H3 Chemistry Preliminary Examination 2009 Mark Scheme

Setter & Marker: Ms Grace Chua

1 a) Narcotic analgesics work by **depressing the CNS**, hence **affecting the capacity** of the **brain to appreciate pain** **[1]**

Non–narcotic analgesics work on the **pain receptors** themselves, preventing them from responding normally to pain stimuli. **[1]**

b) Natural products, current drugs etc **[2]**

ci)

Mode of action (1)	Aspirin
Mode of action (2)	Ibuprofen
Mode of action (3)	Indomethacin

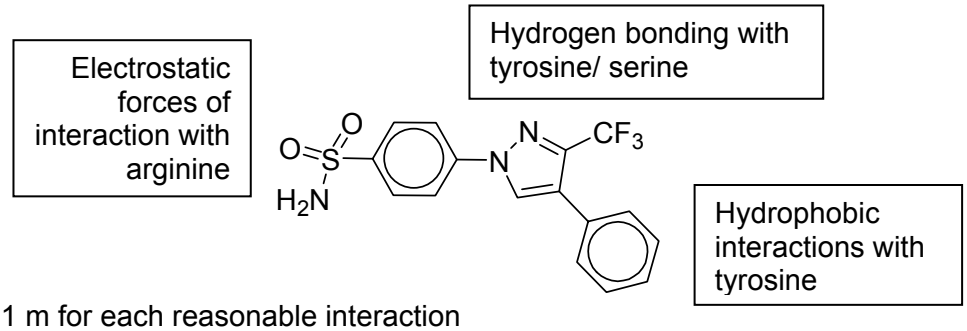
[1]

Mechanism (1) takes place with the formation of a covalent bond with serine. Aspirin can form an ester linkage with the hydroxy residue. **[1]**

Mechanism (2) should take place with substances that mimic arachidonic acid. Ibuprofen has the most similar structure to arachidonic acid. **[1]**

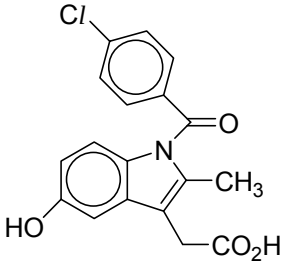
Mechanism (3) should involve electrostatic interactions between the basic group on arginine and hydrogen bonding/ dispersion forces with the tyrosine group for it to be reversible. Indomethacin fits the description. **[1]**

cii)



1 m for each reasonable interaction **[2]**

di) Precursor:



[1]

Reagents and conditions:
(1) NaOH(aq)
(2) CH_3I, heat **[1]**

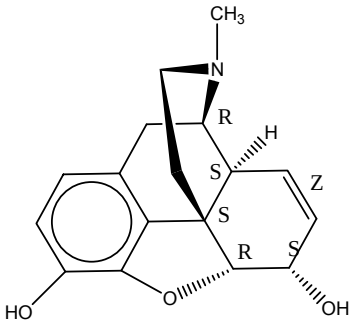
dii) S_N2. **[1]**

If the mechanism were S_N1, the carbocation formed is very unstable/ less steric hindrance

