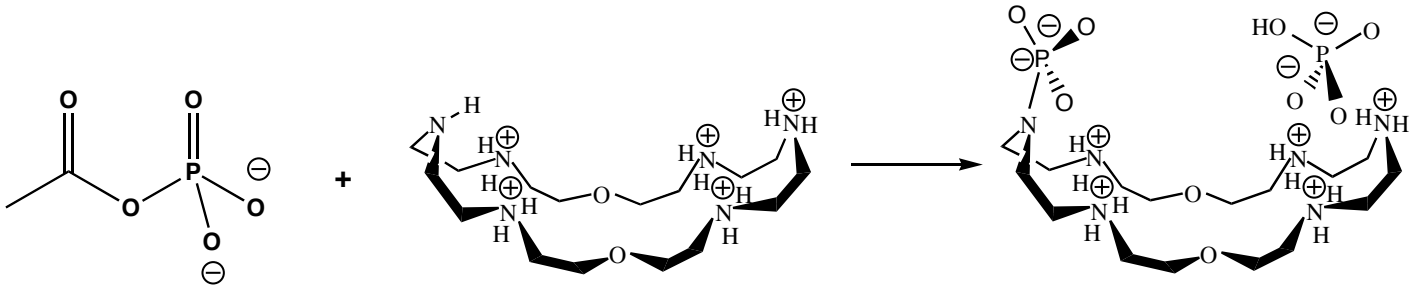
Hydrolyse			ΔG_{libre} (Kcal) pH7, 25 °C
ATP	→	AMP + PP	-10.1
ATP	→	ADP + P	-8.1
ADP	→	AMP + P	-7.7
PP	→	P + P	-6.6

Hydrolyse catalysée de l'ATP par un catalyseur supramoléculaire

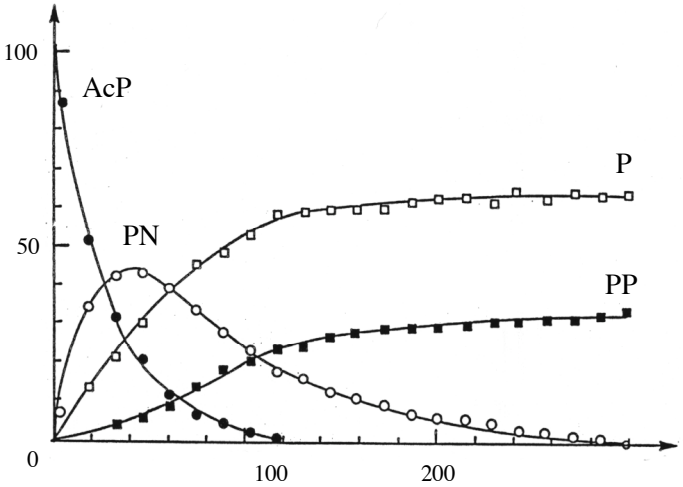


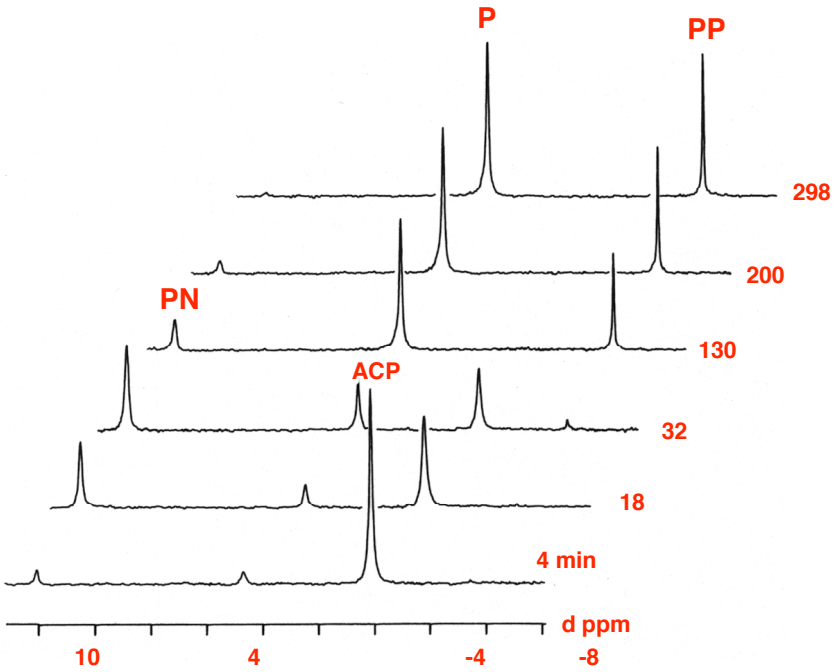


Catalyse de la réaction de formation de liaison P-O-P

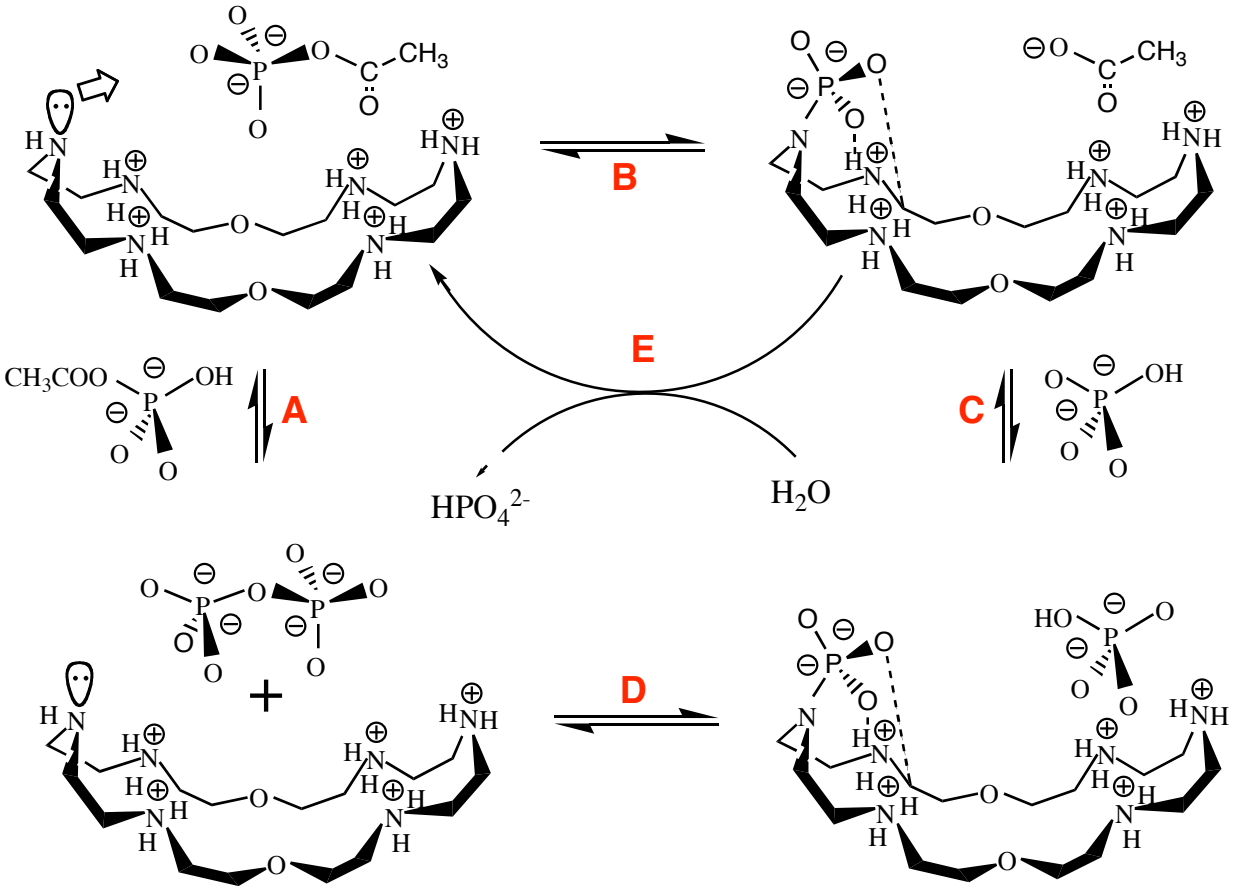


Acétylphosphate (AcP)

