SECOND YEAR Ring Synthesis and Carbohydrate Chemistry

Hilary Term | Prof. Ben Davis | 8 Lectures

This course provides an extension of principles learnt in conformational analysis and reactivity of cyclic systems into the logical construction of rings, including key reaction types.
This is complemented by an analysis of the most vital class of cyclic compounds in nature: carbohydrates. Their chemistry and utility as a vital feedstock will be explored.

Recommended General Books:
Some modern methods of Organic Synthesis Carruthers
An excellent text full of interesting examples. There is a good new later edn.
Advanced Organic Chemistry Parts A & B Carey & Sundberg
Great general text.
Advanced Organic Chemistry March
A mainstay of textbooks but with a good section on ring synthesis, as well as key reactions
Recommended Specific Books:
OCP 36 Kirby
Probably the best introduction to stereoelectronics that there is.
OCP 54 Grossel
A solid text covering some useful aspects of alicyclic chemistry; not comprehensive but some good examples.
OCP 98 Davis and Fairbanks
Carbohydrate Introduction - Obviously sheer class.
Monosaccharides Collins and Ferrier
A great book that is not too large but quite comprehensive – very well referenced and provides a really good view of a long standing field
Carbohydrate Building Blocks Bols
A more specialized book but near unique in its format: this allows one to readily relate sugar feedstock to potential synthons. Full of vision for those designing syntheses.

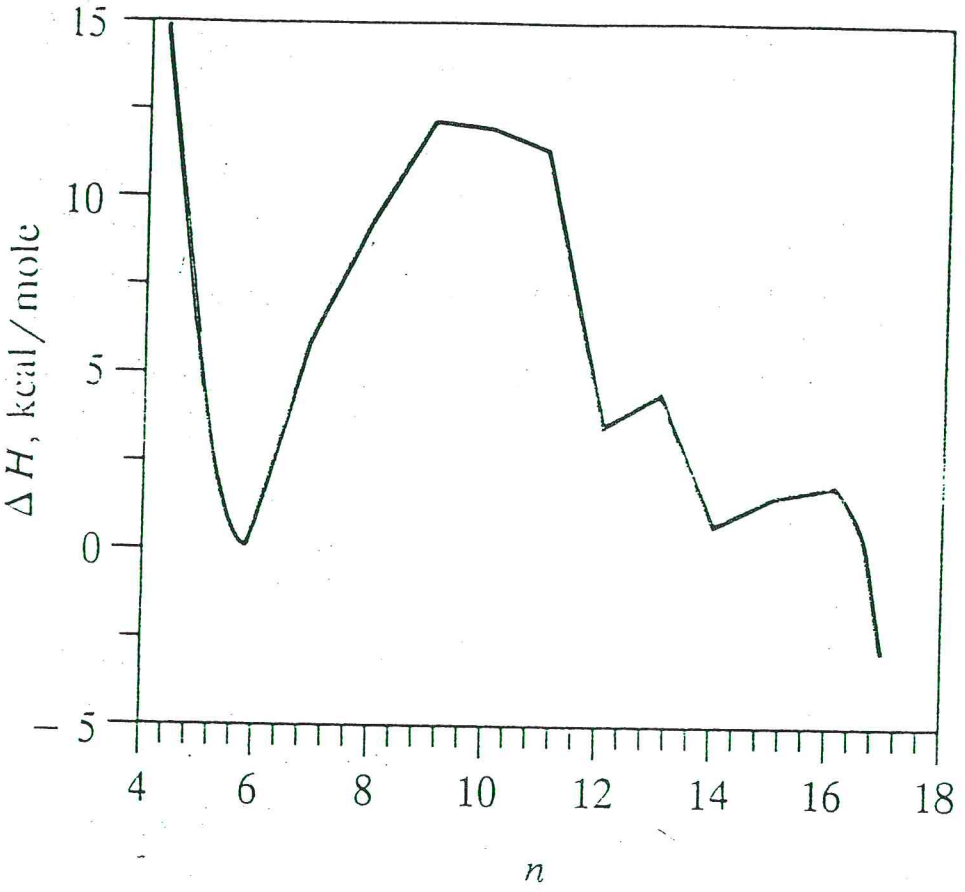
Lecture	*Topic*
1	**General aspects of ring synthesis**. Dependence of K and k on ring size. Conformational effects. Thorpe–Ingold and gem-dialkyl effects. Stereoelectronics (Baldwin's rules). Template effects. Ring size as a guide for strategy
2-4	**Methods of Synthesis.** Considertaion of reactions and types according to ring type/size. Epoxides vs Oxetanes. Carbenes, Simmons–Smith reaction, alkylation of enolates, anions stabilised by S, [2+2] cycloadditions. Thorpe–Ziegler reaction. 1,3 dipolar cycloadditions. Dieckmann condensation; intramolecular aldol reactions; Michael reactions, Robinson ring annelation. [4+2] cycloadditions, the Diels–Alder reaction (syn/endo selectivity). Radical anion methods (acyloin, McMurray). Macrolactonization. Ring Expansion Strategies.
5	**Introduction to Carbohydrates**. Brief biology. Structure and Nomenclature. Aldehyde-Hemiacetal ambiguity. Mutarotation. Anomeric Effect.
6	**Carbohydrate Chemistry 1.** Acetals and Ketals. Other reactions of hydroxyls. The many faces of C-1 reactivity. Protection of Sugars. Substitutions (related to prior analyses of reactivity), epoxide opening (Fürst–Plattner rule).
7	**Sugars as Non-petroleum Feedstocks.** Most abundant organic compounds on Earth. Strategies for alternative synthetic chemistry based on sugars: chirons.
8	**Carbohydrate Chemistry 2.** The anomeric centre: substitution, glycosylation, stereoselectivity.

