Synthesis and characterization of molecular and supramolecular compounds based on 11th group metals for optoelectronics and/or biological applications

Rossana Galassi

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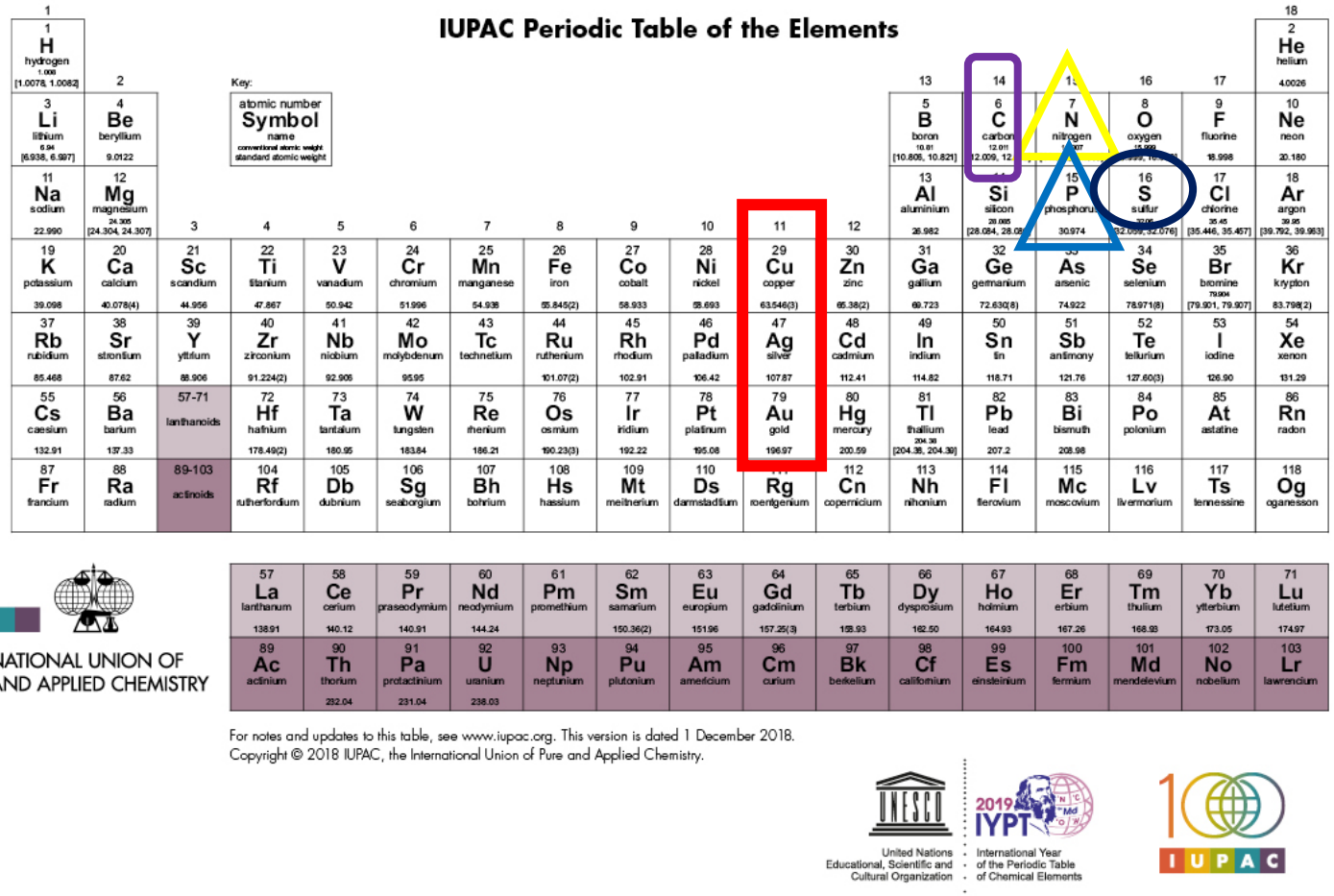
Synthesis and characterization



Synthesis and characterization of molecular and supramolecular compounds based on 11th group metals for optoelectronics and/or biological applications

- Optoelectronics is the study and application of electronic devices that detect control and emit the light
- Some important technological applications:
- Solar cells

- Lasers

- Sensors

- OLEDS

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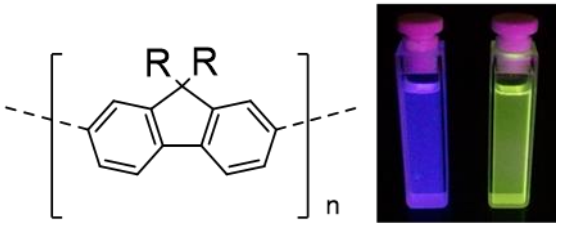
Most important classes of emitters:

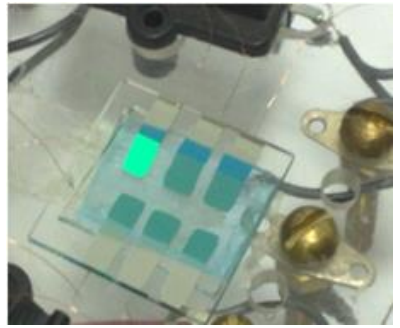
- Organic Polymers or small organic molecules with extended
- π-π* framework



Polyfluorene based emitters

- Rare earth metal coordination complexes

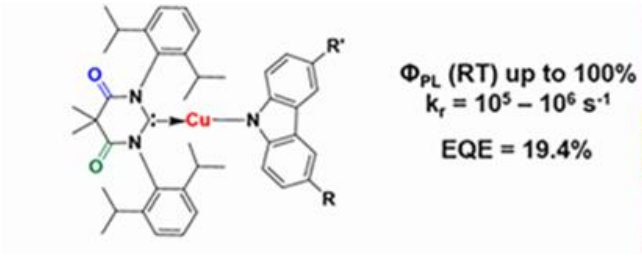
  (mostly Eu(III),Tb(III) and Tm(III))



Tb(III) based OLED

- Transition metal coordination
- complexes

  (mostly Re(I), Ir(III), Pt(II), Ru(II), Cu(I))



Copper(I) based emitter

Biological applications

What are biological properties of 11° group coordination compounds?

GOLD

Antiarthritic

Antiinfective (antiparasitic, antibacterial, antiviral)

Anticancer several cancers or leukemia (e.g., lung cancer, recurrent ovarian epithelial cancer, chronic lymphocytic leukemia)

COPPER

Anticancer Exhibit a potent *in vitro* **cytotoxicity** in H460 human lung carcinoma cells, comparable to that displayed by Adriamycin

