

A Study on Organic Synthesis *via* Ketene

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Short Communication

Received: 15-Apr-2022,
Manuscript No. JAAS-22-60958;
Editor assigned: 18- Apr-2022,
Pre QC No. JAAS-22-60958 (PQ);
Reviewed: 03-May-2022, QC No.
JAAS-22-60958; **Revised:** 17-
Jun-2022, Manuscript No. JAAS-
22-60958 (R); **Published:** 24-
Jun-2022, DOI: 10.4172/2347-
226X.11.4.006

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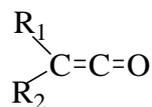
Keywords: Acetylating agent;
Ethane; Ketene; Ketene chemistry;
Organic synthesis

ABSTRACT

Ketene is a colourless toxic gas with a sharp penetrating odour. It is most important member of the class being Ketene itself, which is used to make other important chemicals such as aspirin, acetate, acetic anhydride and other industrial organic compounds. It is soluble in essentially all organic solvents. This knowledge will help to the people who are interested to work in manufacturing of industrial organic compounds. Ketene chemistry remains a very active area of research worldwide.

INTRODUCTION

A ketene is an organic compound of the form:



The first ketene to be prepared and characterized was diphenyl ketene. It was made by Hermann Staudinger in 1905.

Ketenes are highly unstable and cannot be stored. The utility of ketenes in both laboratory and industrial practice was quickly recognized, and these species have been extensively utilized, including as intermediates in the manufacture of acetic acid and acetic anhydride and pharmaceutical intermediates [1-5]. Ketenes are highly electrophilic at the curious Sp carbon atom. Ketenes are characterized by presence of grouping as

If $R_1=R_2=H$, then the simplest member of ketene series is ketene.

If $R_1=R$ and $R_2=H$, then it is known as Aldoketene.

If $R_1=R$ and $R_2=R'$ then it is known as Ketoketene.

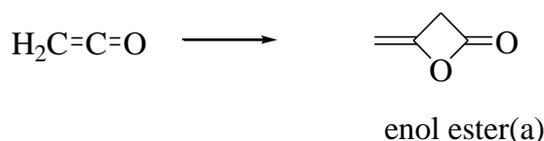
There are various types of ketenes depending upon R_1 and R_2 may be alkyl, aryl, alkenyl, alkynyl, acyl, imidoyl etc.

Ketenes in organic synthesis: Ketene is a colourless, poisonous, pungent, gas. Boiling point $-41^\circ C$ which oxidizes in air to the unstable peroxide, the structure of which may be shown as

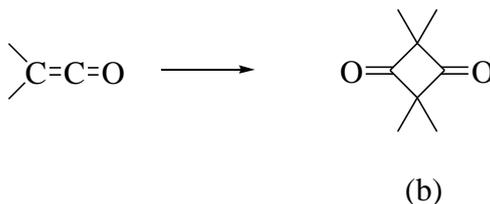


Ketenes are unstable and can't be stored. So ketenes react with nucleophile if present and in the absence of nucleophile they dimerise.

Ketene itself gives an ester [6,7].

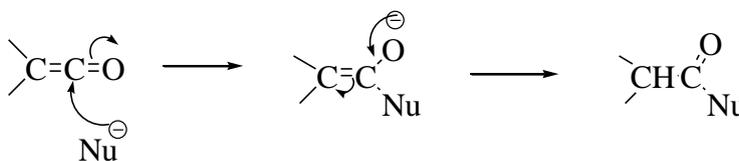


Disubstituted ketenes give **cyclobutadiones**.

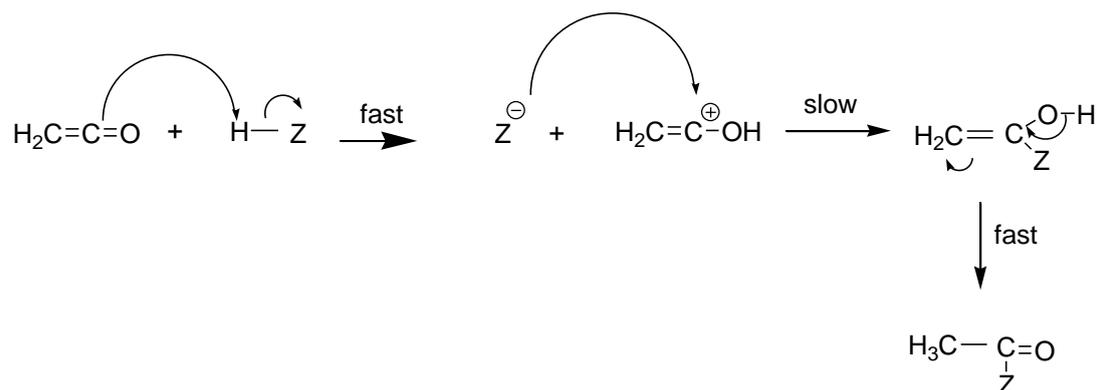


Monosubstituted ketenes may give either of the products (a) or (b)

