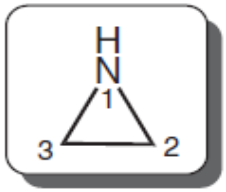
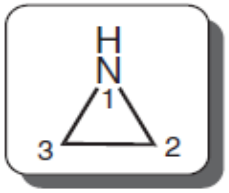
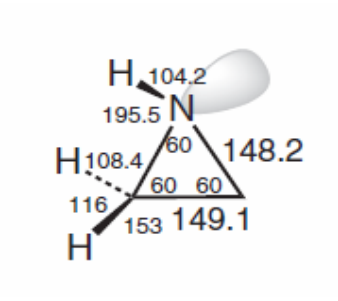
Aziridine



Aziridine was once known as *ethylene imine*.

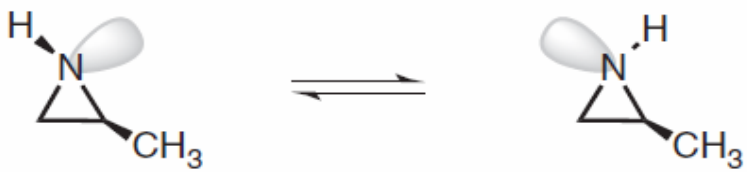


Bond lengths and bond angles are essentially the same as those in oxirane.



Structure of aziridine

2-Methylaziridine would be expected, therefore, to display diastereoisomerism. Trivalent N-atoms are, however, liable to pyramidal inversion.



Chemical properties of Aziridine:

Care is advisable when handling aziridines, because many of them show considerable toxicity. The following reactions of aziridines are due to their nitrogen basicity and to their ability to undergo ring-opening reactions.

Acid-base reactions

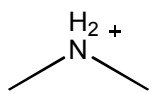
Aziridines unsubstituted on the N-atom behave like secondary amines; N-substituted aziridines behave like tertiary amines. They react with acids to give aziridinium salts:

$$pK_a = 7.98$$

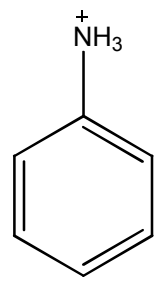
The protonated Aziridine can be acted in polymerization reactions.

Power of basicity:

Aniline<Aziridine<dimethyl amine



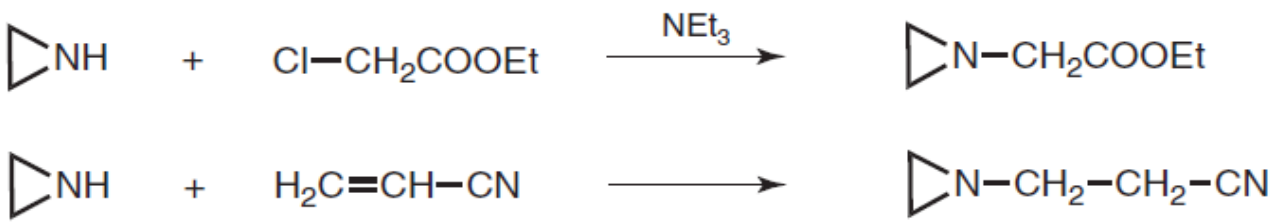
$pK_a =$ 10.87



$pK_a =$ 4.62

Reactions with electrophilic reagents

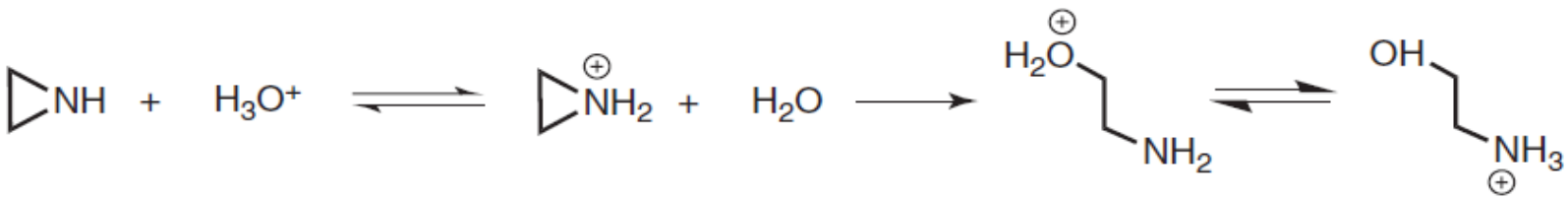
Aziridines, like amines, are nucleophiles and react with electrophiles. Nucleophilic substitution on a saturated C-atom and MICHAEL addition to an acceptor-substituted olefin serve as examples:



