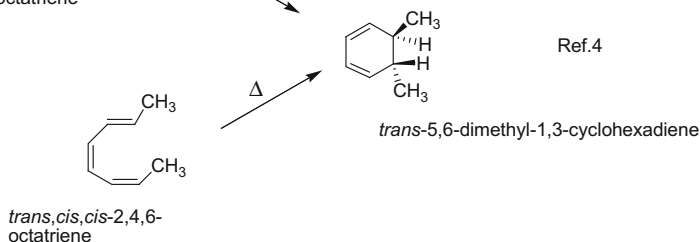
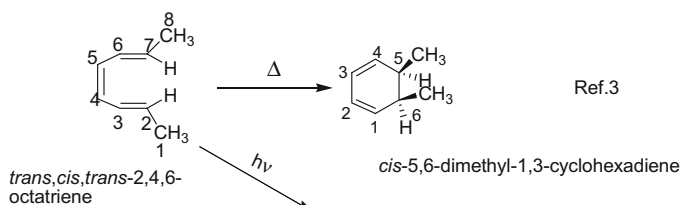
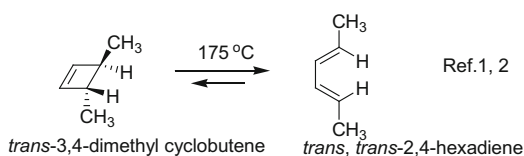
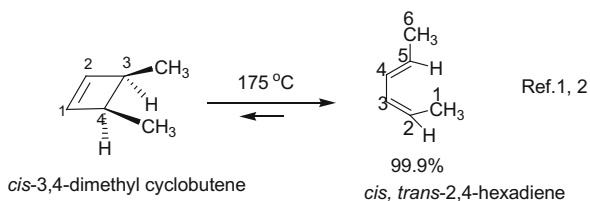


Chapter 2

Electrocyclic Reactions

2.1 Introduction

An electrocyclic reaction is defined as the thermal or photochemical conversion of an acyclic conjugated system into a ring system by formation of a σ bond between the ends of the conjugated system in a concerted process, or the reverse of this reaction. These reactions are reversible in nature.



2.2 Orbital Symmetry Basis for Stereospecificity

Woodward and Hoffmann [5] suggested a complete description of the mechanisms of these reactions by introducing the terms ‘conrotatory’ and ‘disrotatory’ motions of the groups at the termini of acyclic conjugated system or of the groups at the sp^3 carbons of a ring system. The motion of the substituents in the same direction clockwise or anticlockwise is known as conrotatory mode of motion, while the motion of the substituents in opposite direction is known as disrotatory mode of motion. They suggested that the stereochemistry of these reactions is controlled by the symmetry properties of HOMO (highest occupied molecular orbital) of the open-chain conjugated system. It was also supported by the frontier molecular orbital (FMO) theory [6].

For thermal reactions of $4n\pi$ conjugated systems, ψ_2 would be HOMO because it contains lowest number of nodes (one node) and provides a transition state of lowest energy similar to Mobius topology as per perturbation molecular orbital (PMO) theory. While for photochemical reactions of $4n\pi$ systems, ψ_3 would be HOMO because it is the first excited state of ground-state ψ_2 . Therefore, in thermal reactions of $4n\pi$ systems, conrotatory motion of the groups in the terminal carbons of the open-chain π system brings the lobes of the same phase for bonding with a Mobius type TS and is orbital symmetry allowed process, while disrotatory motion brings the lobes of the opposite phase for antibonding formation and is said to be orbital symmetry forbidden process. While for photochemical reactions of $4n\pi$ systems, disrotatory motion brings the lobes of same phase, and hence, the reaction will proceed with low activation energy and is said to be orbital symmetry allowed process. On the other hand, conrotatory motion brings the lobes of opposite phase, and hence, reaction is unfavourable for its high activation energy and is referred as symmetry forbidden reaction path (Fig. 2.1).

In case of thermal reactions of $4n+2\pi$ conjugated system, ψ_3 would be HOMO as it has minimum even nodes (two nodes) and is related to Huckel topology (as per PMO theory). Hence, the disrotatory motion of the groups of terminal carbons brings the lobes of same phase for bonding, involving a Huckel-type transition state and is said to be symmetry allowed path, while conrotatory motion would be symmetry forbidden path as it leads to a TS of high activation energy. For their photochemical reactions, ψ_4 would be HOMO and hence conrotatory motion would be symmetry allowed path (Fig. 2.2).

Woodward–Hoffmann rules for electrocyclic reactions are summarized in Table 2.1.

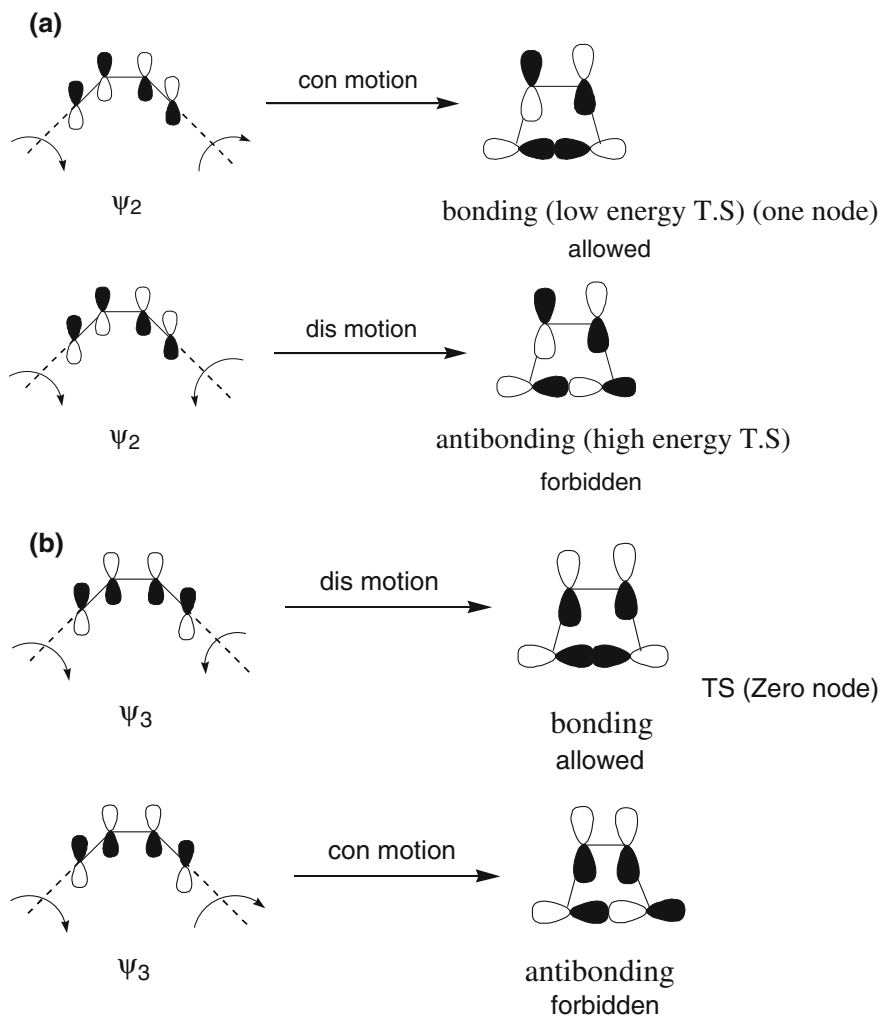


Fig. 2.1 **a** Thermal electrocycization of $4n\pi e$ conjugated system; **b** photochemical electrocycization of $4n\pi e$ conjugated system

