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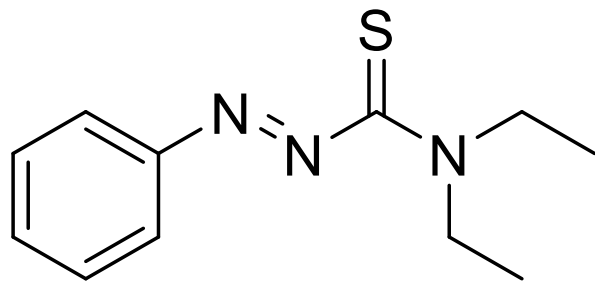
**ARYLAZOTHIOFORMAMIDE (ATF)  
LIGANDS: A FLEXIBLE FOUNDATION FOR  
COORDINATION COMPLEXES AND THEIR  
DIVERSE BIOLOGICAL ACTIVITY**

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**DEPARTMENT OF CHEMISTRY**  
**PH.D. FIFTH SEMESTER**

# OUTLINES

- I Background and Introduction of the ATF ligands**
- I Applications of the ATF ligands**
- I Coordination and Binding of Cu(I) salts with ATF ligands**
  - **Electronic effect**
  - **Steric effect**
- I Biological Activities**
  - **Antimicrobe**
  - **Anti-cancer activities**
- I Conclusion and Further work**
- I Acknowledgement**

# BACKGROUND AND INTRODUCTION

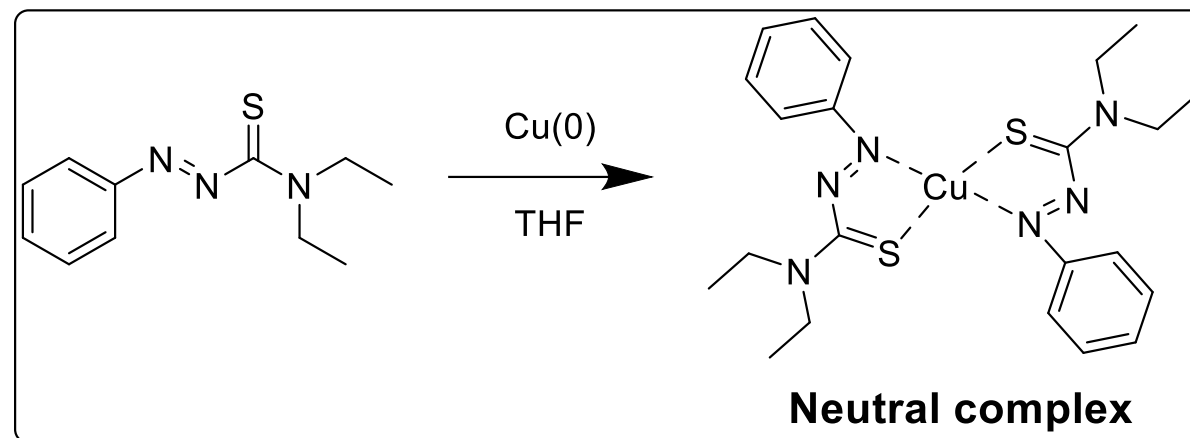
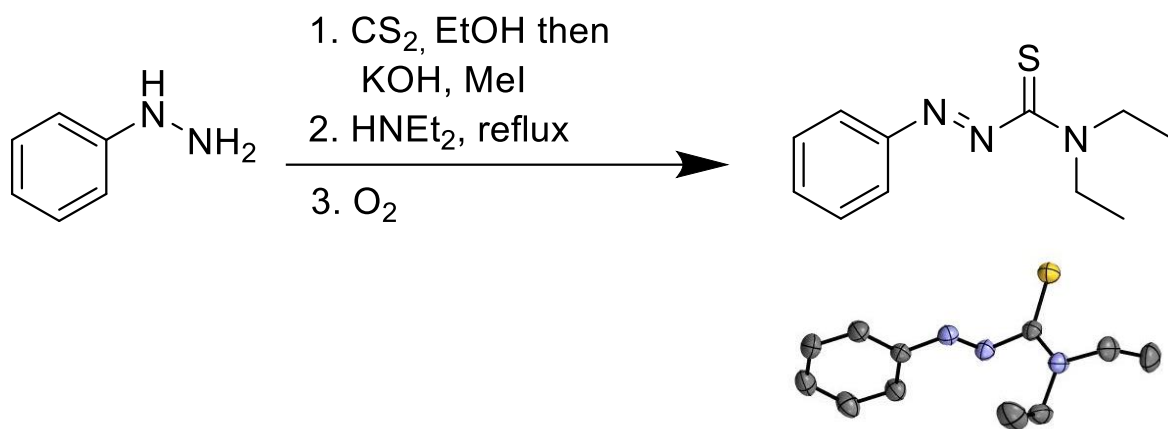


**N,N-diethylphenylazothioformamide**



- ATF ligands, first synthesized in the late 70's, react with zerovalent late transition metals: Cu, Pt, Pd, and Ni, to produce 2:1 complexes.
- Used for metal nanoparticle removal from polymers and shown to dissolve solid metals.

## Synthetic scheme



Bechgaard, K. *Acta Scan. Chem.* **1977** A31 683-688.

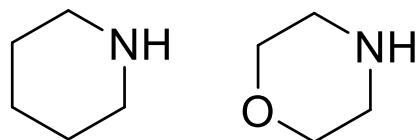
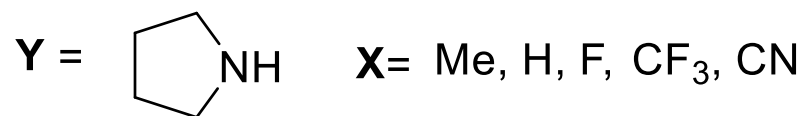
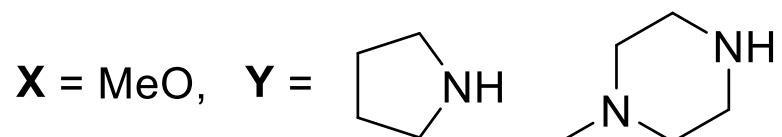
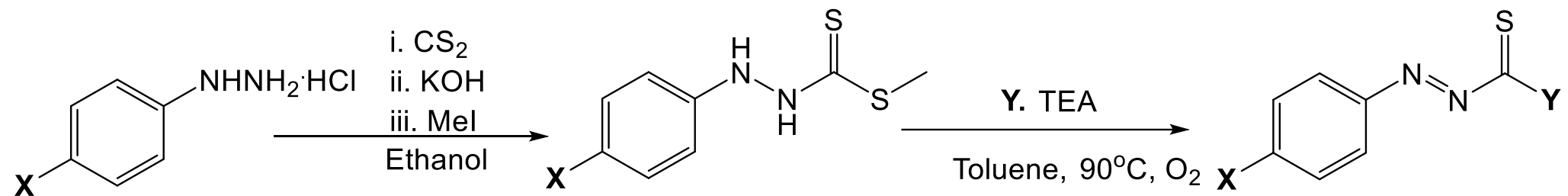
Nielsen, K.T.; Harris, P.; Bechgaard, K.; Krebs, F.C. *Acta Cryst. B.* **2007** 63B, 151-6.

Krebs, F.C. et al. *Synthesis* **2006**, 1639-44.

Waynant et al. *Eur. J. Inorg. Chem.* **2017**, 47, 5576-81

# SYNTHESIS OF ATF LIGANDS

## Synthetic scheme of ATF



# Applications of ATF ligands

```
graph TD; A[Applications of ATF ligands] --> B[Coordination Mechanism Modelling]; A --> C[Biological studies]; A --> D[Catalysis]; A --> E[Metal separation and recovery];
```

Coordination  
Mechanism  
Modelling

Biological  
studies

Catalysis

Metal  
separation  
and recovery

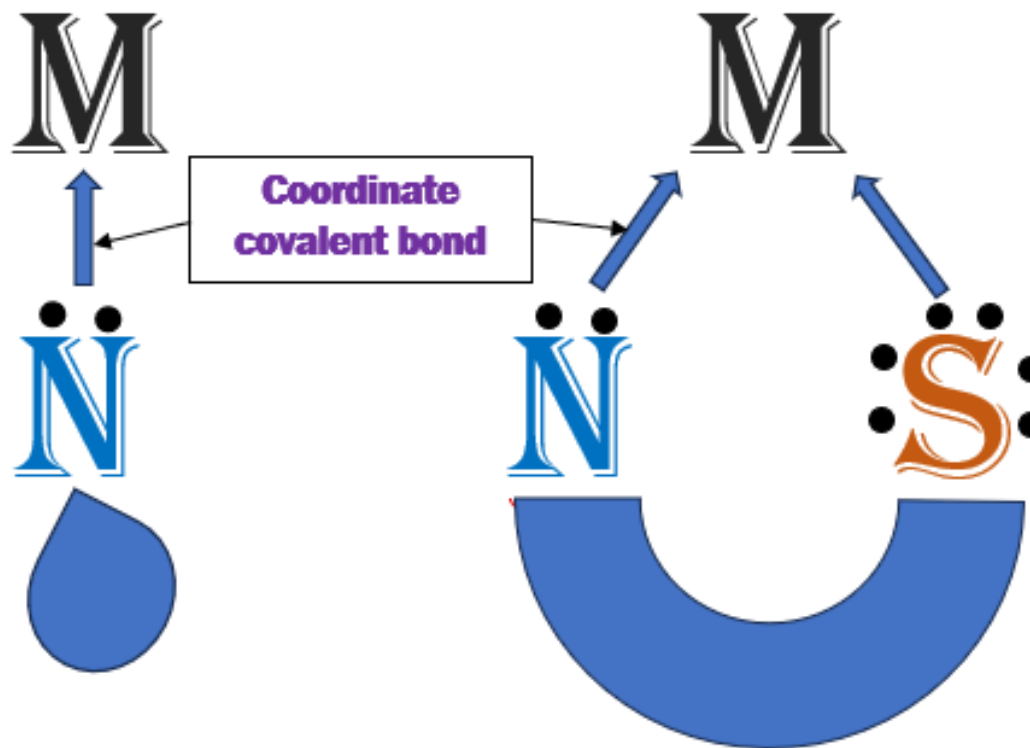
# METAL COORDINATION



Ligands with lone pair

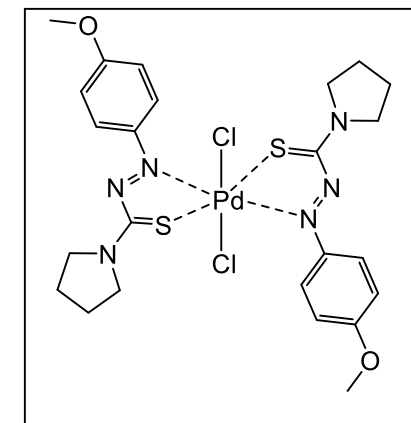
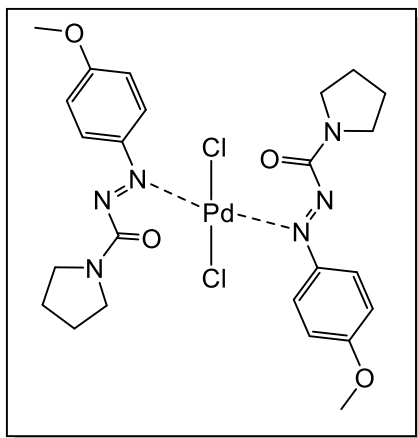
Vacant orbital in metal ion

Formation of coordinate covalent bond



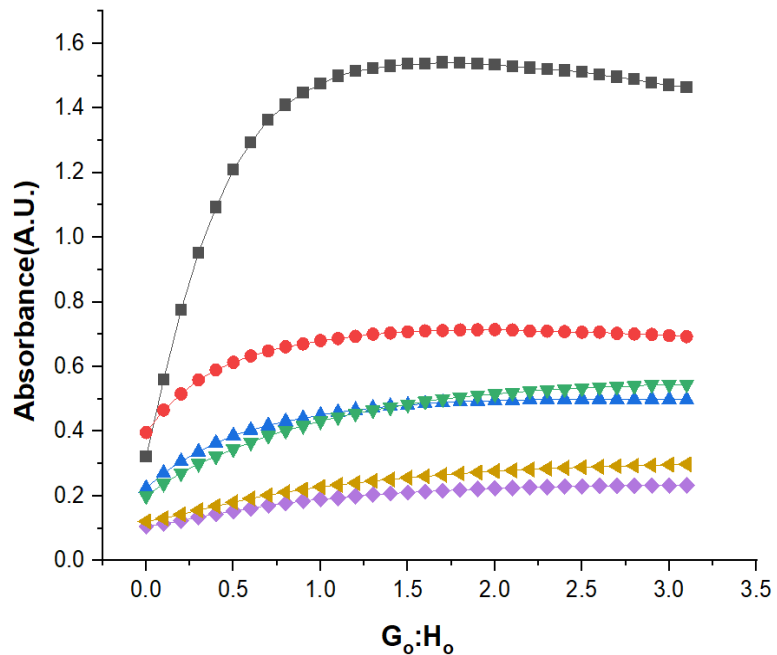
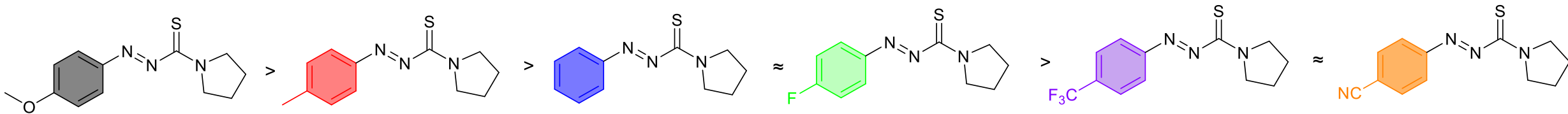
Monodentate ligand

Bidentate ligand

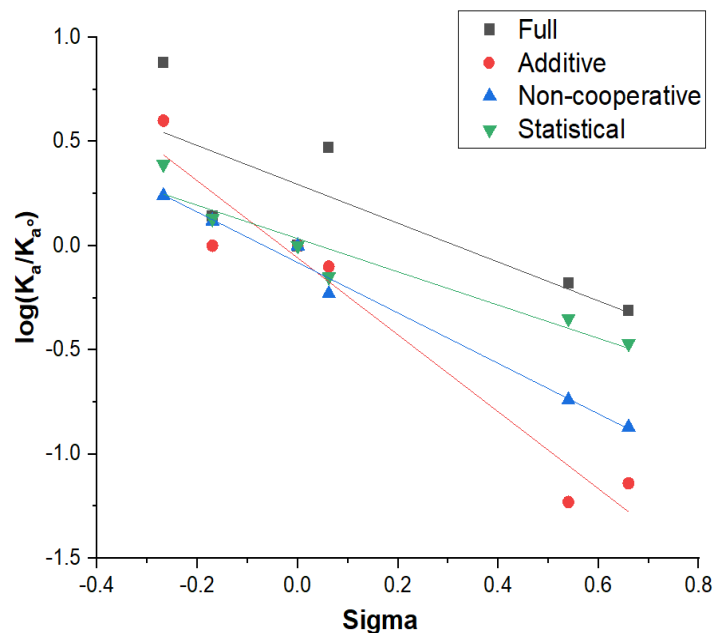


# Substitution effects on ATF ligands for binding of metals

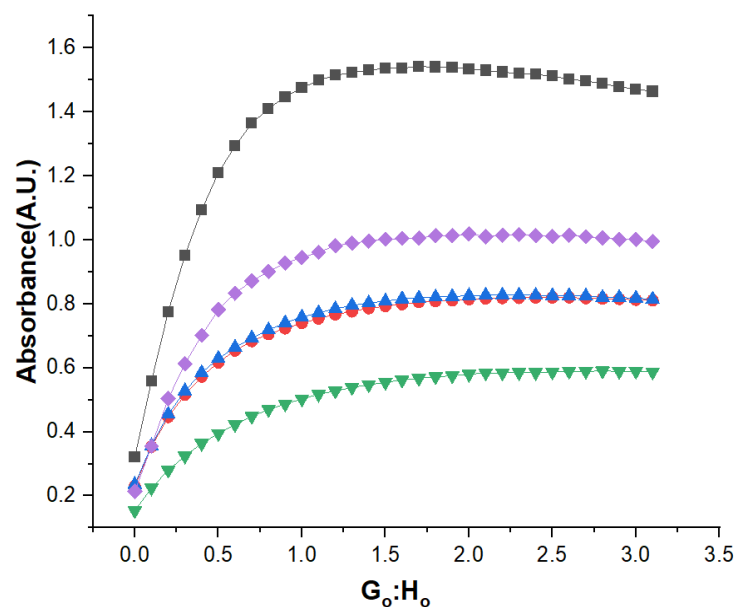
## Electronic Effect on binding Cu(I) salts with ATFs (graph 1)



Graph1: Binding isotherm of CuBr with various ATF ligands

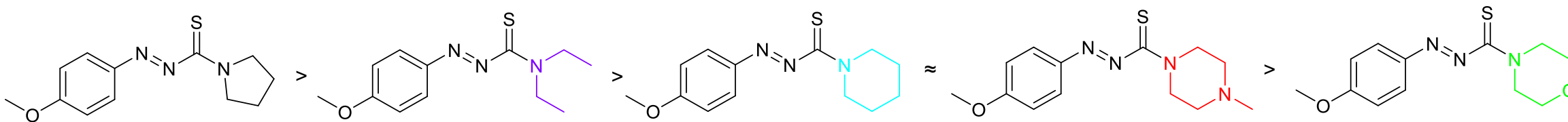


Hammett Plot of Cu(I)Br with ATF ligands

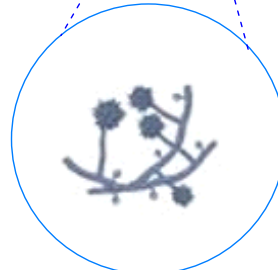
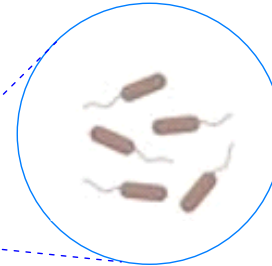
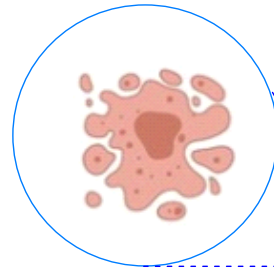
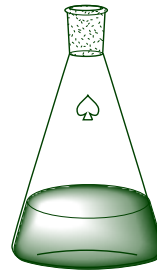
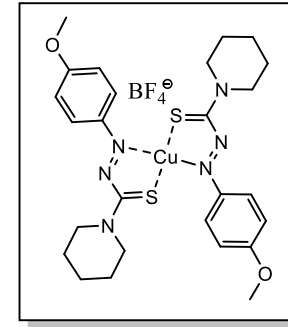
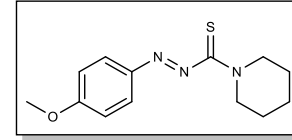
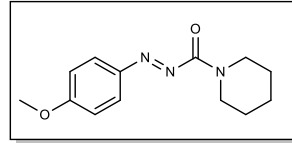
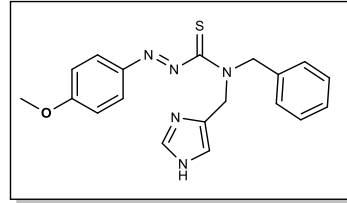
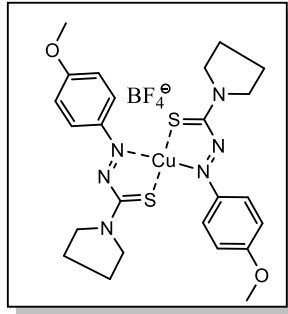


Graph 2: Binding isotherm of Cu(I)Br with various ATF ligands

## Steric Effect on binding Cu(I) salts with ATFs (graph 2)



# BIOLOGICAL STUDIES



## Anticancer

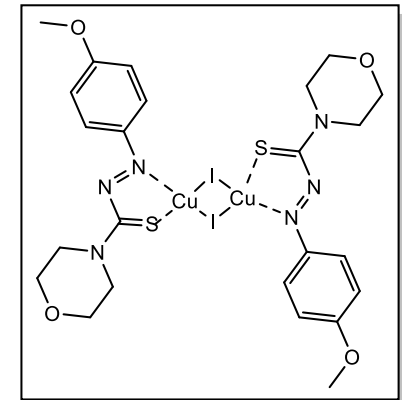
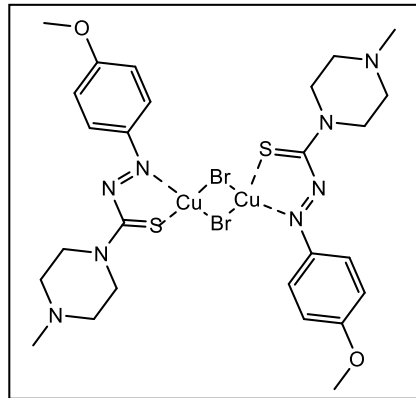
A549  
HT-1080  
MDA-MB-231  
K562  
MRC-5  
HFF

## Antibacterial

*Staphylococcus aureus*  
*Escherichia coli*

## Antifungal

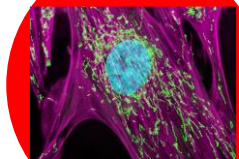
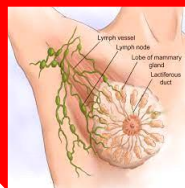
*Candida albicans*





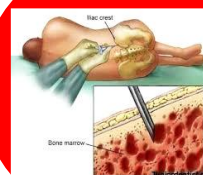
# Cancer cell lines with their location on human body

$IC_{50} = 0.99 \mu\text{M}$ ,  
MDA-MB-231  
Human breast  
cancer cell line



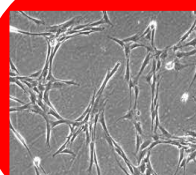
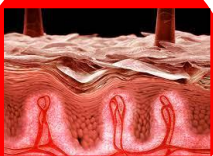
$IC_{50} = 1.5 \mu\text{M}$ ,  
MRC-5, Human  
fetal lung fibroblast  
cancer cell line

$IC_{50} = 12.7 \mu\text{M}$   
A549  
Lung tissue  
cancer cell line

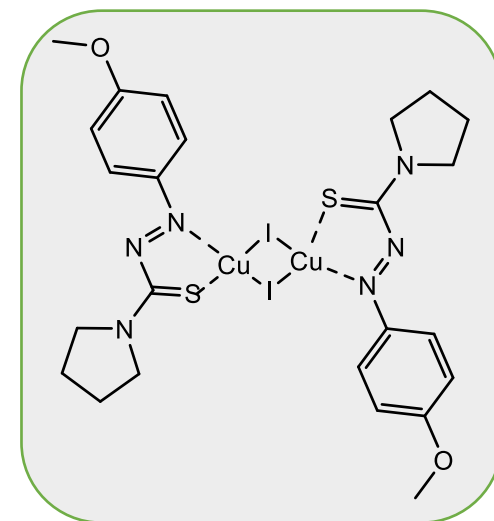
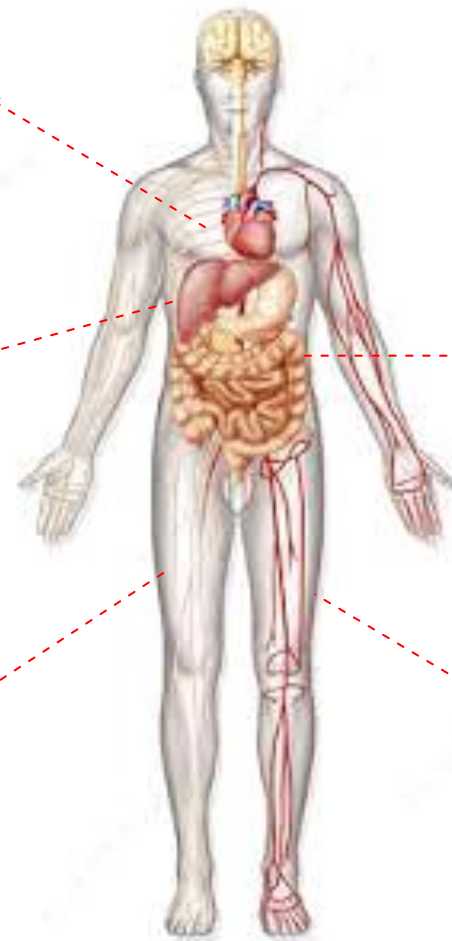


$IC_{50} = 1.1 \mu\text{M}$ ,  
K-562  
bone marrow  
cancer cell line

$IC_{50} = 2.2 \mu\text{M}$ ,  
HFF, Human  
foreskin fibroblasts  
cancer cell line



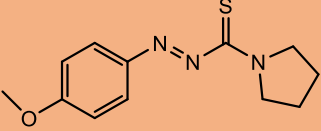
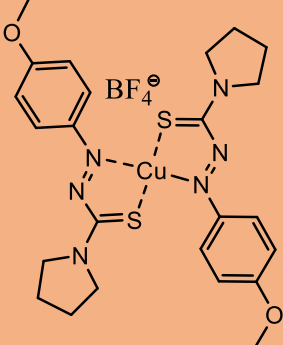
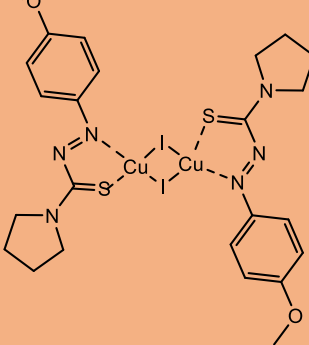
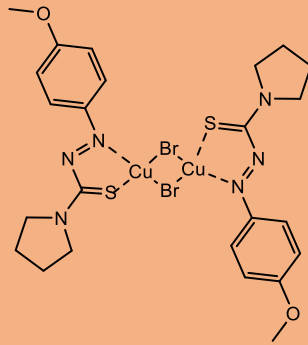
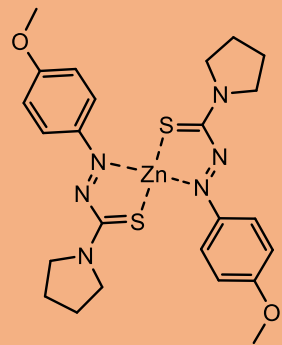
$IC_{50} = 0.52 \mu\text{M}$ ,  
HT-1080,  
connective  
tissue Epithelial cell  
cancer cell line



# Preliminary data\*

## IC<sub>50</sub> values for pyrrolidine ATF-metal chelating compounds

### Compound IC<sub>50</sub>, μM (± SEM)

					
<b>Microbes:</b>					
<i>S. aureus</i>	>50	21.1 (6.7)	3.4 (0.8)	4.1 (0.1)	17.3 (8.2)
<i>E. coli</i>	>50	>50	>50	>50	>50
<i>C. albicans</i>	>50	>50	5.0 (2.6)	2.7 (0.7)	>50
<b>Cell Line:</b>					
A549	>50	20.8 (1.8)	12.7 (1.7)	3.5 (0.7)	>50
HT-1080	>50	10.0 (1.8)	0.52 (0.04)	1.1 (0.2)	16.1 (0.8)
MDA-MB-231	>50	14.9 (3.1)	0.99 (0.015)	3.2 (0.9)	18.2 (1.0)
K-562	>50	16.3 (3.3)	1.1 (0.1)	9.6 (3.9)	>50
MRC-5	>50	18.0 (1.1)	1.5 (0.4)	9.6 (1.1)	10.2 (0.8)
HFF	>50	19.6 (3.8)	2.2 (0.0)	3.9 (0.8)	>50

\*In collaboration with Ken Cornell, Boise State Univ.

# CONCLUSION

## ATF is a Versatile Ligand

- ❖ Synthesized redox-active azothioformamide (ATF), and their different metal complex, and then fully characterized
- ❖ Both the electronic and steric factor plays vital role in the coordination of the metal with ligands
- ❖ Metal complexes are reportedly more efficient than their parent ligands against microbes and cancer cell line

# FUTURE WORK

- Synthesize ligands featuring dimeric, trimeric, polymeric binding sites, and with a central cavity designed for metal binding
- Further expand from coordination and separation to study the metal dissolution rates
- More testing on the cancer cell line and microbes and study the mechanism for the biological activities

# ACKNOWLEDGEMENT

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- Department of Chemistry, University of Idaho
- College of Science, University of Idaho
- Collaborator
  - Dr. James G. Moberly (University of Idaho, Chemical and biological engineering)
  - Dr. Ken Cornell (Boise State University, Chemistry and Biochemistry)
  - Dr. Paul Rowley (University of Idaho, Biological Sciences)

**Thank you!**