SILVER

Antifungal properties

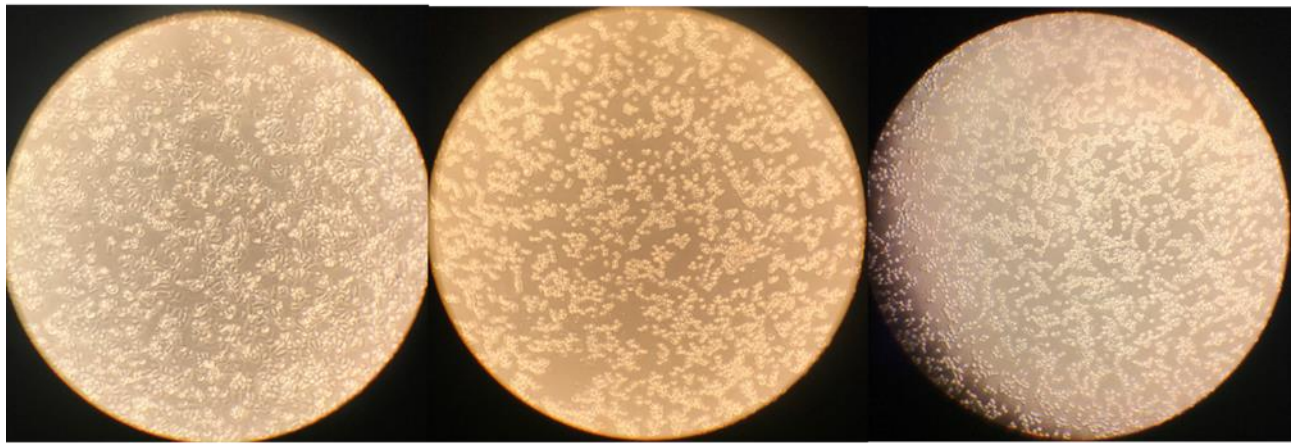
Antimicrobial properties

Ag(I) carbene **and phosphane** complexes is an emerging class of **anticancer agents**

biological applications

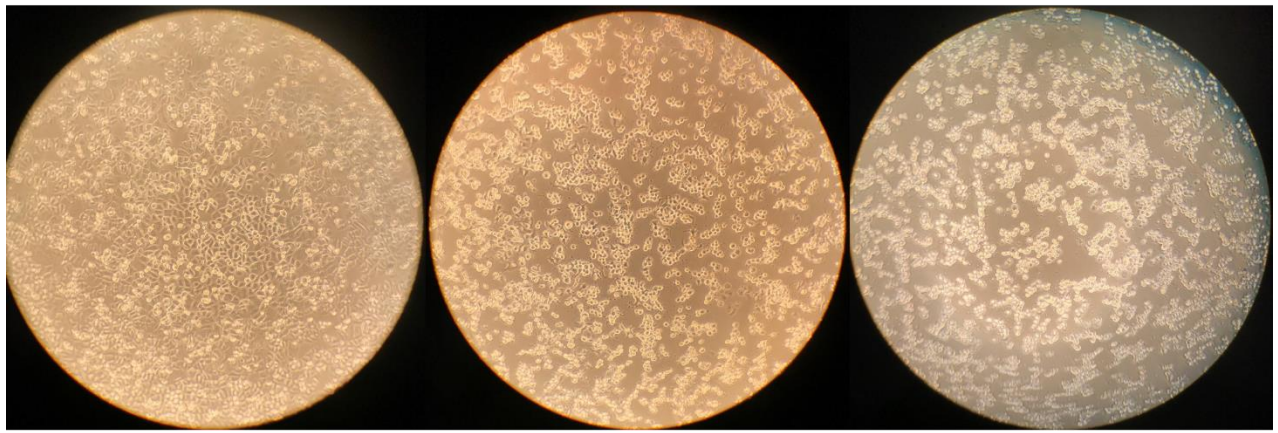
Anticancer activity

SKBR3 cells treated with 6 µM compound 5 and compound 6 for 4 hours



Control 6 µM compound 5 6 µM compound 6

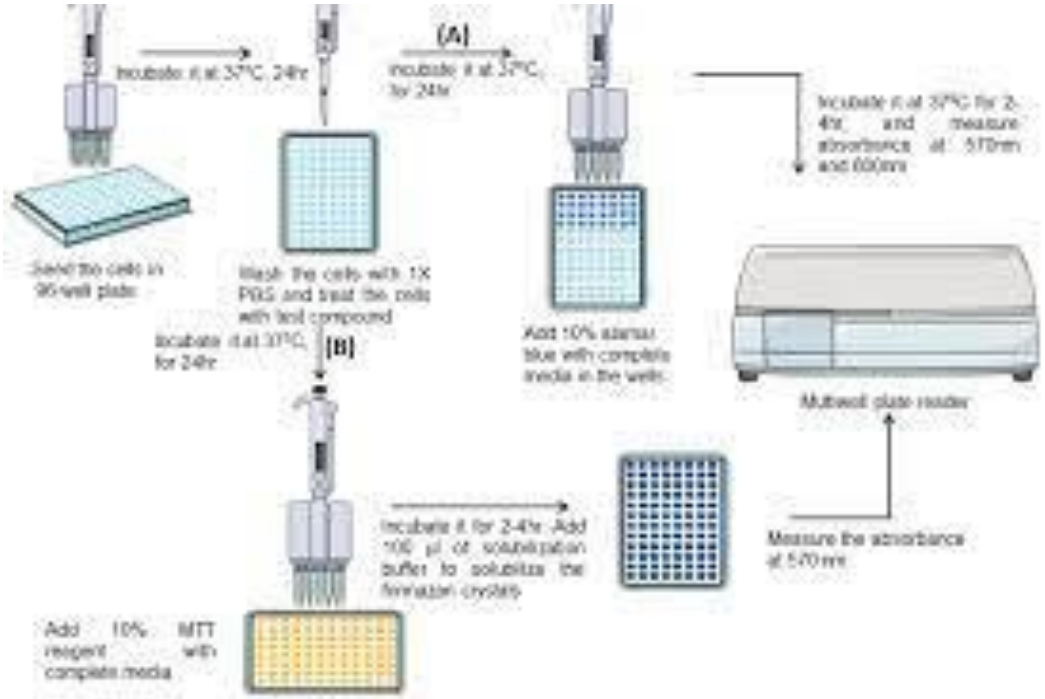
SKBR3 cells treated with 0, 3, 6 µM compound 6 for 12 hours



Control 3 µM compound 6 6 µM compound 6

biological applications

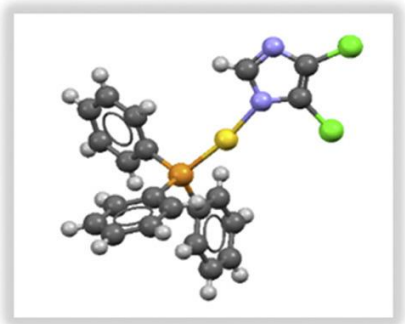
Anticancer activity: In vitro tests

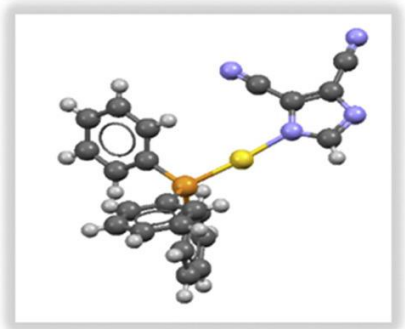


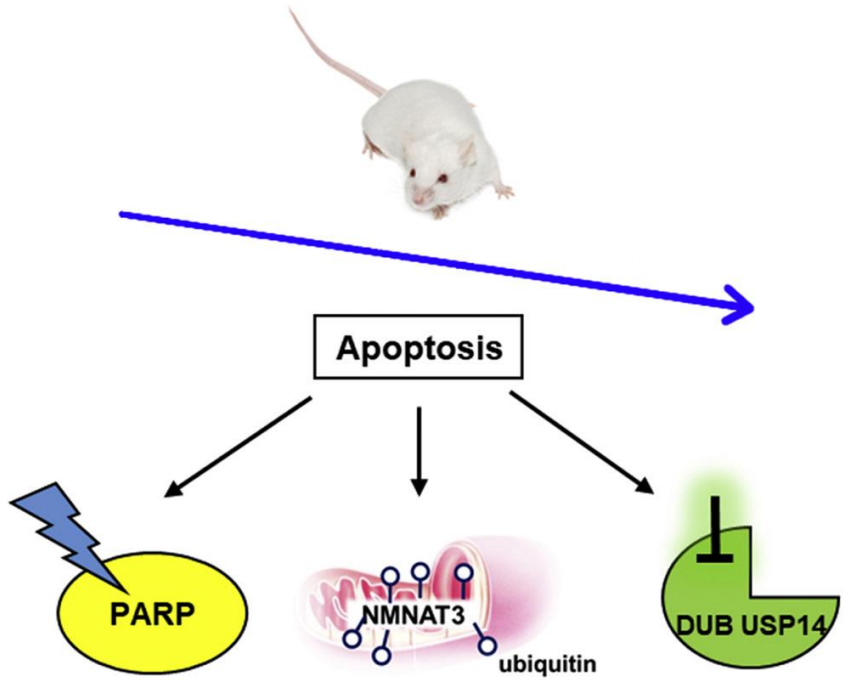
Compound	Cell Line	Time	IC_{50} Mean ± SD[a] [µM]
Compound 1	A17	24 h	11.38 ± 1.05
	MDA-MB-231	24 h	19.28 ± 1.06
	MDA-MB-468	24 h	13.62 ± 1.05
	HMLE/FoxQ1	24 h	7.41 ± 1.06
Compound 2	A17	24 h	11.95 ± 1.04
	MDA-MB-231	24 h	14.83 ± 1.05
	MDA-MB-468	24 h	11.25 ± 1.14
	HMLE/FoxQ1	24 h	9.27 ± 1.06
Cisplatin	A17	24 h	15.86 ± 1.17
	MDA-MB-231	48 h	50.49 ± 2
	MDA-MB-468	24 h	32.50 ± 1.12
	HMLE/FoxQ1	48 h	34.12 ± 2.17

