Chemistry 2211a – Bioinorganic Chemistry MJ Stillman

Contacts: e-mail: Martin.Stillman@uwo.ca
Office: ChB 064 (Office hours: 1-2; 3-4 MWF by appointment – simply email).

Term Test Syllabus:

All lectures from 1st lecture to Thursday, Oct 22nd – that is to the end of the BIO unit. Topics treated evenly. Yes, there will be a calculation of K's. No Periodic Table provided or allowed.

This list is not exclusive of topics in the lecture notes – it just provides a roadmap of those topics the lecture notes are the prime source for any test in Chem 2211a.

Introduction – know descriptions and examples as given or extra – as follows:

Metals exist as free ions; sometimes coordinated free ions; in structures; covalently bonded
Metals concentrations vary – high to very low – bulk to trace
Essential and Toxic metals – definitions – explanation – an example of each – effect of complexed form or speciation

Periodic Table

– know examples from groups 1,2, and d-block: Fe, Co, Cu, Zn, important non-metals
Sizes – account for sizes given – do not memorize values
Configurations – know from memory group 1 and 2, and main groups 13-18 in 1st 3 rows, as indicated in class, and transition metals, especially, Fe, Co, Cu, Zn, and anions of halides, O, F, S, Se, Cl, Br. Know where Se, As, Pb, Bi are located in the Periodic Table. Know triads down from Cu, Zn.

Orbitals: recgnise shapes of s, p, d
Know arrangement of 3d orbitals for octahedral complexes; where are the electrons in Fe(II)? LS and HS

Ligands

-definition – hard (example), soft (example), and hard & soft metal example
-example soft amino acids; hard amino acids – why?
-the porphyrin ligand – be able to draw PPIX – called heme b when it has the iron in it

Concentrations – convert ppm to molarity

Equilibrium – see the example calculations at the very end of this file….

derive the equation – calculate K – calculate K_a ; chelate effect ; cumulative binding constant "beta"; stepwise binding constants "$K_1..K_n$"

Free energy – how enthalpy and entropy connect –

-effect of entropy in changing free energy for chelating ligands - sub numbers provided
Equilibrium constants for sequential ligand reactions $M+L \rightarrow \rightarrow ML_n$
Difference between $K_{1\text{-}N}$ and β_N
Calculate overall values given data – especially – chelate effect

Essential Metals

Know an example of group 1 and 2
Know example charge/size rule
Know concentrations in and out of cells – concept of pumps
Know what these metals do – simple examples
Transition Metals – important metals: Cr, Fe, Cu, Zn, Co

Heme Proteins

Know about myoglobin and hemoglobin - and difference in heme 5th position and oxidation states for catalase vs myoglobin - see questions below

Toxic metals

Know key metals
Know example of mercury – speciation – toxicity – where - when
Know cadmium, lead and arsenic

Section 1- Introduction to Metals in Life or Bioinorganic Chemistry

a. Answer questions about metals and their roles
b. What processes involve metals directly?
c. Which are toxic and why?
d. How can we use metals therapeutically? Which metals are used?
   i. Treat deficiencies
   ii. Treat disease
e. Bioavailability of metals and metalloproteins – Essential metals
   i. The timescale for life on this planet – know how evolution influence the incorporation of metals
   ii. Composition in man – how to calculate ppm etc.
   iii. Bulk-macro- & microminerals- ultratrace levels – which are Bulk – Macro, Micro? Don't need to memorize ultratrace.
   iv. How many elements do we require? 25 for sure, possibly up to 35. Types of metals – essential, toxic – Mg, As, Cd, Pb, - examples
   v. Availability vs change in atmosphere
   vi. Strange molecules – Vit B12
   vii. Where do the metals come from? Diet
   viii. B12 – what happens without it?
   ix. And, Ca, Fe, Cu, etc. come from? And why we need them..
   x. The different essential elements

xi. Why these elements?
xii. Functions of representative essential elements – we are what we eat – Ca-Cr-Co-Fe-Mg-Zn –know what to eat to absorb each –
What do they do – know major roles – p 19
xiii. Structural roles
f. Biologically important ligands that coordinate metals
g. The role of cobalt in vitamin B12
h. The role of zinc (an essential group 12 metal)
i. Toxicity of metals: As, Pb, Cd, Hg
i. How to quantify – the Bertrand Diagram
j. Metals in disease and drugs: Therapeutic metals: Au, Ag, and Pt
k. Mg: The key to plant life in chlorophyll
l. Iron - as an example of diet to function - much more to come
i. Heme iron – overview of heme proteins and heme enzymes – know 2 examples
ii. Heme iron – mechanism of oxygen binding in myoglobin and hemoglobin

See questions at the end of the unit.