for primary halide therefore S_N2 favoured. **[1]**

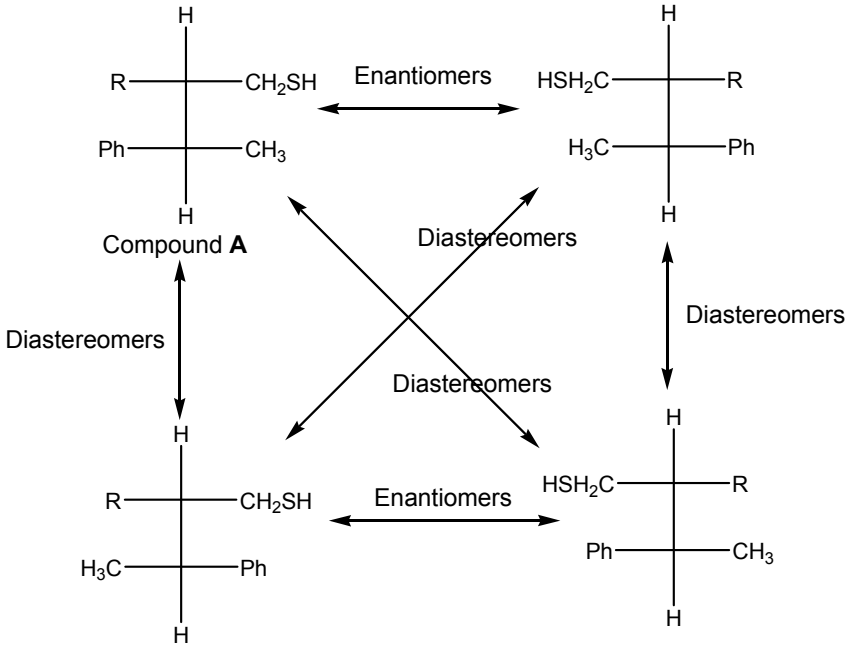
Note: Answer must be accompanied with reason, if not no marks awarded.

e)



[1/2] for each correct assignment. **[3]**

(f)



[3]
[Total: 20m]

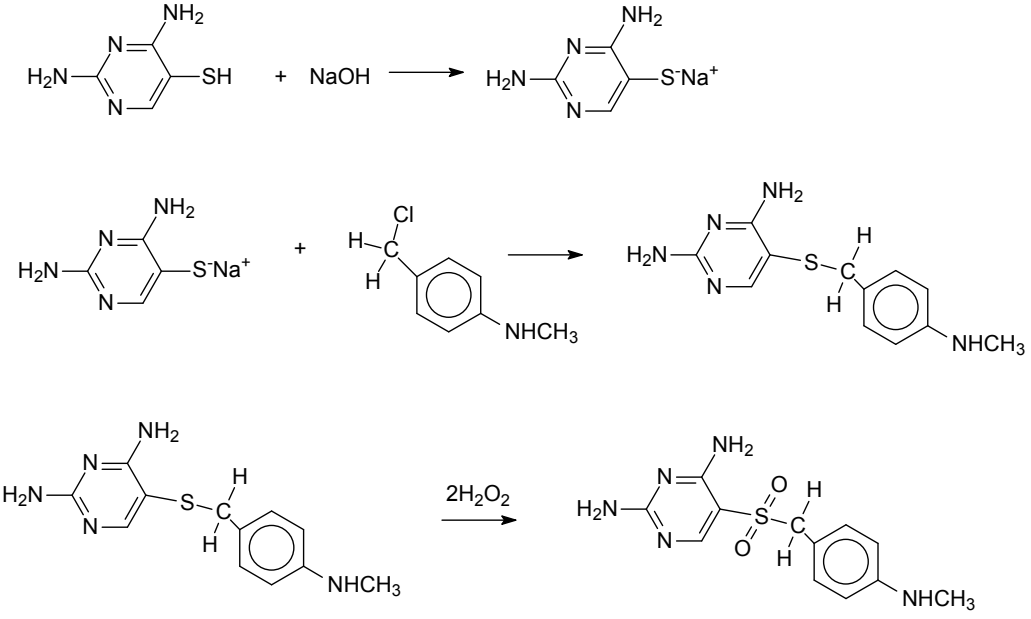
Setter & Marker: Ms Jessie Koh

2 ai) Rate of hydrolysis **A**<penicillin-G<**B** **[1]**

A should hydrolyse slower due to the electron-withdrawing C*l* group, **B** should hydrolyse faster due to the electron-donating CH_3CH_2 group. **[1]**

The electron-withdrawing C*l* group withdraws electrons from the C=O attached to the R group, thus makes the O of this C=O a poorer nucleophile which will have lower tendency to attack the carbonyl carbon of β-lactam ring to cause ring-opening. **[1]**

ii) 1 mark for each equation:



[3]

bi) Agonists compete for the receptor site, causing the necessary change in shape there. Antagonists block the site without causing the necessary change in shape. **[2]**

bii) Agonist: Compound **I**, **III**, **IV**.
Agonist should promote growth hence tumor grows to a larger size. **[1]**

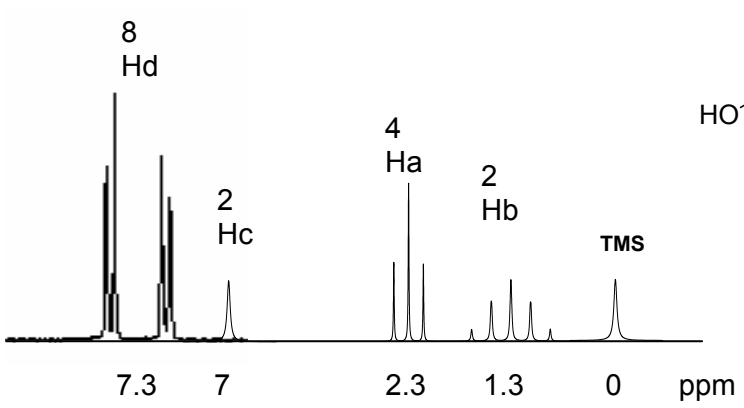
biii) Hydrogen bonding of phenol group **[1]**
Van der Waals forces of attraction of hydrophobic benzene ring or alkyl group **[1]**
(-1 m if student identifies ether)

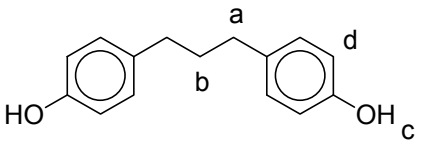
c) IR spectrum for **compound III** contains **broad –OH stretch** at about 3300- 3500 cm^{-1} that is missing in IR spectrum for **compound II.** **[1]**

di) TMS is used in ^{1}H NMR spectroscopy because it has 12 hydrogen atoms all of which are in exactly the same environment, i.e. they are equivalent and absorb energy at the same frequency. This produces a single but intense peak. **[1]**

Other accepted answers:
It is **inert** and would not react with the sample. /It is non-toxic, hence, safe to handle. /It is volatile (boiling point = $26.6^{0}C$) and can be distilled

dii)





- Axis and TMS peak **[1]**
- NMR spectrum shows 4 peaks: Ha, Hb, Hc and Hd **[1]**
- NMR spectrum shows correct splitting of the 4 peaks: Hd is multiplet, Hc is singlet, Ha is triplet, Hb is multiplet (quintet) **[1]**
- NMR spectrum shows correct relative area integrations under the peaks:
  Ha: Hb: Hc: Hd
  4 :2: 2 : 8 (or 2:1:1:4) **[1]**

diii) The Hd protons are aromatic protons which are very deshielded in the 7 – 8ppm region, due to **anisotropic diamagnetic effect** shown by H atoms attached to a benzene ring. **[1]**

Hc protons are also deshielded as it is bond to the **electron withdrawing O atom**, thus the electron density around the H nucleus is reduced, resulting in Hc protons being **deshielded.** **[1]**

div) The singlet due to the phenolic –OH will disappear in the presence of deuterated water as it is a labile proton.

[Total: 20m]

Setter & Marker: Mr Colin Loy

3 ai) As viruses use the host cell's biochemical reactions to reproduce themselves, it is difficult to design drugs which target the viruses but do not affect healthy cells as well. **[1]**