2.3 The Orbital Correlation Diagrams of Reactants and Products

Longuet-Higgins and Abrahamson [6] suggested that in any concerted process, the orbitals of the starting material and product have the same symmetry. This is also supported by Woodward and Hoffmann [5]. The cyclobutene–butadiene interconversion may be considered as an example to verify the fact by construction of a correlation diagram. For cyclobutene, the bonding orbitals are σ and π , while the

Fig. 2.2 **a** Thermal electrocyclization of $4n+2$ π conjugated system; **b** photochemical electrocyclization of $4n+2$ π conjugated system

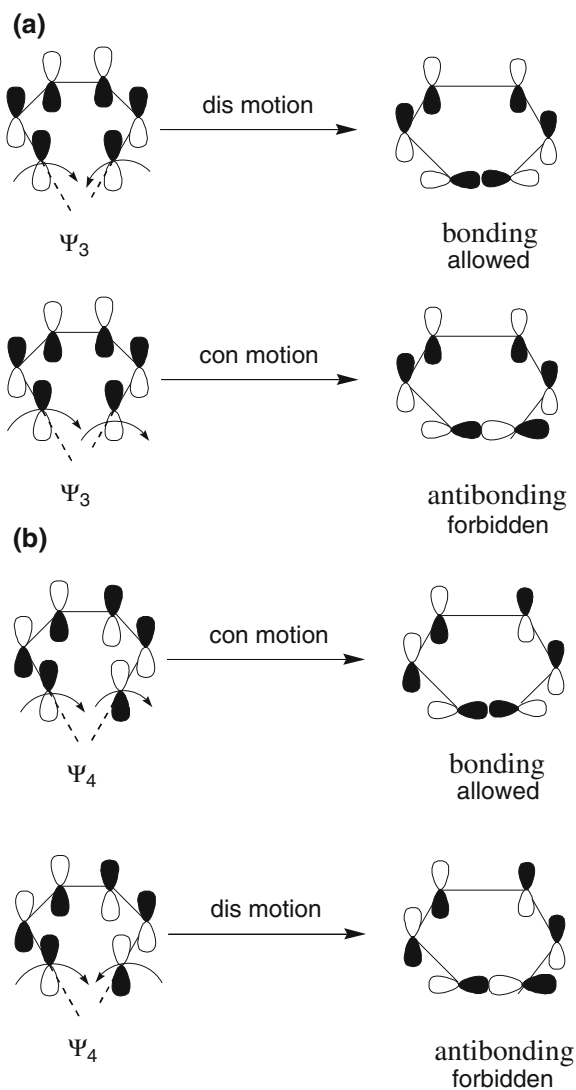


Table 2.1 Woodward–Hoffmann rules for electrocyclic reactions

Acyclic conjugated system	Reaction allowed	Motion
$4n$ π	Thermal	Conrotatory
	Photochemical	Disrotatory
$(4n+2)$ π	Thermal	Disrotatory
	Photochemical	Conrotatory

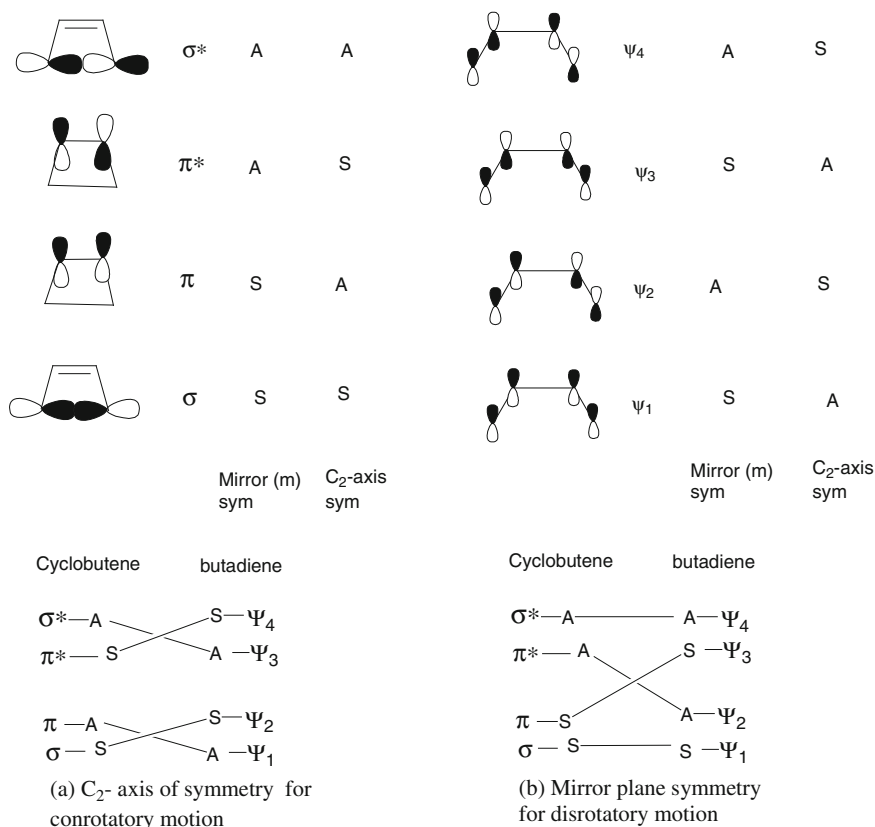


Fig. 2.3 **a** C_2 -axis of symmetry is maintained in thermal conversion of cyclobutene to butadiene; **b** mirror plane symmetry is maintained in photochemical conversion of cyclobutene to butadiene

antibonding orbitals are σ^* and π^* (Fig. 2.3). For butadiene, the bonding orbitals are ψ_1 and ψ_2 , and antibonding orbitals are ψ_3 and ψ_4 . In thermal reaction, conrotatory ring opening of cyclobutene to butadiene, C_2 (twofold) axis of symmetry is maintained throughout the reaction, while for photochemical reaction, disrotatory ring opening, a mirror plane (m) symmetry is maintained throughout the reaction (Fig. 2.3).