Section 2. Important chemistry and special inorganic chemistry for bioinorganic chemistry

2.1. Periodic table
2.1.1. The key elements in Group 1 & 2; d-block metals; triads from Cu and Zn down.
2.1.2. C Hopkins coffee mug with salt
2.1.3. Is cobalt a bulk, macro, micro mineral? Where is it used commonly?
2.1.4. Configurations
2.1.5. Shapes of orbitals
2.1.6. 3d orbitals
2.1.7. Ionization energies across the periodic table
2.1.8. Elements, transition metals, trends, electronic configurations, d orbitals
2.1.9. Biologically common oxidation states – esp. of Na, K, Mg, Ca, Fe, Co, Cu, Zn – configurations for these oxidation states –
2.1.9.1. Also of toxic metals
2.1.10. Where do we find high oxidation states?
2.1.11. And fixed ox. states?
2.1.12. Size of cations and anions

- 2.1.12.1. How this is an important part of biological processes
- 2.2. Special molecules that bind metals
  - 2.2.1. Forming complexes with metals
  - 2.2.2. Ligands – special features of ligands
  - 2.2.3. Nomenclature of complexes
  - 2.2.4. Electronegativity – what the Periodic Table shows
  - 2.2.5. Hard and Soft metals and ligands – very important to know the classes for each element in the table.
    - 2.2.5.1. Know all metals of biological interest
    - 2.2.5.2. Special ligands- EDTA
    - 2.2.5.3. Need to know this set of amino acids – note the donor atoms
  - 2.2.6. Shapes of complexes
- 2.3. Metal-Ligand complex formation
- 2.4. Special ligands that bind metals – and why
  - 2.4.1. Identify from a table the structures of: EDTA, BAL, Lewisite, Desferrioxamine B, D-penicillamine- corrin, chlorin, PPIX, heme b, glutathione, cyclic polyethers, inclusion compounds
  - 2.4.2. How does BAL work
  - 2.4.3. Recognize: All the different porphyrins and how to remember PPIX
  - 2.4.4. Cyclic polyethers, cryptands
  - 2.4.5. Inclusion compounds
  - 2.4.6. Shapes of molecules
  - 2.4.7. d- orbital splitting – high or strong field, low or weak field ligands
  - 2.4.8. Compounds of oxygen
    - 2.4.8.1. Which proteins react with which oxygen compound?
  - 2.4.9. Equilibrium constants – K_F
    - 2.4.9.1. Set up equations for K_A, K_B, K_{SP}, K_F, K_D, K_{EQ}
    - 2.4.9.2. Calculate pH from data for weak acid/base
    - 2.4.9.3. Denticity of ligands
    - 2.4.9.4. Concentrations
    - 2.4.9.5. Competitive equilibria dissolves insoluble salts, why?
    - 2.4.9.6. Step-wise vs Cumulative binding constants
    - 2.4.9.7. Calculate ΔG^0 and ΔH and ΔS from appropriate data
    - 2.4.9.8. Why do chelating ligands have large K's?

See questions at the end of the unit.

Section 3. Biology for bioinorganic chemistry

3.1. Amino acids
3.2. Proteins – peptide bond
3.3. Nonenzymatic proteins; enzymes
3.4. Special absorption spectral properties of amino acids
3.5. Aromatic amino acids
3.6. Protein structure – peptide bond
3.7. Denaturation
3.8. Folding – primary, secondary, tertiary and quaternary structures
3.9. Cofactors and their role
3.10. Special molecules

Some Review Points:

3.1.1. Know an example of basic, acidic, aromatic amino acid - from the metal-binding set
3.1.2. Know names and structures of all metal N- binding; S- binding; -O^- binding amino acids – select correct metal-binding amino acid from data table
3.1.3. Know form of peptide bond –why is it 'planar'
3.1.4. Know the 5 structural features of proteins with examples
3.1.5. Know how they bind using hydrogen bonding - see the course outline above

1) Consider what trace essential and trace toxic metals are.

2) Answer the questions:

4 essential metals are? 3 toxic metals are?