COMPARING THE THERMODYNAMICS AND KINETICS OF RING CLOSURE

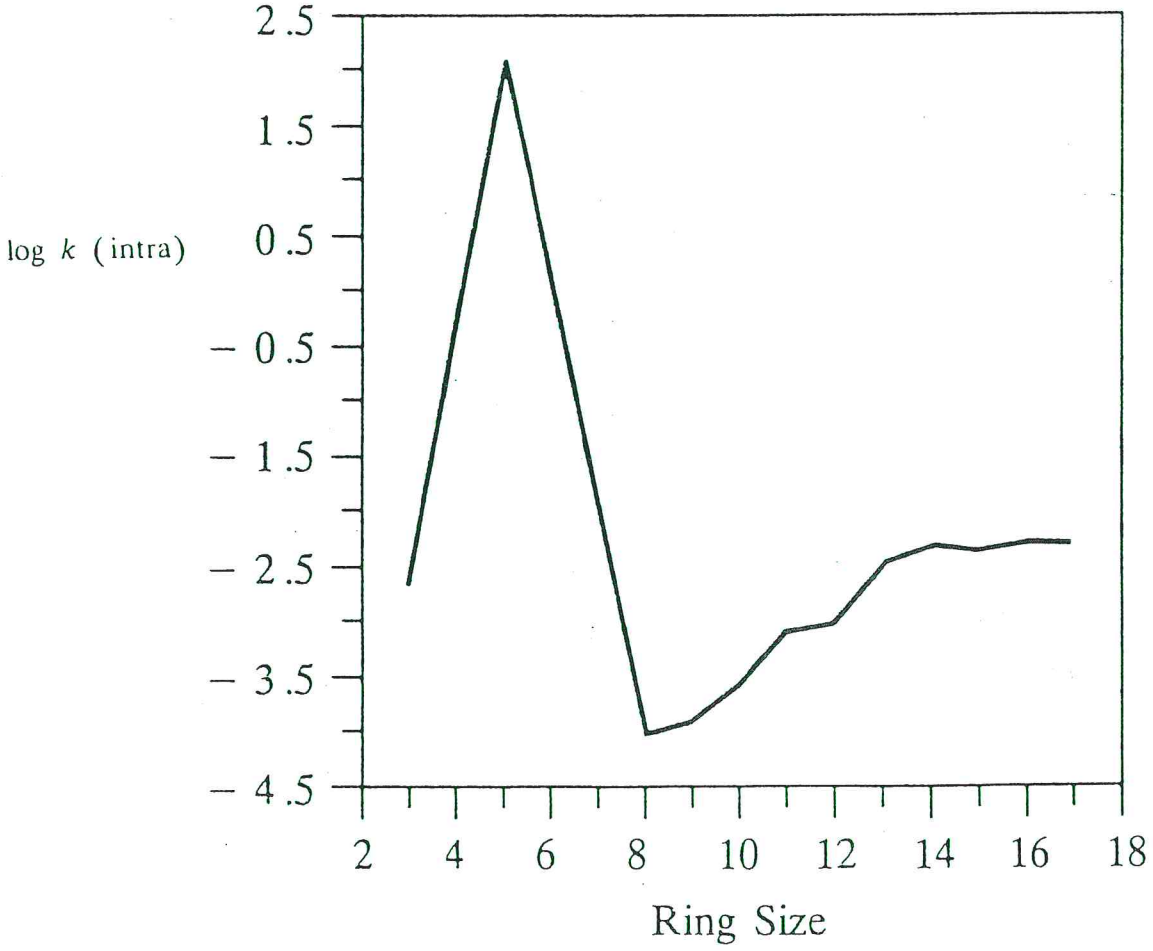
Enthalpy of cycloalkanes (C_nH_{2n}).

