Michela Vargiu
ESR1 Fellow

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Meeting 2
Edinburgh, 3rd February 2020

Innovative Training Networks (ITN) – Marie Skłodowska-Curie Actions
H2020-MSCA-ITN-2017 (THERACAT-765497)

Research Project: overview

NEW SOLUTIONS FOR MORE EFFECTIVE AND SIDE EFFECT-FREE CHEMOTHERAPY

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ACTIVATE CHEMOTHERAPEUTIC PRODRUGS SELECTIVELY AND EFFICIENTLY IN THE TUMOR SITE

Several scientific and technical issues have to be addressed, such as:
i) the availability of metal-labile protective groups fully stable under physiological conditions;
ii) highly stable and active catalysts system that can be implanted or targeted at the site of interest; and
iii) a full understanding of in vivo catalysts localization, catalytic activity, toxicity and anticancer activity.

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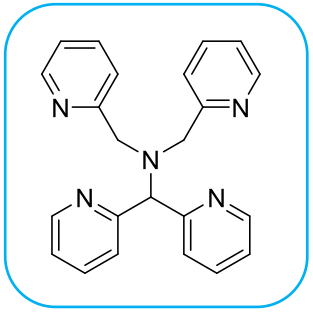
Research Project: overview

N4Py



Was designed to mimic the all nitrogen ligand environment of the iron center in Fe BLM

Is it possible use this ligand to vehicular A T.M. with deprotecting capabilities inside a tumor cell?

Is a chemotherapeutic drug able to oxidatively cleave DNA

Mononuclear iron(III) species with end-on and side-on peroxide have been proposed or identified in the catalytic cycles of the antitumor drug bleomycin and a variety of enzymes

Previous studies shows good cellular uptake. Different metals can affect the intracellular properties of the synthetic BLM-mimic N4Py

Feringa and Que et al.; *Angew. Chem. Int. Ed.*, **1995**, 34, 1512
Roelfes et al.; *Journal of Molecular Catalysis A: Chemicall*, **1997**, 117, 223.
Roelfes et al.,; *Inorganic Chemistry*, **2003**, 8, 2639.
Roelfes et *al.; Inorganic Chemistry* , **2018**, 57, 7748.

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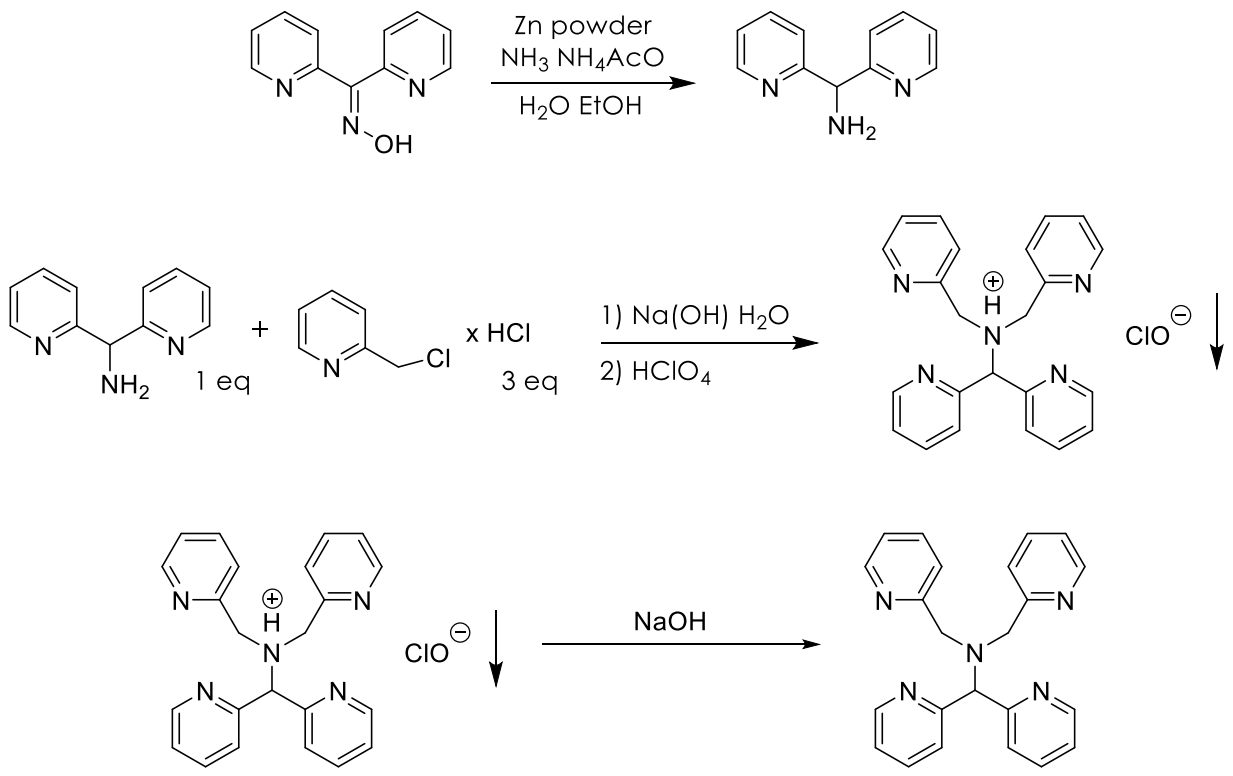
Results: Synthesis of N4Py ligand