5) Copper is an essential metal –answer the questions:

What are the oxidation states that copper adopts in the body?
What does copper do in the body?
..and for interest (with no recommendations) you might find the following interesting… (one question though – does oxidative stress arise from a compound oxidizing or reducing biological molecules, do you think? And is Cu(II) an obvious choice? If not which copper oxidation state would you choose and why?

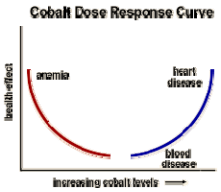
Seems is for real..
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3359723/

6) Review the information here – learn the role of the following metals – note they are the same as above:

Metals that we cannot live without are sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), iron (Fe), cobalt (Co), copper (Cu), zinc (Zn)

Metal:	Function:
cobalt (Co)	core of Vit B_{12} (required to make blood cells) –it's a co-factor for enzymes
copper (Cu)	part of redox enzymes used in defense against oxidative damage, for example superoxide dismutase (SOD)
sodium (Na)	important for extra cellular cations (positively charged ions or molecules) and nerve function
calcium (Ca)	part of bones; important for blood clotting
potassium (K)	major cation in intracellular fluids; essential for nerve and heart function
zinc (Zn)	part of dozens of enzymes; plays a role in reproduction and sexual maturation
iron (Fe)	found in hemoglobin and other proteins and enzymes

7) Explain the dose response for all metals.



As an example: Cobalt is an essential metal for humans. People who don't get enough cobalt in their diet have trouble making enough red blood cells. Cobalt is a component of vitamin B_{12} which helps in the process of making red blood cells. Without enough red blood cells, anemia develops. People with anemia experience symptoms of tiredness, weakness and listlessness. However, too much cobalt is also dangerous. When someone is exposed to too much cobalt, they may develop blood diseases and heart problems. Some people exposed to cobalt occupationally have developed lung disease and it may be linked to lung cancer. This diagram is not like the one in the lectures – what extra comes from the 2211a lecture version?

8) Consider the following questions –

Which of the following is NOT a normal function/role of the stated metal in the body?

A. iron in the heme of hemoglobin

B. calcium in bones

C. cobalt in Vitamin B_{12}

D. phosphorus in ATP

E. arsenic in ATP

9) Which of the following is NOT characteristic of metals?

A. Metals are often charged ions.

B. Metals can be destroyed or degraded in the body.

C. Metals easily bond to other molecules.

D. Metals can have various oxidation states.

10) Some comments – consider these facts:

Metals are elements, so they cannot be destroyed or broken down. Metals can remain in the environment and in human bodies for long periods of time. Metals cannot be broken down to reduce toxicity but the speciation – that is – the form of the ligand molecules bound to the metals can havea profound effect on toxicity. EG, ionic, trivalent arsenic can be made less toxic by the addition of a methyl (CH_3) group. For which metal is the biological toxicity exactly the opposite of this?

11) How does the size of the metal change with its oxidation state?

12) What controls the ability of a metal to form a complex with a ligand?

Background: Metals can have different species with different amounts of charge and these charged atoms easily and quickly form complexes with enzymes and other biological molecules. The amount of charge also affects how easily the metal can get into cells. Iron, for example, in the Fe(III) species, cannot cross membranes very easily. This restricts where it can go in the body. Hg can only easily penetrate membranes and be quickly distributed around the body if it is what form? Which form of Hg will not be so toxic to humans? Why not?

13) Who is LEAST likely to be exposed to toxic metals?

A. a technician working on a computer component board assembly line

B. a person who drinks water from a ground water well

C. a person smoking a cigarette

D. a person working on a new home computer

E. a painter renovating an 100 year old home

Background:

Metals can occur naturally

Metals occur in nature in rock formations, and are all around us in our environment. Most people are usually not exposed to metals, but sometimes, metal exposures do occur. For example, arsenic is sometimes found in drinking water that comes from a ground water source. It gets into the ground water by the normal process of leaching out of rocks and soil. Arsenic can be toxic to humans and is associated lung cancer and skin cancer.

Cadmium and human activities

Many metals exposures are due to human activities. For example, almost everyone is occasionally exposed to cigarette smoke and cigarette smoke contains cadmium, a potentially toxic metal. Cadmium is also found in lead and zinc ores. Symptoms of

cadmium poisoning include nausea and vomiting, and if inhaled, lung lesions and chronic bronchitis.