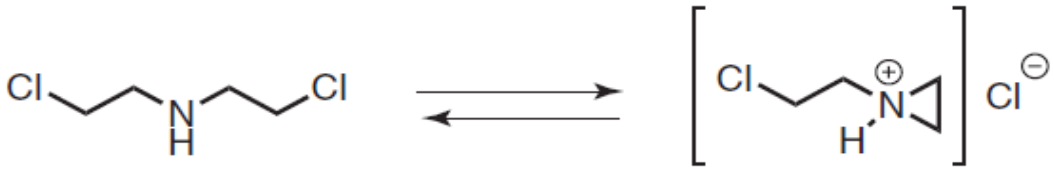
Ring-opening by nucleophiles

Ammonia and primary amines react with aziridines to give 1,2-diamines. The mechanism and the stereochemistry of this reaction are similar to the corresponding reactions of the oxiranes [42].

The ring-opening of the aziridines is catalyzed effectively by acids (A2 mechanism, see p. 20). The acid-catalyzed hydrolysis to give amino alcohols serves as an example:



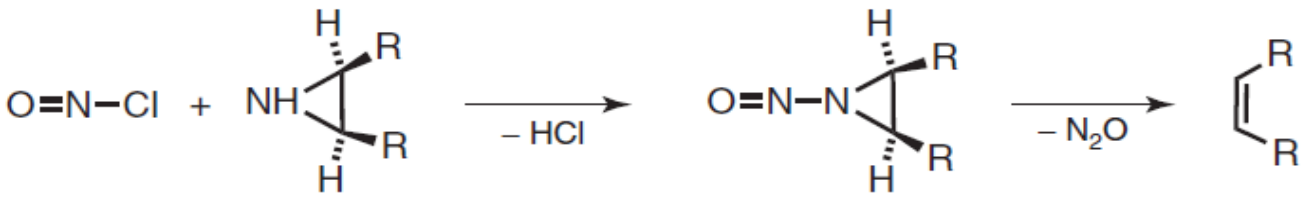
This process can be envisaged as alkylation of a nucleophilic system (here: H_2O) by the protonated aziridine. Reactions of this type can be used to explain the cytostatic and antitumor activity of aziridines and (β-chloroethyl)-substituted amines. An example is bis(2-chloroethyl)amine (**1**), which in solution forms an equilibrium with 1-(2-chloroethyl)aziridinium chloride (**2**):



1 **2**

Deamination to alkenes

Aziridines unsubstituted at the N-atom are stereospecifically deaminated by nitrosyl chloride; via the corresponding *N*-nitroso compound, alkenes are formed stereoselectively:



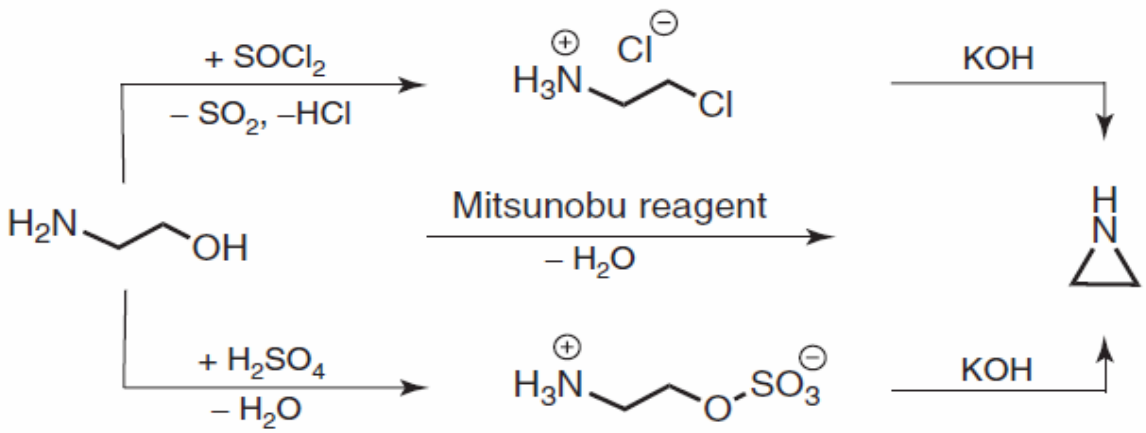
Synthesis of Aziridines:

The syntheses of aziridines fall into four major categories:

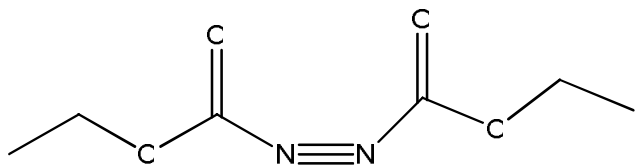
(1) cyclization of N–C–C systems with a leaving group in β-position to nitrogen,
(2) (N + C=C)-cycloaddition (aziridination of alkenes),
(3) (C + C=N)-cycloaddition (aziridines from imines),
(4) cyclization of β-(*N*-chloroethylamino)carbanions.

Cyclization of β-substituted amines

β-Amino alcohols, which are conveniently prepared from oxiranes and ammonia or amines, react with thionyl chloride to give chloramines, which can be cyclized to aziridines by alkali hydroxide (Gabriel, 1888).

