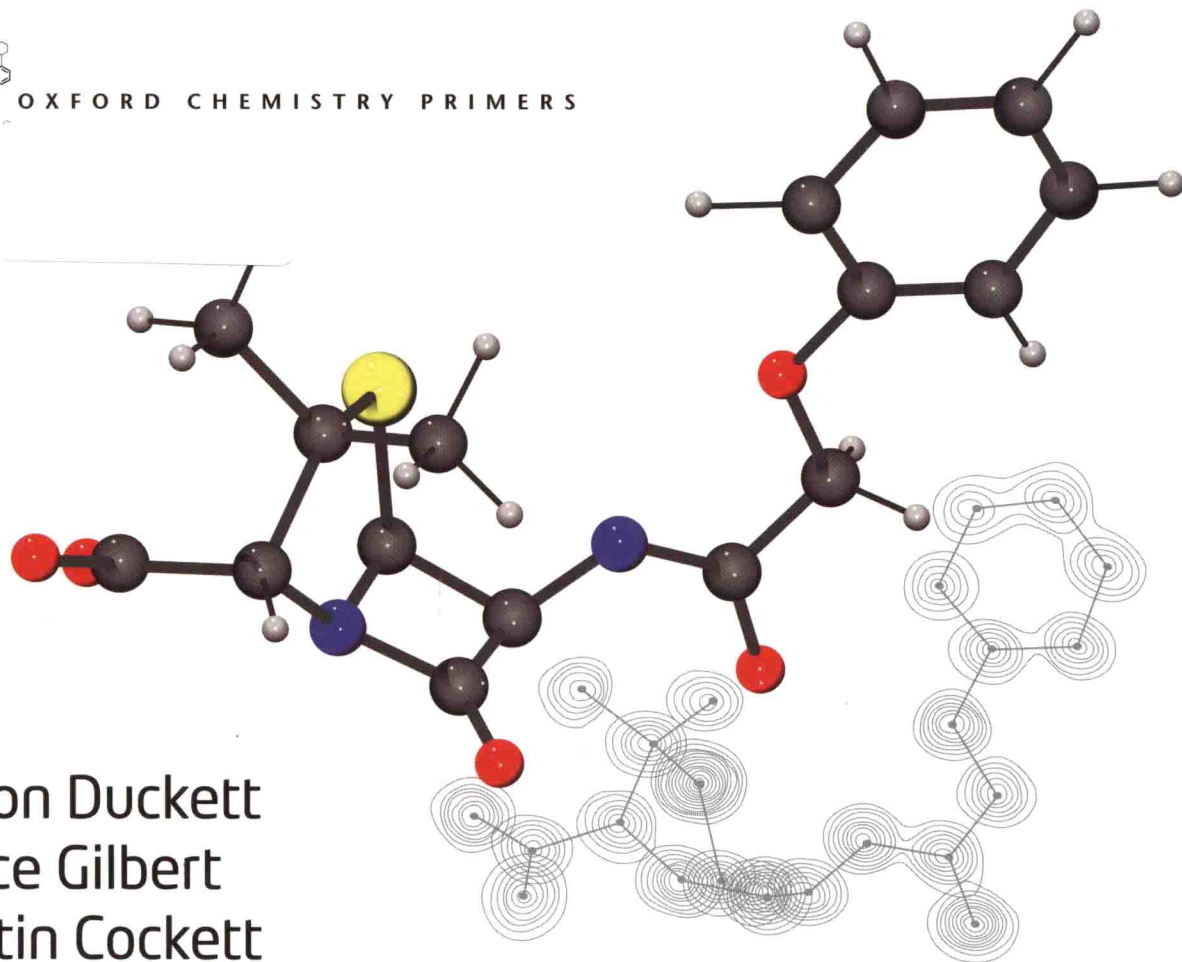


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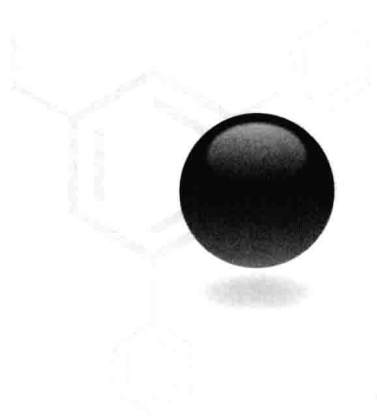
Simon Duckett  
Bruce Gilbert  
Martin Cockett