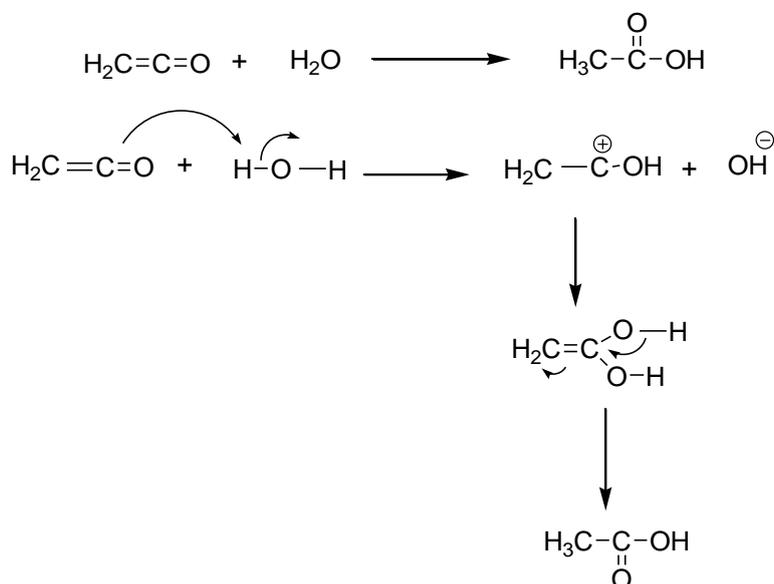
Reaction with nucleophile: Ketene react with nucleophiles give acyl derivatives via. enolate.



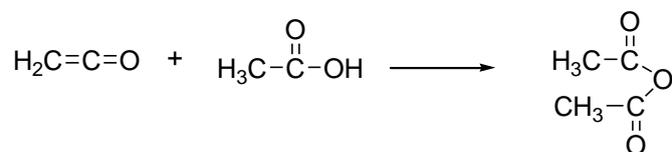
Acetylation by ketenes: Ketenes acetylates most of the compounds with an active H-atom. The much of acetylation by ketenes can be generalized in terms of the addition of a nucleophile as the rate determining step.



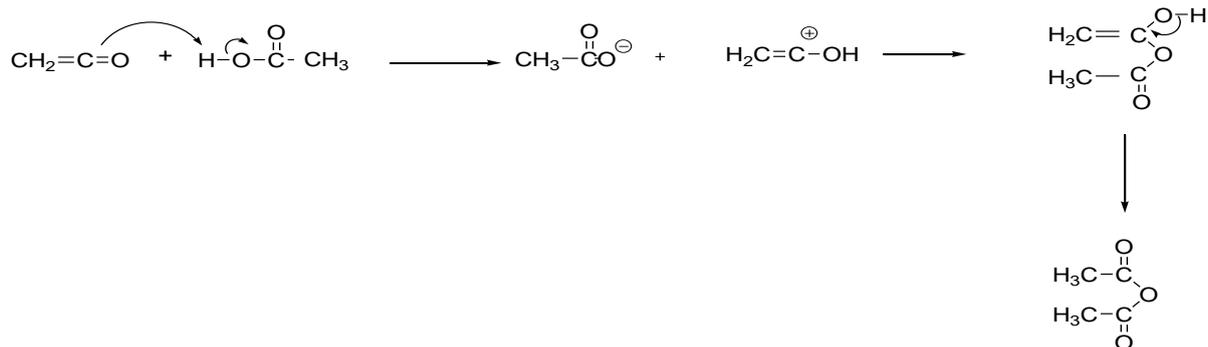
It reacts with water and acetic acid is formed as shown



When ketene is passed into glacial acetic acid, acetic anhydride is formed:

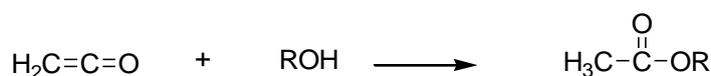


Mechanism:

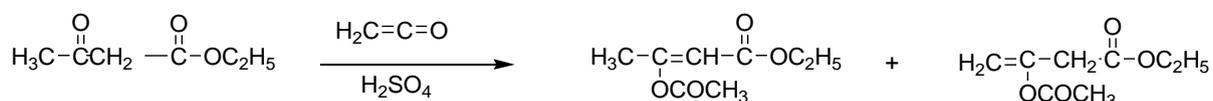


Ketene reacts with aliphatic or aromatic hydroxyl compound.

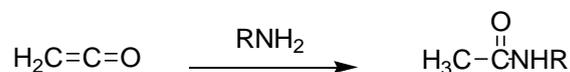
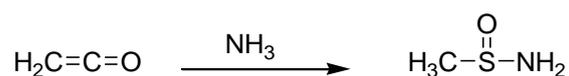
For e.g: It reacts with alcohol to form ester



It also acetylates the enolisable compounds

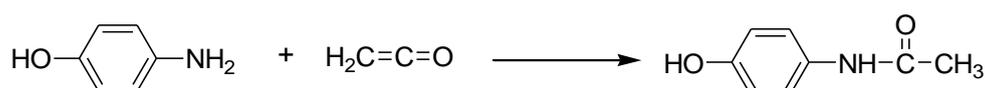


Ketene reacts with ammonia to form acetamide, and with primary or secondary to form N-alkyl acetamides:

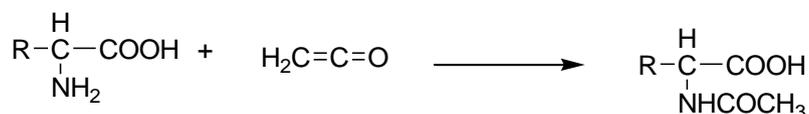


Primary amino group are acetylated extremely readily and hence it is possible to acetylate this group selectively in compound containing both an amino group and hydroxyl group.

For example: p-aminophenol:



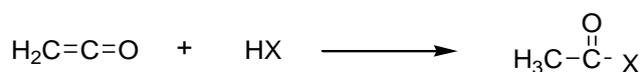
A particularly useful reaction of this type is the acetylation of amino acids.