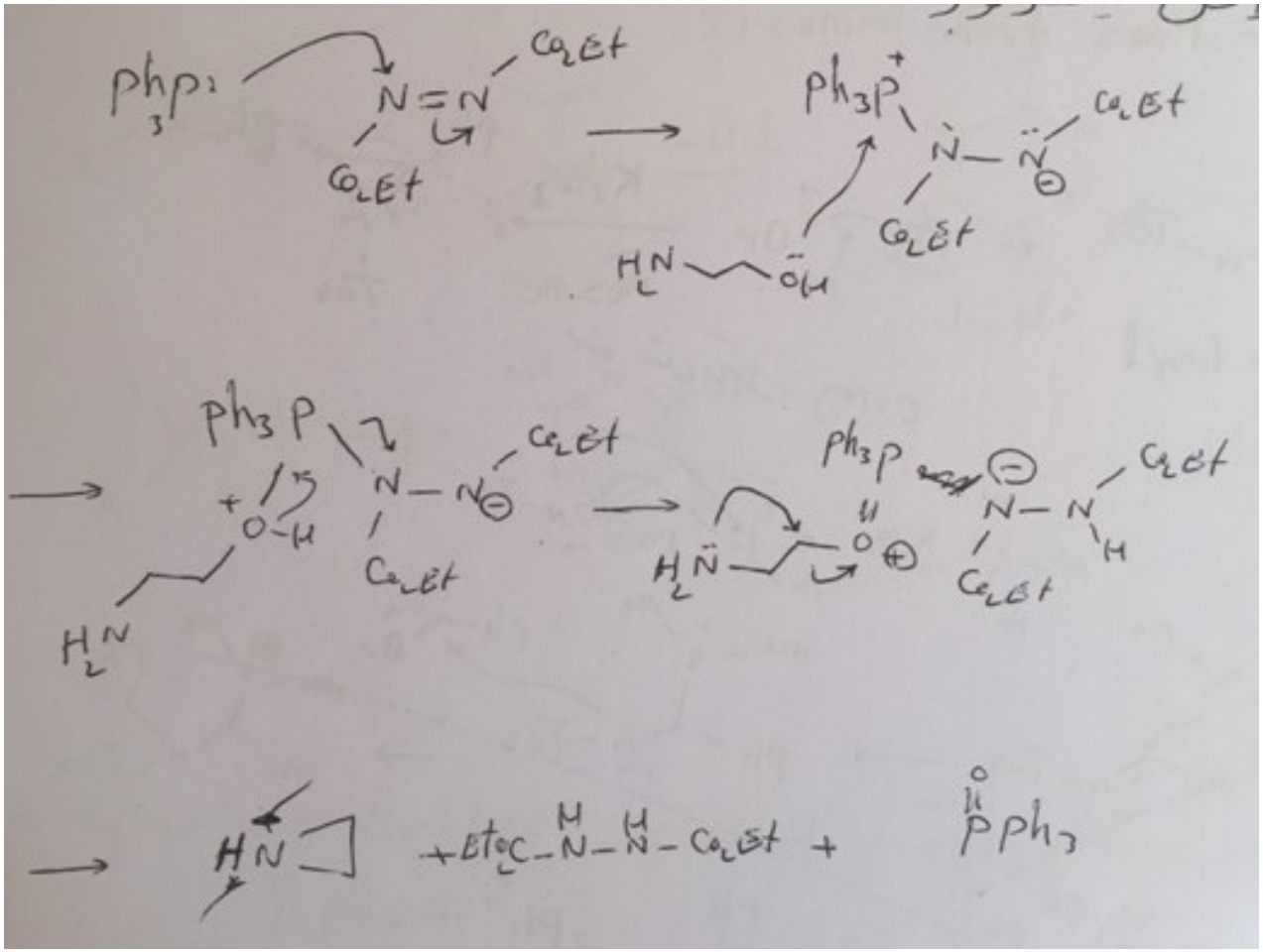


Mitsunobu reagent : Ph3P/diethylazodicarboxylate



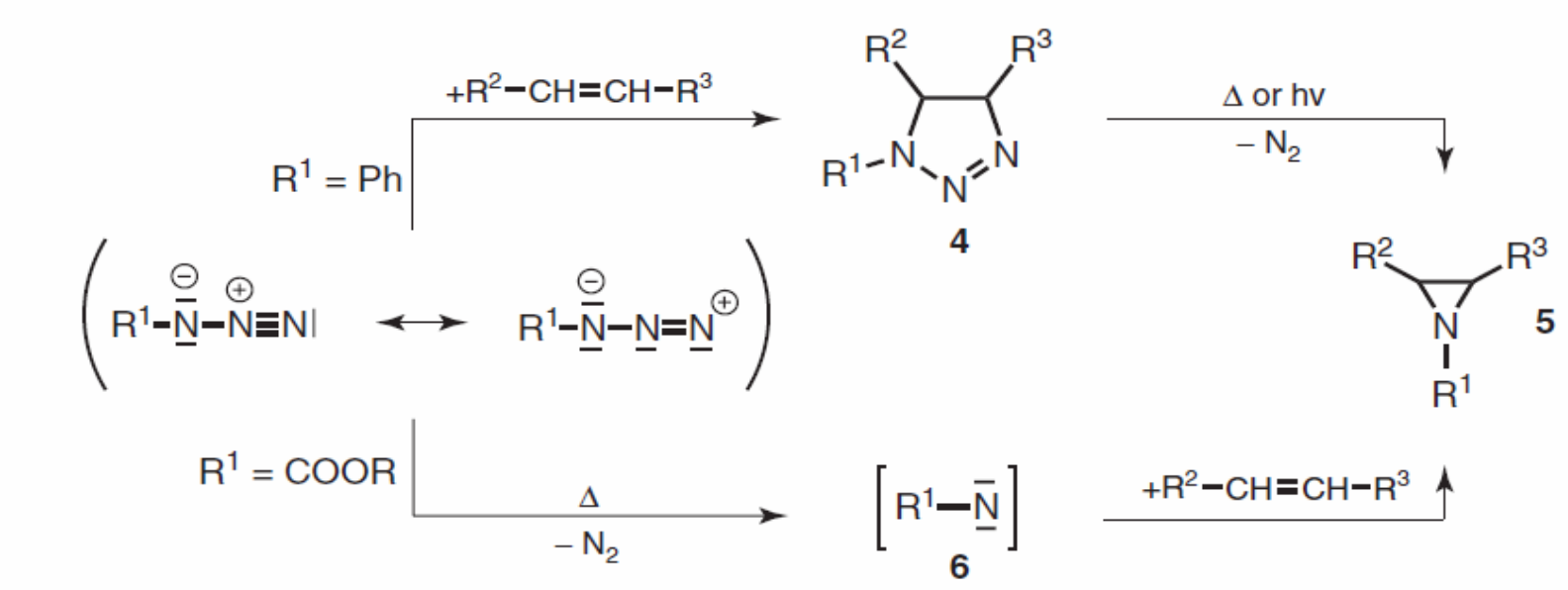
QUESTION: write the mechanism of mitsunobu reaction.

