Synthsis of A Tethered Bis-oxazoline Ligand for Silver(I) Binding

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Outline

1. Silver and its ligands
2. Applications of ligands for silver: silver extraction and catalysis
3. Design and synthesis of Westiellamide analoges: 6 generations
4. Conclusion and future work

Silver

- A group 1B Metal
- Common oxidation state: Ag(I), Ag(II), Ag(III)
- Few catalytic applications in organic synthesis
  - Commonly acts as an oxidant or Lewis acid
  - A ligand is often required

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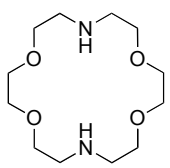
Ligands for Silver(I)

- Halide and pseudo-halide ligands:
  Cl^-, Br^-, I^-, SCN^-, CN^-
- Silver-carbon bonds:
  $Ag(CO)\{B(OTeF_5)_4\}$
- Oxygen donor ligands:
  $HOCH_2CO_2^-$, 18-crown-6 (logKa=1.60)

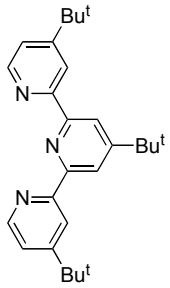
Housecroft, C.E., *Coordination Chemistry Reviews*, **l994,** *131,* 1

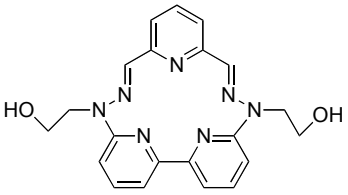
Ligands for Silver(I) – N Donors

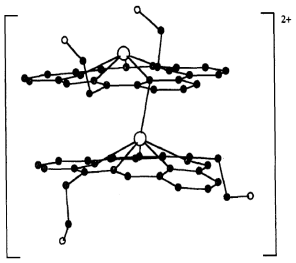
- Nitrogen donor ligands



logKa=7.80



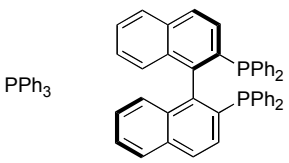




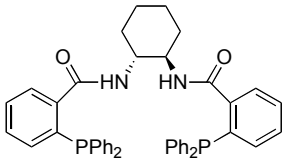
Housecroft, C.E., *Coordination Chemistry Reviews*, **l994,** *131,* 1
Cui, Y., He, C., *Angew. Chem. Int. Ed.* **2004**, *43*, 4210
Steed, J.W., Atwood, J. L., "Supramolecular Chemistry", John Wiley and Sons, Ltd

Ligands for Silver(I) – P Donors

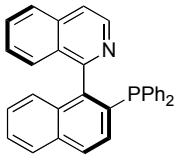
- Phosphorous donor ligands



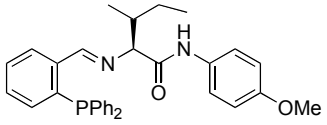
BINAP



Trost ligand



Quinap

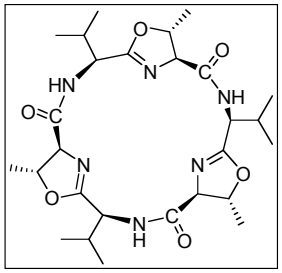


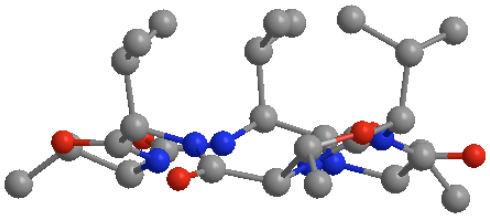
- Other ligands: sulfur, arsenic, selenium

Longmire, J.M., Wang, B., Zhang, X., *J. Am. Chem. Soc.* **2002**, *124*, 13400
Josephsohn, N.S., Snapper, M.L., Hoveyda, A.H., *J. Am. Chem. Soc.* **2003**, *125*, 4018