Next, consider the thermal conversion of a 1,3,5-hexatriene to a 1,3-cyclohexadiene by the disrotatory motion where mirror (m)-symmetry is maintained in the orbitals of the reactant and product (Fig. 2.4). In photochemical conversion of 1,3-cyclohexadiene into 1,3,5-hexatriene or vice versa, the C_2 -axis of symmetry is maintained in conrotatory motion of the termini groups (Fig. 2.4).

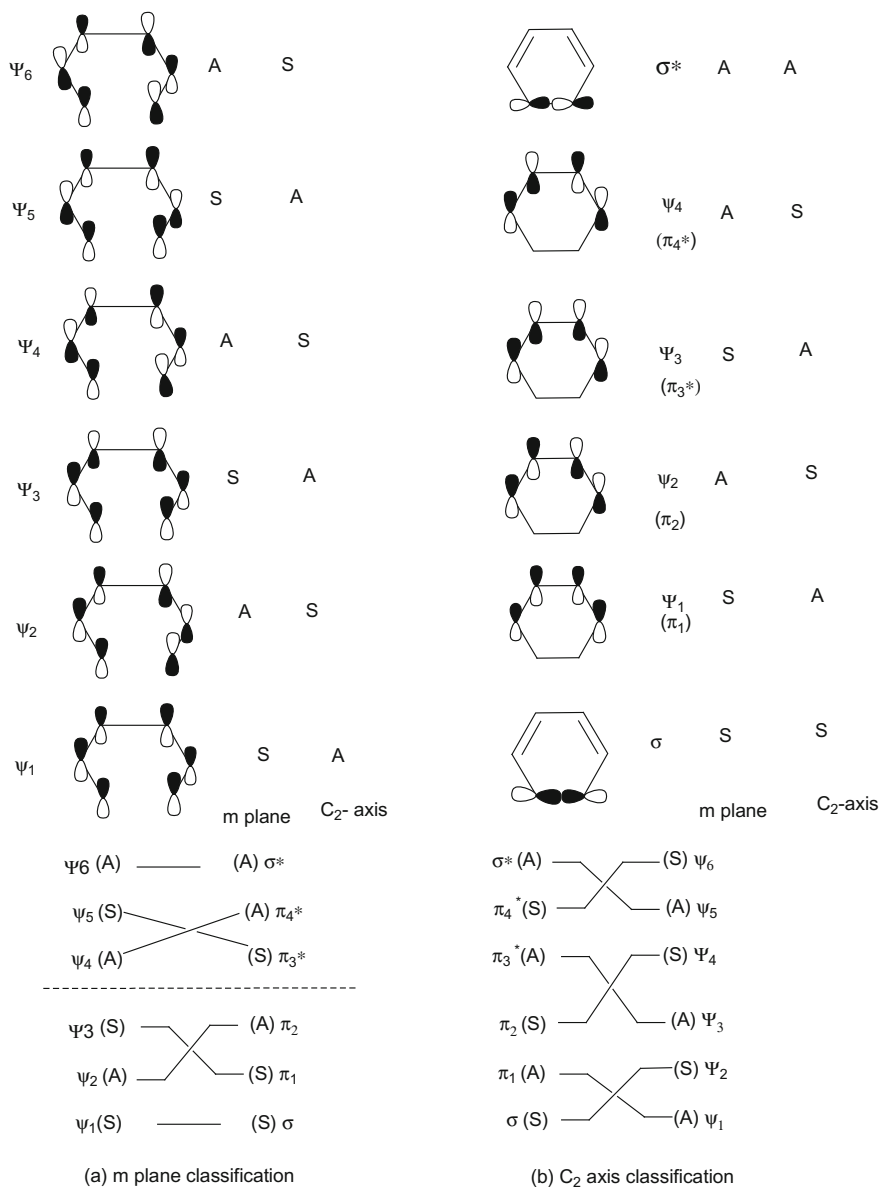
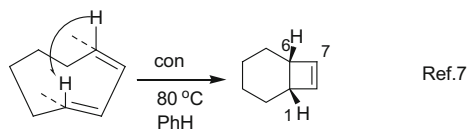


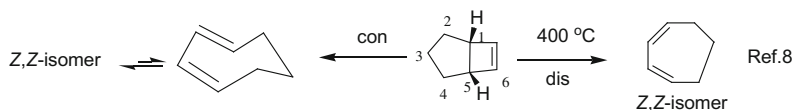
Fig. 2.4 **a** Mirror plane (m) symmetry is maintained in thermal conversion of 1,3,5-hexatriene into 1,3-cyclohexadiene; **b** C_2 -axis of symmetry is maintained in photochemical conversion of 1,3-cyclohexadiene into 1,3,5-hexatriene or vice versa

2.4 Applications of Neutral Conjugated Systems in Electrocyclic Reactions

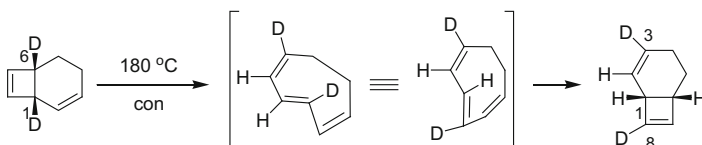
Electrocyclic reaction of *E*, *Z*-1, 3-cyclooctadiene leads to *cis*-bicyclo[4.2.0]-oct-7-ene because of strain associated with *trans* double bond.



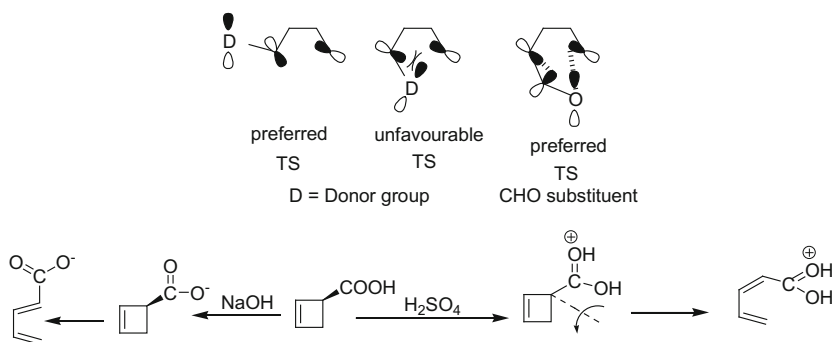
Although cyclobutenes are converted into butadienes on heating to get relief of ring strain, *cis*-bicyclo[3.2.0]-hept-6-ene on heating gave *Z,Z*-1,3-cycloheptadiene by forbidden disrotatory motion. This anomaly of the Woodward–Hoffmann rules can be accounted for by the stability of the product formed. In this case, allowed conrotatory motion gives the strained *E,Z*-1,3-cycloheptadiene, which is less stable due to ring strain and hence rapidly isomerizes to *Z,Z*-isomer at the reaction temperature in low yield.