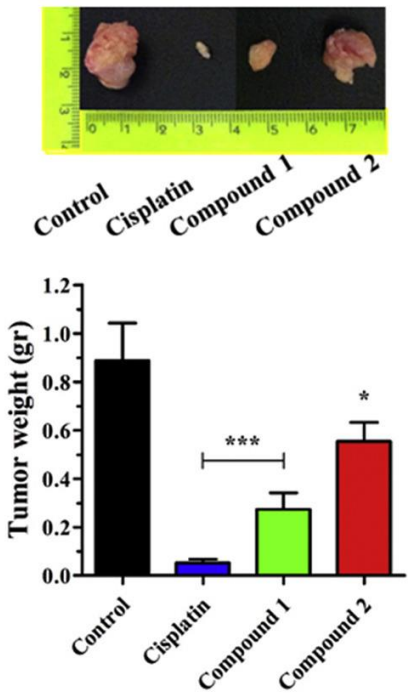
biological applications

Anticancer activity: In vivo tests



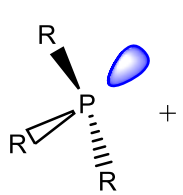






Galassi et al European Journal of Medicinal Chemistry, Volume 155, 2018, 418-427,ISSN 0223-5234, https://doi.org/10.1016/j.ejmech.2018.06.002.