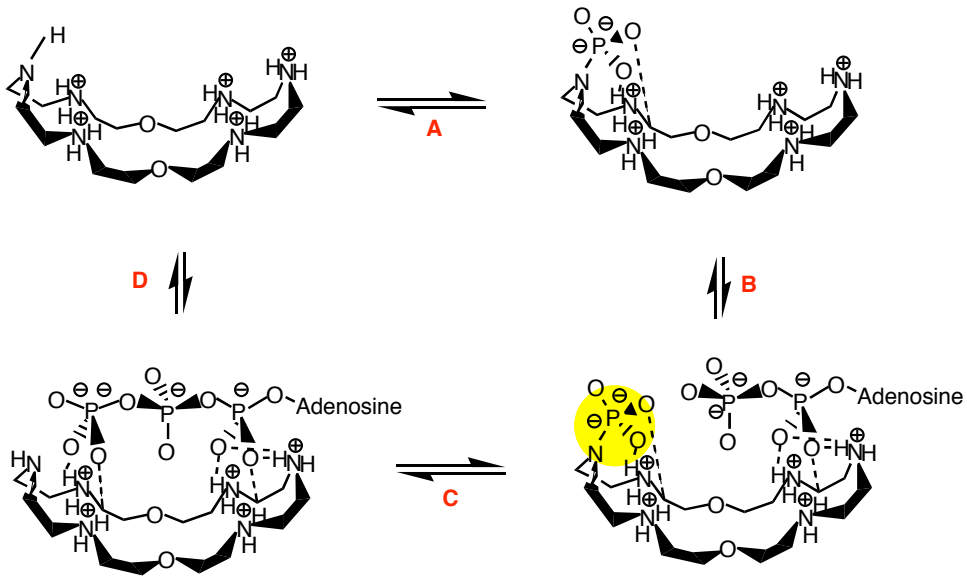


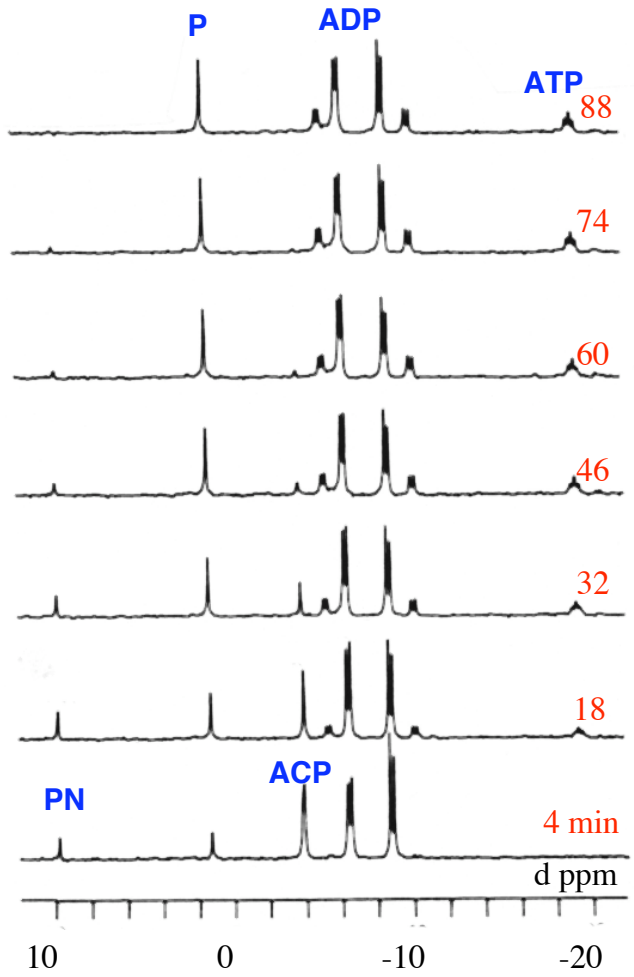


Mécanisme de la réaction de phosphorylation du phosphate

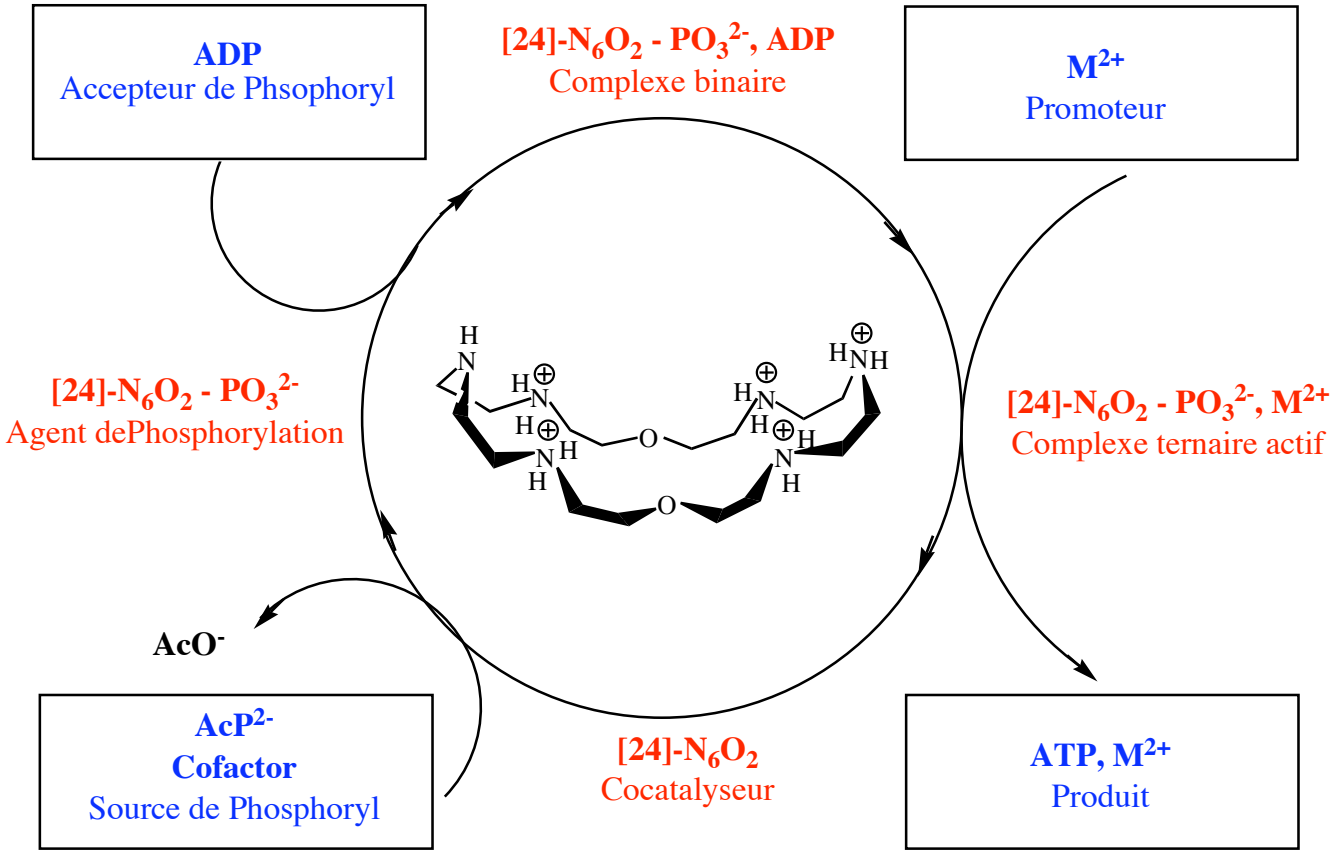


Catalyse de la synthèse d'ATP par un catalyseur supramoléculaire

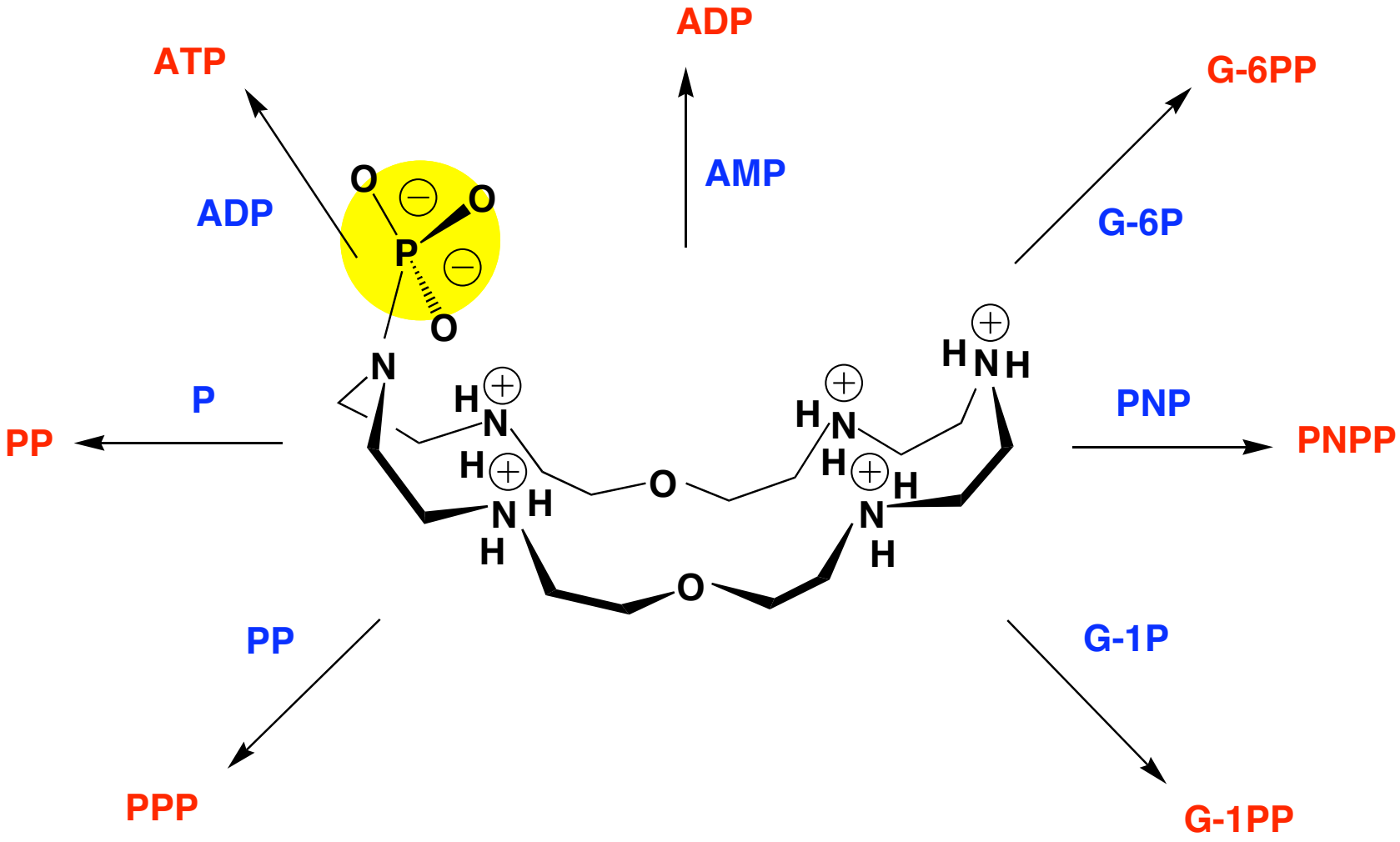




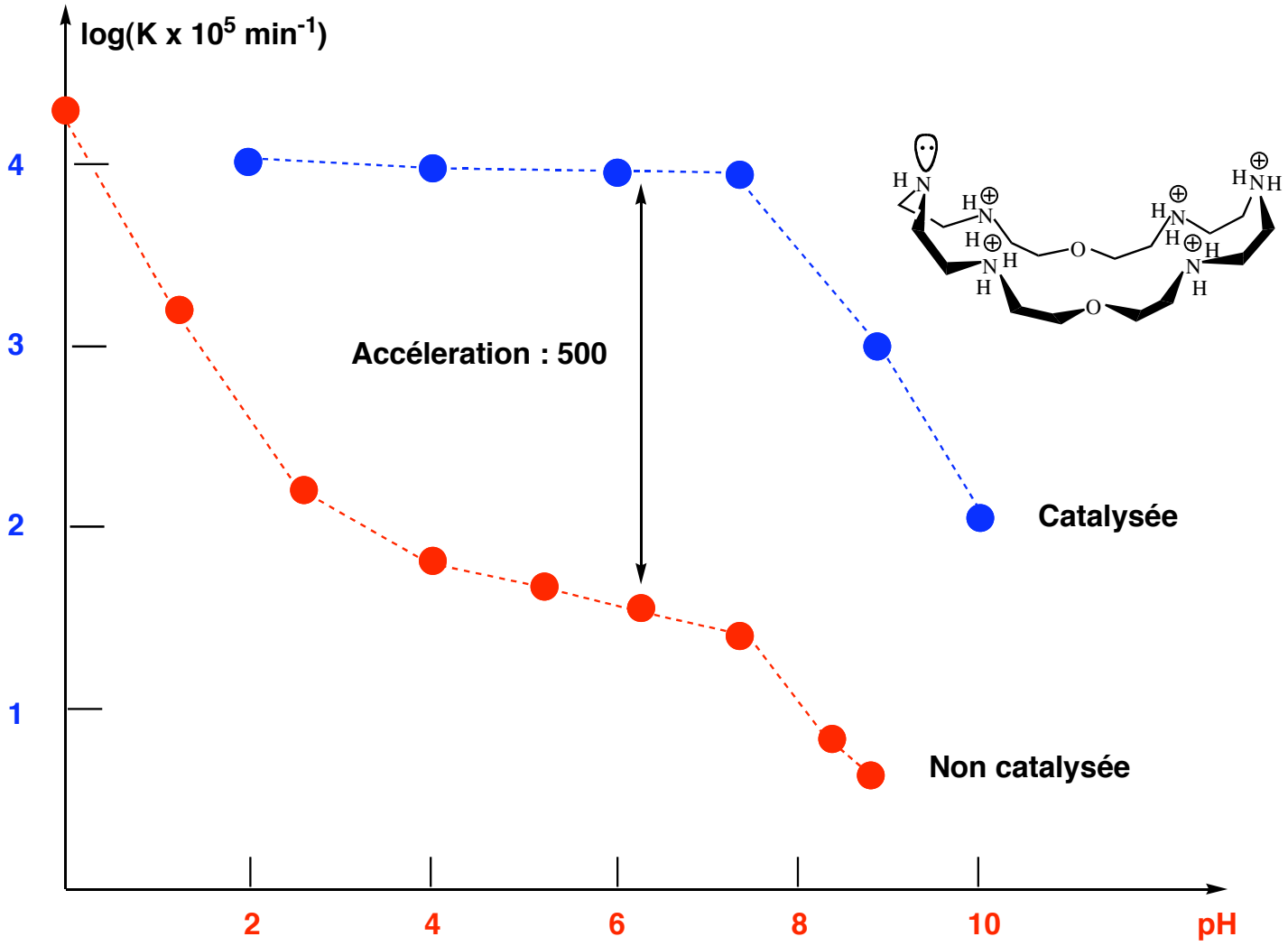
Enzyme artificielle



Vértitable agent de phosphorylation

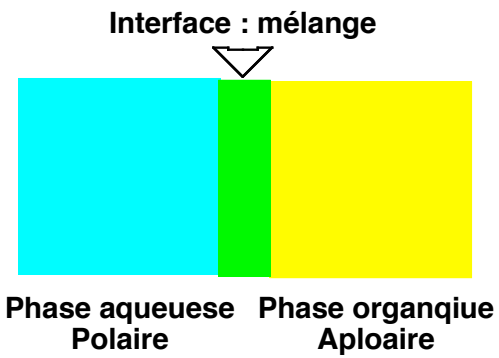


Catalyse de l'hydrolyse de l'ATP: Accélération

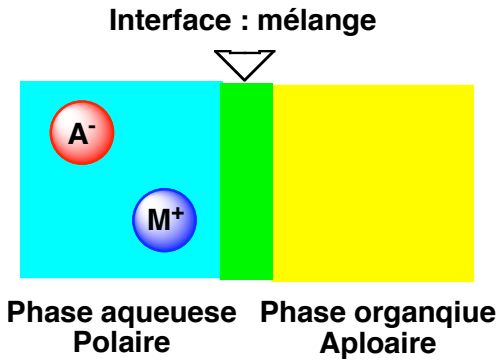


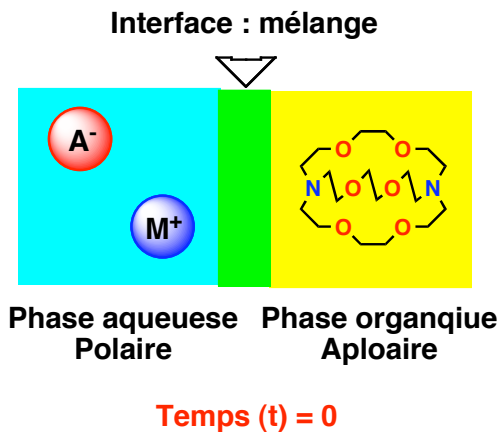
Extraction à l'aide de récepteurs moléculaires

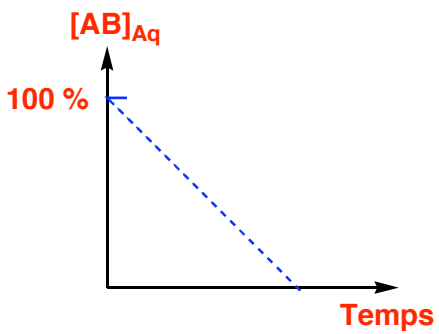
Catalyse de transfert de phase : solubiliser un sel, par définition ionique; dans un milieu apolaire

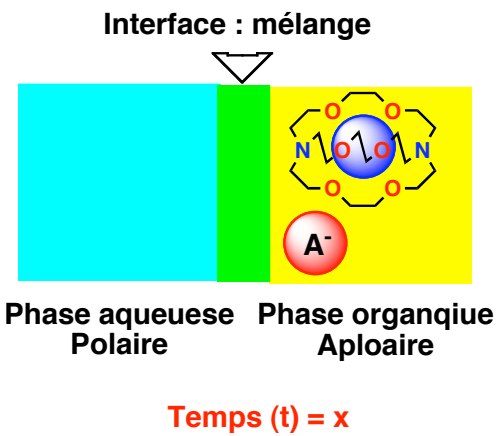


Dans un systéme biphasique (eau, organique), le sel est fortement solvaté par l'eau et sa produit de solubilité dans la phase organique est très faible. En présence d'un extractant, le sel devient soluble dans la phase organique.

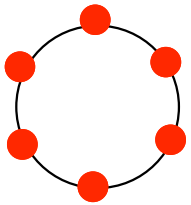








