Coordination Chemistry and Reactivity of f Elements

Cours 2 Electronic spectroscopy and magnetism of 4f elements. MRI contrast agents

Marinella Mazzanti
Coordination Chemistry Group

Learning Outcomes

-Use Hunds rules to calculate the lanthanide ground state

-Calculate the magnetic moment of lanthanide ions

-Understand why spin-only formula is not adequate

-Explain why excitation (electronic) spectra are not dependent on ligand environment

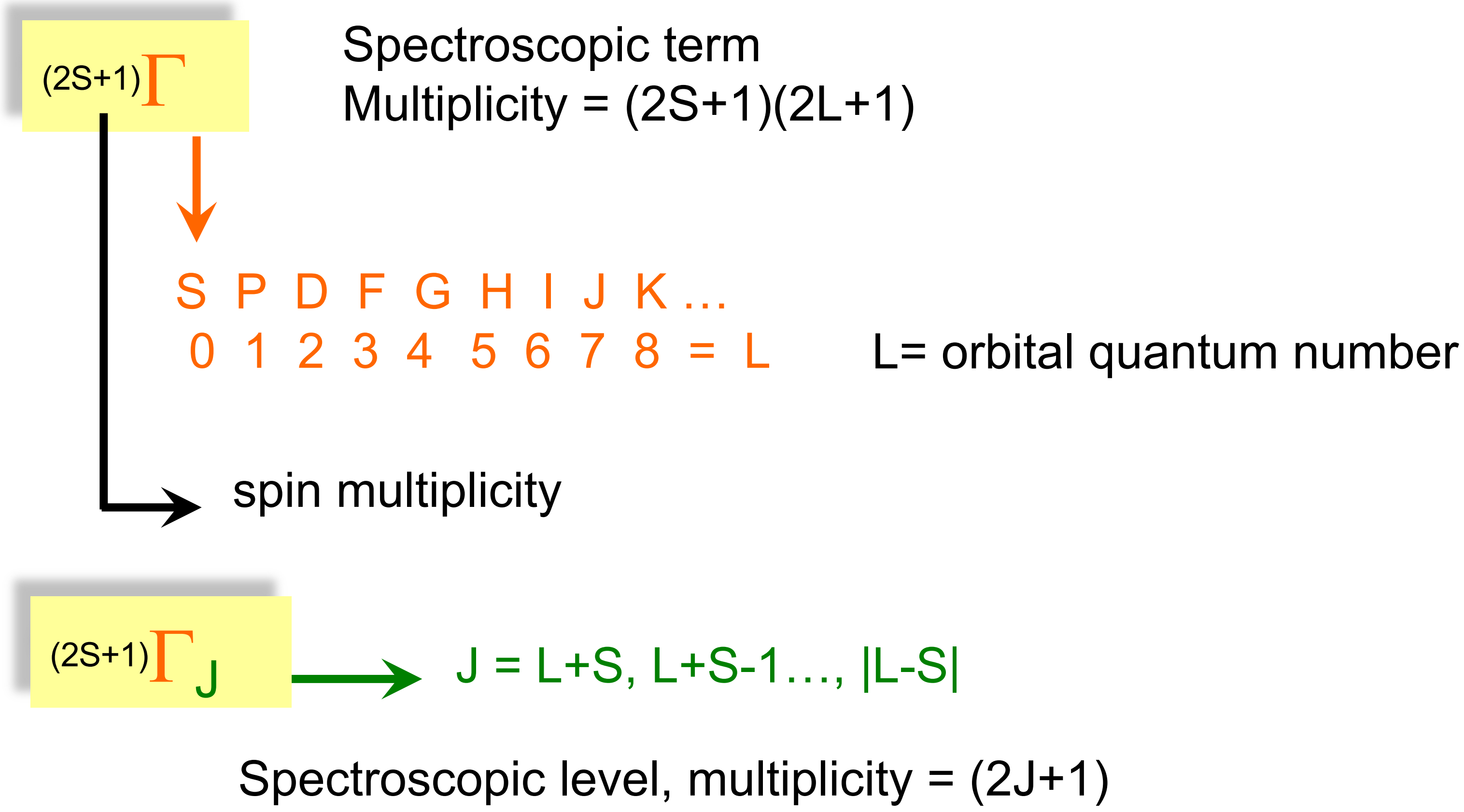
-Explain the use of lanthanides as MRI agent and NMR Shift Reagents

-Know the properties needed for use of Gd complexes as MRI contrast agents

Electronic levels

2.1.1 Electronic structure of 4f elements

Russel-Saunders coupling usually works well



$^{(2S+1)}\Gamma$

Spectroscopic term
Multiplicity = (2S+1)(2L+1)

S P D F G H I J K …
0 1 2 3 4 5 6 7 8 = L

L= orbital quantum number

spin multiplicity

$^{(2S+1)}\Gamma_J$

J = L+S, L+S-1…, |L-S|

Spectroscopic level, multiplicity = (2J+1)

Electronic levels

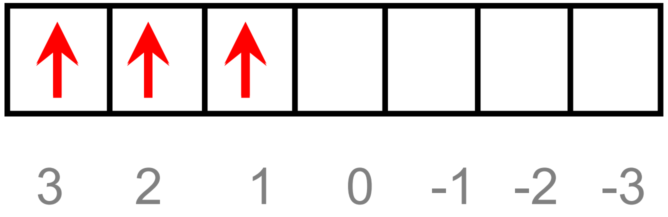
Hund's rules for ground state:

- Spin multiplicity must be the highest possible (S_{max})
- If more than one term have the highest multiplicity, the term with the highest value of L is the ground state (L_{max})
- The ground level has J_{min} if the subshell is less than half filled, J_{max} if the subshell is more than half filled

S_{max} = 3´½ = 3/2

L_{max} = 6   J = 15/2……9/2

Example: Nd^{3+}, $4f^3$



m_ℓ (ℓ = 3)

J = L+S, L+S-1…, |L-S|

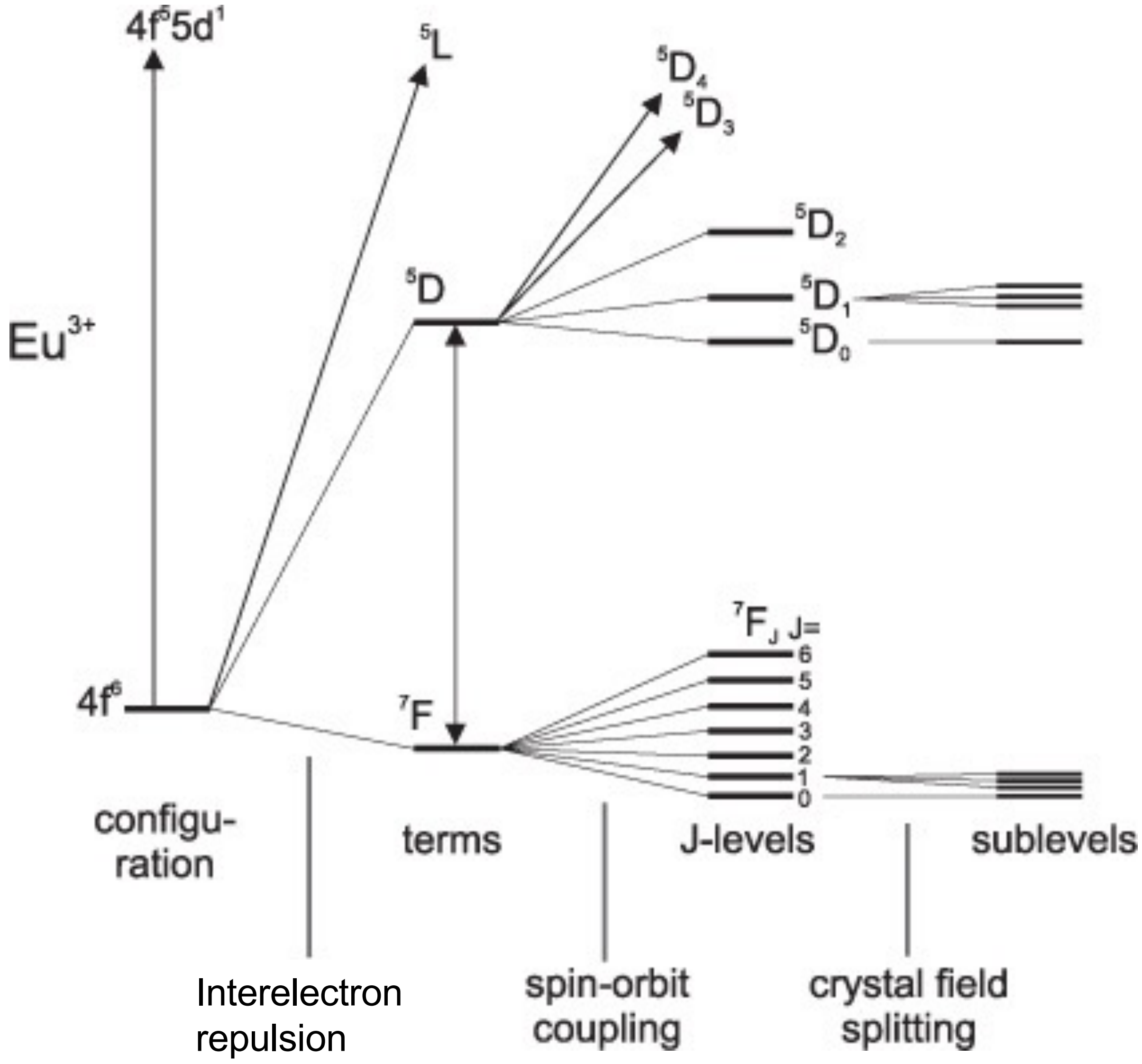
$^{(2S+1)}\Gamma_J$

$^4I_{9/2}$

Electronic levels in lanthanides

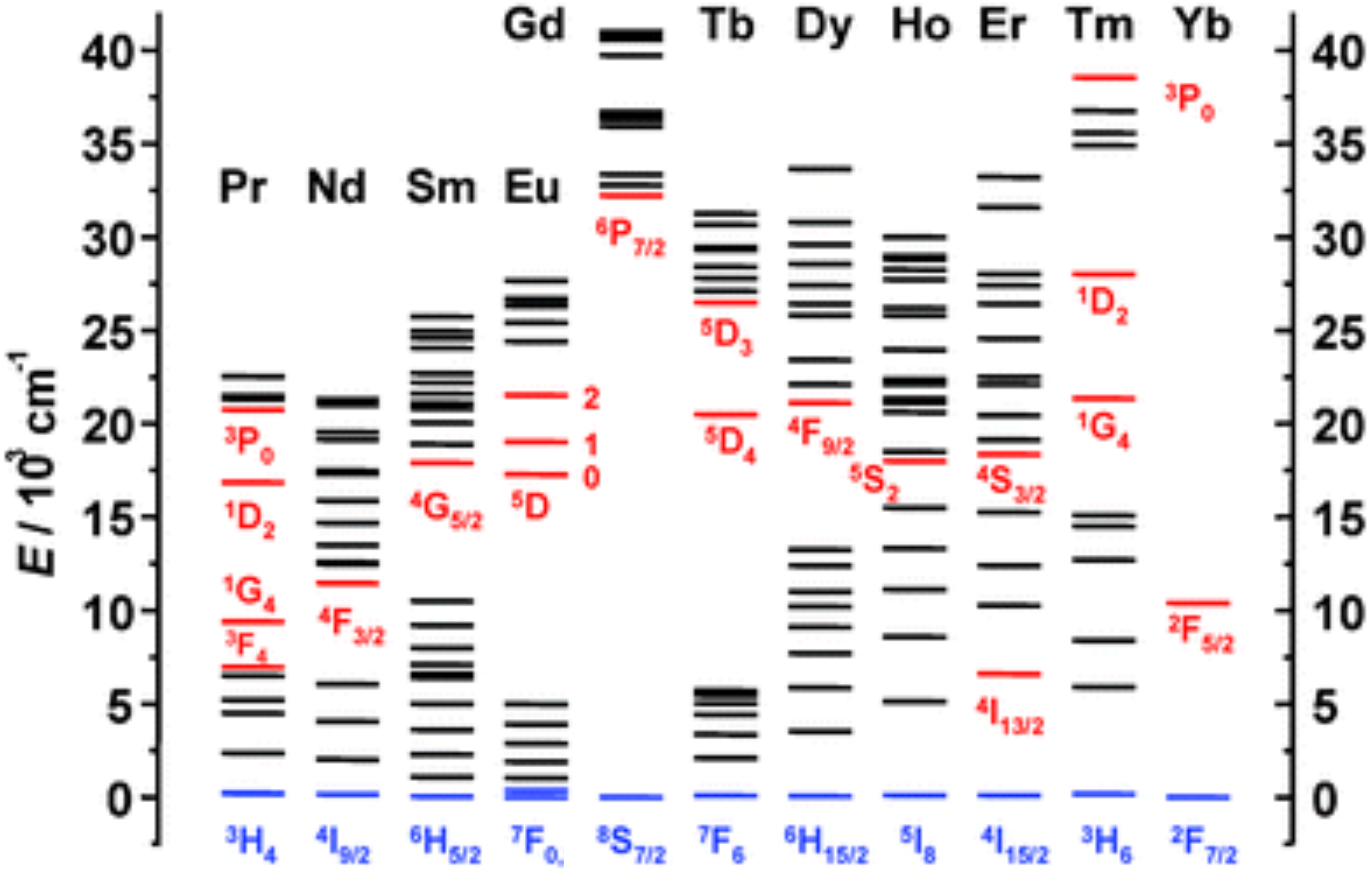
Ligand field effects in lanthanides

They are very weak, a few hundreds cm^{-1} as compared to a few thousands for spin-orbit coupling, and 10^{4} cm^{-1} for electron repulsion.



Electronic levels

Some electronic levels…



Partial energy diagrams for the lanthanide aquo ions.
The main luminescent levels are drawn in red, while the fundamental level is indicated in blue.