Brown et al.; *Inorganic Chemistry*, **2017**, 56 , 900.
Roelfes et al.; *Journal of Molecular Catalysis A: Chemical*, **1997**, 117, 223

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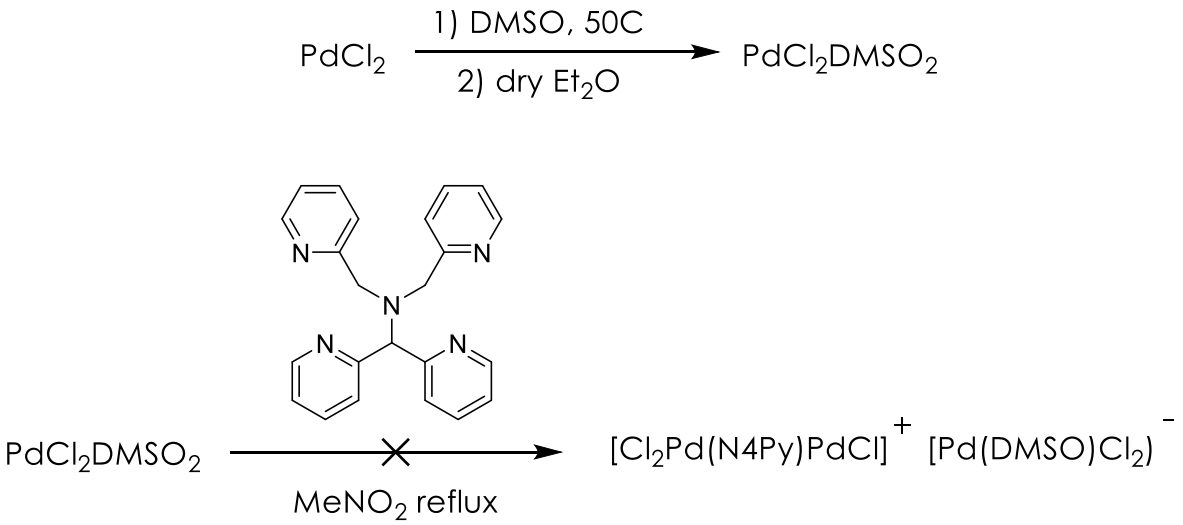
Results: Palladium complexation with N4Py



Following a modification of a procedure already present in literature for platinum.

Wayland et al.; *Inorganic Chemistry*, **1972**, 6, 1280.
Crawly et al.; *Inorganic Chemistry*, **2015**, 54, 6671