Westiellamide

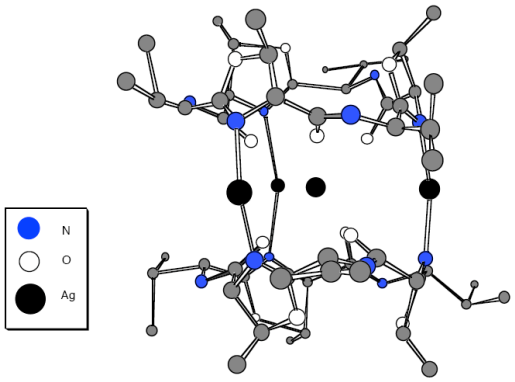
- A marine cytotoxin isolated from the ascidian *Lissoclinum bistratum*
- C-3 symmertry element in the molecule
- First total synthesis by Wipf group
- **Selective binding to Ag(I) (Ka>10^5) , forming a We_2Ag_4 complex**





Wipf, P., Miller, C. P., *J. Am. Chem. Soc.* **1992**, *114*, 10975
Wipf, P., Venkatraman, S., Miller, C. P., Geib, S., *Angew. Chem. Int. Ed.* **1998**, *37*, 78

Crystal Structure of Westiellamide-Ag(I) Complex



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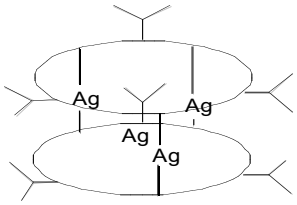


•Features:
- Multiple accessible Ag(I)s with low coordination number in an asymmertric environment (Bis-oxazolines)
- Side chains adopt equatorial positions
- Releases Ag(I)s at elevated temperature (~50ºC)

•Potential applications: Ag extraction, Ag catalysts

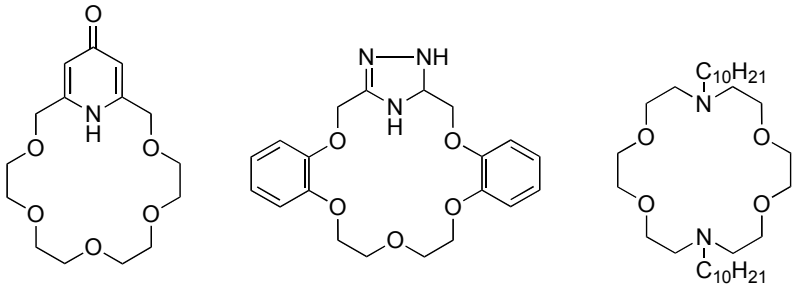
Wipf, P., Venkatraman, S., Miller, C. P., Geib, S., *Angew. Chem. Int. Ed.* **1998**, *37*, 78

Traditional Ag Extraction Techniques

- Silver Recovery: both economical and environmental friendly
- Common Ag recovery methods in film processing industry and their shortcomings:
  - Concentration of Ag in waste range from 5 mg/L to 12000 mg/L
  - For concentrated Ag waste:
    - Electrolytic recovery: large capital expenditure, percentage recovery <95%
    - metallic replacement: not reusable, percentage recovery <95%
  - For dilute Ag waste:
    - Chemical precipitation with Na_2S: handling of chemicals, H_2S formation
    - Ion exchange, reverse osmosis: Low selectivity

Extraction of Ag With Ligands

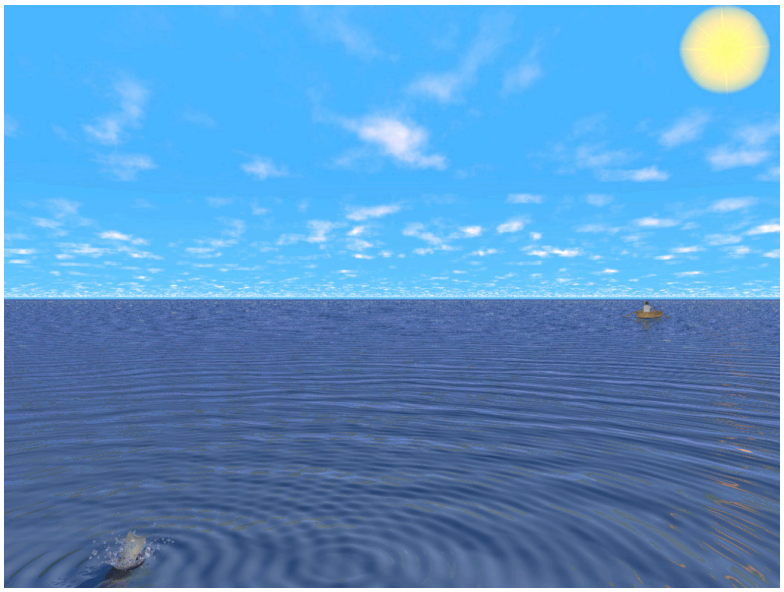
- Organophosphorous Ligands: tri-isobutylphosphine sulfide
- Macrocycles



- Drawbacks: selectivity, requires membranes for separation

Sirlin, C., Burgard, M., Leroy, M.J.F., *J. Membr. Sci.*, **1990**, *54,* 299
Izatt, R.M., LindH, G.C., Bruening, R.L., Huszthy, P, McDaniel, C.W., Bradshaw, J.S., Christensen, J.J., *Anal. Chem*., **1988**, *60*, 1694

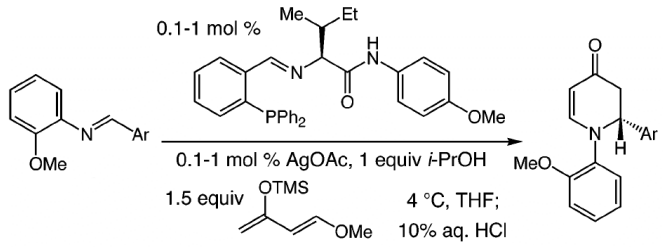
Extraction of Ag From Sea Water



- Average Ag concentration 0.24 ug/L
- For westiellamide system (We_2Ag_4), Ka~$10^{33}M^{-5}$ is required (10mM Ligand, 90% Ag bound)
- Recovery of the precious ligand

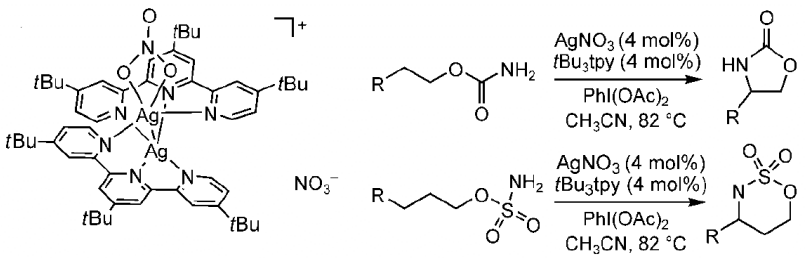
Ag-catalyzed Reactions

- Cycloaddition reaction



78%-98% yield
88%-95% ee

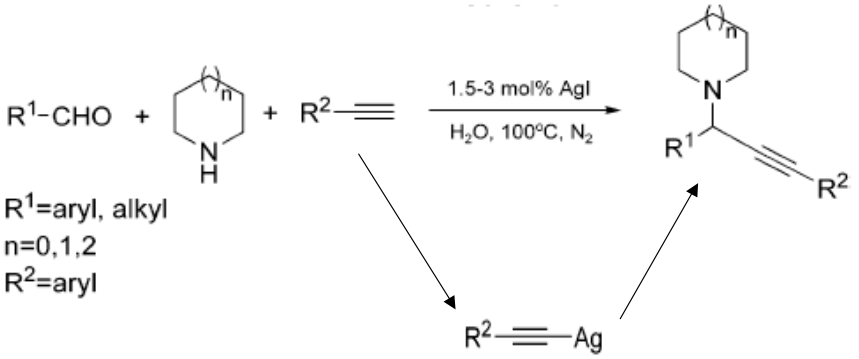
- Oxidative insertion to C-H bond



58%-90% yield

Josephsohn, N.S., Snapper, M.L., Hoveyda, A.H., *J. Am. Chem. Soc.* **2003**, *125*, 4018
Cui, Y., He, C., *Angew. Chem. Int. Ed.* **2004**, *43*, 4210

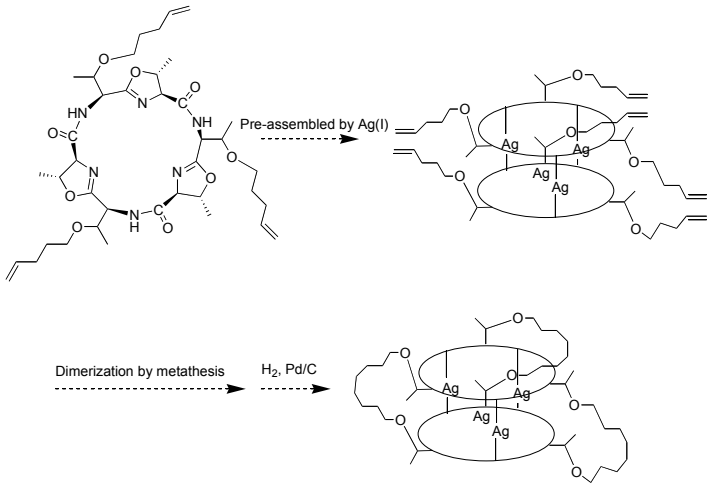
Silver Catalyst in A "Transition Metal Sense"



47%-99% yield

Wei, C., Li, Z., Li, C, *Org. Lett.* **2003**, *5*, 4473

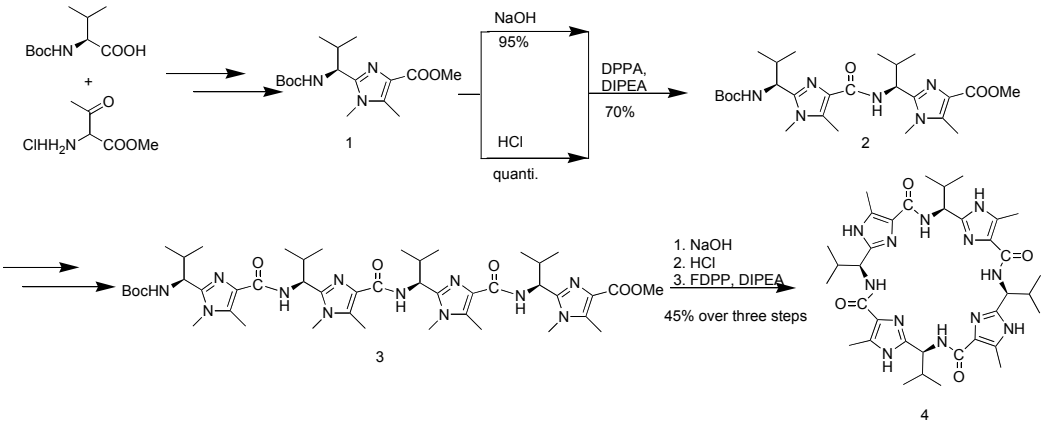
Design of A Westiellamide Analogue: Gen I



