

PHARMACEUTICAL CHEMISTRY

HIGHER 3

(Syllabus 9812)

INTRODUCTION

The objectives of the syllabus are to provide students who have exceptional ability and interest in Chemistry the opportunity to:

- (a) apply the principles of chemistry for an understanding of drug action and design
- (b) understand and apply various analytical techniques to chemical analysis
- (c) be enthused to engage in research and rationalise ethical issues

Candidates should simultaneously offer H2 Chemistry, and will be assumed to have knowledge and understanding of Chemistry at H2 level.

SYLLABUS DESIGN

The syllabus is based on about 140 hours of teaching and self-directed independent learning out of curriculum time. It is pitched at approximately undergraduate year one level.

SUGGESTED TEACHING APPROACH

Learning can be via:

- lectures, possibly including guest lectures from industry and research
- laboratory exercises
- literature review
- group work and presentations
- case studies

ASSESSMENT OBJECTIVES

A *Knowledge with understanding*

Students should be able to demonstrate knowledge with understanding in relation to:

1. scientific phenomena, facts, laws, definitions, concepts, theories;
2. scientific vocabulary, terminology, conventions (including symbols, quantities and units);
3. scientific instruments and apparatus, including techniques of operation and aspects of safety;
4. scientific quantities and their determination;
5. scientific and technological applications with their social, economic and environmental implications;

The Syllabus Content defines the factual knowledge that candidates may be required to recall and explain. Questions testing these objectives will often begin with one of the following words: *define, state, describe, explain or outline*. (see the Glossary of Terms.)

B *Handling, applying and evaluating information*

Students should be able in words or by using symbolic, graphical and numerical forms of presentation to:

1. locate, select, organise and present information from a variety of sources;
2. handle information, distinguishing the relevant from the extraneous;
3. manipulate numerical and other data and translate information from one form to another;
4. analyse and evaluate information so as to identify patterns, report trends and conclusions, and draw inferences;
5. present reasoned explanations for phenomena, patterns and relationships.
6. construct arguments to support hypotheses or to justify a course of action;
7. apply knowledge, including principles, to novel situations;
8. evaluate information and hypotheses.
9. demonstrate an awareness of the limitations of Chemistry theories and models.
10. bring together knowledge, principles and concepts from different areas of chemistry, and apply them in a particular context.
11. use chemical skills in contexts which bring together different areas of the subject.

These assessment objectives cannot be precisely specified in the Syllabus Content because questions testing such skills may be based on information which is unfamiliar to the candidate. In answering such questions, candidates are required to use principles and concepts that are within the syllabus and apply them in a logical, reasoned or deductive manner to a novel situation. Questions testing these objectives will often begin with one of the following words: *predict, suggest, construct, calculate* or *determine*. (see the Glossary of Terms.)

SCHEME OF ASSESSMENT

Candidates will take a 2 h 30 min paper (100 marks total). Candidates choose five out of six free-response questions. Each question carries 20 marks, and requires integration of knowledge from the different sections in the syllabus.

WEIGHTING OF ASSESSMENT OBJECTIVES

Assessment Objectives		Weighting
A	Knowledge with understanding	30%
B	Handling, applying and evaluating information	70%

ADDITIONAL INFORMATION

Data Booklet

A *Data Booklet* is available for use in the examination paper. The booklet is reprinted at the end of this syllabus document.

Nomenclature

Students will be expected to be familiar with nomenclature used in the syllabus but otherwise the ASE (The ASE Companion to 16-19 Science) conventions will be used.

In particular, the names sulphite, nitrite, sulphur trioxide, sulphurous acid and nitrous acid will be used in question papers.

SUBJECT CONTENT

1. EFFECTS AND DEVELOPMENT OF DRUGS

This section introduces the general properties and functions of drugs. It gives a general idea of how drugs are designed, developed, and tested, including the use of structural modification, asymmetric synthesis to get the desired optical isomer, and drug testing made before drugs are introduced to the public. Candidates should be aware of the contribution that science has made (and continues to make) towards maintaining the health and well-being of the world's population.

1.1 EFFECTS OF DRUGS

Learning Outcomes

Candidates should be able to:

- (a) list the general effects of drugs
- (b) identify the properties of an ideal drug
- (c) recognise the importance of the body's natural healing processes
- (d) recognise the implications of the placebo effect

1.2 DEVELOPMENT OF DRUGS

Learning Outcomes

Candidates should be able to:

- (a) describe the various aspects of a drug discovery program
- (b) understand the different sources of potential drug candidates
- (c) explain the modification of molecular structure to optimise drug activity
- (d) describe the importance of stereochemistry in drug action, and the use of asymmetric synthesis to get the desired optical isomer
- (e) describe the basic steps in drug testing

2. PROPERTIES OF FUNCTIONAL GROUPS AND INTERMOLECULAR INTERACTIONS

This section focuses on the properties of some functional groups and ring systems in drug molecules, and how drug molecules interact with receptors to bring about a biological effect.

2.1 PROPERTIES OF SOME FUNCTIONAL GROUPS AND RING SYSTEMS IN DRUG MOLECULES

Learning Outcomes

- **Lactones**

Candidates should be able to:

- (a) describe the chemistry of lactones in the following reactions:
 - (i) hydrolysis
 - (ii) reaction with ammonia
 - (iii) reduction

- **Lactams**

Candidates should be able to:

- (a) describe the chemistry of lactams in the following reactions:
 - (i) hydrolysis
 - (ii) reduction

- **Ethers**

Candidates should be able to:

- (a) describe the preparation of ethers from
 - (i) alcohols
 - (ii) Williamson ether synthesis
- (b) describe the acidic cleavage of ethers

- **Sulphides**

Candidates should be able to:

- (a) describe the preparation of sulphides from the reaction between an alkyl halide and thiolate ion
- (b) describe the oxidation of sulphides

- **Thiols and Disulphides**

Candidates should be able to:

- (a) describe the preparation of thiols from an alkyl halide and the hydrosulphide ion
- (b) describe the oxidation of thiols to disulphides, and reduction of disulphides to thiols.