243 ## Lead-based paint

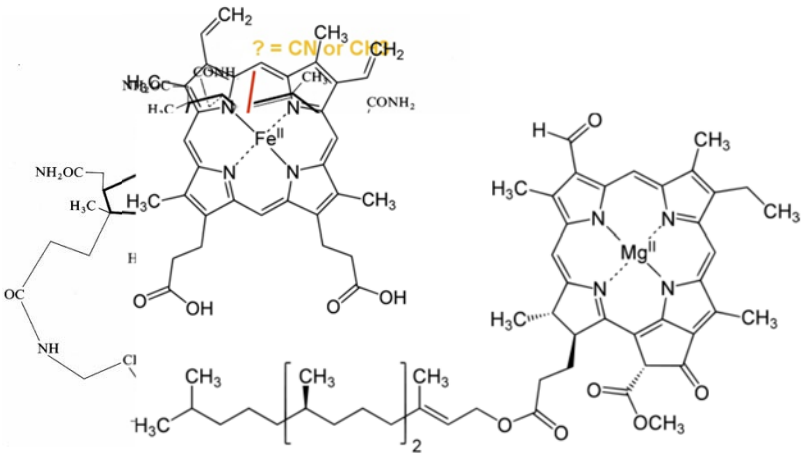
Another common source of metals in our environment is old paint. Paint applied before 1973 is very likely to contain lead, a toxic metal. Old paint can often be 100% lead salt because the original organic solvents have evaporated, so chips of the paint are deadly to young children and dust can be inhaled by adults doing renovations. Lead poisoning in adults can result in a wide range of symptoms from weakness and loss of appetite to coma and death in very acute or massive exposures.

244 ## Metals in computers

The semiconductor industry uses many types of metals. Semiconductors are parts of personal computers. During the manufacturing process, toxic metals are often created as by products. There is no exposure from the use of the finished product.

245 ## Mercury in fish

Some people have been exposed to mercury in the fish that they eat. Many of the fish in the Great Lakes region of Canada and the United States are contaminated with methylmercury. People are often requested to limit their intake of fish from these lakes. Mercury was deposited in the lakes from air contaminated by the smokestacks of coal-burning power plants, waste incinerators, and factories, as well as from pulp and paper run-off. Bacteria in the lakes convert many forms of mercury into methylmercury, which can be concentrated in fish. Mercury is a "neurotoxin." It damages the brain and nervous system. Symptoms include weakness, fatigue, not being able to concentrate, headaches, tremors in the hands, and memory loss. Even more severe symptoms are possible.



246

247 **14) Big ligands – enough of salts – covalently bound metals are important too**

248 Nomenclature of Tetrapyrroles – that is the generic name of the chlorins, corrins, corroles,
249 porphyrins

250 **Chlorin**

251 - notice how chlorin is not the same as protoporphyrin IX – takes a bit of searching for the very
252 subtle changes – that means everything to the way chlorophyll works.

253 http://www.chem.qmul.ac.uk/iupac/tetrapyrrole/TP/E2.html

Chlorophyll *a* – notice the R = phytyl chain – what is that?

Cobalamin – the corrin ring

Protoporphyrin IX - heme

15) Which metals typically bind in chlorophyll, corrin, and protoporphyrin IX in biology?

What is the difference between these 3 metals?

16 Calculations to try

Equilibrium:

1) Calculate K for $N_2 + 3H_2 \rightarrow 2NH_3$
if at equilibrium, $[N_2] = 1.03$ mol/L; $[H_2] = 1.62$ mol/L; and $[NH_3] = 0.102$ mol/L
(=0.00238)

2) Calculate $\log_{10}\beta_6$, β_6, $\Delta G^0{}_1$ and $\Delta S^0{}_1$ (that is for the 1st step – NOTE THE SUBSCRIPT "1")
using these data:
$[Ni(H_20)_6]^{2+} + NH_3 \rightarrow [Ni(NH_3)(H_20)_5]^{2+}$ $+ NH_3 \rightarrow [Ni(NH_3)_2(H_20)_4]^{2+}$ etc to $[Ni(NH_3)_6]^{2+}$
in 6 steps with the following log K_n values:
n=1-6: 2.79, 2.26, 1.69, 1.25, 0.74, 0.03 at 303 K. $\Delta H^0{}_1 = -16.8$ kJ/mol and R= 8.314 $JK^{-1}mol^{-1}$
(8.76; 5.75×10^8; -16.2 kJ mol^{-1}; 1.98 $JK^{-1}mol^{-1}$)

Keywords for text books you check

d-orbitals;
Essential metals; toxic metals; dose relationships
Stability constants for coordination complexes

QUESTIONS - 4

What are metals? Why are metals so prevalent in the environment today?
How many metals are essential? Have no known use? Are toxic?
Is it clear cut which metals are toxic?
How can you define an a metal as essential – see url 3 above
Iron is essential – how much is best? Is 'too much' possible?
Are essential metals always present in mg/kg quantities?
Are roles for all metals known?
Are all essential metals now known?
Can an essential metal become toxic? Give examples.