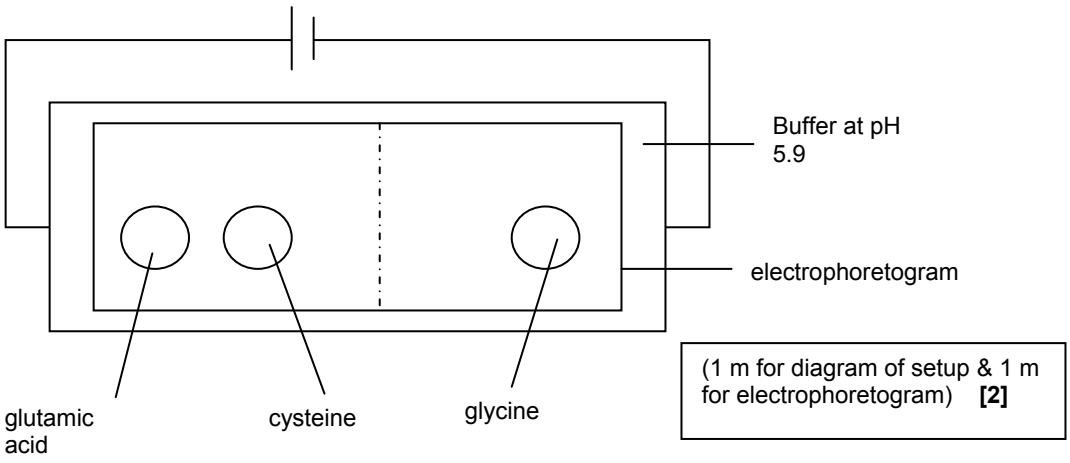
aii) Antibody: protein whose synthesis in the body in B lymphocytes is triggered by the presence of a specific antigen on the surface of an invading bacterium or virus. **[1]**

Monoclonal: antibody which has been isolated and generated in unlimited quantities from one particular B lymphocyte. **[1]**

aiii) J has an additional NH_2 group which may exist as a charged NH_3^+ at physiological pH leading to favourable interactions with water. **[1]**

In catalyzing deamination, the enzyme adenosine deaminase is rather specific. J may now be too different from the natural substrate adenosine/ unable to fit into the active site due to larger size. **[1]**

bi)



(1 m for diagram of setup & 1 m for electrophoretogram) **[2]**

bii) At pH 5.8, glutamic acid and cysteine are positively charged. Serine if present would also be positively charged and there would have been 3 amino acids (3 spots) migrating towards the anode. **[1]**
Glycine is negatively charged and migrated towards the cathode as shown in the expected electrophoretogram. **[1]**

ci) All have cyclic/ring structure with overlapping p orbitals/ π electron from carbon atoms or heteroatom. **[1]**

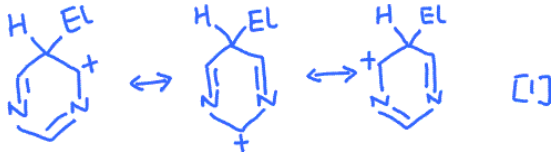
All satisfy Huckel's Rule (4n+2 π electrons) with n=1 for benzene, pyridine and pyrimidine and n=2 for quinoline. **[1]**

cii) Nitrogen is more electronegative than carbon and withdraws π electron density from the ring. **[1]**

Or

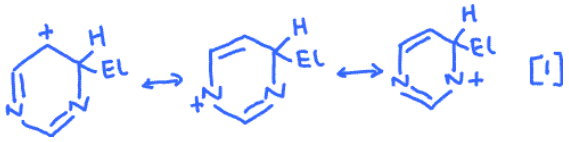
The nonbonding electrons on the nitrogen are perpendicular to the π system and cannot stabilize the positively charged intermediate effectively. **[1]**

ciii) For 5-bromopyridine:

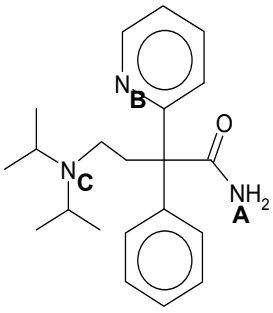


The positive charge in the intermediate does not lie at any of the nitrogen atoms in any of the resonance structures, which would be unfavourable. **[1]**

For 4-bromopyridine:



civ)

