HL Paper 3

Lutetium-177 is used in radiotherapy. It emits beta radiation when it decays.

a. State a nuclear equation to show the decay of lutetium-177. [2]

b. The half-life of lutetium-177 is 6.73 days. Determine the percentage of a sample of lutetium-177 remaining after 14.0 days. [2]

c. Explain the low environmental impact of most medical nuclear waste. [2]

Markscheme

a. ${}^{177}_{71}\mathrm{Lu} \rightarrow {}^{177}_{71}\mathrm{Hf} + {}^{0}_{-1}\mathrm{e}$ «+ ν»

Hf

correct *A* and *Z* ***AND*** beta product

Accept "β/ β^-/e/e^-" for "${}^{0}_{-1}\mathrm{e}$".

Accept "$^{177}Lu \rightarrow {}^{177}Hf + e^-$ «+ ν»".

b. number of half-lives = $\frac{t}{t_{\frac{1}{2}}}$ = 2.08

OR

$\frac{N(t)}{N_0} = 0.5^{\frac{14.0}{6.73}}$

OR

$\lambda = \text{«}\frac{\ln 2}{t_{\frac{1}{2}}} = \frac{\ln 2}{6.73} \text{=»}$ 0.103 «day^{-1}»

OR

$\frac{N(t)}{N_0} = e^{-0.103 \times 14.0}$

23.6 «%»

*Award **[2]** for correct final answer.*

c. *Any two of:*

emits weak ionising radiation

OR

low activity/radioactivity

can be stored until material becomes inactive ***AND*** then disposed with normal waste

«isotopes» have short lives

OR

exist for a short period of time

*Award **[1 max]** for "low-level waste/LLW".*

[Max 2 Marks]

Examiners report

a. [N/A]
b. [N/A]
c. [N/A]

Targeted Alpha Therapy (TAT) is a technique that involves using alpha-radiation to treat leukemia and other dispersed cancers.

Yttrium-90 and lutetium-177 are used in radiotherapy.

a.i. Explain why alpha-radiation is particularly suitable for this treatment. [2]

a.ii. Outline how the alpha-radiation in TAT is directed to cancer cells. [1]

b.i. Identify the type of radiation emitted by these two radioisotopes. [1]

b.ii. State an equation for the one-step decay of yttrium-90. [1]

b.iii. The half-life of lutetium-177 is 6.75 days. Calculate the percentage remaining after 27 days. [1]

Markscheme

a.i. more damaging than other radiation types

OR

very damaging to «cancer» cells

OR

high ionizing density «of alpha particles»

absorbed within a very short range of emission
OR
causes little damage to surrounding tissues

Accept "high ionizing power «of alpha particles»" for M1.

Accept "low penetrating power «of alpha particles»" for M2.

[2 marks]

a.ii. «radioactive isotope/radionuclide/alpha-emitter» administered using carrier drug/protein/antibodies

[1 mark]

b.i. beta/β «radiation»

[1 mark]

b.ii. $^{90}_{39}Y \rightarrow {}^{90}_{40}Zr + \beta$

Accept "$^{0}_{-1}e/e/e^{-}$" ***OR*** "$^{0}_{-1}\beta/\beta^{-}$"

Accept ECF from (b) (i) if incorrect radiation identified, eg, $^{90}_{39}Y \rightarrow ^{86}_{37}Rb + ^{4}_{2}He$

[1 mark]

b.iii **ALTERNATIVE 1:**

«4 half-lives»

6.25 «%»

ALTERNATIVE 2:

«$N_t = N_0(0.5)^{\frac{t}{t_{1/2}}} = 100(0.5)^{\frac{27}{6.75}} =$» 6.25 «%»

[1 mark]

Examiners report

a.i. [N/A]
a.ii. [N/A]
b.i. [N/A]
b.ii. [N/A]
b.iii. [N/A]

A number of drugs have been developed to treat excess acidity in the stomach.

Outline how ranitidine (Zantac) functions to reduce stomach acidity.

Markscheme

Blocks/binds H2-histamine receptors «in cells of stomach lining»

OR

prevents histamine molecules binding to H2-histamine receptors «and triggering acid secretion»

Accept "H2 receptor antagonist"

[1 mark]

Examiners report

[N/A]

Technetium-99m is the most widely used medical radioisotope. It is usually made on-site in medical facilities from isotopes of molybdenum.

a. Deduce equations for the following nuclear reactions: [2]

(i) Molybdenum-98 absorbs a neutron.

(ii) The isotope produced in (a) (i) decays into technetium-99m.

b. Molybdenum-99 has a half-life of 66 hours, while technetium-99m has a half-life of 6 hours. Outline why technetium-99m is made on-site. [1]

c. Outline **two** reasons, other than its half-life, why technetium-99m is so useful in medical diagnosis. [2]

d. Outline the nature of the radioactive waste that is generated by the use of technetium-99m in medical diagnosis. [1]

Markscheme

a. i

$^{98}_{42}\mathrm{Mo} + {}^{1}_{0}\mathrm{n} \rightarrow {}^{99}_{42}\mathrm{Mo}$

Accept $^{98}Mo + {}^{1}n/n \rightarrow {}^{99}Mo$.

ii

$^{99}_{42}\mathrm{Mo} \rightarrow {}^{99\,\mathrm{m}}_{43}\mathrm{Tc} + {}^{0}_{-1}\beta$

Accept "$^{0}_{-1}e$" for "$^{0}_{-1}\beta$".

Accept "$^{99}Mo \rightarrow {}^{99\,\mathrm{m}}Tc + \beta$".

Accept "$^{0}_{-1}e/e^{-}/e$" for "β".

Do not penalize "^{99}Tc" for "$^{99\,\mathrm{m}}Tc$".

b. molybdenum-99 can be easily transported «before it decays»/more stable

OR

«most of» technetium-99m will decay during transportation

*Do **not** accept just "short half-life of Tc-99m"*

c. emits gamma rays

OR

emissions escape from body

OR

emissions detected by gamma camera

OR

radiation dose is low

chemically reactive/versatile/transition metal bonds to a range of «biologically active» substances

*Do **not** accept "short half-life of Tc-99m".*
Accept "energy of photons produced is «relatively» low" and "no high energy beta emission" for M1.
Accept "…has ability to form tracers" for "…bonds to a range of «biologically active» substances".

d. low-level «radioactive» waste/LLW

OR

small amounts of ionizing radiation for short time

Examiners report

a. [N/A]

b. [N/A]
c. [N/A]
d. [N/A]

Taxol is produced using a chiral auxiliary. Describe how the chiral auxiliary functions to produce the desired product.

Markscheme

chiral molecule/auxiliary/optically active species added/connected/attached «to non-chiral starting molecule to force reaction to follow a certain path»

one enantiomer produced
OR
chiral auxiliary creates stereochemical condition «necessary to follow a certain pathway»
OR
stereochemical induction
OR
existing chiral centre affects configuration of new chiral centres

«after new chiral centre created» chiral auxiliary removed «to obtain desired product»

[3 marks]

Examiners report

[N/A]

Aspirin, paracetamol (acetaminophen), morphine and diamorphine (heroin) are all pain killers. Their structures are given in Table 20 of the Data Booklet.

Suggest a reagent that could be used to convert morphine into diamorphine and state the name of the type of reaction taking place.

Markscheme

ethanoic acid / ethanoic anhydride / ethanoyl chloride;

Accept formula instead of name.

diesterification / esterification / condensation;

Examiners report

Most could name the type of the reaction, and many did not name the reagent, with “carboxylic acid” being a common answer.

Radioactive isotopes are used in a variety of medical procedures including medical imaging and radiotherapy.

b. Lead-212 is a radioisotope that is used in the treatment of cancer. It is produced from another radioisotope by alpha decay. Formulate the equation for its production. [2]

c. Identify **one** advantage of using Targeted Alpha Therapy (TAT) and one form of cancer commonly treated by this method. [2]

Advantage:

Cancer treatment:

d. Technetium-99m, used for radioimaging scans, has a half-life of 6.01 hours. Calculate the mass of a 5.80×10^{-9} g dose remaining after 24.04 hours. [2]

e. Outline an ethical implication of using nuclear treatments in medicine. [1]

Markscheme

b. $^{216}_{84}\mathrm{Po} \rightarrow {}^{4}_{2}\mathrm{He} + {}^{212}_{82}\mathrm{Pb}$

correct reactant

correct alpha particle

Atomic numbers not required for mark.
Accept "α"/"$^{4}_{2}\alpha$" for "$^{4}_{2}\mathrm{He}$".

c. *Advantage*:

selectively kills cancer cells/targets cancer cells only

OR

does not damage healthy cells

*Do **not** accept "targets cancer". Reference must be made to "cells".*

Cancer treatment:
melanoma
OR
leukemia
OR
rectal
OR
breast
OR
ovarian
OR
prostate
OR
pancreatic
OR
cancers that spread around the body/produce metastasis/dispersed cancers

Accept "skin cancer".

d. ***ALTERNATIVE 1:***

$\lambda \ll= \frac{\ln 2}{6.01} \gg\approx 0.115 \ll \mathrm{h}^{-1} \gg$

«remaining mass = $5.80\times10^{-9}\times e^{-0.115 \times 24.04}$=»$3.63\times10^{-10}$ «g»

ALTERNATIVE 2:

$\ll \frac{24.04}{6.01} =\gg 4 \ll \mathrm{halflives} \gg$

$\ll \frac{5.80\times10^{-9}}{2^4} =\gg 3.63 \times 10^{-10} \ll \mathrm{g} \gg$

*Award **[2]** for correct final answer.*

e. risk vs benefit «patient and environment»

OR

providing adequate information to patients about risks

OR

security concerns if nuclear radioactive material ended up with terrorists

OR

cultural resistance/superstition/lack of education

OR

«potential» exposure of health workers «to radioactivity»

OR

proper training «in radioactive hazards» not always given to workers

OR

proper disposal of radioactive materials

Accept other valid ethical implications (note that risk of cancer to the patient is not an ethical issue, while risk of cancer to the health worker is).

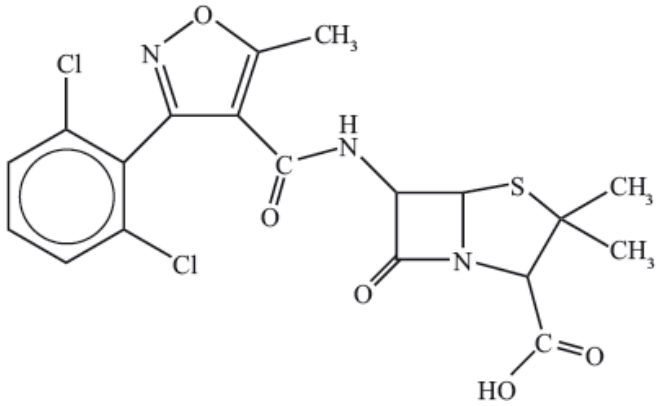
*Do **not** accept "security concerns" alone – there must be some reference to an ethical implication.*

Examiners report

b. [N/A]
c. [N/A]
d. [N/A]
e. [N/A]

The discovery of penicillin by Alexander Fleming in 1928 is often given as an example of serendipity in science.

The structure of a particular type of penicillin called dicloxacillin is shown below.

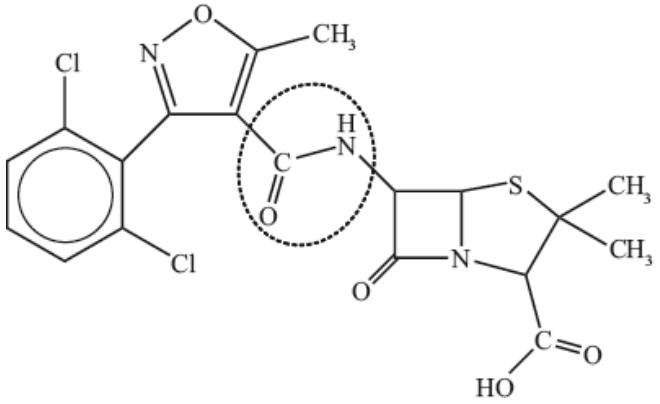


c. Describe what happens to bacteria when they come into contact with penicillin. [2]

d. (i) Identify the β-lactam ring by drawing a circle around it. [5]

(ii) Explain why the β-lactam ring is so important in the mechanism of the action of penicillin.