- **Furan, Thiophene, Pyrrole**

Candidates should be able to:

- (a) compare the relative aromaticity of furan, thiophene, and pyrrole
- (b) describe the electrophilic substitution reactions, as exemplified by nitration, Friedel-Crafts acylation and alkylation
- (c) explain the effect of electron-withdrawing groups on the reactivity and position of substitution on the aromatic ring

- **Pyridine**

Candidates should be able to:

- (a) explain the basicity of pyridine
- (b) explain its inertness to electrophilic substitution
- (c) describe the mechanism of nucleophilic substitution in pyridine

2.2 INTERMOLECULAR FORCES AND RECEPTOR INTERACTIONS

Learning Outcomes

Candidates should be able to:

- (a) apply their understanding of the following types of bonding to explain how a general receptor interacts with a drug molecule and changes shape to bring about a biological effect
 - (i) covalent bonding
 - (ii) ionic interaction
 - (iii) hydrogen bonding
 - (iv) ion-dipole interaction
 - (v) van der Waals interaction (based on permanent and induced dipoles)

[Details of types and sub-types of receptors are **not** required]

- (b) understand the effects of competitive and non-competitive inhibition on drug-receptor interaction
- (c) explain the design of agonists and antagonists
- (d) use the concept of drug-receptor interactions to explain tolerance and dependence on a drug

2.3 BONDING AND MOLECULAR PROPERTIES OF ORGANIC DRUG MOLECULES

Learning Outcomes

Candidates should be able to:

- (a) apply their understanding of the effects of the following factors to explain the behaviour of drug molecules:
 - (i) hydrophilicity vs hydrophobicity (polarity)
 - (ii) acidity and basicity
 - (iii) electronic effects (inductive effects; mesomeric effects)
 - (iv) steric effect

3. MOLECULAR STEREOCHEMISTRY

The importance of stereochemistry in drug action is well-known. Different stereoisomers can have very different biological effects. This section builds on the study of stereochemistry in H2 Chemistry.

3.1 GEOMETRICAL ISOMERISM

Learning Outcomes

Candidates should be able to:

- (a) explain the importance of geometrical isomerism to drug action
- (b) use the *E*, *Z* nomenclature to label geometrical isomers

3.2 OPTICAL ISOMERISM

Learning Outcomes

Candidates should be able to:

- (a) explain the importance of optical isomerism to drug action
- (b) understand the terms *enantiomers*, *diastereomers* and *meso* compounds
- (c) use stereochemical projections (e.g. Fischer and Newman projections) to represent organic molecules
- (d) use *R*, *S* configurations to label optical isomers
- (e) understand the concepts of optical activity and optical purity

3.3 CONFORMATIONAL ISOMERISM

Learning Outcomes

Candidates should be able to:

- (a) describe the different conformations of alkanes and cycloalkanes
- (b) understand the energy barriers to rotation and interconversion among conformational isomers

4. UNDERSTANDING REACTION MECHANISMS

The synthesis of drug molecules, as well as their reactions, involves a variety of reaction mechanisms. This section builds on the study of reaction mechanisms in H2 Chemistry.

4.1 NUCLEOPHILIC SUBSTITUTION

Learning Outcomes

Candidates should be able to:

- (a) describe and compare the mechanisms and kinetics of S_N1 and S_N2 reactions, using nucleophilic substitution reactions of bromoalkanes as an example
- (b) explain how the relative rate of nucleophilic substitution is affected by the nature of the nucleophile
- (c) explain the inductive and steric effects of substituents on the rate of substitution reactions
- (d) use stereochemical projections to represent the stereochemistry at different stages in a nucleophilic substitution reaction

4.2 ELIMINATION

Learning Outcomes

Candidates should be able to:

- (a) describe and compare the mechanisms and kinetics of E1 and E2 reactions, using the elimination of HBr from bromoalkanes as an example
- (b) use stereochemical projections to represent the stereochemistry at different stages in an elimination reaction

4.3 ADDITION

Learning Outcomes

Candidates should be able to:

- (a) use stereochemical projections to represent the stereochemistry at different stages in electrophilic and nucleophilic addition reactions

5. SEPARATION AND ANALYTICAL TECHNIQUES

Analytical techniques are widely used in the development and testing of pharmaceutical products. This section emphasises problem solving and using the information gained from one or more analytical techniques to provide evidence of structural features in molecules. Students should understand the chemical principles behind each analytical technique, but are not expected to have a detailed knowledge of the instruments themselves.

For questions which require candidates to interpret several spectra, candidates may be expected to:

- explain the contribution that each of the spectra makes to a possible identification.
- use evidence from up to three spectra to suggest a probable structure for a given compound.
- suggest what further evidence might be required to confirm a structure suggested by the study of spectra.

Candidates are encouraged to use the analytical instruments covered in this section to analyse simple organic compounds/mixtures.

5.1 USE OF ANALYTICAL TECHNIQUES IN SYNTHESIS AND DRUG DEVELOPMENT

Learning Outcomes

Candidates should be able to:

- (a) recognise the importance of analytical techniques in drug development, for example, in isolation of drugs, and in the determination of drug structure and purity

5.2 BASIC PRINCIPLES OF SPECTROSCOPY

Learning Outcomes

Candidates should be able to:

- (a) understand qualitatively the range of wavelengths (frequencies, energies) with different types of radiation used in spectroscopy
- (b) understand the concept of quantized energy levels

[Quantal formulae and selection rules are **not** required]

5.3 ULTRA-VIOLET/VISIBLE SPECTROSCOPY

Learning Outcomes

Candidates should be able to:

- (a) use Beer's Law, absorbance = $\lg(I_0/I) = \epsilon cl$, where ϵ is taken merely as a constant characteristic of the substance concerned, to calculate the concentration of a given species in solution
- (b) explain that ultraviolet/visible absorption in organic molecules requires electronic transitions between energy levels in chromophores which contain a double or triple bond, a delocalised system or a lone pair of electrons

[Detailed theory of why chromophores have absorptions of appropriate energy is **not** required, **nor** is any consideration of molecular orbitals involved]

- (c) predict whether a given organic molecule will absorb in the ultraviolet/visible region
- (d) explain qualitatively how increasing conjugation in an organic molecule decreases the gap between energy levels and hence shifts the absorption towards longer wavelength
- (e) apply uv/visible spectroscopy to quantitative analysis of a given species in solution.

5.4 INFRA-RED (IR) SPECTROSCOPY

Learning Outcomes

Candidates should be able to:

- (a) explain the origin of IR absorption of simple molecules
- (b) predict the number of IR absorptions for a given simple molecule (such as CO_2 or SO_2), and identify the molecular vibrations which give rise to them
- (c) identify characteristic absorptions in the IR spectrum of a compound containing up to three functional groups (from H2 syllabus)

[Absorptions of common functional groups as in the H2 syllabus will be provided in the Data Booklet.]

- (d) suggest structures for a compound from its IR spectrum

5.5 NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY

Learning Outcomes

Candidates should be able to:

- (a) outline, in simple terms, the principles of nuclear magnetic resonance
- (b) explain the use of the δ scale with TMS as the reference
- (c) explain how the chemical environment of a proton affects the magnetic field it experiences, and hence the absorption of energy at resonance
- (d) explain how diamagnetic anisotropy, as in alkyne, aldehyde, and benzene molecules affects the absorption of energy at resonance
- (e) describe the effects of adjacent protons on the magnetic field experienced by a given proton
- (f) predict, from an NMR spectrum, the number of protons in each group present in a given molecule by integration of peak area
- (g) predict, from an NMR spectrum, the number of protons adjacent to a given proton from the spin-spin splitting pattern, limited to splitting patterns up to a quadruplet only

[Knowledge of the theory of why coupling occurs is **not** required.]

- (h) identify protons in chemically identical environments in simple molecules
- (i) interpret ^1H NMR spectra of simple organic molecules containing no more than three functional groups (from H2 syllabus)

[Chemical shifts of common functional groups as in the H2 syllabus will be provided in the *Data Booklet*.]

- (j) describe how the addition of D_2O may be used to identify labile protons

5.6 MASS SPECTROMETRY

Learning Outcomes

Candidates should be able to:

- (a) identify the basic features of the mass spectrometer
[Detailed knowledge of instrumentation is **not** required, but students should be aware of the functions of the main parts of the instrument.]
- (b) calculate the relative atomic mass of an element given its mass spectrum
- (c) analyse mass spectra in terms of isotopic abundances and molecular fragments
- (d) recognise that rearrangements accompanying fragmentation processes are possible

[mechanism of rearrangement is **not** required]

- (e) suggest the identity of major fragment ions in a given mass spectrum, and hence the possible structure of a molecule
- (f) use the molecular ion peak to determine relative molecular mass
- (g) explain the use of high resolution mass spectrometry in distinguishing between molecules of similar relative molecular mass
- (h) use the (M + 1) peak caused by ^{13}C for determining the number of carbon atoms in organic molecules
- (i) use the (M + 2) and (M + 4) peak(s) in the identification of halogen compounds with up to two halogen atoms (chlorine and bromine)

5.7 CHROMATOGRAPHY : PRINCIPLES OF PAPER, THIN LAYER (TLC), HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC), GAS/LIQUID CHROMATOGRAPHY (GLC)

Learning Outcomes

Candidates should be able to:

- (a) describe simply and explain qualitatively, these types of chromatography in terms of adsorption and/or partition
- (b) explain what is normal and reverse-phase HPLC
- (c) interpret one-way and two-way chromatograms in the identification of particular species present in a mixture.
- (d) interpret gas/liquid chromatograms in terms of the percentage composition of a mixture
- (e) apply their understanding (e.g. polarity, volatility) to decide which is the best chromatographic method to use for a given situation

5.8 ELECTROPHORESIS

Learning Outcomes

Candidates should be able to:

- (a) describe simply the process of electrophoresis, and the effect of pH, using the separation and detection of the products of hydrolysis of proteins as an example.

6. SOME CLASSES OF DRUG

This section exposes candidates to some common classes of drug, classified according to their pharmacological effects, and the chemistry of their actions. Memorising of complex formulae is not required, but candidates should be able to recognise the fundamental structures and relevant functional groups of these drugs, and be able to distinguish between them. Candidates are encouraged to carry out the synthesis of some drugs so that they will be exposed to some techniques in organic synthesis.

6.1 ANTI-BACTERIALS

Learning Outcomes

Candidates should be able to:

- (a) outline the different ways anti-bacterials work, including disruption of cell metabolism, inhibition of cell wall synthesis, damage to plasma membrane structure and impairment of protein synthesis
- (b) compare and contrast the chemical structures and chemistry of the common penicillin types (I-IV) or (F, G, X, K)
- (c) describe the various forms of a semi-synthetic penicillin like ampicillin
- (d) discuss and identify the side effects of penicillin and the effect of over prescription, including in animal feedstock

6.2 ANALGESICS

Learning Outcomes

Candidates should be able to:

- (a) classify analgesics into narcotic and non-narcotic
- (b) outline the different ways analgesics prevent pain
- (c) describe the use of derivatives of salicylic acid as a mild analgesic
- (d) compare the advantages and disadvantages of using aspirin and paracetamol
- (e) describe the structure-activity relationship of morphine and its derivatives
- (f) discuss the social and physiological effects of using analgesics

6.3 STIMULANTS

Learning Outcomes

Candidates should be able to:

- (a) outline the physiological effects of stimulants
- (b) discuss the short- and long-term effects of nicotine consumption
- (c) discuss the effects of caffeine and compare its structure with that of nicotine
- (d) compare and contrast amphetamines and adrenaline

6.4 ANTIVIRALS/MONOCLONAL ANTIBODIES

Learning Outcomes

Candidates should be able to:

- (a) distinguish between viruses and bacteria
- (b) outline the different ways antiviral drugs work
- (c) describe the importance of monoclonal antibodies
- (d) discuss the difficulties of finding appropriate antiviral drugs

6.5 HALLUCINOGENS (MIND-ALTERING DRUGS)

Learning Outcomes

Candidates should be able to:

- (a) discuss the effects of LSD, and look-alike drugs
- (b) compare and contrast the chemical structures and chemistry of these drugs

References

Organic reaction mechanisms, stereochemistry and spectroscopy:

Organic Chemistry, by J McMurry, published by Brooks/Cole

Organic Chemistry, by J Morrison, R Boyd, published by Prentice Hall International

Organic Chemistry: A Problem-Solving Approach, by Cane and Tomlinson, published by Mills and Boon

Introduction to Spectroscopy, by Pavia, Lampman and Kinz, published by Saunders College Publishing

Investigation of Molecular Structure, by B.C. Gilbert, published by Mills and Boon

Spectrometric Identification of Organic Compounds, by Silverstein, Bassler, Morrill, published by John Wiley and Sons, Inc

Chromatography:

Fundamentals of Analytical Chemistry, by Skoog, West and Holler, published by Saunders College Publishing

Medicines and drugs:

An Introduction to Medicinal Chemistry, by Graham L. Patrick, published by Oxford University Press

Modern Medicinal Chemistry, by John B. Taylor and Peter P. Kennewell, published by Ellis Horwood

Review of Organic Functional Groups/Introduction to Medicinal Organic Chemistry, by Thomas L. Memk, published by Lippincott

Medicinal Chemistry into the Millennium, by Campbell, M. M., published by Royal Society of Chemistry, Cambridge

Essentials in Pharmaceutical Chemistry, by Cairns, Donald, published by Pharmaceutical Press, London

Drugs and the Human Body - With Implications for Society, by Ken Liska, published by Prentice Hall

Biopharmaceuticals: Biochemistry and Biotechnology, by Walsh, Gary, published by John Wiley.

New Trends in Synthetic Medicinal Chemistry, by Gualtieri, Fulvio, published by Wiley-VCH, Weinheim

Strategies for Organic Drug Synthesis and Design, by Lednicer, Daniel, published by Wiley, New York

SUMMARY OF KEY QUANTITIES AND UNITS

The list below is intended as a guide to the more important quantities which might be encountered in teaching and used in question papers. The list is not exhaustive.

Quantity	Usual symbols	SI unit
Base quantities		
mass	m	kg, g
length	l	m
time	t	s
electric current	I	A
thermodynamic temperature	T	K
amount of substance	n	mol
Other quantities		
chemical shift	δ	ppm
temperature	θ, t	$^{\circ}\text{C}$
volume	V, v	m^3, dm^3
density	ρ	$\text{kg m}^{-3}, \text{g dm}^{-3}, \text{g cm}^{-3}$
pressure	p	Pa
frequency	ν, f	Hz
wavelength	λ	m, mm, nm
speed of electromagnetic waves	c	m s^{-1}
Planck constant	h	J s
electric potential difference	V	V
(standard) electrode redox } potential	$(E^{\ominus}) E$	V
electromotive force	E	V
molar gas constant	R	$\text{J K}^{-1} \text{mol}^{-1}$
half-life	$T_{1/2}, t_{1/2}$	s
atomic mass	m_a	kg
relative { atomic isotopic } mass	A_r	—
molecular mass	m	kg
relative molecular mass	M_r	—
molar mass	M	kg mol^{-1}
nucleon number	A	—
proton number	Z	—
neutron number	N	—
number of molecules	N	—
number of molecules per unit volume	n	m^{-3}
Avogadro constant	L	mol^{-1}
Faraday constant	F	C mol^{-1}
enthalpy change of reaction	ΔH	J, kJ
standard enthalpy change of reaction	ΔH^{\ominus}	$\text{J mol}^{-1}, \text{kJ mol}^{-1}$
ionisation energy	I	kJ mol^{-1}
lattice energy	—	kJ mol^{-1}
bond energy	—	kJ mol^{-1}
electron affinity	—	kJ mol^{-1}
rate constant	k	as appropriate
equilibrium constant	K, K_p, K_c	as appropriate
acid dissociation constant	K_a	as appropriate
order of reaction	n, m	—
mole fraction	x	—
concentration	c	mol dm^{-3}
partition coefficient	K	—
ionic product, solubility product	K, K_{sp}	as appropriate
ionic product of water	K_w	$\text{mol}^2 \text{dm}^{-6}$
pH	pH	—

MATHEMATICAL REQUIREMENTS

It is assumed that candidates will be competent in the techniques described below.

Make calculations involving addition, subtraction, multiplication and division of quantities.

Make approximate evaluations of numerical expressions.

Express small fractions as percentages, and vice versa.

Calculate an arithmetic mean.

Transform decimal notation to power of ten notation (standard form).

Use tables or calculators to evaluate logarithms (for pH calculations), squares, square roots, and reciprocals.

Change the subject of an equation. (Most such equations involve only the simpler operations but may include positive and negative indices and square roots.)

Substitute physical quantities into an equation using consistent units so as to calculate one quantity.

Check the dimensional consistency of such calculations, e.g. the units of a rate constant k .

Solve simple algebraic equations.

Comprehend and use the symbols/notations $<$, $>$, \approx , $/$, Δ , \equiv , \bar{x} (or $\langle x \rangle$).

Test tabulated pairs of values for direct proportionality by a graphical method or by constancy of ratio.

Select appropriate variables and scales for plotting a graph, especially to obtain a linear graph of the form $y = mx + c$.

Determine and interpret the slope and intercept of a linear graph.

Choose by inspection a straight line that will serve as the 'least bad' linear model for a set of data presented graphically.

Understand (i) the slope of a tangent to a curve as a measure of rate of change, (ii) the 'area' below a curve where the area has physical significance, e.g. Boltzmann distribution curves.

Comprehend how to handle numerical work so that significant figures are neither lost unnecessarily nor used beyond what is justified.

Estimate orders of magnitude.

Formulate simple algebraic equations as mathematical models, e.g. construct a rate equation, and identify failures of such models.

Calculators

If calculators are to be used, it is suggested that they should have the following functions:

$+$, $-$, \times , \div , \sqrt{x} , x^2 , x^y , $\lg x$. A *memory* function may be useful but is not essential.

GLOSSARY OF TERMS

It is hoped that the glossary (which is relevant only to science subjects) will prove helpful to candidates as a guide, i.e. it is neither exhaustive nor definitive. The glossary has been deliberately kept brief not only with respect to the number of terms included but also to the descriptions of their meanings. Candidates should appreciate that the meaning of a term must depend in part on its context.

1. *Define (the term(s)...) is intended literally. Only a formal statement or equivalent paraphrase being required.*
2. *What do you understand by/What is meant by (the term(s)...) normally implies that a definition should be given, together with some relevant comment on the significance or context of the term(s) concerned, especially where two or more terms are included in the question. The amount of supplementary comment intended should be interpreted in the light of the indicated mark value.*
3. *State implies a concise answer with little or no supporting argument, e.g. a numerical answer that can be obtained 'by inspection'.*
4. *List requires a number of points, generally each of one word, with no elaboration. Where a given number of points is specified, this should not be exceeded.*
5. *Explain may imply reasoning or some reference to theory, depending on the context.*
6. *Describe requires candidates to state in words (using diagrams where appropriate) the main points of the topic. It is often used with reference either to particular phenomena or to particular experiments. In the former instance, the term usually implies that the answer should include reference to (visual) observations associated with the phenomena.*
In other contexts, describe and give an account of should be interpreted more generally, i.e. the candidate has greater discretion about the nature and the organisation of the material to be included in the answer. Describe and explain may be coupled in a similar way to state and explain.
7. *Discuss requires candidates to give a critical account of the points involved in the topic.*
8. *Outline implies brevity, i.e. restricting the answer to giving essentials.*
9. *Predict implies that the candidate is not expected to produce the required answer by recall but by making a logical connection between other pieces of information. Such information may be wholly given in the question or may depend on answers extracted in an early part of the question.*
10. *Deduce is used in a similar way as predict except that some supporting statement is required, e.g. reference to a law/principle, or the necessary reasoning is to be included in the answer.*
11. *Comment is intended as an open-ended instruction, inviting candidates to recall or infer points of interest relevant to the context of the question, taking account of the number of marks available.*
12. *Suggest is used in two main contexts, i.e. either to imply that there is no unique answer (e.g. in chemistry, two or more substances may satisfy the given conditions describing an 'unknown'), or to imply that candidates are expected to apply their general knowledge to a 'novel' situation, one that may be formally 'not in the syllabus'.*
13. *Find is a general term that may variously be interpreted as calculate, measure, determine etc.*
14. *Calculate is used when a numerical answer is required. In general, working should be shown, especially where two or more steps are involved.*

15. *Measure* implies that the quantity concerned can be directly obtained from a suitable measuring instrument, e.g. length, using a rule, or angle, using a protractor.
16. *Determine* often implies that the quantity concerned cannot be measured directly but is obtained by calculation, substituting measured or known values of other quantities into a standard formula, e.g. relative molecular mass.
17. *Estimate* implies a reasoned order of magnitude statement or calculation of the quantity concerned, making such simplifying assumptions as may be necessary about points of principle and about the values of quantities not otherwise included in the question.
18. *Sketch*, when applied to graph work, implies that the shape and/or position of the curve need only be qualitatively correct, but candidates should be aware that, depending on the context, some quantitative aspects may be looked for, e.g. passing through the origin, having an intercept, asymptote or discontinuity at a particular value.

In diagrams, sketch implies that a simple, freehand drawing is acceptable: nevertheless, care should be taken over proportions and the clear exposition of important details.
19. *Construct* is often used in relation to chemical equations where a candidate is expected to write a balanced equation, not by factual recall but by analogy or by using information in the question.
20. *Compare* requires candidates to provide both the similarities and differences between things or concepts.
21. *Classify* requires candidates to group things based on common characteristics.
22. *Recognise* is often used to identify facts, characteristics or concepts that are critical (relevant/appropriate) to the understanding of a situation, event, process or phenomenon.

Special Note

Units, significant figures. Candidates should be aware that misuse of units and/or significant figures, i.e. failure to quote units where necessary, the inclusion of units in quantities defined as ratios or quoting answers to an inappropriate number of significant figures, is liable to be penalised.

Data Booklet

for

Chemistry
(Advanced Level)

for use in all papers for the H1, H2, H3 Chemistry syllabuses, except practical examinations

TABLES OF CHEMICAL DATA

Important values, constants and standards

molar gas constant	R	$= 8.31 \text{ J K}^{-1} \text{ mol}^{-1}$
the Faraday constant	F	$= 9.65 \times 10^4 \text{ C mol}^{-1}$
the Avogadro constant	L	$= 6.02 \times 10^{23} \text{ mol}^{-1}$
the Planck constant	h	$= 6.63 \times 10^{-34} \text{ J s}$
speed of light in a vacuum	c	$= 3.00 \times 10^8 \text{ m s}^{-1}$
rest mass of proton, ${}^1_1\text{H}$	m_p	$= 1.67 \times 10^{-27} \text{ kg}$
rest mass of neutron, ${}^1_0\text{n}$	m_n	$= 1.67 \times 10^{-27} \text{ kg}$
rest mass of electron, ${}^0_{-1}\text{e}$	m_e	$= 9.11 \times 10^{-31} \text{ kg}$
electronic charge	e	$= -1.60 \times 10^{-19} \text{ C}$
molar volume of gas	V_m	$= 22.4 \text{ dm}^3 \text{ mol}^{-1}$ at s.t.p V_m $= 24 \text{ dm}^3 \text{ mol}^{-1}$ under room conditions
(where s.t.p. is expressed as 101 kPa, approximately, and 273 K (0 °C))		
ionic product of water	K_w	$= 1.00 \times 10^{-14} \text{ mol}^2 \text{ dm}^{-6}$ (at 298 K [25 °C])
specific heat capacity of water		$= 4.18 \text{ kJ kg}^{-1} \text{ K}^{-1}$ ($= 4.18 \text{ J g}^{-1} \text{ K}^{-1}$)

Ionisation energies (1st, 2nd, 3rd and 4th) of selected elements, in kJ mol^{-1}

	Proton Number	First	Second	Third	Fourth
H	1	1310	-	-	-
He	2	2370	5250	-	-
Li	3	519	7300	11800	-
Be	4	900	1760	14800	21000
B	5	799	2420	3660	25000
C	6	1090	2350	4610	6220
N	7	1400	2860	4590	7480
O	8	1310	3390	5320	7450
F	9	1680	3370	6040	8410
Ne	10	2080	3950	6150	9290
Na	11	494	4560	6940	9540
Mg	12	736	1450	7740	10500
Al	13	577	1820	2740	11600
Si	14	786	1580	3230	4360
P	15	1060	1900	2920	4960
S	16	1000	2260	3390	4540
Cl	17	1260	2300	3850	5150
Ar	18	1520	2660	3950	5770
K	19	418	3070	4600	5860
Ca	20	590	1150	4940	6480
Sc	21	632	1240	2390	7110
Ti	22	661	1310	2720	4170
V	23	648	1370	2870	4600
Cr	24	653	1590	2990	4770
Mn	25	716	1510	3250	5190
Fe	26	762	1560	2960	5400
Co	27	757	1640	3230	5100
Ni	28	736	1750	3390	5400
Cu	29	745	1960	3350	5690
Zn	30	908	1730	3828	5980
Ga	31	577	1980	2960	6190
Ge	32	762	1540	3300	4390
Br	35	1140	2080	3460	4850
Sr	38	548	1060	4120	5440
Sn	50	707	1410	2940	3930
I	53	1010	1840	2040	4030
Ba	56	502	966	3390	-
Pb	82	716	1450	3080	4080

Bond energies**(a) Diatomic molecules**

Bond	Energy/kJ mol⁻¹
H—H	436
D—D	442
N≡N	994
O=O	496
F—F	158
Cl—Cl	244
Br—Br	193
I—I	151
H—F	562
H—Cl	431
H—Br	366
H—I	299

(b) Polyatomic molecules

Bond	Energy/kJ mol⁻¹
C—C	350
C=C	610
C≡C	840
C [⋯] C (benzene)	520
C—H	410
C—Cl	340
C—Br	280
C—I	240
C—O	360
C=O	740
C—N	305
C=N	610
C≡N	890
N—H	390
N—N	160
N=N	410
O—H	460
O—O	150
Si—Cl	359
Si—H	320
Si—O	444
Si—Si	222
S—Cl	250
S—H	347
S—S	264

Standard electrode potential and redox potentials, E^\ominus at 298 K (25 °C)

For ease of reference, two tabulations are given:

- (a) an extended list in alphabetical order;
 (b) a shorter list in decreasing order of magnitude, i.e. a redox series.

(a) E^\ominus in alphabetical order

Electrode reaction	E^\ominus/V
$\text{Ag}^+ + \text{e}^- \rightleftharpoons \text{Ag}$	+0.80
$\text{Al}^{3+} + 3\text{e}^- \rightleftharpoons \text{Al}$	-1.66
$\text{Ba}^{2+} + 2\text{e}^- \rightleftharpoons \text{Ba}$	-2.90
$\text{Br}_2 + 2\text{e}^- \rightleftharpoons 2\text{Br}^-$	+1.07
$\text{Ca}^{2+} + 2\text{e}^- \rightleftharpoons \text{Ca}$	-2.87
$\text{Cl}_2 + 2\text{e}^- \rightleftharpoons 2\text{Cl}^-$	+1.36
$2\text{HOCl} + 2\text{H}^+ + 2\text{e}^- \rightleftharpoons \text{Cl}_2 + 2\text{H}_2\text{O}$	+1.64
$\text{Co}^{2+} + 2\text{e}^- \rightleftharpoons \text{Co}$	-0.28
$\text{Co}^{3+} + \text{e}^- \rightleftharpoons \text{Co}^{2+}$	+1.82
$[\text{Co}(\text{NH}_3)_6]^{2+} + 2\text{e}^- \rightleftharpoons \text{Co} + 6\text{NH}_3$	-0.43
$\text{Cr}^{2+} + 2\text{e}^- \rightleftharpoons \text{Cr}$	-0.91
$\text{Cr}^{3+} + 3\text{e}^- \rightleftharpoons \text{Cr}$	-0.74
$\text{Cr}^{3+} + \text{e}^- \rightleftharpoons \text{Cr}^{2+}$	-0.41
$\text{Cr}_2\text{O}_7^{2-} + 14\text{H}^+ + 6\text{e}^- \rightleftharpoons 2\text{Cr}^{3+} + 7\text{H}_2\text{O}$	+1.33
$\text{Cu}^+ + \text{e}^- \rightleftharpoons \text{Cu}$	+0.52
$\text{Cu}^{2+} + 2\text{e}^- \rightleftharpoons \text{Cu}$	+0.34
$\text{Cu}^{2+} + \text{e}^- \rightleftharpoons \text{Cu}^+$	+0.15
$[\text{Cu}(\text{NH}_3)_4]^{2+} + 2\text{e}^- \rightleftharpoons \text{Cu} + 4\text{NH}_3$	-0.05
$\text{F}_2 + 2\text{e}^- \rightleftharpoons 2\text{F}^-$	+2.87
$\text{Fe}^{2+} + 2\text{e}^- \rightleftharpoons \text{Fe}$	-0.44
$\text{Fe}^{3+} + 3\text{e}^- \rightleftharpoons \text{Fe}$	-0.04
$\text{Fe}^{3+} + \text{e}^- \rightleftharpoons \text{Fe}^{2+}$	+0.77
$[\text{Fe}(\text{CN})_6]^{3-} + \text{e}^- \rightleftharpoons [\text{Fe}(\text{CN})_6]^{4-}$	+0.36
$\text{Fe}(\text{OH})_3 + \text{e}^- \rightleftharpoons \text{Fe}(\text{OH})_2 + \text{OH}^-$	-0.56
$2\text{H}^+ + 2\text{e}^- \rightleftharpoons \text{H}_2$	0.00
$\text{I}_2 + 2\text{e}^- \rightleftharpoons 2\text{I}^-$	+0.54
$\text{K}^+ + \text{e}^- \rightleftharpoons \text{K}$	-2.92
$\text{Li}^+ + \text{e}^- \rightleftharpoons \text{Li}$	-3.04
$\text{Mg}^{2+} + 2\text{e}^- \rightleftharpoons \text{Mg}$	-2.38
$\text{Mn}^{2+} + 2\text{e}^- \rightleftharpoons \text{Mn}$	-1.18
$\text{Mn}^{3+} + \text{e}^- \rightleftharpoons \text{Mn}^{2+}$	+1.49
$\text{MnO}_2 + 4\text{H}^+ + 2\text{e}^- \rightleftharpoons \text{Mn}^{2+} + 2\text{H}_2\text{O}$	+1.23
$\text{MnO}_4^- + \text{e}^- \rightleftharpoons \text{MnO}_4^{2-}$	+0.56
$\text{MnO}_4^- + 4\text{H}^+ + 3\text{e}^- \rightleftharpoons \text{MnO}_2 + 2\text{H}_2\text{O}$	+1.67
$\text{MnO}_4^- + 8\text{H}^+ + 5\text{e}^- \rightleftharpoons \text{Mn}^{2+} + 4\text{H}_2\text{O}$	+1.52
$\text{NO}_3^- + 2\text{H}^+ + \text{e}^- \rightleftharpoons \text{NO}_2 + \text{H}_2\text{O}$	+0.81
$\text{NO}_3^- + 3\text{H}^+ + 2\text{e}^- \rightleftharpoons \text{HNO}_2 + \text{H}_2\text{O}$	+0.94
$\text{NO}_3^- + 10\text{H}^+ + 8\text{e}^- \rightleftharpoons \text{NH}_4^+ + 3\text{H}_2\text{O}$	+0.87
$\text{Na}^+ + \text{e}^- \rightleftharpoons \text{Na}$	-2.71
$\text{Ni}^{2+} + 2\text{e}^- \rightleftharpoons \text{Ni}$	-0.25

(a) continued...

Electrode reaction		E^{\ominus}/V
$[\text{Ni}(\text{NH}_3)_6]^{2+} + 2\text{e}^-$	\rightleftharpoons Ni + 6NH ₃	-0.51
$\text{H}_2\text{O}_2 + 2\text{H}^+ + 2\text{e}^-$	\rightleftharpoons 2H ₂ O	+1.77
$\text{O}_2 + 4\text{H}^+ + 4\text{e}^-$	\rightleftharpoons 2H ₂ O	+1.23
$\text{O}_2 + 2\text{H}_2\text{O} + 4\text{e}^-$	\rightleftharpoons 4OH ⁻	+0.40
$\text{O}_2 + 2\text{H}^+ + 2\text{e}^-$	\rightleftharpoons H ₂ O ₂	+0.68
$2\text{H}_2\text{O} + 2\text{e}^-$	\rightleftharpoons H ₂ + 2OH ⁻	-0.83
$\text{Pb}^{2+} + 2\text{e}^-$	\rightleftharpoons Pb	-0.13
$\text{Pb}^{4+} + 2\text{e}^-$	\rightleftharpoons Pb ²⁺	+1.69
$\text{PbO}_2 + 4\text{H}^+ + 2\text{e}^-$	\rightleftharpoons Pb ²⁺ + 2H ₂ O	+1.47
$\text{SO}_4^{2-} + 4\text{H}^+ + 2\text{e}^-$	\rightleftharpoons SO ₂ + 2H ₂ O	+0.17
$\text{S}_2\text{O}_8^{2-} + 2\text{e}^-$	\rightleftharpoons 2SO ₄ ²⁻	+2.01
$\text{S}_4\text{O}_6^{2-} + 2\text{e}^-$	\rightleftharpoons 2S ₂ O ₃ ²⁻	+0.09
$\text{Sn}^{2+} + 2\text{e}^-$	\rightleftharpoons Sn	-0.14
$\text{Sn}^{4+} + 2\text{e}^-$	\rightleftharpoons Sn ²⁺	+0.15
$\text{V}^{2+} + 2\text{e}^-$	\rightleftharpoons V	-1.20
$\text{V}^{3+} + \text{e}^-$	\rightleftharpoons V ²⁺	-0.26
$\text{VO}^{2+} + 2\text{H}^+ + \text{e}^-$	\rightleftharpoons V ³⁺ + H ₂ O	+0.34
$\text{VO}_2^+ + 2\text{H}^+ + \text{e}^-$	\rightleftharpoons VO ²⁺ + H ₂ O	+1.00
$\text{VO}_3^- + 4\text{H}^+ + \text{e}^-$	\rightleftharpoons VO ²⁺ + 2H ₂ O	+1.00
$\text{Zn}^{2+} + 2\text{e}^-$	\rightleftharpoons Zn	-0.76

All ionic states refer to aqueous ions but other state symbols have been omitted.