Synthesis and characterization: classic methods



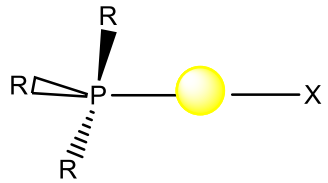
+

Cu+

Ag+

Au+

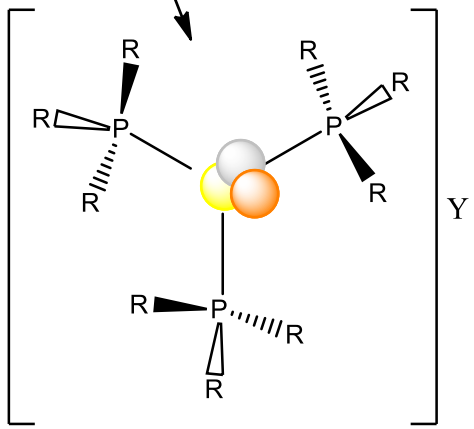
1:1

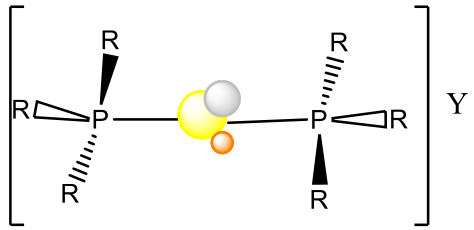


X = Heterocycles, Halides, Counterions

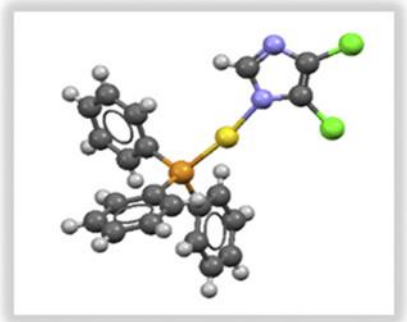
1:2

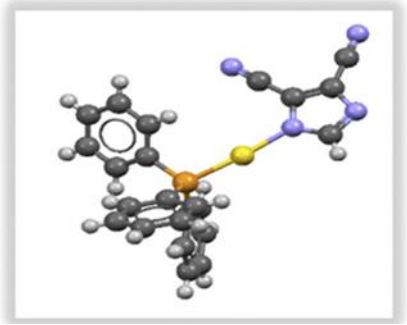
1:3

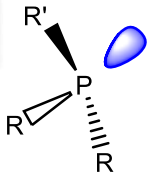




Y = Counterions



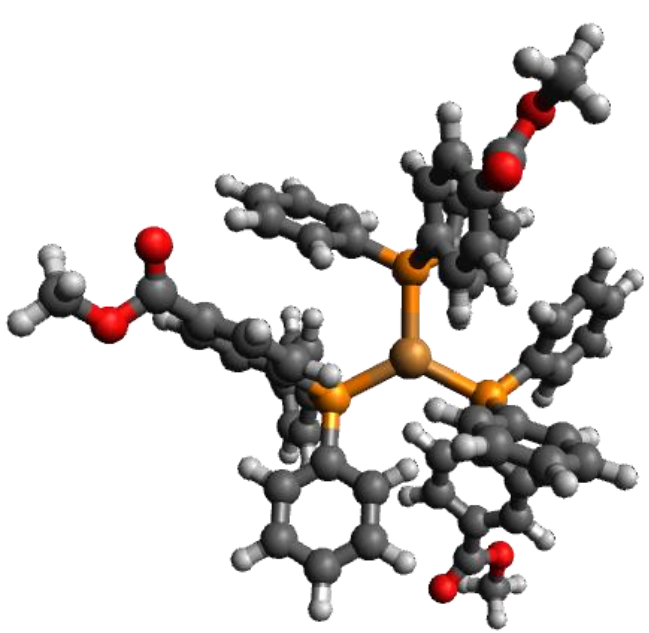


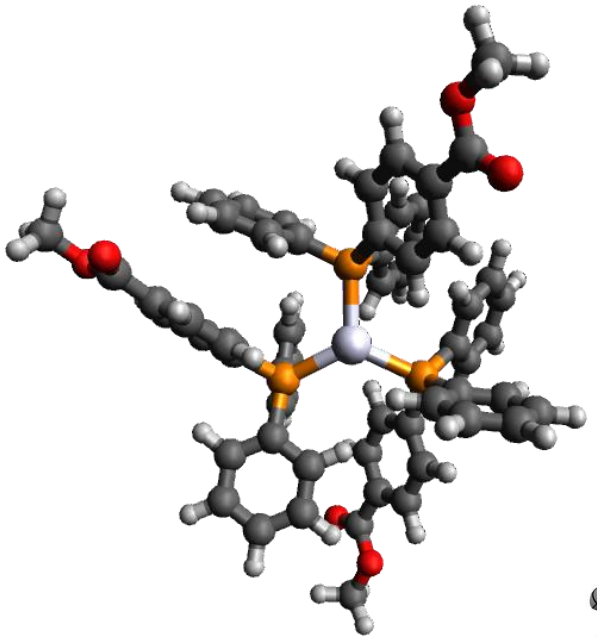


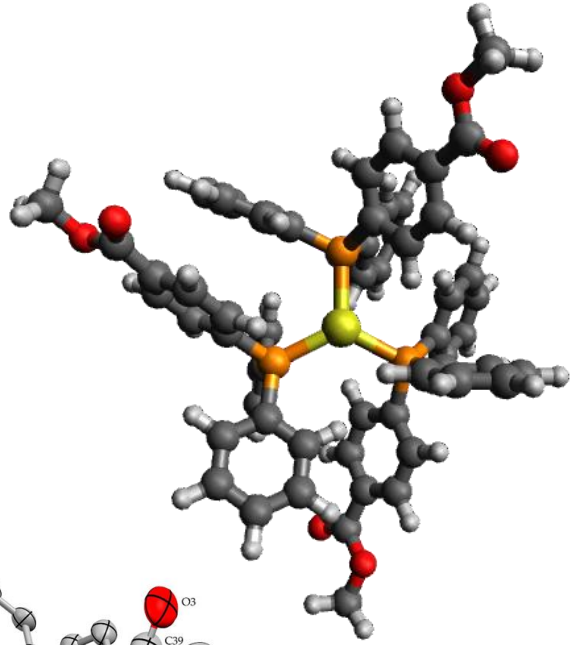
R' = 4-diphenyl-phosphane benzoic acid and ester, or amide derivatives

Characterization of molecular compounds

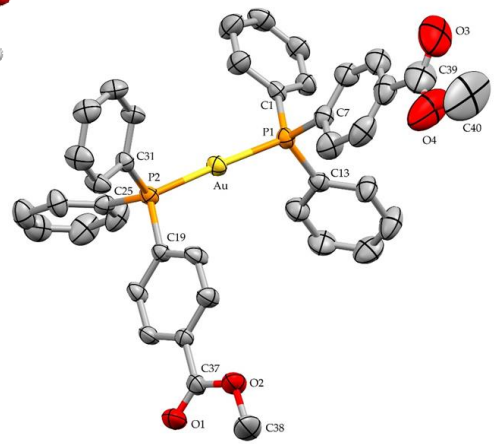
DFT OPTIMIZATION OF COMPLEXES $[M(PR_3)_3]^+$ (M = Cu, Ag, Au)





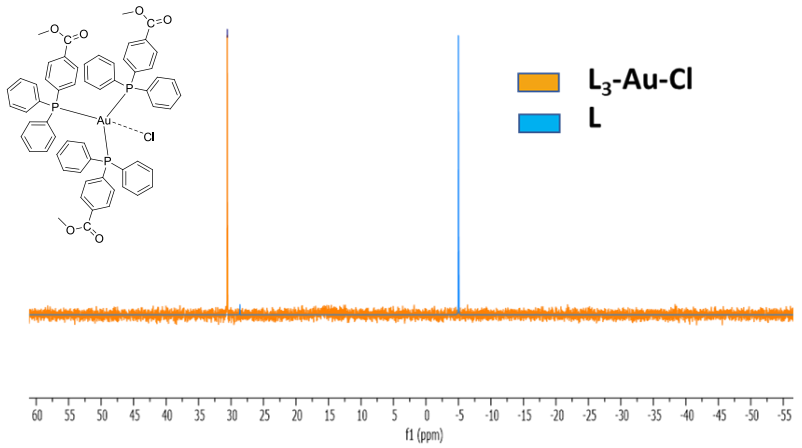


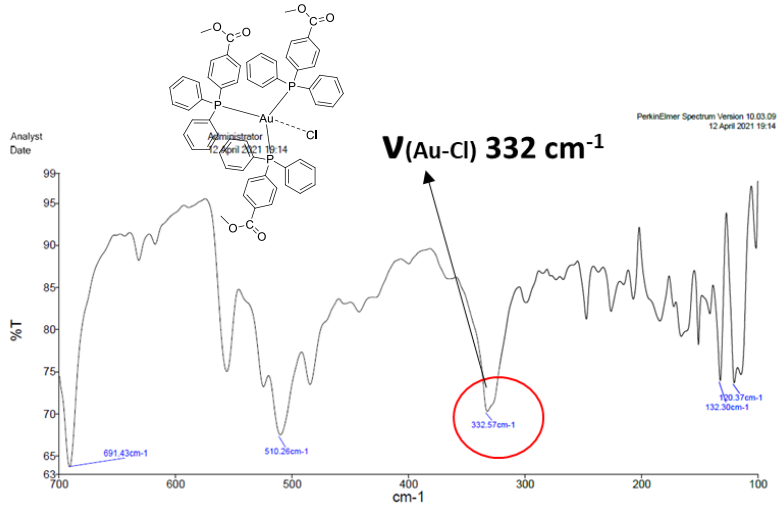
X-ray crystal structure determination

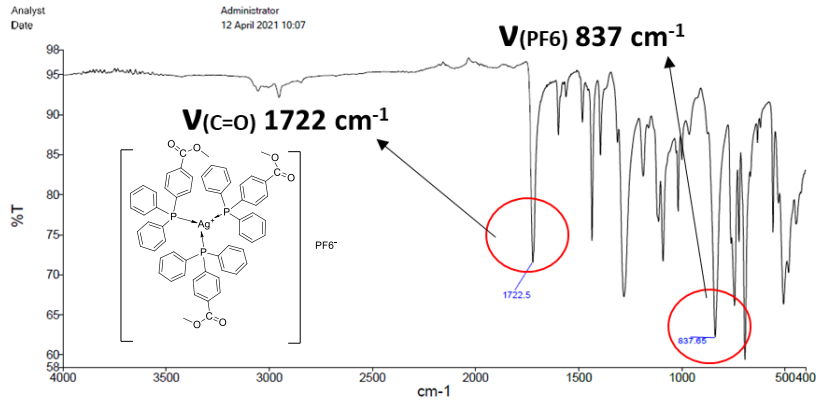


Characterization of molecular compounds

L_3-Au(I)-Cl\		L3-Cu(I)-BF_4		L3-Ag(I)-PF_6	
Calculated (%)	Found (%)	Calculated (%)	Found (%)	Calculated (%)	Found (%)
C 60,39	C 60,16	C 64,85	C 65,03	C 59,37	C 59,09
H 4,31	H 4,47	H 4,63	H 4,68	H 4,24	H 4,24







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Characterization: in vitro acitivity

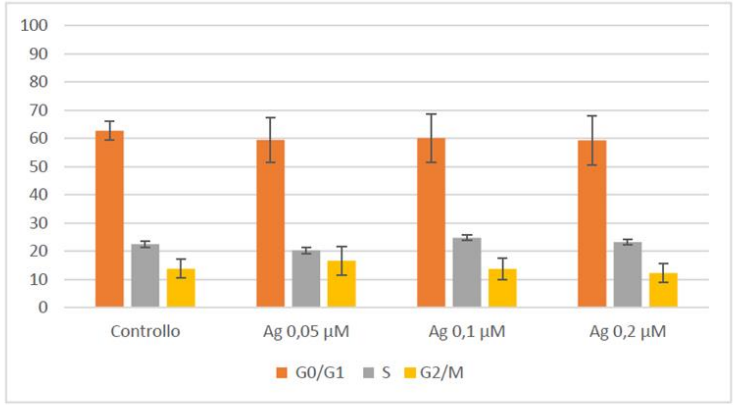
Compounds	A2780 (GI_{50} µM)	A2780cis (GI_{50} µM)	HT-29 (GI_{50} µM)	MDA-MB-231 (GI_{50} µM)
Ligand (**L**)	>20	>20	> 20	> 20
L_3-Ag-PF_6	0, 17 ± 0,07	0,94 ± 0,10	2,98 ± 0,40	4,33 ± 0,45
L_3-Au-Cl	0,17 ± 0,03	4,68 ± 0,86	8,17 ± 0,61	12,64 ± 0,93
L_3-Cu-BF_4	1,78 ± 0,15	4,40 ± 0,18	4,80 ± 0,50	10,78 ± 0,88
Cisplatin (reference)	1,08 ± 0,35	4,50 ± 0,88	3,02 ± 0,47	23 ± 0,53

- The ligand (**L**), is **not active** in all the studied cell lines
- The most active complex is the **L_3-Ag-PF_6**
- **GI_{50}** of the **L_3-Ag-PF_6** on the *A2780cis* is almost 5 times smaller with respect to the cisplatin
- The **GI_{50}** of the **L_3-Au-Cl** and the **L_3-Cu-BF_4** are comparable in almost all studied cell lines
- The **GI_{50}** of the **L_3-Au-Cl** is the same of the **L_3-Ag-PF_6** for the *A2780* cell line.