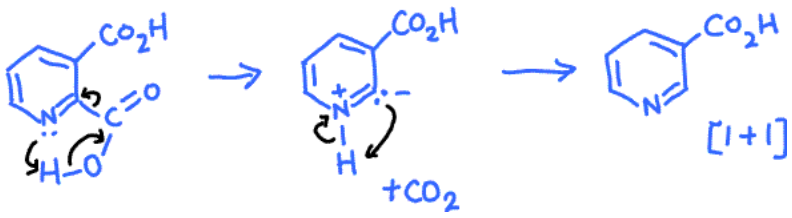


The N in the amide group is least basic (N_A) as the lone pair is delocalized over the 3 atoms O-C-N and is hence unavailable.

The N in the pyridine is basic (N_B) as it is available for coordination to form pyridinium ions.

The N in the tertiary amine is most basic (N_C) as the availability of its lone pair is enhanced by the electron donating effect of the alkyl groups.

cv)



[Total: 20m]

Setter & Marker: Ms Liew PC

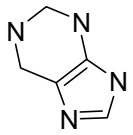
4 ai) **Placebo** is a "blank" pill/ injection that contains no active pharmaceutical agent, but should look and taste as similar as possible to the preparation of the actual drug. **[1]**

aii) The caffeine increases the time to exhaustion for non-user as compared to the regular caffeine users. **[1]**

The caffeine still exerts an effect on the non-users after 6 hours, but not on the regular users. **[1]**

aiii) (35-20)/ (25-20) X 100% = **300%** **[1]**

aiv)



[1]

av) Longer hydrophobic alkyl side group increases its ability to dissolve the lipophilic cell membrane/ blood brain barrier of the central nervous system. **[1]**

Longer alkyl side group allows it to fit into the hydrophobic pocket of the binding site and thus result in a better fit. **[1]**

avi) Caffeine, as a competitive antagonist, prevents the natural ligand from binding to the receptors on the surfaces of cells in the CNS. **[1]**

The cell has to adjust to the continual presence of an antagonist/caffeine by forming more receptors. **[1]**

Reduction of caffeine intake will upset the new balance and drug user craves for a continued high dose of caffeine to produce the same level of stimulation, leading to addiction. **[1]**

bi) $A = \varepsilon c l$ **[1]**

A – no units; ε - $mol^{-1}dm^3\ cm^{-1}$; c – mol dm^{-3} ; l – cm **[1]**

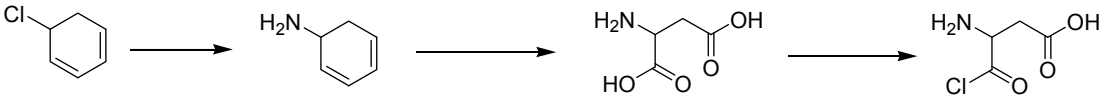
bii) H^+ protonates the basic N atom and decreases the degree of conjugation, **[1]**
thus increasing the energy gap and decreases the wavelength at which it absorbs. **[1]**

biii) [caffeine] diluted = 50/100 x (25 x 10^{-3}/194) = **6.44×10^{-5} mol dm^{-3}** **[1]**

A_{273} = 6.44 x 10^{-5} x 10000 = **0.64** **[1]**

biv) The reading is higher than expected as the other food addictives such as food colourings and flavourings maybe able to absorb at 273 nm, thus increasing the absorbance. (no mark if student just specify "impurities/ contaminants" without adding that they absorb at 273 nm as well). **[1]**

bv)