QUESTIONS - 5

What is the difference between Hb and Mb
What binds oxygen?
How many oxygen molecules per protein molecule?
Is oxygen binding the same in both Mb and Hb?

How does the Hb oxygen binding work? - to come in detail
Why does smoking affect Hb action? How?
Describe the secondary structure of myoglobin. Does it consist mainly of alpha helices, beta pleats, or a combination of both?

Use the following to answer the questions about toxic metals – most work for me
https://www.dartmouth.edu/~toxmetal/index.html
http://www.osha.gov/SLTC/metalsheavy/
http://www.osha.gov/SLTC/mercury/
http://www.osha.gov/SLTC/cadmium/index.html

QUESTIONS - 6

What are toxic metals?
Which metals are very toxic?
What sort of diseases do toxic metals cause?
Where are toxic metals found around the home?
How is mercury released into the environment?
How does mercury affect health of humans?
What are the conditions toxic metals become a concern?
What cases of poisoning by toxic metals are well known? Which metals?
Why do acidic drinks pose a hazard?
How is cadmium different from mercury in its toxicity?
Why is cadmium a problem in the workforce?
Is it a problem in the home?
Why is dental amalgam considered potentially dangerous?
What is the concern with some vaccine solutions?
Are there restrictions on the consumption of fish? Why?
Why is smoking so dangerous (other than nicotine and lung cancer)?
Why are computers a problem?
Where in the world is mercury a current problem?
Are there any elements/compounds that protect mammals from the effects of toxic metals? What are they?

Are the statements here all correct?
http://www.world-action.co.uk/poisoning.html

Some typical questions - the style to be adopted - note - as these questions are from previous years - both the style and the questions will be different this year.

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1. About how many elements are for certain essential with known biological roles in life's chemistry? Answers

A) Less than 10
B) Less than 15
C) Less than 20
D) 21—30
E) 31—40

D

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2. Except for C, N, O, S, all other essential elements exist at about the same, but much lower concentration?

A) Yes (B) No — B

3. The identity of all essential elements in life's chemistry are now known precisely.

A) Yes (B) No — B

4. Which statements are True concerning the elements in a typical human that are frequently classified as: — T

(i) bulk, that includes P and S — T

(ii) macronutrients, that includes Ca, Fe, and K — T

(iii) micronutrients, that includes Cr, Zn, and Cu — T

(iv) ultra-trace elements, that includes As

A) All B) (i), (ii) and (iii) only, C) (ii) and (iii), D) (i), (ii) and (iv) E) None — A

5. Which of the following is/are True concerning the elemental composition of a typical human?

(i) Iron, Fe, is only present at about 50 mg although essential — F

(ii) Essential metals with known roles include Fe, Cu, and Zn — T

(iii) The presence of As is due to exposure to toxic materials and always indicates some form of toxicity is occurring — F

(iv) Cr is highly toxic under all conditions — F

(v) Ag, Au, and Pt are known to be essential elements — F

A) All are true
B) Only (i), (ii), (iv) are true
C) Only (ii) is true — C
D) Only (i) and (ii) are true
E) None are true

6. In the Periodic Table, which statement(s) is/are true?

(i) Mg, Ca are known as alkali metals — T

(ii) Mg, Ca are known as alkaline earths — F

(iii) Mg, Ca exist with 1+ and 2+ oxidation states in biological molecules — F

(iv) Mg, Ca are in Group 1 — T

(v) Mg, Ca are in Group 2 — F

(vi) The electronic configuration of the cations is [RG] ns^1 (RG = nearest rare gas) — F

(vii) The electronic configuration of the cations is [RG] ns^2 (RG = nearest rare gas) — F

(n – depends on the row number of the metal)

A) (ii) and (v) only; B) (i) and (iv) only; C) (i), (iv) and (vi) only; D) (ii) and (iii) only; — A
E) (ii), (v) and (vii) only) only