Mechanism of mitsunobu reaction:



Aziridination of alkenes

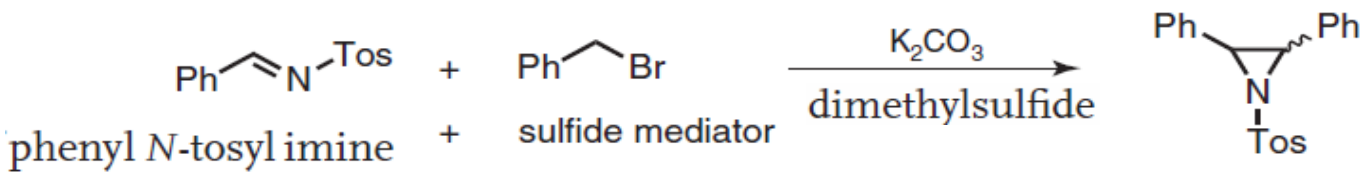
Aziridination of C=C double bonds is readily accomplished by azides as nitrogen donors. The mechanism of nitrogen transfer is markedly influenced by the azide substituent (R^1).



Nitrene

Aziridines from imines

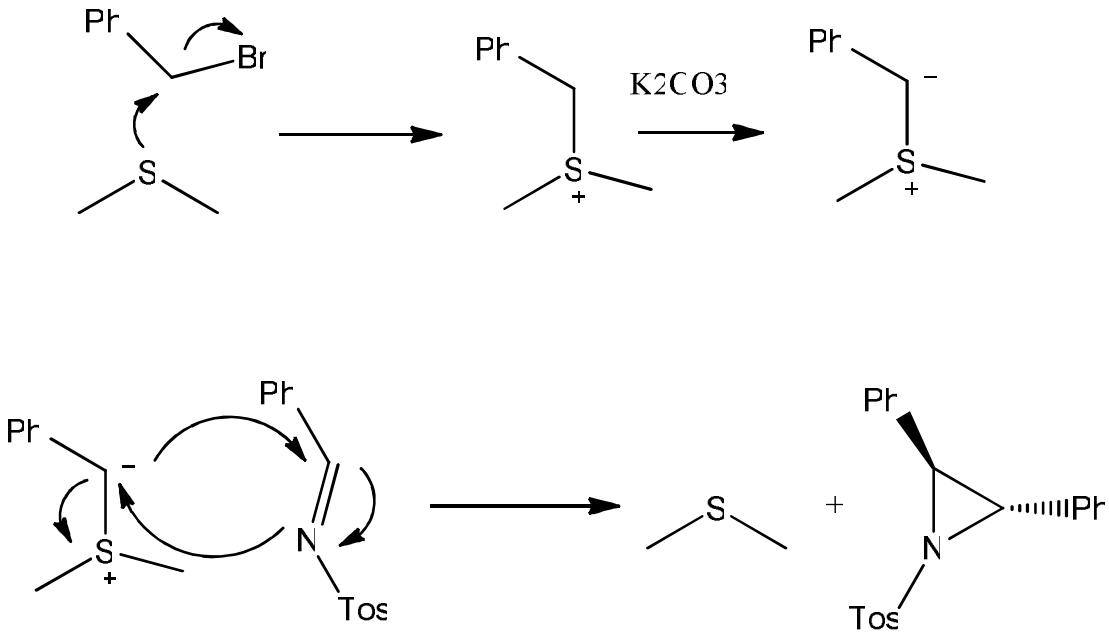
Imines can be transformed to aziridines by addition of suitable C_1-building-blocks, as shown



