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## Lecture Synopses for Course B

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### *Key Organic Reactions: 12 lectures*

This course is divided into two sections. The first deals with flat compounds as reagents and products, and the second with chemistry in three dimensions. Reactions of aromatic compounds and of enols and enolates are the key reactions in the first part. In the second part we consider the “handedness” or *chirality* of molecules and how that affects their structure and reactivity. Molecules can be right- or left-handed: the creation and manipulation of this chirality are the key reactions in this part. Each reaction can be used in chemistry and in biology often with strikingly different results.

**Dr I. R. Baxendale****1–9 Flat Chemistry****1. Electrophilic Substitution on Aromatic Compounds.**

Many drugs, flavouring substances and dyestuffs contain aromatic rings. The structure and reactivity of the benzene ring will be explored using the attack of electrophiles as the key reaction.

**2. Formation and Reactions of Enols and Enolates.**

Carbonyl compounds are in equilibrium with enols and some enols are stable - vitamin C is an example. The formation of enols and enolate ions and their reaction with halogen and silicon electrophiles are the key reactions here

**3. Enols as Reaction Products: Conjugate Addition.**

Unsaturated carbonyl compounds add nucleophiles at the remote end of the alkene. This key reaction – conjugate addition – can be constructive in the assembly of new organic molecules or destructive in the irreversible inhibition of enzymes. Anti-cancer drugs are designed with this key reaction in mind.

**10–12 Chemistry in Three Dimensions****4. Introduction to Chirality.**

What makes objects / molecules chiral? How do we know they are chiral? The structures of natural left-handed amino acids and important synthetic molecules reveal some of the answers here.

**5. The Creation and Destruction of Chirality.**

Chemical processes normally produce equal amounts of right and left handed molecules while biological processes give just one form. Chemical and biological versions of the reduction of ketones will be a key reaction here.

**6. Transformation of Chirality by Reactions on Chiral Compounds.**

Purely chemical processes on one chiral form of a molecule can produce new molecules with fixed handedness. Key reactions will include stereospecific Inversion by the  $S_N2$  mechanism and retention by of stereochemistry by double inversion.

***Structure Determination: 6 lectures*****Dr N. Bampos**

Molecular structure is the foundation of chemistry. We need to be able to understand and determine structures before we can seriously study synthesis, reaction mechanisms, or the nature of chemical bonding. In this course we shall look at how structures can be determined by spectroscopic methods. The aim of the course is to allow you to build on the methods (IR, NMR) you learned last year, so that you can look at these and other spectra (mass, ESR, UV and visible) from an unknown compound, and deduce its structure.

**Topics** The mass spectrum for the determination of molecular weight and molecular formula, and simple fragmentation for identifying substructures; the UV/visible spectrum for identifying conjugated systems; and spin-coupling in the  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra to determine connectivity between carbon atoms.

***Co-ordination Chemistry: 8 lectures*****Dr S. R. Boss**

The coordination chemistry of first row transition metals will be explored, focusing on the role of *d*-orbitals and *d*-electrons in their chemistry.

Qualitative molecular orbital diagrams to explain the splitting of the  $d$  orbitals in an octahedral geometry will be described. The effect of both ligand and metal on the extent of octahedral splitting energy ( $\Delta_{\text{oct}}$ ) will be included. The discussion of how coordination geometries effect  $d$ -orbital splitting will be extended to include tetrahedral and square planar examples. An introduction to the effects of the  $d$ -orbital splitting on complex properties will be given, focusing on trends in ionisation energy, preferred geometries, oxidation states, high spin and low spin complexes and the magnetic properties of transition metal ions (spin-only approximation).

### *Organometallic Chemistry: 6 lectures*

Dr P. D. Barker

This course deals with compounds formed by the combination of an organic moiety with a metal-containing species and which incorporate at least one metal-carbon interaction. Their study has contributed greatly to inorganic chemistry but its relevance goes far beyond, having important applications in catalytic, synthetic and polymer chemistries. The aim of this course is to provide an introduction to the chemistry of these fascinating compounds. Their syntheses will be described and the methods of characterisation outlined. Emphasis will be placed on the structures they adopt and the various treatments of their bonding modes. Where relevant there will be discussion of their reactions, especially where this is pertinent to their industrial application.

Specific topics covered will include:  $\pi$ -acceptors and the Dewar–Chatt model, the spectroscopic study of metal carbonyls, the eighteen-electron rule and exceptions to it, catalysis, sandwich complexes, hapticity, fluxionality and metal–metal single bonds.