(b) E^\ominus in decreasing order of oxidising power

(see also the extended alphabetical list on the previous pages)

Electrode reaction	E^\ominus/V
$F_2 + 2e^- \rightleftharpoons 2F^-$	+2.87
$S_2O_8^{2-} + 2e^- \rightleftharpoons 2SO_4^{2-}$	+2.01
$H_2O_2 + 2H^+ + 2e^- \rightleftharpoons 2H_2O$	+1.77
$MnO_4^- + 8H^+ + 5e^- \rightleftharpoons Mn^{2+} + 4H_2O$	+1.52
$PbO_2 + 4H^+ + 2e^- \rightleftharpoons Pb^{2+} + 2H_2O$	+1.47
$Cl_2 + 2e^- \rightleftharpoons 2Cl^-$	+1.36
$Cr_2O_7^{2-} + 14H^+ + 6e^- \rightleftharpoons 2Cr^{3+} + 7H_2O$	+1.33
$Br_2 + 2e^- \rightleftharpoons 2Br^-$	+1.07
$NO_3^- + 2H^+ + e^- \rightleftharpoons NO_2 + H_2O$	+0.81
$Ag^+ + e^- \rightleftharpoons Ag$	+0.80
$Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$	+0.77
$I_2 + 2e^- \rightleftharpoons 2I^-$	+0.54
$O_2 + 2H_2O + 4e^- \rightleftharpoons 4OH^-$	+0.40
$Cu^{2+} + 2e^- \rightleftharpoons Cu$	+0.34
$SO_4^{2-} + 4H^+ + 2e^- \rightleftharpoons SO_2 + 2H_2O$	+0.17
$Sn^{4+} + 2e^- \rightleftharpoons Sn^{2+}$	+0.15
$S_4O_6^{2-} + 2e^- \rightleftharpoons 2S_2O_3^{2-}$	+0.09
$2H^+ + 2e^- \rightleftharpoons H_2$	0.00
$Pb^{2+} + 2e^- \rightleftharpoons Pb$	-0.13
$Sn^{2+} + 2e^- \rightleftharpoons Sn$	-0.14
$Fe^{2+} + 2e^- \rightleftharpoons Fe$	-0.44
$Zn^{2+} + 2e^- \rightleftharpoons Zn$	-0.76
$Mg^{2+} + 2e^- \rightleftharpoons Mg$	-2.38
$Ca^{2+} + 2e^- \rightleftharpoons Ca$	-2.87
$K^+ + e^- \rightleftharpoons K$	-2.92

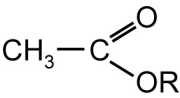
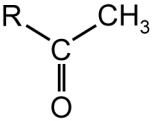
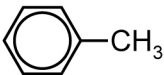
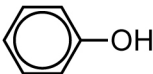
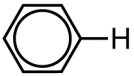
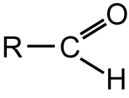
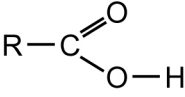
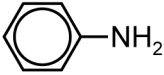
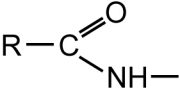
Atomic and ionic radii

(a)	Period 3	atomic/nm		ionic/nm	
	metallic	Na	0.186	Na ⁺	0.095
		Mg	0.160	Mg ²⁺	0.065
		Al	0.143	Al ³⁺	0.050
	single covalent	Si	0.117	Si ⁴⁺	0.041
		P	0.110	P ³⁻	0.212
		S	0.104	S ²⁻	0.184
		Cl	0.099	Cl ⁻	0.181
	van der Waals	Ar	0.192		
(b)	Group II				
	metallic	Be	0.112	Be ²⁺	0.031
		Mg	0.160	Mg ²⁺	0.065
		Ca	0.197	Ca ²⁺	0.099
		Sr	0.215	Sr ²⁺	0.113
		Ba	0.217	Ba ²⁺	0.135
		Ra	0.220	Ra ²⁺	0.140
(c)	Group IV				
	single covalent	C	0.077		
		Si	0.117	Si ⁴⁺	0.041
		Ge	0.122	Ge ²⁺	0.093
	metallic	Sn	0.162	Sn ²⁺	0.112
		Pb	0.175	Pb ²⁺	0.120
(d)	Group VII				
	single covalent	F	0.072	F ⁻	0.136
		Cl	0.099	Cl ⁻	0.181
		Br	0.114	Br ⁻	0.195
		I	0.133	I ⁻	0.216
		At	0.140		
(e)	First row transition elements				
	single covalent	Sc	0.144	Sc ³⁺	0.081
		Ti	0.132	Ti ²⁺	0.090
		V	0.122	V ³⁺	0.074
		Cr	0.117	Cr ³⁺	0.069
		Mn	0.117	Mn ²⁺	0.080
		Fe	0.116	Fe ²⁺	0.076
				Fe ³⁺	0.064
		Co	0.116	Co ²⁺	0.078
		Ni	0.115	Ni ²⁺	0.078
		Cu	0.117	Cu ²⁺	0.069
		Zn	0.125	Zn ²⁺	0.074

Characteristic values for infra-red absorption (due to stretching vibrations in organic molecules).

Bond		Characteristic ranges Wavenumber (reciprocal wavelength) /cm ⁻¹
C—C/		700 to 800
C—O	alcohols, ethers, esters	1000 to 1300
C=C		1610 to 1680
C=O	aldehydes, ketones, acids, esters	1680 to 1750
C≡C		2070 to 2250
C≡N		2200 to 2280
O—H	'hydrogen-bonded' in acids	2500 to 3300
C—H	alkanes, alkenes, arenes	2840 to 3095
O—H	'hydrogen-bonded' in alcohols, phenols	3230 to 3550
N—H	primary amines	3350 to 3500
O—H	'free'	3580 to 3650

Typical proton chemical shift value (δ) relative to T.M.S.=0

<i>Type of proton</i>	<i>Chemical shift (ppm)</i>
$R-CH_3$	0.9
$R-CH_2-R$	1.3
R_3CH	1.4–1.7
	2.0
	2.1
	2.3
$R-C\equiv C-H$	1.8–3.1
$R-CH_2-Hal$	3.2–3.7
$R-O-CH_3$	3.3–4.0
$R-O-H$	0.5–6.0*
$R_2C=CH-$	4.5–6.0
	4.5–7.0*
	6.0–9.0
	9.0–10.0
	9.0–13.0*
$R-NH_2$	1.0–5.0*
	3.0–6.0*
	5.0–12.0*

*Sensitive to solvent, concentration