(iii) State the name of the functional group in dicloxacillin, circled below.



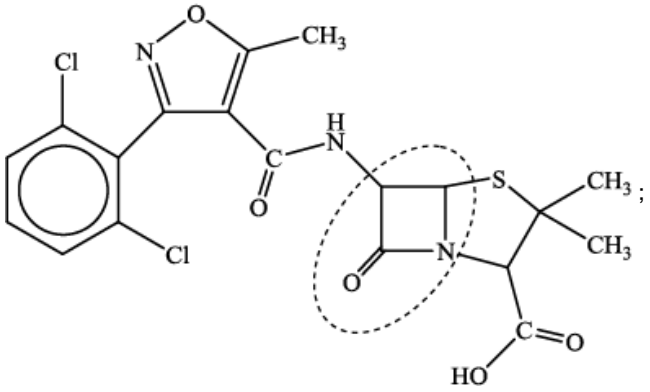
e. Comment on the fact that many bacteria are now resistant to penicillins. [2]

Markscheme

c. interferes with enzymes/chemicals that bacteria need to make <u>cell walls</u> / interferes with <u>cell wall</u> formation;

osmosis/osmotic pressure causes cell wall to break/burst / water enters cell causing it to burst / *OWTTE*;

d. (i)



;

(ii) ring strain / bond angles are approx 90° / should be 109° or 120° / *OWTTE*;

ring breaks / produces reactive amide group / *OWTTE*;

(so) penicillin can become bonded to enzyme/penicillinase;

(iii) amide;

e. caused by overprescription/overuse/overdose / not completing course of penicillin / use of antibiotics in animal feed / *OWTTE*;

penicillins with modified side chains must be developed/cocktail of drugs must be taken to overcome resistant bacteria / *OWTTE*;

Examiners report

c. Most answers scored at least one mark in (c), or came close to it – most that did not were not specific enough or failed to mention cell walls.

d. In (d), the β-lactam ring was usually correctly identified, as was the circled amide group. In part (d)(ii), few answers scored full marks, although most identified the relevance of the bond angles in causing ring strain.

e. In (e), many more scored the overprescription mark than the one for modifying the side chain.

Nuclear radiation is dangerous because of its ability to damage cells but it can also be used in nuclear medicine.

Iodine-131 is released in nuclear explosions but is used in scanners for thyroid cancer. The half-life of iodine-131 is 8.02 days.

a. Yttrium-90 is used in treating certain cancers. [1]

Formulate a nuclear equation for the beta decay of yttrium-90.

b. Lutetium-177 is a common isotope used for internal radiation therapy. [1]

Suggest why lutetium-177 is an ideal isotope for the treatment of certain cancers based on the type of radiation emitted.

c.i. Calculate the rate constant, λ, in day^{-1}, for the decay of iodine-131 using section 1 of the data booklet. [1]

c.ii. Calculate the time, in days, for 90% of the sample to decay. [2]

d. A breathalyser measures the blood alcohol content from a breath sample. Formulate half-equations for the reactions at the anode (negative electrode) and the cathode (positive electrode) in a fuel cell breathalyser. [2]

Anode (negative electrode):

. . . . . .

Cathode (positive electrode):

. . . . . .

Markscheme

a. $^{90}Y \rightarrow {}^{90}Zr + \beta^-$

Accept β, e or e^-.
Accept $^{90}Y \rightarrow {}^{90}Zr + \beta^- + \nu$

[1 mark]

b. beta-radiation/emission ***AND*** targets tumour/cancer cells

OR

beta-radiation/emission ***AND*** limited damage to healthy cells/tissues

OR

beta-radiation/emission ***AND*** produces «small amount of» gamma-rays «for visualizing tumours/monitoring treatment»

[1 mark]

c.i. $\lambda \left(= \frac{\ln 2}{t_{\frac{1}{2}}} = \frac{0.693}{8.02\ day} \right) = 8.64 \times 10^{-2} / 0.0864$ «day^{-1}»

[1 mark]

c.ii. ***ALTERNATIVE 1:***

«N_0 = initial amount = 100%»

N «= 100 – 90» = 10% at time t

«$\ln\left(\frac{100}{10}\right) = 2.303 = 0.0864t$»

«$t = \frac{2.303}{0.0864\ \text{day}^{-1}}$ =» 26.7 «days»

Accept 26.6 or 27 «days»
Award [2] for correct final answer.

ALTERNATIVE 2:
«$N_t = N_0(0.5)^n$ where n = number of half-lives»

$10 = 100(0.5)^n$

«$\log\left(\frac{1}{10}\right) = n \times \log\ 0.5$»

«$-1 = n\,(-0.301)\,/n = \frac{1}{0.301}$»

«$t = \frac{1}{0.301} \times 8.02$ =» 26.6 «days»

Accept 26.7 or 27 «days»

Award [2] for correct final answer.

[2 marks]

d. *Anode (negative electrode):* $C_2H_5OH + H_2O \rightarrow CH_3COOH + 4H^+ + 4e^-$

Cathode (positive electrode): $O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$

[2 marks]

Examiners report

a. [N/A]
b. [N/A]
c.i. [N/A]
c.ii. [N/A]
d. [N/A]

Ethanol slows down the reaction time of a driver leading to traffic accidents. Explain how the concentration of ethanol in a sample of breath can be determined using a fuel cell breathalyser.

Markscheme

ethanol is oxidized «to ethanoic acid»

OR

electrons are released

current/potential proportional to concentration «of ethanol»

OR

current compared to a reference «to determine concentration»

Accept "ethanol reacts with oxygen" for M1.

Accept "voltage" for "potential".

Examiners report

[N/A]

Some drugs can be converted into ionic salts in order to increase their solubility in water.

a.i. State the equation for the formation of the ionic salt of aspirin, $\mathrm{CH_3COO(C_6H_4)COOH}$. [1]

b. Chiral auxiliaries are used in drug design. Describe how a chiral auxiliary works. [2]

Markscheme

a.i. $\mathrm{CH_3COO(C_6H_4)COOH + NaOH \rightarrow CH_3COO(C_6H_4)COONa + H_2O}$;

Accept Na_2CO_3 or $NaHCO_3$.

Accept ions for strong base and salt or net ionic equation.

b. chiral auxiliaries are enantiomers/optically active;

auxiliary creates stereochemical condition necessary to follow a certain pathway / is used to manufacture one enantiomer (so avoids need to separate a racemic mixture);

attaches/connects itself to non-chiral molecule / makes it optically active;

only desired/one enantiomer/molecule formed (and chiral auxiliary removed);

Examiners report

a.i. The equations for the formation of the ionic salt of aspirin and the ionic salt of fluoxetine were poorly done with $\mathrm{H_2O}$, NaCl, HCl and Na used in the first case instead of NaOH and $\mathrm{H_2O}$ and NaOH used in the second case instead of HCl.

b. Description of how a chiral auxiliary works was not well understood and chiral axillaries function in synthesis was also sometimes confused.

A polarimeter can be used to determine the optical rotation of an optically active substance.

a. Describe what happens to plane-polarized light when it passes through a solution of an optically active compound. [1]

b. A mixture of enantiomers shows optical rotation. [1]

Suggest a conclusion you can draw from this data.

Markscheme

a. plane of polarization is rotated

Award zero if answer refers to plane-polarized light being bent.

[1 mark]

b. not a racemic mixture

OR

two enantiomers not equimolar

OR

mixture contains optically active impurity

OR

relative proportions of enantiomers in mixture can be determined

[1 mark]

Examiners report

a. [N/A]
b. [N/A]

Amphetamine and methamphetamine are widely abused drugs.

d. Amphetamine exists as optical isomers. Describe how chiral auxiliaries can be used to synthesize only the desired enantiomeric form of a drug from a non-chiral starting compound. [3]

e. The structures of morphine and heroin are shown in Table 20 of the Data Booklet. Explain the increased potency of heroin compared to morphine. [2]

Markscheme

d. a chiral auxiliary is itself an enantiomer/optically active;

it is bonded to the reacting molecule so that reaction forms one product;

(remove chiral auxillary) to give one enantiomer;

e. polar hydroxyl groups in morphine are replaced by less/non-polar ester groups;

Accept morphine more polar/heroin less polar without mentioning hydroxyl and ester groups for M1.

allows transport into the non-polar central nervous system / more soluble in nonpolar lipids / penetrates/crosses blood-brain barrier / *OWTTE*;

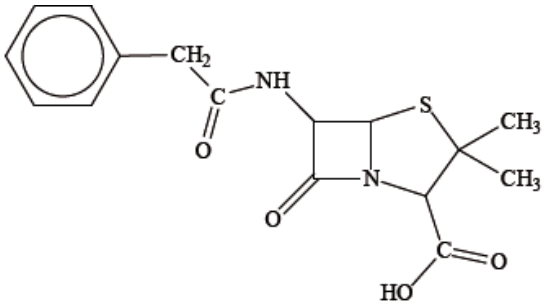
Reference to difference in polarity needed for first mark.

Examiners report

d. Candidates found it more difficult to explain the use of chiral auxiliaries.

e. Discussion of polarity with regard to morphine and heroin was often omitted in (e), again suggesting poor chemical understanding by many candidates.

The first penicillin to be used was benzylpenicillin (Penicillin G), its structure is shown below.



The active part of penicillins is the beta-lactam ring. Determine the functional group present in the beta-lactam ring and explain why the ring is important in the functioning of penicillin as an antibacterial.

Markscheme

amide group / –CONH– / peptide;

ring is strained / *OWTTE*;

ring breaks easily so (the two fragments similar to cysteine and valine) then bond(s) covalently to the enzyme that synthesizes the bacterium cell wall (so blocking its action);

Examiners report

Surprisingly few candidates identified the amide in (c). The idea of the strained ring was well known, but very few stated that the opened molecule binds to the enzyme that synthesizes the cell wall, some stated that it binds to the cell wall itself.

Some drugs are extracted from natural sources and others are synthetic.

Explain the role of the chiral auxiliary in the synthesis of Taxol.

Markscheme

Any three of:

chiral auxiliary is optically active

is attached to non-optically active/non-chiral substrate

creates stereochemical condition necessary to follow a certain pathway

allows only the required enantiomer to form «so avoids need to separate a racemic mixture»

[Max 3 Marks]

Examiners report

[N/A]

Analgesics are used to relieve pain in the body. Aspirin and paracetamol (acetaminophen) are both mild analgesics.

The structures of the strong analgesics morphine and heroin (diamorphine) can be found in Table 20 of the Data Booklet.

Explain the increased potency of heroin (diamorphine) compared to morphine.

Markscheme

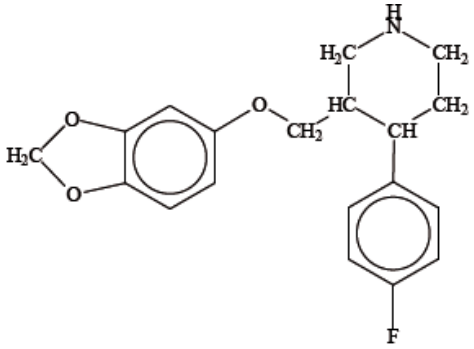
polar hydroxyl groups in morphine are replaced by less polar/non-polar ester groups;

so facilitate transport into the non-polar environment of the central nervous system / increases the solubility in lipids / *OWTTE*;

Examiners report

Very few were able to fully explain the increased potency of heroin – some referred to polarity but did not identify the groups, and some the other way round, a few correctly stated that heroin was more lipid soluble so could cross the blood brain barrier more easily.

Paroxetine, whose structure is shown below, is a drug prescribed to people suffering from mental depression.