### *Inorganic Ring Chemistry: 6 Lectures*

Dr A. E. H. Wheatley

This course describes the synthesis, structures and bonding in a range of p-block ring systems, exemplified by borazine, phosphazene and thiazene (B/N, P/N and S/N) rings. Emphasis is placed on synthetic methodologies and chemical reactivity. A range of arguments have been proposed to rationalize the structure and bonding in these rings. Whilst  $p_{\pi}$ – $p_{\pi}$  bonding in borazines is generally accepted, the use of  $d$  orbitals in bonding is more contentious and the way our view of bonding in phosphazenes has changed recently (with  $p_{\pi}$ – $d_{\pi}$  bonding models giving way to more ionic perspectives) will be discussed. Students will be expected to extend structure and bonding concepts to other related systems such as boroxane and siloxane (B/O, Si/O) derivatives.

**Topics** There are many thousands of compounds that fall into the category of inorganic rings. Rather than survey all of them, three types of N-containing ring system are introduced to exemplify concepts in synthesis, structure and reactivity of these rings:

Synthesis, bonding and reactivity in borazines; the importance of  $p_{\pi}$ – $p_{\pi}$  bonding in inorganic rings. Substitution by addition elimination reactions and comparisons with organic aromatics;

Synthesis, bonding and reactivity in phosphazenes;  $p_{\pi}$ – $d_{\pi}$  vs ionic approaches to bonding; gem and non-gem substitution patterns;

Synthesis, bonding and reactivity of thiazene rings; stabilization of weak S/N bonds.

## *Shape and Organic Reactivity: 10 lectures*

Dr P. D. Wothers and Dr J. M. Goodman

Molecular shape and reactivity is the foundation of organic chemistry. We need to be able to understand the critical, and often subtle, interactions between the shape of a molecule and its reactions. In two dimensions, shape concerns molecules with rigidity conferred by  $\pi$ -bonds, such as alkenes and imines, whose formation can be controlled kinetically or by product stability and whose reactions depend on the substitution and geometry of the double bond. In three dimensions, molecules have more flexible shapes and these determine the course of many reactions. This builds on the stereochemical principles already introduced in the *Key Organic Reactions* course.

**Focus on 2D Shape** Geometry of alkenes, reactions of alkynes, elimination reactions, reactions of alkenes with electrophiles.

**Focus on 3D Shape** Stereochemistry with two or more chiral centres, resolution of enantiomers by forming diastereoisomers, elimination reactions, stereospecific and stereoselective reactions, conformational analysis, cyclisation reactions.

## *Introduction to Chemical Biology: 11 lectures*

Dr A. Ciulli and Prof. C. Abell

This course introduces the chemistry of the three most important constituents of the cell, the biopolymers - DNA, RNA and proteins. The course will explore their structure, function and chemistry, and show how they perform their biological role. The role of metal ions and non-covalent interactions in determining the structure and function of biomolecules will be described.

Basic physical organic chemical concepts such as general acid and general base catalysis, transition state theory, free energy profiles, isotope effects etc. will be illustrated by reference to enzyme chemistry. The chemical mechanisms of proteases and other enzymes will be discussed along with the principles of enzyme inhibition and its role in medicine. This course looks forward to Part II and Part III courses when some of the most exciting recent advances in biological chemistry and chemical biology will be discussed. The approach throughout the course will be based on structure and mechanism - we will not assume any previous biochemical knowledge.

1–5 Basic background of molecular biology. The central dogma: DNA-RNA-protein. DNA structure: heterocycles, sugars, phosphate esters, the double helix. The genetic code. Translation: protein synthesis. Molecular biology techniques: PCR and site-directed mutagenesis.

Protein structure and amino acids. Non-covalent interactions: electrostatics, hydrogen bonding, van der Waals forces,  $\pi$ - and cation- $\pi$ , the hydrophobic effect. Secondary, tertiary and quaternary structures. Protein folding. Homology and sequence identity. The Protein Data Bank (PDB).

Synthesis of peptides and the use of protecting groups. Solid phase synthesis.

6–11 Thermodynamic and kinetic concepts relevant to biological chemistry including transition state theory, kinetic isotope effects, free energy diagrams. General acid catalysis, general base catalysis, electrophilic catalysis by metal ions, nucleophilic catalysis.

The mechanisms of serine proteases, metalloproteases and other types of proteases.

Enzyme inhibition and its role in medicinal chemistry.

Metabolic pathways.

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## Recommended Books for Chemistry B

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These recommended books should be in your College Library. They can also be consulted in the Departmental Library, and some are available on short-term loan.