Chem. Soc. Rev., 2005, 34, 1048–1077

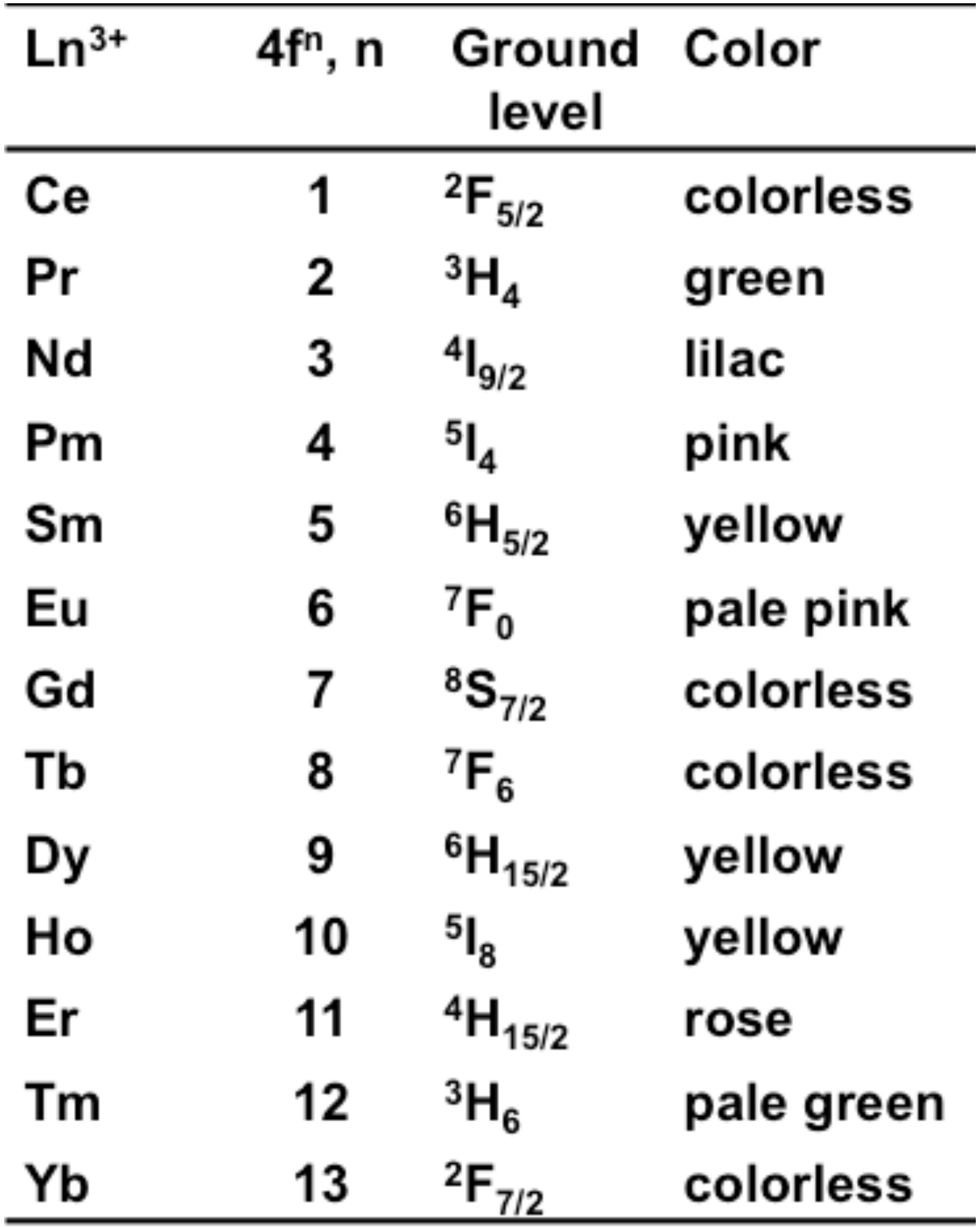
Electronic absorption spectra of Ln(III) Ions

f-f transitions

- Narrow bands
- Low absorption coefficient (forbidden transitions by Laporte and selection rules)

- Bary-centers of LF (ligand field) sublevels are not much dependent on the nature of the Ln^{III} environment therefore energy of the transitions is more or less constant

Electronic levels



Ln^{3+}	$4f^n$, n	Ground level	Color
Ce	1	$^2F_{5/2}$	colorless
Pr	2	$^3H_4$	green
Nd	3	$^4I_{9/2}$	lilac
Pm	4	$^5I_4$	pink
Sm	5	$^6H_{5/2}$	yellow
Eu	6	$^7F_0$	pale pink
Gd	7	$^8S_{7/2}$	colorless
Tb	8	$^7F_6$	colorless
Dy	9	$^6H_{15/2}$	yellow
Ho	10	$^5I_8$	yellow
Er	11	$^4H_{15/2}$	rose
Tm	12	$^3H_6$	pale green
Yb	13	$^2F_{7/2}$	colorless

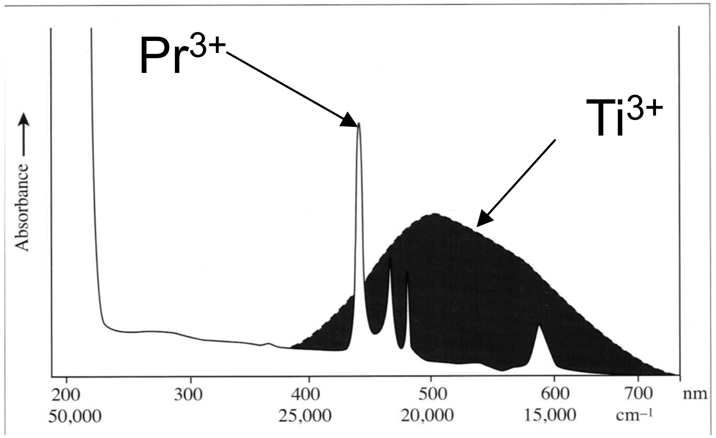
Transitions f-f

- Spectra of complexes ≈ spectra of free ions, not affected by geometry

- Narrow Bands

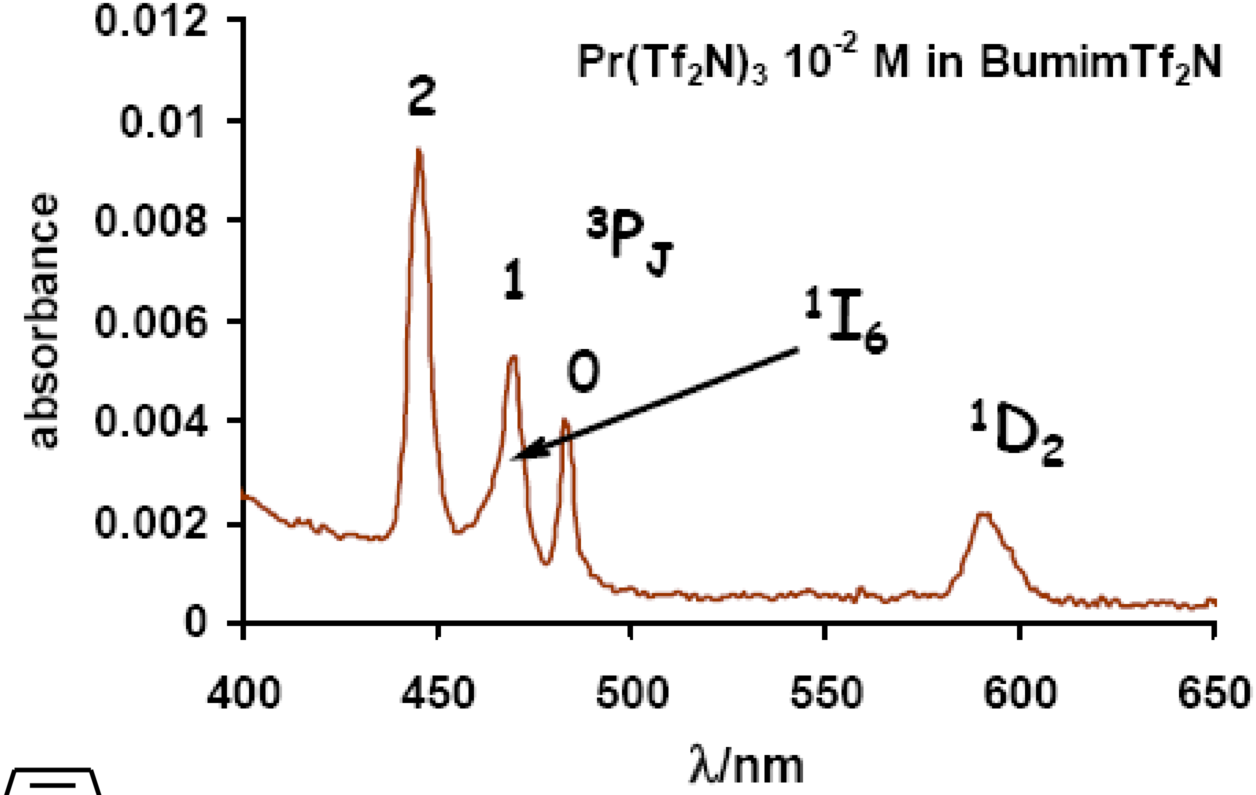
- Forbidden transitions by Laporte selection rules ($\Delta l : \pm 1$) $\varepsilon < 10\ M^{-1}cm^{-1}$ colours less intense than d metal complexes

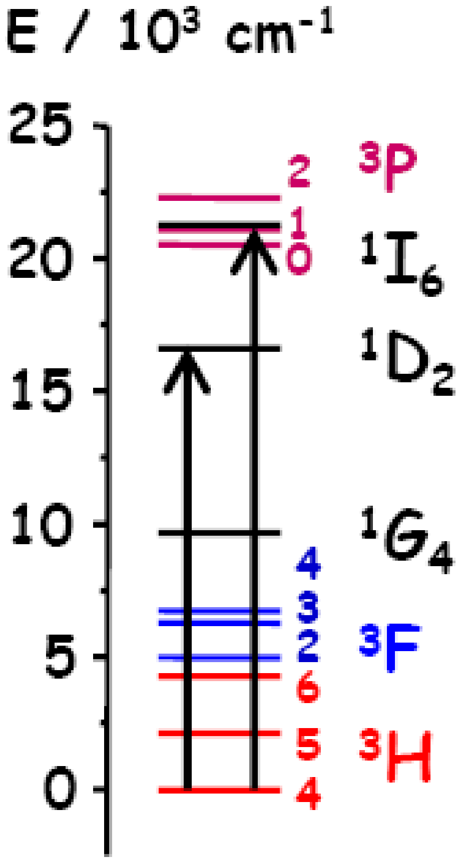
d-d transitions ~ 100 $M^{-1}cm^{-1}$ (rules relaxed by vibronic coupling) and π-π ~ $10^5 M^{-1}cm^{-1}$
Pale colour of lanthanide(III) complexes
Relaxation of the Laporte selection rule occurs by spin-orbit coupling (l and s)



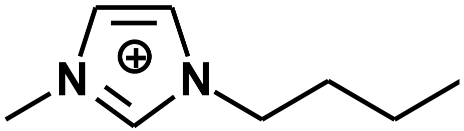
Electronic spetrum of Pr^{3+} (f^2) (narrow line)
Electronic spetrum of $Ti(H_2O)^{3+}$ (d^1) (broad line)

Transitions f-f

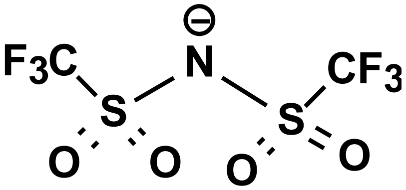




Pr^{III} $4f^{2}$, $^{3}H_{4}$



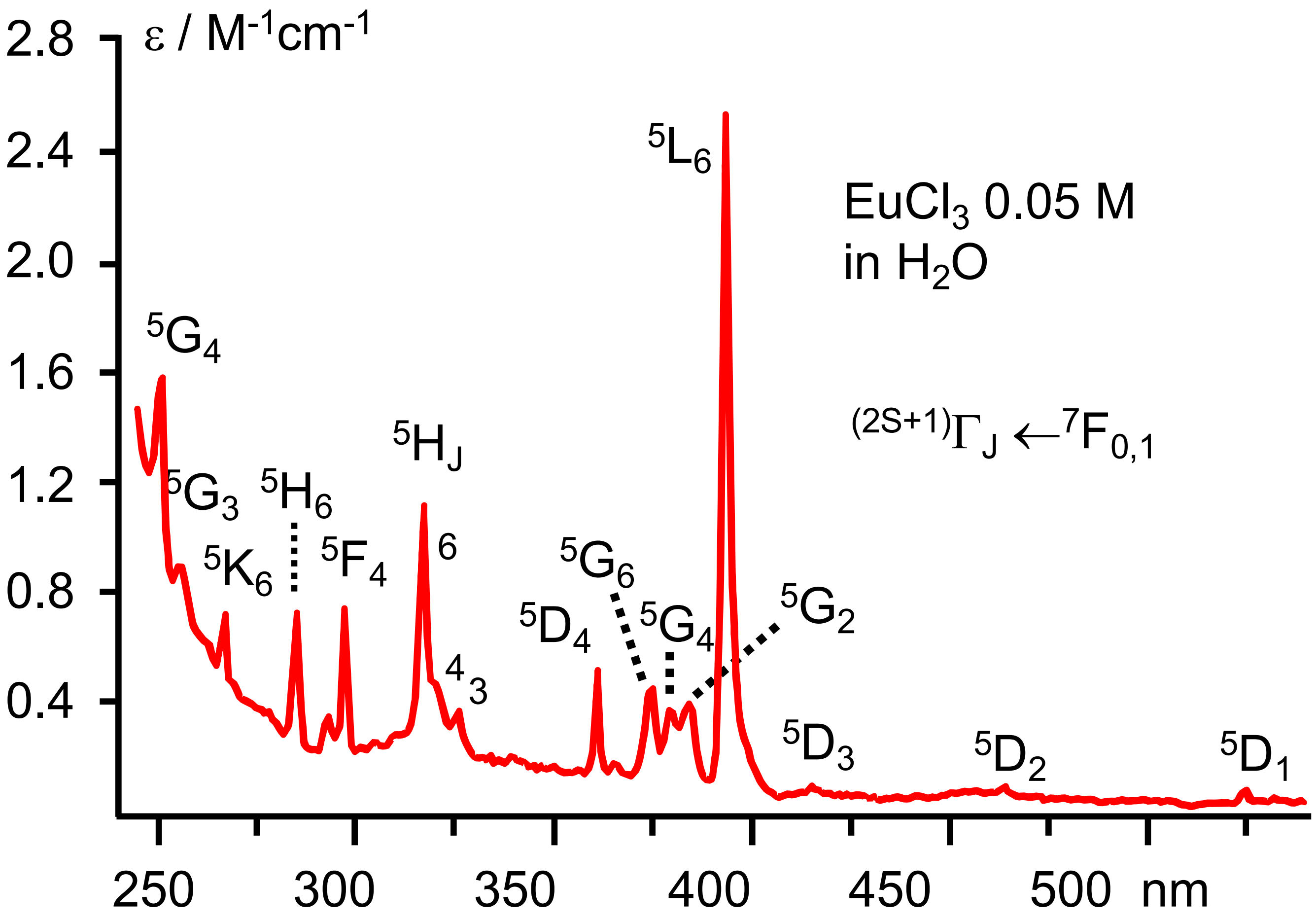
Tf$_2$N



- Line-like absorption and emission spectra
- Transitions between states derived from Russell-Saunders spin orbit coupling (J)
- Pale colours (formally forbidden transitions)