Characterization: in vitro acitivity

5.1 Cellular cycle alterations

Figure 1 and 2: A2780 percentages in the different cellular phases



	Controllo	Ag 0,05 µM	Ag 0,1 µM	Ag 0,2 µM
G_0/G_1	62.7 ± 3.3	59.5 ± 7.9	60.1 ± 8.4	59.3 ± 8.7
S	22.5 ± 1.0	20.3 ± 2.1	24.8 ± 5.9	23.2 ± 3.8
G_2/M	13.8 ± 3.3	16.6 ± 5.1	13.7 ± 3.8	12.3 ± 3.3

Treatment: 48 ore Fluorophore: Propidium iodide

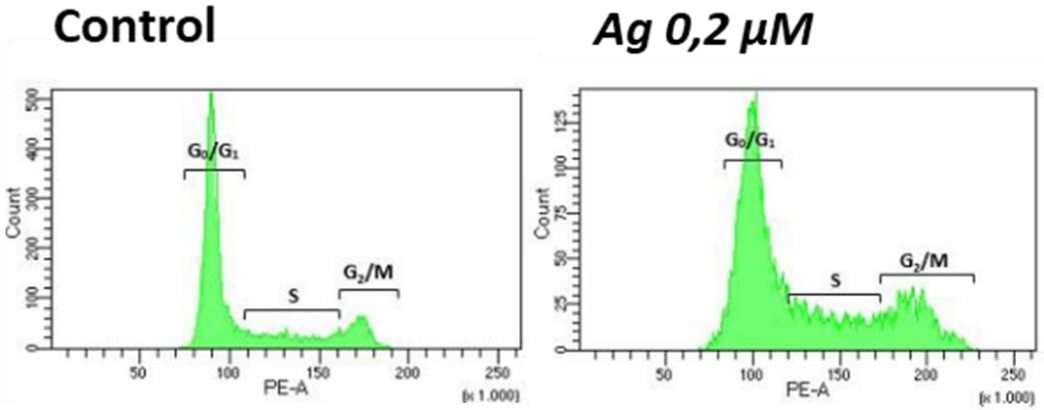


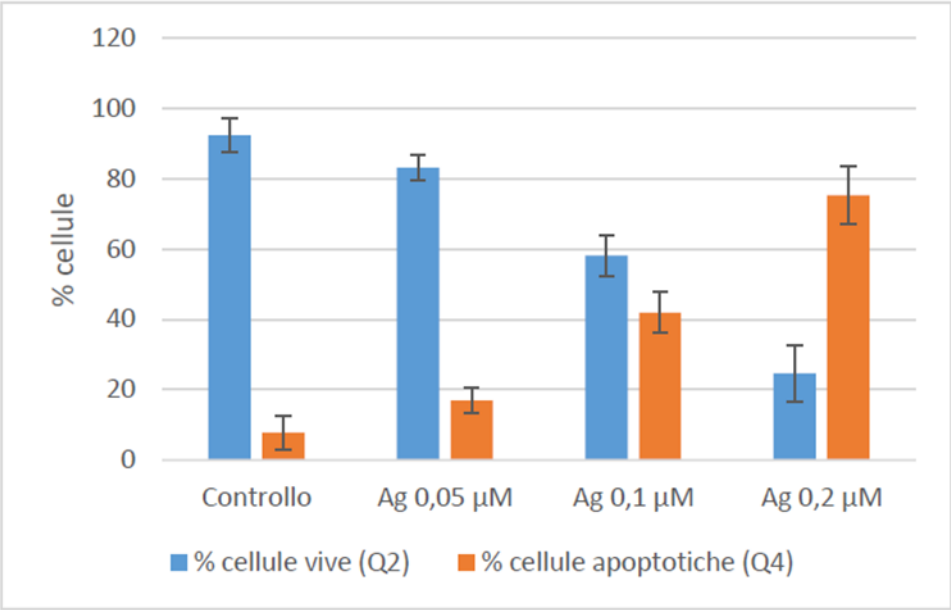
Figure 3: Cytofluorimetric analysis of the A2780 cellular cycle of untrated (control) and Silver treated (Ag 0,2 µM) cells.

- Cytofluorimetric analysis highlights that the **L_3-Ag-PF_6** complex does not modify the cellular cycle

Characterization: in vitro acitivity

5.3 Mitochondrial Membrane Depolarization

Figure 6: histogram (up) and table (down) of A2780 cells percentage.



	Controllo	**Ag** 0,05 µM	**Ag** 0,1 µM	**Ag** 0,2 µM
% cellule vive	92.2± 4.8	83.1 ± 3.5	58.1 ± 5.8	24.7 ± 8.1
% cellule apoptotiche	7.8 ± 4.8	16.9 ± 3.7	41.9 ± 5.8	75.3 ± 8.1

Treatment: 48 hours
Fluorophore: JC1

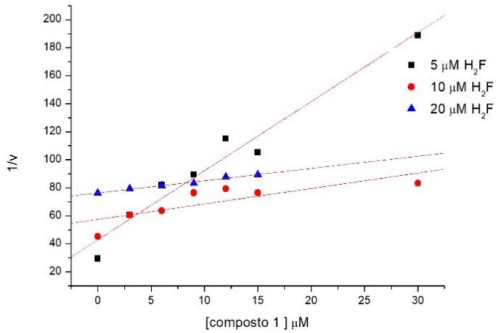
Q2: healthy cells with high mitochondrial membrane potential. Fluorescence in red region

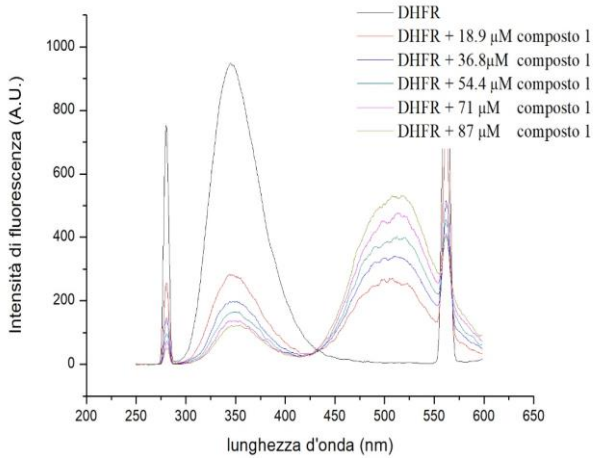
Q4: Apoptotic cells with collapsed mitochondrial potential. Fluorescence in the green region