Modulation de réactivité



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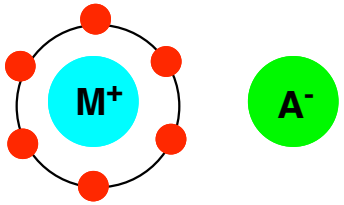
Paire d'ions intimes



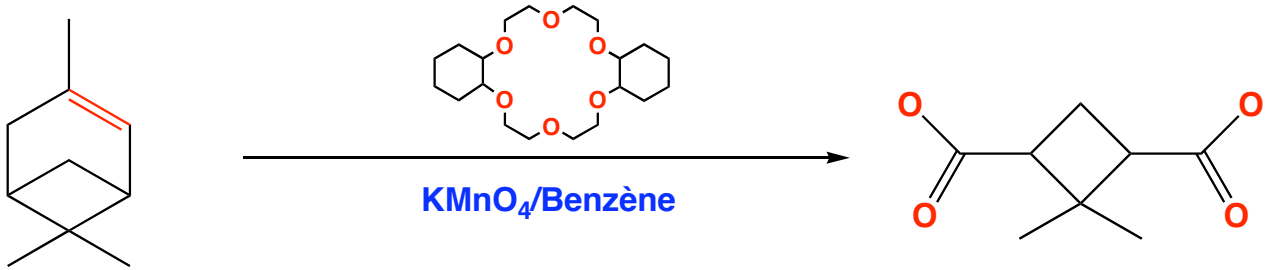
Paire d'ions séparés

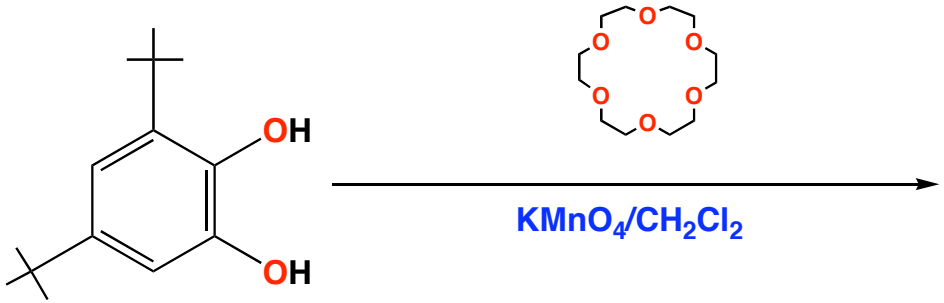
Récpeteur-extractant
soluble en milieu organique

Réactif salin insoluble
en milieu organique

Complexe soluble en milieu
organique

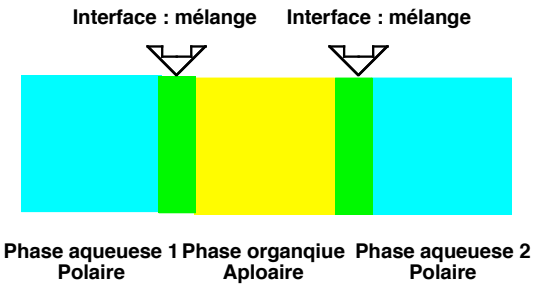
Coupure oxidante d'une double liaison



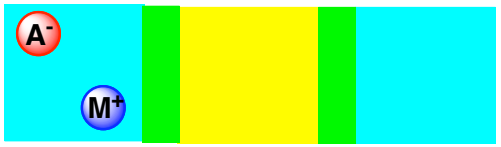


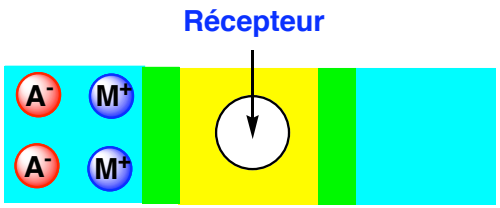
Transport à l'aide de récepteurs moléculaires

Transport passif de cation dans le sens du gradient de concentration

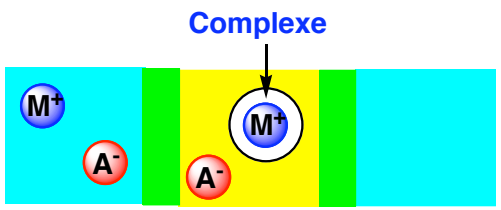


En abscence de transporteur, comme le produit de solubilité du sel en phase organique est très faible, seule la phase 1 reste chargée en sel

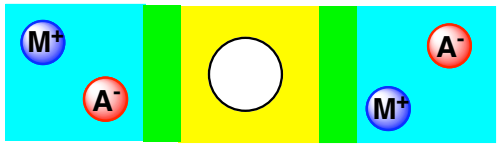




Temps (t) = 0

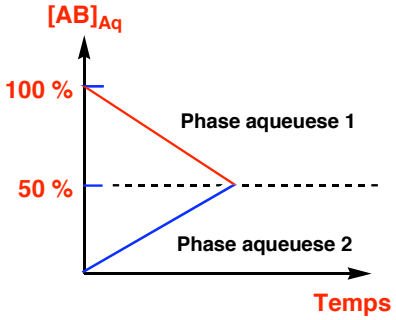


Temps (t) = intermédiaire



Temps (t) = fin

Al fin du processus de transport les concentrations du sel dans les phases aqueuses 1 et 2 sont identiques