Thiols are acetylated as shown below:



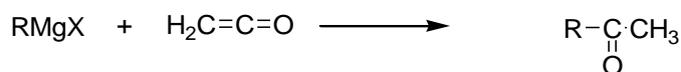
Ketenes react with halogen acid to form the acetyl halide:



Ketenes react with alkyl halide to form acid chloride:

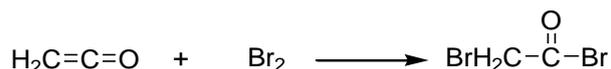


Ketene reacts with Grignard reagent to form methyl ketones



In addition to behaving as an acetylating reagent, ketene behaves as unsaturated compounds.

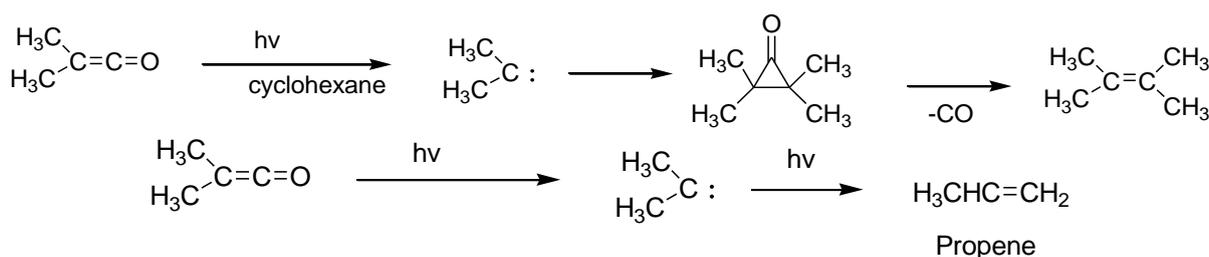
- Ketenes add on bromine to form bromoacetyl bromide.



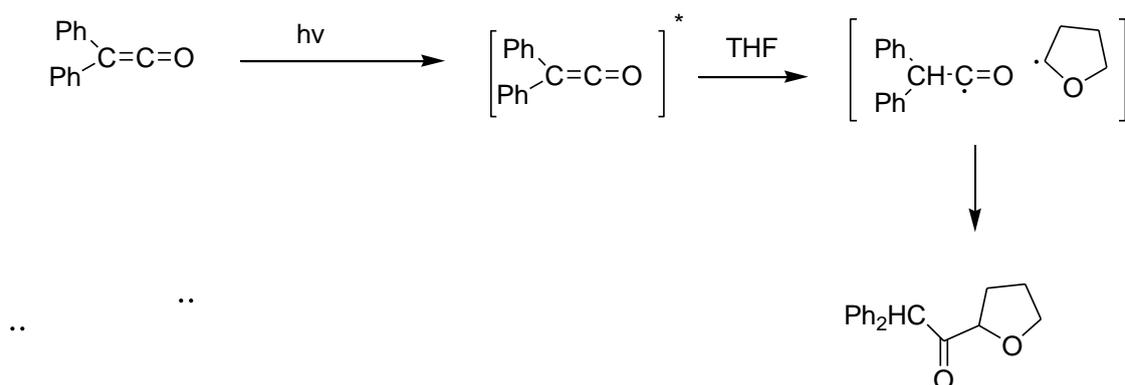
DESCRIPTION

Photolysis of ketenes: Ketene undergoes photochemical decomposition resulting into the formation of methylene (carbene). Photolysis of higher ketene $MeHC=C=O$ and $Me_2C=C=O$ formed the corresponding carbene, and in the gas phase $H_2C=CH_2$ and $MeHC=CH_2$, respectively are the major product.

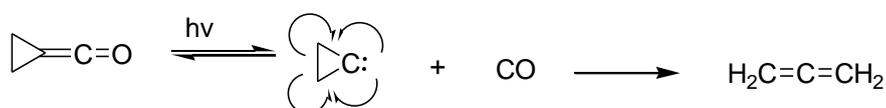
Photolysis of $Me_2C=C=O$ in cyclohexane solution also gave $Me_2C=CMe_2$ which was proposed to form via the cyclopropanone, which was observed by IR at 1840 cm^{-1} .



Photolysis of diphenylketene in several solvents gave product derived from diphenyl carbene, but in THF the diphenyl acetyl derivative was formed. This was proposed to form by Hydrogen abstraction by photo excited ketene forming a radical pair that recombined.