conc NH_3

heat in sealed tube

or ethanolic NH_3, heat

1) $KMnO_4$(aq), H_2SO_4(aq), heat
2) NaOH(aq), controlled addition

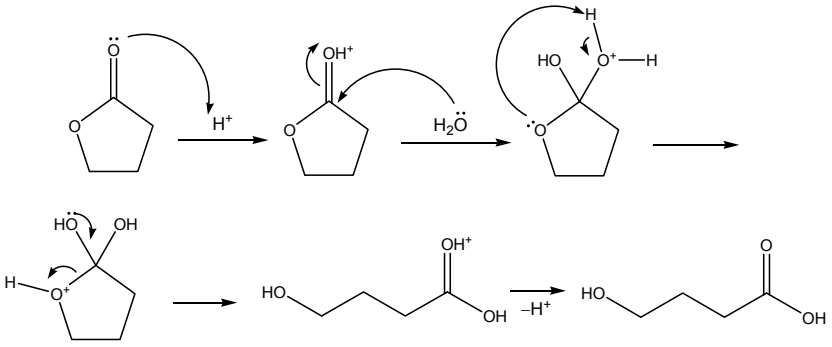
1 equiv PCl_5 (or limited amount)

½ m for each reagent & ½ m for intermediate **[3]**

[Total: 20m]

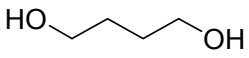
Setter & Marker: Ms Tan CS

5 ai)



[3]

aii)



[1]

aiii) (**I**) The sample is vaporized and carried through the column by an **inert gas (mobile phase)** such as He or N_2. **[1]**

The sample is passed through a column containing **non-volatile liquid coated onto small inert particles as the stationary phase**. **[1]**

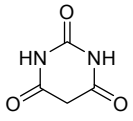
The separation is based on the **volatility of the solute** as well as the **nature of interaction** between the component and the stationary and mobile phase. **[1]**

(**II**)

$$K_c = = \frac{[GBL][H_2O]}{[GHB]} = \frac{\left(\frac{1}{2}\times 3\times 4.6\right)(55.0)}{\left(\frac{1}{2}\times 4\times 1\right)} = 190 \text{ mol dm}^{-3} \text{ (3.s.f)}$$

(1 m for the peak areas, 1 m for the correct K_c) **[2]**

bi)



[1]

bii) From MS spectrum:

No of carbon atoms = $\frac{0.3}{2.7}\left(\frac{100}{1.1}\right) = 10$ **[1]**

biii) From MS spectrum:
Peak at m/z = 167 ⇒ Loss of 210 – 167 = 43 ⇒ loss of CH_3CHCH_3 **[1]**
Peak at m/z = 41 ⇒ $[CH_2{=}CHCH_2]^+$ fragment **[1]**

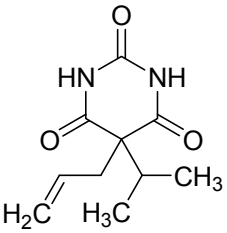
From ^{1}H NMR spectrum:

chemical shift / ppm	integration	multiplicity	deduction	
1.0	6	doublet	2 equivalent CH_3 group next to CH group	**[1]**
2.3	1	multiplet	CH group attached to 2 equivalent CH_3	**[1]**
2.4	2	doublet	CH_2 next to CH	**[1]**
5.0	2	multiplet	H of CH_2=C group	**[1]**
5.7	1	multiplet	H of CH=C group	
10.0	2	singlet	H attached to N	**[1]**

H attached to N is highly deshielded as it is next to two electron withdrawing C=O group. **[1]**

From IR spectrum:

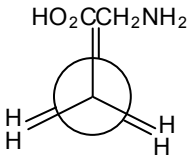
wavenumber / cm^{-1}	deduction	
3200	N–H stretch	**[1]**
1700	C=O stretch	**[1]**

Aprobarbital is  . **[1]**

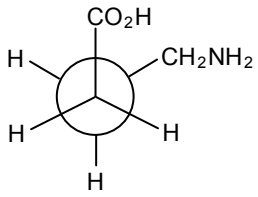
11 marking points. Max **[9]**
[Total: 20m]

Setter & Marker: Mr Rudy Lee

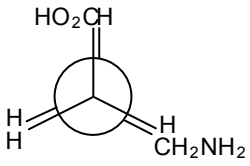
6 ai)



