

Carbocyclic Rings

Medium and Large Rings

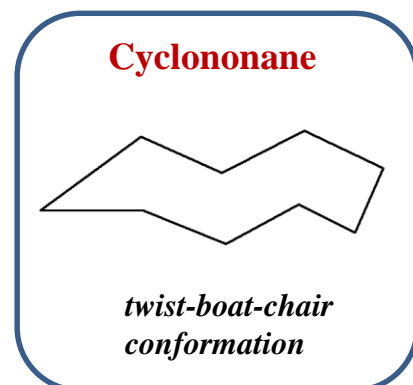
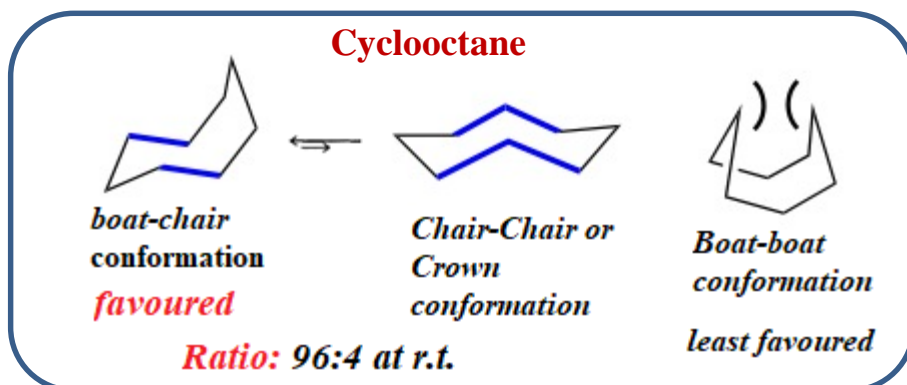
Paper 4201 B
Organic Chemistry
(Special-II)

CHEMISTRY OF MEDIUM AND LARGE RING COMPOUNDS

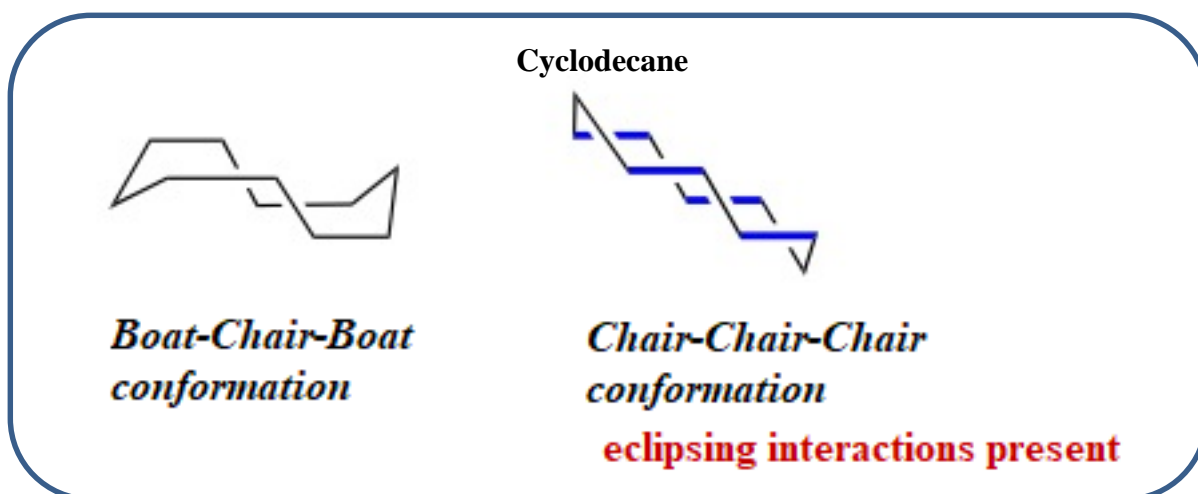
- 8-11 C-atoms: **Medium rings**
 - >12 C-atoms: **Large rings**
- MACROCYCLES**

CONFORMATION OF MEDIUM AND LARGE SIZED RINGS

- **Cyclooctane:** *boat-chair*, *chair-chair (crown)* or *boat-boat* conformations
- favored conformation- **boat-chair** due to minimum number of eclipsing ethane interactions (*shown in blue*), as well as torsional strain.
- The chair-chair or **crown conformation**- *less stable*
- **boat-boat conformation**- *least stable*



- **Cyclononane:** most favourable conformation- *twist-boat-chair*
- **Cyclodecane:** Boat-chair-boat and Chair-chair-chair conformation
- **Boat-chair-boat** conformation- **energetically minimized**
- **Chair-chair-chair** conformation- **eclipsing interactions**.