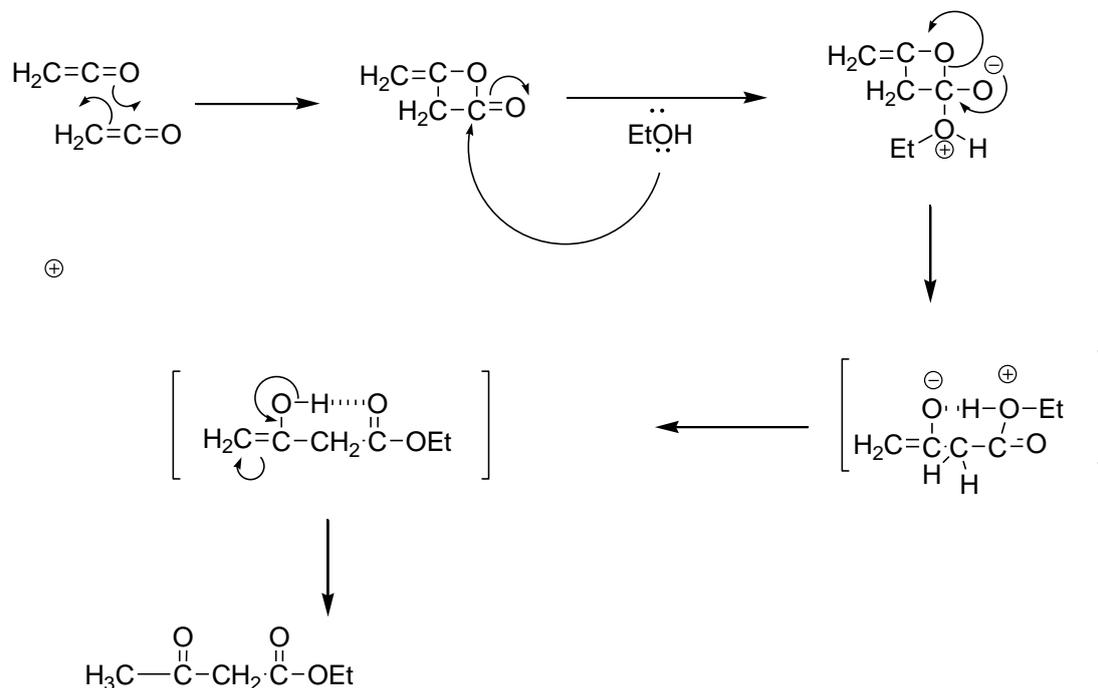


Formation of alkenes: Photolysis of cyclopropylideneketene gives carbene, which result in to the formation of alkene.

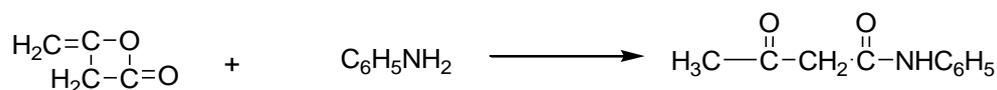


Thermolysis of ketenes: Staudinger and Endle observed in 1913 that diphenylketene undergo thermolysis with loss of CO

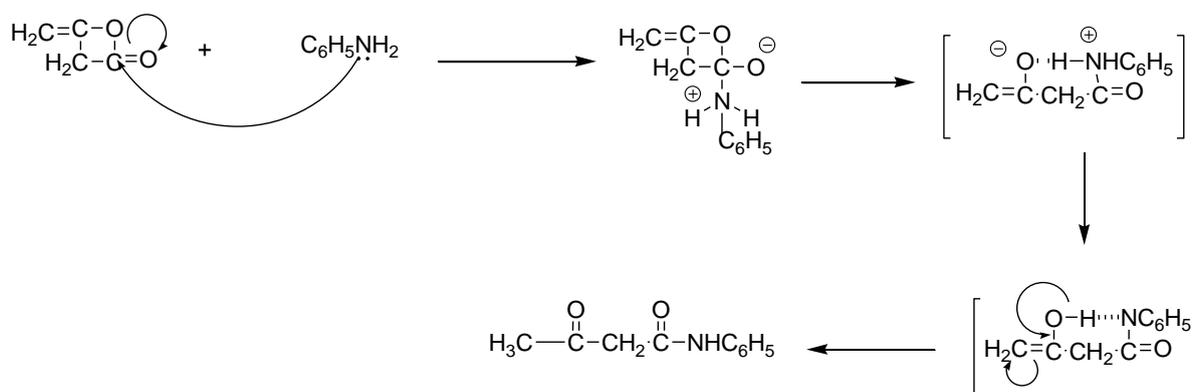
also prepared industrially by polymerising ketene in acetone solution to diketene, which is then treated with ethanol. A possible mechanism is:



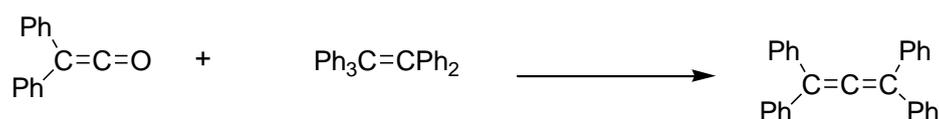
Formation of N-substituted acetamide: Diketene also reacts with primary amines to form N-substituted acetamide. For eg.



Mechanism:

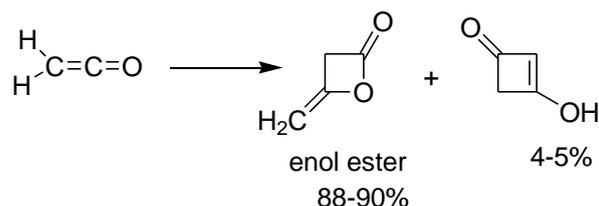


Formation of alkenes: Diphenyl ketene was found to react with the phosphorous ylide to form tetraphenylallene by Luscher. This reaction was later developed by Wittig and Haeg.



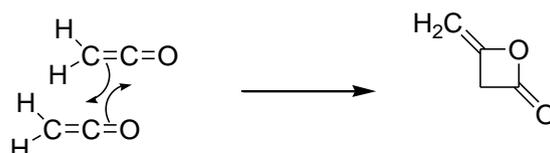
Cycloaddition reaction of ketenes: Cycloaddition reactions have been a characteristic feature of ketene chemistry from the very beginning, with the isolation of the ketene dimer by Chick and Wilsmore. Staudinger found that ketene reacted with cyclopentadiene to form an addition compound that was later shown to result from net [2+2] cycloaddition, and that it reacted with imines to form beta-lactams and with aldehydes to form beta-lactones. Since that time, cycloaddition has

remained the most distinctive, useful and intellectually challenging aspect of ketene chemistry. Ketene itself gives ester:-

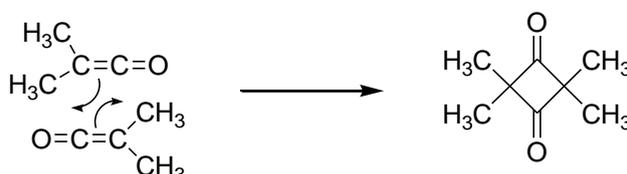


Mechanism:

Cycloaddition of ketene with carbonyl group.