Like corey reaction

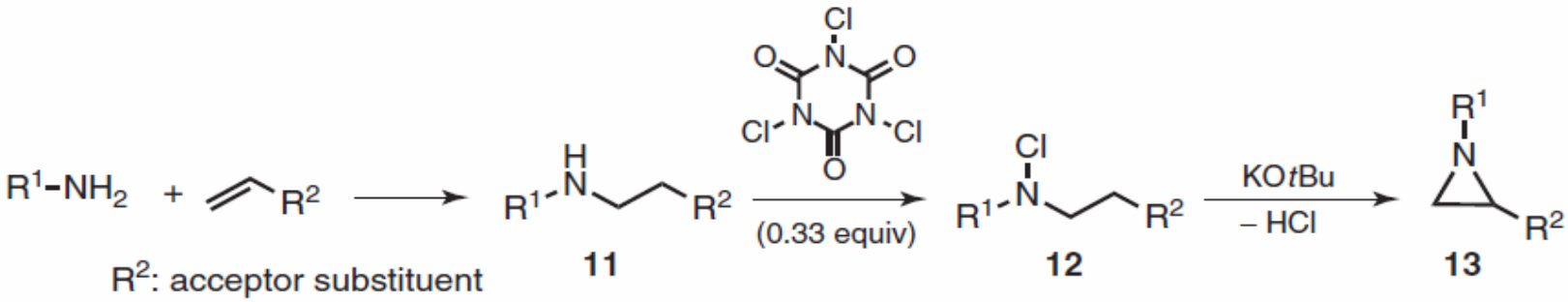
Write the mechanism of above reaction.

Mechanism of previous reaction:



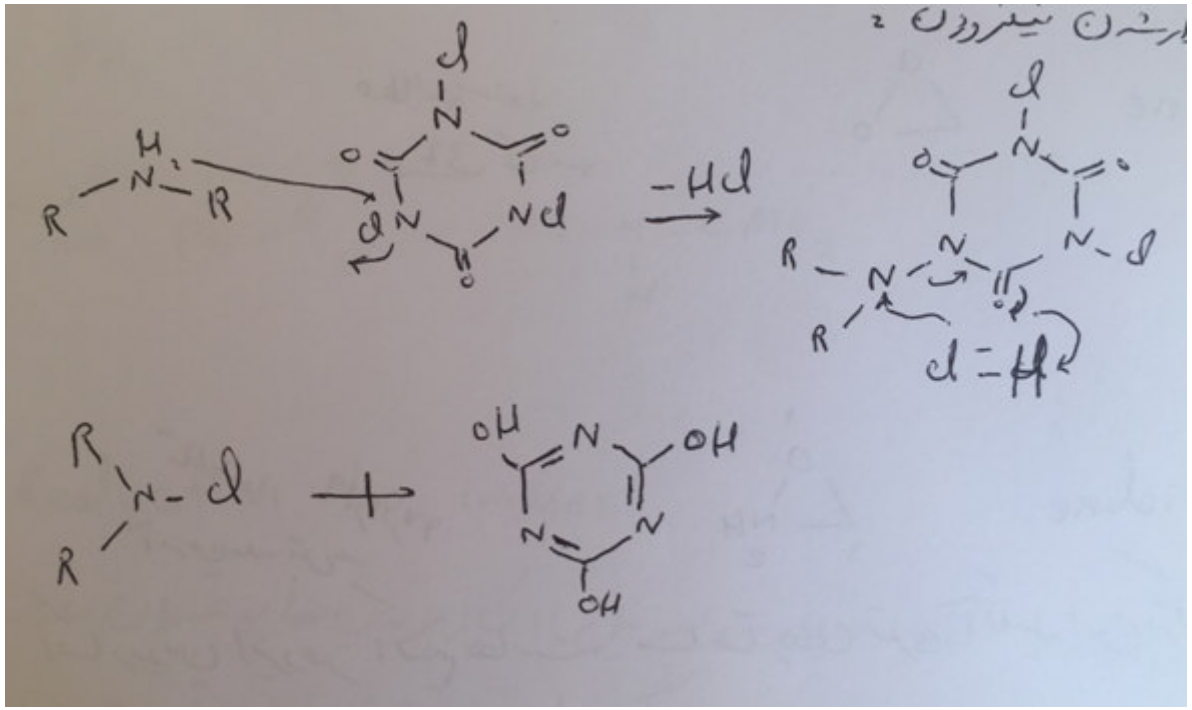
Cyclization of β-(N-chloroethylamino)carbanions