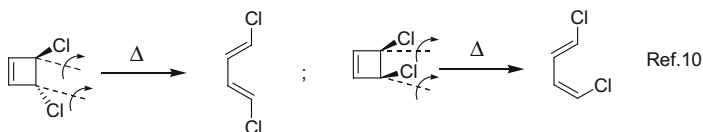
It was supported by the thermal conversion of *cis*-1,6-dideuterio-bicyclo[4.2.0]-oct-2,7-diene to *cis*-3,8-dideuterio-isomer via *trans*-isomer.



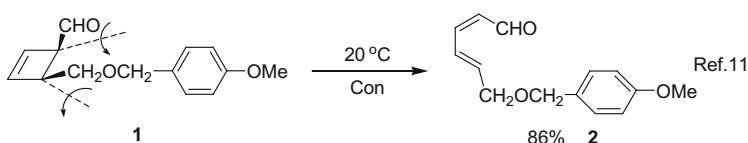
Cyclobutene-3-carboxylic acid on heating in acidic and basic solutions gives isomeric *cis*- and *trans*-pentadienoic acids [9]. In thermal ring opening of cyclobutenes, electron-donating substituents tend to move outward of the butadiene chains to minimize the repulsive interaction with π system of butadiene in the TS, while the π electron-accepting substituents tend to move inward of butadiene chains to stabilize the HOMO TS by interaction with the donor lobes of p-orbitals of breaking C(3)–C(4) σ bond. This preferential direction of movement of C(3) substituent in cyclobutene ring opening is called torquoselectivity and it works in ranges far beyond the 4π -electrocyclic system [9].



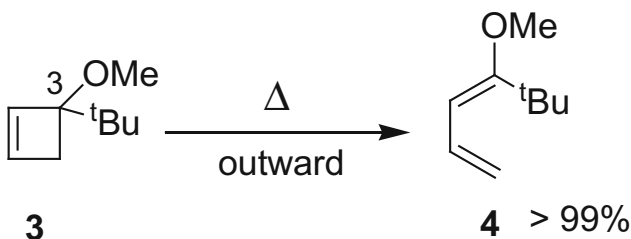
Study of the electrocyclic ring opening of *cis*- and *trans*-3,4-dichlorocyclobutenes indicated that *trans*-isomer reacts at lower temperature. This is due to ring opening by outward conrotatory motion of donor chlorine substituents while in case of *cis*-isomer, activation energy is higher as one of the chlorines rotates inward.



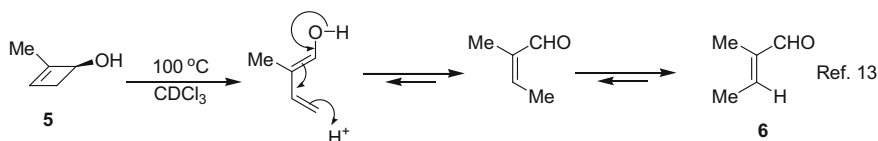
When a cyclobutene ring contains both electron-donating and electron-accepting substituents, conrotatory outward or inward motion of the substituents depends on the size of the substituents. Thus, **1** gives **2**.



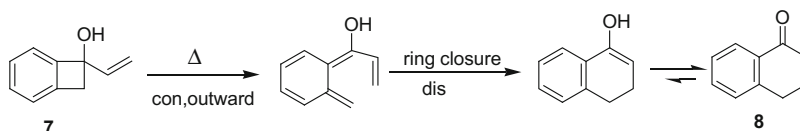
When a cyclobutene ring contains two electron-donating substituents at C-3 position, the substituent with greater donor ability will move outward [12]. For example, **3** gives **4**.



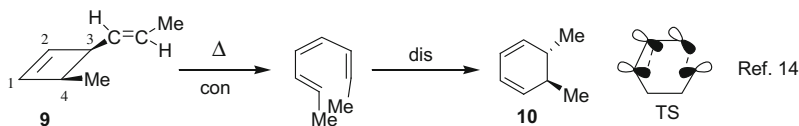
3-Hydroxy-2-methylcyclobutene **5** on electrocyclic ring opening undergoes keto-enol tautomerization to afford the product **6**.



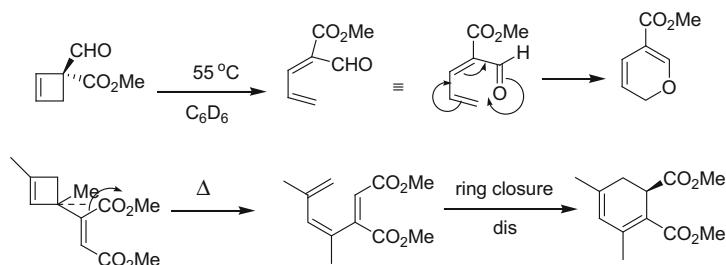
When a cyclobutene ring contains both donor hydroxyl and olefinic substituents at C-3, the inward con-motion of the olefinic substituent occurs preferentially to increase the stability of the TS. For example, **7** gives **8**.



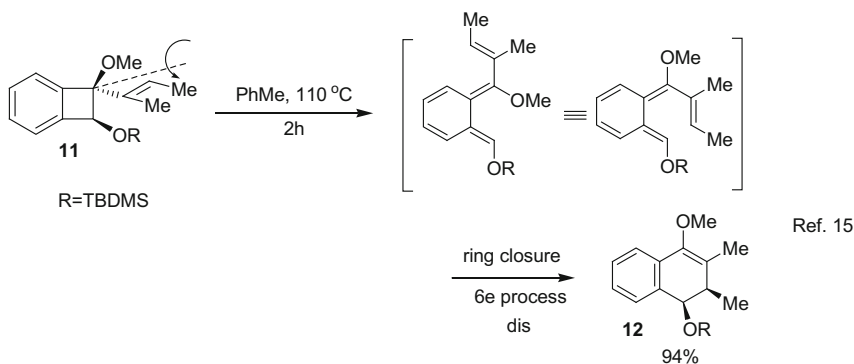
Cyclobutene **9** having olefinic function at C-3 or C-4 position undergoes inward ring opening from the olefinic substituent site followed by ring closure to give the product. This inward motion of the olefinic substituent stabilizes the HOMO of the TS by π -orbital interaction of the substituent with the donor lobes of p-orbitals of the breaking σ bond of the ring carbons [14].



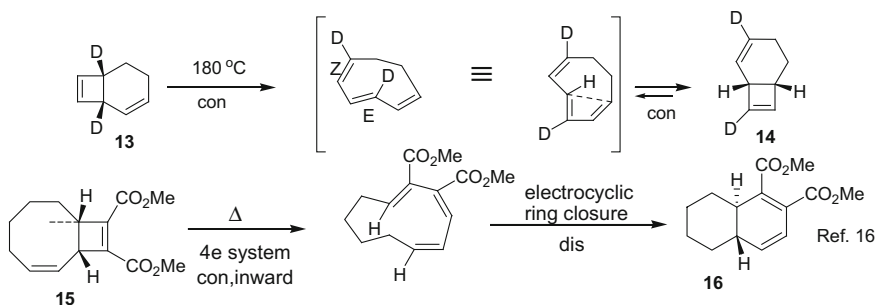
Similarly, when both electron-withdrawing substituents are present at C-3, inward conrotatory motion of the less bulky substituent takes place. When alkyl and olefinic substituents are present at C-3 or C-4 position, the olefinic substituent will move inward to provide more stable TS by closer interaction with the π -orbitals of C-1 and C-2. The following examples are illustrative [12].



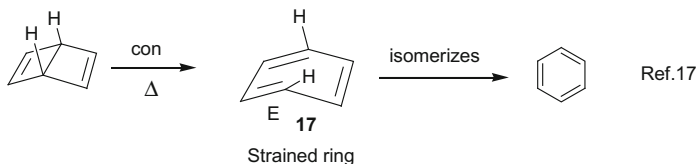
Cyclobutene **11** containing two *ortho*-alkoxy groups at C-3 and C-4 positions gives major product **12** by inward movement of smaller alkoxy group [15].



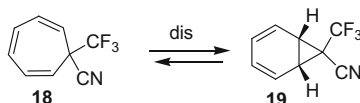
Cyclobutene fused with a carbocyclic ring gives isomeric product by more than one electrocyclic processes. For example, cyclobutene **13** gives **14** and cyclobutene **15** gives **16**.



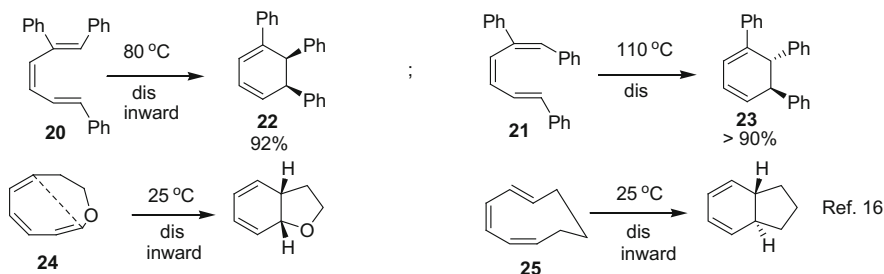
Dewar benzene having two cyclobutene rings on heating gives benzene rather than the expected product **17** from an allowed conrotatory opening. This is due to the presence of strained *E*-double bond in the expected product, which rapidly isomerizes to benzene.



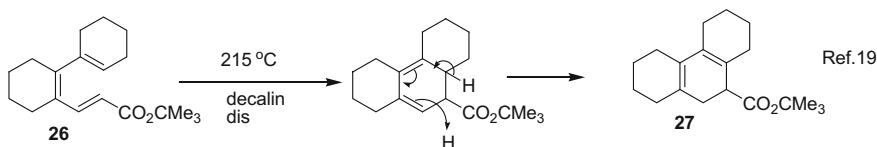
Heptatriene **18** having electron-withdrawing substituents, undergoes rapid conversion into bicyclo[4.1.0]-hepta-2,4-diene **19** and both the isomers remain in equilibrium because of low activation energy $E_a < 10$ kcal/mol. This transformation is known as valence tautomerism [18].



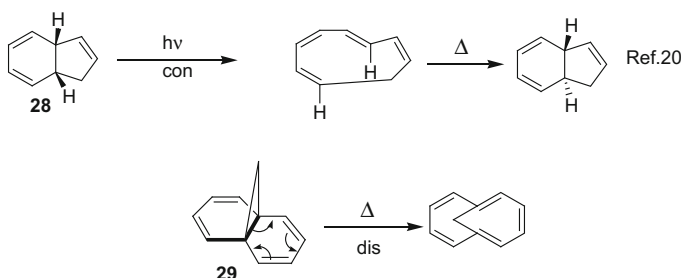
Triphenylhexatrienes **20** and **21** undergo ring closures by dis-motion to give **22** and **23**, respectively. Similarly, cyclic trienes **24** and **25** undergo allowed disrotatory reactions to give products.



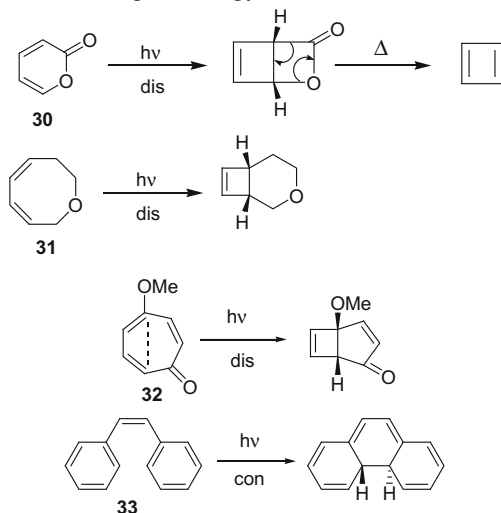
Substituted 1,3,5-hexatriene **26** on electrocyclicization, followed by isomerization gives **27**.



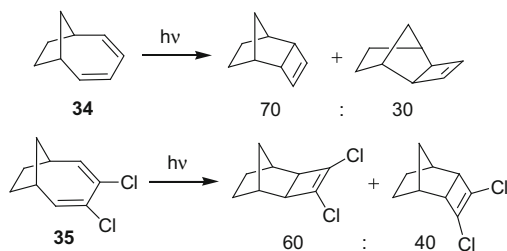
Bicyclic conjugated dienes **28** and **29** undergo ring opening by electrocyclic process.