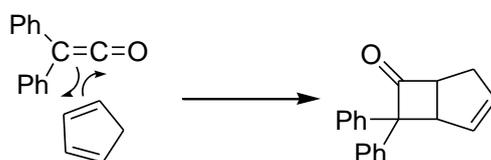
Dimethyl ketene gives cyclobutanones:



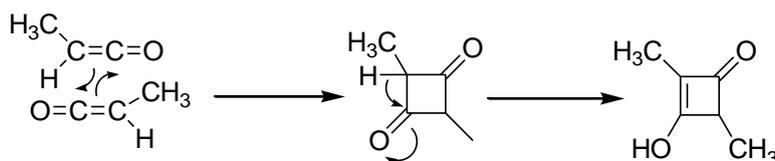
Thus ketenes have a unique propensity for giving facile [2+2] cycloaddition reactions, even when other pathways are available.

This feature of ketene chemistry is of major importance for preparative purposes in that the reaction with diene and alkene gives cyclobutanone.

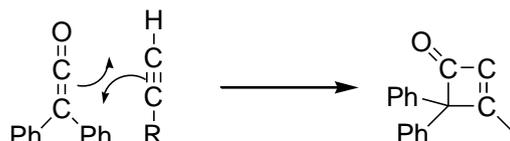
Formation of cyclobutanone:



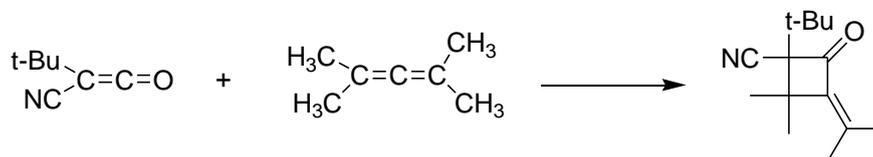
Formation of enol:



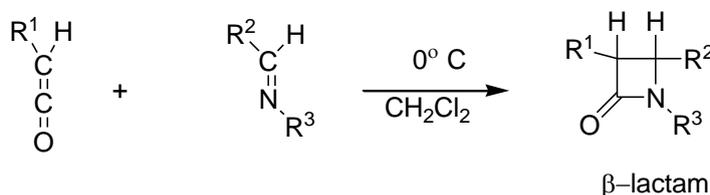
Formation of enone:



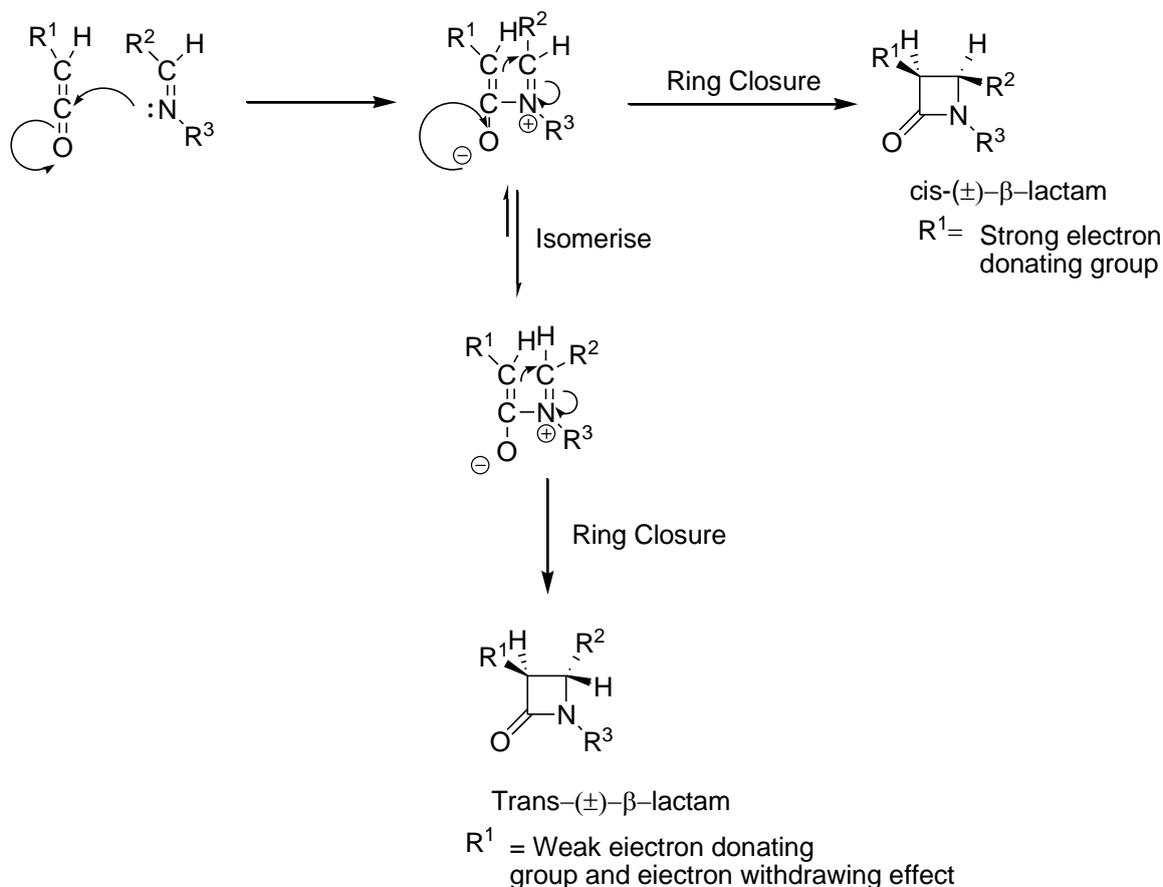
[2+2] cycloaddition of ketenes with alkenes:



Formation of beta-lactams: Cycloaddition of ketenes with imines: The reaction of ketene with imines forming beta-lactams is the most straight forward method for the synthesis of these compounds, which have valuable application in the synthesis of antibiotics.