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# FOUNDATIONS OF MOLECULAR STRUCTURE DETERMINATION

SECOND EDITION

OXFORD



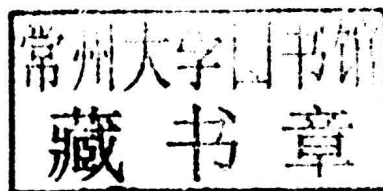
# Foundations of Molecular Structure Determination

SECOND EDITION

Simon Duckett

Bruce Gilbert

Martin Cockett



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First edition 2000

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## Foundations of Molecular Structure Determination

The front cover shows the three-dimensional structure and hand-drawn electron density map of phenoxymethylpenicillin obtained from x-ray diffraction experiments by Dorothy Hodgkin (kindly provided by Dr Adrian Whitwood).

# Preface to the First Edition

This book is written primarily for those studying first-year University courses in Chemistry and for those preparing to do so.

It is designed to reflect significant recent advances in the use of spectroscopic and diffraction methods, not only for obtaining an analysis of elements and groups present in a molecule but also for establishing the arrangement of the constituent atoms. These developments have had a profound effect by increasing scientific knowledge in the fields of chemistry and molecular biology, reflected in the elucidation of the structure and function of a wide range of compounds including drugs, proteins and enzymes, and nucleic acids.

It is important that such work and its appreciation should find its place in the curriculum — as a means of educating chemistry students about essential principles and wide-ranging applications and to show how problem-solving skills are developed and applied in industrial and research environments. We also hope to convey the enjoyment and satisfaction of successful spectrum analysis.

We have included mass spectrometry and X-ray diffraction, along with traditional spectroscopic techniques; the former is the method *par excellence* for molecular mass and formulae determination and the latter provides details of molecular structure, providing information complementary to IR, NMR and UV-visible spectroscopy. We introduce the essential physical principles of each method, many examples of spectral analysis, and some problems; further reading and practice are strongly encouraged.

SI units have been adopted, with IUPAC nomenclature; trivial names accompany the recommended names in parentheses. Accurate mass data are taken from *Mass and Abundance Tables for Use in Mass Spectrometry* by J. H. Beynon and A. E. Williams, Elsevier, Amsterdam, 1963, and fragmentation patterns from *Compilation of Mass Spectral Data* by A. Cornu and R. Massot, Heyden, London, 1966.

We thank especially the following for assistance in recording spectra: Kin MyaMya, Anthony Crawshaw, Zygmunt Derewenda, Guy Dodson, Chris Hall, Reuben Girling, Rod Hubbard, Robert Liddington, and Ted Parton. We acknowledge permission to use Fig. 6.19 (The Royal Society). We are grateful for particularly relevant advice from schoolteachers including David Bevan, Michael Cane, Peter Gradwell, Geoff Liptrot, Bill Pickering, and George Walker. Finally, our special thanks go to David Waddington and Barry Thomas for enthusiasm and encouragement, and to Sue Street and Adrian Whitwood for assistance in producing the manuscript.

York  
1999

S. B. D. and B. C. G.

# Preface to the Second Edition

In preparing this second edition of our primer, we have been very conscious of our commitment to the initial aim 'to reflect recent advances in the use of spectroscopic and diffraction methods, not only for obtaining an analysis of the elements and groups present in a molecule but also for establishing the arrangement of constituent atoms'. This, again, is our major goal, with emphasis placed on the ways in which these approaches provide enhanced understanding and knowledge about molecular structure; and also, of course, how their application provides opportunities (especially for year-one university students) to learn and develop skills in structural analysis. As before, we have chosen to include chapters on mass spectrometry and the diffraction techniques (X-ray, neutron, and electron), as well as the spectroscopic methods of IR, UV, and NMR, to reflect the crucial information they can bring to structural analysis (e.g. on molecular weights, on empirical and structural formulae, and on 3-dimensional structural relationships).

In revising the text and content, we have aimed to provide many opportunities for practice: worked examples; encouragement for self-help; exercises with answers provided; and on-line multi-choice questions. Our policy has been to encourage practice in basic manipulation and understanding of information, before progressing to more advanced examples.

New sections have been included on Raman spectroscopy, alongside infra-red and microwave spectroscopy, and both neutron and electron diffraction, alongside X-ray diffraction. We have increased our coverage of enhancements in methodology and analysis, for example those resulting from advances in computer-based technology. In particular, we have extended our treatment of infra-red and Raman spectroscopy, placing more emphasis on spectroscopic principles involving, for instance, energy levels, populations, selection rules and transitions, and geometric parameters (e.g. bond lengths), as well as those used in structural recognition. We have also placed greater focus on the effects that molecular symmetry, size, and phase play in determining the kinds of information available and how specific methods can be employed to greatest effect.

The range of applications of these techniques has been extended, not least into biological and medical systems (for example in the development of magnetic resonance imaging, MRI). It has also been our intention to highlight the types of changes in instrumentation, to cover, for example, the demand for less expensive spectrometers to operate on a bench-top, as well as those 'top-of-the range' spectrometers for very high sensitivity or even those for operation in remote and hostile environments (e.g. on other planets). But the main emphasis remains on the student readers and their ability to understand and interpret the signals they get from the instruments. Our underpinning philosophy is that tackling problems takes readers to the core of the methods employed, and is likely to provide a stimulus for more advanced study, understanding, and application.

We thank, especially, those who have assisted us by providing helpful comments, or spectra, or both (e.g. via access to their papers in the primary literature); thus our gratitude is extended most warmly to our colleagues Ian Fairlamb, Brendan Keeley,

Jason Lynam, and Peter O'Brien, as well as John Moore and Derek Wann for helpful discussions. We are also indebted substantially to Adrian Whitwood for providing helpful comments, access to papers and computer files, and for computational and on-line assistance. We acknowledge most warmly the care and expertise of Lyndsay Muschamp and Katie Stott, for their invaluable assistance with the production of the manuscripts; and to the staff at OUP, most notably Alice Roberts, for their expertise and patient support.

York  
2015

S. B. D., B. C. G, and M. C. R. C





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# Overview, energy levels, and the electromagnetic spectrum

## 1.1 Introduction

Molecules come in a bewildering variety of shapes and sizes, and with a huge diversity of structural complexity. From the simplest homonuclear diatomic molecules such as  $\text{H}_2$ , to macromolecules such as haemoglobin containing many thousands of constituent atoms, the complexity of any molecule derives from the large number of potential constituent nuclei, the types of bonds which hold the nuclei together, and the degree to which the atoms arrange themselves into symmetric structures. Whilst the universe is seemingly bent on preferring to favour increasing disorder as the natural order of things, nature has a habit of creating molecules of considerable structural order and symmetry. Indeed, the extent to which any given molecule can be regarded as either unsymmetrical and disordered in its form or symmetrical, ordered and, yes, beautiful, is usually directly correlated with the efficiency with which it carries out its chemical functions.

Molecular bonding is absolutely fundamental to all aspects of chemistry, and it is the nature of the interactions that exist between nuclei, both weak and strong, which defines the types of structures that can be constructed from the atomic building blocks. Our understanding of chemical structure derives to a great extent from the theory of the chemical bond and, in particular, from the foundations laid by the development of quantum theory and quantum mechanics in the early part of the 20th century. However, it also depends critically on our ability to determine molecular structures through experiment.

This book presents a number of different experimental strategies to determine the geometrical arrangement of atoms in space that make up a particular molecule. The choice of which technique to use depends on a number of factors such as whether we are dealing with a crystalline, liquid or gas phase sample, whether the molecule is small or large, how symmetric it is and whether we need precise determination of bond lengths and bond angles. In cases where we need more general structural information, we might be interested, for example, in: the structural relationship between functional groups in an organic molecule; or the arrangements of ligands around a metal centre in a transition metal complex; or indeed in the way in which a cardiovascular drug molecule might bind within the protein cavity in haemoglobin.

Most of the methods described in this book rely on the interaction of photons or electrons with the molecule of interest. Those that use photons exploit whichever regions of the electromagnetic spectrum are appropriate to: the probing of rotational,

It is worth noting that mass spectrometry uses a wide variety of alternative ionization methods other than electron impact. These include fast atom bombardment, chemical ionization, electrospray ionization, matrix-assisted laser desorption/ionization, and inductively coupled plasmas. Similarly, diffraction experiments are not limited to X-rays and electrons but can also be conducted with neutrons.

vibrational, or electronic degrees of freedom in, respectively, rotational, vibrational, and electronic spectroscopy; the interaction of nuclear magnetic moments with externally applied magnetic fields in nuclear magnetic resonance spectroscopy (NMR); or the diffraction of X-rays in X-ray diffraction experiments. The two methods that largely employ electrons use them either as a means to transfer energy to ionize and fragment a molecule (mass spectrometry) or to exploit the wave-particle duality of their nature by observing their diffraction in either the gas or condensed phases.

## 1.2 Energy levels, transitions between them, and the electromagnetic spectrum

Visible light constitutes the part of the electromagnetic spectrum with which we are most familiar, simply because we are equipped with the facility to perceive it most acutely through our vision, but it forms just a small slice of the overall spectrum of light. Visible light assumes a particular historical importance in the development of spectroscopy because in sunlight we have a readily available source of radiation with which to observe certain phenomena. The dark lines discovered in the solar spectrum by Wollaston in 1802 and subsequently rediscovered by Fraunhofer 15 years later were due to absorption of sunlight by the colder gases in the outer regions of the Sun. The realization that discrete line spectra arise from discrete quantum states and, moreover, that the positions of those lines could provide a means to identify which atoms might be present, provided the basis of spectroscopic identification and characterization of gases, not only in remote bodies such as the Sun but also closer to home in our own atmosphere. Similarly, in emission rather than absorption, we can use colour as a means to identify particular elements in vaporized samples in flame tests. The characteristic yellow colour of a sodium flame, visible for example when you place a sample of common table salt into a flame, precisely corresponds in wavelength to one of the dark Fraunhofer lines, thereby identifying sodium as being present in the Sun.

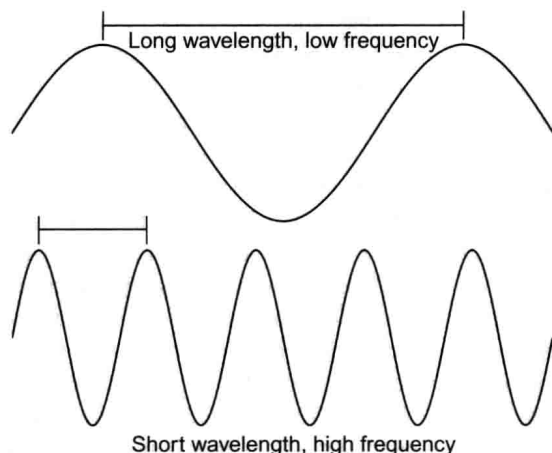
The development of quantum theory, and subsequently of quantum mechanics, formed the basis of our understanding of the relationship between differences in energy between quantum states and the positions of lines appearing in an absorption or emission spectrum. Electromagnetic radiation consists of oscillating electric and magnetic fields that can propagate through space. In a vacuum, all electromagnetic radiation travels with the same speed,  $2.997 \times 10^8 \text{ m s}^{-1}$ . The oscillations associated with different types of electromagnetic radiation can be described simultaneously in terms of their *wavelength* (the distance between successive peaks or troughs in the wave) or their *frequency* (the number of complete wavelengths passing a given point per second). The relationship between the wavelength,  $\lambda$ , and the frequency,  $\nu$ , is given by

$$c = \lambda \times \nu \quad (1.1)$$

where  $c$  is the speed of light in  $\text{m s}^{-1}$ , and the wavelength,  $\lambda$ , and frequency,  $\nu$ , are expressed, respectively, in units of length, m, and reciprocal time,  $\text{s}^{-1}$  or Hz (Hertz). Figure 1.1 shows how wavelength and frequency are inter-related.

The connection between the frequency of light and its ability to change the *energetic* state of matter was provided by Planck at the start of the 20th century when he proposed that frequency is related to energy,  $E$ , through the relationship

$$E = h\nu \quad (1.2)$$



**Figure 1.1** Electromagnetic radiation can be characterized in terms of both its wavelength and frequency. The wavelength provides a measure of the distance between successive peaks or troughs in the wave whilst the frequency provides a measure of the number of complete wavelengths passing a given point per unit time. The energy of the radiation scales linearly with the frequency.

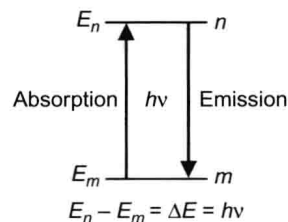
where  $h$  is Planck's constant  $6.626 \times 10^{-34}$  J s. Effectively, the energy is delivered in discrete packets,  $h\nu$ , which we call either quanta or, to use the term coined by G.N. Lewis, photons. Thus, spectroscopy concerns the absorption, emission or scattering of photons by atoms and molecules, with those processes providing direct information about changes in internal quantum state. In the context of absorption or emission, the energy of the photon,  $E$ , supplied or generated by the process has to be exactly the same as the difference in energy,  $\Delta E$ , between the two states involved (see Figure 1.2).

The energy states of an isolated atom are defined solely by the relationship between the orbiting electrons and the positively-charged nucleus. The translational freedom of the atom in space is not one which results in discrete quantum states because the atom's movements are not restricted in any way. Thus, the quantum states of an atom result solely from the fact that the motion of the electrons is constrained by the influence of the nucleus and, consequently, excited states can only result from the promotion of an electron from one orbit to another. To a first approximation then, an absorption spectrum in an atom has a somewhat simple structure involving a series of lines whose separation decreases rapidly as the electron becomes more and more weakly associated with the nucleus, eventually converging to a continuum at the point of ionization.

In a diatomic molecule, in addition to the constraints imposed upon the electrons, the translational motions of the two nuclei are now also constrained, in this case by the 'electronic glue' provided by the chemical bond between the nuclei. Certainly, the molecule as a whole can translate through space but this motion, like that of the isolated atom, is not one which results in stationary quantum states. However, movement of the two nuclei with respect to each other leads to two additional types of motion: rotation about an axis perpendicular to the internuclear axis, and motion of the two nuclei against one another along the internuclear axis. The former is known as a rotational degree of freedom, whilst the latter motion is known as a vibrational degree of freedom.

In addition, when certain nuclei are subjected to an externally applied magnetic field, their energy levels split to an extent which depends on the strength of the field, but this

The almost vanishingly small magnitude of Planck's constant goes some way to explaining why the quantization of energy in microscopic systems escaped notice for so long!



**Figure 1.2** Transitions between states  $m$  and  $n$  requires light to be either absorbed or emitted whose energy exactly equals the energy difference between the two states.

In practice, atomic spectra can be hugely complex. This complexity is most apparent in multi-electron atoms and is the result of electron-electron interactions involving orbital and spin angular momenta as well as interactions between the angular momenta associated with the electrons and those associated with the nuclei.