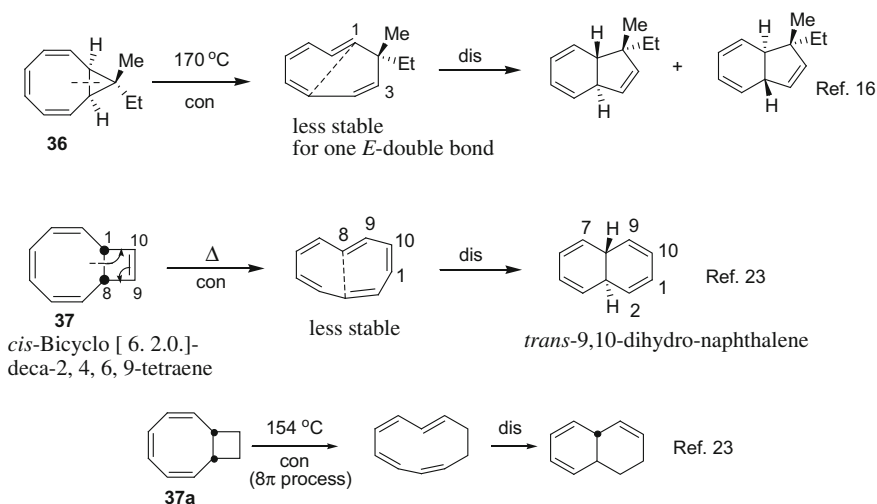
Some photochemical electrocyclic reactions take place to yield products of much higher energy than the starting materials [21]. For example, pyrone **30**, oxocin **31**, cyclic ketone **32** and *cis*-stilbene **33** undergo photo-induced allowed electrocyclization to give products of higher energy.



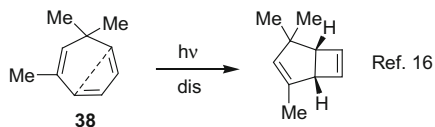
Light-induced electrocyclization of bicyclo-[4.2.1]-nona-2,4-dienes, **34** and **35** gives both *endo*- and *exo*-isomers. Direct irradiation of the unsubstituted diene gives *endo*-isomer as major product through a singlet excited state. The presence of heavy atom, such as chlorine in the diene system facilitates the ISC by spin-orbit coupling and increases the percentage of *exo*-isomer through triplet excited state. Use of photosensitizer gives *exo*-isomer as the major product [22].



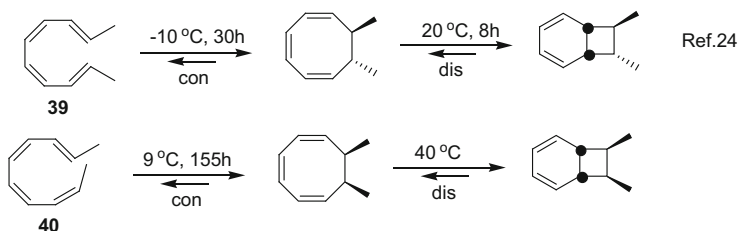
1, 3, 5-Trienes, **36**, **37** and **37a** in a ring system undergo double electrocyclic processes to yield stable products.



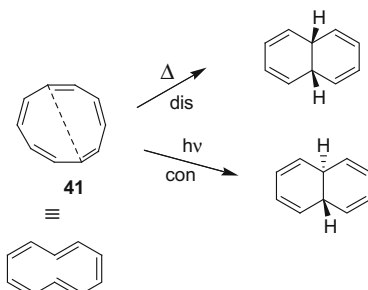
The presence of methyl substituents in cyclic 1, 3, 5-triene **38** causes cyclization involving 4π electrons. Due to steric interaction, one of the olefinic double bonds remains out of plane of other olefinic double bonds.



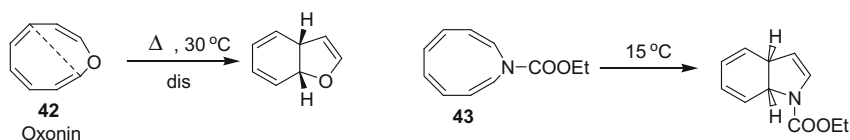
2, 4, 6, 8-Decatetraenes **39** and **40** undergo electrocyclic reactions near room temperature and maintain an equilibrium favouring the cyclooctatriene products. At slightly more elevated temperatures, the cyclooctatriene system undergoes another cyclization to produce bicyclo[4.2.0]-octa-2,4-diene.



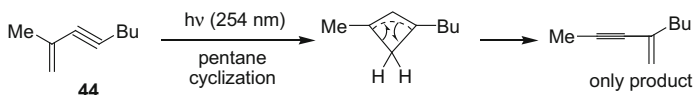
Conjugated decapentaene **41** undergoes electrocyclic ring closure using 6π because of nonplanarity of 10π .



Oxonin **42** and azonine **43** having a tetraene system undergo cyclization using their triene system to bicyclo[4.3.0] systems due to interaction of the lone pair of oxygen and nitrogen, respectively, with one double bond [25].

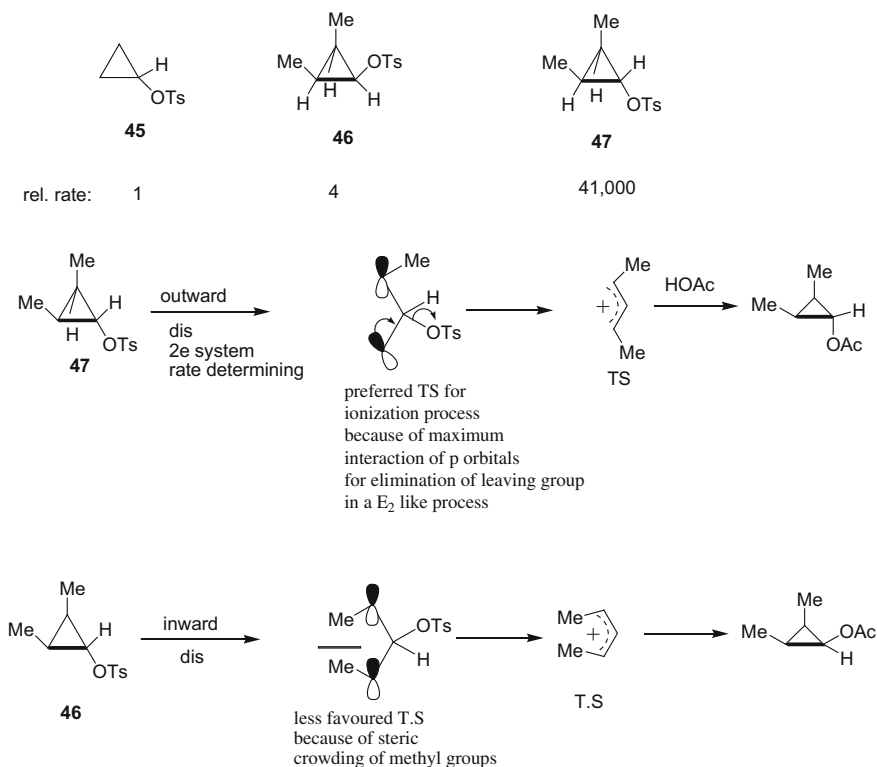


Acyclic conjugated enyne **44** in singlet excited state undergoes skeletal rearrangement via photoelectrocyclization to a highly strained 1,2-cyclobutadiene, followed by ground-state ring opening [26]. Calculation of energies of 1,2-cyclobutadiene suggested its planar geometry of C_2 -symmetry with the vinylic hydrogens twisted 6° out of plane.