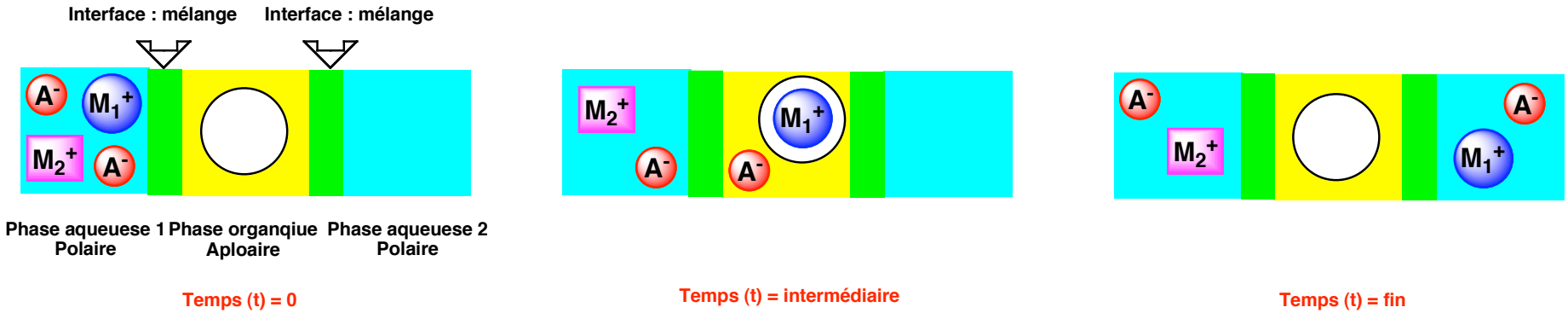


Pour que le transport soit efficace, il faut:

1) solubilité du récepteur dans la phase organique
2) une constante de stabilité non nule pour le complex
3) une constante de stabilité pas trop élevée. Une constante trop grande ne permet pas la dissociation et relargage

Transport à l'aide de récepteurs moléculaires

Transport sélectif de cation dans le sens du gradient de concentration



Récepteur (ρ) + **Substrat** M_1^+ ⇌ **Complexe ρM_1** M_1^+

Complexation / Ks_{M1}

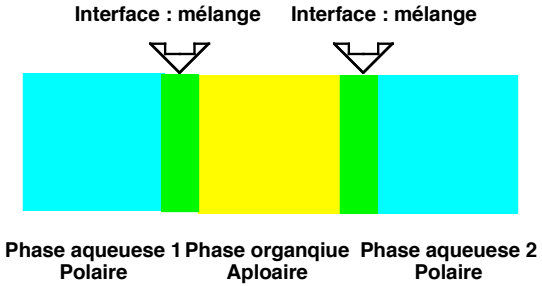
Récepteur (ρ) + **Substrat** M_2^+ ⇌ **Complexe ρM_2** M_2^+

Complexation / Ks_{M2}

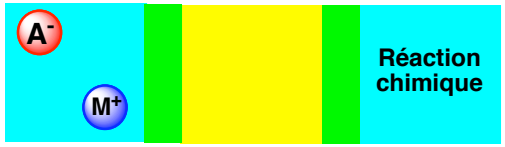
Pour un couple cation/anion, l'anion est le même, la sélectivité de transport dépend de l'affinité du récepteur pour l'un des deux cations.

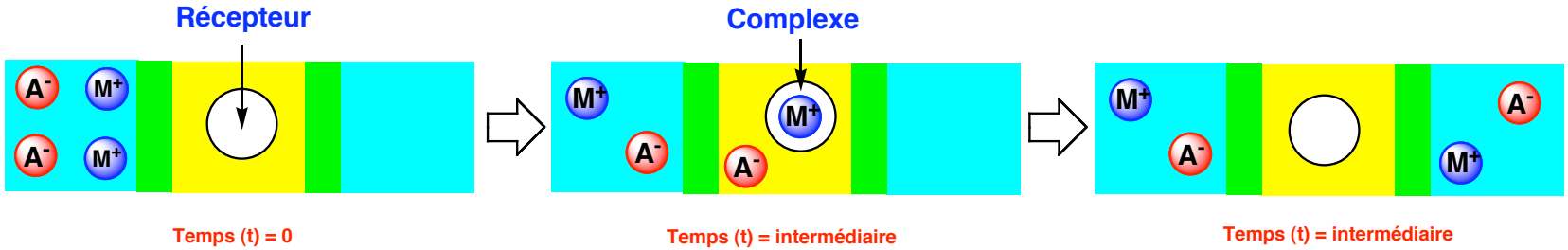
Transport à l'aide de récepteurs moléculaires

Transport actif de cation dans le sens du gradient de concentration

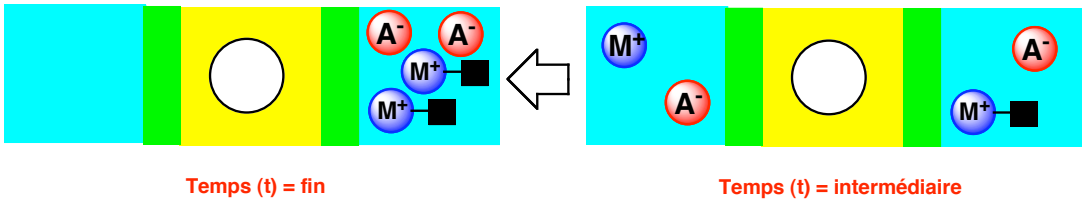


En abscence de transporteur, comme le produit de solubilité du sel en phase organique est très faible, seule la phase 1 reste chargée en sel. En présence du transporteur, le sel passe de la phase 1 à la phase 2.

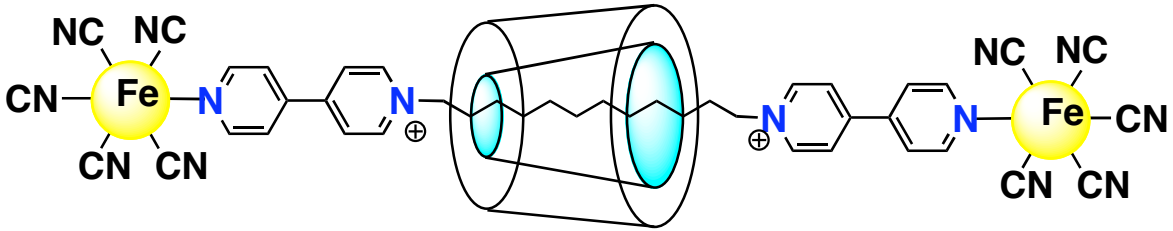




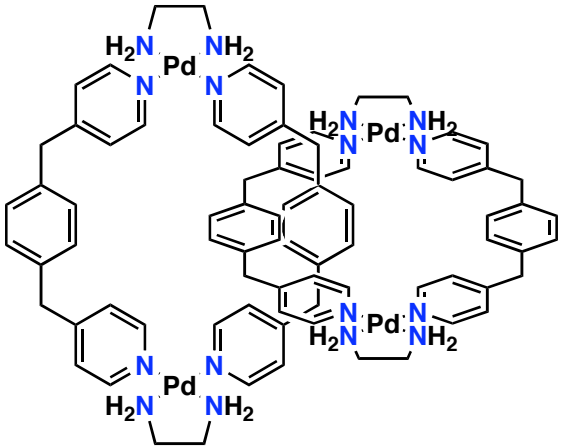
Le transport est dit actif car le chemin retour est bloqué par une réaction chimique qui transforme le cation. Il ne peut plus être complexé par le transporteur. Ainsi, le sel passe intégralement de la phase 1 à la phse 2.

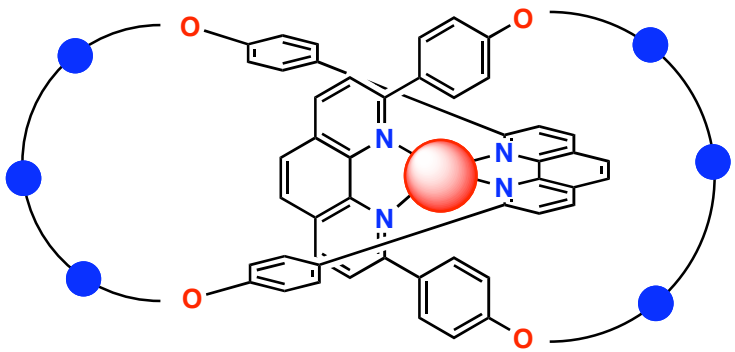


Al fin du processus de transport les concentrations du sel dans les phases aqueuses 1 est nulle



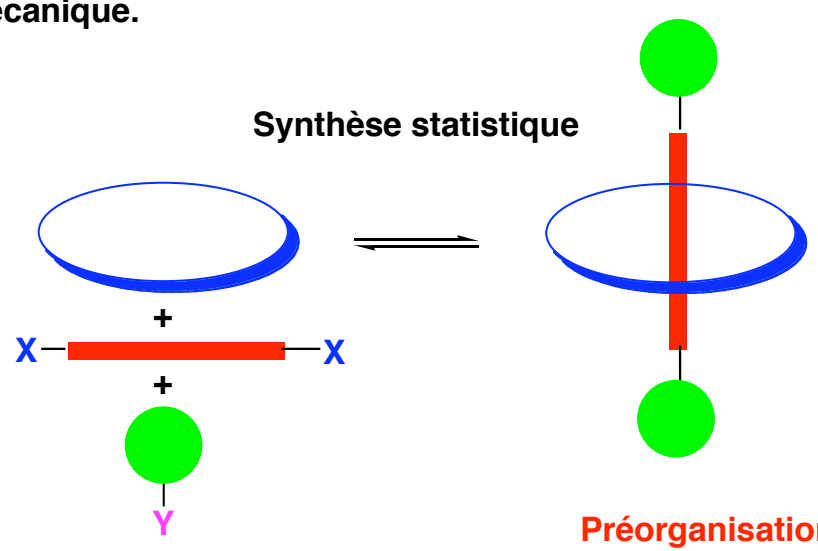
Les rotaxanes et caténanes



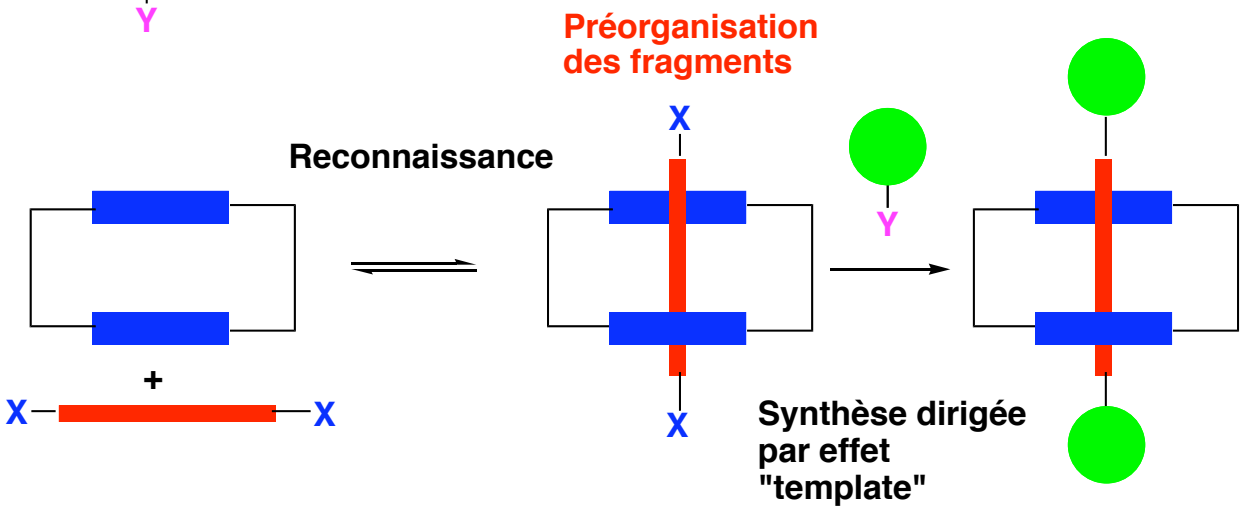


Rotaxanes

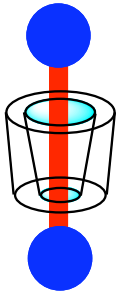
Un rotaxane est un ensemble de deux parties sans lien chimique mais maintenues ensembles par un lien mécanique.