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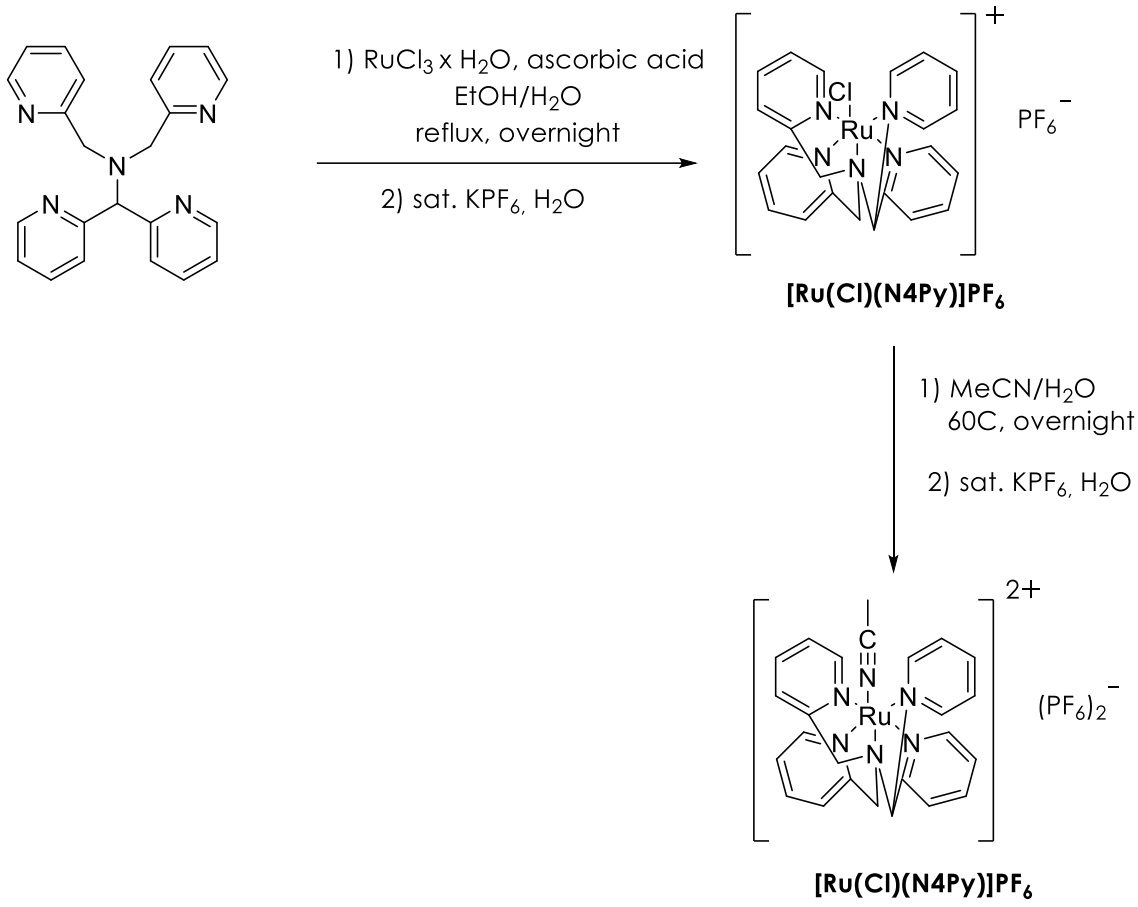
Results: Ruthenium complexation with N4Py



Brown et al.; *Inorganic Chemestry*, **2017**, 56 , 900.