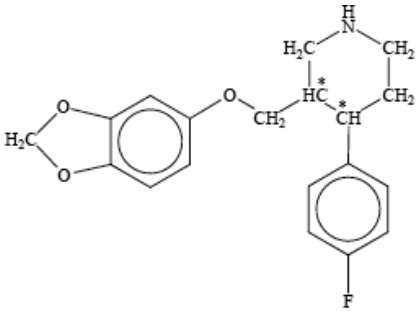
a. Identify the **two** chiral carbon atoms in the structure above with an asterisk (*). [2]

b. Explain, with an example, the importance of chirality in drug action. [2]

c. Describe the use of chiral auxiliaries to synthesize the desired enantiomer of a drug. [2]

Markscheme

a.



*Award **[1]** for each correctly placed asterisk.*

b. different enantiomers can cause different (physiological) effects in the body;

thalidomide – one isomer prevented morning sickness, the other caused fetal abnormalities / ibuprofen – one isomer is more effective than the other / DOPA – one isomer helps manage Parkinson¨disease, the other has no physiological effects;

Accept other correct examples.

c. chiral auxiliaries are themselves chiral;

attach to the non-chiral molecule (to enable the desired enantiomer to be formed);

after the desired enantiomer is formed the chiral auxiliary is removed/recycled;

Examiners report

a. The better candidates could identify the chiral carbon atoms.

b. Many candidates could explain the importance of chirality in drug action with an example.

c. The use of chiral auxiliaries was less known, many candidates failed to recognize that they are chiral themselves and many confusing answers were given.

Diseases may be caused by bacteria or viruses.

a.ii. The beta-lactam ring is highly reactive and enables penicillins to be effective antibacterials. The general structure of penicillin is given in table 20 of the data booklet. Explain, in terms of hybridization and bond angles, why the beta-lactam ring is strained. [2]

b.i. Cytovaricin is an antibiotic that is produced using a chiral auxiliary. Suggest why it may be necessary to use a chiral auxiliary during its production. [1]

b.ii. Describe how a chiral auxiliary is involved in the synthesis of a drug. [3]

Markscheme

a.ii. C=O carbon is sp^2 hybridized **and** others are sp^3;

(normal) bond angles (120° and 109.5°) cannot be achieved in ring;

Accept bond angles in the ring are 90.

b.i. only one enantiomer is active/has required effect / one enantiomer may have adverse effects;

Accept stereo/optical isomer, but not just isomer.

b.ii. chiral auxiliary attaches to non-chiral compound;

creates desired stereochemical conditions for reaction / ensures only one isomer is produced / *OWTTE*;

auxiliary removed/recycled after reaction (to leave desired product);

*Award **[1 max]** for making the compound chiral/optically active / OWTTE.*

Examiners report

a.ii. Many students could correctly explain the mode of action of penicillins, but often explanation of the strain in the bond angle failed to go into the required depth concerning the hybridization of the atoms in the four-membered ring. An encouragingly large number of candidates could explain how chiral auxiliaries are used in drug synthesis, but sometimes their response to the first part of this question failed to identify why it is sometimes necessary to use such an elaborate procedure. Many students could give the mode of action of antiviral drugs, though sometimes these responses lacked the required precision.

b.i. Many students could correctly explain the mode of action of penicillins, but often explanation of the strain in the bond angle failed to go into the required depth concerning the hybridization of the atoms in the four-membered ring. An encouragingly large number of candidates could explain how chiral auxiliaries are used in drug synthesis, but sometimes their response to the first part of this question failed to identify why it is sometimes necessary to use such an elaborate procedure. Many students could give the mode of action of antiviral drugs, though sometimes these responses lacked the required precision.

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necessary to use such an elaborate procedure. Many students could give the mode of action of antiviral drugs, though sometimes these responses lacked the required precision.

Morphine and its derivatives work by temporarily bonding to receptor sites in the brain, preventing the transmission of pain impulses.

Explain why the change in functional groups makes diamorphine (heroin) more potent than morphine.

Markscheme

ester group/diamorphine less polar / hydroxyl group/morphine more polar / diamorphine more soluble in non-aqueous systems/lipids/fats/fatty tissue / morphine less soluble in non-aqueous systems/lipids/fats/fatty tissue;

(ester group means) diamorphine crosses blood-brain barrier/into central nervous system/CNS/brain faster/more easily;

*Award **[1 max]** for answers that correctly describe diamorphine/morphine but do not compare the two.*

Examiners report

Many candidates described morphine (strong analgesic) rather than discussing an advantage of the drug. Most could also identify disadvantages, but sometimes referred to issues applicable to any substance, such as the problems of overdosing. The structural difference between morphine and diamorphine, and why this makes the latter more potent, were well known.

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a. State **two** ways in which viruses are different from bacteria. [2]

b. Describe **two** ways in which antiviral drugs work. [2]

c. Discuss **three** of the difficulties associated with solving the AIDS problem. [3]

Markscheme

a. bacteria are a single cell / viruses are not cellular;

bacteria have cell walls/nuclei / viruses have no nucleus/cell wall;

bacteria larger than viruses / viruses smaller than bacteria;

viruses need host cell to reproduce / viruses take over another cell;

bacteria are organisms/living / bacteria metabolise/can grow/feed/excrete / viruses are not living / viruses do not metabolise/grow/feed/excrete ;

Allow “bacteria have both DNA and RNA / viruses have either RNA or DNA only (but not both)”.

b. alter cell’s genetic material;

block enzyme activity within host cell;

(changes cell membrane so that it) inhibits virus entry/bonding to cell;

prevents virus from leaving cell (after reproduction);

becomes part of DNA of virus / alters virus / blocks enzyme (polymerase) which builds DNA;

prevents virus from using cell to multiply/reproduce/replicate / prevents virus from using cell's metabolism;

c. HIV retrovirus attacks immune system / binds to white blood cells/T-cells;

virus has ability to mutate;

virus makes people vulnerable to other infections;

metabolism of virus is linked closely to metabolism of the (host) cell / *OWTTE*;

antiretroviral agents are expensive / availability dependent on wealth of community/nation / lack of education/knowledge;

(social) "stigma" of diagnosis leads to not getting treatment / *OWTTE*;

Examiners report

a. The ways in which viruses differ from bacteria were well answered but, in (b), how antiviral drugs work was less well described. The AIDS problem had clearly been discussed but some of the answers lacked focus.

b. The ways in which viruses differ from bacteria were well answered but, in (b), how antiviral drugs work was less well described. The AIDS problem had clearly been discussed but some of the answers lacked focus.

c. The ways in which viruses differ from bacteria were well answered but, in (b), how antiviral drugs work was less well described. The AIDS problem had clearly been discussed but some of the answers lacked focus.

The development of new and improved medications for the reduction and management of pain is an important part of 21st-century medicine.

a. Discuss **two** advantages and **two** disadvantages of the medical use of morphine and its derivatives. [2]

Advantages:

Disadvantages:

b. Explain the increased potency of diamorphine (heroin) compared to morphine. [2]

Markscheme

a. *Advantages:*

*Award **[1 max]** for any two of:*

strong pain relief/strong analgesic

sedation / *OWTTE*

treatment of diarrhoea

relieve coughing

Disadvantages:

*Award **[1 max]** for any two of:*

addiction

tolerance

dependence

constipation

depresses respiratory drive

Accept "criminals/drug addicts might get access to strong analgesics intended for medical use" / OWTTE.

*Award **[1 max]** if one advantage **and** one disadvantage are given.*

b. molecule of diamorphine is less polar / polar hydroxyl/OH (groups) in morphine are replaced with less polar/non-polar groups in heroin / diamorphine contains two ester groups;

diamorphine is more fat/lipid soluble / *OWTTE*;

diamorphine more rapidly absorbed into the brain / (less polar molecules such as) diamorphine crosses the blood-brain barrier faster/more easily / diamorphine is more soluble in non-polar environment of the CNS/central nervous system than morphine / *OWTTE*;

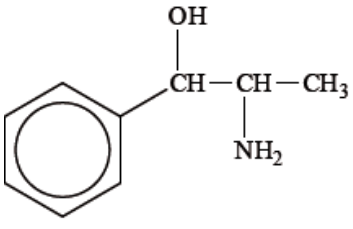
Examiners report

a. Candidates needed to recognize that the question asks about the *medical* use of morphine and its derivatives. Although many candidates struggled to give two advantages most scored the mark for disadvantages. Part (b) was usually answered well except by the candidates who got it the wrong way round.

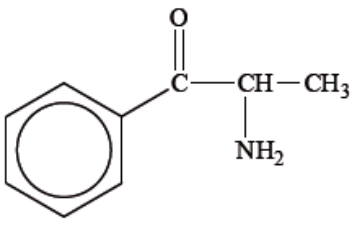
b. Candidates needed to recognize that the question asks about the *medical* use of morphine and its derivatives. Although many candidates struggled to give two advantages most scored the mark for disadvantages. Part (b) was usually answered well except by the candidates who got it the wrong way round.

There is some concern that increased use of the recreational drug khat is causing social problems.

The structures of two substances found in khat are shown below.



Cathine



Cathinone

Cathine and cathinone are both classed as sympathomimetic drugs.

Phenylpropanolamine (PPA) is an optical isomer of cathine used in cough medicines.

c.i. Outline how PPA and not cathine could be synthesized from the same non-chiral starting materials. Details of reagents and conditions are not required. [3]

c.ii. Explain why this is the generally preferred method for the synthesis of optically active drugs. [2]

c.iii Suggest how the aqueous solubility of cathine or PPA could be increased to facilitate its distribution around the body. [1]

Markscheme

c.i. chiral auxiliary/optically active species is used;

that can be connected to a molecule / to make it optically active;

auxiliary creates stereochemical condition necessary to follow a certain pathway / forms (only) one enantiomer / *OWTTE*;

chiral auxiliary removed to obtain (desired) product;

c.ii. other methods produce racemic mixture;

enantiomers difficult to separate because they have same physical properties (except rotation of the plane of plane polarised light);

optical isomers might have different physiological activities/(usually) only one is useful/half product is not used;

c.iii add acid/$\mathrm{H}^{+}(\mathrm{aq})$ (to form ionic compound) / converted to its salt;

Examiners report

c.i. Option D was a popular option. The identification of the wavenumber range used in the determination of ethanol lead to many correct answers. However, why the absorption range 3200-3600 cm^{-1} is not used still eludes a substantial number of candidates. How the transmission of IR radiation changes with increased levels of ethanol was not answered well, showing a poor understanding of transmittance. The question on the mild analgesic was not very well except for being able to identify the amide group in the molecules in question. The physiological effect of the drug as well as the reason for some drugs being less effective when taken orally was both very well answered. The 'mix and split' approach to combinatorial chemistry was generally not done well with answers that were weak showing shallow understanding.

The two structural features found in the sympathomimetic drugs were mostly correctly identified. Although many students were able to identify two chiral centers in the two structures given, not as many could identify the three needed for the mark. In the preferred method for the synthesis of optically active drugs, where many scored full marks but the difficulty of separating enantiomers due to their similar physical properties was the least popular explanation given. Surprisingly, the suggestion for increasing the aqueous solubility of an alkaline drug by adding an acid or converting it to its salt was done poorly showing a lack of understanding of acid-base chemistry and bonding.

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Alcohol abuse is a major problem in many countries, especially when associated with driving. Many police forces now use instruments that detect the presence of ethanol on a person’s breath by its absorption of electromagnetic radiation.

Identify the region of the electromagnetic spectrum used to detect the presence of ethanol.

Markscheme

infrared/IR;

Examiners report

This was well answered. Most students knew that the IR absorption is used for ethanol detection.

Radiotherapy is one type of treatment for cancer.

a. Describe how ionizing radiation destroys cancer cells. [2]

b. Outline how Targeted Alpha Therapy (TAT) is used for treating cancers that have spread throughout the body. [2]

Markscheme

a. *Any two of:*

radiation causes breaks in DNA chains

OR

radiation causes errors in DNA sequences

«damage accumulates and» cells cannot multiply

rapidly dividing/cancer cells more susceptible

Accept "alters DNA".

[2 marks]

b. *Any two of:*

radiation source delivered directly to «targeted» cancer cells

by a carrier drug/protein/antibody

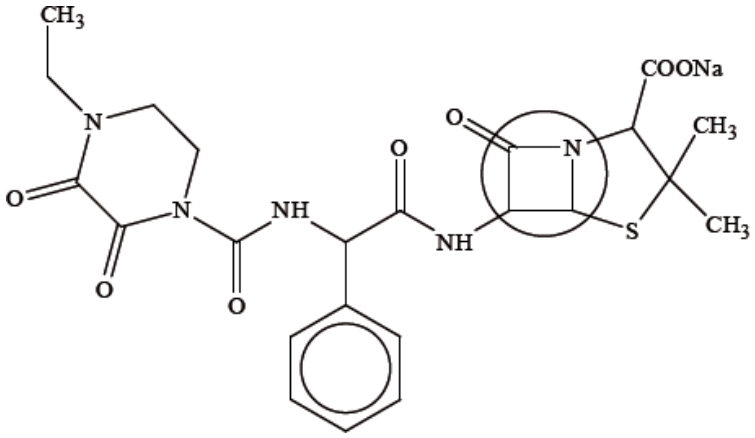
several sites in body can be targeted «at same time»

[2 marks]

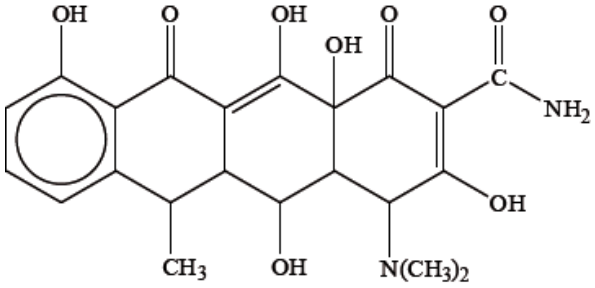
Examiners report

a. [N/A]
b. [N/A]

The structure of a drug is shown below:



Another drug that can have a similar effect to the one shown in (a) is doxycycline, shown below.



a.i. Identify the class of drugs to which this particular drug belongs. [[N/A

a.ii. Explain the high reactivity of the part of the drug that is enclosed in the circle. [2]

a.iii Suggest why the drug is administered as its sodium salt. [2]

b.i. Because it contains several –OH groups and an amine group, doxycycline is slightly polar. Identify the amine group by drawing a circle around it [2]

on the structure above **and** state whether it is a primary, secondary or tertiary amine.

b.ii Suggest **one** way in which the polarity of doxycycline could be substantially increased. [1]

b.iii Deduce the number of chiral carbon atoms in doxycycline **and** explain why chirality is important when considering its action in the body. [2]

Markscheme

a.i. penicillin(s)/antibacterial(s)/antibiotic;

a.ii. (β-lactam) ring is strained;

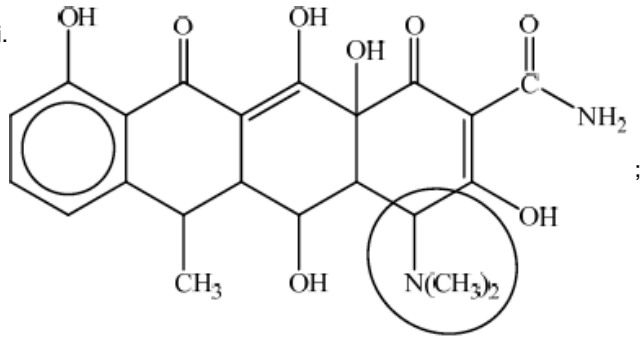
Accept stressed.

sp^3 **and** sp^2 hybridization;

bond angles are 90° / less than 120° and 109.5° / *OWTTE*;

a.iii (the sodium salt) makes the penicillin ionic/<u>more</u> polar;

this increases its solubility in water/more concentrated in bloodstream / makes it more able to be absorbed by the body / *OWTTE*;

b.i. 

;

Circle must go around the N atom (joined to the two CH_3 groups) and not include more than the two CH_3 groups and the carbon atom in the ring directly bonded to it.

Accept a circle around the –$N(CH_3)_2$ without including the carbon atom of the ring.

tertiary;

M2 can only be awarded if M1 is correct.

b.ii. react with hydrochloric acid/any other named strong acid / convert the amine group into a salt/ammonium ion/its hydrochloride/any other named product;

Accept amino for amine group.

react with sodium hydroxide/OH^- / convert a phenolic/OH group on the benzene ring/ into a phenoxide ion/sodium salt;

b.iii. six/6;

The different enantiomers/isomers may have different physiological/pharmacological effects on the body / one enantiomer benefits the body, the other might not / *OWTTE*;

Accept a specific example such as thalidomide.

Accept one enantiomer could have a toxic effect.

Do not allow just "has different effects".

Examiners report

a.i. Part a) (i) was very well answered overall.

a.ii. In a) (ii) while many candidates showed familiarity with the β-lactam ring, not as many were able to convey arguments that allowed them to score.

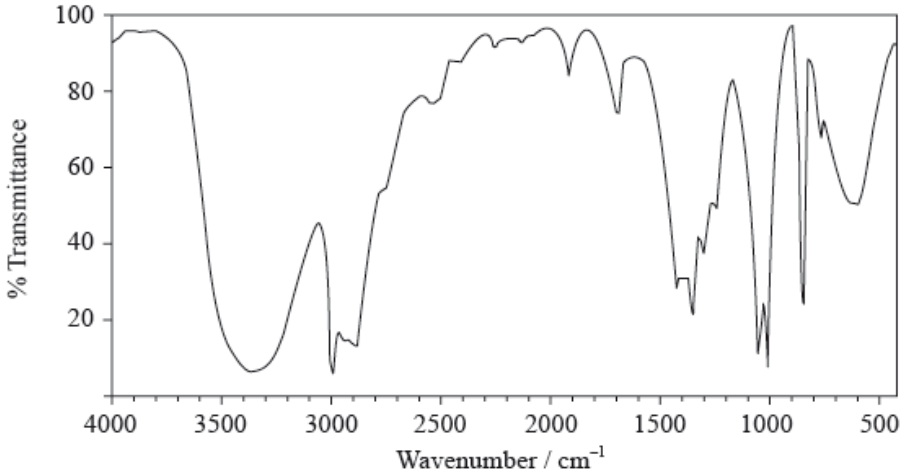
a.iii. Good candidates achieved at least one mark in a) iii) for the increase in polarity although often answers for this question were vague and just referenced an increase in solubility' without specifying 'in water'. The reason for converting the drug into a sodium salt was often incorrectly linked to digestion as opposed to making the molecule more polar.

b.i. A fair number of candidates incorrectly circled the NH_2 group of the amide group and classified this as a primary amine.

b.ii. Many had difficulty explaining how to make the drug more polar in b) ii).

b.iii. Most candidates obtained second mark in this question and very few identified the correct number of chiral carbons.

A modern method for accurately determining ethanol concentrations in the breath is based on the infrared (IR) spectrum of the molecule.



a.i. Use Table 17 of the Data Booklet to identify the wavenumber range used in the determination. [1]

a.ii. State why the absorption in the range 3200 to 3600 cm^{-1} is not used. [1]

b. The concentration of ethanol is determined by passing IR radiation through a breath sample. Outline how the transmittance of IR radiation changes when increased levels of ethanol are present. [1]

Markscheme

a.i. 2850 – 3100 (cm^{-1});

a.ii. (OH absorption present) in water/air/water vapour;

b. transmittance decreases / absorbance increasing (with increasing concentration);

No mark for: transmittance/absorbance changes.

Examiners report

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Analgesics can be prescribed for treating various types of pain.

a.i. The structure of aspirin is shown in table 20 of the data booklet. Suggest a suitable reagent for the conversion of aspirin to its sodium salt. [1]

a.ii. Explain the advantage of converting aspirin into its sodium salt. [2]

b.ii. Suggest a reagent that could be used to convert morphine into diamorphine. [1]

c. Explain why diamorphine is a more potent drug than morphine. [2]

Markscheme

a.i. $\mathrm{NaOH}/\mathrm{Na_2CO_3}/\mathrm{NaHCO_3}$;

Do not accept alkali, base or OH^-.

Accept either a correct chemical formula or name.

a.ii. increases aqueous/water solubility;

facilitates distribution (in the body) by the bloodstream / *OWTTE*;

b.ii. ethanoic acid/$\mathrm{CH_3COOH}$ / ethanoyl chloride/$\mathrm{CH_3COCl}$ / ethanoic anhydride/$(\mathrm{CH_3CO})_2\mathrm{O}$;

Accept "acetic acid", "acetyl chloride", "acetic anhydride" or "ethanoyl-ethanoate".

Do not accept "carboxylic acid".

c. diamorphine is less polar/non-polar / morphine is more polar / polar groups in morphine are replaced with less polar/non-polar groups in diamorphine;

(less polar molecules) cross blood-brain barrier faster/more easily / (diamorphine) more soluble in non-polar environment of CNS/central nervous system / (diamorphine) more soluble in lipids;

Examiners report

a.i. Many candidates were able to give a correct reagent for the conversion of aspirin to its sodium salt. Incorrect answers included NaCl, Na and incorrect chemical formulas for sodium carbonate. In (a) (ii), the increase in aqueous solubility was necessary and increase in solubility alone did not suffice. This threw a number of candidates. The markscheme for (b) (i) was quite broad and most candidates scored one for the two similarities, though some did not understand that benzene is different to benzene ring and that -$\mathrm{C_6H_2}$ is not the phenyl group, which is actually -$\mathrm{C_6H_5}$. As regards the difference, as previously hydroxide was not accepted for hydroxyl. Some candidates mixed up ethers with esters. In (c), many scored both marks though a few did not mention the non-polar nature of diamorphine.

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A variety of techniques can be used to determine the ethanol concentration of the breath, blood or urine.

a.i. The breathalyser, one of the earliest tests, uses the reaction between ethanol and acidified potassium dichromate(VI). Ethanol is first oxidized to ethanal. [1]

Deduce the half-equation for the reaction of ethanol to ethanal.

a.ii. Outline why the colour changes from orange to green. [1]

b. Explain how the ethanol concentration in the breath can be measured by an intoximeter using infrared absorption. [2]

Markscheme

a.i. $\mathrm{CH_3CH_2OH(aq) \rightarrow CH_3CHO(aq) + 2H^+(aq) + 2e^-}$;

Accept equilibrium sign, e for e– and different representations of organic compounds (such as C_2H_6O and *C_2H_4O).*

Ignore state symbols.

*Do **not** accept $CH_3CH_2OH + [O] \rightarrow CH_3CHO + H_2O$ (since half-equation requested).*

a.ii. (orange) dichromate(VI) $\mathrm{ion/Cr_2O_7^{2-}/Cr(VI)/Cr^{6+}}$ is reduced/converted to (green) chromium(III) $\mathrm{ion/Cr(III)/Cr^{3+}}$;

b. absorption (of IR at $2950\ \mathrm{cm^{-1}}$) by C–H bond;

(IR) absorption increases with/proportional to concentration / (IR) intensity compared to an empty/control cell;

Accept area under peak/size of peak (on IR spectrum) can be used to measure ethanol concentration.

Examiners report

a.i. The ability to construct a redox half-equation connecting a given starting material and product was disappointingly rare. The colour change was better explained though many students failed to specifically identify the species involved or their oxidation states. An encouraging number of students were aware of the role of the C-H bond absorption in IR based intoximeters, though frequently mention of the importance of the absorption intensity was omitted.

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The efficiency of a drug depends on the polarity of its molecule. Explain how the polarity of a drug can be modified in order to increase its solubility in water and how it affects the distribution of the drug around the body.

Markscheme

(non-charged) carboxylic acids/groups can be converted into more polar salts/carboxylates;

(non-charged) amines/amino groups can be converted into more polar amines/ammonium groups;
more polar/charged/ionic substances are more soluble in water/concentrate in the bloodstream;

Examiners report

Most candidates stated that polar drugs are more soluble in blood, and some suggested turning the drugs into a salt but didn"t describe how. Most also had a pretty clear understanding of THC and its effects.

Mild analgesics such as aspirin, and strong analgesics such as opiates, differ not only in their potency but also in the ways they act on the central nervous system.

Explain why heroin is a more potent drug than morphine.

Markscheme

molecule of heroin is less polar / molecule of morphine is more polar / polar OH groups in morphine are replaced with less polar/non-polar groups in heroin;

(less polar molecules) cross the blood-brain barrier faster/more easily / (heroin) is more soluble in non-polar environment of the CNS/central nervous system than morphine / *OWTTE*;

Examiners report

Candidates struggled to explain why heroin is a more potent drug than morphine. An explanation based on differences of the polarity of the molecules was expected.

Ethanol can be detected by a variety of instruments.

a. Fuel cells use an electrochemical process to determine the concentration of ethanol. [1]

   Formulate the overall equation for this process.

b. Predict the chemical shifts and integration for each signal in the ^{1}H NMR spectrum for ethanol using section 27 of the data booklet. [3]

Markscheme

a. $C_2H_5OH(g) + O_2(g) \rightarrow CH_3COOH(aq) + H_2O(l)$

   Accept any correct formula for reactants and products.

   [1 mark]

b. *R–O**H**:*

   1.0–6.0 «ppm» ***AND*** 1 H

   *R–O–C**H**$_2$–:*

   3.3–3.7 «ppm» ***AND*** 2 H

   *–C**H**$_3$:*

   0.9–1.0 «ppm» ***AND*** 3 H

   *Award **[1]** for the ratio of 1:2:3 (in any order).*

   *Award **[2]** for three correct chemical shifts without integration.*

   *Award **[1]** for two correct chemical shifts without integration.*

   For each chemical shift accept a specific value within the range.

   *Assignment of proton to fragment (eg, R–O**H**) is **not** required in each case.*

   [3 marks]

Examiners report

a. [N/A]
b. [N/A]

Radioisotopes can be used to treat a wide variety of diseases.

a. Phosphorous-32 undergoes beta decay. Formulate a balanced nuclear equation for this process. [1]

b. The half-life of phosphorus-32 is 14.3 days. Calculate the mass, in g, of ^{32}P remaining after 57.2 days if the initial sample contains 2.63×10^{-8} mol. Use table 1 of the data booklet and $M_r = 31.97$ g mol^{-1}. [2]

c. Explain the targeted alpha therapy (TAT) technique and why it is useful. [3]

Markscheme

a. $^{32}P \rightarrow {}^{32}S + {}^{0}_{-1}\beta$

Accept "e^-/e/β" instead of "$^{0}_{-1}\beta$".

[1 mark]

b. ***ALTERNATIVE 1***

«$\lambda = \frac{\ln 2}{14.3}$ =» 0.04847 «day^{-1}»

«$m(^{32}P) = 2.63 \times 10^{-8}$ mol × 31.97 g mol^{-1} × $e^{-0.04847 \times 57.2}$ =» 5.26×10^{-8} «g»

ALTERNATIVE 2

«$\frac{57.2}{14.3}$ =» 4 «half-lives passed»

OR

«$n(^{32}P) = \frac{2.63 \times 10^{-8}\ \text{mol}}{2^4}$ =» 1.64×10^{-9} «mol»

«$m(^{32}P) = 1.64 \times 10^{-9}$ mol × 31.97 g mol^{-1} =» 5.26×10^{-8} «g»

*Award **[2]** for correct final answer.*

Accept any value in the range "5.24–5.26 × 10^{-8} «g»".

[2 marks]

c. alpha-emitting isotopes/^{212}Pb/^{225}Ac attached to drugs/antibodies/chelating ligands/carriers

*Award **[2 max]** for any two of:*

absorbed by «cancer/growing» cells

OR

bind to «cancer/growing» cell receptors

alpha particles have high ionizing density/power

short-range of emission «of alpha-particles»

OR

healthy tissues less affected «as slower cell growth»

OR

local effect «on dispersed/spread/metastasised cancers»

Accept “radionuclide” for “isotope”.

Accept “alpha particles are highly ionizing”.

Accept “alpha particles have low penetrating power”.

Accept “used to treat dispersed/spread/metastasised cancers” ***OR*** *“can be used to map the distribution of cancer cells in the body”.*

[3 marks]

Examiners report

a. [N/A]
b. [N/A]
c. [N/A]

Many diseases are the result of infection of the body by either bacteria or viruses.

Identify the particular structural feature of penicillins that is responsible for their action and explain how this prevents bacteria multiplying.

Markscheme

4-membered ring/β-lactam ring;

easily broken / very reactive / highly strained ring;

binds to proteins/deactivates proteins that form cell wall / interferes with cell wall formation / prevent formation of crosslinks within cell wall;

makes cell wall porous / allows water to pass;

causes cell to burst;

Examiners report

Most candidates knew that AIDS was a viral disease, but knowledge of a bacterial disease (rather than the name of a bacterium) was more sketchy. The differences between bacteria and viruses and reasons for drug resistance in bacteria were generally well known. Many candidates also gave good answers about the mode of action of penicillin, but the action of antiviral drugs could only be explained by the best candidates.

Three factors which can influence the mechanism of the action of a drug include geometrical isomerism, polarity and ring strain.

a. For each of the following drugs, identify which **one** of these factors is involved. [3]

   Increased potency of diamorphine compared to morphine:

   Penicillin:

b. Explain the action of penicillin with reference to your answer in part (a). [2]

Markscheme

a. *Increased potency of diamorphine compared to morphine*:

polarity / polar hydroxyl groups in morphine replaced by non-polar ester groups in diamorphine;

Penicillin:

ring strain;

b. ring opens (to allow penicillin to bond to enzyme);

which synthesizes bacterial cell walls and so blocks action / prevent cell wall/membrane formation;

Examiners report

a. Most candidates had no problem with (a).

b. in (b), although most candidates knew that penicillin interferes with cell wall synthesis, most did not know the actual mechanism i.e. the fact that the ring opens to allow the penicillin to bond to the enzyme.

Chemists can change structures of substances in order to produce chemicals with desired properties.

Aspirin is virtually insoluble in water. Use Table 20 in the Data Booklet to explain how aspirin can be made more water-soluble. Write an equation for the reaction.

Markscheme

react aspirin with sodium hydroxide/$\mathrm{OH^-}$ to produce the (ionic) salt;

No M1 for reaction with $CaCO_3$ (as calcium salicylate is not water soluble).

$\mathrm{C_6H_4(OCOCH_3)COOH + NaOH \rightarrow C_6H_4(OCOCH_3)COONa + H_2O}$;

Accept ionic equation.

ECF for M2

Examiners report

Few candidates knew how to make aspirin more water-soluble – most answers showed a lack of understanding of the chemistry involved, namely reaction with NaOH to produce the ionic salt of aspirin.

Many drugs, including aspirin, penicillin, codeine and taxol, have been modified from compounds that occur naturally.

Many drugs are chiral. Explain how a polarimeter can be used to determine the relative proportion of two enantiomers.

Markscheme

«pure» enantiomers rotate the plane «of plane-»polarized light «by equal angles» in opposite directions

Any two of:

find angle of rotation of pure enantiomers

measure angle of rotation of mixture

mixture has angle between that of two enantiomers

ratio of angles gives purity

[3 marks]

Examiners report

[N/A]

The discovery of penicillin was one of the most significant scientific discoveries of the last century.

State the type of hybridization of each of the carbon atoms (**I**, **II**, and **III**) in the β-lactam ring of ampicillin by completing the table below, and explain why the amide group is highly reactive.

Carbon atom	I	II	III
Hybridization			

Markscheme

Carbon atom	I	II	III
Hybridization	sp^2	sp^3	sp^3

;

strain in four-membered ring / as angles less than 109°;

Examiners report

In (c), many students could not relate the hybridization of the carbon atoms in the beta-lactam ring to ring strain and a significant number appear to have difficulty linking some key chemical concepts in this option.

Taxol was originally obtained from the bark of the Pacific yew tree.

Outline how Green Chemistry has improved the process of obtaining Taxol.

Markscheme

Any two of:

stripping the bark kills Pacific yew tree

plant cell fermentation «and extraction»/PCF technology/use of plant cell cultures/Taxol «precursors» produced by biosynthesis/fungi/yeast/e-coli/use of natural enzymes «more sustainable process»

OR

Taxol produced semi-synthetically/Taxol from 10-DAB/10-deacetylbaccatin

uses renewable resources

OR

use «needles/leaves/twigs of» European/common yew/yew from Himalayas

«sustainable» process has eliminated «high proportion of» hazardous chemicals/waste

OR

«sustainable» process has eliminated several solvents/«sustainable» process uses greener solvents/«sustainable» process recycles/reuses solvents

OR

«sustainable» process has eliminated several «drying» steps/«sustainable» process has eliminated lots of the work-up after the synthesis

OR

«sustainable» process has increased energy efficiency

OR

«sustainable» process has no intermediates

OR

«sustainable» process uses more efficient catalysts

Accept "Pacific yew rare/slowgrowing/takes 100/200 years to mature" for M1.

Accept "synthesis of Taxol using chiral auxiliaries increases efficiency of process as single enantiomer formed" for M4.

[2 marks]

Examiners report

[N/A]

Excess stomach acid leads to medical conditions that affect many people worldwide. These conditions can be treated with several types of medical drugs.

Omeprazole exists as a racemic mixture whereas esomeprazole is a single enantiomer. Outline how, starting from a non-chiral molecule, esomeprazole but not omeprazole, could be synthesized. Details of chemicals and conditions are not required.

Markscheme

Any two of:

chiral molecule/auxiliary/optically active species is used/added/connected «to the starting molecule to force reaction to follow a certain path»

chiral intermediate forms «only» one enantiomer
OR
auxiliary creates stereochemical condition «necessary to follow a certain pathway» / stereochemical induction
OR
existing chiral centre affects configuration of new chiral centres

«after new chiral centre created» chiral auxiliary removed «to obtain desired product»

Examiners report

[N/A]

Solubility plays an important role in the bioavailability of drugs in the body.

Some mild analgesics contain a solid mixture of acidic aspirin and a non-acidic organic chemical of similar polarity to asprin.

Discuss how acid-base properties and the process of solvent extraction can be used to separate aspirin from the mixture.

Markscheme

dissolve compounds in an organic solvent

add NaOH(aq)/OH^-(aq) «to the mixture» to convert aspirin to its water soluble salt

separate the two «immiscible» layers

convert salt «in aqueous layer» back to aspirin by reacting with acid/H^+

«evaporate solvents and dry»

Accept organic solvents immiscible with water such as hexane, ethyl ethanoate, butyl acetate.

Accept any other base.

Need explanation for mark.

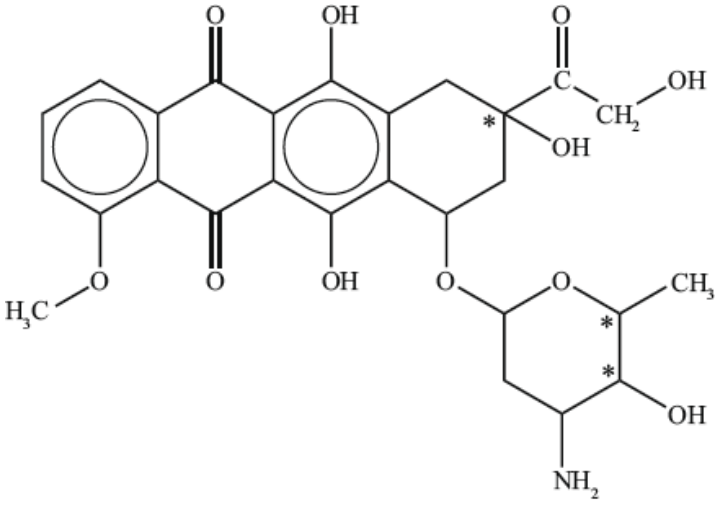
[3 marks]

Examiners report

[N/A]

Thalidomide is currently used to treat several different diseases including certain types of cancer. Research to compare its effectiveness with other cancer drugs, such as doxorubicin, is ongoing.