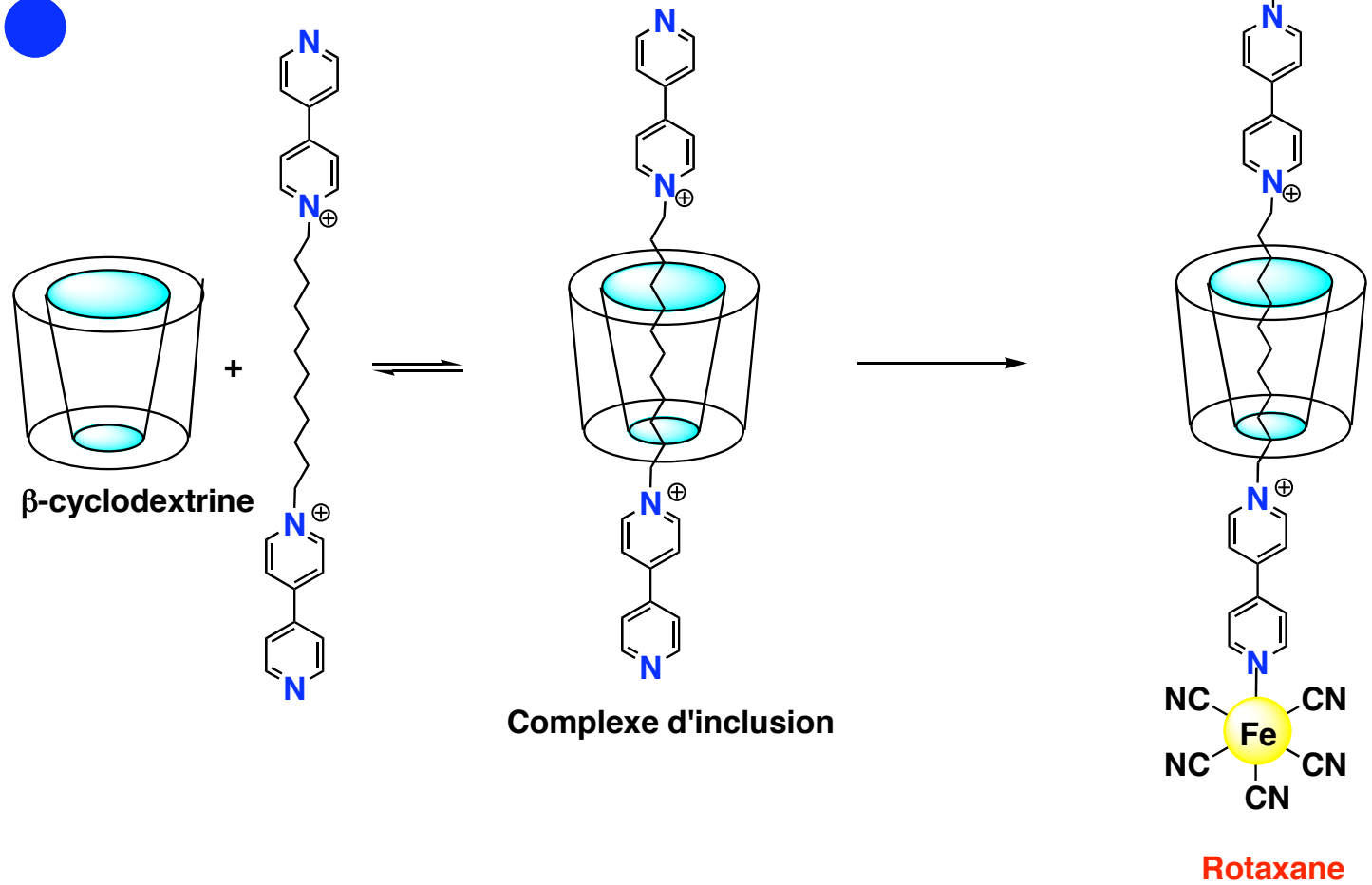


X et Y fonctions réactives complémentaire

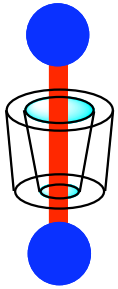


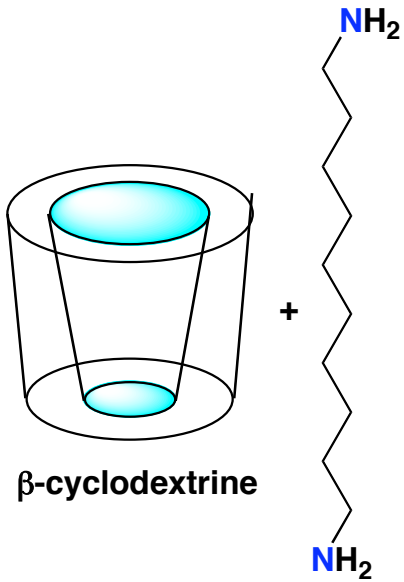
Les Rotaxane





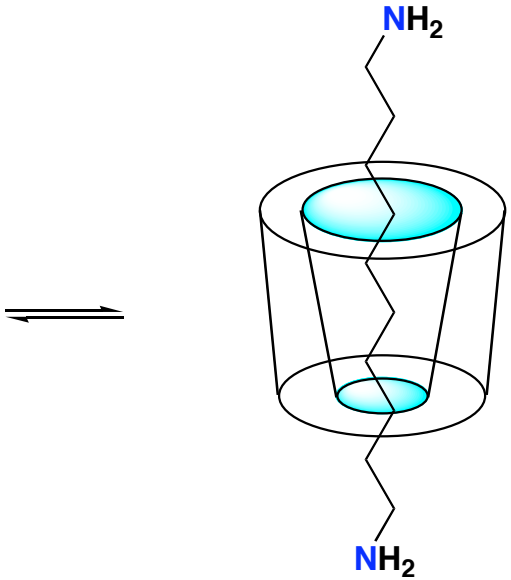
Les Rotaxane



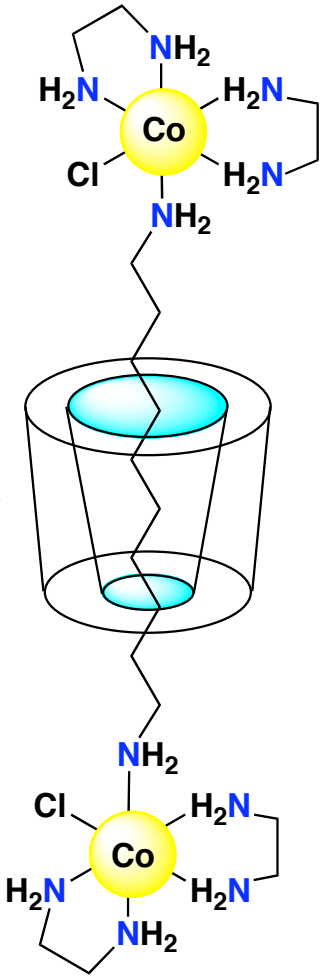


β-cyclodextrine

1,12-diaminododécane



Complexe d'inclusion

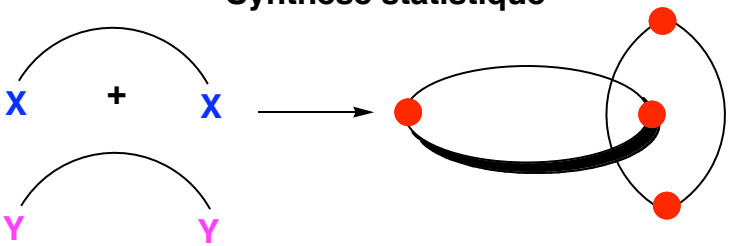


Rotaxane

Caténands

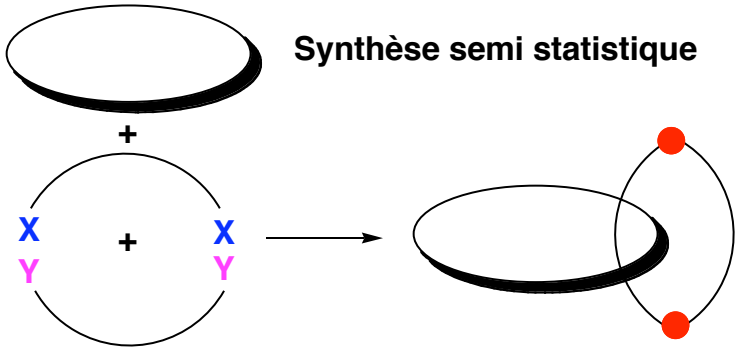
Un caténand est une architecture composée d'au moins deux anneaux entrelacés. Le seul lien maintenant les deux ensembles est un lien physique et non chimique. On qualifie ceci de lien mécanique

