KENYATTA UNIVERSITY

UNIVERSITY EXAMINATIONS 2011/2012

FIRST SEMESTER EXAMINATION FOR THE DEGREE OF BACHELOR OF EDUCATION AND BACHELOR OF SCIENCE

SCH 411: HETEROCYCLIC CHEMISTRY

DATE: **Thursday 8th December 2011** **TIME: 4.30p.m – 6.30p.m**

INSTRUCTIONS

Answer ALL questions

Q1. (a) Explain fully the following differences in physical and chemical properties of 5- membered heterocycles on the basis of electronic (inductive, mesomeric , electronegativity) and related effects.

(i) The resonance (delocalisation) energies of 5-membered hetero-aromatic compounds with one S, N or O atom are **lower** than that of benzene, 150 kJ $mole^{-1}$, and **varies** as follows: thiophene 122 kJ $mole^{-1}$, pyrrole 90 kJ $mole^{-1}$, and furan 68 kJ $mole^{-1}$. **[6 marks]**

(ii) The relative rate of electrophilic attack (e.g. with $AcONO_2$) on the three heterocycles is in the following order: pyrrole > furan > thiophene; electrophilic substitution in all the three compounds occurs mainly at the 2-position adjacent to the heteroatom (rather than at position 3). **[6 marks]**

(iii) Electrophilic reaction of the bicyclic heteroaromatic indole (pyrrole with benzene) occurs preferably on the pyrrole moiety rather than benzene. Electrophilic attack occurs at position 3 rather than 2 of the pyrrole ring. **[8 marks]**

(b) In the following reaction sequence, identify the products formed in each step and outline the electronic factors and mechanisms that underlie their formation:

$$\text{Pyrrole} \xrightarrow{CH_3MgBr} ? \xrightarrow{PhSO_2Cl} ? \xrightarrow{Ac_2O,\ AlCl_3} ? \xrightarrow{NaOH} ?$$

[10 marks]

Q2. (a) Account for the following differences or variations in the physical and chemical properties of pyridine and its derivatives on the basis of electronic and related effects.

(i) Electronic polarisation in both pyridine and its saturated analogue (piperidine) is in the direction of the heteroatom (N); however, this polarisation is almost x2 in pyridine compared to that in piperidine as reflected in their dipole moments (pyridine, 2.2D; piperidine, 1.17D). **[4 marks]**

(ii) The IR spectrum of 2-hydroxypyridine in solid phase shows no absorption due to O-H, but absorption due to amide C=O. In cyclohexane, its UV spectrum shows two maxima (234 and 310 nm), closely resembling that of 1-methyl-2-pyridone. However, in the gas phase or very dilute solutions its UV spectrum shows one maximum at about 273 nm. **[6 marks]**

(iii) Exposure of 2- or 4-bromopyridines to ammonia at 200^{o}C gives corresponding aminopyridines (2- or 4-). However, 3-bromopyridine does not react with ammonia under similar conditions. **[6 marks]**

(iv)Treatment of quinoline with a mixture of concentrated nitric acid and sulphuric acid at 0^{o} C gives approximately equal amounts (1:1) of 5- and 8-nitroquinolines. Under the same conditions isoquinoline gives mainly the 5-nitro isomer (9:1). **[8 marks]**

(b) In the following reaction sequences (each involving equimolar amounts of reactants), identify the products formed in each step and outline the electronic factors and mechanisms that underlie their formation:

(i) 4-Ethylpyridine $\xrightarrow{NaNH_2}$? $\xrightarrow{\text{Benzaldehyde}}$? **[6 marks]**

(ii) 2,3-Dimethylpyridine $\xrightarrow{NaNH_2}$? $\xrightarrow{CH_3CH_2Br}$? **[6 marks]**

Q3. (a) Fischer indole synthesis involves two steps: formation of an imine-enamine tautomeric intermediate; and acid (including a Lewis acid) cyclisation of the enamine tautomer to an indole.

(i) Put down the structures of the imine and 2 possible enamine tautomers that can be formed from the following reactants indicating which enamine tautomer is likely to be favoured and why:

$PhNHNH_2 + PhCH_2COCH_2CH_3 \longrightarrow ?$ **[6 marks]**

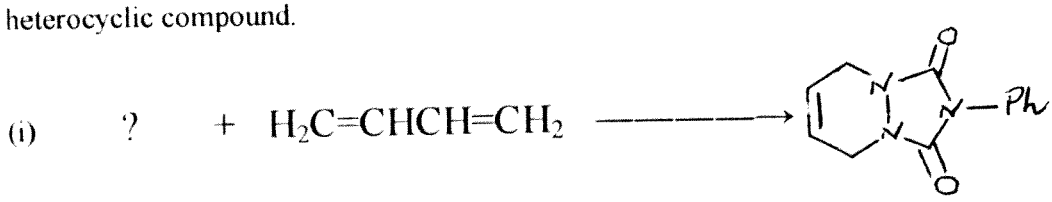
(ii) Trace the cyclisation of the enamine to the indole likely to be formed indicating the mechanism of the reaction pathway. **[6 marks]**

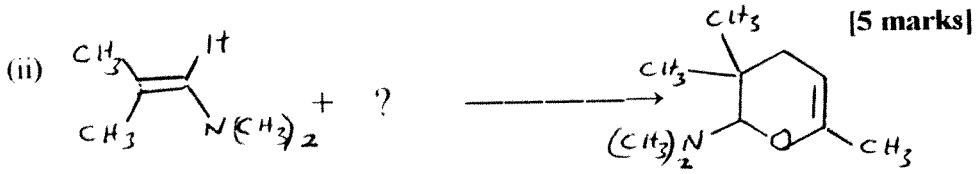
(b) Conrad-Limpach synthesis of quinolones involves acid-catalysed reaction of an aniline and a β-ketoester. Two products can initially be formed depending upon temperature and presence of water. Low temperatures (25-100^{o}C) and removal of water favour the formation of one (kinetic product) and higher temperatures (~150 ^{o}C) favour the other (thermodynamic product).

(i) Put the structures of the two products formed when 4-methylaniline and ethyl acetoacetate are allowed to react under the two reaction conditions and explain why one is favoured kinetically and the other thermodynamically. **[4 marks]**

(ii) Two different isomers of quinolones (2- or 4-quinolone) are formed when the products are exposed to appropriate conditions, the kinetic product to high temperatures in an appropriate medium (e.g. in diphenyl ether) and the thermodynamic product to concentrated sulphuric acid. Trace the cyclisation reactions of each product to the appropriate quinolone isomer. **[8 marks]**

(c) In the following hetero-Diels-Alder reactions, identify the missing heterodiene or dienophile/heterodienophile in the formation of the given heterocyclic compound.

(i) 

(ii) 

[5 marks]

[5 marks]