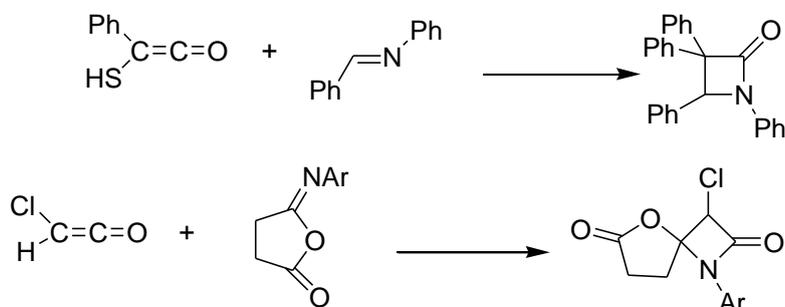
Mechanism:



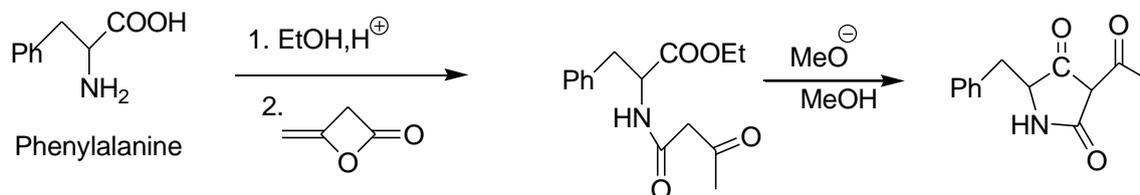
The stereoselectivity is generated as a result of the competition between the direct ring closure and the isomerisation of imine moiety in the zwitterionic intermediate. The ring closure step is the most likely an intramolecular nucleophilic

addition of enolate to the imine moiety, which is obviously affected by the electronic effect of the ketene and imine substituent. Electron donating ketene substituents and electron withdrawing imine substituents accelerate the direct ring closure leading to a preference for cis beta-lactam formation. While electron withdrawing ketene substituents and electron donating imine substituents slow the direct ring closure, leading to a preference for trans beta-lactam formation.

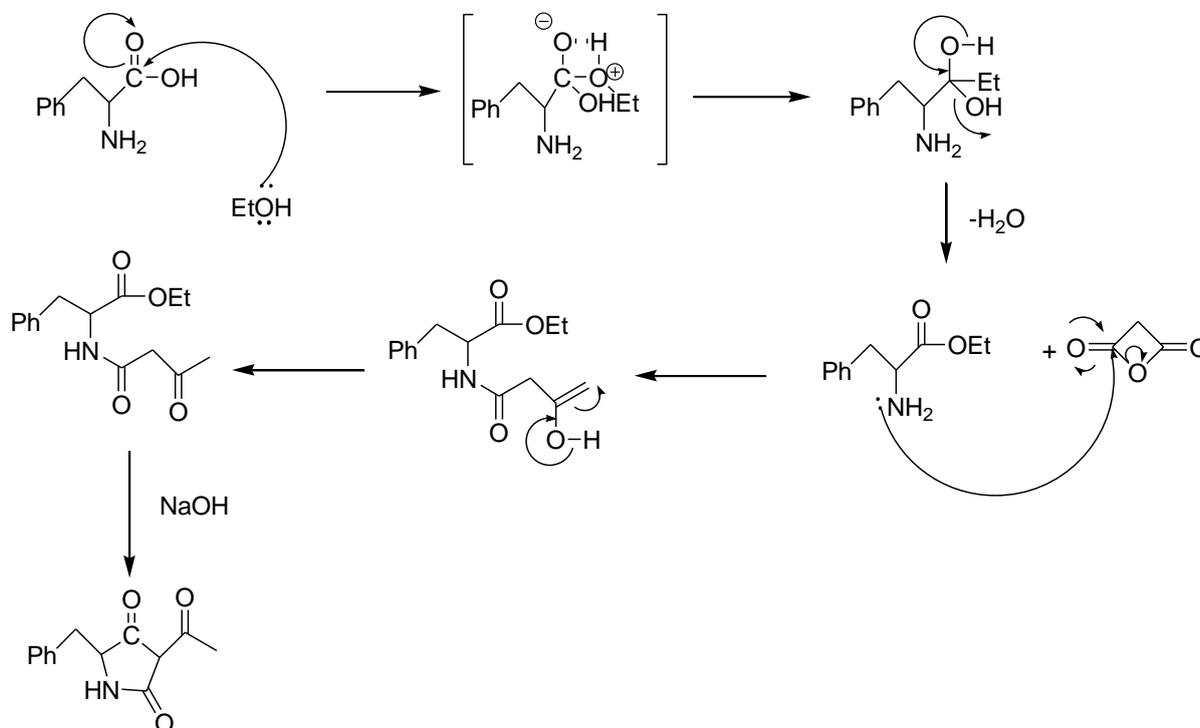
Examples:



Formation of heterocyclic compounds: Heterocyclic compound, an intermediate in a cytochalasin synthesis can be made from acid phenyl alanine and ketene dimer in the presence of ethanol.