Synthèse statistique

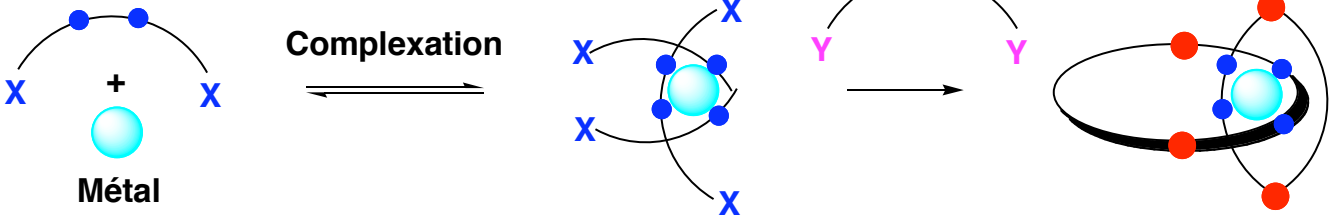


X et Y fonctions réactives complémentaire

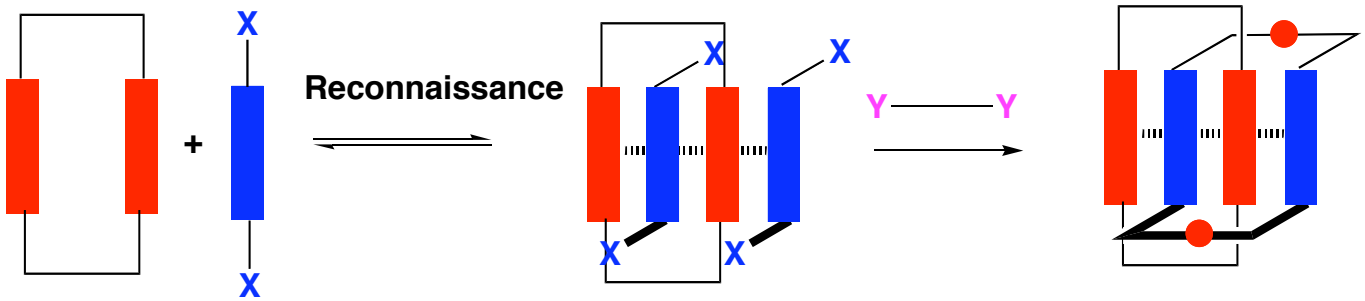
Synthèse semi statistique



Synthèse dirigée par effet "template"

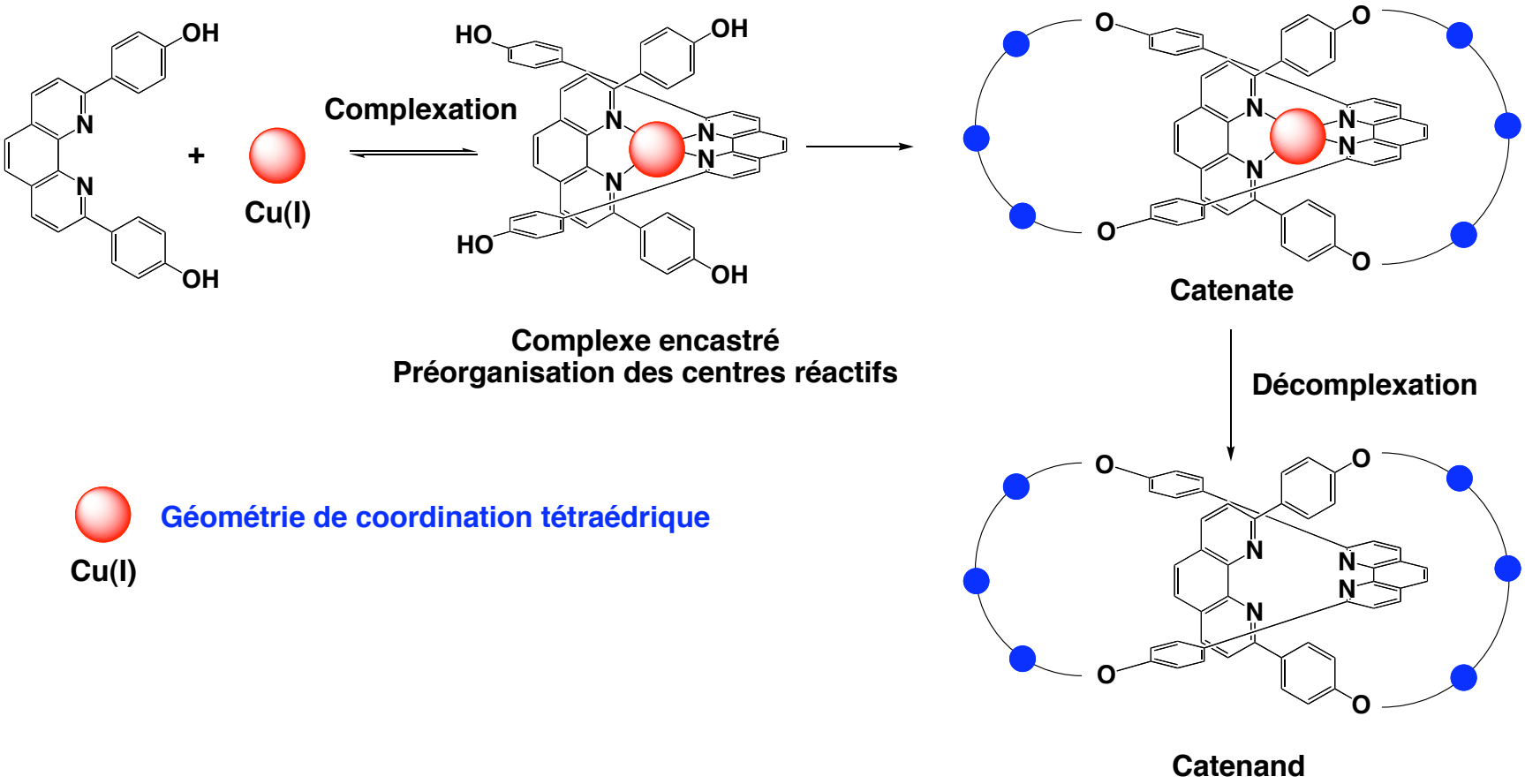


Préorganisation des fragments



Synthèse de catenands par effet "Template"

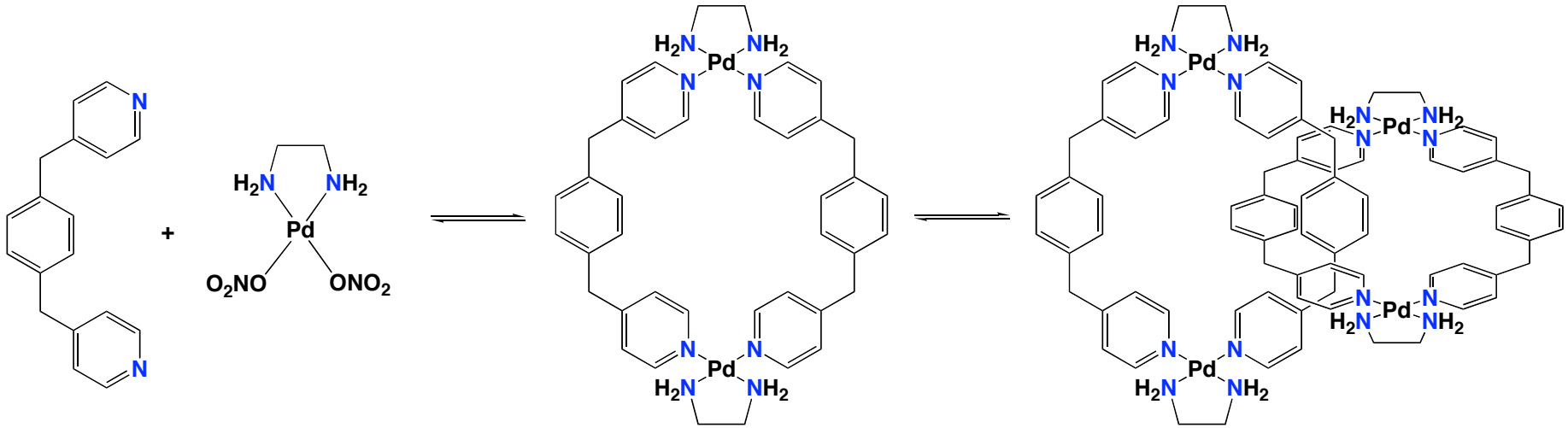
Création de liens mécaniques (des anneaux entrelacés)



Cu(I)