Transitions f-f

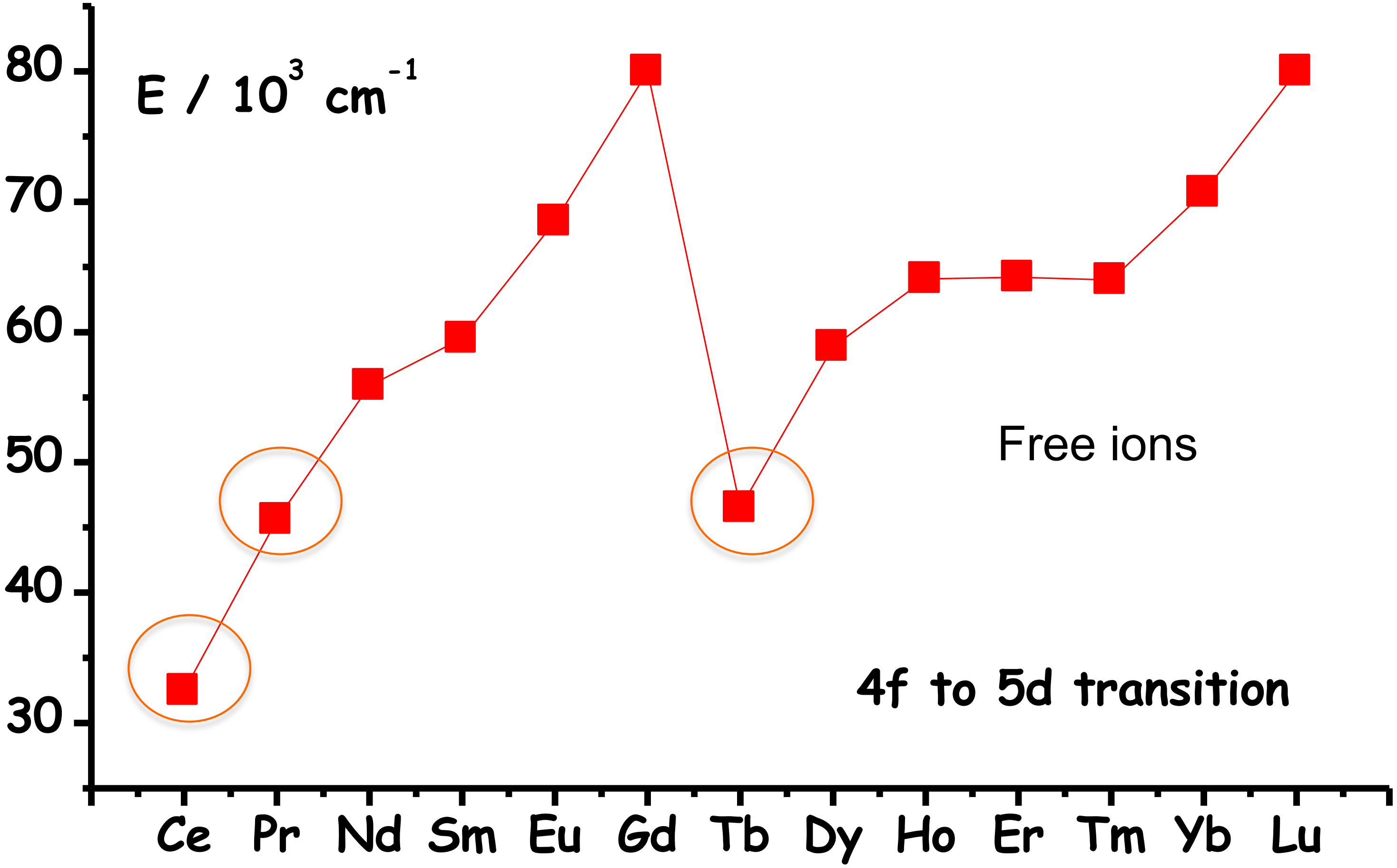
Europium(III), $4f^6$



Transitions f-d

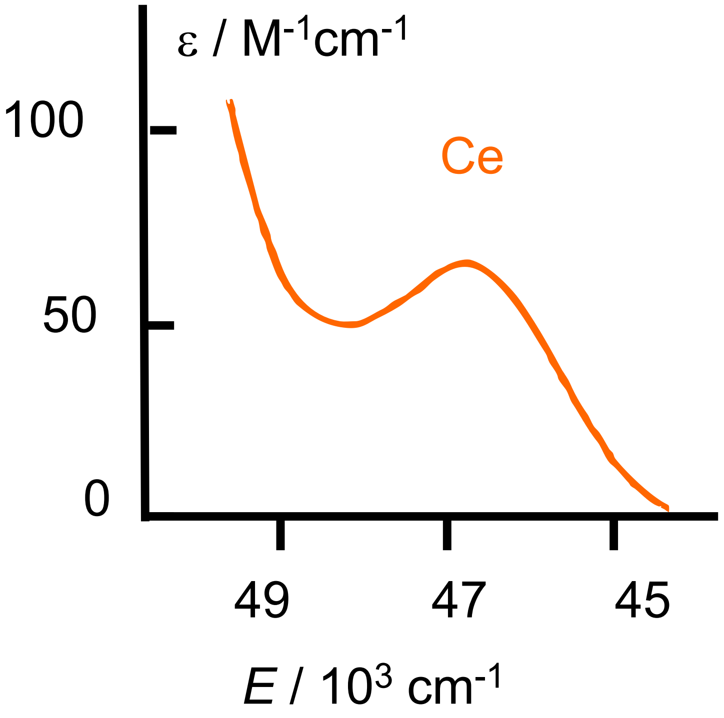
Allowed by Laporte's rule, ≈ 100-1000 $M^{-1}cm^{-1}$

Highly energetic, except for Ce^{III}, Pr^{III} and Tb^{III}
The Ce^{3+} transition $4f^1$ to $4f^05d^1$ varies with the ligand :
49737 cm^{-1} for Ce^{3+} gas, 17650 cm^{-1} for $[Ce\{C_5H_3(SiMe_3)_2\}_3]$

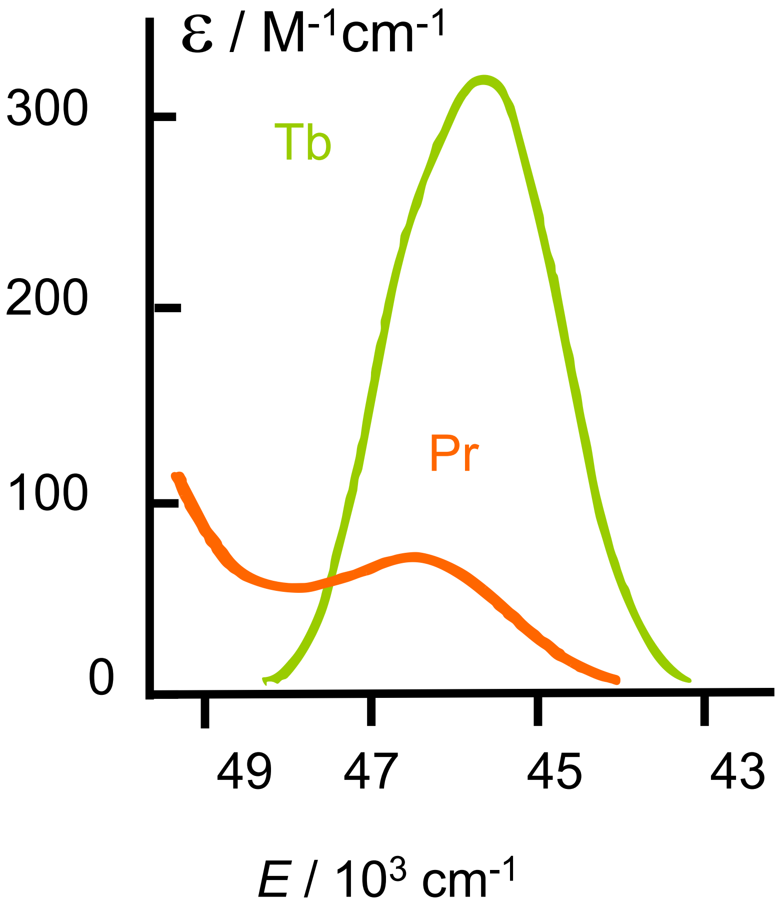


Transitions f-d

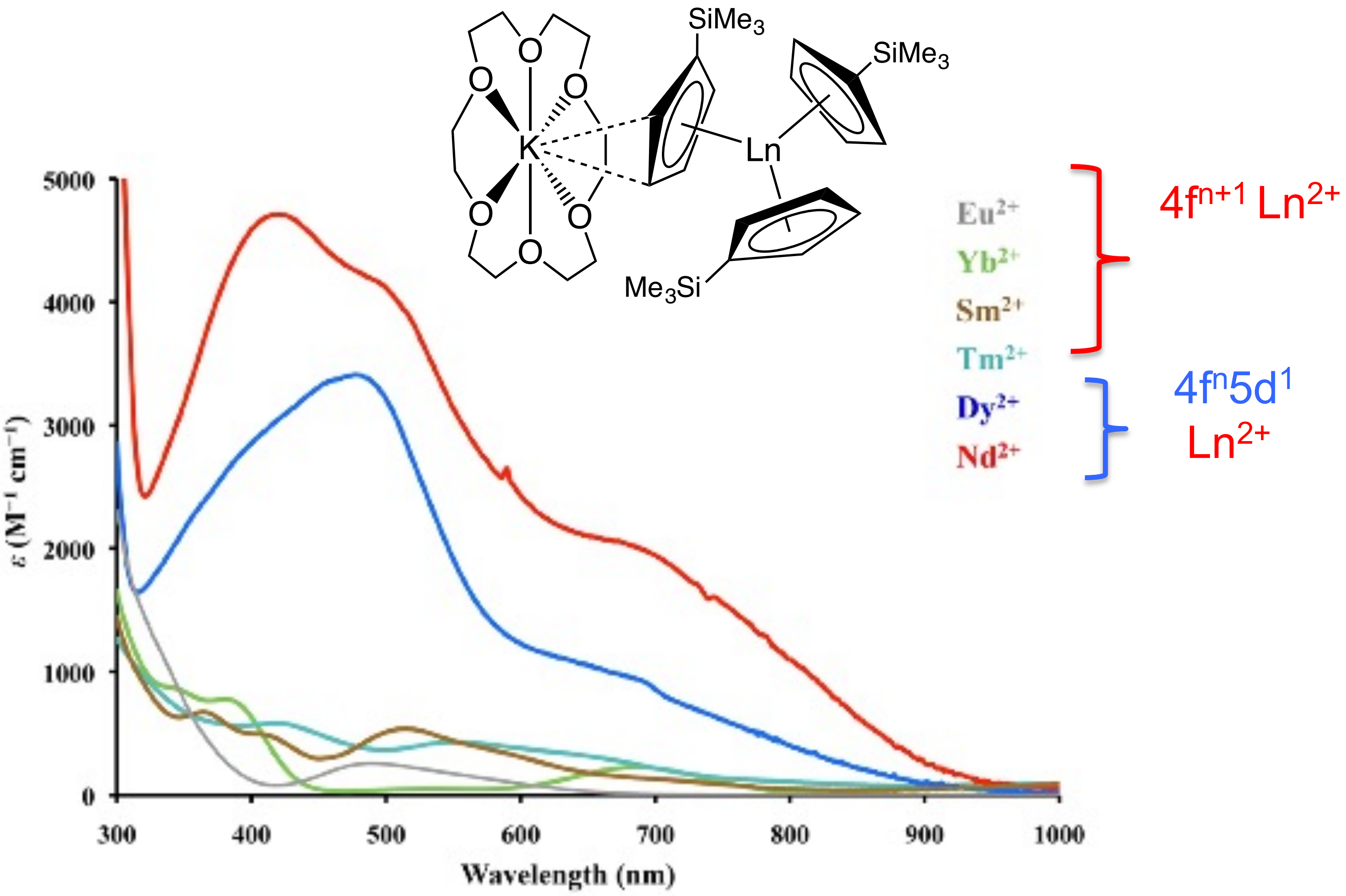
Observed f-d transitions for
$LnBr_3$ in anhydrous EtOH:



Ln^{III} (aq)



Electronic absorption spectra of Ln(II) Ions



$4f^{n+1}$ Ln^{2+}

$4f^n5d^1$ Ln^{2+}

Experimental UV−vis spectra of [K(2.2.2-cryptand)][Cp'_3Ln], (Ln = Nd, Sm, Eu, Dy, Tm, Yb), in THF at 298 K.

High ε of non-classical Ln^{2+} is due to metal-ligand mixing in the $4f^n5d^1$ configuration

Absorption for $4f^{n+1}$ Ln^{2+} is due to f-d mixing

J. Am. Chem. Soc. 2015, 137, 369−382

Magnetic Properties

A paramagnetic substance placed in the magnetic field contributes its own magnetic field due to the circulating charges. The total field strength is then increased by the field strength of the sample called magnetisation **M.**

This quantity can be measured by the magnetic susceptibility χ = M/H
The measured quantity is the susceptibility per mass unit χ_w
The molar susceptibility is obtained multiplying per the molecular mass $\chi_w = \chi_m \times M_m$

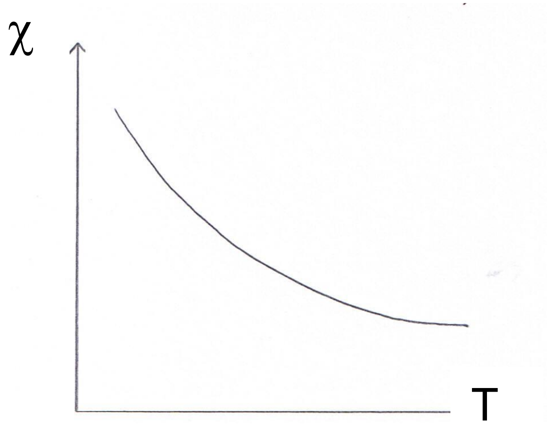
$$\boxed{\chi_M = \chi_M^{\text{dia}} + \chi_M^{\text{para}}}$$

χ^{dia}

Diamagnetic
repelled
by the magnetic field
< 0 weak
T independant

Paramagnetic
attracted by the field
> 0 strong
Varies in 1/T
(χ=C/T with C curie constant)

χ = C/T (loi de Curie)



χ_M = -1 à -500.10^{-6} cm^{3}mol^{-1}

χ_M = + 0 à 1.10^{-2} cm^{3}mol^{-1}

Magnetic Moment

If we have a collection of identical molecules each of magnetic moment μ and free to orient itself in a magnetic field , then in the field there will be some alignement but this will be opposed by the thermal motion of the molecules.