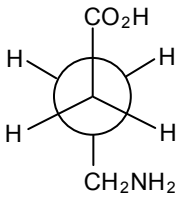
I (most unstable eclipsed)



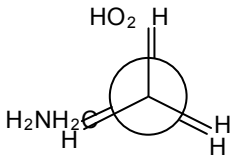
II (gauche)



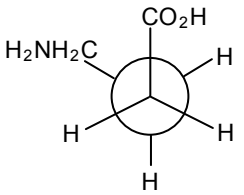
III (eclipsed)



IV (anti-staggered)

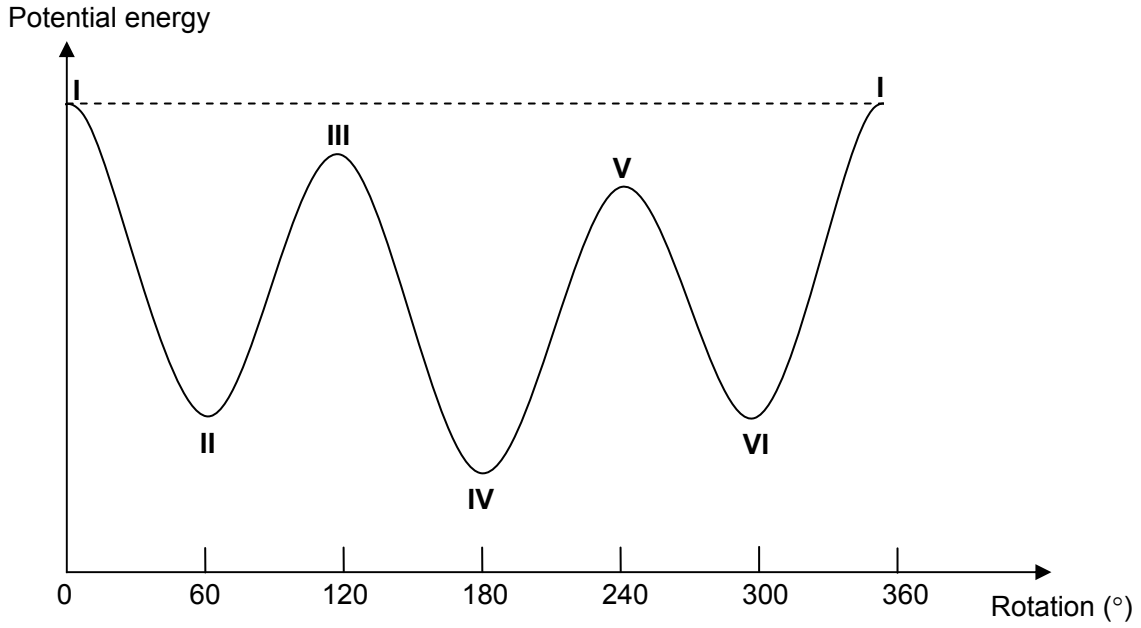


V (eclipsed)



VI (gauche)

[2]

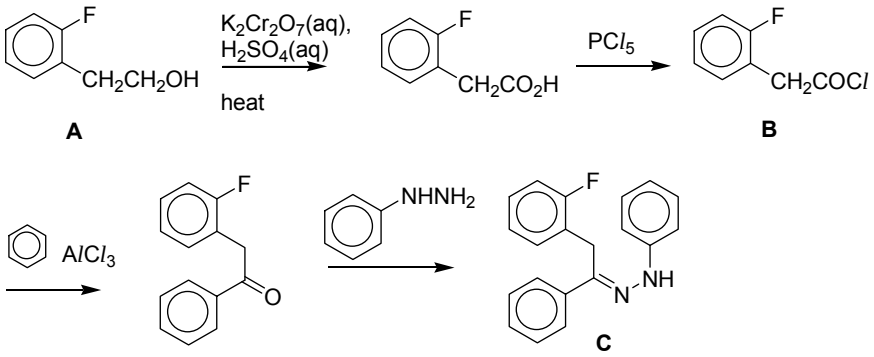


Correct potential energy diagram, with labelling. **[2]**

aii) Flunitrazepam is an agonist at the $GABA_A$ receptor site since a conformational change occurs in the receptor when it binds to $GABA_A$, enhancing the binding of GABA. **[1]**

bi) A drug causing hallucinations or affecting the subjective qualities of thought and perception. **[1]**