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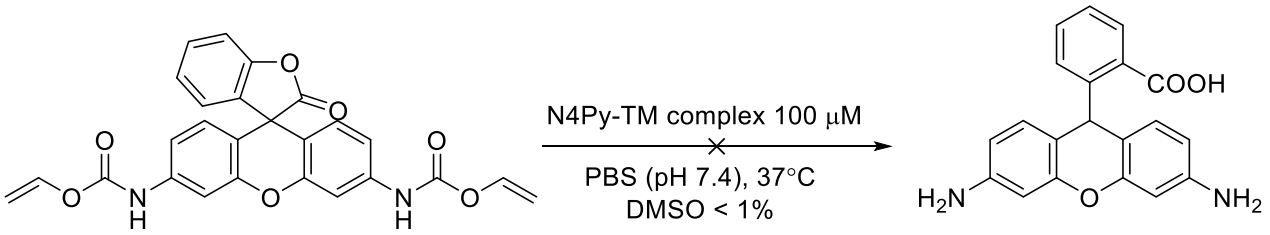
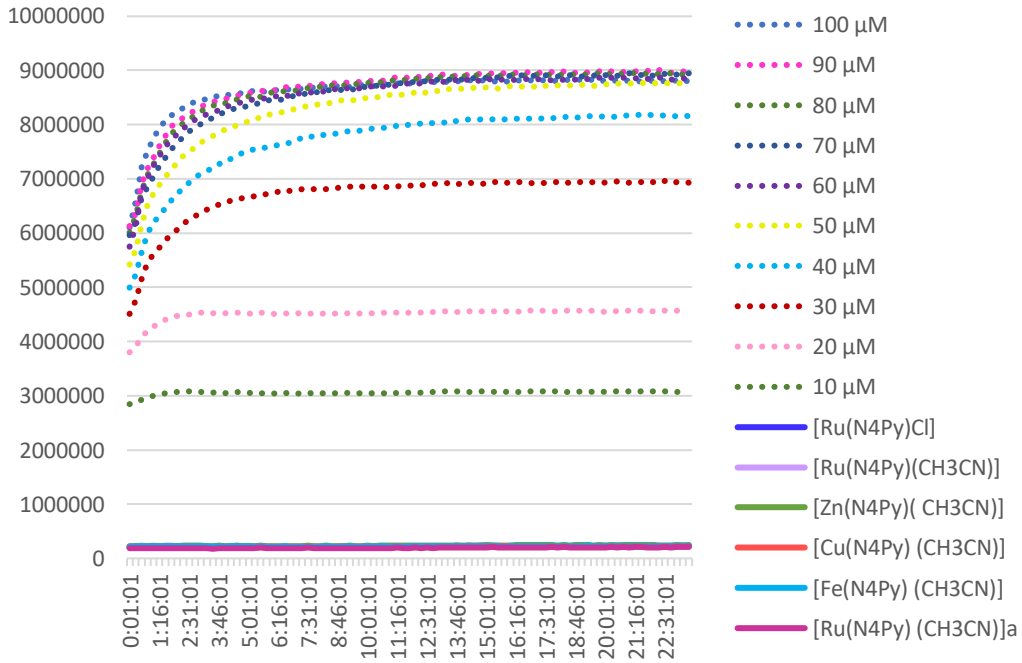
Results: Uncaging of pro-Rhodamine110



100 μM

Complexes: [Ru(N4Py)Cl] [Ru(N4Py)(CH_3CN)] [Zn(N4Py)(CH_3CN)] [Cu(N4Py) (CH_3CN)] [Fe(N4Py) (CH_3CN)] [Ru(N4Py) (CH_3CN)][a]

[a]200 μM



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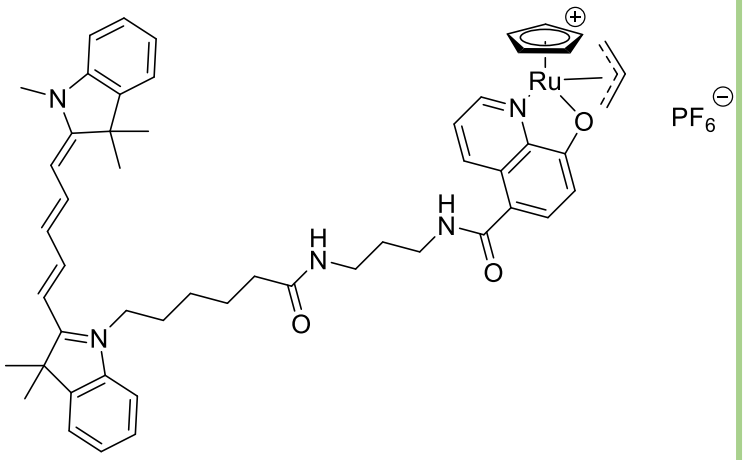
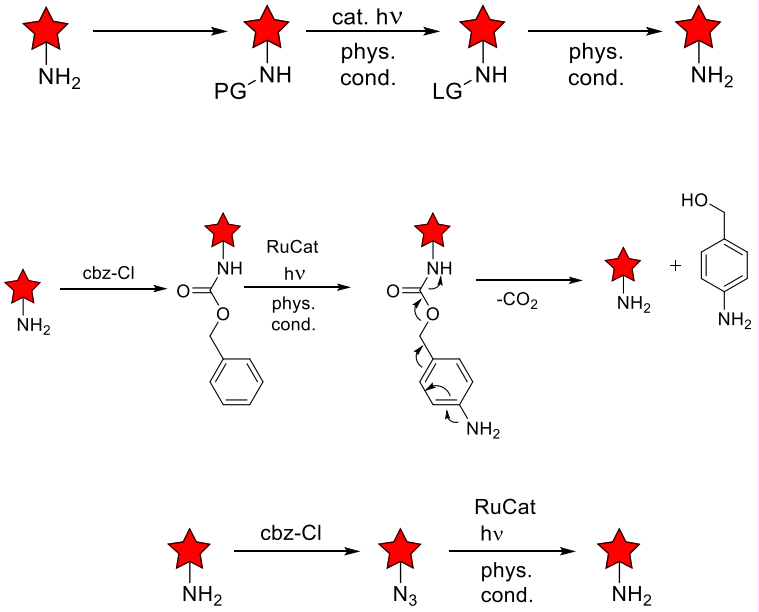
Research Project: New ideas

USE OF A NEW CATALYST FOR THE OLD REACTION.