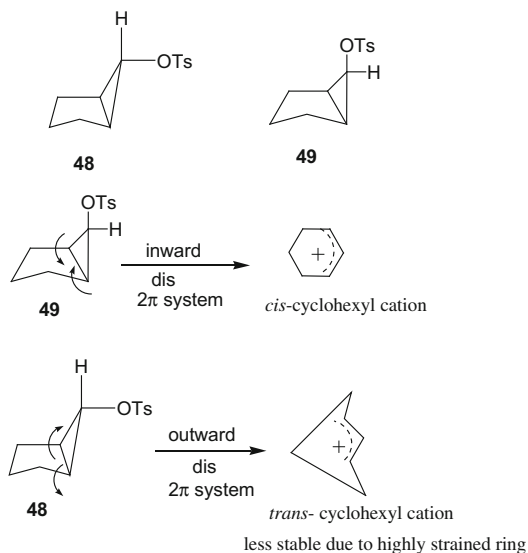


2.5 Applications of Ionic Conjugated Systems in Electrocyclic Reactions

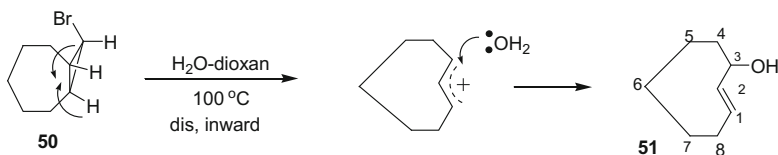
The acetolysis of isomeric cyclopropyl tosylates (**45**–**47**) at 100 °C takes place by concerted electrocyclic ring opening and ionization. The loss of tosyloxy group in ionization step is assisted by the electron density of the developing p-orbitals that are *trans* to the leaving group. Hence, the isomer **47** undergoes much faster acetolysis than the other isomers [27].



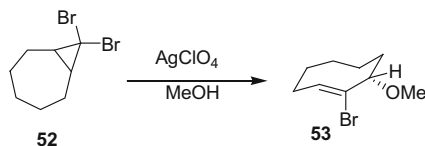
The rate of acetolysis of bicyclic tosylates **48** and **49** with acetic acid at 150 °C depends on the geometry of the generated allyl cation. Isomer **49** reacts about 2×10^6 times faster than **48** because in the former the reaction proceeds via the formation of stable cis-cyclohexenyl cation [28].



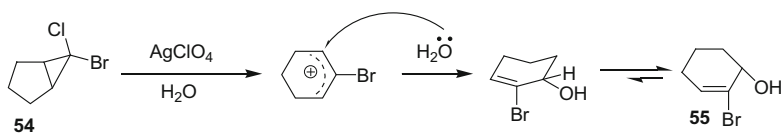
The similar electrocyclic reaction of bicyclic bromide **50** in aqueous dioxane at 100 °C gives *trans*-cyclooctene-3-ol **51** [29]. The generated *p*-orbitals from the breaking of a σ bond in cyclopropane ring by inward dis-motion participate in the removal of bromine atom in an E_2 -like process. The outward ring opening will provide less stable *trans*-cyclooctenyl cation.



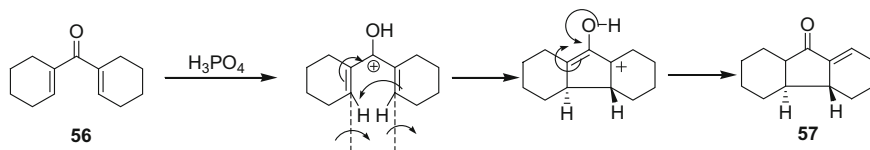
Methanolysis of bicyclic dibromide **52** with MeOH in the presence of AgClO_4 gives *trans* product **53** [30].



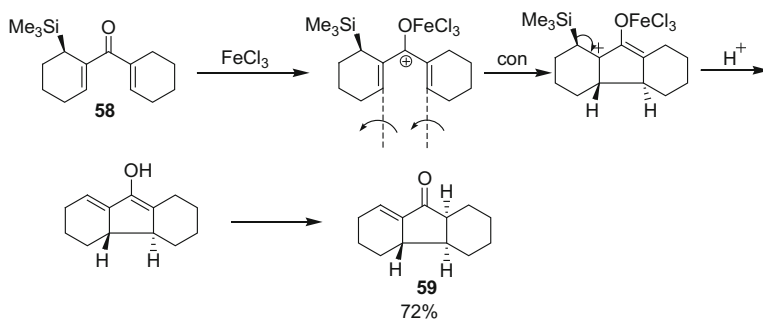
Hydrolysis of *endo*-2-chloro-*exo*-2-bromo-bicyclo[3.1.0]-hexane **54** gives 2-bromo-3-cyclohexenol **55** [16]. The inward disrotatory motion of ring opening is preferred because it provides the movement of *endo*-chlorine atom inside the cyclopropane ring to acquire an antigeometry with respect to electron-rich lobes of the *p*-orbitals generated by cleavage of a sigma bond of cyclopropane ring and helps to participate in an E_2 -like elimination process for faster elimination. Moreover, it provides a more stable *cis*-cyclohexenyl cation [16].



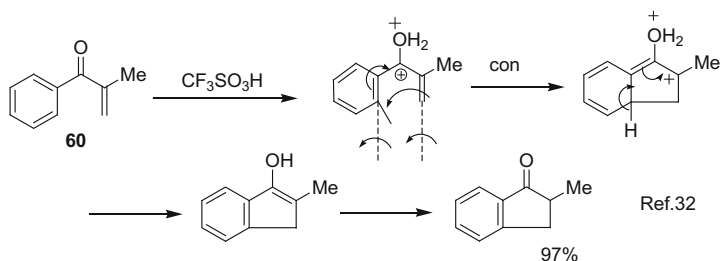
Acid-catalyzed cyclization of divinyl ketone **56–57** occurs by conrotatory cyclization of 3-hydroxy pentadienyl cation [31]. This type of cyclization reaction is known as Nazarov cyclization reaction [31].



