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1. Learning Outcomes

After studying this module, you shall be able to

- Know what are cheletropic reactions
- Learn mechanism of cheletropic reactions
- Identify stereochemistry of cheletropic addition reactions
- Evaluate carbene insertion mechanism in double bonds
- Analyze utility of cheletropic reactions in synthesis of natural products

2. Introduction

An important class in pericyclic reactions belongs to cycloaddition reactions. In cycloaddition reactions two components having suitably placed double bonds come together to form two new σ bonds, one at each end of both components, joining them together to form a ring. Like other pericyclic reactions, cycloadditions involve a cyclic transition state and are concerted and stereospecific in nature. Diels-Alder reaction and 1, 3-dipolar cycloadditions are the most important and useful of all pericyclic cycloaddition reactions. They are reversible, and the reverse reaction is called a retro-cycloaddition or a cyclo-reversion reaction.
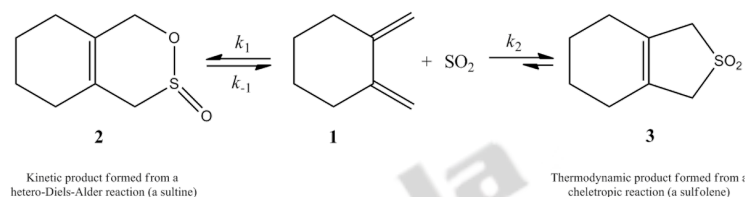
Cheletropic reactions which falls under a subclass of cycloaddition reactions are also a type of pericyclic reactions. The salient feature of cheletropic reactions is that both new bonds are being made to the same atom but only on one of the reagents Like other pericyclic reactions, cheletropic reactions are reversible in nature. A few illustrative examples of cheletropic reactions are shown below;
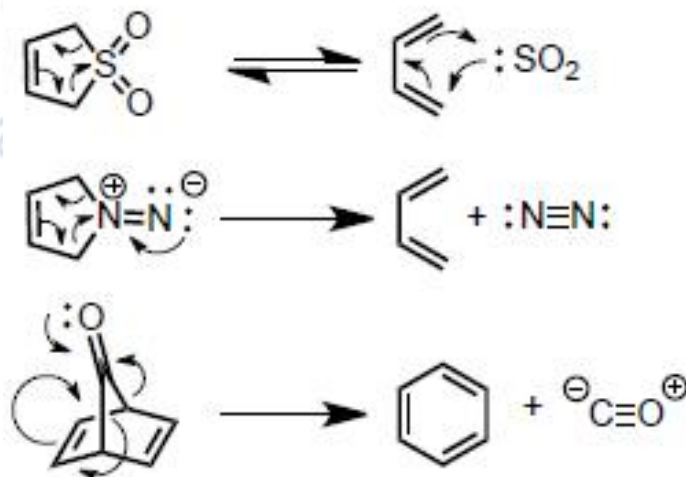
The above written reactions present examples of cheletropic addition (first reaction) as well as cheletropic extrusions, because a small stable molecule is given off in the reaction. The driving force for cheletropic extrusion reactions is often the entropic benefit of gaseous evolution fore.g.

in the above examples removal of SO_2, N_2 and CO. The important observation here is that these small molecules that are extruded or get added to the dienes have a filled and vacant orbital available on the same atom for bonding to other atoms which enables them to undergo cheletropic reactions.

The classical example of cheletropic addition reaction is adding sulfur dioxide to a diene. It has been shown experimentally that this reaction may lead to a [4+2] Diels-Alder adduct (**2**) which is the kinetic product but is thermally unstable and readily undergoes a retro-Diels-Alder reaction to give back the starting material the 1,3-diene and sulphur dioxide.

Kinetic product formed from a
hetero-Diels-Alder reaction (a sultine)

Thermodynamic product formed from a
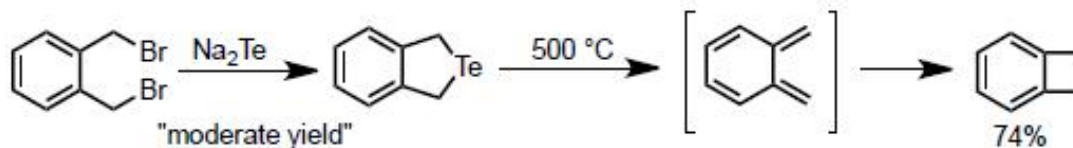cheletropic reaction (a sulfolene)

A thermodynamically more favourable addition (cheletropic reaction) then takes place which is a [4+1] cheletropic cycloaddition leading to formation of a stable five-membered ring adduct (**3**). In the five member adduct there is proper loss of 1 π-bond in the substrate and there is an increment in the coordination number of the sulfur atom of the reagent which changes to six from being four initially.