7. The electronic configuration of Co^{2+} includes:

A) $4s^23d^7$ B) $4s^13d^7$ C) $4s^03d^9$ D) $4s^03d^8$ E) $4s^03d^7$ — E

8. In the Periodic Table, which statement(s) is/are true?

(i) Metals in group 15 and 16 are electropositive — F

(ii) Metals in group 15 and 16 are electronegative — T

(iii) Metals in group 1 and 2 are electropositive — T

(iv) Metals in group 1 and 2 are electronegative — F

(v) Metals in groups 3-12 are all electronegative — F

A) (i) and (iv) only; B) (ii) and (iii) only; C) (i) only; D) (ii) only; E) (iii) only — B

9. If the $K_{1\text{-}6}$ values for this reaction are:

$K_1 = 3.8 \times 10^4$ 1.45×10^{15}

$K_2 = 17.2 \times 10^3$

$K_3 = 4.3 \times 10^2$

$K_4 = 3.2 \times 10^2$ B

$K_5 = 1.8 \times 10^1$

$K_6 = 0.9$

$\text{Log}_{10}\ \beta_6$ is closest to: A) 10^{-3} B) 15 C) 150 D) 1,500 E) 10^7

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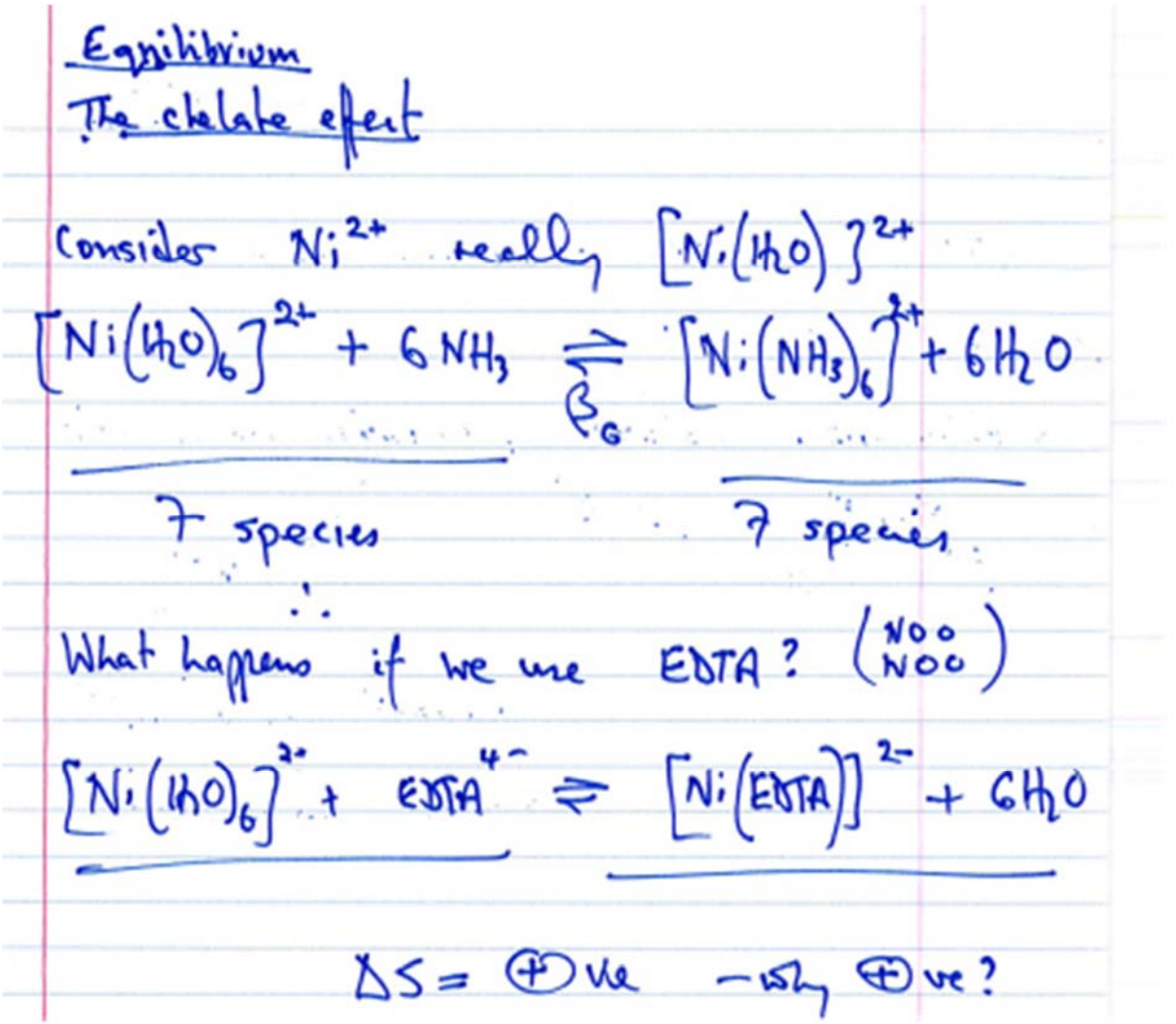
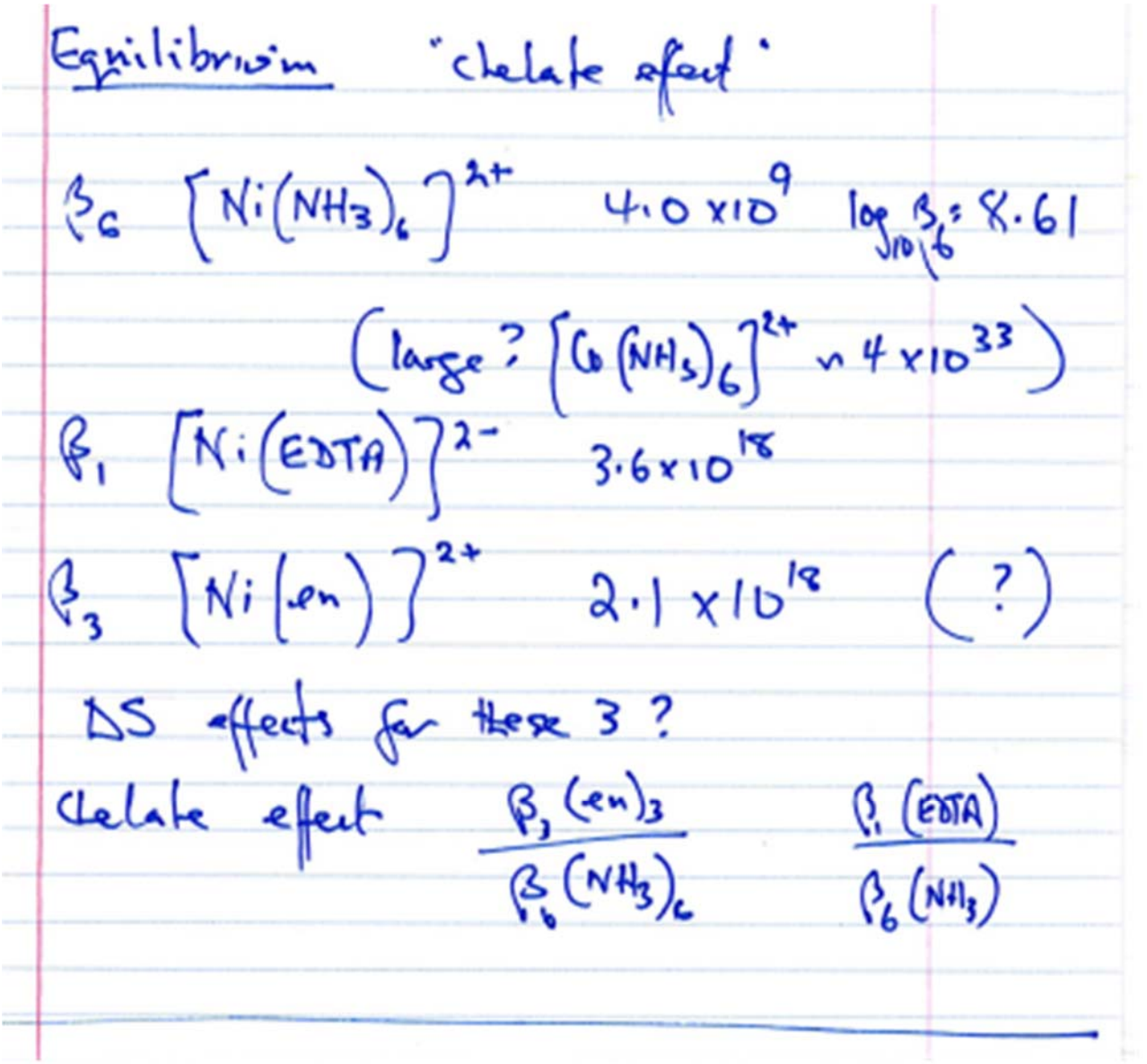


Look at the last Multiple choice question above.



