Orbitals in Organic Chemistry – Stereoelectronic Effects & Pericyclic Reactions

Overview

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Aims

The first part of this module addresses stereoelectronic effects in organic synthesis and aims to demonstrate the role of orbital interactions in controlling the conformation of molecules and in influencing the reactivity of molecules and the outcome of reactions. Familiar reactions as well as new reactions will be used to illustrate the ideas. The second part of this module addresses pericyclic reactions and aims to demonstrate how the Woodward-Hoffman rules and frontier molecular orbital (FMO) theory can be used to rationalise many aspects of this chemistry.

Summary

In the stereoelectronic part of this module, how orbital interactions influence molecular shape and conformation in the 'ground state' (*i.e. structure*) will be explained before examining how 'transition state' stereoelectronic effects influence *reactivity*. Ionic reactions (*i.e.* those involving electrophiles/nucleophiles, carbanions/carbocations *etc.*) will be used to illustrate these ideas. In the pericyclic part of this module we will see how for *concerted* reactions involving conjugated arrays of orbitals, the *phases* of the reacting molecular orbitals and their *symmetry* properties have a controlling influence on their outcome. Four classes will be studied: cycloaddition reactions, group transfer reactions, sigmatropic rearrangements and electrocyclic reactions.

Objectives:

On completion of this course you will be able to:

- Recognise anti-periplanar relationships between reacting bonds in synthetic transformations,
- Draw orbital representations and energy diagrams for stereoelectronic interactions and for conjugated π-systems that participate in pericyclic reactions.,
- Discuss the factors that affect orbital overlap and lead to important (stabilising) interactions,
- Explain the role of stereoelectronic interactions in determining the conformations of functional groups,
- Explain the influence of orbital control in ionic reactions, particularly in carbonyl chemistry, substitution reactions and ring opening/closure reactions,
- Rationalise the stereochemical outcome of synthetically important rearrangements and fragmentations based on stereoelectronic analysis,
- Identify a pericyclic reaction and categorise it as a cycloaddition, a group transfer reaction, a sigmatropic rearrangement, or an electrocyclic reaction,
- Apply the Woodward-Hoffmann rules to predict the viability and/or stereochemical outcomes of certain pericyclic reactions,
- Apply frontier molecular orbital (FMO) theory to rationalise selectivity and reactivity aspects of pericyclic reactions.

Course delivery (8 lectures)

Lecture 1:	Key stereoelectronic principles.
Lecture 2:	Conformational analysis of selected functional groups. The anomeric effect.
Lecture 3:	Thermodynamic *vs*. kinetic control of reactions. 1,2-Diaxial reactivity of cyclohexanes. Baldwin's rules for ring-closure. Reactions of the carbonyl group – Burgi-Dunitz nucleophilic attack and α-deprotonation to give enolates – control of stereochemistry.
Lecture 4:	Neighbouring Group Participation (NGP). Non-classical carbocations. Wagner-Meerwein rearrangements. Other ionic 1,2-rearrangements (pinacol, semi-pinacol, Baeyer-Villiger & Beckmann). Ionic fragmentations (Grob, Eschenmoser ring-expansion).

Lecture 5:	Definition of pericyclic reactions. Types of pericyclic reaction. Drawing molecular orbitals for conjugated systems. FMO theory recap. Symmetry correlation diagrams.
Lecture 6:	The Woodward-Hoffmann rules and application to selected pericyclic reactions. Frontier Molecular Orbital (FMO) theory treatment of selected pericyclic reactions.
Lecture 7:	*Cycloadditions*: the Diels-Alder reactions and 1,3-dipolar cycloadditions.
Lecture 8:	*Sigmatropic rearrangements*: Claisen, Cope, hydride and alkyl shifts. *Electrocyclic reactions*: hexatriene.

Reference material

The following texts all contain information pertinent to the course content.

Clayden, Greeves and Warren, *Organic Chemistry*, 2nd Edition, Oxford University Press, **2012**.
Alabugin, *Stereoelectronic Effects – A bridge between structure and reactivity*, Wiley, **2016**.
Fleming, *Molecular Orbitals and Organic Chemical Reactions – Reference Edition*, Wiley, **2010**.

Fleming, Pericyclic Reactions, Oxford Chemistry Primer, **1998**

Kirby, *Stereoelectronic Effects*, Oxford Chemistry Primer, **1996**.

Harwood, *Polar Rearrangements*, Oxford Chemistry Primer, **1992**.