M is a constant but the measured moment decreases with temperature

$$\mu = \frac{\sqrt{3RT.\chi_M}}{N_A}$$

$$\boxed{\mu_{eff} = \frac{\sqrt{3RT.\chi_M}}{N_A.\beta}}$$

μ is given in Bohr magnetons :

$$\mu = \mu_{eff}.\beta$$

$\beta = 9.2741 \text{x} 10^{-24}$ JT

Magnetic Properties

Paramagnetism

- The spin-only formula is used to predict the magnetic moment:

Only spin contribution, (métaux d):

$$\mu_{eff} = \mu_S = g_e\sqrt{S(S+1)} = \sqrt{n(n+2)}$$

Or μ est exprimé en magnéton de Bohr BM or μ_β $\mu_\beta = 9.2741\text{x}10^{-24}$ JT

S = spin quantum number (½ for each unpaired electrons)
g_e= giromagnetic ratio around 2.00

n = number of unpaired electrons

Magnetic Moment of Ln^{3+}

Ln	conf.	n	Fond	1^{er} ex.	ΔE (cm^{-1})	**Spin Only formula** μ_{calc}		μ_{exp}
Ce	f^1	1	$^2F_{5/2}$	$^2F_{7/2}$	2200	1,73		2,5-2,8
Pr	f^2	2	$^3H_4$	$^3H_5$	2100	2,83	wrong	3,2-3,6
Nd	f^3	3	$^4I_{9/2}$	$^4I_{11/2}$	1900	3,87		3,2-3,6
Pm	f^4	4	$^5I_4$	$^5I_5$	1600	4,90		
Sm	f^5	5	$^6H_{5/2}$	$^6H_{7/2}$	1000	5,92		1,3-1,5
Eu	f^6	6	$^7F_0$	$^7F_1$	300	6,93		3,1-3,4
Gd	f^7	7	$^8S_{7/2}$	$^6P_{7/2}$	32000	7,94	Gd^{3+} OK	7,9-8,1
Tb	f^8	6	$^7F_6$	$^7F_5$	2000	6,93		9,2-9,7
Dy	f^9	5	$^6H_{15/2}$	$^6H_{13/2}$	3300	5,92		10,1-10,6
Ho	f^{10}	4	$^5I_8$	$^5I_7$	5300	4,90		10,0-10,5
Er	f^{11}	3	$^4I_{15/2}$	$^4I_{13/2}$	6500	3,87	wrong	9,2-9,6
Tm	f^{12}	2	$^3H_6$	$^3F_4$ d)	5800	2,83		7,0-7,3
Yb	f^{13}	1	$^2F_{7/2}$	$^2F_{5/2}$	10000	1,73		4,3-4,6

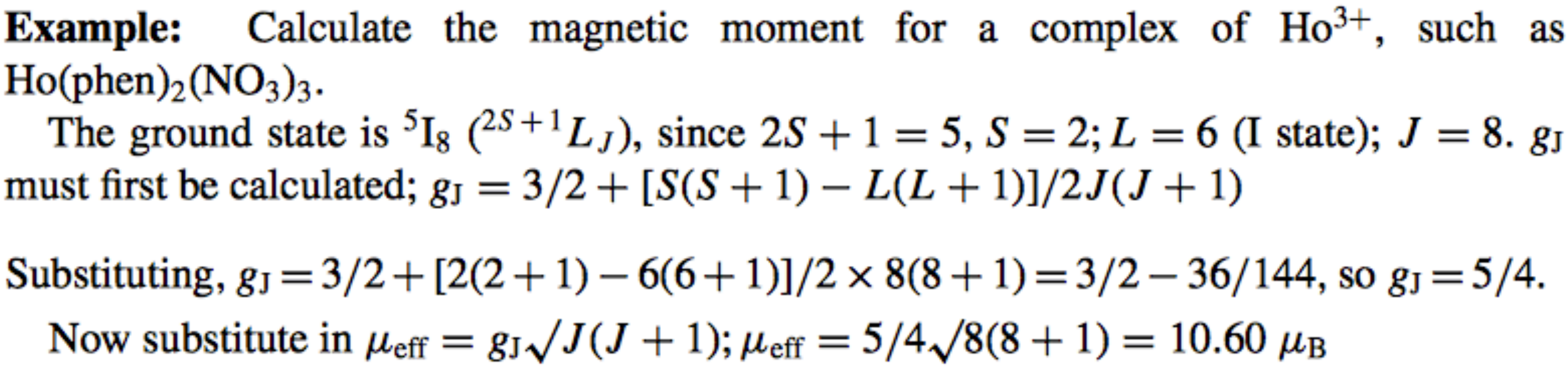
Magnetism

When Russell-Saunders scheme for spin-orbit coupling (SOC) is valid and when the ground state is pure and well separated from excited states, the following formulae are well adapted to predict the effective magnetic moment:

$$\boxed{\mu_{eff} = \mu_{j} = g_{J}\sqrt{(J(J+1)}}$$

$$g_J = 1 + \frac{J(J+1) + S(S+1) - L(L+1)}{2J(J+1)}$$

$$\chi T = g \cdot J(J+1)/8$$



Example: Calculate the magnetic moment for a complex of Ho^{3+}, such as $Ho(phen)_2(NO_3)_3$.

The ground state is $^5I_8$ ($^{2S+1}L_J$), since $2S+1=5$, $S=2$; $L=6$ (I state); $J=8$. g_J must first be calculated; $g_J = 3/2 + [S(S+1) - L(L+1)]/2J(J+1)$

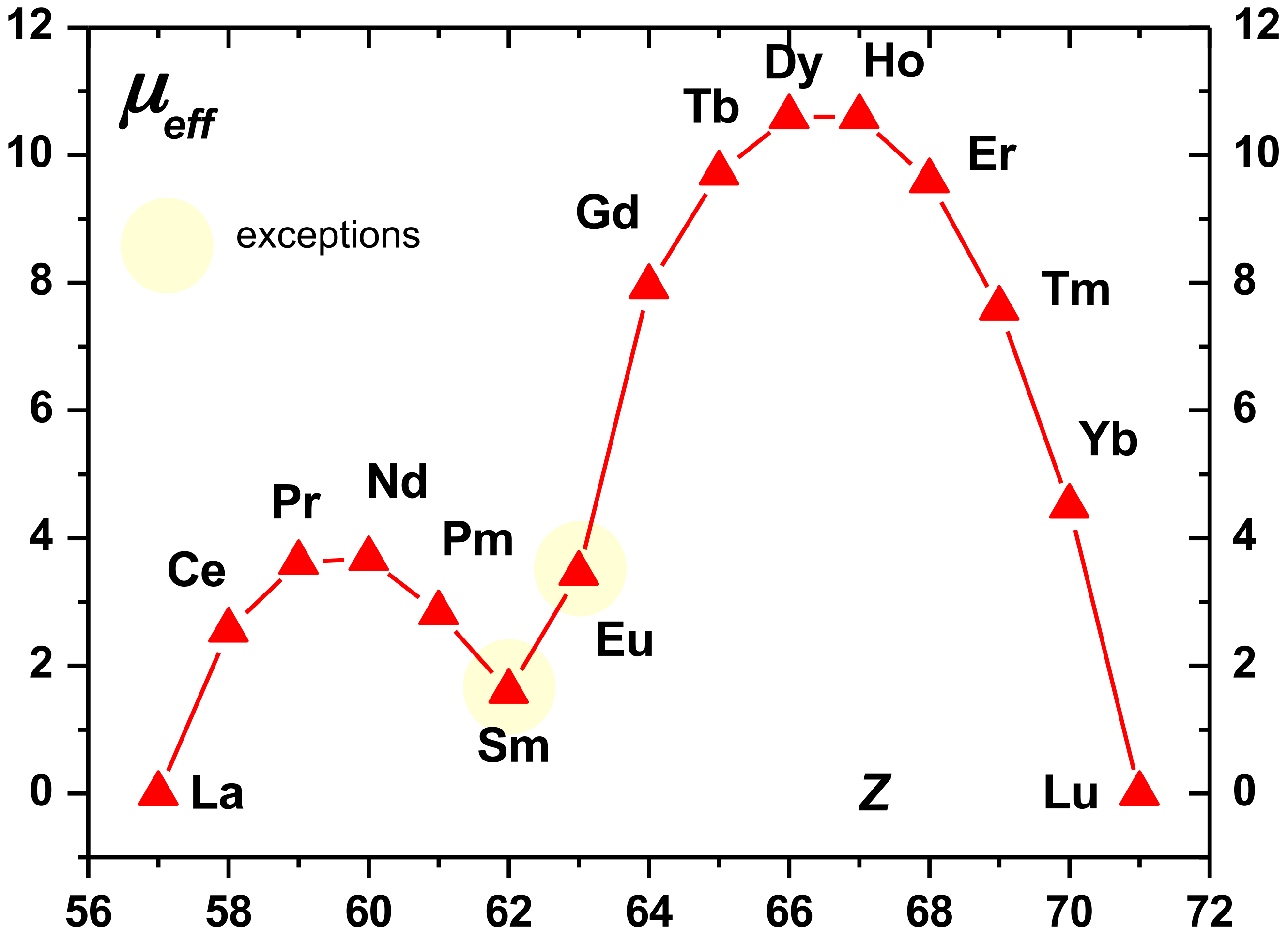
Substituting, $g_J = 3/2 + [2(2+1) - 6(6+1)]/2 \times 8(8+1) = 3/2 - 36/144$, so $g_J = 5/4$.

Now substitute in $\mu_{eff} = g_J\sqrt{J(J+1)}$; $\mu_{eff} = 5/4\sqrt{8(8+1)} = 10.60\ \mu_B$

Electronic levels and magnetic moments

Ln^{3+}	$4f^n$, n	Ground level	Color	Magnetic moment	
				exp.	Calc.with SOC formula
Ce	1	$^2F_{5/2}$	colorless	2.3-2.5	2.54
Pr	2	$^3H_4$	green	3.4-3.6	3.58
Nd	3	$^4I_{9/2}$	lilac	3.5-3.6	3.62
Pm	4	$^5I_4$	pink	n.a.	2.68
Sm	5	$^6H_{5/2}$	yellow	1.4-1.7	0.85
Eu	6	$^7F_0$	pale pink	3.3-3.5	0
Gd	7	$^8S_{7/2}$	colorless	7.9-8.0	7.94
Tb	8	$^7F_6$	colorless	9.5-9.8	9.72
Dy	9	$^6H_{15/2}$	yellow	10.4-10.6	10.6
Ho	10	$^5I_8$	yellow	10.4-10.7	10.6
Er	11	$^4H_{15/2}$	rose	9.4-9.6	9.58
Tm	12	$^3H_6$	pale green	7.1-7.5	7.56
Yb	13	$^2F_{7/2}$	colorless	4.3-4.9	4.54

Magnetic moment



The number of unpaired electrons is given by the electronic configuration (small CFT)

In the case of Eu and Sm the first excited states are close to the ground state at room T
So the exp magnetic moment is the mix of ground and excited state moments

Magnetic Moment of Ln^{3+}

Including excited states

Ln	conf.	n	Fond	1^{er} ex.	ΔE (cm^{-1})	g_J	SO μ_{calc}	SOC μ_{calc}	μ_{calc}	μ_{exp}
Ce	f^1	1	$^{2}F_{5/2}$	$^{2}F_{7/2}$	2200	0,86	1,73	2,54	2,56	2,5-2,8
Pr	f^2	2	$^{3}H_4$	$^{3}H_5$	2100	0,80	2,83	3,58	3,62	3,2-3,6
Nd	f^3	3	$^{4}I_{9/2}$	$^{4}I_{11/2}$	1900	0,73	3,87	3,62	3,68	3,2-3,6
Pm	f^4	4	$^{5}I_4$	$^{5}I_5$	1600	0,60	4,90	2,68	2,83	
Sm	f^5	5	$^{6}H_{5/2}$	$^{6}H_{7/2}$	1000	0,29	5,92	0,85	1,60	1,3-1,5
Eu	f^6	6	$^{7}F_0$	$^{7}F_1$	300		6,93	0	3,45	3,1-3,4
Gd	f^7	7	$^{8}S_{7/2}$	$^{6}P_{7/2}$	32000	2,00	7,94	7,94	7,94	7,9-8,1
Tb	f^8	6	$^{7}F_6$	$^{7}F_5$	2000	1,50	6,93	9,72	9,72	9,2-9,7
Dy	f^9	5	$^{6}H_{15/2}$	$^{6}H_{13/2}$	3300	1,33	5,92	10,65	10,6	10,1-10,6
Ho	f^{10}	4	$^{5}I_8$	$^{5}I_7$	5300	1,25	4,90	10,61	10,6	10,0-10,5
Er	f^{11}	3	$^{4}I_{15/2}$	$^{4}I_{13/2}$	6500	1,20	3,87	9,58	9,6	9,2-9,6
Tm	f^{12}	2	$^{3}H_6$	$^{3}F_4$ d)	5800	1,17	2,83	7,56	7,6	7,0-7,3
Yb	f^{13}	1	$^{2}F_{7/2}$	$^{2}F_{5/2}$	10000	1,14	1,73	4,54	4,5	4,3-4,6