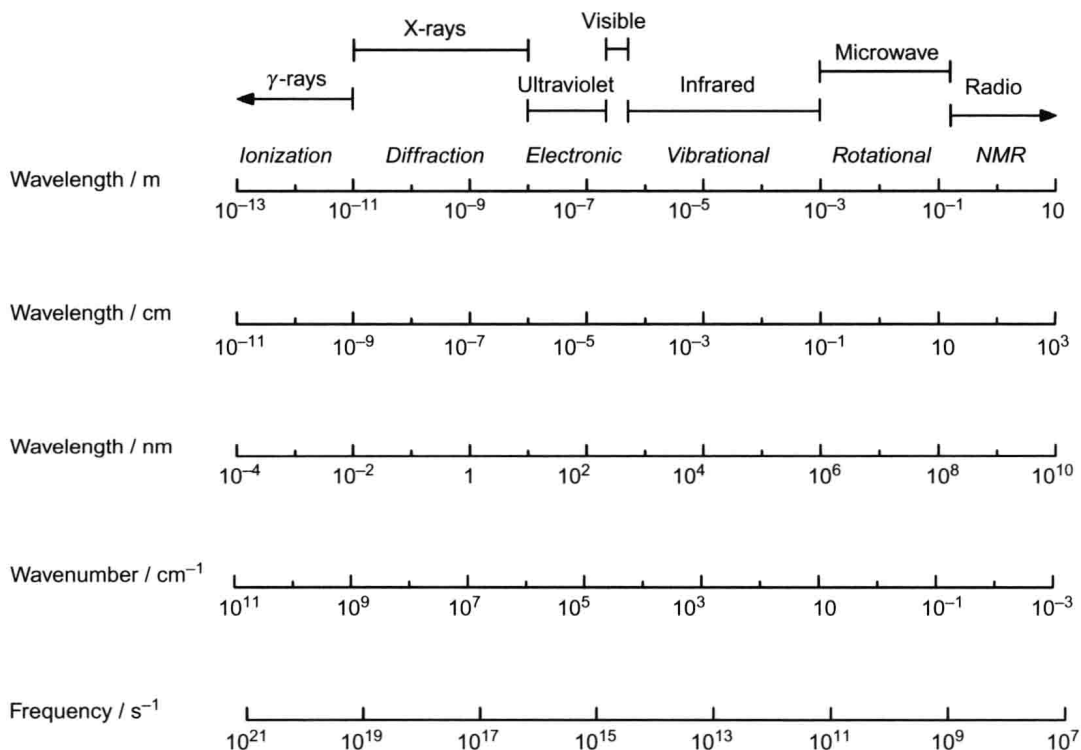
The wavenumber unit,  $\text{cm}^{-1}$ ,  $\tilde{\nu}$ , is simply the reciprocal of the wavelength expressed in cm, and is commonly used by spectroscopists as a matter of convenience when working in certain parts of the electromagnetic spectrum. More generally, you will find that some scientific disciplines favour wavelength, and some frequency or wavenumber, both of which scale linearly with energy. In each case, the preferred units will depend largely on the magnitude of number resulting from their use but also in some cases simply as a consequence of historic convention.

splitting is of a very small order indeed and requires energy in the radiofrequency part of the electromagnetic spectrum to probe. This is the basis of NMR spectroscopy.

These principles extend to molecules of all shapes and sizes. All of them exhibit discrete line spectra as a result of the constraints imposed upon the motions of their constituent nuclei, on the electrons that form the bonds between them and as a result of perturbations provided by externally applied fields. We can get a sense of the relationship between the energy level spacings between electronic, vibrational, rotational, and nuclear magnetic energy levels by referencing them to the electromagnetic spectrum, presented in terms of wavelength, wavenumber and frequency (see Figure 1.3). So let's take a wander through the spectrum to orient ourselves and to get a sense of which types of light excite particular degrees of freedom in the molecule.

Visible light extends from about 390 to 770 nm, which in frequency terms spans about  $7.7 \times 10^{14}$  to  $3.9 \times 10^{14}$  Hz (i.e. 770 to 390 THz). With frequencies so large, you can see why spectroscopists prefer working in units of wavenumber,  $\text{cm}^{-1}$ , for which the same region covers about 26000 to 13000  $\text{cm}^{-1}$ . Visible light is generally used to excite transitions between electronic energy levels, typically those in which the electrons are moving between valence orbitals.

Moving to longer wavelengths, lower energy, and hence lower frequencies, we find ourselves in the *infrared* region which covers 770 nm to about 1000  $\mu\text{m}$ . In frequency terms this spans 390 THz to 300 GHz or, in wavenumbers, 13000 to 10  $\text{cm}^{-1}$ . Infrared



**Figure 1.3** The electromagnetic spectrum extends from  $\gamma$ -rays and X-rays at the very short wavelength, high energy end of the spectrum to microwaves and radiowaves at the very long wavelength, low energy end. We can see from the figure that the visible region actually constitutes only a very narrow slice of the overall spectrum.