ALICYCLIC CHEMISTRY (EHS) SYNOPSIS

Textbooks:

"Alicyclic Chemistry", F. J. McQuillin, M. S. Baird, Cambridge, 2nd Ed. 1983.
"Alicyclic Chemistry", M. Grossel, OUP, 1997.
"Stereochemistry of Organic Compounds", E. L. Eliel, S. H. Wilen, Wiley, 1994.
"Conformational Analysis", E. L. Eliel, N. L. Allinger, S. J. Angyal, G. A. Morrison, Interscience, 1967.

1. Ring Strain

(a) *1st Lecture*: Angle (Baeyer) Strain.- As tetrahedral angle is compressed p-character of ring C-C bond increases. In cyclopropane internal bond 105° with approx. $sp^{3.7}$ for C-C and $sp^{2.3}$ for C-H. Thus the C-H shorter and stronger shown by IR, CH acidity, ^{13}C NMR; C-C weaker and longer (π-like) shown by UV, ^{1}H NMR.

(b) Torsional (Pitzer) Strain.- Eclipsing of groups along a σ-bond which cannot be relieved by rotation. Planar and puckered cyclobutanes.

(c) *2nd Lecture*: Transannular Strain.- In medium rings groups project towards one another inside the ring.

(d) Cycloalkenes and Cycloalkynes.- Increase in angle strain is balanced to some extent by reduction in torsional strain. Oxirenes, 1H-azirines, 2H-azirines. *Trans* –cycloalkenes – optical isomerism.
3rd Lecture: Strain measured by Ag^+ complexation. Cycloalkyne-Cycloallene equilibrium.

2. Conformational Analysis (Alicyclic only)

(a) Thermodynamic Aspects.- Cyclohexane chair and boat. Axial and equatorial hydrogens in chair. Ring flipping equilibrium in monosubstituted cyclohexanes. Rigid *trans* –decalin and steroid systems (Handout).

(b) *4th Lecture*: Kinetic Aspects.- (i) Steric control: Base hydrolysis of esters (TS more crowded than SM). Dichromate oxidation of alcohols (TS less crowded than SM).
(ii) Stereoelectronic control: E2 elimination. HOBr addition. Epoxide formation (neighbouring group participation). Ring opening of epoxides. Anti-periplanar rearrangements.

3. Synthesis of Three-Membered Rings (Irreversible reactions only)

(a) *5th Lecture*: Additions of "X" to a double bond: carbenes, carbenoids, nitrenes, oxene equivalents (peroxyacids)

(b) *6th Lecture*: Intramolecular S_N2 displacements of leaving group by carbanions, oxyanions and amines.

4. Reactivity of Cyclopropanes, Epoxides and Aziridines

(a) Ring Opening by Electrophilic Attack

(b) *7th Lecture*: Ring Opening by Nucleophilic Attack

(c) Catalytic Hydrogenation of Cyclopropanes
(d) Ring Opening by Electrocyclisation
(e) Effect of Increasing Angle Strain in Cyclopropanes and Aziridines
(f) Cheletropic Reactions of Aziridines

5. **Synthesis of Four-Membered Rings** (Irreversible reactions only)
"[2 + 2]" – Cycloadditions – (i) hν + alkene + enone (ii) Paterno-Buchi reaction (iii) Ketene + alkene (iv) ketene + imine, Staudinger reaction (v) chlorosulphonylisocyanate + alkene.

6. Reactivity of Cyclobutanes, Cyclobutenes, Oxetanes and Azetidin-2-ones

(a) Cyclobutyl – cyclopropyl – homoallyl cation
(b) Cyclobutenes – electrocyclic reaction to butadienes.
(c) Nucleophilic attack on oxetanes and azetidin-2-ones.

7. **Synthesis of Medium Rings**

(a) Acyloin synthesis.
(b) Ni^0 – catalysed dimerisation of butadiene.
(c) Cope rearrangement / expansion of smaller rings.

8. **Reactivity of Medium Rings**

(a) Transannular hydride shifts.
(b) Transannular ring closures.