Magnetic Moment of Ln^{2+}

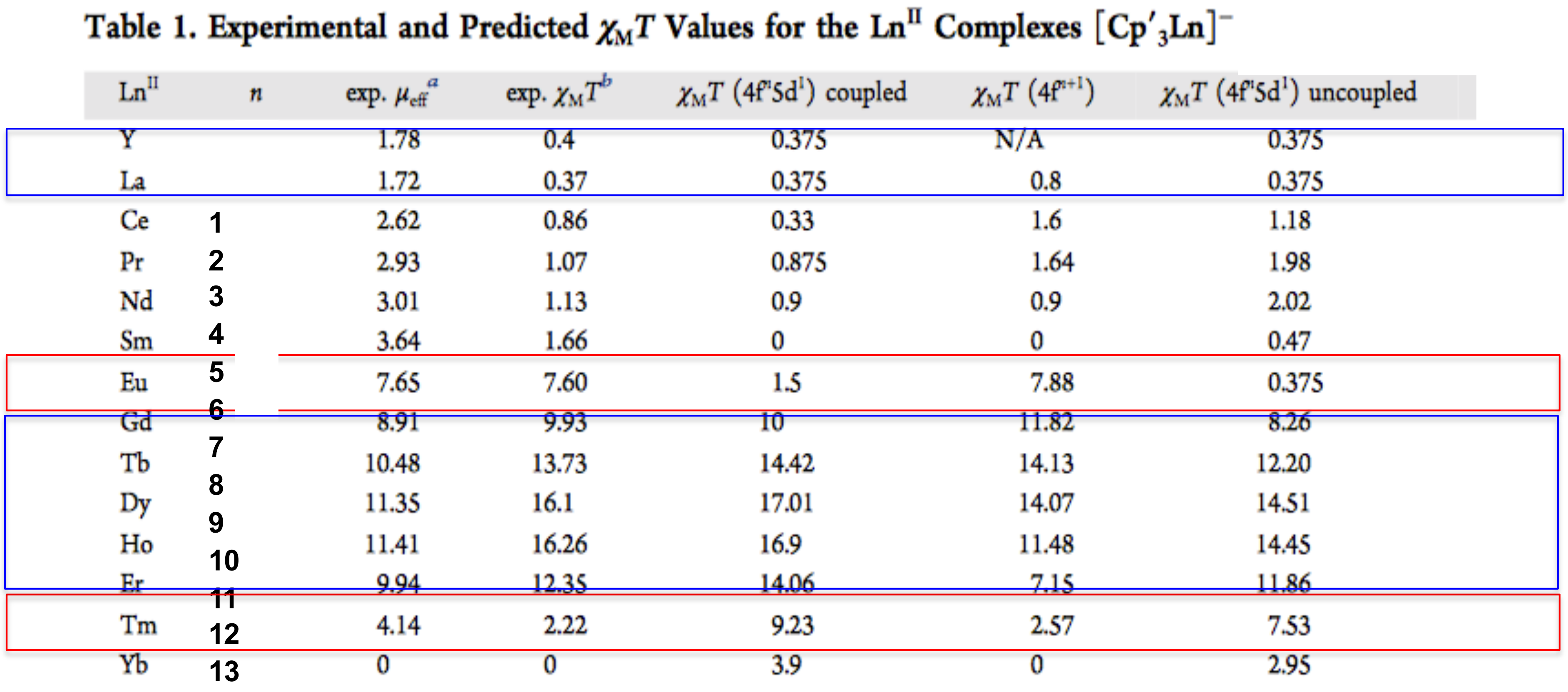


Table 1. Experimental and Predicted $\chi_M T$ Values for the Ln^{II} Complexes $[Cp'_3Ln]^-$

Ln^{II}	n	exp. μ_{eff}[a]	exp. $\chi_M T$[b]	$\chi_M T$ ($4f^n5d^1$) coupled	$\chi_M T$ ($4f^{n+1}$)	$\chi_M T$ ($4f^n5d^1$) uncoupled
Y		1.78	0.4	0.375	N/A	0.375
La		1.72	0.37	0.375	0.8	0.375
Ce	1	2.62	0.86	0.33	1.6	1.18
Pr	2	2.93	1.07	0.875	1.64	1.98
Nd	3	3.01	1.13	0.9	0.9	2.02
Sm	4	3.64	1.66	0	0	0.47
Eu	5	7.65	7.60	1.5	7.88	0.375
Gd	6	8.91	9.93	10	11.82	8.26
Tb	7	10.48	13.73	14.42	14.13	12.20
Dy	8	11.35	16.1	17.01	14.07	14.51
Ho	9	11.41	16.26	16.9	11.48	14.45
Er	10	9.94	12.35	14.06	7.15	11.86
Tm	11 12	4.14	2.22	9.23	2.57	7.53
Yb	13	0	0	3.9	0	2.95

Very high magnetic moments with Dy and Ho

$4f^{n+1}$ Ln^{2+}

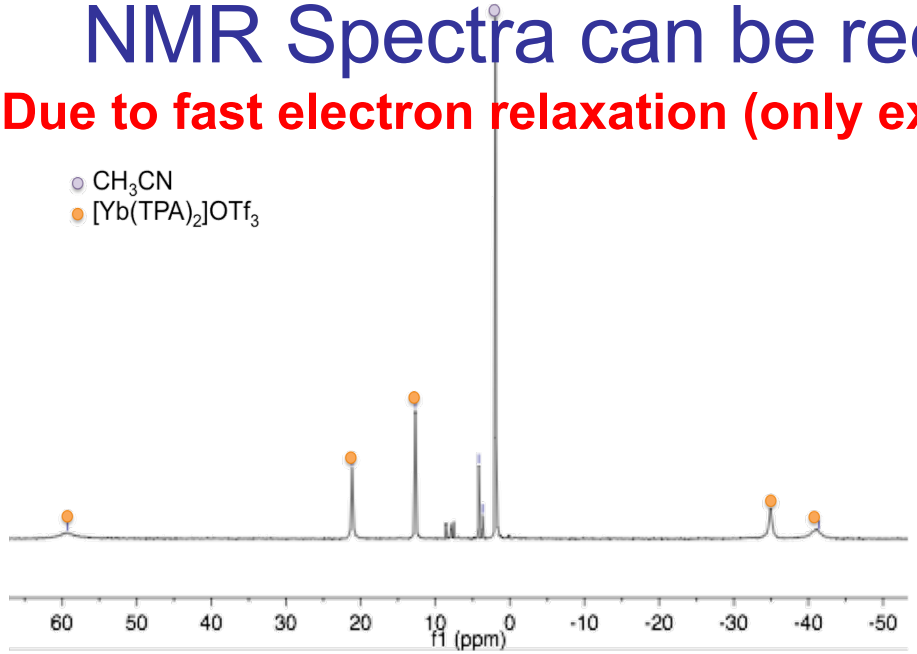
$4f^n5d^1$

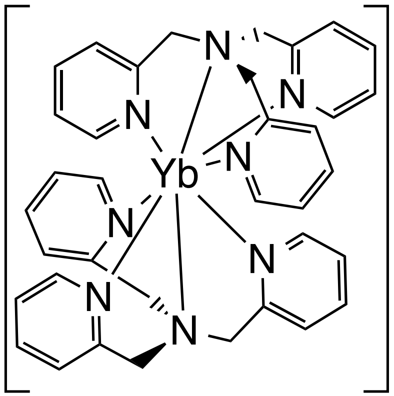
Evans J. Am. Chem. Soc. 2015, 137, 9855−9860

Ce, Pr, Nd :mixed configuration??

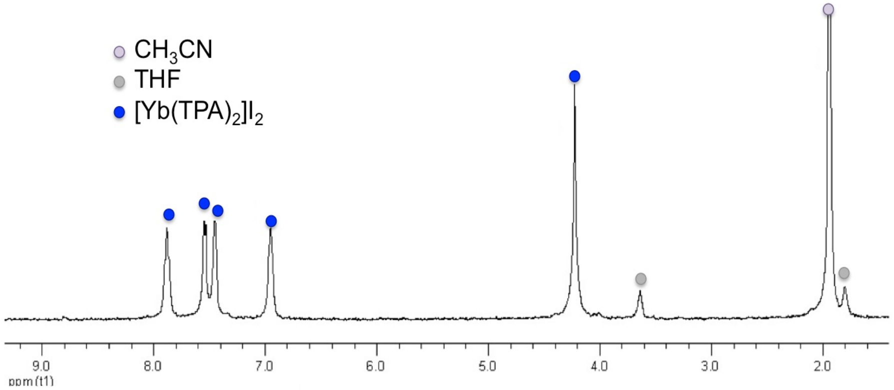
NMR Spectra can be recorded in spite of large **μ**

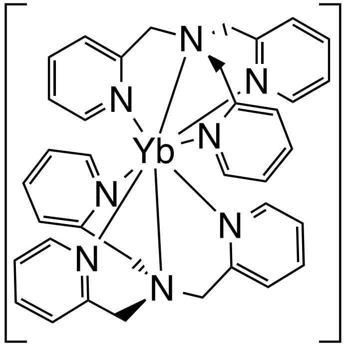
Due to fast electron relaxation (only exception Gd^{3+})





f^1





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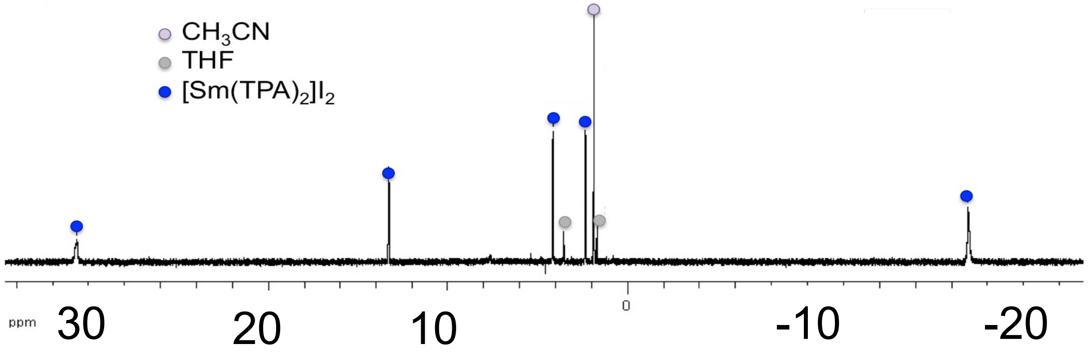
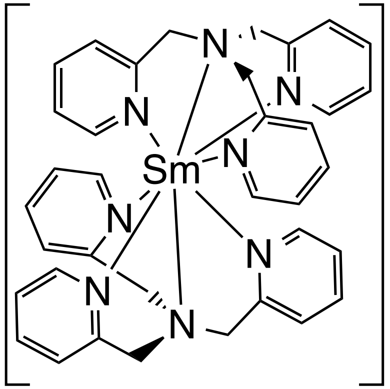




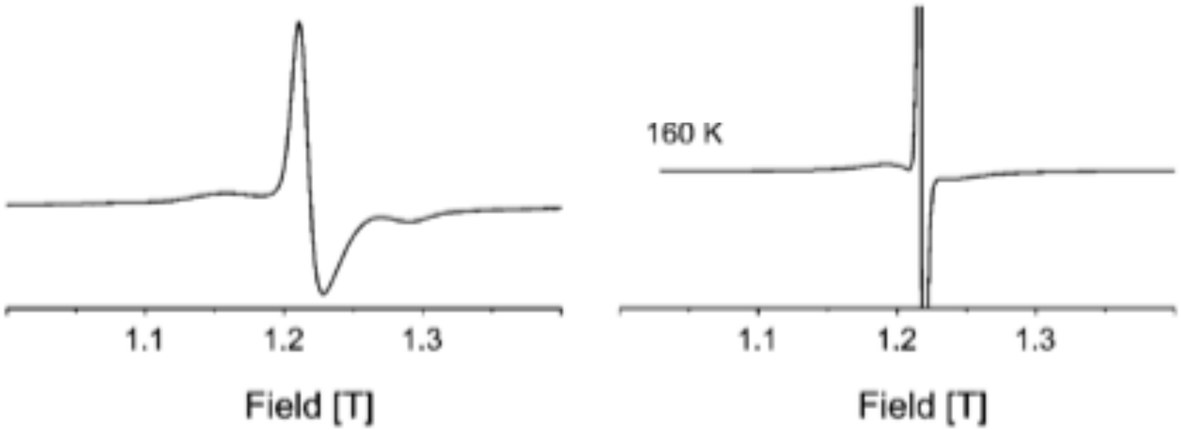
f^6

EPR Spectra

Due to the **rapid** electronic relaxation NMR spectra are observed , but for most ions EPR spectra can only be recorded at low T (20 K) (very rapid electron relaxation, ≈10^{-13} s).

Gd^{3+} ($4f^7$) ^8S ground state with no orbital contribution

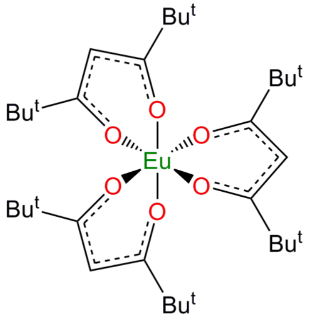
Very slow electron relaxation time (≈10^{-9} s), EPR can be measured at room temperature



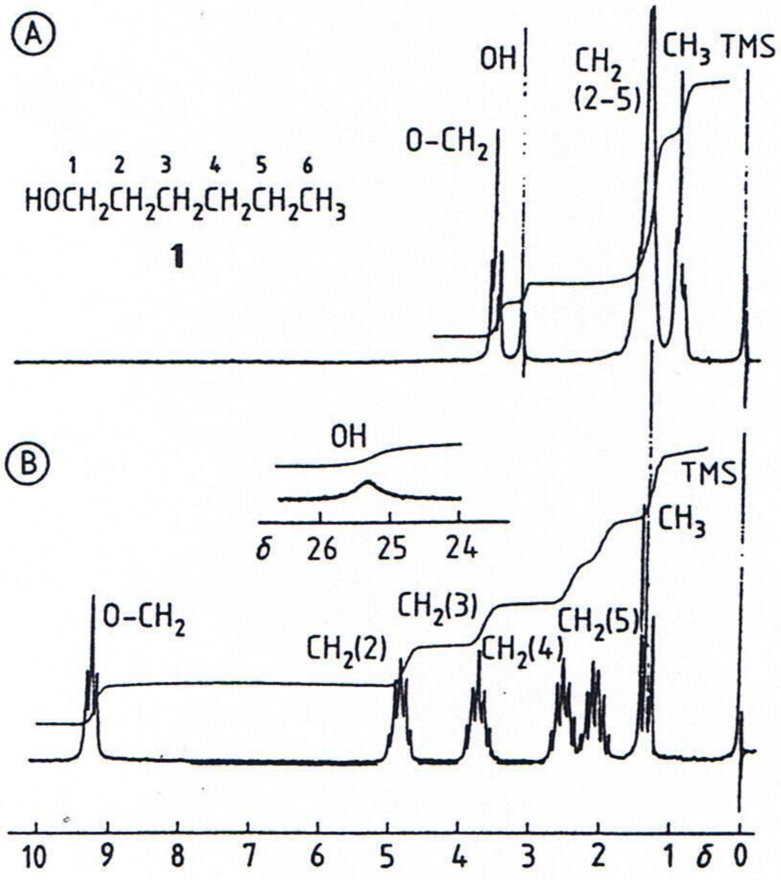
EPR can give informations on crystal field splitting