Géométrie de coordination tétraédrique

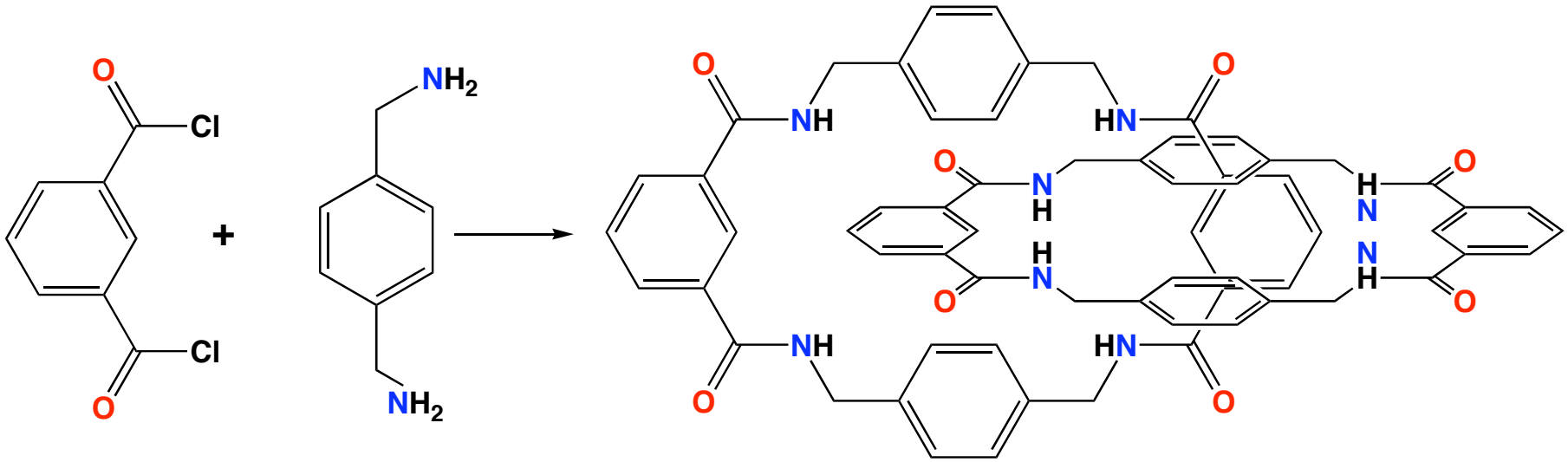
Catenand

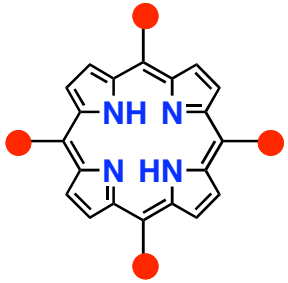


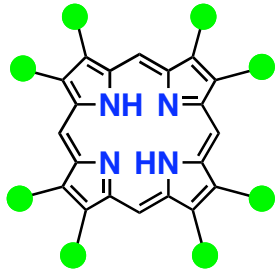
Métallamacrocycle

Catenand

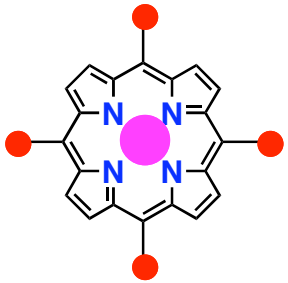
Caténand purement organique

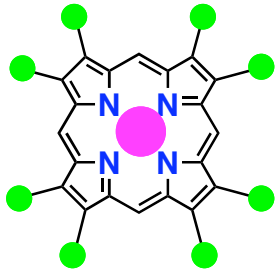




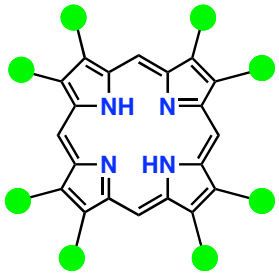


Les Porphyrines

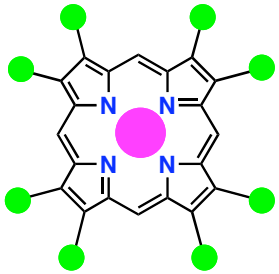




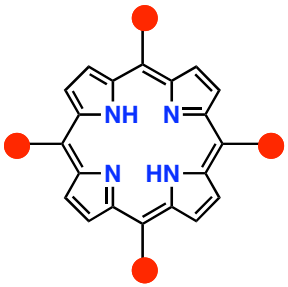
Porphyrine



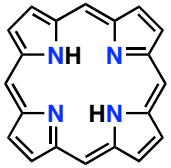
β-Pyrr-substitution



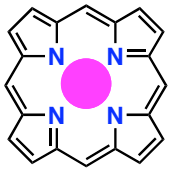
β-Pyrr-substitution



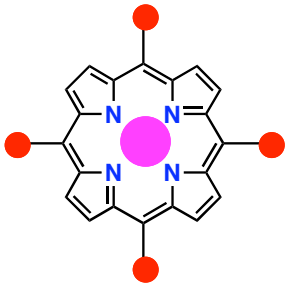
Meso-substitution



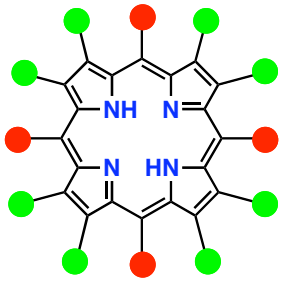
Porphyrine



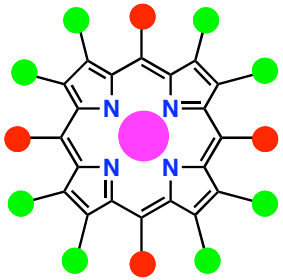
Métallaporphyrine



Meso-substitution

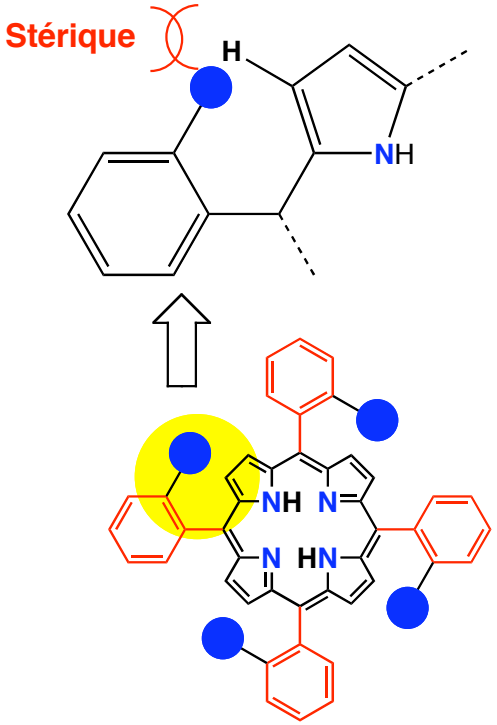


Meso et *β-Pyrr*-substitution

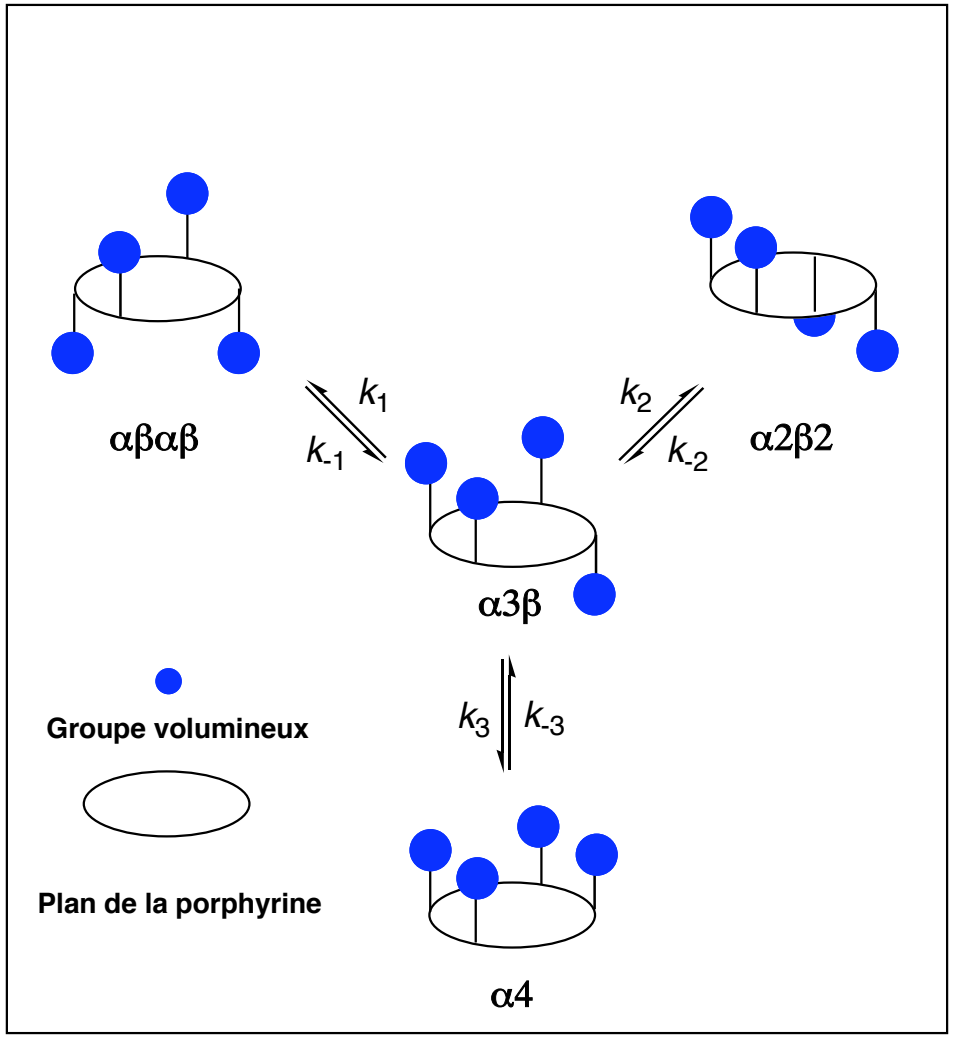


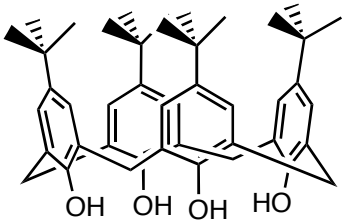
Meso et *β-Pyrr*-substitution

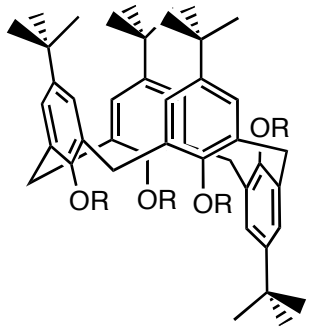
Atropoisomérie



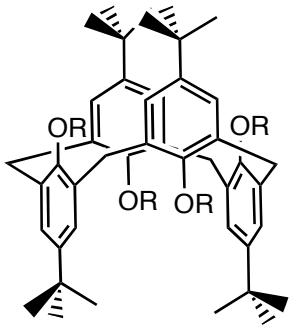
Tétra(o-Xphényl)porphyrine

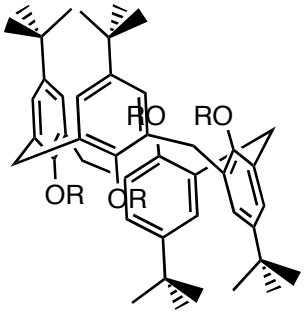




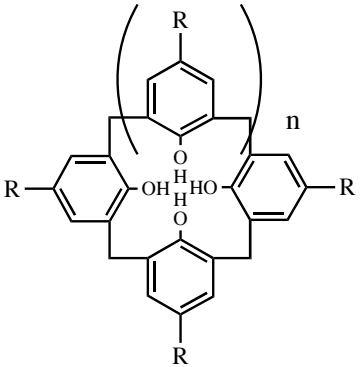


Les Calixarènes

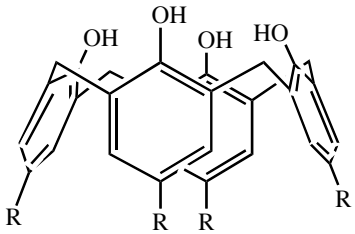




CALIXARENES



calixarene : n = 1 to 4



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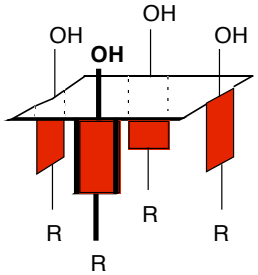
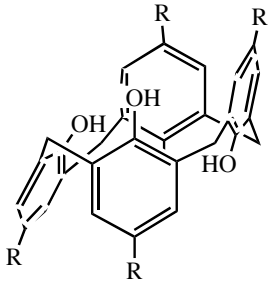
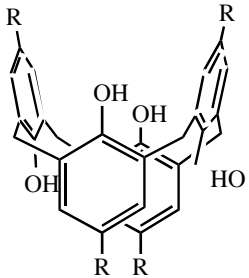
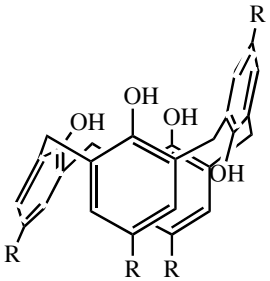