There are other examples of cheletropic extrusion followed by ring closing reactions as sown below.

Thermal extrusion of SO_2 leading to formation of benzocyclobutene.
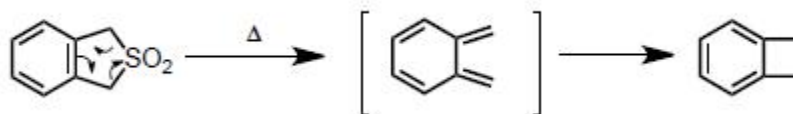
Tellurium extrusion leading to synthesis of benzocyclobutene


3. Stereochemistry and Woodward-Hoffmann rules for cheletropic reactions

Like all other pericyclic reactions, cheletropic reactions also follow Woodward Hoffmann rules. The generalized Woodward-Hoffmann rule applicable to all pericyclic reaction states that, in a thermal pericyclic reaction the total number of $(4q + 2)_s$ and $(4r)_a$ components should be odd. According to rules for cheletropic reactions specifically, the linear cheletropic reactions in which the polyene is a suprafacial component (i.e., involving disrotatory motion of the termini) will be

allowed if it has a total of (4n + 2) electrons. But linear cheletropic reactions in which the polyene is an antarafacial component (i.e., involving conrotatory movement of the termini) are allowed if it has a system of 4n electrons. These rules are reversed for a non-linear cheletropic change.

Linear and non linear geometry

For a cheletropic addition reaction in the transition state, a small molecule donates two electrons towards the ring formation with the diene component. The incoming small molecule may approach the diene in a linear or non-linear fashion thus giving rise to two different geometries. To explain the linear and non linear geometry let us consider the addition of a singlet carbene (:CCl_2) to an alkene to make a cyclopropane ring which is a [2+1] cycloaddition. A carbene is a neutral electrophile with six electrons in its valence shell. Due to this, carbenes are highly reactive, where a singlet carbene contains an empty p orbital and a sp^2 hybrid orbital that has two electrons.
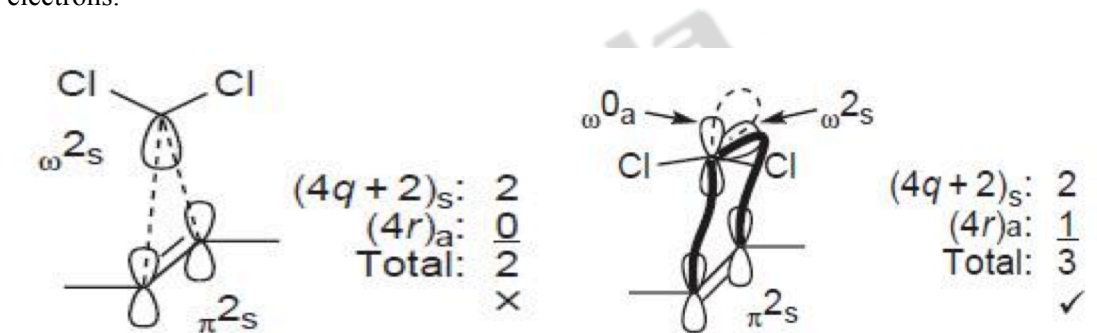

Linear arrangement   Non-linear arrangement

As can be seen (in the scheme) in the linear approach, the carbene (:CCl_2), with its two substituents lined up where they will be in the product, comes straight down into the middle of the double bond. Based on Woodward Hoffmann rules this linear approach addition of carbene is disallowed as the total number of coponents is even.

In the alternative nonlinear approach, in order to arrive in their proper orientation in the product the carbene approaches the double bond on its side, and then has the two substituents tilt upwards as the reaction proceeds. In this fashion, the carbene is effectively able to take up the role of the antarafacial component. Based on Woodward Hoffmann rules non-linear addition of carbene is allowed as the total number of coponents is odd in this case. Interestingly, similar to ketenes, it is possible for carbenes to connect up the orthogonal orbitals of diene in an antarafacial mode.