Ln(III) complexes as NMR “Shift reagents”

Some Ln β-diketonate complexes are used to resolve ^{1}H NMR spectra in busy overlapping regions. For example 1-hexanol



[Eu(dpm)$_3$]



^{1}H NMR 90 MHz of 1-hexanol

A. hexan-1-ol in CCl_4

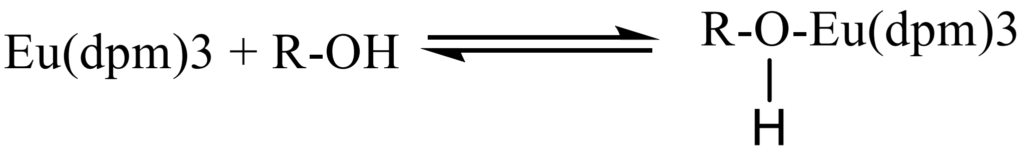
Overlapped signals

B. hexan-1-ol in presence of Eu(dpm)$_3$ in CCl_4

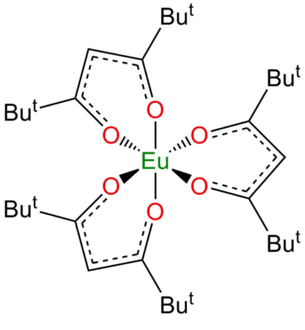
Shifted signals

Less used with spreading of high field NMR

Ln(III) complexes as NMR “Shift reagents”



$$\mathrm{Eu(dpm)3 + R\text{-}OH \rightleftharpoons R\text{-}\underset{\displaystyle H}{\underset{|}{O}}\text{-}Eu(dpm)3}$$



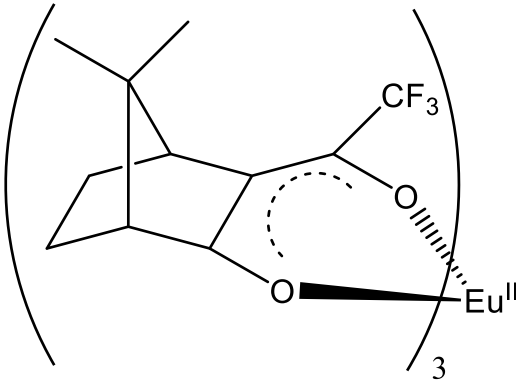
[Eu(dpm)$_3$]

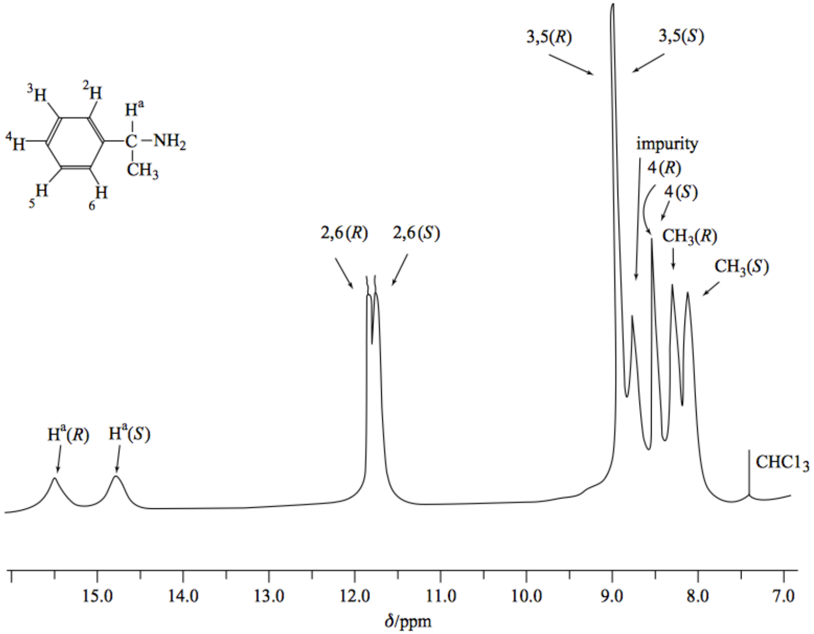
OH coordinates to Eu, protons experience paramagnetism.

Paramagnetic effects vary with distance, spreading out the signals.

Chiral Eu Complexes:

Eu(TFC)$_3$ =





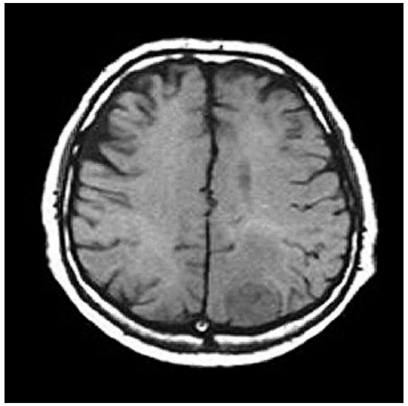
One cans also use chiral Ln β-diketonate complexes to analyse mixtures of enantiomers [(R)- and (S)- diasteromeric complexes formed.

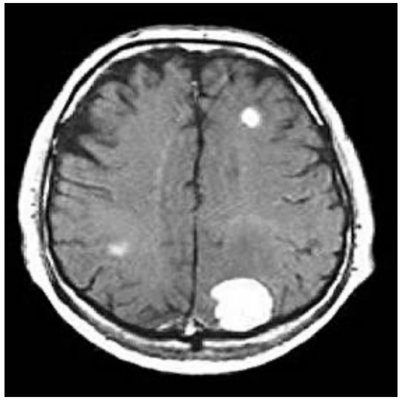
Application of Ln^{3+} Magnetic Properties in MRI

MRI: Detection of the water protons (^1H NMR)

Signal intensity = f (T_1, T_2)
Depends of tissues

Addition of contrast agents ($T_1 \searrow$, $T_2 \searrow$)


Without contrast agent


With contrast agent

❖ *improve the contrast cancerous vs healthy tissues*

❖ *target a specific organ of function (blood pool…)*

Binding of the water to a metal with high magnetic moment will **decrease** the nuclear relaxation time. A good contrast agent needs large number of water molecules coordinated to a metal with high magnetic moment.

Gd^{3+} ion has a large number of unpaired electrons ($S = 7/2$) and its magnetic properties are isotropic. It has a relatively long electron-spin relaxation time, $\sim 10^{-9}$ s, which makes it more suitable than other very paramagnetic ions such as Dy^{3+}, Eu^{3+}, and Yb^{3+} ($\sim 10^{-13}$ s). These factors are very favourable for nuclear spin relaxation.

Gd^{3+} toxic so we need to include it in stable complexes.

Stability of Lanthanide Complexes

For the following reaction:

$M^{n+} + L^{y-} \leftrightarrow [ML]^{(n-y)+}$

We can define the stability constant, β_1:

$\beta_1 = [ML^{(n-y)+}]/[M^{n+}][L^{y-}]$

The stability generally increases across the Ln series

Electrostatic interaction prevails: higher stability at the end of the series due to the high density charge (lanthanide contraction)

Ln^{3+} are hard ions and form higher stability complexes with hard bases such as water, negative oxygen and negative N donors

Higher stability with more electron donor ligands

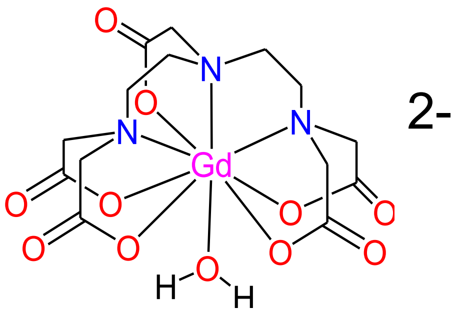
Multidentate ligands have higher stability values as for TM due to chelate effect (large ΔS).

Complexes Stability in Water

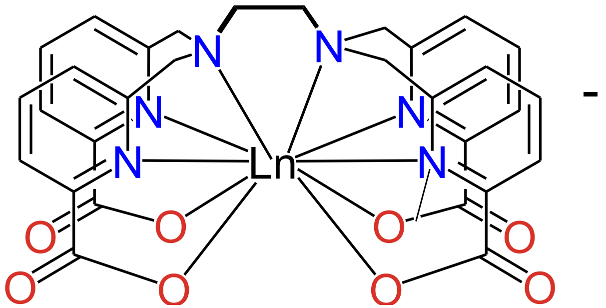
High stability in water (as required by biomedical applications is achieved with

- Polydentate ligands with negative O, N donors
  aminocarboxylate ligands , aminophenolate etcc

Thermodynamic stability is proportional to the sum of pKas
and pre-organisation



$[\mathrm{Gd(\ DTPA)}]\mathrm{K}_2$ Log$K$ = 22.1



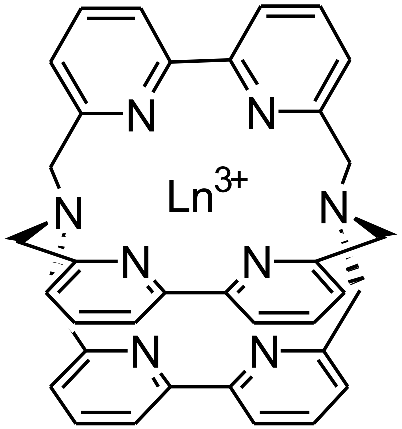
[Gd(tpaen)]K Log$K$ = 15.3

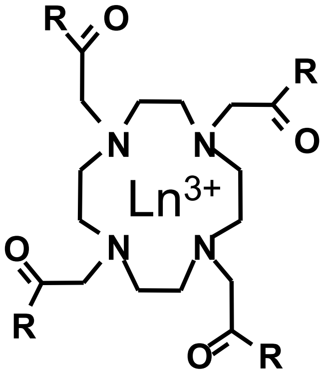
Kinetic Stability in Water

The crystal field of coordinated ligands does not remove the degeneracy of the 4f orbitals.

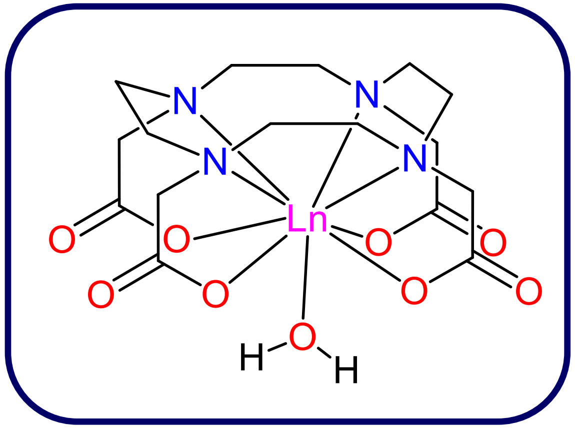
As there is no Crystal Field Stabilisation Energy, there are often low barriers to ligand substitution.
Therefore these complexes are often **kinetically labile**.

Kinetic Stability is found with macrocycles and cryptates ligands can form stable cationic complexes