NOTE – $Ni(en)_3$ the "3" indictaed by beta3 because en (ethylenediamine) is a didentate ligand (2 donor atoms); but EDTA is just "1" because it is a hexadentate ligand

So these data are given – you can only calculate the chelate effect by dividing one K or beta by the other.

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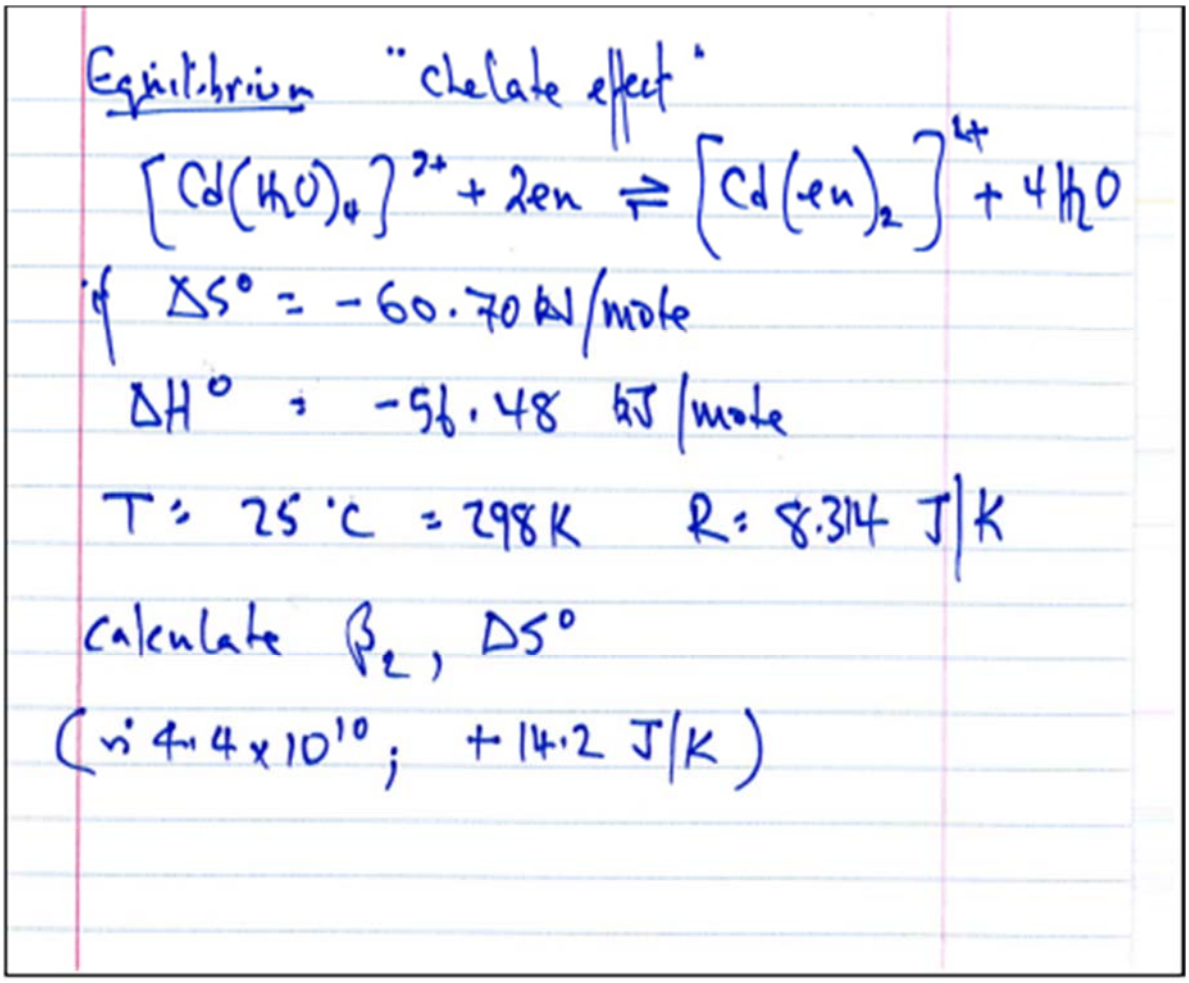

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350 **Note Delta(G)^0 and Delta(H)^0 are in kJ/mol but Delta(S)^0 is in J/mol**

351