Heavy carbene analogues Stannylenes (R_2Sn:) are singlet species that react with dienes via a concerted thermal [2+4] cycloaddition which is a cheletropic reaction of the linear type allowed by the Woodward-Hoffmann rules to give cyclic products.

where X= CH(SiMe$_3$)$_2$
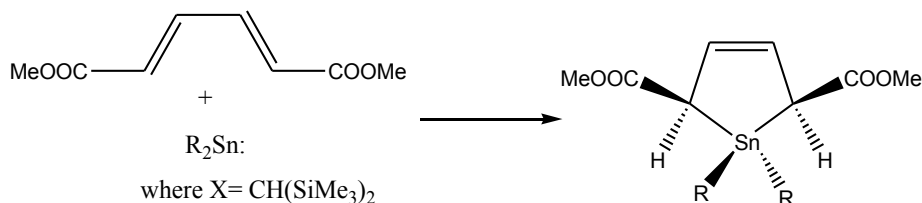
The reaction was reported to be possible only for most electron deficient dienes to give the cyclic product.

Let us now look at the application of Woodward-Hoffmann rules to cheletropic extrusion and addition of SO$_2$, which can take place via a suprafacial disrotatory electrocyclization or an antarafacial conrotatory electrocyclization, depending on the trajectory of SO$_2$.

Head on trajectory
Disrotatory, suprafacial

Side on trajectory
Conrotatory, suprafacial
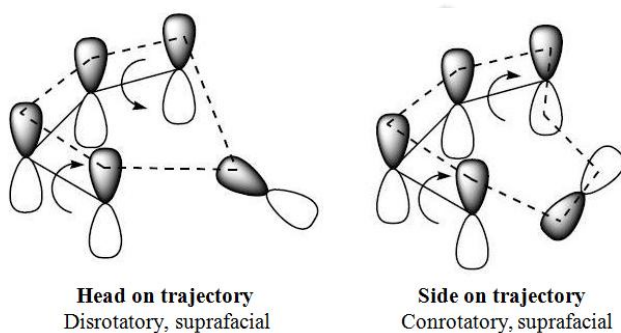
Extrusion of SO$_2$

Woodward-Hoffmann rules and geometry for the reverse of extrusion i.e. addition of SO$_2$ to diene are summarized in the following diagram.
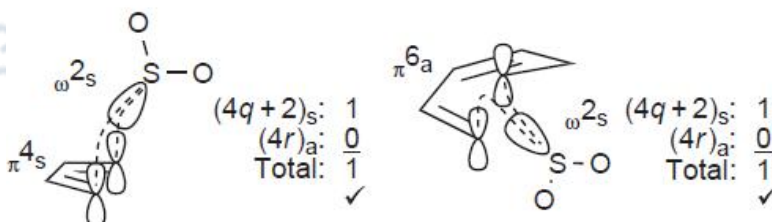
Addition of SO$_2$

The reaction between sulfur dioxide and butadiene also uses linear and non linear approaches, and are both allowed, according to Woodward-Hoffmann rules, the former because the total number of electrons (6) is a (4n+2) number, and the latter because the triene is flexible enough to take up the role of antarafacial component.

4. Examples of cheletropic reactions

The **Ramberg-Backlund** reaction is an important example of cheletropic reaction accompanying extrusion of sulfur dioxide. The reaction involves base-mediated conversion of α-halosulfones into E or Z alkenes. Z alkenes are often observed with weak bases, whereas strong bases give predominantly E alkenes. The overall transformation is the conversion of the carbon–sulfur bonds to a carbon-carbon double bond.
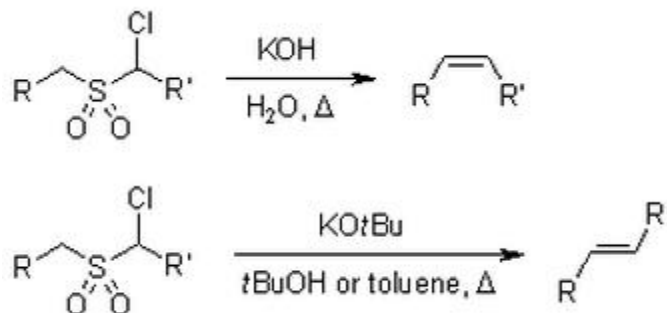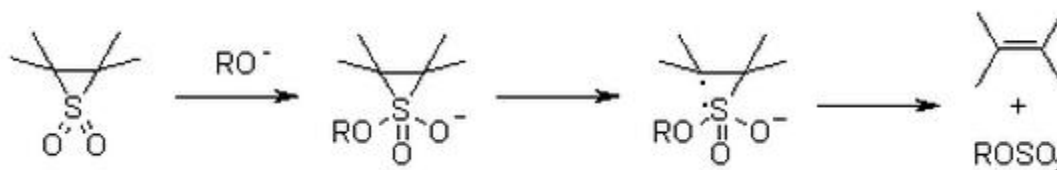
Mechanism of the Ramberg-Backlund Reaction