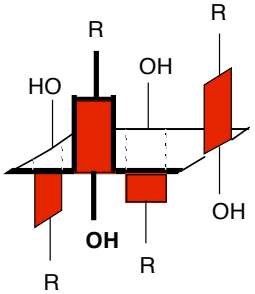
1-2 alternate

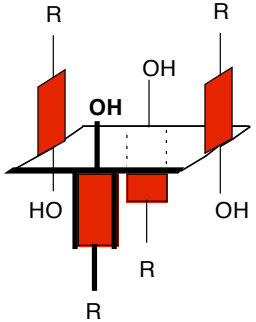


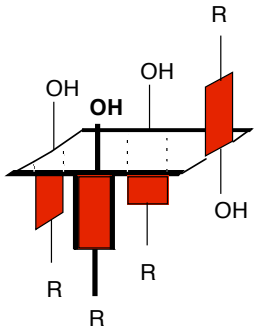
1-3 alternate

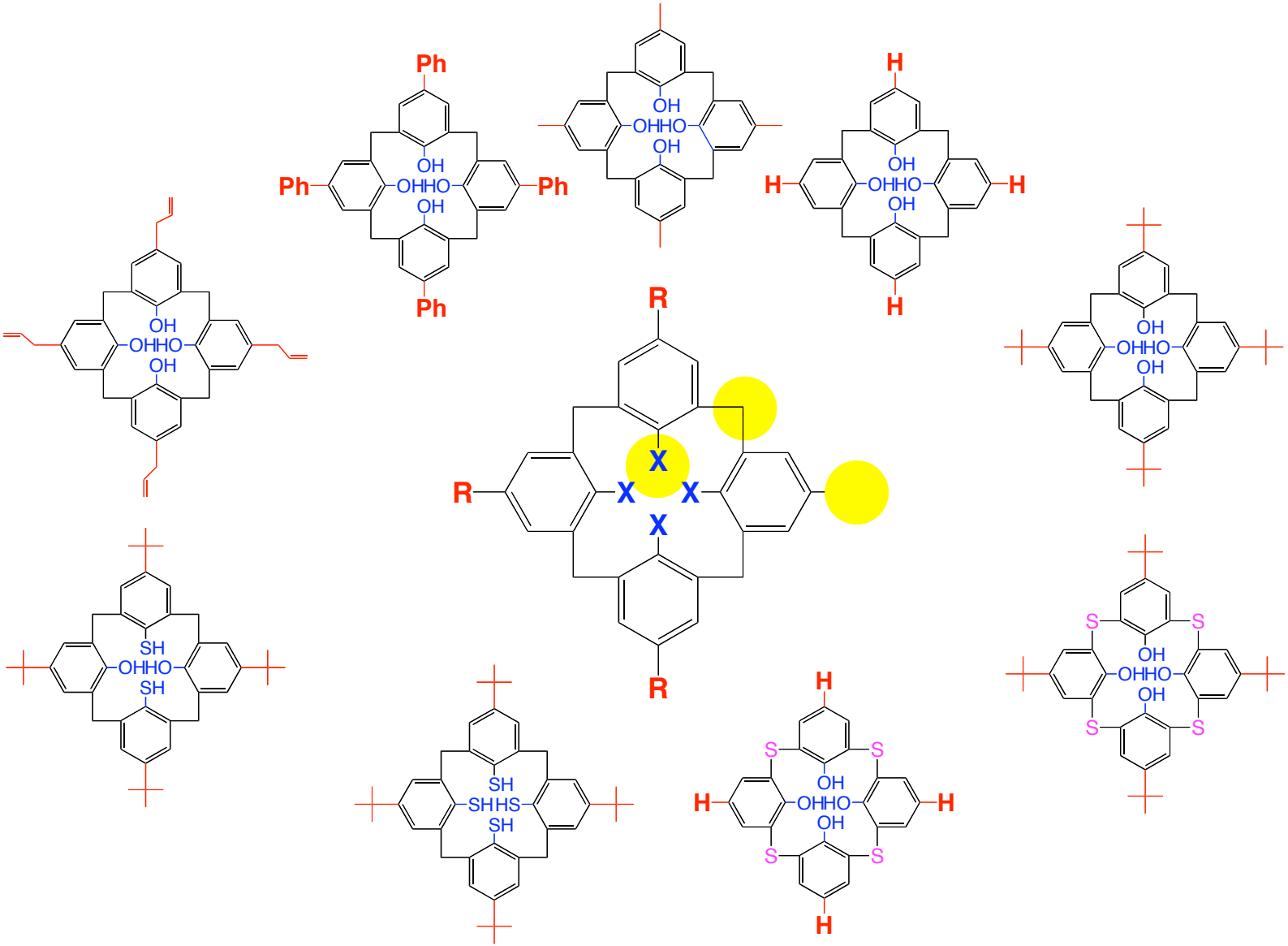


partial cone





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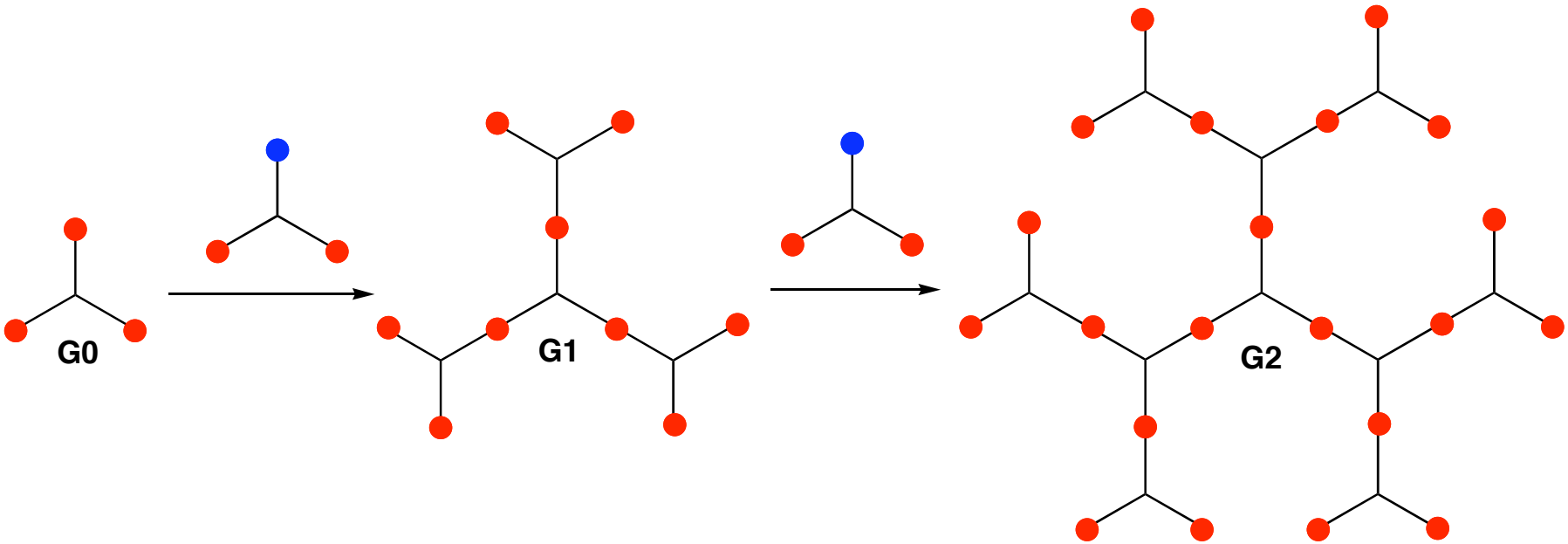
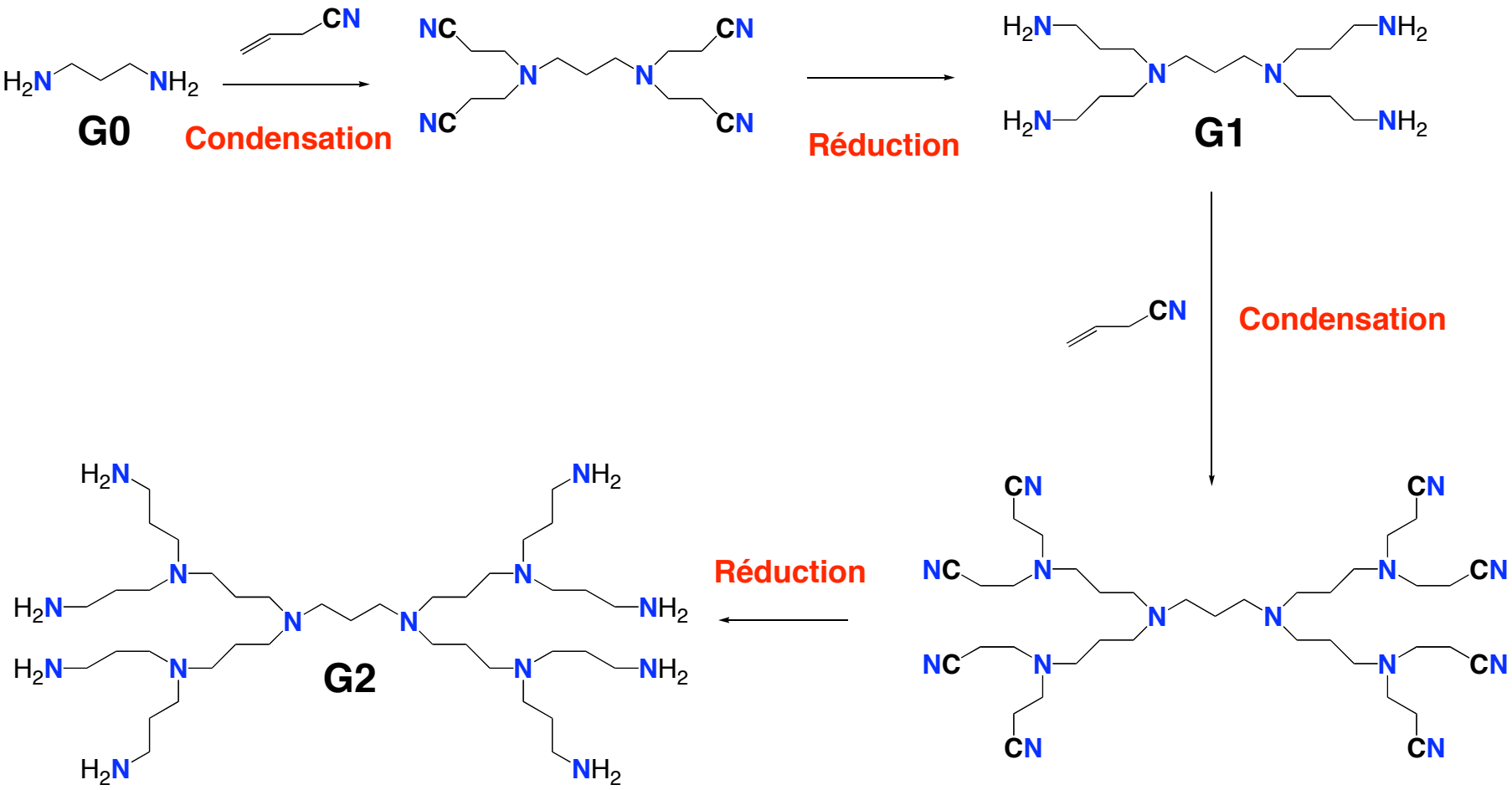
Les dendrimères



Un dendrimère aminé