### Key Organic Reactions

- Clayden J., Greeves N., Warren S. and Wothers P. *Organic Chemistry*, OUP 2000.  
Carey F. A. and Sundberg R. J., *Advanced Organic Chemistry*, 5th Edn, Springer 2007.  
Part A: Structure and Mechanism  
Part B: Reactions and Synthesis  
Sainsbury M., *Aromatic Chemistry*, Oxford Chemistry Primer No. 4, OUP.

The following Organic textbooks are also useful (earlier editions are fine):

- McMurray J., *Organic Chemistry*, 7th Edn, Brooks/Cole 2008.  
Vollhardt K. P. C. and Schore N. E., *Organic Chemistry*, 5th Edn, Freeman 2007.

### Structure Determination

- Williams D. H. & Fleming I. *Spectroscopic Methods in Organic Chemistry* McGraw Hill 5th Edition 1995.  
Silverstein R.M. Bassler G.C. & Morrill T.C. *Spectrometric Identification of Organic Compounds* Wiley 5th Edn 1991.  
Field, L.D., Sternhell R.M. & Kalman, J.R. *Organic Structures from Spectra, 2nd Edition*, Wiley 1995.  
Abraham R.J. Fisher J. & Loftus P. *Introduction to NMR Spectroscopy* Wiley 1988.  
Sanders J.K.M. Constable E.C. Hunter B.K. & Pearce C.M. *Modern NMR Spectroscopy: Workbook of chemical problems* OUP 2nd Edn 1993.

### Electron Deficient Compounds

- W.L. Jolly *Modern Inorganic Chemistry*, McGraw-Hill, 2nd Ed., 1991.  
D.F. Shriver & P.W. Atkins *Inorganic Chemistry*, OUP, 3rd Ed., 1999.  
F.A. Cotton, G. Wilkinson, C.A. Murillo & M. Bochmann, *Advanced Inorganic Chemistry*, John Wiley & Sons, 6th Ed, 1999.  
C.E. Housecroft & A.G. Sharpe *Inorganic Chemistry*, Prentice Hall, 1st Ed. 2001.  
Ebsworth E.A.V. Rankin D.W.H & Craddock S. *Structural Methods in Inorganic Chemistry* Blackwell 2nd Edn 1991.  
Housecroft C.E. *Cluster Molecules of the p-Block Elements*, OUP, 1994.

### Co-ordination Chemistry

- M.J. Winter *d-Block Chemistry*, Oxford Chemistry Primer 27, OUP.  
J. McCleverty *Chemistry of the First-Row Transition Metals*, Oxford Chemistry Primer 71, OUP.

### Organometallic Chemistry

- Shriver D. F. and Atkins P. W. *Inorganic Chemistry* 3rd Ed. OUP (1999).  
Cotton F.A., Wilkinson G., Murillo C.A. & Bochmann, M., *Advanced Inorganic Chemistry*, John Wiley & Sons, 6th Ed (1999).  
Spessard, G.O. and Miessler, G.L., *Organometallic Chemistry*, Prentice Hall (1996).  
Elschenbroich, C., *Organometallics*, Wiley-VCH 3rd Ed. (2006).  
Bochmann M. *Organometallics Volumes 1 and 2*, OUP Primers (1994).

### Shape and Organic Reactivity

- Clayden, J., Greeves, N., Warren, S. and Wothers, P., *Organic Chemistry*, OUP 2000.  
Carey F.A. & Sundberg R.J. *Advanced Organic Chemistry* Plenum 3rd Edn, 1990.  
Fox M.A. & Whitesell J.K. *Organic Chemistry* Jones & Bartlett 1994.  
Streitwieser A. & Heathcock C.H. *Introduction to Organic Chemistry* Macmillan 4th Edn 1992.  
Solomons T.W.G. *Organic Chemistry* Wiley 5th Edn 1992.  
McMurry J. *Organic Chemistry* Brooks/Cole 3rd Edn 1992.  
Carey F.A. *Organic Chemistry* McGraw Hill 2nd Edn 1992.

### Introduction to Chemical Biology

- C.R. Calladine & H.R. Drew, *Understanding DNA*, Academic Press, 1997.  
C.-I. Branden & J. Tooze, *An Introduction to Protein Structure*, 2nd Edition, 1999.  
A. R. Fersht, *Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding*, 3rd edition, W. H. Freeman, 1998.  
T. Bugg, *An Introduction to Enzyme and Coenzyme Chemistry*, Blackwell, 1997.  
C. M. Dobson, J. A. Gerard & A.J. Pratt, *Foundations of Chemical Biology*, Oxford Chemistry Primers, OUP, 2001.