**Semester I Examinations 2012-2013**

Exam Code(s) 4BS; 4BPC
Exam(s) 4th year Chemistry and 4th year Biopharmaceutical Chemistry
Module Code(s) CH431
Module(s) Organic Chemistry I

Paper No.

External Examiner(s) Professor Tim Gallagher
Internal Examiner(s) Prof. Paul V. Murphy
Dr. Fawaz Aldabbagh
Dr. Peter B. Crowley
Dr. Patrick O’Leary

**Instructions:** Answer one question from Section A, one question from Section B and one question of Section C

All questions carry 100 marks distributed as shown where appropriate. Leave the first page of the answer book blank and list on it clearly the numbers of the questions attempted.

**Duration** 2 hours
No. of Pages 8 (incl. this one)
Discipline(s) Chemistry

Requirements None
Section A
Answer either question 1 or question 2

1. Answer all parts:

(i) What is the isoprene rule? [10 marks]

(ii) Identify the isoprene units in the following terpenes.

(iii) Rationalise the biosynthesis of limonene from geranyl pyrophosphate using a curly arrow mechanism.

(iv) Identify organic products A and B in Scheme 1.

(v) Provide a curly arrow mechanism for the formation of product A. [20 marks]

(vi) Accurately draw the three dimensional conformation of steroid C, where methyl esters occupy equatorial positions only. [30 marks]
2. **Answer all parts**

(i) The acetylation of D-glucose carried out using a large excess of acetic anhydride (Ac₂O) and pyridine gives two isomeric pyranose products **C** and **D**.

Draw structures for **C** and **D** and explain in detail the role played by pyridine during the acetylation reaction.

![Chemical structures](image)

(ii) 2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl chloride **E** when treated with tetraethylammonium chloride (Et₄NCl) gives an equilibrium mixture that contains >90% of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl chloride. Draw the structure of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl chloride and give a detailed explanation for the outcome from this reaction.

![Chemical structures](image)
(iii) Write structures for the products F-K. Provide mechanisms and explain the stereoselectivity that results in the reactions that give H, J and K. Give reagents and conditions that would be required to convert G into the tripeptide Lys-Asp-Ser.

[60 marks]
Section B
Answer either question 3 or question 4

3. (i) In a reaction to assess if a complex catalyses alkene isomerisation by an allyl or alkyl mechanism the reagents below were used. What are the possible products for the alkyl and allyl mechanisms? Show the mechanism of either alkyl or allyl isomerisation.

\[ \text{Isomerisation catalyst} \]

[30 Marks]

(ii) The X-ray structure of the complex \((\text{C}_5\text{H}_5)\text{Rh}(\text{C}_2\text{H}_4)(\text{C}_2\text{F}_4)\) is shown below. The structure has some interesting features including the deviation of the alkenes from their normal planarity. The \(\text{C}_2\text{F}_4\) is seen to deviate to a greater degree from planarity than the \(\text{C}_2\text{H}_4\). The relevant bond lengths are marked in picometers. Discuss in detail the bonding of the alkenes to the rhodium in the complex showing the nature of the interactions and comparing the bonding of the two different alkenes.

[40 Marks]

(iii) In the complexes below which of the two dihydrogen bonds will be longer. Explain your answer.

[16 Marks]
(iv) What are the products C and D of the reactions below?

\[
\text{Bu}_3\text{Sn} \text{C} \text{Br} \xrightarrow{\text{Pd}_2\text{dba}_3, \ As\text{Ph}_3, \ THF, \ \Delta} \text{C} \xrightarrow{\text{Pd}_2\text{dba}_3} \text{D}
\]

[14 Marks]

4.

(i) Determine by means of electron counting whether the following complexes are stable or not. Explain your reasoning.  

[16 Marks]

(ii) The scheme below shows a hydroformylation reaction of hept-1-ene. The two main products are the expected linear and branched aldehyde. The third product is hept-2-ene which is formed via an unwanted elimination during the catalytic cycle. Show by means of the mechanism how all of these products may be formed.  

[30 Marks]
(iii) Choose three of the four compounds from the top row of compounds below and one from the lower row.
Give a synthesis for each of the compounds you selected from the top row. In your answers include all reagents and at least one organometallic reagent. The bond marked should be the one formed in the reaction.
For the lower row of compounds two bonds need to be formed in two separate reactions. Indicate which reagents you would use for the compound you have chosen and the order you would carry out the reactions and why.

![Chemical structures](Image)

(iv) In the reaction of an alkyne with an aldehyde as shown below (-)DIAB is used as a chiral ligand. Give the structures for the intermediates (J-L) and discuss how the ligand influences the chirality of the product.

![Chemical structures](Image)
5. **Answer all parts:**

The cationic side chains of lysine and arginine are potential targets for protein recognition by small molecules.

(i) Draw physiologically-relevant structural diagrams of the side chains of Lys and Arg. Comment on the typical location of Lys and Arg in protein structure. **[25 marks]**

(ii) Discuss the differences in charge density of the side chain atoms in Lys and Arg. Comment on the typical contribution of Lys and Arg to protein interactions. **[25 marks]**

(iii) Describe in detail, including structural diagrams, the types of interactions that Lys can form with p-sulfonatocalix[4]arene. **[30 marks]**

(iv) Name and draw structural diagrams of three posttranslational modifications of Lys. With reference to part (iii) discuss how one of these modifications can affect the interaction with p-sulfonatocalix[4]arene. **[20 marks]**

6. **Answer all parts:**

NMR spectroscopy and X-ray crystallography are two essential techniques used to characterize protein interactions.

(i) Outline the sample requirements for the characterization of a protein by NMR spectroscopy and X-ray crystallography. Comment on how these techniques can provide complementary information. **[15 marks]**

(ii) Describe with the aid of diagrams the application of $^1$H-$^{15}$N HSQC spectroscopy to study a protein-ligand complex. Include a method to determine the binding affinity of the interaction. **[40 marks]**

(iii) The crystal structure of a protein-protein complex reveals a non-covalent interaction between a Tyrosine and an Arginine residue. The side chains are observed to pack in a co-planar fashion. Draw a structural diagram of the side chain packing and name the interaction. Comment on the electrostatics that contribute to the non-covalent bond. **[25 marks]**

(iv) The resolution of the crystal structure is 1.1 Å. Discuss why the resolution of the structure is important. With reference to part (iii) explain if the observed non-covalent interaction is reliable. **[20 marks]**