The anionic mechanism for the Ramberg-Backlund reaction includes a rapid deprotonation which is followed by a slow cyclization to generate a thiirane dioxide intermediate.
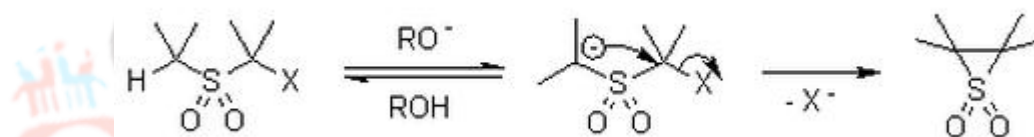
Formation of the thiirane dioxide is followed by extrusion of SO_2. The above elimination step is regarded as a concerted cycloelimination. The extrusion reaction might have a linear geometry and this would make the loss of SO_2 symmetry forbidden. Due to this reason, this step has somehow been suggested to involve a dipolar and diradical stepwise mechanisms by some researchers. Concentration of base highly influences the rate of the reaction, thus some facts about its mechanism i.e whether the successive decomposition involves a rotationally hindered diradical mechanism or a concerted symmetry-allowed non-linear cheletropic pathway has not been answered uptill now.

The radical anion mechanism

A refined verson of the Meyers' modification of the Ramberg-Backlund reaction employ CBr_2F_2 in the presence of alumina-supported KOH and tBuOH as solvent which allows the conversion of

α- and α'-hydrogen-bearing sulfones of various structural types into alkenes. An example is shown below;
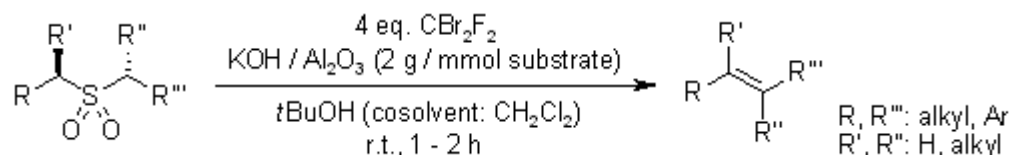

In another cheletropic extrusion reaction thermolysis of the substituted sulfone at 210 ºC in di-n-butyl phthalate solution generated the corresponding o-quinodimethanes by cheletropic elimination of SO_2 and led to the indicated polycycles by intramolecular [4+2]cycloaddition.
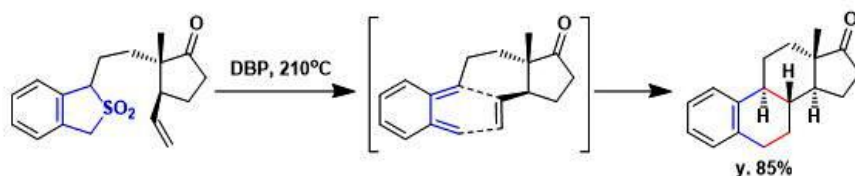
The [4 + 1] cycloaddition between a carbene and a diene give a cyclopentene adduct. For example, heating bis-heteroatom carbene, an oxadiazoline gave diastereomerically pure acetal in 80% yield.
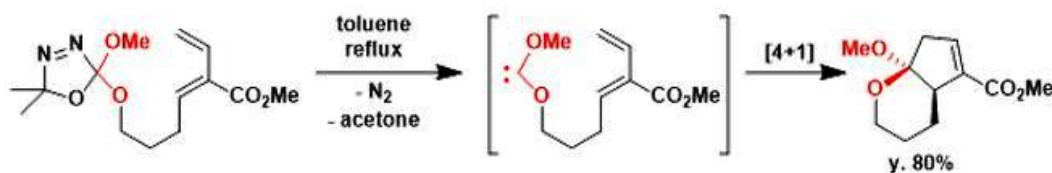