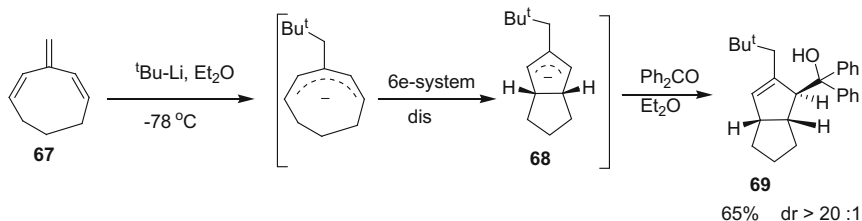
Divinyl ketone **58** undergoes Lewis acid-catalyzed electrocyclization to give **59** [21].



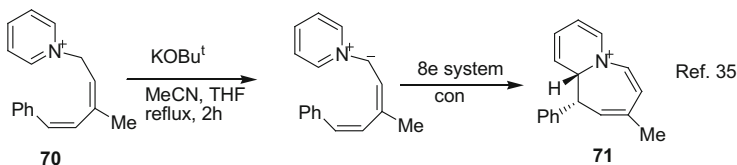
Similar electrocyclic ring closure occurs in aryl vinyl ketone **60** by strong acid.



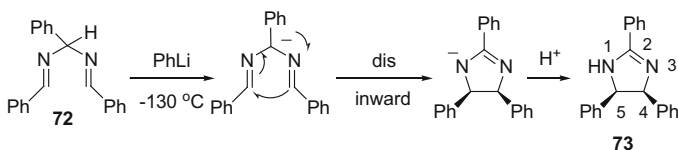
Cyclooctadienyl anion obtained from carbolithiation of 3-methylene-1,4-cyclooctadiene **67**, on electrocyclization gives a *cis*-bicyclo-product **68**, which on trapping with an electrophile gives *exo*-isomer **69** as major product [33].



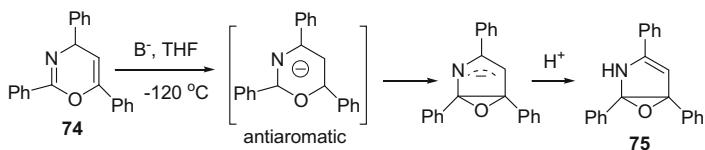
Butadienyl pyridinium ylide **70** on electrocyclization gives stereoselective 1,2-annulated-2,3-dihydroazepine **71** as major product [35].



Hydrobenzamide **72** on treatment with phenyl lithium gives a pentadienyl anion, which on electrocyclization gives dihydroimidazole, amarine **73** [36].

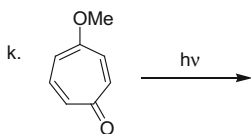
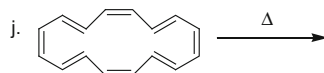
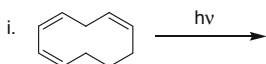
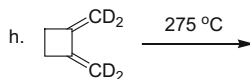
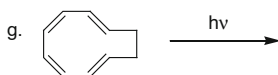
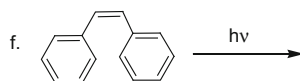
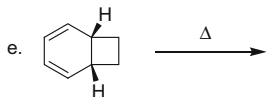
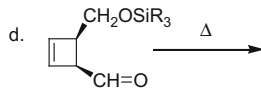
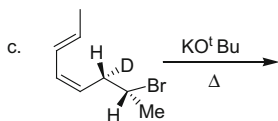
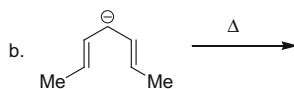
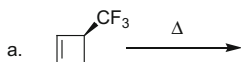


Similarly, heterocyclic compound **74** in the presence of a strong base gives **75** by disrotatory reaction [36].

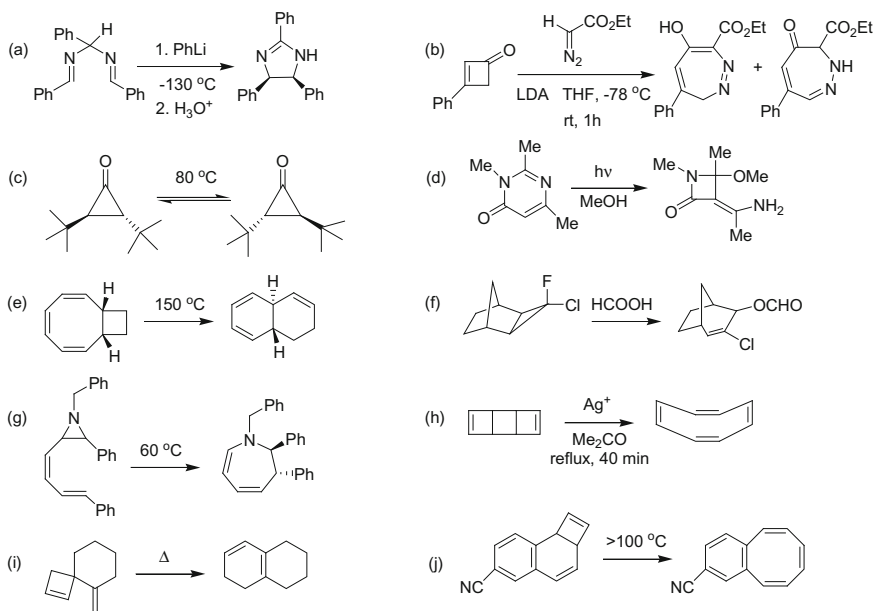


2.6 Problems

2.6.1. Predict the structure, including stereochemistry, of the product for each of the following reactions.

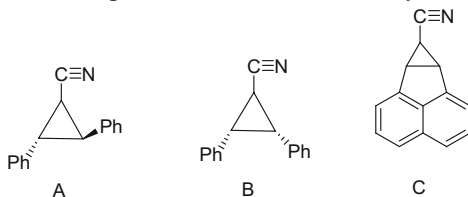


2.6.2 Rationalize the following reactions.

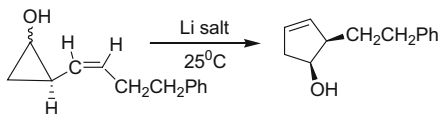


2.6.3. Offer a mechanistic explanation for each of the following observations.

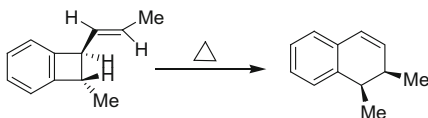
a. It has been found that both compound A and B undergo ring opening about 10^4 times faster than C in the presence of lithium di-*t*-butylamide.



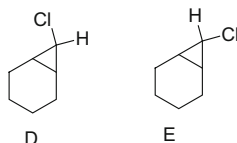
b. 2-Vinylcyclopropanols undergo facile rearrangement to give cyclopent-3-enols.



c.



d. Compound D undergoes solvolysis readily with AcOH at 125 °C, whereas compound E remains unchanged on prolonged heating with AcOH at 210 °C.



2.7 Further Reading

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