N.B.

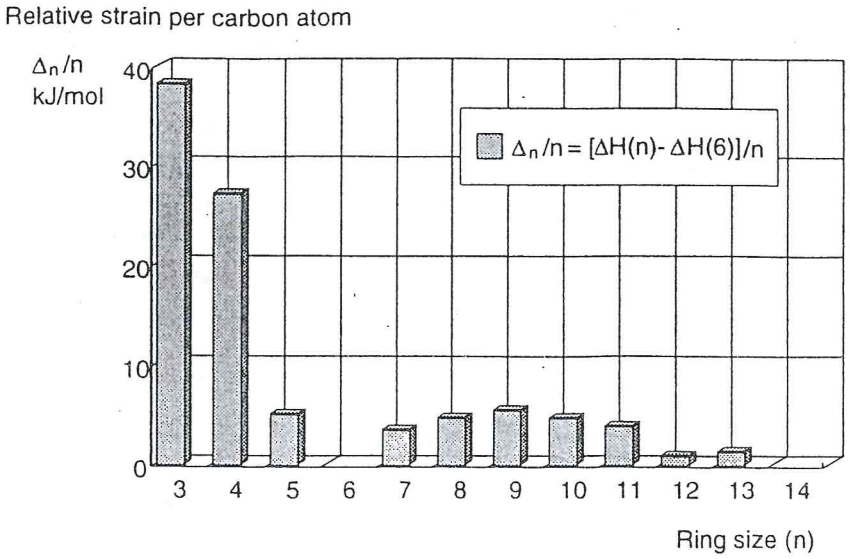
1 kcal = 4.2 kJ



Reactivity profile for lactone formation.