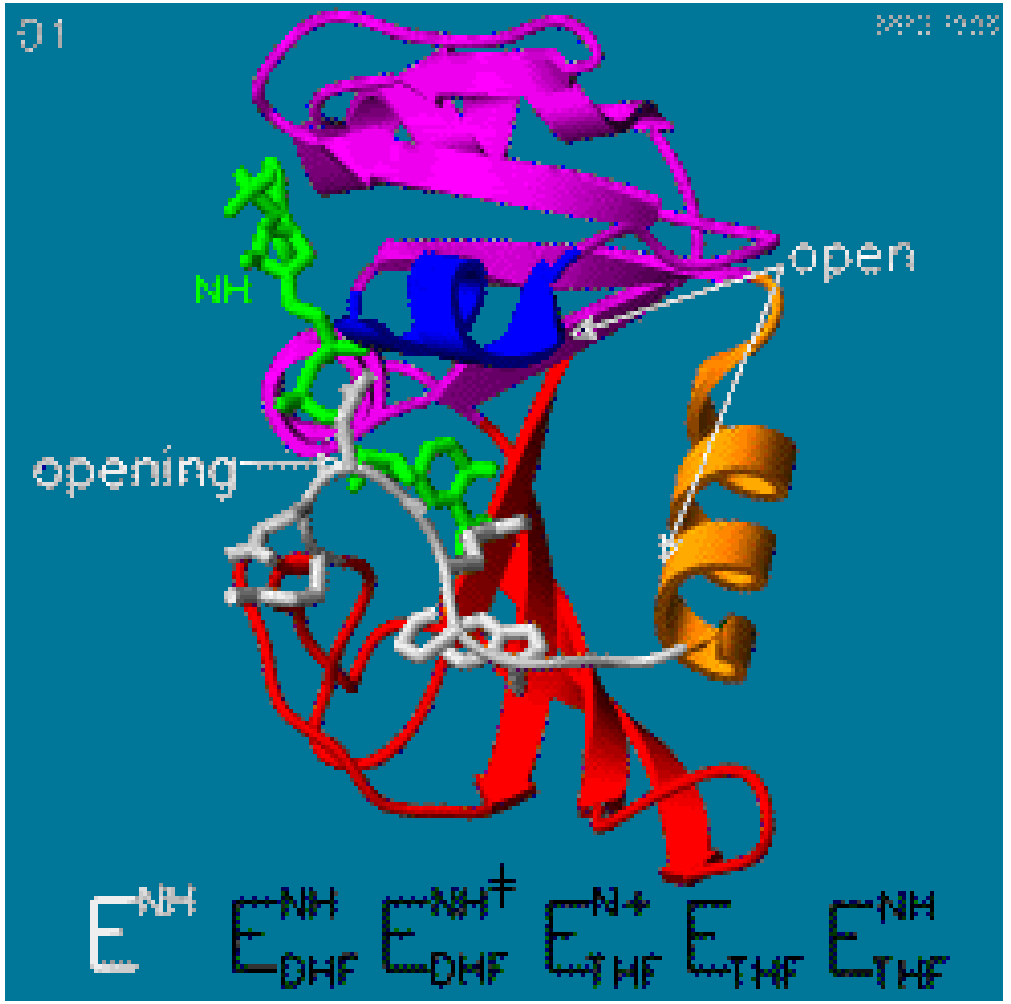
- The treatment of **A2780** cells with growing concentrations of **Silver** complex increases the percentage of cells with collapsed **mithocondrial** transmembrane potential

Characterization: in vitro activity

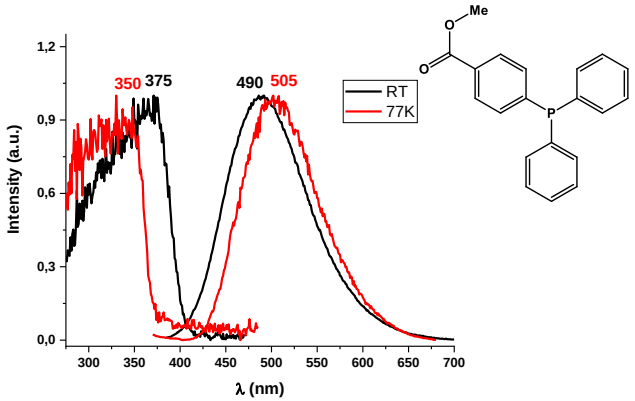
5.4 Enzyme inhibition



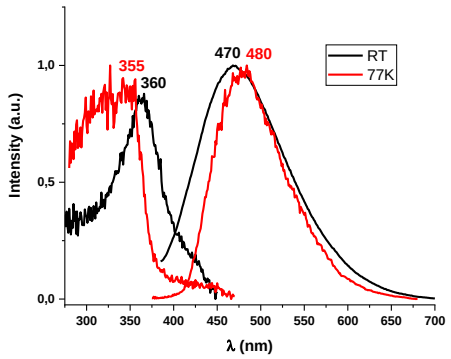




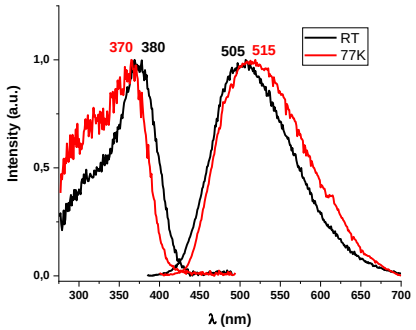
Characterization: emissive properties



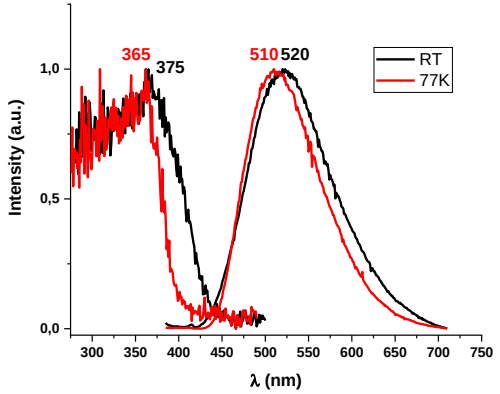
L_3AgPF_6)



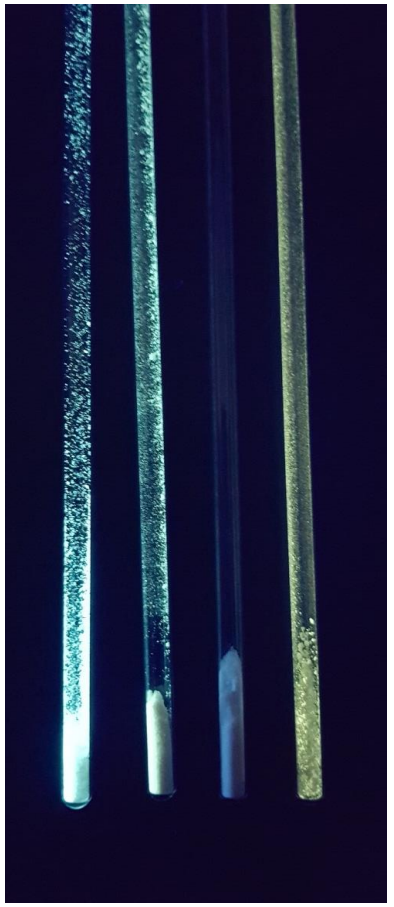
(L_3CuBF_4)



(L_3AuCl)