Meggers et al.; *ChemBioChem*, **2017**, 18, 1083.

USE OF THE OLD CATALYST FOR A NEW REACTION.



Wissinger et al.; *Chem. Com.*, **2011**, 47, 4364.
Robillard et al.; *Angew. Chem. Int. Ed.*, **2013**, 52, 14112,
Brown et al., *Inorg. Chem.*, **2017**, 56, 900,

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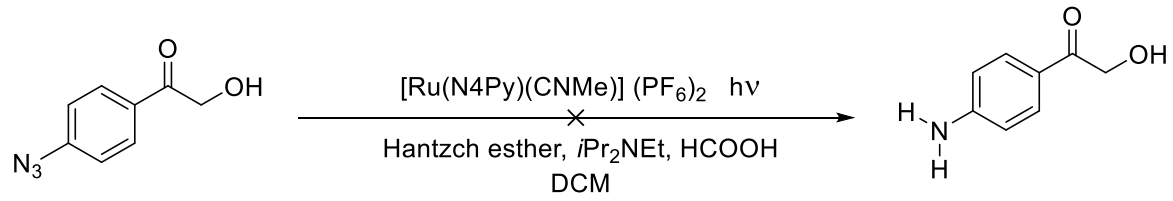
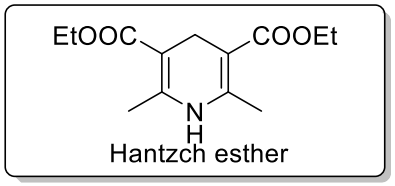
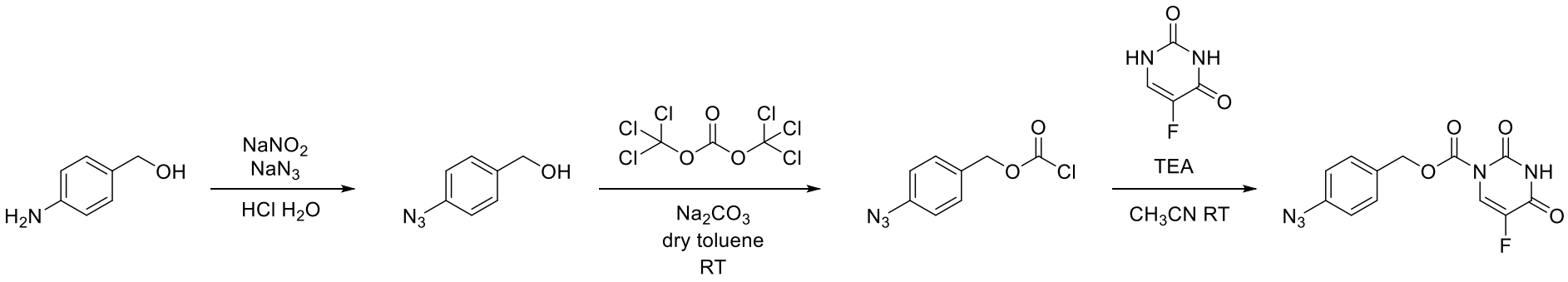
Results: photo-than-release, preliminary studies





Follow a modification of:
Liu et al., *Nature Chemistry*, **2011**, 3, 146.



Follow modifications of:
Liu et al., *Nature Chemistry*, **2011**, 3,146.
Jiang et al., *Org. Biomol. Chem.*, **2013**, 11, 4577.
Zang et al., *Org. Lett.*, **2018**, 20, 3635.