(i) Doxorubicin contains six different chiral carbon atoms. Three of them are identifi ed with an asterisk, *. Identify the locations of the other three by placing circles around the relevant carbon atoms.



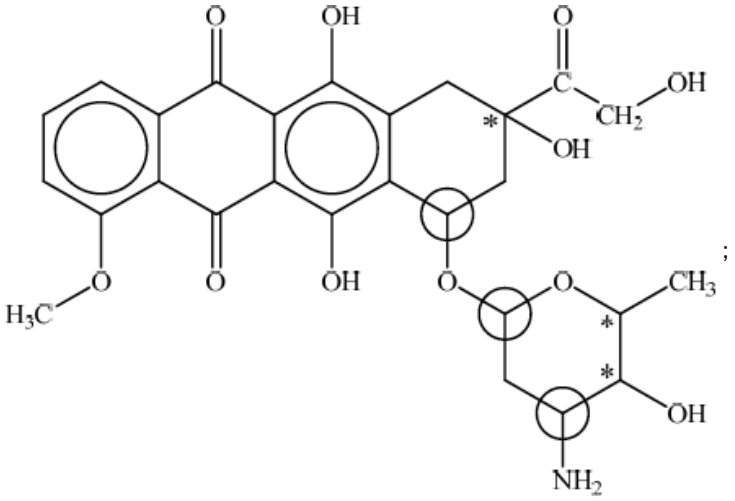
Doxorubicin

(ii) Only one of the possible enantiomers is really effective as an anti-cancer drug.

Describe the general principles behind the use of chiral auxiliaries to form the desired enantiomer when several different enantiomers of a drug exist.

(iii) From its structure it can be seen that doxorubicin contains several polar hydroxyl groups. However, when it is given intravenously it needs to be in an ionic form to make it even more soluble in an aqueous medium. Describe how doxorubicin can be converted into a salt.

Markscheme

(i)  ;

*Award **[1]** for each correct circle.*

(ii) a chiral auxiliary (which is itself optically active/chiral) attaches to nonchiral molecule (to force reaction to follow a certain path);

chiral auxiliary is removed (once stereospecific intermediate has been formed to leave desired enantiomer) / *OWTTE*;

(iii) **EITHER**

doxorubicin contains an amino group (which is basic);

Allow (primary) amine.

can react with acid/hydrochloric acid (to form acid salt);

OR

doxorubicin contains OH/hydroxyl groups some of which are acidic;

can react with sodium hydroxide/NaOH/hydroxide ions/OH^- (to form sodium/alkaline salt);

Accept other suitable base such as potassium hydroxide/KOH.

Allow "can react with alkali".

*Award **[2]** for a correct equation.*

Examiners report

In (a), enantiomers typically were not referred to and few stated that since drugs can pass from mother to foetus all drugs must be tested for their effect on pregnant women. In (b) (i) most candidates got one chiral centre but surprisingly at HL only the better students got all three. In (b) (ii) although M2 was generally scored, few scored M1 *i.e.* the fact that a chiral auxiliary attaches to a non-chiral molecule. In (iii) few candidates scored both marks. Many stated that doxorubicin can react with an acid but did not mention the fact that it contains an amino group *etc.*

Morphine is a strong analgesic which is administered parenterally.

Diamorphine (heroin) is a more effective painkiller than morphine. The structures of morphine and diamorphine are shown in Table 20 of the Data Booklet. Explain at the molecular level why diamorphine is absorbed into fatty tissue more rapidly than morphine.

Markscheme

diamorphine has (2) ester/acetyl/$\mathrm{COOCH_3}$ groups instead of hydroxyl/OH groups;

diamorphine is less polar/non-polar;

Examiners report

Most candidates answered the question satisfactory, though some did not name the difference in polarity in (b).

Many factors can be involved in the action of a particular drug.

The structures of morphine and diamorphine (heroin) are given in Table 20 of the Data Booklet. With reference to the structures, explain why diamorphine (heroin) is more potent than morphine.

Markscheme

two (polar) hydroxyl groups/OHs in morphine replaced by ester groups in diamorphine;

Do not allow hydroxide for hydroxyl.

Accept two alcohols instead of hydroxyl.

diamorphine less polar / morphine more polar;

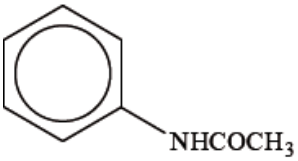
diamorphine capable of rapid penetration of (lipid-based) blood-brain barrier / diamorphine more quickly absorbed into non-polar environment of central nervous system/CNS / *OWTTE*;

Allow diamorphine more soluble/easily dissolved in lipids/fatty tissue.

Examiners report

In contrast (b) was very well answered by nearly all students and several got all three marks.

The drug Antifebrin was first used as a medicine in 1886.



Antifebrin

The structures of some medicines and drugs are given in Table 20 of the Data Booklet.

a.i. Identify the molecule which is most similar to Antifebrin in terms of size and structure. [1]

a.ii. State the names of the **two** functional groups that both molecules have in common. [1]

c. Outline why some drugs can be less effective when taken orally rather than through other methods of administration. [1]

Markscheme

a.i. paracetamol/acetaminophen;

a.ii. phenyl **and** (secondary) amide;

Accept benzene ring for phenyl.

Do not allow just benzene or arene instead of phenyl.

c. drugs broken down by acids/enzymes/digestive system before they are absorbed / drugs reach target more slowly / *OWTTE*;

Examiners report

a.i. Option D was a popular option. The identification of the wavenumber range used in the determination of ethanol lead to many correct answers. However, why the absorption range 3200-3600 cm^{-1} is not used still eludes a substantial number of candidates. How the transmission of IR radiation changes with increased levels of ethanol was not answered well, showing a poor understanding of transmittance. The question on the mild analgesic was not very well except for being able to identify the amide group in the molecules in question. The physiological effect of the drug as well as the reason for some drugs being less effective when taken orally was both very well answered. The ‘mix and split’ approach to combinatorial chemistry was generally not done well with answers that were weak showing shallow understanding.

The two structural features found in the sympathomimetic drugs were mostly correctly identified. Although many students were able to identify two chiral centers in the two structures given, not as many could identify the three needed for the mark. In the preferred method for the synthesis of optically active drugs, where many scored full marks but the difficulty of separating enantiomers due to their similar physical properties was the least popular explanation given. Surprisingly, the suggestion for increasing the aqueous solubility of an alkaline drug by adding an acid or converting it to its salt was done poorly showing a lack of understanding of acid-base chemistry and bonding.

In one argument for and one against the legalization of cannabis, while many candidates scored at least one mark out of two, some journalistic answers were seen. Description of the bonding changes that occur when the anti-cancer drug cisplatin attaches to the DNA chain was typically not well answered questions with many candidates being able to provide only one of the two ideas, usually the missing one was that Cl^- leave $\mathrm{Pt}/\mathrm{Pt}^{2+}$. Why the *trans*-cisplatin is ineffective in the treatment of cancer elicited fewer correct answers than expected. Question 18 was not on AIDS *per se* but rather on why viral infections are more difficult to treat than bacterial infections. A significant number of students scored part marks thus illustrating shallow understanding and deserves further attention in class. Very often marks were lost due to incomplete arguments.

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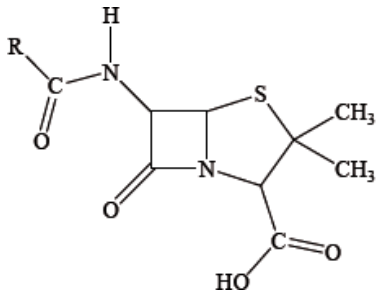
Antibacterials are drugs that kill or inhibit the growth of microorganisms that cause infectious diseases. The general structure of penicillin, an antibacterial, is given below.



Describe the composition and structure of the beta-lactam ring in penicillin and explain its importance.

Markscheme

ring consists of one nitrogen atom and three carbon atoms (and three hydrogen atoms);

4 membered/square ring structure / bond angles of 90°;

ring under stress/strain / increased (chemical) reactivity / ring opens (due to angle of 90° instead of about 109°);

bonds to/blocks action of enzyme/transpeptidase;

reaction with the enzyme not reversible / prevents cross linking of peptides / inhibits synthesis and growth of bacterial cell walls / *OWTTE*;

Examiners report

Many candidates were unable to explain the importance of the beta-lactam ring in penicillin. The bonds in the opened structure blocks the action of the enzyme, transpeptidase, a non-reversible reaction that prevents cross linkage of peptides in the bacteria, which inhibits the synthesis and growth of bacterial cell walls.

The first commercially available antibiotic came from a class of compounds known as the penicillins.

b. Explain how penicillins work and why it is necessary to continually modify the side-chain. [3]

c. Explain the importance of the beta-lactam ring in the action of penicillin. [3]

Markscheme

b. penicillins interfere with (enzymes involved with) development of cell wall/(cross-link) structure of bacteria;

(due to damage) cells absorb water (by osmosis) **and** burst / *OWTTE*;

modifying side-chain overcomes resistance (by bacteria) / *OWTTE*;

c. beta lactam ring has strained structure/(four-membered ring with) 90° bond angles on the carbon and nitrogen atoms;

atoms should have larger bond angles based on VSEPR theory / *OWTTE*;

ring stress increases chemical reactivity and opens;

open ring reacts/bonds with enzyme/penicillinase to prevent formation of bacteria cell walls (prevents cross-linking of peptides);

Examiners report

b. The role of Florey and Chain did not seem to be too well known with many incorrectly listing large-scale production. In (b), the side-chain modification was better known than the working of penicillins. Whilst many had the correct general idea of the importance of the beta-lactam ring in (c), a precise explanation was needed.

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A commonly used mild analgesic is aspirin, 2-acetoxybenzoic acid, whose structure is given in Table 20 of the Data Booklet.

One form of soluble aspirin is $\mathrm{Ca(C_9H_7O_4)_2}$.

Morphine, codeine and diamorphine (heroin) are examples of strong analgesics.

Their structures are given in Table 20 of the Data Booklet.

a. Describe how mild analgesics function. [1]

b. (i) Outline why this substance is more soluble than standard aspirin in water. [2]

(ii) Deduce the balanced ionic equation for the reaction that occurs between soluble aspirin and the acid in the stomach.

c. (i) Deduce **two** named functional groups present in both aspirin and diamorphine. [8]

(ii) Deduce **one** named functional group present in morphine but not in diamorphine.

(iii) State **two** short-term advantages and **two** long-term disadvantages of using codeine as a strong analgesic.

Short-term advantages:

Long-term disadvantages:

(iv) Explain the increased potency of diamorphine compared to morphine.

Markscheme

a. intercepts pain stimulus at source / inhibits release of substances/prostaglandins that cause pain/swelling/fever;

b. (i) ionic compound (which dissociates);

(ii) $C_9H_7O_4^-(aq) + H^+(aq) \rightarrow C_9H_8O_4(aq)$;

Ignore state symbols.

Ignore arrow.

c. (i) phenyl/benzene ring;

Do not allow just benzene or arene or the formula C_6H_6.

ester;

Do not allow –COO– or carbonyl/CO.

(ii) hydroxyl / phenol; ***[1]***

Allow alcohol/hydroxy but not hydroxide.

Do not allow –OH.

(iii) *Award any **[1] for any two** short-term advantages from*:

strong/powerful (pain reliever);

fast-acting / effective;

has a wide safety margin;

can quickly stop diarrhoea;

can be used in cough mixtures/medicines / antitussive properties;

works effectively with paracetamol/acetaminophen;

*Award **[1] for any two** long-term disadvantages from*:

(regular use) can lead to addiction/dependence/withdrawal symptoms;

tolerance can lead to toxic dosages;

can result in depression / apathy;

can cause mental health problems;

can result in constipation;

can result in sterility/sexually related problems;

memory loss;

serious health risk to babies who are breastfed;

*Award **[1 max]** for one correct advantage and one correct disadvantage.*

(iv) two (polar) hydroxyl groups in morphine replaced by less polar ester groups in diamorphine/heroin;

Do not allow hydroxide for hydroxyl.

Accept alcohols for hydroxyl groups.

diamorphine/heroin more soluble in non-polar lipids / diamorphine/heroin more soluble in non-polar environment of central nervous system/CNS;

Reference to solubility required.

diamorphine/heroin can penetrate blood-brain barrier more quickly / diamorphine/heroin can act more quickly in CNS (leading to increased potency);

Examiners report

a. In Q15, the function of mild analgesics was well understood but few stated that the calcium salt is ionic and fewer still managed the ionic equation. The named functional groups were usually correctly identified although “benzene” was one of the incorrect answers as was “esther”. For the short-term advantages there was a tendency to repeat the stem of the question but the long-term disadvantages were better understood. Many scored one mark by including one correct short-term and one correct long-term answer. One respondent suggested that asking candidates about codeine was unfair – but this was regarded as a reasonable extension of D.3.4. Answers about the increased potency of diamorphine over morphine were better than in the past but if a mark were to be lost it would be for not commenting on the greater solubility of diamorphine in lipids specifically.

b. In Q15, the function of mild analgesics was well understood but few stated that the calcium salt is ionic and fewer still managed the ionic equation. The named functional groups were usually correctly identified although “benzene” was one of the incorrect answers as was “esther”. For the short-term advantages there was a tendency to repeat the stem of the question but the long-term disadvantages were better understood. Many scored one mark by including one correct short-term and one correct long-term answer. One respondent suggested that asking candidates about codeine was unfair – but this was regarded as a reasonable extension of D.3.4. Answers about the increased potency of diamorphine over morphine were better than in the past but if a mark were to be lost it would be for not commenting on the greater solubility of diamorphine in lipids specifically.

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Acquired immune deficiency syndrome (AIDS), a disease caused by the HIV virus, has resulted in millions of deaths worldwide since it was first identified in 1981.

Explain why viral infections, such as AIDS, are generally more difficult to treat than bacterial infections.

Markscheme

viruses mutate quickly so adapt to drugs/evade immune system response / *OWTTE*;

bacteria are more complex and thus can be targeted in more ways / viruses lack sub-units/functions targeted by antibacterials / *OWTTE*;

different types of bacteria employ similar metabolic processes and thus can be targeted by common antibacterials / each kind of virus usually requires special drugs/approaches / *OWTTE*;

bacteria can be killed by interfering with cell wall production without attacking host cell / difficult to attack the virus without attacking host cell;

Examiners report

Option D was a popular option. The identification of the wavenumber range used in the determination of ethanol lead to many correct answers. However, why the absorption range 3200-3600 cm^{-1} is not used still eludes a substantial number of candidates. How the transmission of IR radiation changes with increased levels of ethanol was not answered well, showing a poor understanding of transmittance. The question on the mild analgesic was not very well except for being able to identify the amide group in the molecules in question. The physiological effect of the drug as well as the reason for some drugs being less effective when taken orally was both very well answered. The 'mix and split' approach to combinatorial chemistry was generally not done well with answers that were weak showing shallow understanding.

The two structural features found in the sympathomimetic drugs were mostly correctly identified. Although many students were able to identify two chiral centers in the two structures given, not as many could identify the three needed for the mark. In the preferred method for the synthesis of optically active drugs, where many scored full marks but the difficulty of separating enantiomers due to their similar physical properties was the least popular explanation given. Surprisingly, the suggestion for increasing the aqueous solubility of an alkaline drug by adding an acid or converting it to its salt was done poorly showing a lack of understanding of acid-base chemistry and bonding.

In one argument for and one against the legalization of cannabis, while many candidates scored at least one mark out of two, some journalistic answers were seen. Description of the bonding changes that occur when the anti-cancer drug cisplatin attaches to the DNA chain was typically not well answered questions with many candidates being able to provide only one of the two ideas, usually the missing one was that Cl^- leave $\mathrm{Pt}/\mathrm{Pt}^{2+}$. Why the *trans*-cisplatin is ineffective in the treatment of cancer elicited fewer correct answers than expected. Question 18 was not on AIDS *per se* but rather on why viral infections are more difficult to treat than bacterial infections. A significant number of students scored part marks thus illustrating shallow understanding and deserves further attention in class. Very often marks were lost due to incomplete arguments.

Organic solvents are commonly used in the pharmaceutical industry.

a. Hexane and propanone have vapour pressures of 17 kPa and 24 kPa respectively at 20 °C. [1]

   Calculate the vapour pressure, in kPa, at 20 °C of a mixture containing 60% hexane and 40% propanone by mole fraction, using Raoult's law and assuming the mixture is ideal.

b. Explain how hexane and propanone may be separated by fractional distillation. [3]

Markscheme

a. «vapour pressure = 0.6 × 17 + 0.4 × 24 =»

   19.8 «kPa»

   [1 mark]

b. *Any three of:*

   different molar masses

   OR

   different strength of intermolecular forces

   different boiling points

   temperature in «fractionating» column decreases upwards

   «components» condense at different temperatures/heights

OR

«component with» lower boiling point leaves column first

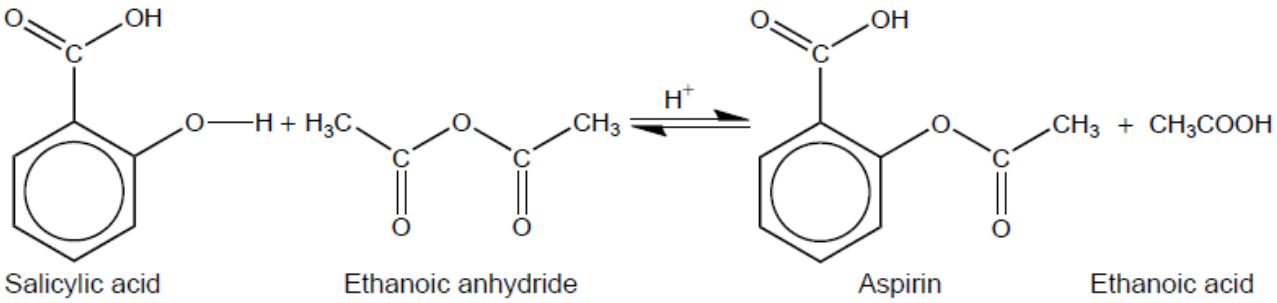
[3 marks]

Examiners report

a. [N/A]
b. [N/A]

Aspirin is one of the most widely used drugs in the world.

Aspirin was synthesized from 2.65 g of salicylic acid (2-hydroxybenzoic acid) (M_r = 138.13) and 2.51 g of ethanoic anhydride (M_r = 102.10).



a.iii Suggest **two** absorbances, other than the absorbances due to the ring structure and C–H bonds, that would be present in the infrared (IR) spectrum of aspirin. [2]

a.iv State **two** techniques, other than IR spectroscopy, which could be used to confirm the identity of aspirin. [2]

Markscheme

a.iii *Any two of:*

2500–3000 «cm^{-1}» / «absorbance» due to O–H in carboxyl

1700–1750 «cm^{-1}» / «absorbance» due to C=O in carboxyl/ethanoate

1050–1410 «cm^{-1}» / «absorbance» due to C–O bond in carboxyl/ethanoate

Accept "carboxylic acid" for "carboxyl", "acetate/ester" for "ethanoate".

Accept specific wavenumber once within indicated range.

*Do **not** award mark if reference is made to an alcohol/ether.*

[2 marks]

a.iv *Any two of:*

melting point

mass spectrometry/MS

high-performance liquid chromatography/HPLC

NMR/nuclear magnetic resonance

X-ray crystallography

elemental analysis

Accept "spectroscopy" instead of "spectrometry" where mentioned but ***not*** *"spectrum".*

Accept "ultraviolet «-visible» spectroscopy/UV/UV-Vis".

Do ***not*** *accept "gas chromatography/GC".*

Accept "thin-layer chromatography/TLC" as an alternative to "HPLC".

[2 marks]

Examiners report

a.iii. [N/A]

a.iv. [N/A]

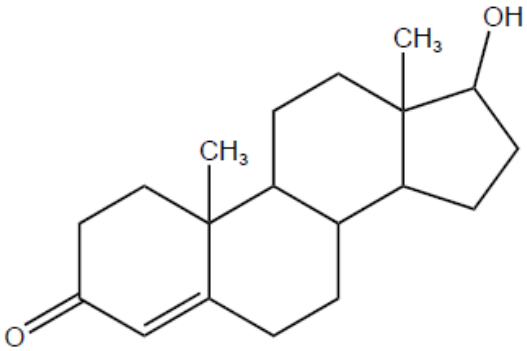
The use of performance-enhancing drugs presents a challenge in the world of competitive sports. New regulations have lowered the acceptable concentrations of certain drugs in athletes' bodies.

a. Suggest what may have led to these changes in acceptable concentrations. [1]

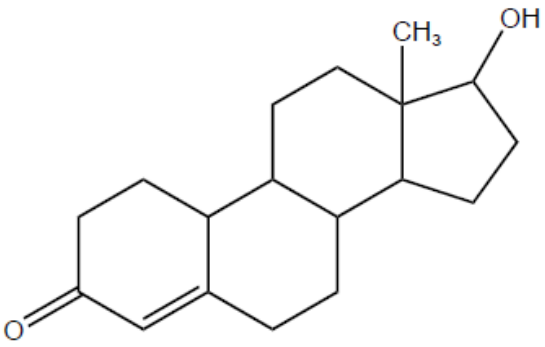
b. One class of performance-enhancing drugs is the anabolic steroids. Detection of these drugs in urine samples uses a combination of gas chromatography and mass spectrometry (GC/MS). [4]

(i) Describe how gas chromatography enables the components of urine to be analysed.

(ii) The structures of two steroids, testosterone and nandrolone, are given below.

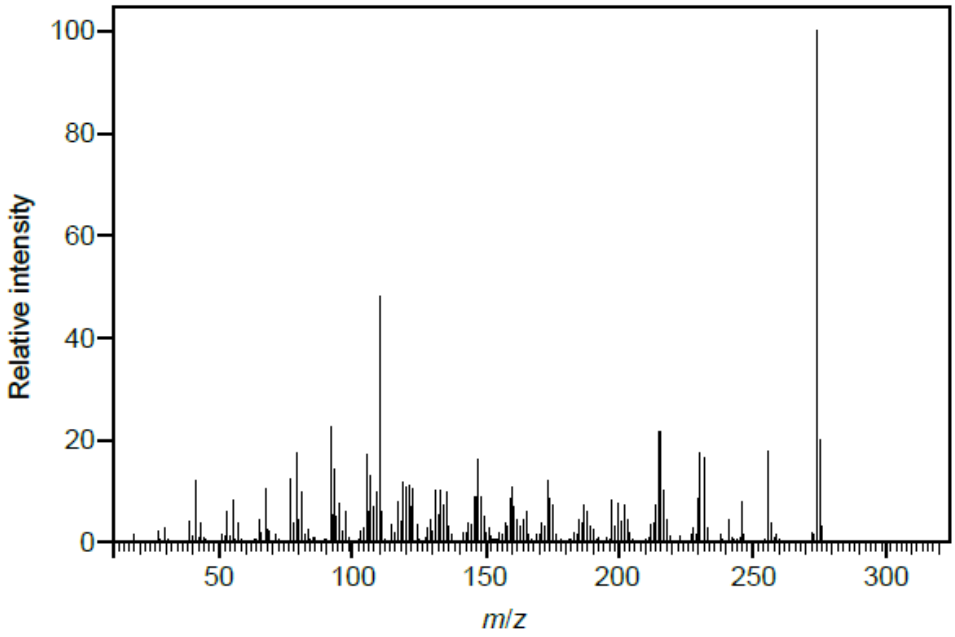


Testosterone $C_{19}H_{28}O_2$



Nandrolone $C_{18}H_{26}O_2$

With reference to the molar masses of the two steroids, determine, with a reason, which can be identified from the mass spectrum below.



[Source: http://sdbs.db.aist.go.jp/ accessed 2015-08-23]

Markscheme

a. improvements in technology/instrumentation/analytical techniques/precision of measurements

Accept "greater awareness/knowledge of the negative effects of the drugs".

b. i

«components have» different affinities for/partition between 2 phases/mobile and stationary phase

move at different rates through instrument
OR
have different retention times

ii

nandrolone M = 274 «g mol^{-1}»
OR
testosterone M = 288 «g mol^{-1}»

nandrolone identified because «molecular ion peak of» m/z = 274

Accept non-integer molar masses, ie, 274.44 «g mol^{-1}» and 288.47 «g mol^{-1}».

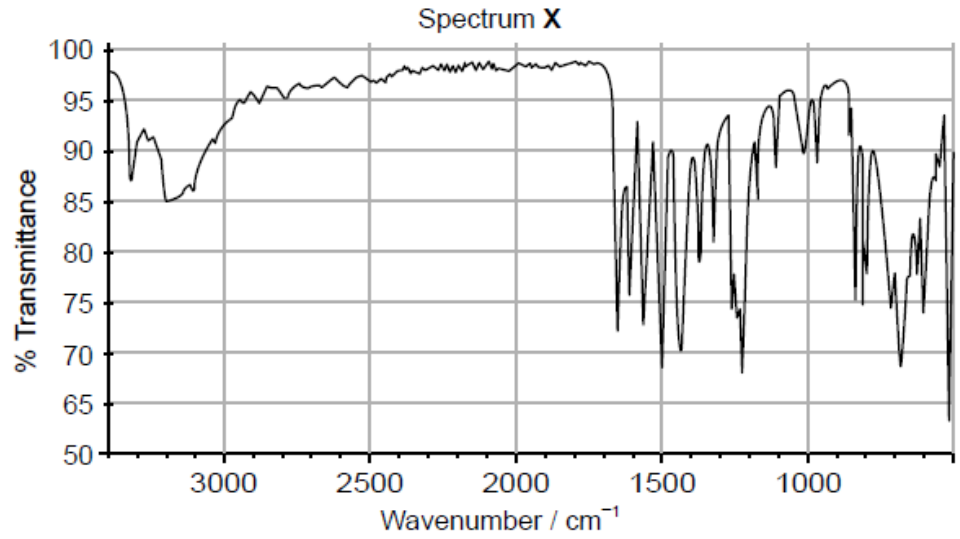
Accept also "m/z = 275" for "m/z = 274" in M2.

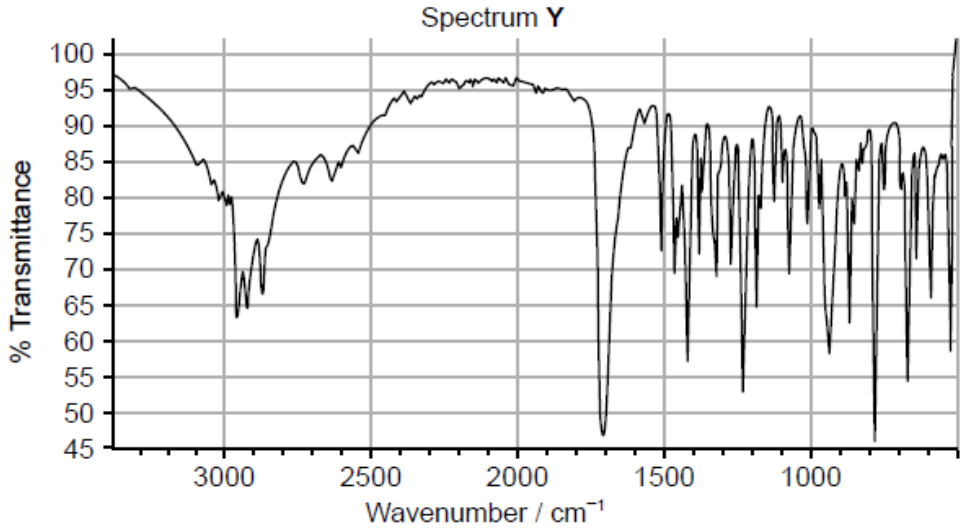
Accept "absence of peak with m/z = 288"

Examiners report

a. [N/A]
b. [N/A]

Ibuprofen and paracetamol are mild analgesics. One of the IR spectra below belongs to ibuprofen and the other to paracetamol. The structures of both compounds are given in section 37 of the data booklet.





[Source: chemspider.com]

a.i. Both spectra show a peak at wavenumber 1700 cm^{-1}. Identify the bond responsible for this peak. [1]

a.ii. Deduce which spectrum belongs to paracetamol, giving two reasons for your choice. Use section 26 of the data booklet. [2]

X or **Y**:

. . . . . .

Reason 1:

. . . . . .

. . . . . .

Reason 2:

. . . . . .

. . . . . .

b. Describe how mild analgesics function. [2]

Markscheme

a.i. C=O

Accept "carbonyl".

a.ii. **X** (must be identified) ***AND***

Any two of:

For **X**:

N–H «absorption» ***AND*** at 3300 – 3500 «cm^{-1}» ✔

O–H «absorption» in phenol ***AND*** at 3200 – 3600 «cm^{-1}» ✔

absence of OH «absorption» in carboxylic acid ***AND*** 2500 – 3000 «cm^{-1}»

Accept any specific wavenumber in the range 3300–3380 «cm^{-1}» for M1.

Accept any specific wavenumber in the range 3100–3200 «cm^{-1}».

*Award **[1 max]** if **Y** is incorrectly identified for paracetamol but if a correct reason/reasons is/are given for the bond absorption(s).*

[Max 2 Marks]

b. prevents/interferes with the production of prostaglandins

OR

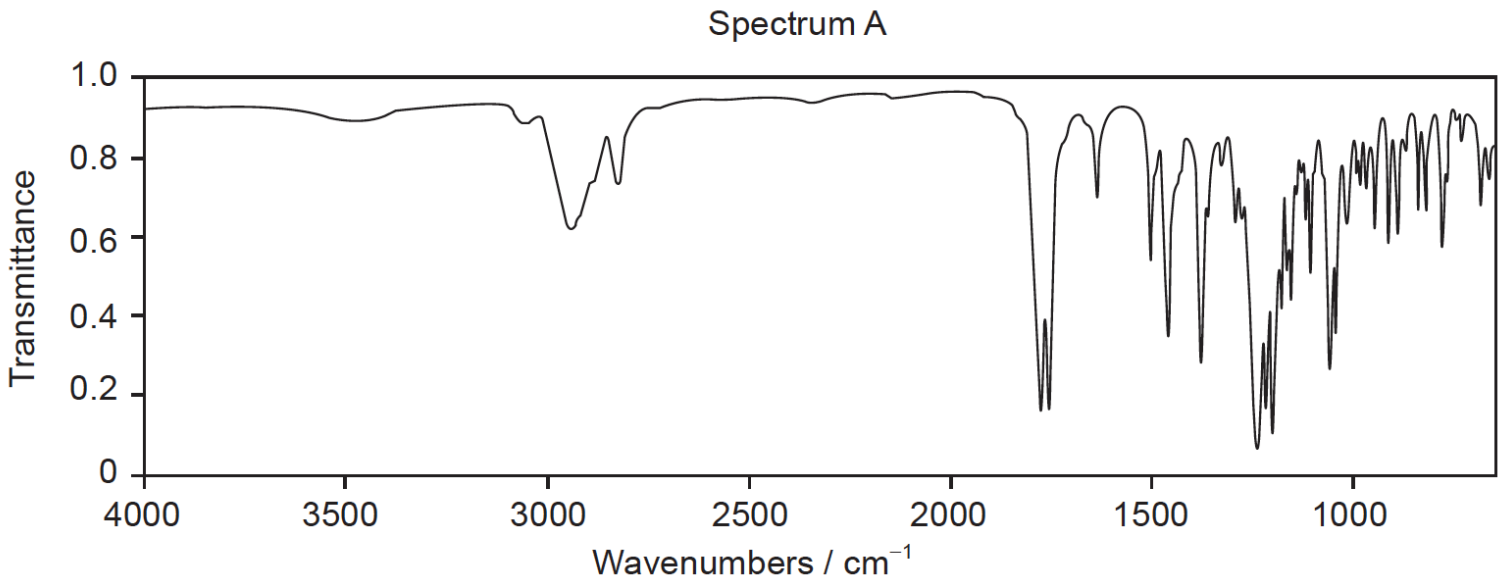
prevents/interferes with the production of substances responsible for inflammation/pain/fever at the site of injury/source of pain

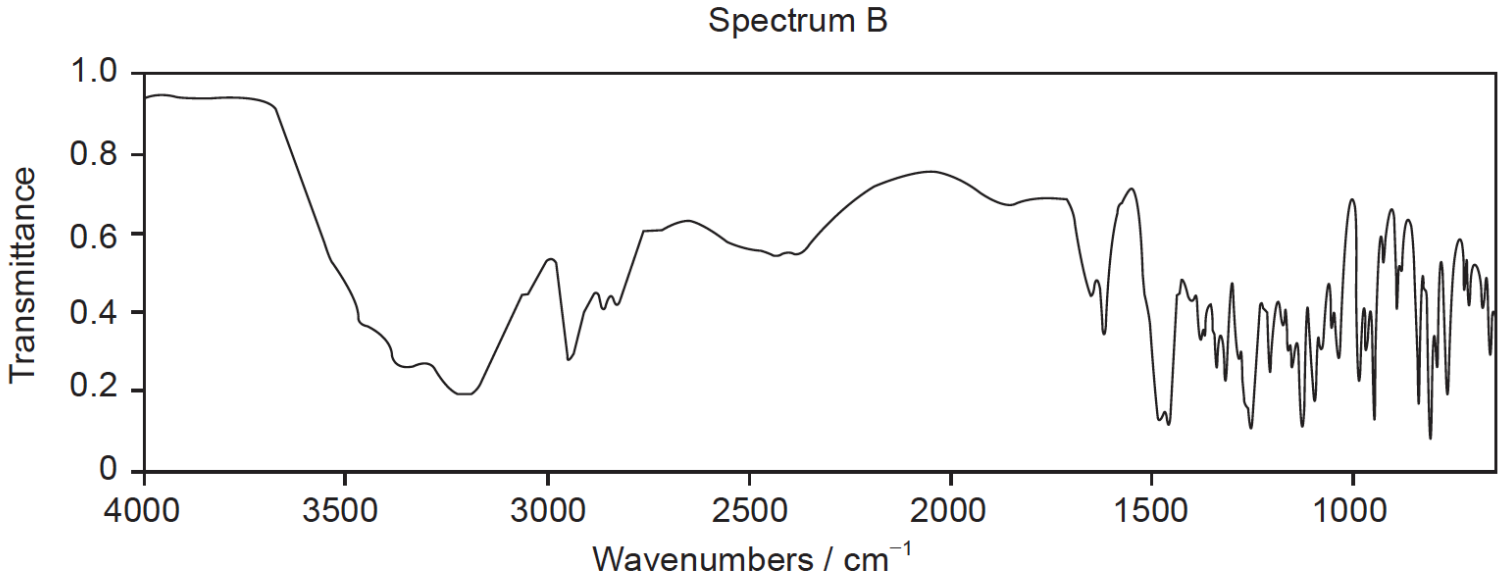
Examiners report

a.i. [N/A]
a.ii. [N/A]
b. [N/A]

Opiates have been used for thousands of years to alleviate pain. The structures of opiates are found in section 37 of the data booklet.

Using sections 26 and 37 of the data booklet, deduce, giving **two** reasons, which spectrum is that of morphine and which is diamorphine.





[Source: http://webbook.nist.gov]

Markscheme

spectrum A is diamorphine because it has a «strong» peak at 1700–1750 «cm^{-1}»

OR

spectrum A is diamorphine because it has a C=O/carbonyl (group)/ester

spectrum B is morphine because it has a «strong broad» peak at 3200– 3600 «cm^{-1}»
OR
spectrum B is morphine because it has a –OH/hydroxyl (group)

*Award **[1 max]** for "spectrum A is diamorphine **AND** spectrum B is morphine" **OR** correctly identified peaks associated with the correct compounds (eg. C=O for diamorphine etc.).*

Accept "alcohol/hydroxy" for "hydroxyl" but not "hydroxide".

Examiners report

[N/A]