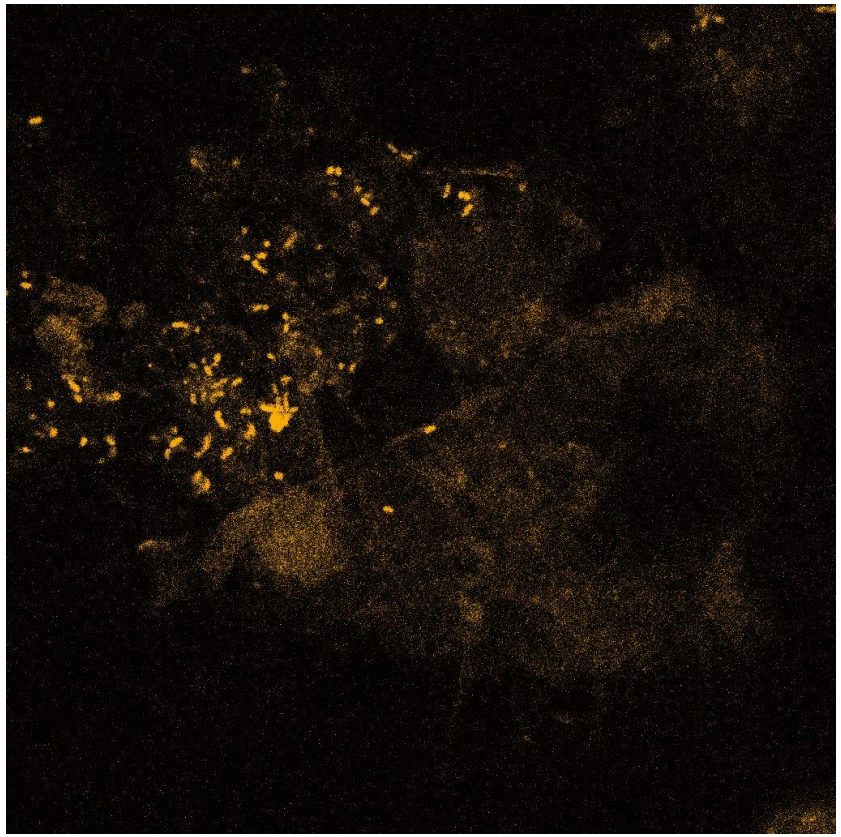


L Cu Ag Au



Future remarks

5.5 Theranostics



Composto di oro luminescente all'interno di una cellula tumorale A2780 visto con il microscopio confocale

Biological applications: collaborations

Dipartimento di Scienze del Farmaco
Dipartimento di Medicina Molecolare

- School of Biosciences and Veterinary Medicine
- School of Drugs and Health Products Sciences,

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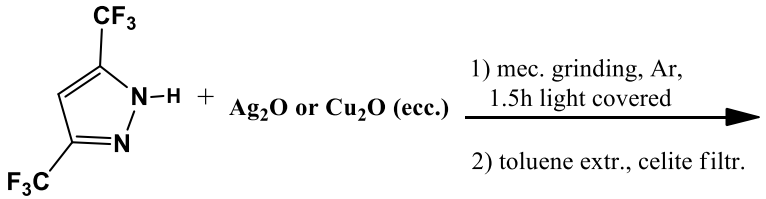
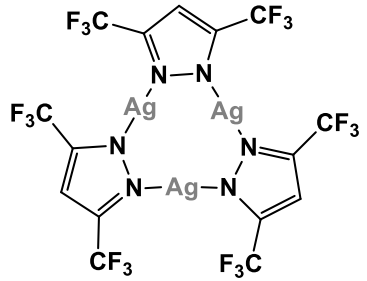
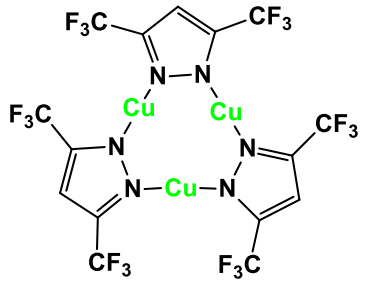
Molecular and supramolecular … means what?