Annulenes are conjugated monocyclic hydrocarbons. Cheletropic elimination of CO from the product of following cycloaddition reaction leads to formation of annulenes.
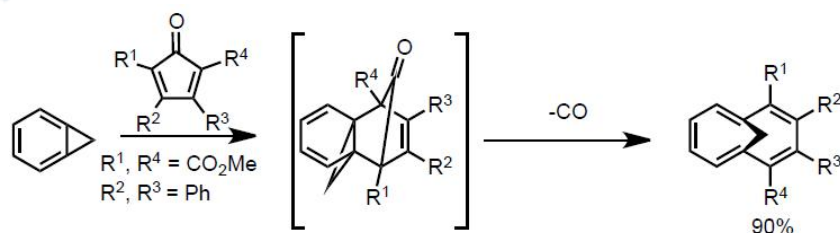
Nitrous oxide elimination from nitroso heterocyclic compounds such as shown below involves Chelotropic extrusion leading to formation of alkenes and NO. In the following series of compounds the molecules **1**, **2**, **5** and **6** were found to be thermally stable and thus do not undergo

fast cheletropic fragmentation. Rapid decomposition was observed only for nitroso aziridine **1** and compound **5** at a temperature below 0 °C and at 45 °C, respectively.
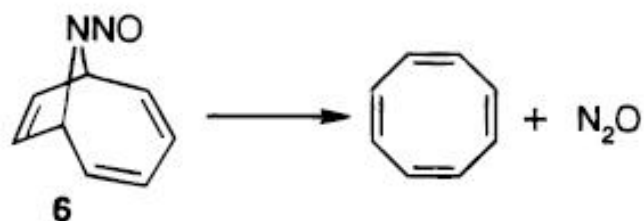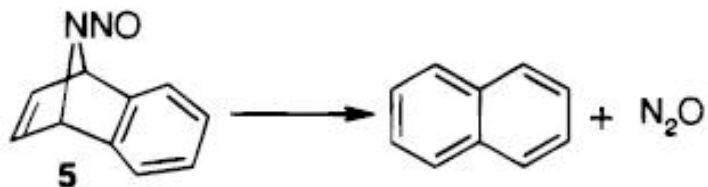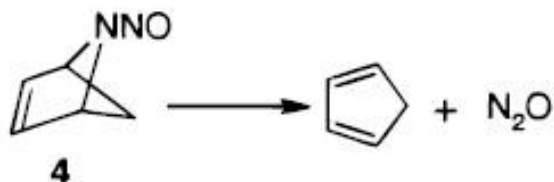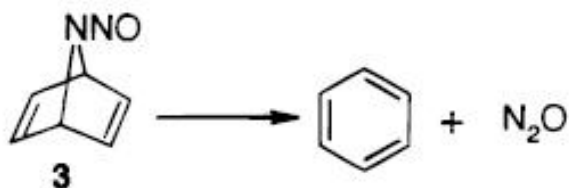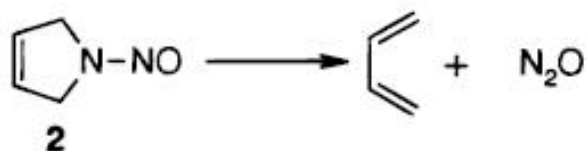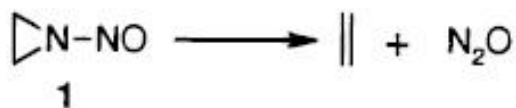
It was shown that ring strain is the critical factor for the cheletropic decomposition of cyclic nitrosoamines. Based on theoretical studies it was shown that the ring strain destabilizes the ground state of the nitrosoamines and increases the electron donor and acceptor abilities of the carbon-nitrogen bonds. This results in decrease in the activation barrier for the cheletropic fragmentation with increasing ring strain in the cyclic nitroso amines. Further, it was also shown that the cheletropic fragmentation proceeds via a highly asynchronous transition state with a (more or less) planar ring nitrogen atom with the exception of aziridine system took place.

In terpenes, taxanes forms a large family which comprises of over 350 members, out of which, the most famous one is Taxol (paclitaxel), which is a billion-dollar anticancer drug. The total synthesis of Taxane ring system involvs a cheletropic extrusion of sulphur dioxide..

