

Synthesis and Characterization of a Series of Zinc and Nickel Dithiolate Complexes

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Importance of Zinc

- Essential cofactor for many enzymes active in digestion and metabolism, and in transcription factors active in the control of gene expression.
- Plays critical roles in the nervous, reproductive and immune systems, as well as in embryonic development.
- The role of Zn can be structural, catalytic, or regulatory.



Zinc Fingers

• Structural:

Zinc Fingers have a structural role, these domains coordinate Zn ions to help stabilize protein folds.

A Cys₂His₂Zn Finger (**ZnS₂N₂**) that interacts with the DNA major groove.



DNA & its major groove



DNA **IS** the genetic information of most living organisms (**B-DNA** form shown)

Proteins bind at grooves, using specific binding: H-bonds, and non specific binding: van der Waals interactions, generalized electrostatic interactions.

Importance of Zinc

• Catalytic:

The most common motif in **Zn enzymes** is a tetrahedral Zn ligated by three amino acid residues (typically His, Glu, Asp, or Cys), with the fourth being occupied by the catalytically important water (or hydroxide) ligand.

eg. Alcohol Dehydrogenase (ADH): converts alcohols to aldehydes/ketones. [humans ADH breaks down alcohols; in yeast/bacteria ADH catalyzes the opposite (fermentation)

$CH_{3}CH_{2}OH + NAD^{+} \rightarrow CH_{3}CHO + NADH + H^{+}$



ADH



The human ADH **isozyme** is a dimer containing two Zn²⁺ ions. One Zn is coordinated to **four Cys**, and plays a structural role. The other Zn is coordinated to **two Cys and one His**, is <u>catalytic</u> and holds the hydroxyl group of the alcohol in place.



Importance of Nickel



- Ni plays important roles in <u>microorganisms and</u> <u>plants</u>:
- The NiFe-hydrogenases (H₂ases) contain Ni in addition to a series of iron-sulfur clusters.
 - A nickel-tetrapyrrole **coenzyme F**₄₃₀, is present in the methyl coenzyme M reductase which powers methanogenic archaea.
- One of the carbon monoxide dehydrogenase (CODH) enzymes consists of an Fe-Ni-S cluster.
- Other enzymes: glyoxalases (glx), superoxide dismutases (SOD)



NiFe-Hydrogenases

$2 H^+ + 2 e^- \implies H_2$

Active site of [NiFe]-H₂ase





NiFe-Hydrogenases & Energy

Why Hydrogen (H₂) ? It is lightweight, abundant, and when used as fuel generates only H₂O

$$H_2(g) + O_2(g) \rightarrow H_2O$$
 (liq)

Fuel	kJ/kg (specific enthalpy)
Anthracite	32,500 - 34,000
Bituminous coal	17,000 - 23,250
Butane	49,510
Charcoal	29,600
Coke	28,000 - 31,000
Diesel	44,800
Ethanol	29,700
Gasoline	47,300
Hydrogen	141,790
Methane	55,530
Oils, vegetable	39,000 - 48,000
Propane	50,350
Wood (dry)	14,400 - 17,400
Kerosene	35,000





WE CAN EXPLOIT HYDROGENASES: Biomimetic Chemistry



Synthesis of the ligands

- The generic method involved a one-step synthesis of the ligand:
- The appropriate sulfide is added to the diamine in benzene. The reaction is kept under high temperature (90°C) and pressure in a reaction tube for 24hrs. The reaction mixture then washed with water, dried and reduced on a rotary evaporator. All the ligands are **smelly viscous oils**.
- NMR and IR data is consistent with the formulations.
- Example:





Use of Schlenk techniques since the reagents and products are air/moisture sensitive





A Rotary Evaporator



CH3

CH3 9

Synthesis of the Ni & Zn Complexes

- The complexes were synthesized using a template reaction with Zn²⁺ or Ni²⁺ acetate salts in MeOH/EtOH solvent. After 24hrs, the reaction volume is reduced, ether was carefully layered and the mixture was placed in a refrigerator for several days to generate crystalline material.
- IR analysis was consistent with the formulations and structures given.
- Ni complexes: red/brown colored
- Zn complexes: white colored



(ORTEP plot) Molecular structure of a Ni complex (Pr-Pr ligand)



Complexes Synthesized & Characterized in 8 weeks:

(The work on Co is not reported here)

All appropriate characterization data (NMR, IR) is consistent with formulations and structures given for each complex.







Future...?

- Some of the problems encountered along the way can be avoided if I
 paid more attention to the air sensitivity aspect of the synthesis.
- Ran out of time, but would have liked to have made more ligands, particularly those that add more features to the α-C adjacent to the thiolates.
- If had more time, would like to have varied the N₂S₂ donor ligand set, perhaps N₃S, NS₃, S₄.
- Different metals: there is an interest in making 'similar' lanthanide complexes, particularly in the biophysical world.
- Kinetic and thermodynamic studies still remain
- Of course, do these complexes have functionality are these biomimetics functional or just structural mimics ?

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