An Introduction to Reaction Stereoelectronics

Overview

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Aims

To demonstrate the role of orbital interactions and the importance of stereoelectronic effects 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.

Building Upon: Year 2 'Pericyclic Reactions' course.
Looking forward to: Year 4 'Advanced Stereochemistry, Synthesis and Biosynthesis' course.

Summary

Building upon the concepts introduced in the 'Pericyclic Reactions' course regarding the importance of orbital interactions in influencing reactions, this course explains how orbital interactions influence molecular shape and conformation in the 'ground state' (*i.e. structure*) and explores 'transition state' stereoelectronic effects which influence *reactivity*. The course will concentrate on 'ionic' reactions (*i.e.* those involving electrophiles/nucleophiles, carbanions/carbocations *etc.*) since these constitute the majority of synthetically useful transformations.

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 several stereoelectronic interactions
- 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
- Appreciate 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

Course delivery (6 lectures + 1 problem class)

Lecture 1:	Recap on key stereoelectronic principles.
Lecture 2:	Conformational analysis of selected functional groups. The anomeric effect.
Lecture 3:	Thermodynamic *vs*. kinetic control of reactions. Recap on anomeric effect & 1,2-diaxial reactivity of cyclohexanes. Sterics *vs* stereoelectronics – ester hydrolysis and dichromate oxidation of alcohols. Baldwin's rules and the Thorpe-Ingold effect.
Lecture 4:	Reactions of the carbonyl group – Burgi-Dunitz nucleophilic attack, Felkin-Ahn diastereoselectivity, α-deprotonation to give enolates – control of stereochemistry.
Lecture 5:	Neighbouring Group Participation (NGP). Non-classical carbocations. Wagner-Meerwein rearrangements.
Lecture 6:	Other ionic 1,2-rearrangements (pinacol, semi-pinacol, Baeyer-Villiger & Beckmann). Ionic fragmentations (Grob, Eschenmoser ring-expansion).
Problem class:	Revision of the whole module and exam-style questions.

Reference material

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

Fleming, *Molecular Orbitals and Organic Chemical Reactions – Reference Edition*, Wiley, **2010**.
Bruckner, *Advanced Organic Chemistry,* Harcourt-AP, **2002**
Clayden, Greeves & Warren, *Organic Chemistry*, 2nd Ed. Oxford University Press, **2012**.
Eliel, Wilen, *Stereochemistry of Organic Compounds*, Wiley-InterScience, **1994**.
Kirby, *Stereoelectronic Effects*, Oxford Chemistry Primer, **1996**.
Harwood, *Polar Rearrangements*, Oxford Chemistry Primer, **1992**.