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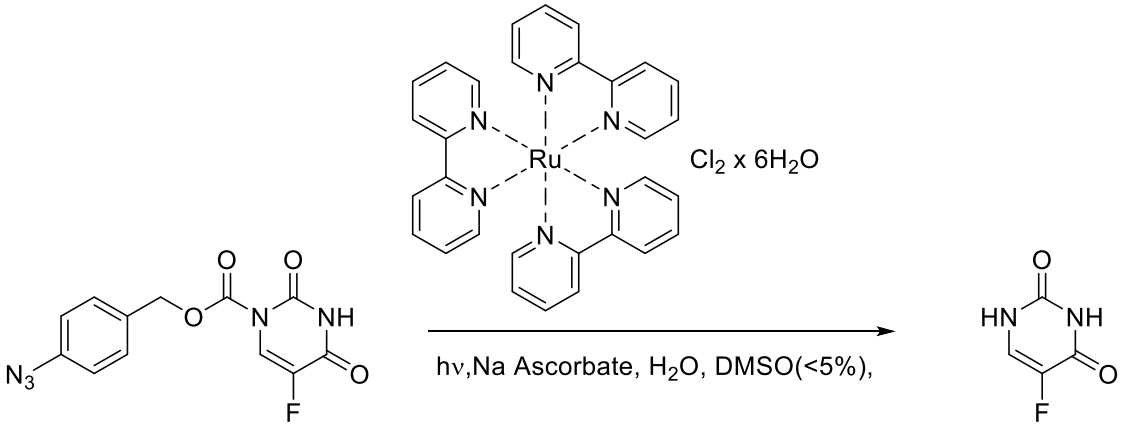
Results: photo-than-release on pro 5-FU



Follow a modification of:
Liu et al., *Nature Chemistry*, **2011**, 3, 146.

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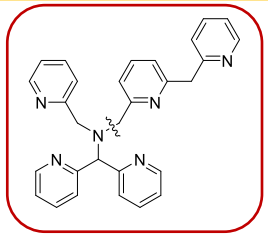
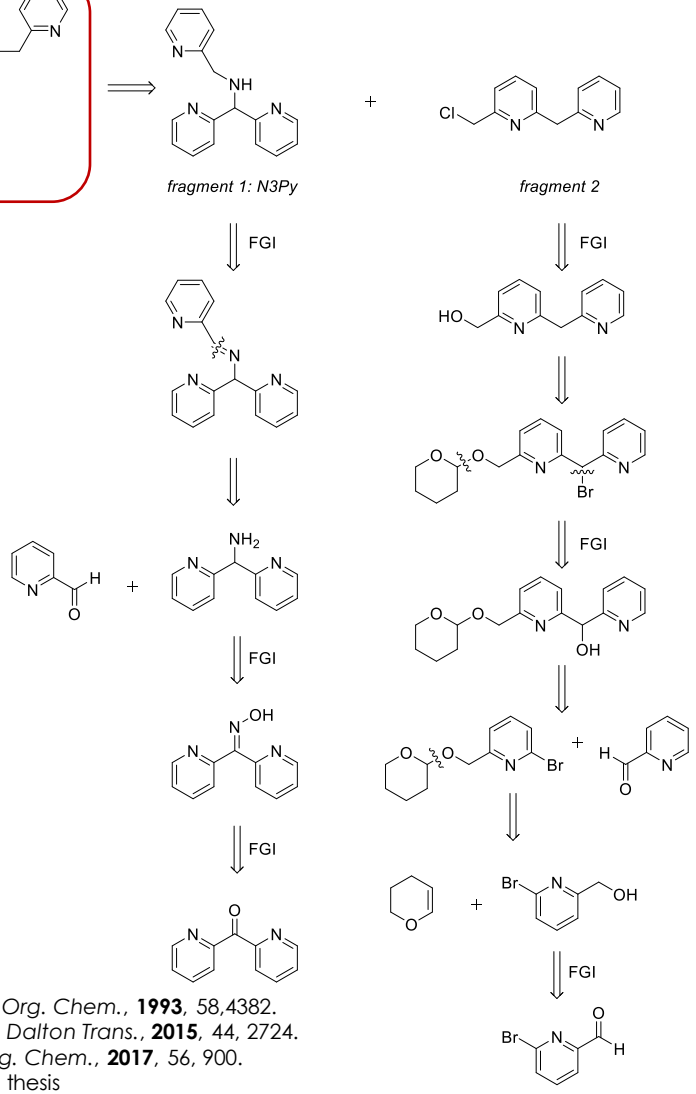
Results: Synthesis of N5Py ligand