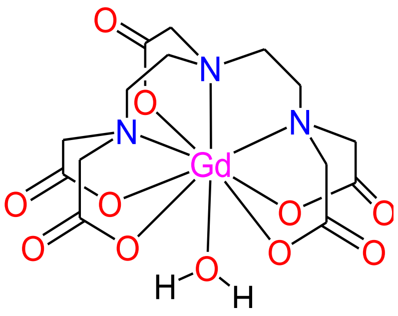
R = NH_2 dotam



High stability
Kinetic and thermodynamic

Commercial MRI Contrast Agents

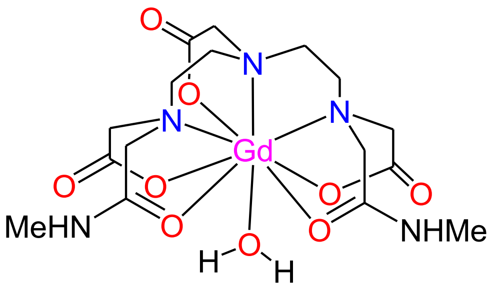
$[Gd(dtpa)(H_2O)]^{2-}$



Magnevist®

Log*K* = 22.1

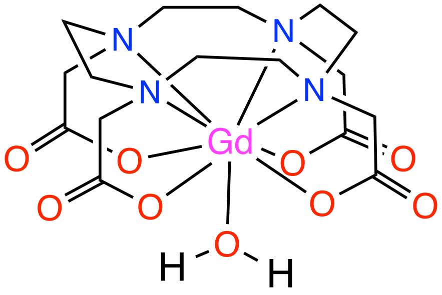
$[Gd(dtpa\text{-}bma)(H_2O)]^{-}$



Omniscan®

Log*K* = 16.9

$[Gd(dota)(H_2O)]^{-}$



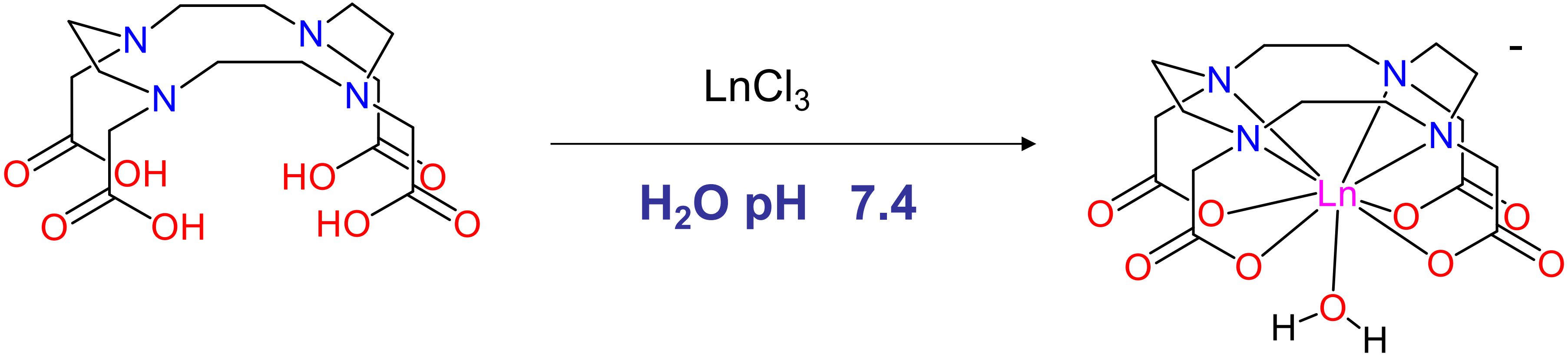
Dotarem®

Log*K* = 25.8

☞ The ligand is crucial for the control of the stability

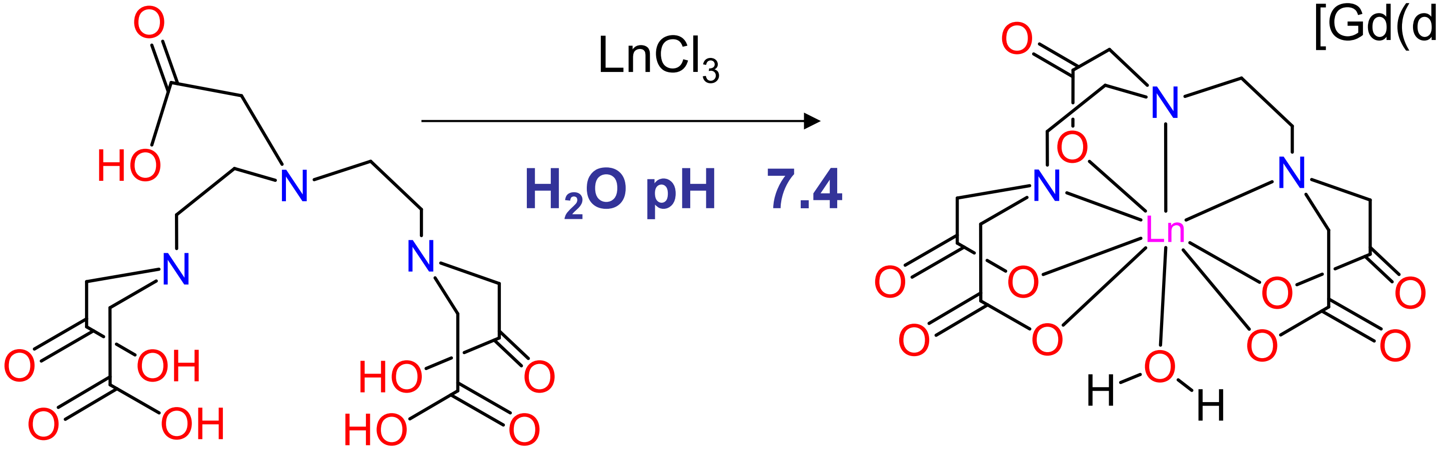
Anionic Multidentate N,O-donors: Thermodynamic stability

H_4dota



$[Gd(dota)(H_2O)]^-$

H_5dtpa



$[Gd(dtpa)(H_2O)]^{2-}$

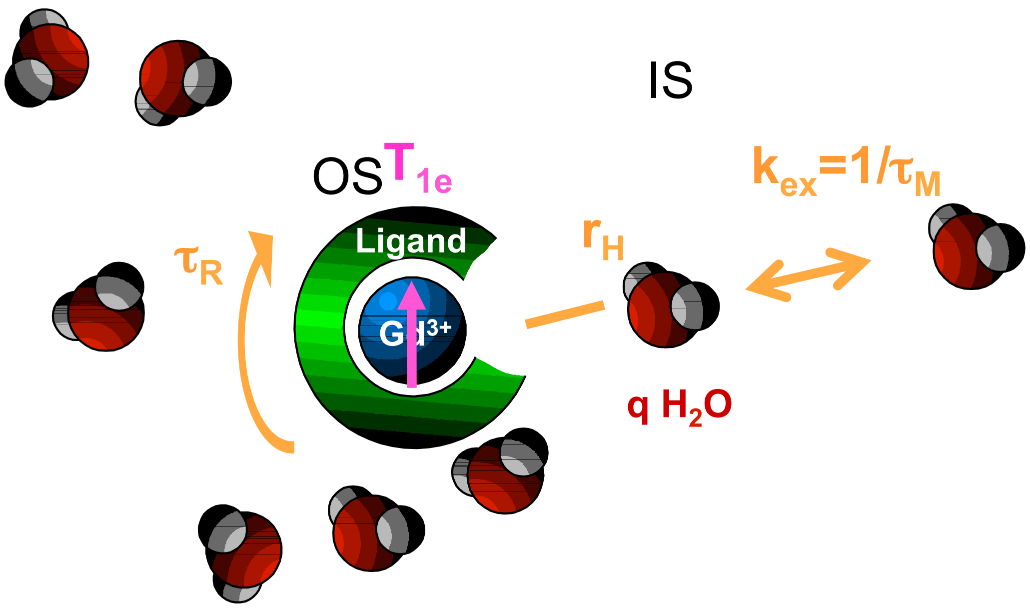
Gd(III) Complexes as Contrast Agents

- High water solubility, Thermodynamic and kinetic stabilities
- Efficiency = Relaxivity r measures the ability of magnetic compounds to increase the relaxation rates of the surrounding water proton spins.

$$r_1 = \frac{1}{T_{1\,para}} \times \frac{1}{[GdL]} \quad (\mathrm{s^{-1}mM^{-1}})$$

$$r = r_{IS} + r_{OS} + r_{SS}$$

$$r_{1,p}^{IS} = c \times \frac{q}{55.55} \times \frac{1}{T_{1\mathrm{m}} + \tau_{\mathrm{M}}}$$



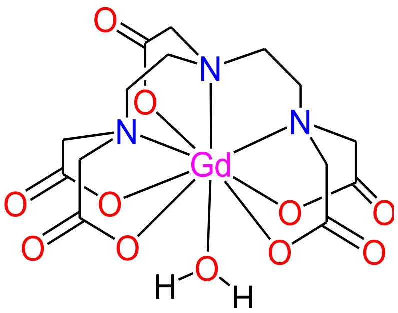
☞ To increase IS relaxivity :

- maximise q at any field
- optimise τ_R, k_{ex} and T_{1e} at low-medium fields

$$T_{1\mathrm{m}}\left(\frac{1}{\mathrm{r_H^6}}, \mathrm{T_{1e}}, \tau_R, \tau_M\right)$$

Commercial MRI Contrast Agents

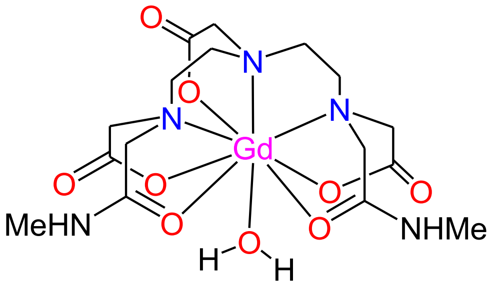
$[Gd(dtpa)(H_2O)]^-$



Magnevist®

Log*K* = 22.1

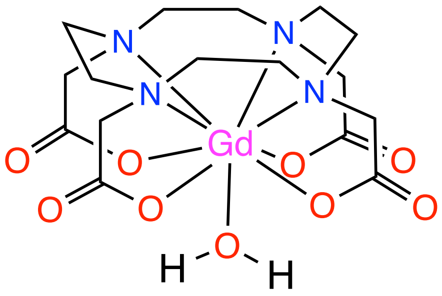
$[Gd(dtpa\text{-}bma)(H_2O)]^-$



Omniscan®

Log*K* = 16.9

$[Gd(dota)(H_2O)]^-$



Dotarem®

Log*K* = 25.8

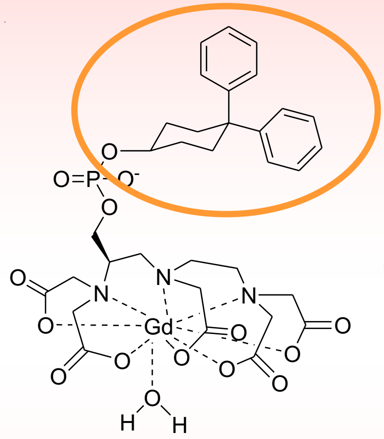
Low relaxivity r_1 ~ 4 mM^{-1} s^{-1} (20 MHz – 0.5 T) High stability

☞ The ligand is crucial for the control of the complex properties
But also to optimize relaxivity and to build responsive agents

Different parameter are optimized at different fields

New Generation Contrast Agents

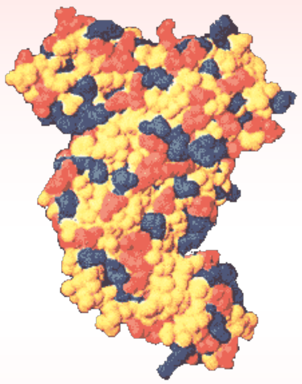
Contrast at clinical fields ($0.5 < B < 1.5$ T) can be increased by increasing the rotational time ⇨ Macromolecular complexes



MS-325

$r_1 = 5.8\ mM^{-1}s^{-1}$

+



HSA

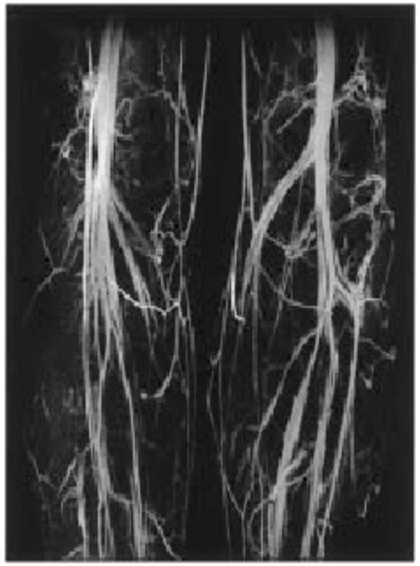
PM = 67 kDa
4.5% in plasma

⟶

Supramolecular adduct

(hydrophobic interactions)

$\mathbf{r_1 = 42\ mM^{-1}s^{-1}}$ (0.5 T)

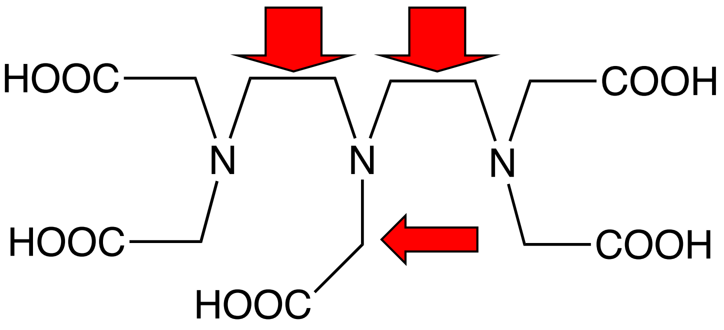


Angiography (visualizes blood vessels)

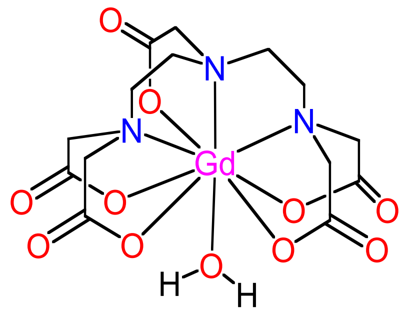
Caravan, Epix

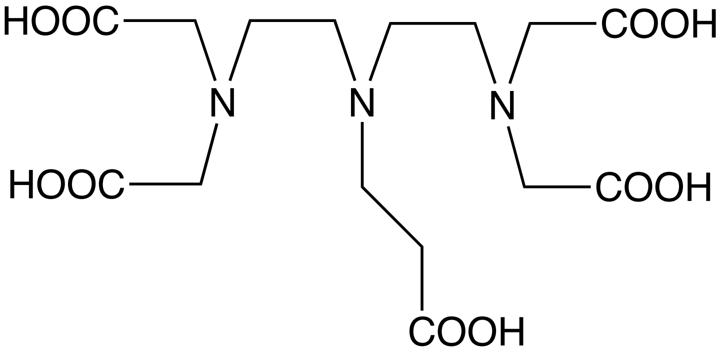
Increasing Water Exchange Rate

- ☞ In a dissociatif mechanism the water exchange rate is increased by steric compression

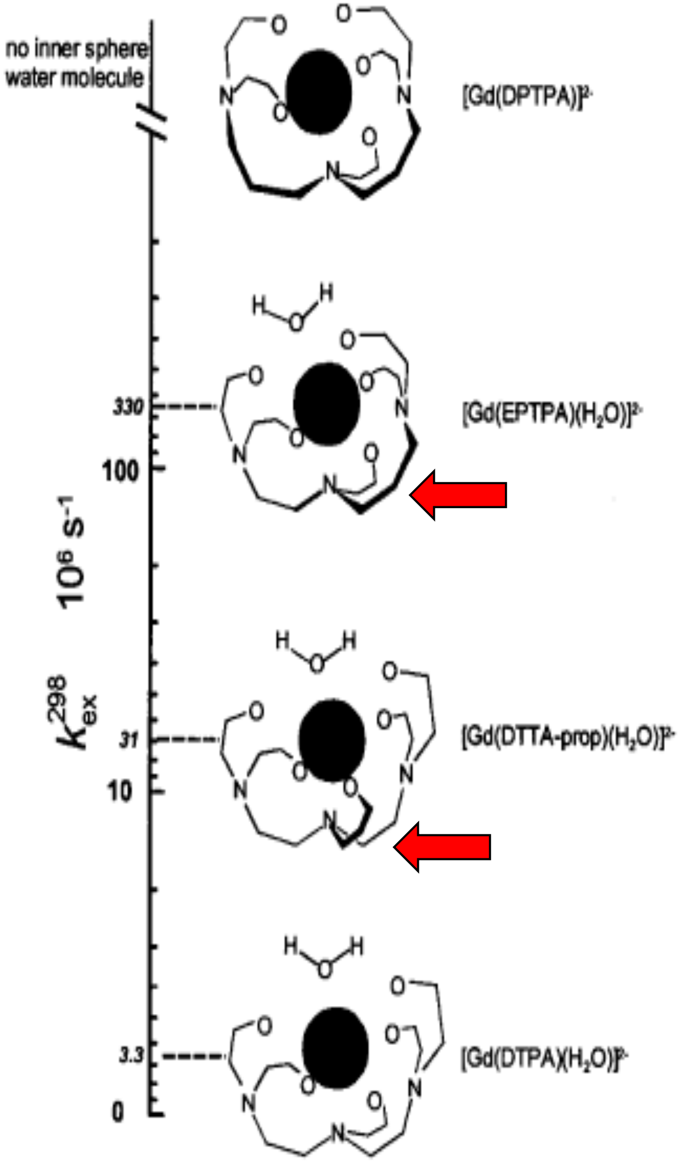


H_3DTPA





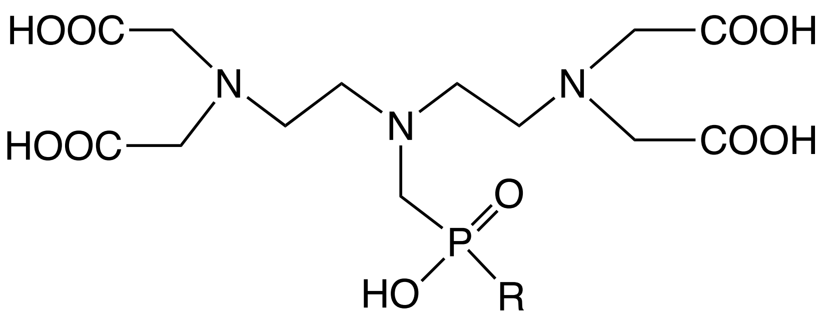
H_3DTPA-prop



A. Merbach, (2003)

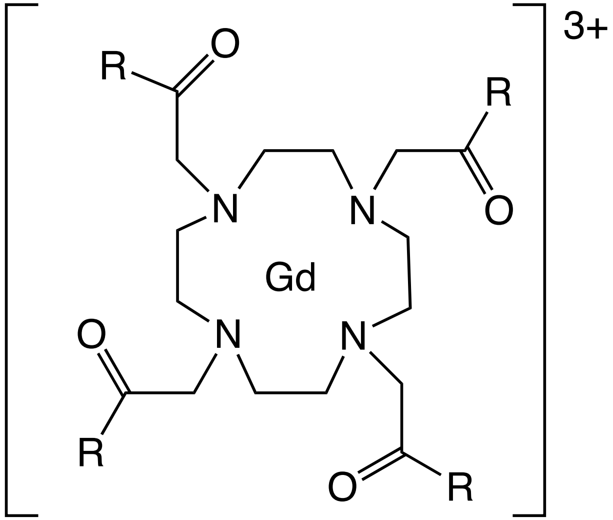
☞ Increasing water exchange rate:

- steric compression



R = OH

- **Complex charge has also an effect**

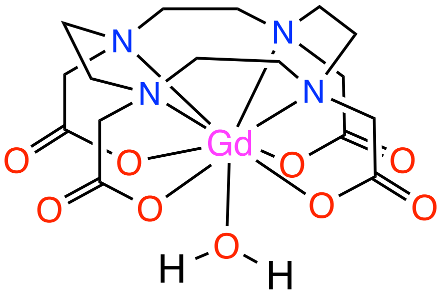


R = NH_2 **dotam**

$k_{ex} \sim 0.053.\ 10^6\ s^{-1}$

<<<

$[Gd(dota)(H_2O)]^-$

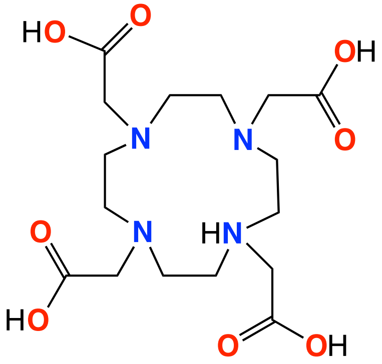


$k_{ex} \sim 4.\ 10^6\ s^{-1}$

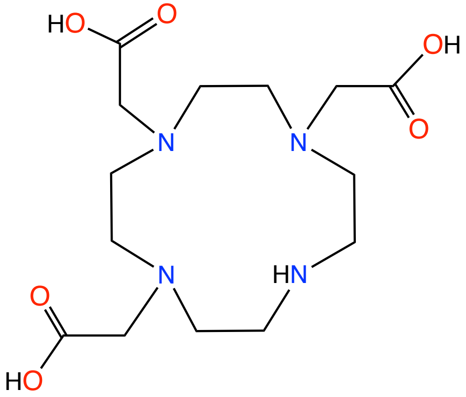
Increasing the number of coordinated water molecules

q>1 → Higher efficiency at all fields

Lower stability



H_4dota

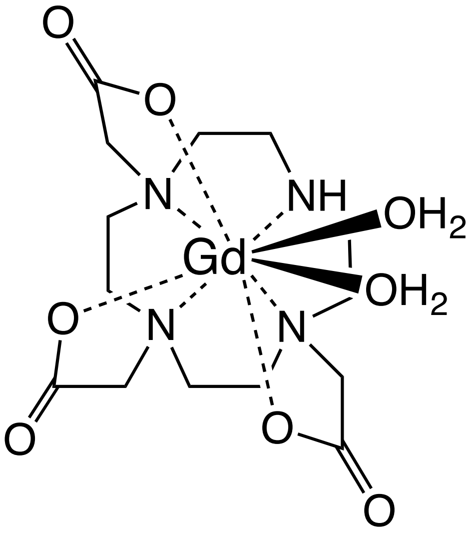


Heptadentate

logKGdL = 21.1

q = 2

r = 6.1 mM^{-1} s^{-1}



$[Gd(DO3A)(H_2O)_2]$

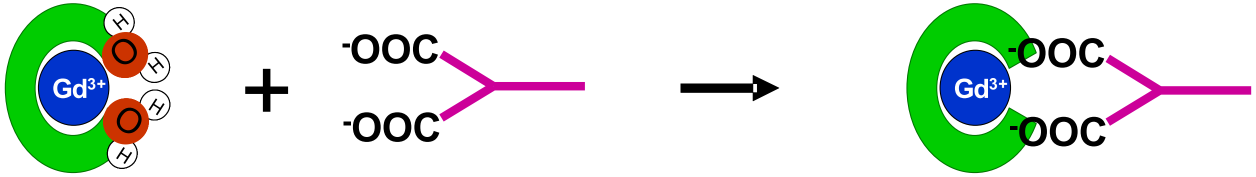
☹ Neutral complex : water exchange is slower

In biological media anion binding displaces water and reduces efficiency

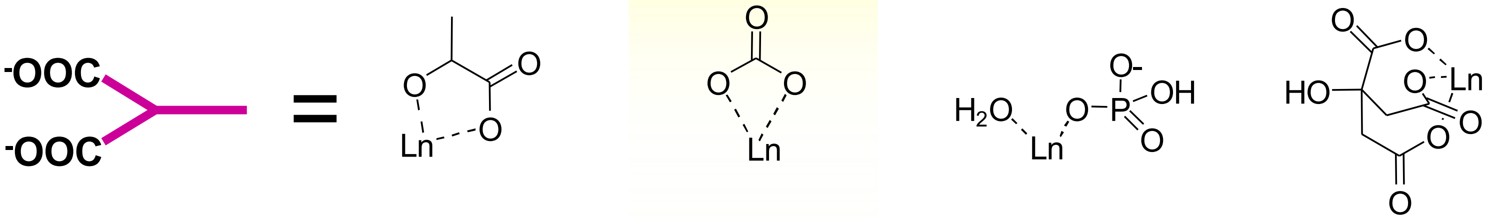
Limitations of Gd^{3+} Complexes with q>1

1) ↘ Lower thermodynamic stability (effet chelate)

2) Competition with endogenous carboxylates → Physiologic anions / proteins

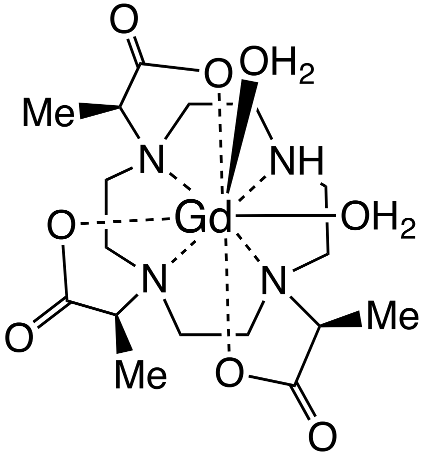


↘ q → ↘ relaxivity



lactate	**carbonate**	**phosphate**	**citrate**
2.3 mM	30 mM	0.9 mM	0.13 mM

Increasing the number of coordinated water molecules



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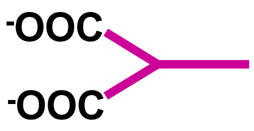
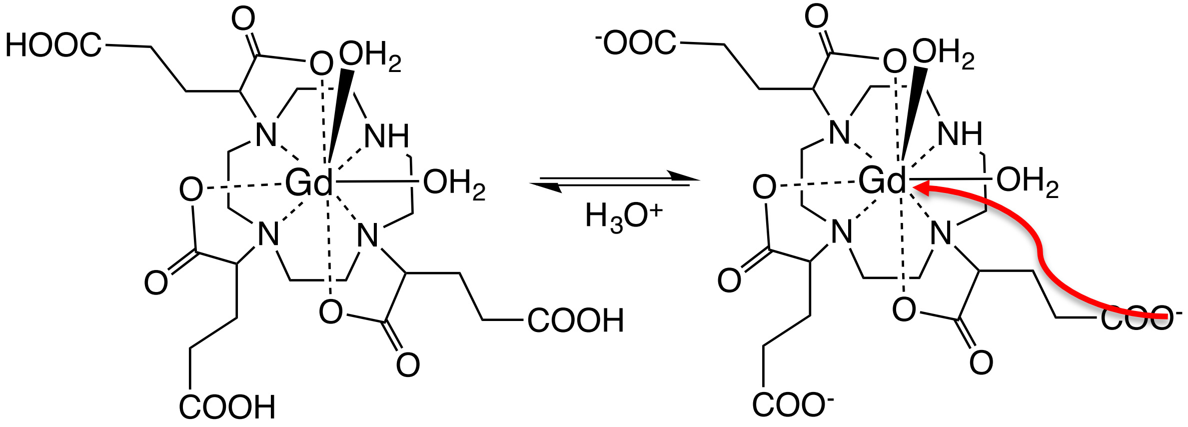


↘ q → ↘ relaxivité



$r_{1(PH\ 7.2)} = 5.4\ mM^{-1}\ s^{-1}$

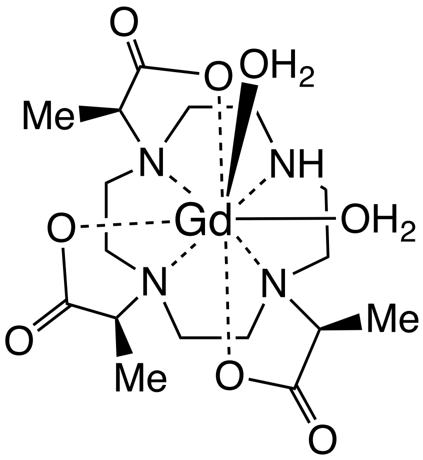
Anion binding can be prevented by introducing negative charges on the ligand (adding carboxylate groups)

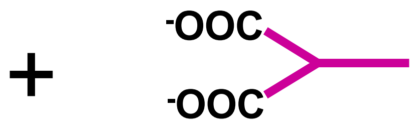
But we need to prevent binding to metal center!!

Increased charge on the ligand leads also to higher water exchange rate

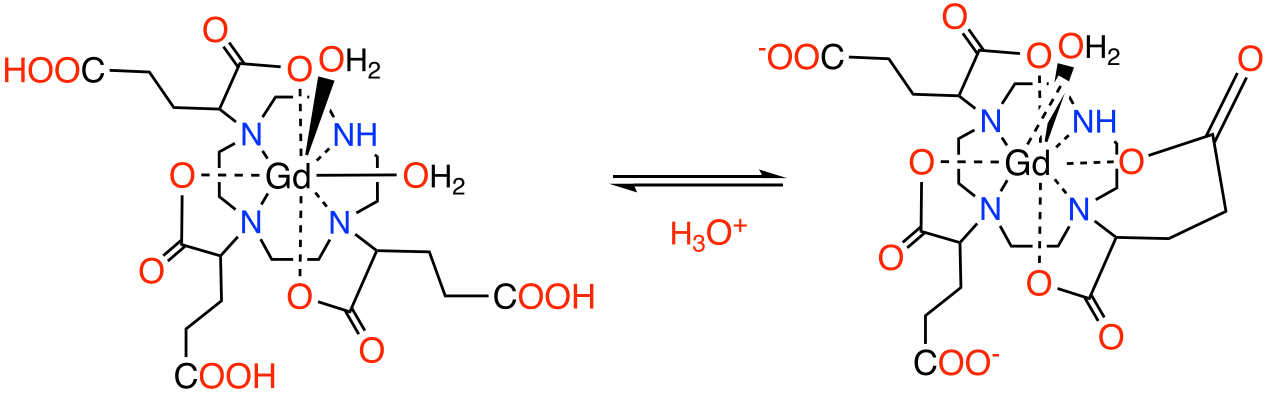
D. Parker 2001

Increasing the number of coordinated water molecules

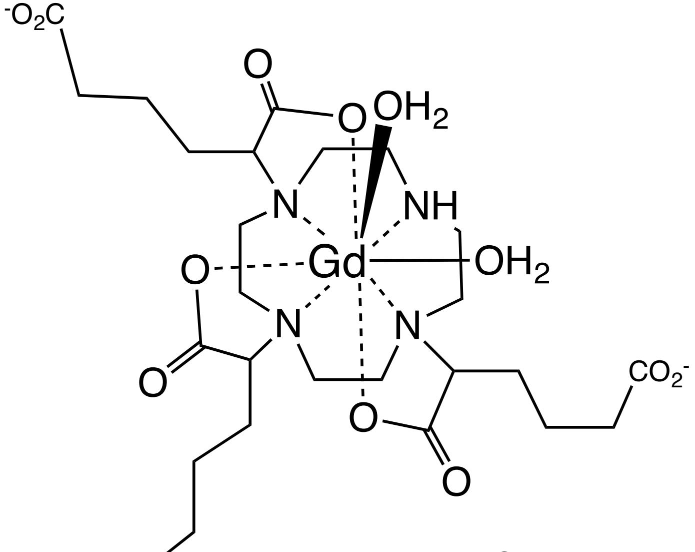




↘ q → ↘ relaxivité



$r_{1(PH\ 7.2)}$= 5.4 mM^{-1} s^{-1}



$[GdaDO3A]^{3-}$

$r_{1(PH\ 7.2)}$= 12.3 mM^{-1} s^{-1}

High relaxivity in serum

Anion binding can be prevented by introducing negative charges on the ligand (adding carboxylate groups)

But we need to prevent binding to metal center!!

Increased charge on the ligand leads also to higher water exchange rate

D. Parker 2001

Summary

-Spectroscopic states: small ligand field effects

-Ln(III) show narrow and low intensity absorption lines (f-f)
except for f-d transitions, Ln(II) M-L mixing lead to higher intensities

-Magnetic moment, spin-orbit coupling importance

-Application of magnetic properties in Shift reagents and MRI CAs

-Importance of ligand design in the development of MRI Gd Cas

-Stability and number of water molecules very important