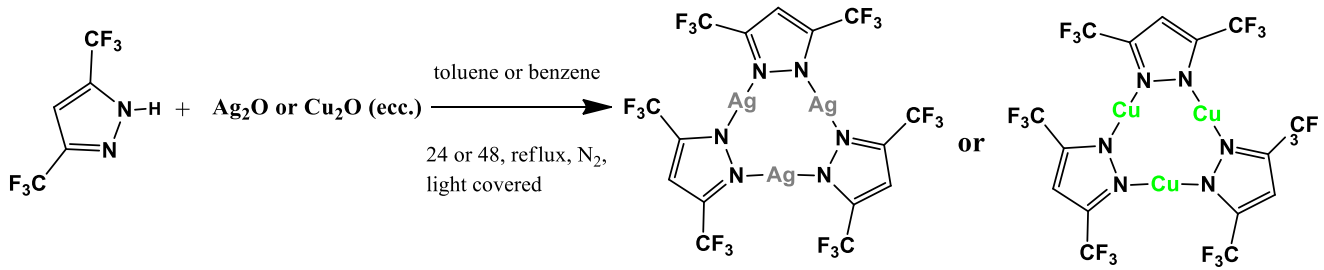




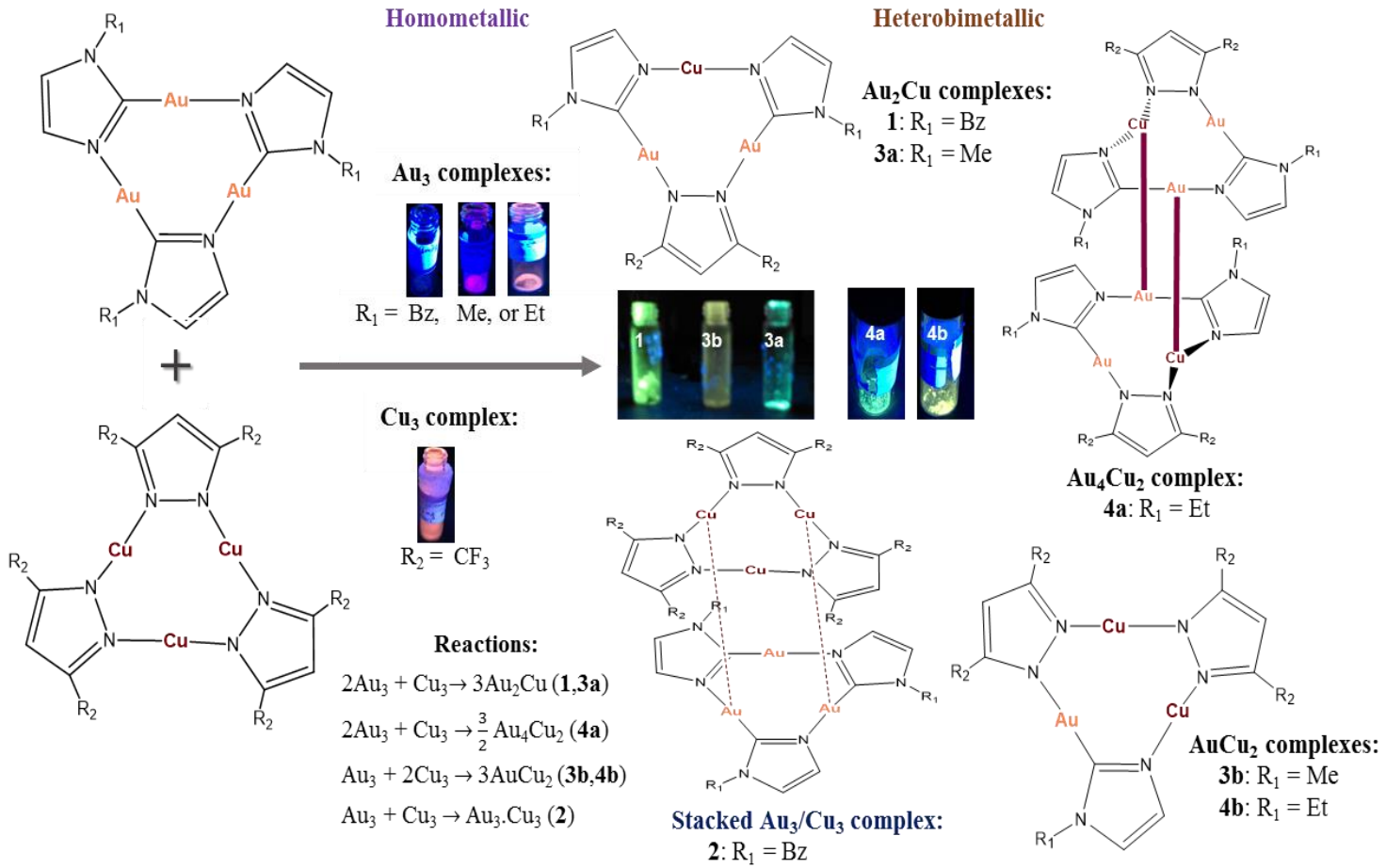
or



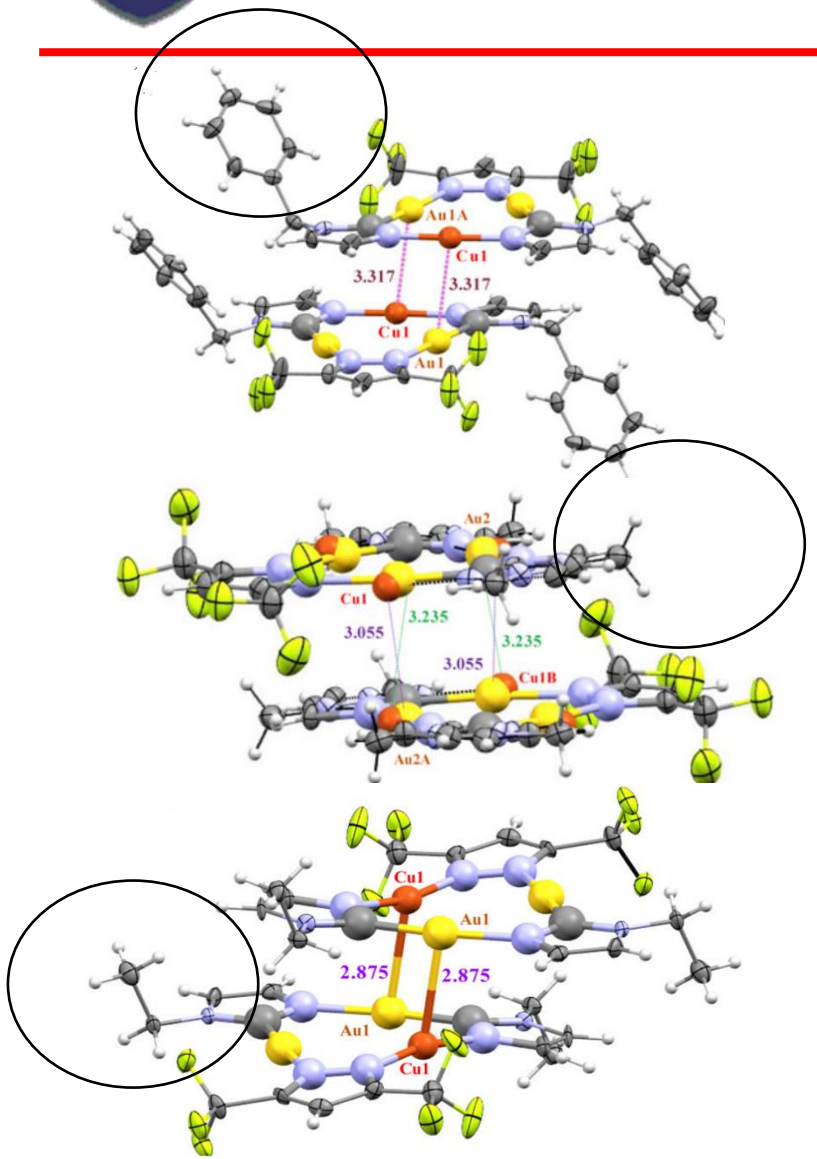
Conventional syntheses

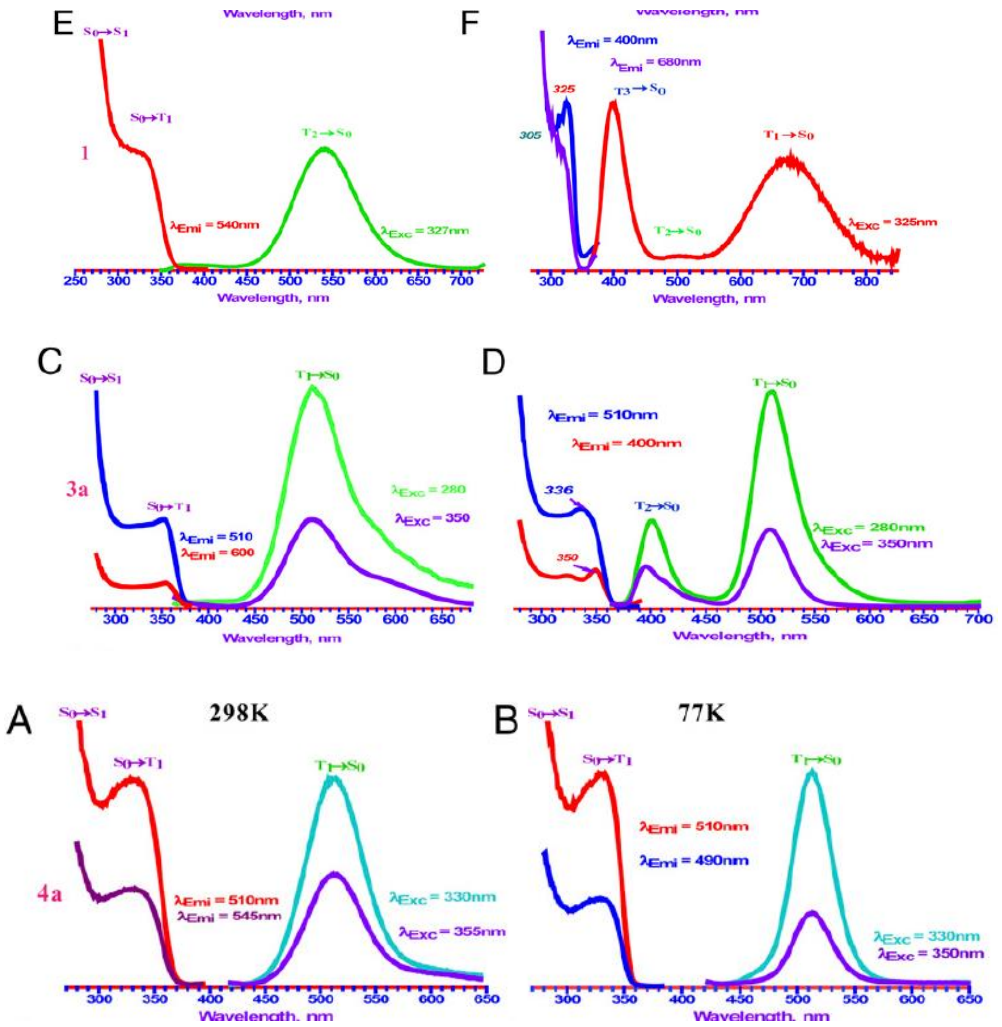


Molecular → supramolecular



Proprietà emissive





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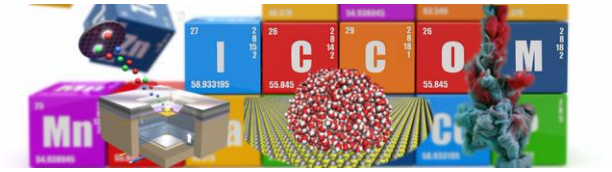
Galassi et al Inorg. Chem. 2019, 58, 22, 15303–15319

Mohammad Omary



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Grazie!