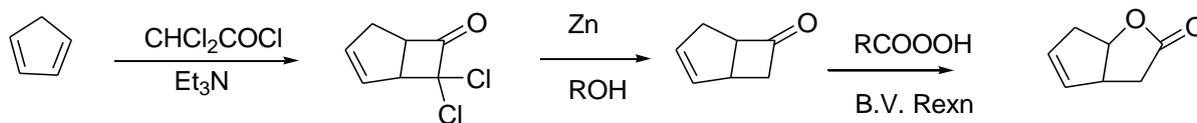


Mechanism:

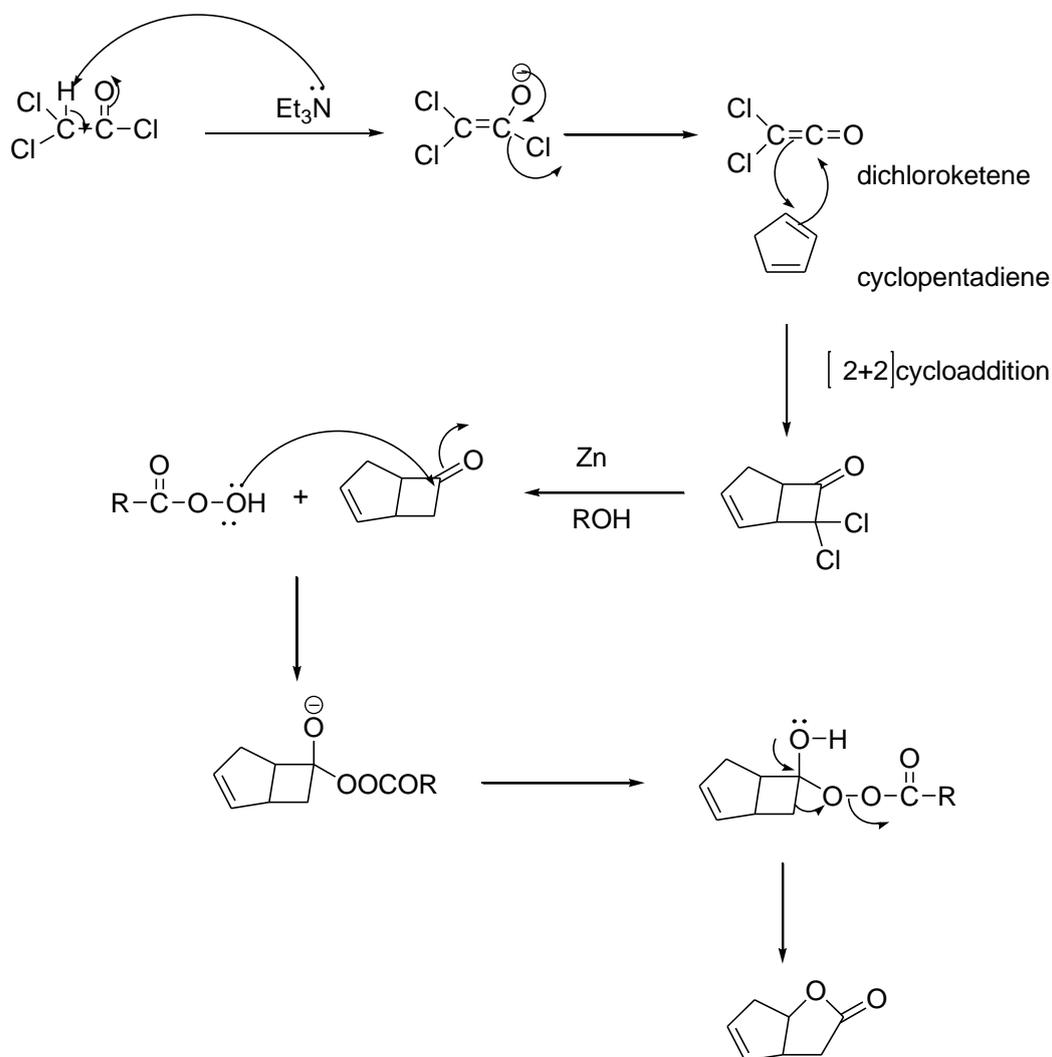


Formation of lactones: Generally lactones are made by Baeyer-villiger rearrangement. Lactones can also be prepared from ketene. Let us consider lactone which is an important intermediate in the synthesis of Prostaglandins. In actual practice, dichloroketene is much easier to make and handle than ketene itself.

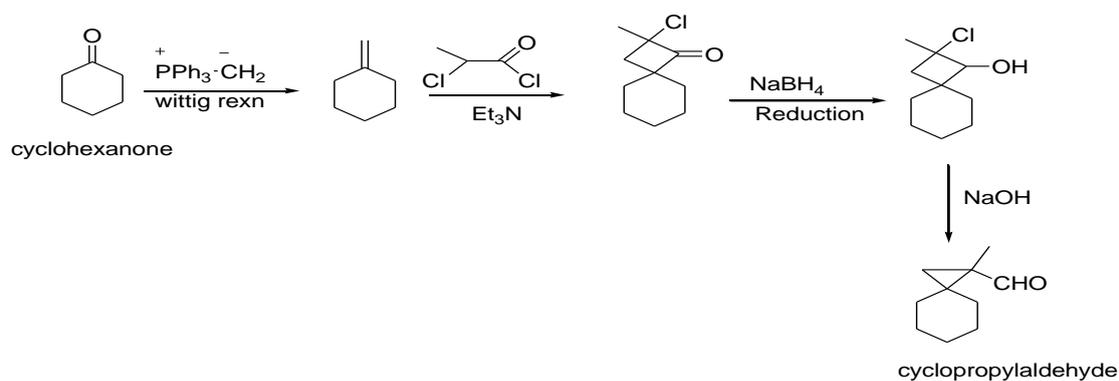
Synthesis:

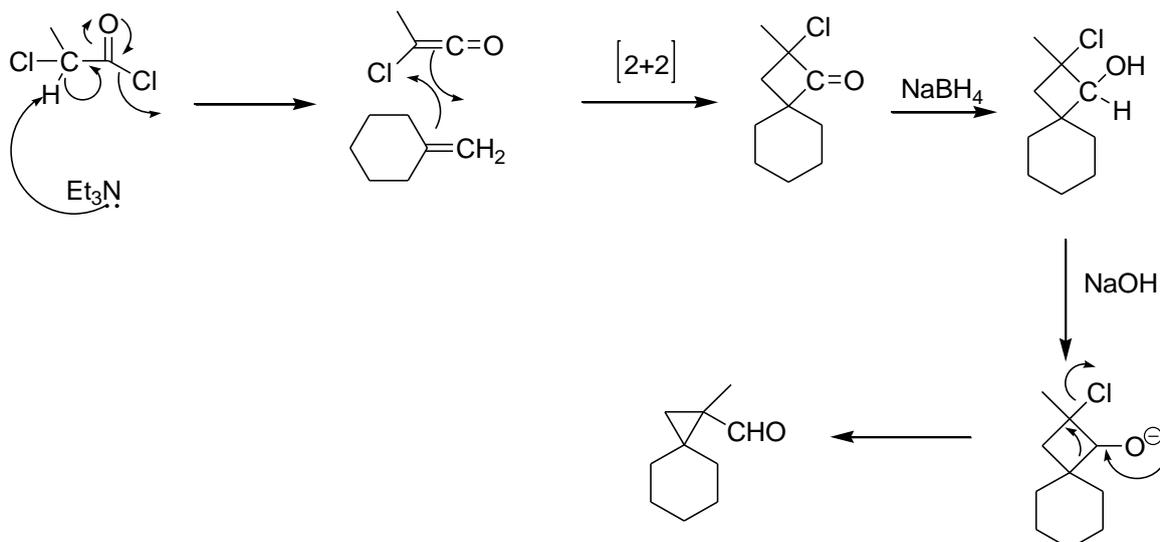


Mechanism:

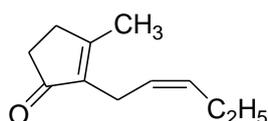


Formation of cyclopropyl aldehyde: Cyclopropyl aldehyde can be from cyclic ketones *via*. ketene formation.



Mechanism:


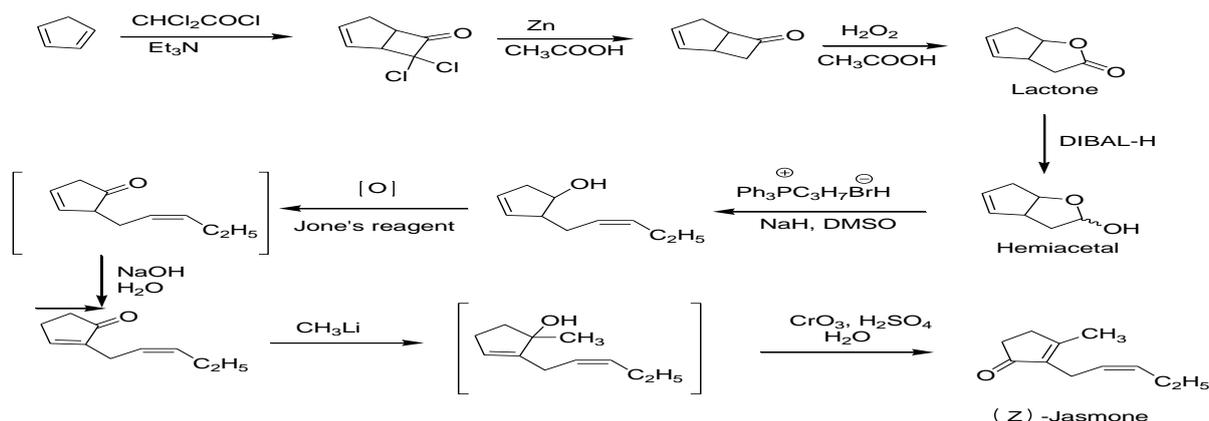
Synthesis of Z-Jasmone from cyclopentadiene: Jasmine flowers contain Z-Jasmine which is responsible for jasmine fragrance and used in perfumery.



Z-Jasmone

Synthesis:

- Dichloro ketene (formed in situ by reaction of dichloroacetyl chloride with tri-ethylamine) reacts with cycloalkene by [2+2] cycloaddition.
- Reductive dehalogenation with zinc in the presence of acetic acid.
- Baeyer-villiger oxidation to give a lactone.
- Reduction of the lactone to hemiacetal.
- A wittig reaction on hemiacetal affords a gama-hydroxy alkene.
- Oxidation of the alcohol to an unsaturated ketone and conversion to more stable conjugated isomer.
- Reaction with methyl lithium to yield a tert.alcohol.
- Oxidation under acidic condition is attended with allylic rearrangement to give jasmone.



CONCLUSION

A variety of hydroxylic compounds can add as nucleophiles, forming either enol or ester products. As examples, a water molecule easily adds to ketene to give 1,1-dihydroxyethene and acetic anhydride is produced by the reaction of acetic acid with ketene. Reactions between diols (HO-R-OH) and bis-ketenes (O=C-CH-R'-CH=C=O) yield polyesters with a repeat unit of (-O-R-O-CO-R'-CO).

Ethyl acetoacetate, an important starting material in organic synthesis, can be prepared using a diketene in reaction with ethanol. They directly form ethyl acetoacetate, and the yield is high when carried out under controlled circumstances; this method is therefore used industrially. This knowledge will help to the people who are interested to work in manufacturing of industrial organic compounds.

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