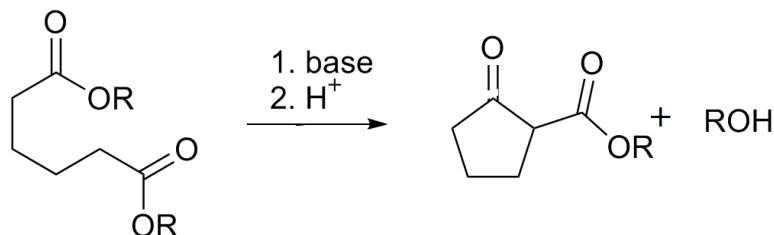
SYNTHESIS OF MEDIUM AND LARGE SIZED RINGS

Challenges

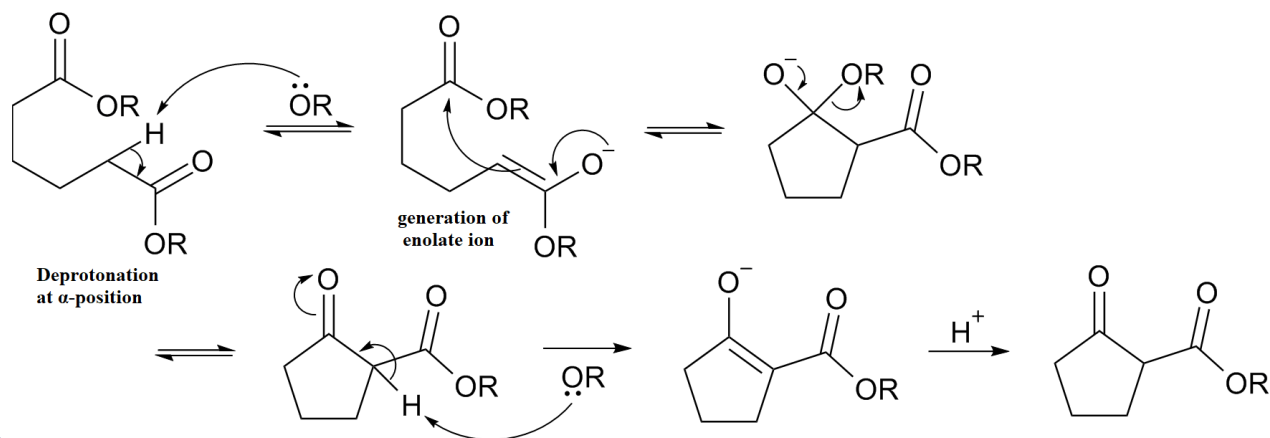
- Generally difficult to synthesize from open-chain compounds as the probability of reactive groups on the two ends of a long hydrocarbon chain undergoing cyclization is low.
- The reactions are carried out in very dilute solutions (*high-dilution technique*) to reduce the possibility of coupling of reactive groups on the ends of *different* molecules.

THE DIECKMANN REACTION

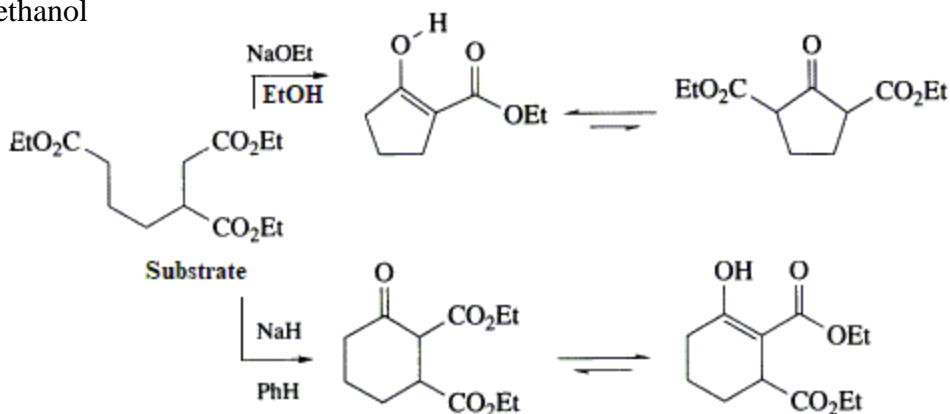
- Intramolecular reaction of diesters in the presence of base to give cyclic products.
- Usually used to prepare five- or six-membered rings.



