School of Chemistry

Aims and Objectives: Session 2022-2023

Module CH4614: Heterocyclic and Pericyclic Chemistry

Duration: 20 hours

Lecturers: Dr R. A. Aitken and Dr E. R. Kay*

(*Module Convenor)

Aims: This module covers the important areas of heterocyclic and pericyclic chemistry in detail. In heterocyclic chemistry, the nomenclature and numbering of single and fused ring systems, and structure, reactivity, synthesis and applications of the main five and six-membered ring systems with one and two heteroatoms will be covered. Selected industrial syntheses of heterocyclic medicinal compounds are used to illustrate the basic principles as well as the factors to be considered in large-scale synthesis. In pericyclic chemistry, both a frontier molecular orbital approach and the concept of conservation of orbital symmetry will be applied to explain the observed reactivity and stereochemistry for this class of reactions. The Woodward–Hoffman rules governing all pericyclic processes will be developed and their use to predict the outcome of cycloadditions, electrocyclic processes, sigmatropic rearrangements and group transfer reactions will be demonstrated. Synthetic applications of these processes will also be illustrated.

Objectives:

1. Know the most important simple heterocyclic ring systems containing one and two heteroatoms and their systems of nomenclature and numbering.
2. Understand, in general terms, the reactivity and stability of heteroaromatic compounds.
3. Know the main synthetic routes and reactivity for furans, pyrroles and thiophenes.
4. Know the main syntheses and selected reactions of imidazoles, oxazoles and thiazoles and pyrazoles, isoxazoles and isothiazoles.
5. Know the major synthetic routes and reactivity of pyridines and pyrylium salts.
6. Know the structure and importance of pyridazines, pyrimidines and pyrazines.
7. Know the structure and selected syntheses of indoles, quinolines and isoquinolines. Know the Reissert reaction and briefly consider phthalazines, quinazolines, quinoxalines, cinnolines and benzodiazepines.
8. Discuss the problems involved in process development and the scale-up of synthesis of commercially important compounds.
9. Discuss the design of synthetic routes, choice of reagents and conditions taking into account cost, safety and environmental factors.

10. Understand, be able to identify and draw the mechanisms for each of the different types of pericyclic reaction: cycloadditions, electrocylic reactions, sigmatropic reactions and group transfer reactions.

11. Be able to discuss how pericyclic reactions may be analysed in terms of the symmetry of the molecular orbitals involved, thus explaining experimental observations of ‘allowed’ and ‘forbidden’ reactions; be able to predict reaction outcome (stereochemistry) and/or mode of activation (thermal vs. photochemical) by applying the Woodward–Hoffmann rules.

12. Be able to identify examples of cycloadditions involving neutral conjugated alkenes (e.g. Diels-Alder reactions), conjugated cations, and 1,3-dipoles. Be able to predict and rationalize aspects of selectivity including exo vs. endo selectivity, the Alder rule and regioselectivity. Be able to rationalize and predict effects on reaction kinetics including the electronic and steric effects of substituents and catalysis of cycloadditions.

13. Understand conrotatory and disrotatory electrocyclic ring-opening and ring-closure. Be able to link each reaction pathway with the correct stereospecific outcome. Understand and be able to apply the orbital symmetry explanation for which pathway is allowed under thermal and photochemical activation conditions.

14. Sigmatropic rearrangements: Cope and Claisen and related processes; supra and antarafacial migration of hydrogen and carbon-based groups. Be able to apply molecular orbital arguments to rationalize or predict stereochemical outcomes and relative rates of reactions.

15. Group transfer reactions – The ene reaction. Be able to apply molecular orbital arguments to rationalize or predict stereochemical outcomes and relative rates of reactions.