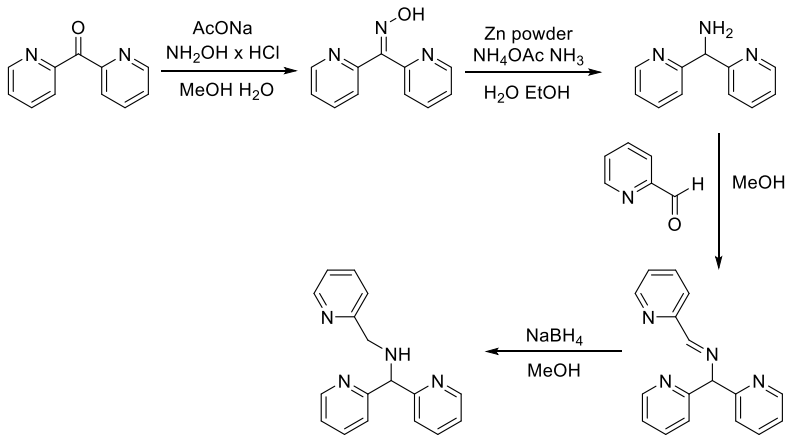


N5Py

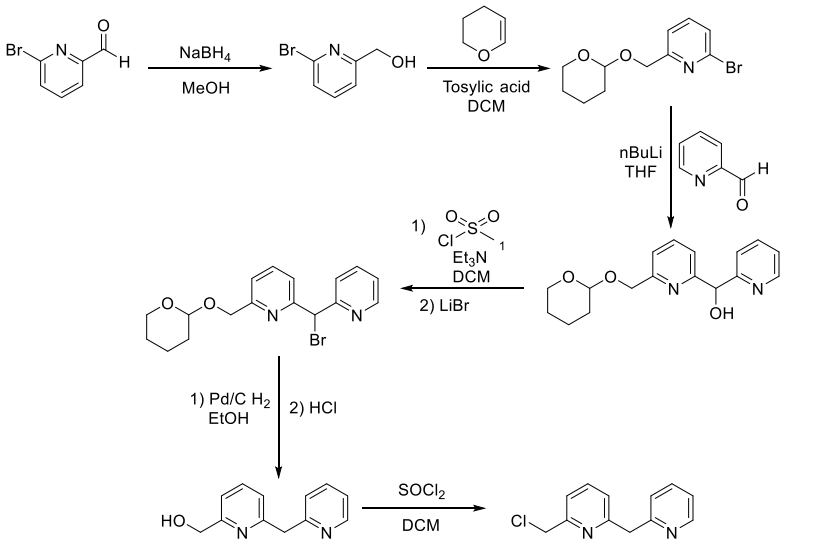


Tsukube et al., *J. Org. Chem.*, **1993**, 58,4382.
Wadephol et al., *Dalton Trans.*, **2015**, 44, 2724.
Brown et al., *Inorg. Chem.*, **2017**, 56, 900.
Prof. Roelfes PhD thesis

fragment 1: N3Py



fragment 2



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Mass-spectroscopy course (December 3-4 2019):

- Part 1: General introduction, mass analyzers, resolution, isotopes
- Part 2: Ionization techniques
- Part 3: LC-MS, tandem mass spectrometry (MS/MS)
- Part4: Analysis and identification of proteins and peptides.

Interfaculty Mass Spectrometry Center Groningen

Teaching Synthesis and Analysis practical course (January 08-28 2020):

- Assign an experiment and teach the required techniques
- Correct the reports
- Grade students

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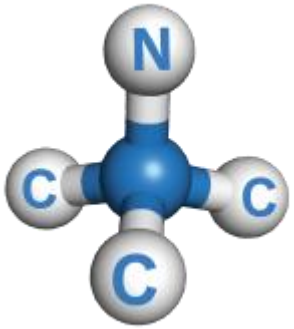

The Netherlands' Catalysis and Chemistry Conference.

XXIst conference: March 2-4 2020 in Noordwijkerhout

Topics:

- Applied Heterogeneous Catalysis
- Fundamental Heterogeneous Catalysis
- Bio-catalysis
- Coordination Chemistry
- Homogeneous Catalysis
- Photo and Electro Catalysis
- Alternative feedstocks: renewables, carbon dioxide, waste streams
- Catalysis in confinement: Zeolites, Cages and MOFs
- Catalysis in Organic Synthesis

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Thank you for your attention.

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