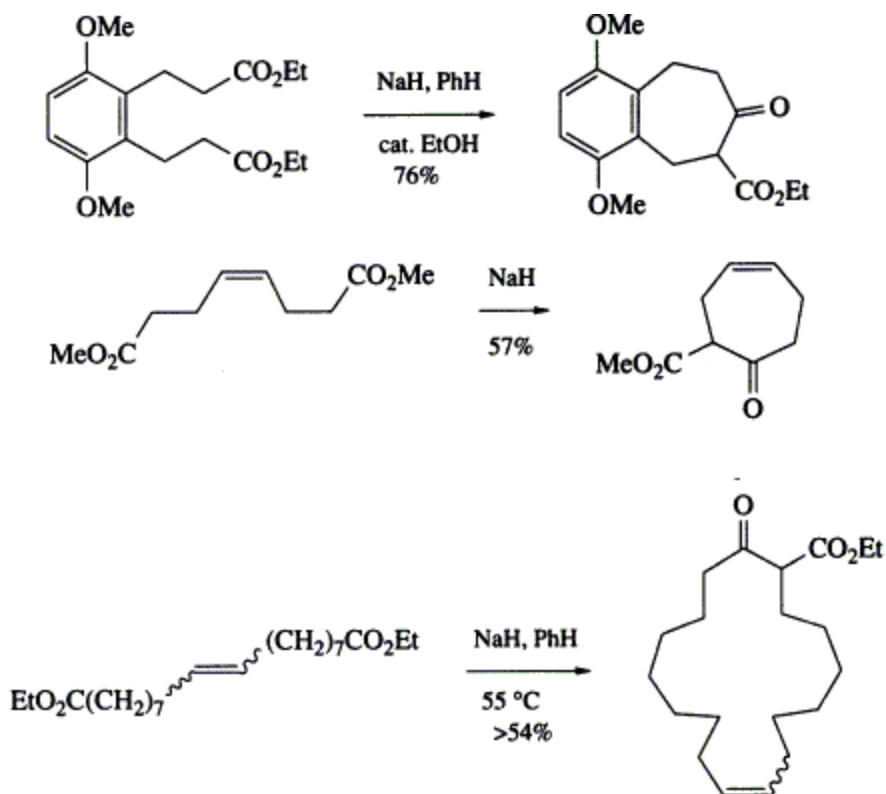
Mechanism



- Products depend on the substrate and conditions. e.g., diethyl 3-ethoxycarbonylheptanedioate gives the 6-membered ring product with NaH in benzene and the 5-membered ring product with NaOEt in ethanol

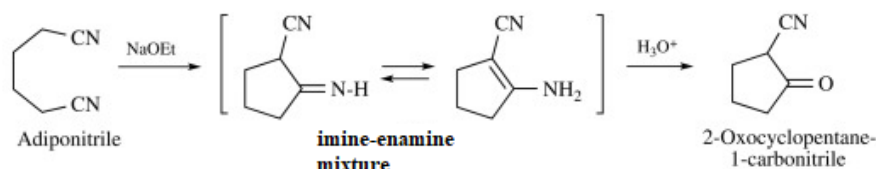


- **7-membered and larger rings can also be prepared by this method** (under high dilution techniques) and the yields can often be satisfactory.

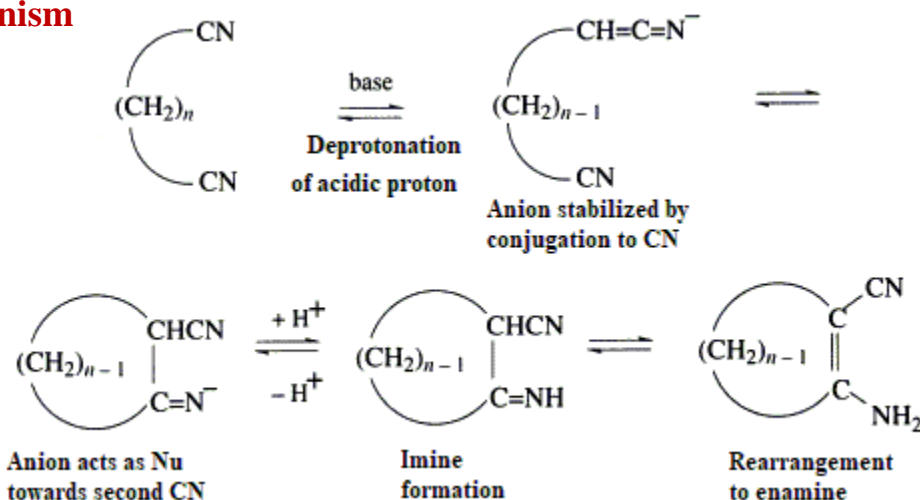


THE THORPE-ZIEGLER REACTION

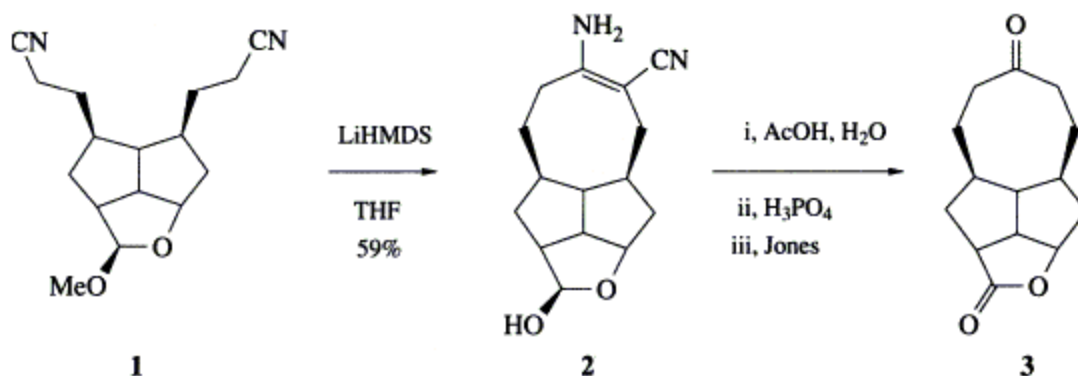
- Reaction of α,ω -dinitrile with a base leads to cyclization.
- e.g., the reaction of adiponitrile with sodium ethoxide, lead to cyclization and formation of the imine-enamine mixture. Cyclic cyano-ketone obtained upon hydrolysis.



Mechanism



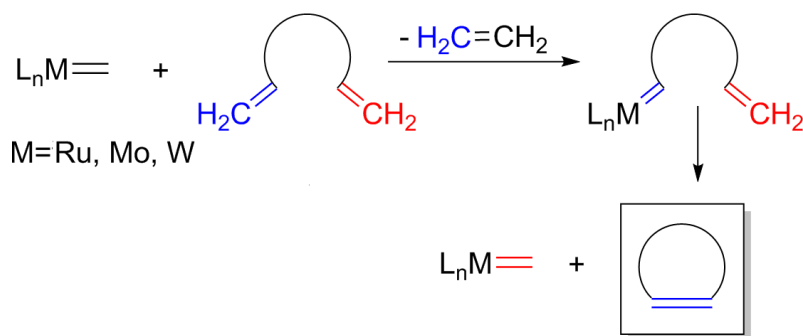
Example of Formation of 8-membered ring



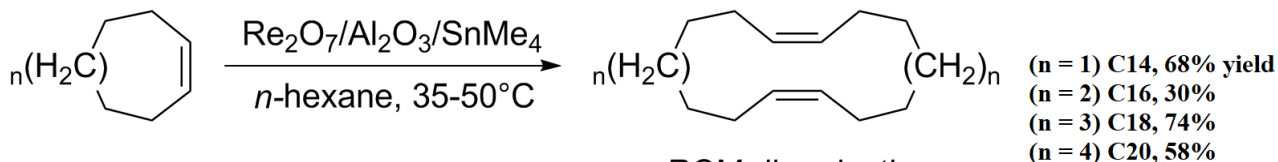
Disadvantages: The reaction has found much less general use than the Dieckmann reaction because dinitriles are less readily available than diesters and the resulting cyanoenamines are both more difficult to hydrolyze and less versatile in their transformation into other groups.

SYNTHESIS OF LARGE RINGS BY RING CLOSING METATHESIS (RCM) REACTION

- **RCM**, is a widely used for the synthesis of various unsaturated rings via the intramolecular metathesis of two terminal alkenes.
- Forms *E*- or *Z*- cycloalkenes
- **Advantages:** 1. formation of rings, which were previously difficult obtain in good yields
2. broad substrate scope
3. Atom economical reaction- ethylene is the only major by-product

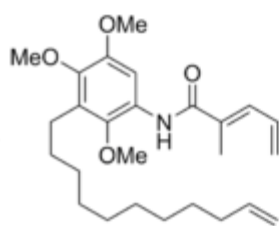


Examples

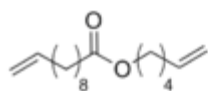
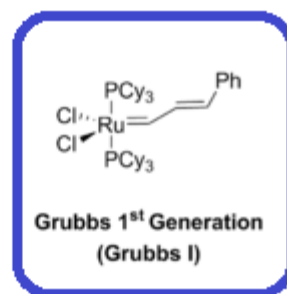
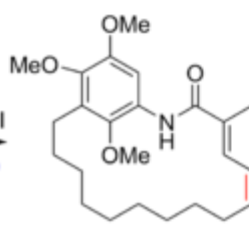


Warwel, S.; Katker, H. . *Synthesis*, 1987, 935-937.

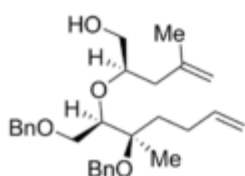
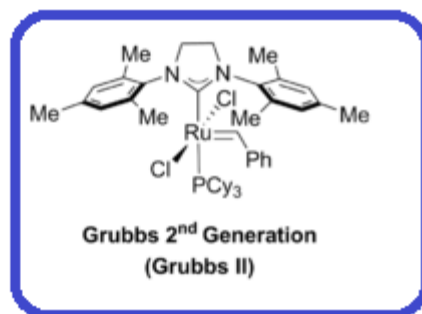
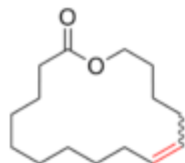
RCM dimerization



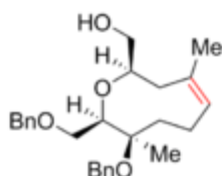
10 mol% Grubbs I
 CH_2Cl_2 , (0.5 mM)
 40°C, 20 h, 68%

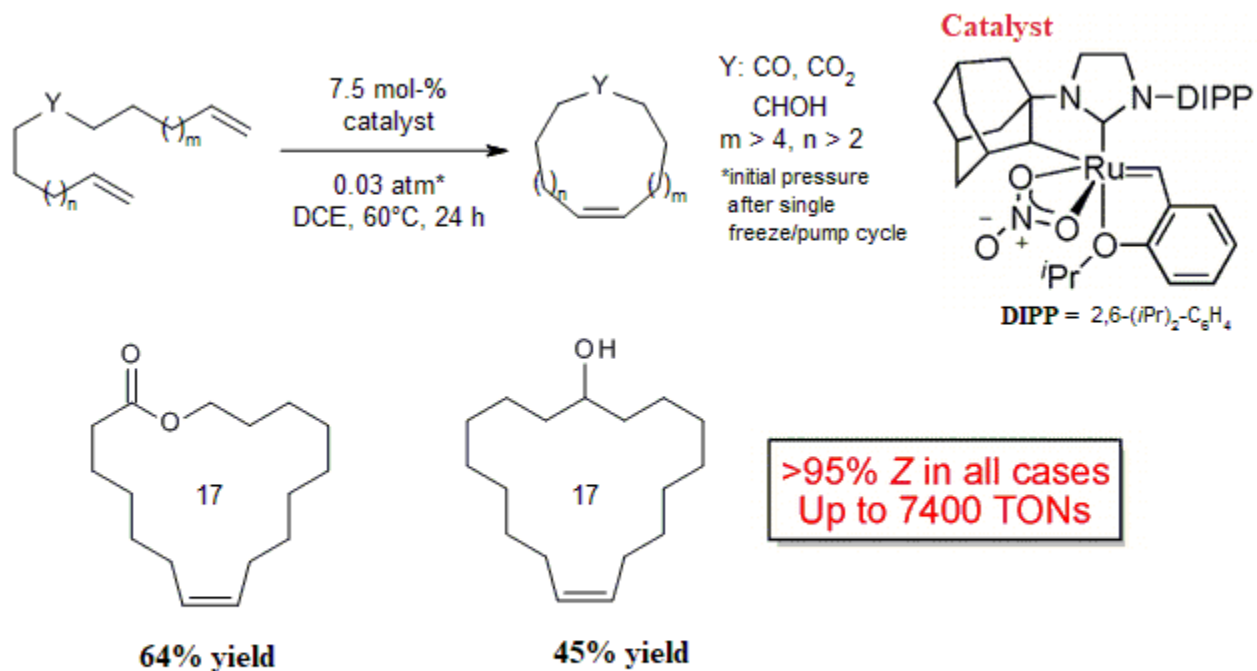


5 mol% Grubbs II
 CH_2Cl_2 , (5 mM)
 40°C, 5h
 99% RCM



10 mol% Grubbs II
 C_6H_6 (2 mM)
 80°C, 5h, 89%
 15:1 RCM/dimer





R. H. Grubbs *et.al.* *J. Am. Chem. Soc.*, **2013**, *135*, 1276-1279

- Ring-closing metathesis is important in total synthesis.
- **Limitations**: use of high dilution technique, selectivity issues, and unwanted isomerization.