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Lectura recomendada

The Organic Chemistry of Isotopic Labelling

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Chapter 1 The discovery and detection of isotopes.

The aim of this chapter is present a brief history of the impact of isotopic labelling on the development of organic chemistry and biochemistry.

Some general principles are described concerning the selection of an isotopic label for specific purposes and the underlying physical methods for their detection. A summary of the nomenclature of isotopically labelled compounds is given.

Chapter 2 Labelling compounds with carbon-13 and carbon-14.

The aim of this chapter is to describe and exemplify the major methods for introducing a carbon-13 or carbon-14 label into an organic compound. These include methods based on the use of the cyanide ion, organometallic methods including the Grignard and Wittig reactions and various carbonyl condensation reactions. The synthetic routes are exemplified by the synthesis of biosynthetic intermediates such as mevalonic acid and various aromatic and heterocyclic systems such as the nucleic acid bases and intermediates in alkaloid biosynthesis.

Chapter 3 Labelling with deuterium and tritium.

The aim of this chapter is to describe general and site-specific methods for introducing deuterium and tritium into organic compounds. The role of the kinetic isotope effect is described. Methods which involve exchange reactions on aromatic rings and adjacent to carbonyl groups and also decarboxylation reactions are exemplified. Reduction,



Chapter 4 Stereochemical aspects of labelling with hydrogen isotopes.

The Cahn–Ingold–Prelog sequence rules for designating the stereochemistry of chirally labelled centres are outlined. The stereochemical outcomes of reactions used to introduce a label particularly into cyclic systems are outlined. These are exemplified by the stereospecific introduction of labels into the steroids and gibberellin plant hormones. Methods for the preparation of the chiral methyl group and various chirally labelled biosynthetic precursors such as mevalonic acid, isopentenyl diphosphate and 1-deoxy-D-xylulose are discussed, in addition to the determination of the stereochemistry of hydrogen transfer from the nicotinamide coenzymes.

Chapter 5 The synthesis of labelled amino acids.

The syntheses of amino acids containing both stable isotopes and radioisotopes are described. The methods are divided into those which lead to the racemic amino acid and those which lead to enantiomerically pure amino acids. A number of the methods involve a combination of chemical and enzymatic methods.

Chapter 6 The labelling of some compounds of pharmaceutical interest.

The isotopic labelling of pharmaceutical compounds is an important requirement for establishing their metabolism. Strategies for introducing labels are exemplified by lidocaine, some non-steroidal anti-inflammatory agents, amphetamines, sulfonamides, morphine and its relatives, galanthamine, tropane alkaloids and tryptamine derivatives.

Chapter 7 Labelling compounds with the stable isotopes of nitrogen and oxygen.

The organic chemistry of labelling of amino acids, nucleic acid bases and other heterocyclic compounds with the stable isotope nitrogen-15 is described. The introduction of oxygen-17 and oxygen-18 into compounds by nucleophilic substitution and the hydrolysis of acetals is reviewed. The preparation of chiral [^{16}O , ^{17}O , ^{18}O]phosphate is described.

Chapter 8 Labelling compounds with isotopes of phosphorus, sulfur and the halogens.

The organic chemistry of labelling compounds with radioactive isotopes of phosphorus, sulfur and chlorine is reviewed. The use of radioisotopes of iodine as therapeutic radiopharmaceuticals and in radioimmunoassay is reviewed.

Chapter 9 Labelling organic compounds for diagnostic imaging.

The organic chemistry of labelling compounds for use in diagnostic imaging techniques such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) is reviewed. Methods for the rapid introduction of carbon-11, fluorine-18, nitrogen-13, oxygen-15, technetium-99m and iodine-123 for these purposes are described.

The book ends with some conclusions and recommendations for further reading concerning the material in the individual chapters together with a glossary of terms used in isotope chemistry.



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