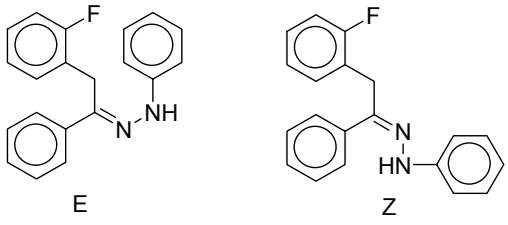
bii)



A B C

[4]

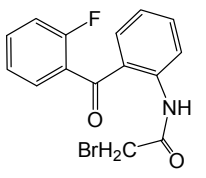
biii) Geometric isomerism



E Z

[1]

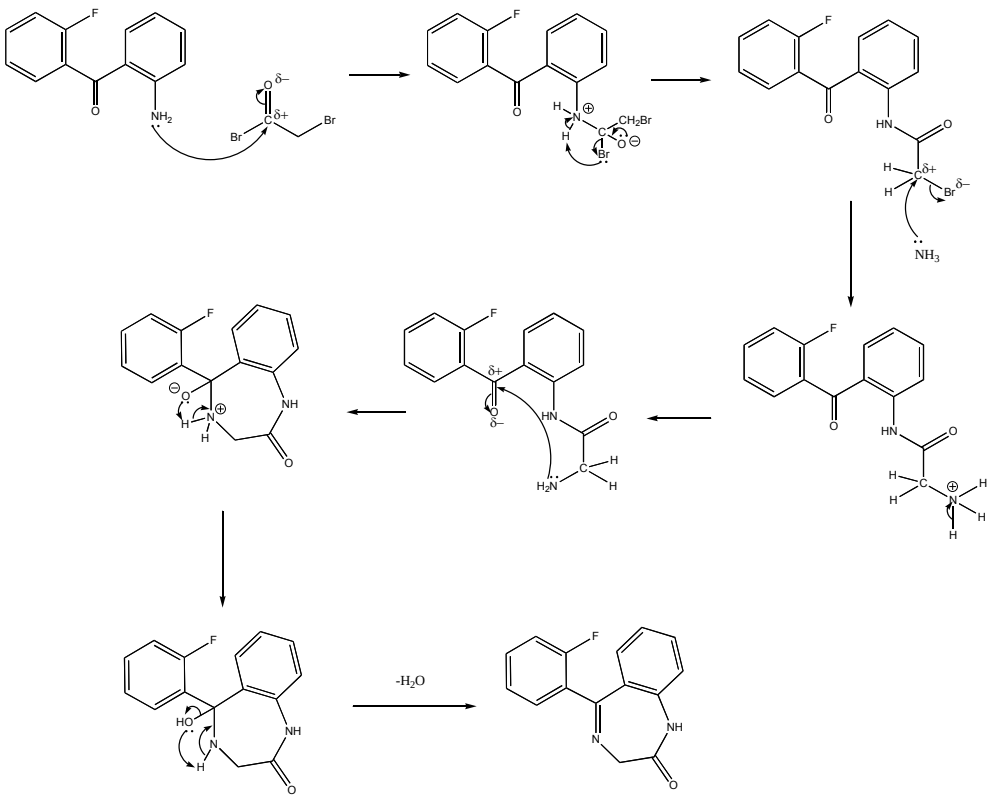
biv)



F

[1]

bv)



[2]

[3]

bvi) (I) G → H : Electrophilic Substitution **[1]**

(II) H → flunitrazepam: Nucleophilic Substitution **[1]**

[Total: 20m]