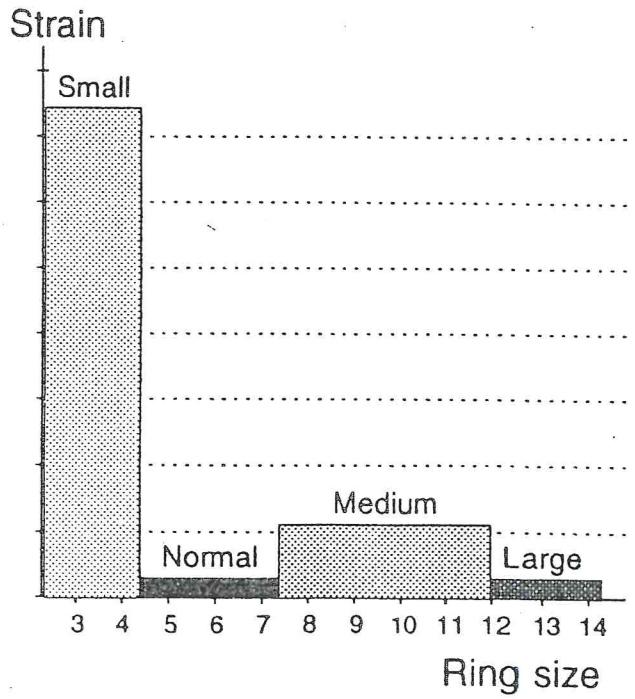


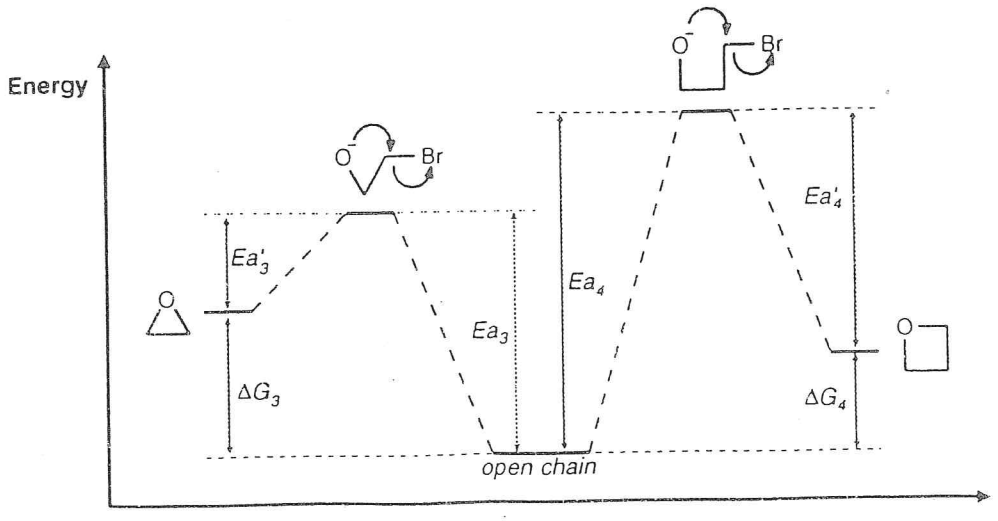
RING SIZE AND PROPERTIES



Estimation of strain in alicyclic rings (relative to cyclohexane)

Classification of alicyclic rings based on the degree of strain:





BALDWIN'S RULES FOR RING CLOSURE

These rules only consider the transition state and therefore only give an idea of the kinetics of ring closure.

5 - endo - trig

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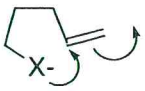

5 - exo - trig

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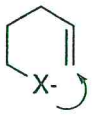

6 - endo - trig

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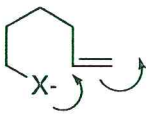

6 - exo - trig

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5 - endo - tet

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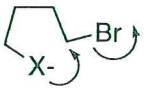

5 - exo - tet

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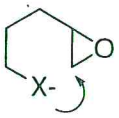

6 - endo - tet

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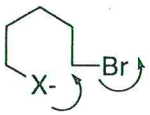

6 - exo - tet

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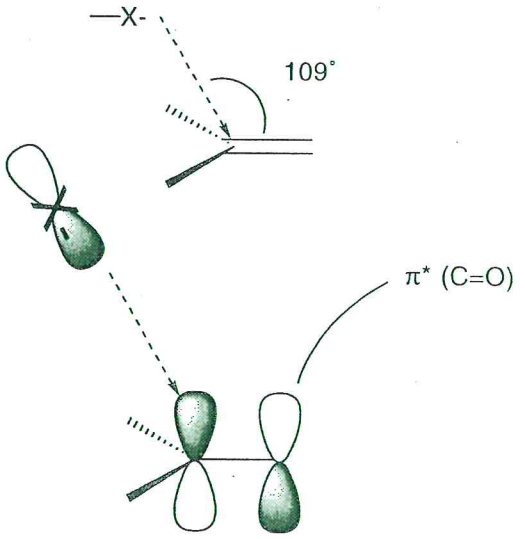

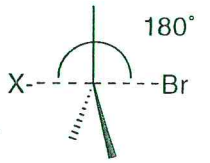

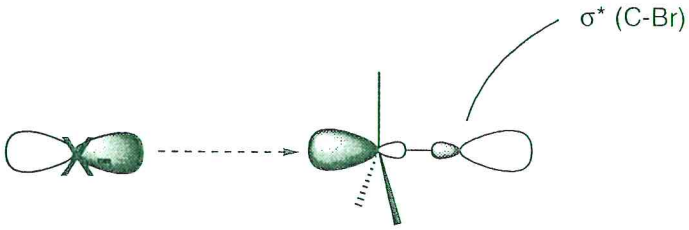

FULL RULES

a. The number refers to the ring size that is made

b. **Endo** describes the electrons moving round the ring or a leaving group attached to the ring
Exo describes the electrons movingout of the ring or a leaving group becoming detached from the ring

c. **Dig** means the nucleophile or radical attacks an sp hybridized carbon (e.g., C≡C)
Trig means the nucleophile or radical attacks an sp^2 hybridized carbon (e.g., C=C, C=O)
Tet means the nucleophile or radical attacks an sp^3 hybridized carbon (e.g., C-Br, C-O)