Winkler's retrosynthetic analysis:
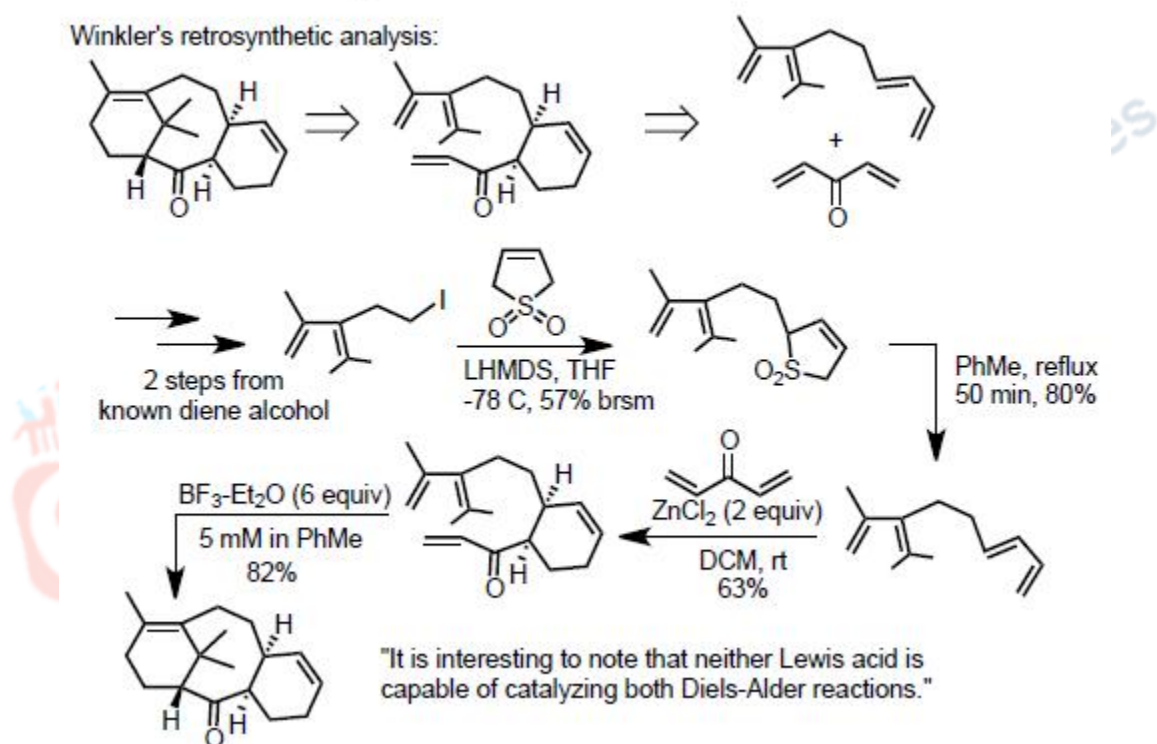
5. Summary

- ➢ Cheletropic reactions are a class of pericyclic cycloaddition reactions.
- ➢ Cheletropic reactions are those reactions where two σ bonds are made or broken to the same atom in the reagent.
- ➢ Like all other pericyclic reactions, cheletropic reactions are also reversible, concerted and include a cyclic transition state.
- ➢ Cheletropic extrusion reactions are the reverse of cheletropic addition reactions these are assisted by elimination of a stable molecule from the reactant such as nitrogen or carbon monoxide.
- ➢ The addition of sulphur dioxide to a diene is a classical example of [4+1] cycloaddition.
- ➢ Cheletropic reactions follow Woodward-Hoffmann rules. According to the rules the conjugated fragment of (4n+2) π electrons systems react in a disrotatory (conrotatory) mode in linear (non linear) reactions. In (4n) π electron systems it reacts in a disrotatory (conrotatory) mode in non linear reaction.
- ➢ Cheletropic addition reactions involve two geometries linear and non linear based on orientation of incoming molecule relative to the diene.
- ➢ Addition of carbine to double bond is an elegant example of cheletropic addition to double bond.
- ➢ Ramberg-Bucklund reaction is an important example of cheletropic extrusion reaction that leads to transformation of a carbon-sulfur bond to a carbon-carbon double bond.
- ➢ Nitrous oxide elimination from nitroso heterocycles are decided by ring strain in the system.
- ➢ The total synthesis of important anticancer agent taxane involves cheletropic extrusion reaction.