- Crosslinking reinforces Ag binding and allows attaching to a solid support

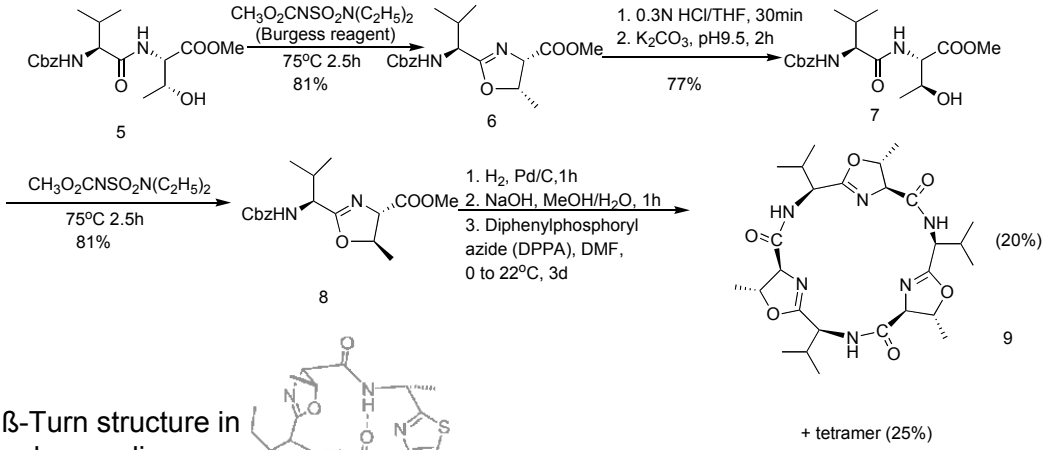
Clark, C. T., Ghadiri, M. R., *J. Am. Chem. Soc.* **1995**,*117*, 12364

General Approaches to The Cyclic Peptide: I. Linear Coupling Approach

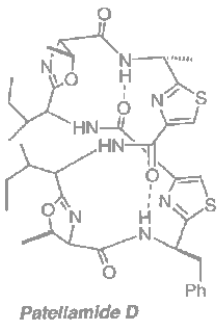


Haberhauer, G., Rominger, F., *Eur. J. Org. Chem*. **2003**, 3209

II. Cyclooligomerization Approach: Total Synthesis of Westiellamide

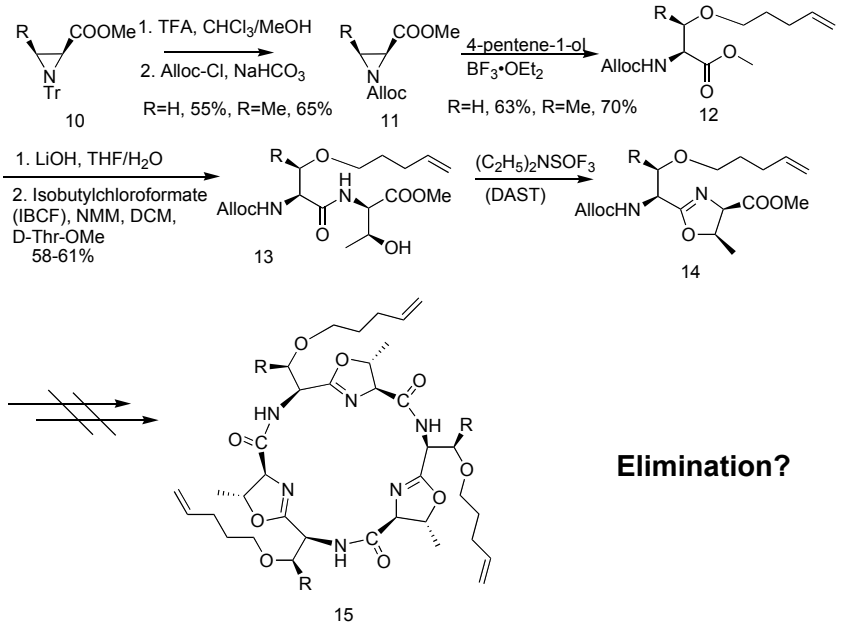


ß-Turn structure in polyoxazoline facilitates cyclization:



Wipf, P., Miller, C. P., *J. Am. Chem. Soc.* **1992**, *114*, 10975
Schmitz, F. J.; Ksebati, M. B.; Chang, J. S.; Wang, J. L.; Hossain,
M. B.; Helm, D. v. d.; Engel, M. H.; Serban, A.; Silfer, J. A. *J. Org. Chem*. **1989**, *54*, 3463

Work Done On The Gen I



Majundar, D. Master degree's thesis