N-Chloroethylamines **12** bearing an acceptor-functionality (ester, benzoyl, cyano, phenylsulfonyl) in β-position to nitrogen are readily cyclized in a 1,3-elimination of HCl by strong base (e.g., *t*BuOK) to give *N*-alkyl-2-acceptor-substituted aziridines **13** [46]:



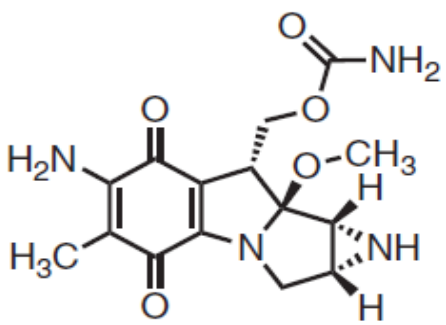
QUESTION: Write the mechanism of chlorination of Nitrogen.

mechanism of chlorination of Nitrogen:



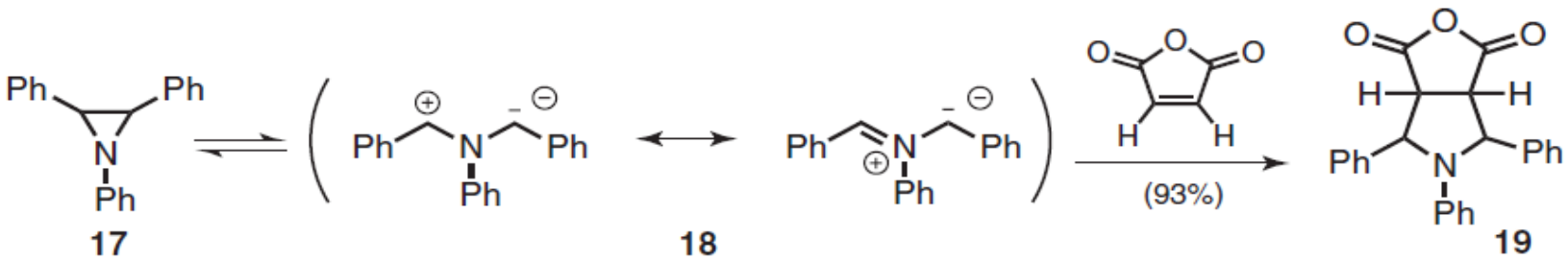
D **Aziridine**, a colorless, water-soluble, poisonous liquid (bp 57 °C) of ammoniacal odor is relatively stable, thermally, but is best stored in a refrigerator over sodium hydroxide.

Some natural products contain an aziridine ring, for example, mitomycins



mitomycins

antitumor activity

Application in synthesis:

Aziridines (e.g., **17**) have the potential to undergo heterolytic ring-opening at the C-2/C-3 bond (facilitated by C-2/C-3 acceptor substituents) leading to 1,3 dipoles (e.g., **18**) which can be trapped by 1,3-dipolar cycloaddition to electron-deficient olefins (e.g., maleic anhydride) to give pyrrolidine derivatives (e.g., **19**) [48]: