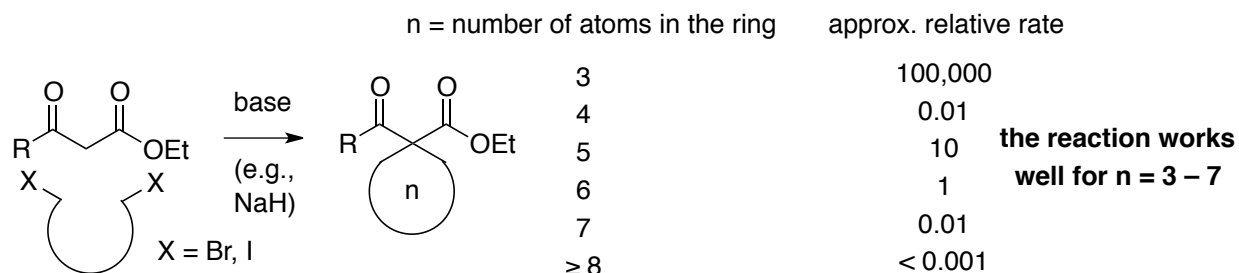


CHEM 330

Topics Discussed on Sept 25

Approximate relative rates of ring formation in the above process:



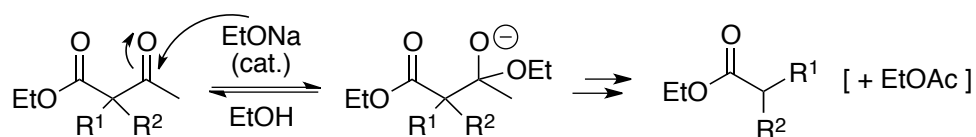
Irreversible nature of the S_N2 reaction leading to the alkylation of an enolate and consequent success of the formation of strained 3- and 4- membered rings by alkylation chemistry

Recall, one cannot create such strained rings by Claisen-Dieckmann reactions taking place under conditions of reversibility (thermodynamic control): see notes of Sept. 15

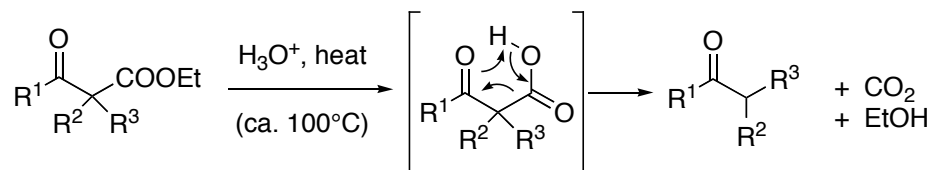
Significance of Claisen and Dieckmann products in contemporary synthetic chemistry:

- conversion of simpler 1,3-dicarbonyl compounds into more complex structures by alkylation of their enolates
- preparation of cyclic structures
- assembly of more complex esters and ketones — themselves valuable building blocks — from simpler starting materials
- synthesis of heterocyclic compounds of common occurrence in pharmaceuticals.

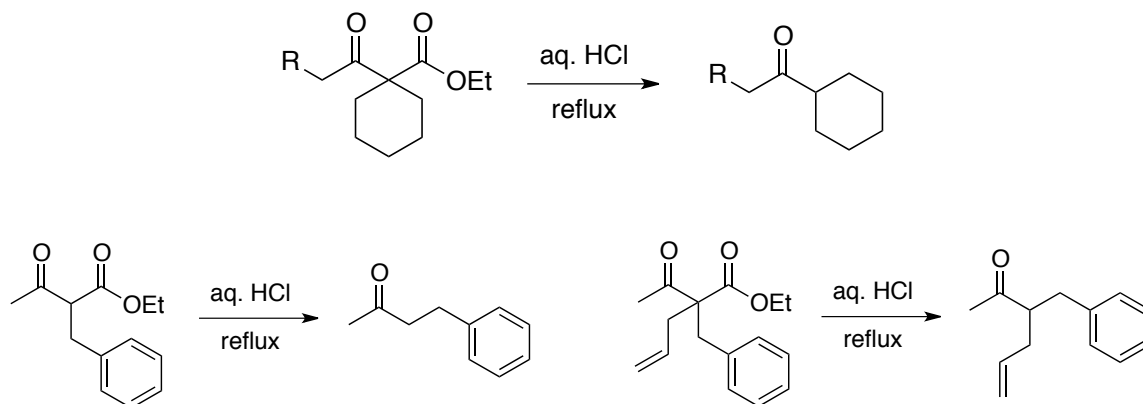
Preparation of new esters by retro-Claisen reaction of the above alkylated derivatives (no longer an important method):



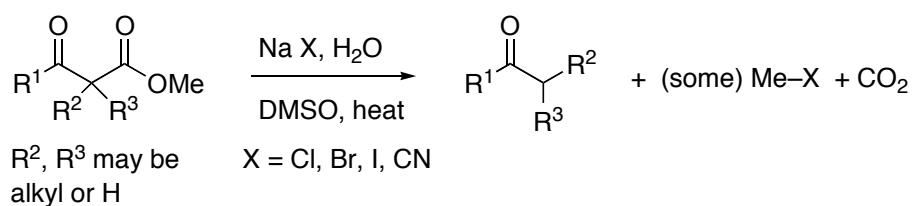
Preparation of ketones by decarboxylation of β -ketoesters— especially under acidic conditions (still very useful)



Examples:



The **Krapcho** reaction: a mild method for the decarboxylation of β -ketoesters:



Possible mechanisms for the Krapcho reaction

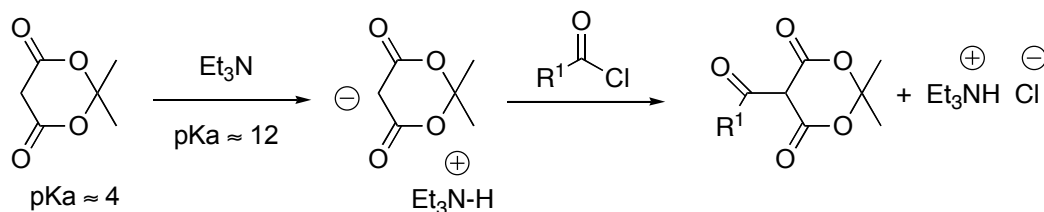
Practical importance of simple β -ketoesters of the type $\text{R-CO-CH}_2\text{-COOEt}$ in synthetic organic chemistry.

The **Yonemitsu reaction**: a technologically important method for preparation of β -ketoesters of the type $\text{R-CO-CH}_2\text{-COOEt}$. This reaction illustrates a special case of successful cross-Claisen condensations of acid chlorides through reaction with stabilized ($\text{pK}_a < 10$) carbonyl enolates, especially with enolates of active methylene compounds ($\text{R}^1\text{-CO-CH}_2\text{-CO-R}^2$):

Meldrum's acid: a type of cyclic malonic ester that exhibits enhanced C-H acidity ($\text{pK}_a \approx 4$) relative to ordinary malonic esters ($\text{pK}_a \approx 14$)

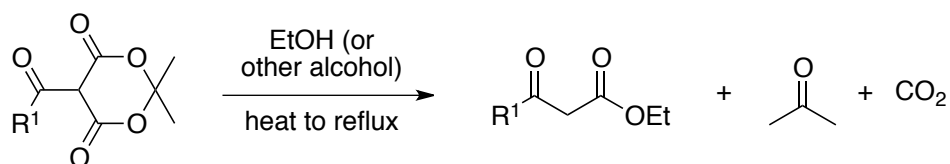


Base-promoted acylation of the anion of Meldrum's acid with an **aliphatic** acid chloride:



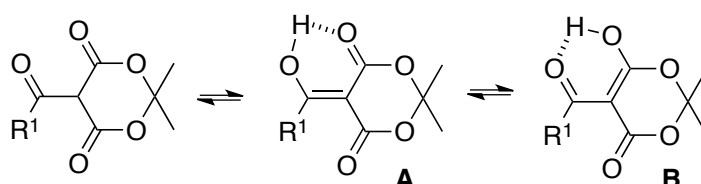
note: aromatic acid chlorides are much less reactive than their aliphatic counterparts, and do not perform adequately in the Yonemitsu reaction

Thermal decomposition of acylated Meldrum's acids in alcohol solution:

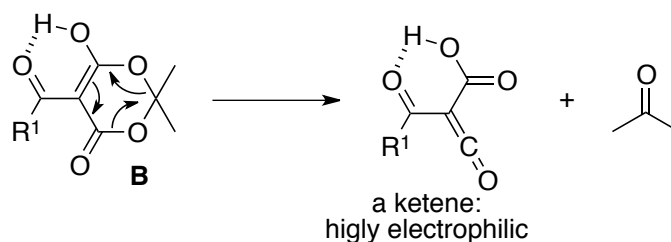


Presumed mechanism of the above reaction:

i. facile equilibration of the acylated Meldrum's acid with enol tautomers **A** and **B**:

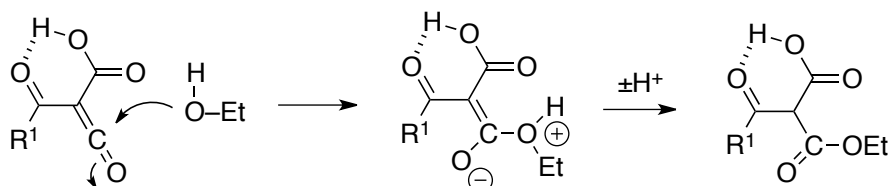


ii. facile retro-Diels-Alder reaction of tautomer **B** leading to a ketene and a molecule of acetone:



ketenes (carbonyl compounds incorporating the functional group $\text{C}=\text{C}=\text{O}$), allenes (olefinic compounds incorporating the functional group $\text{C}=\text{C}=\text{C}$), etc., as "cumulenes": molecules in which a carbon atom establishes **two** double bonds with a pair of contiguous atoms.

iii. rapid reaction of the extremely electrophilic ketene with EtOH (or any other alcohol)



iv. decarboxylation / tautomerization

