

**M.Sc. Semester-IV
Core Course-9 (CC-9)
Synthetic Organic Chemistry**



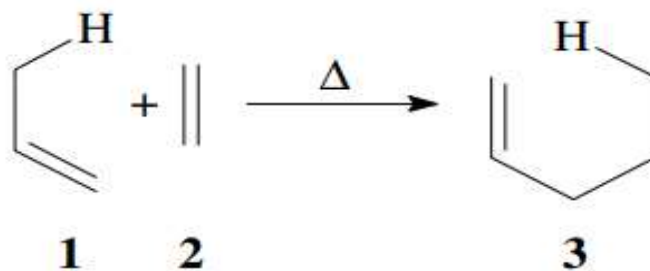
**II. Pericyclic Reactions
10. Ene Reaction**



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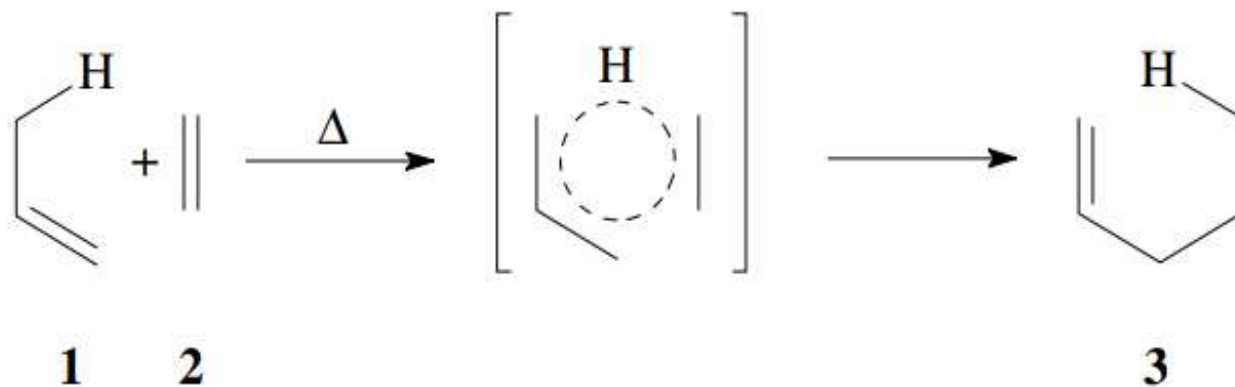
Ene Reaction

Addition of a double bond to an alkene with allylic hydrogen

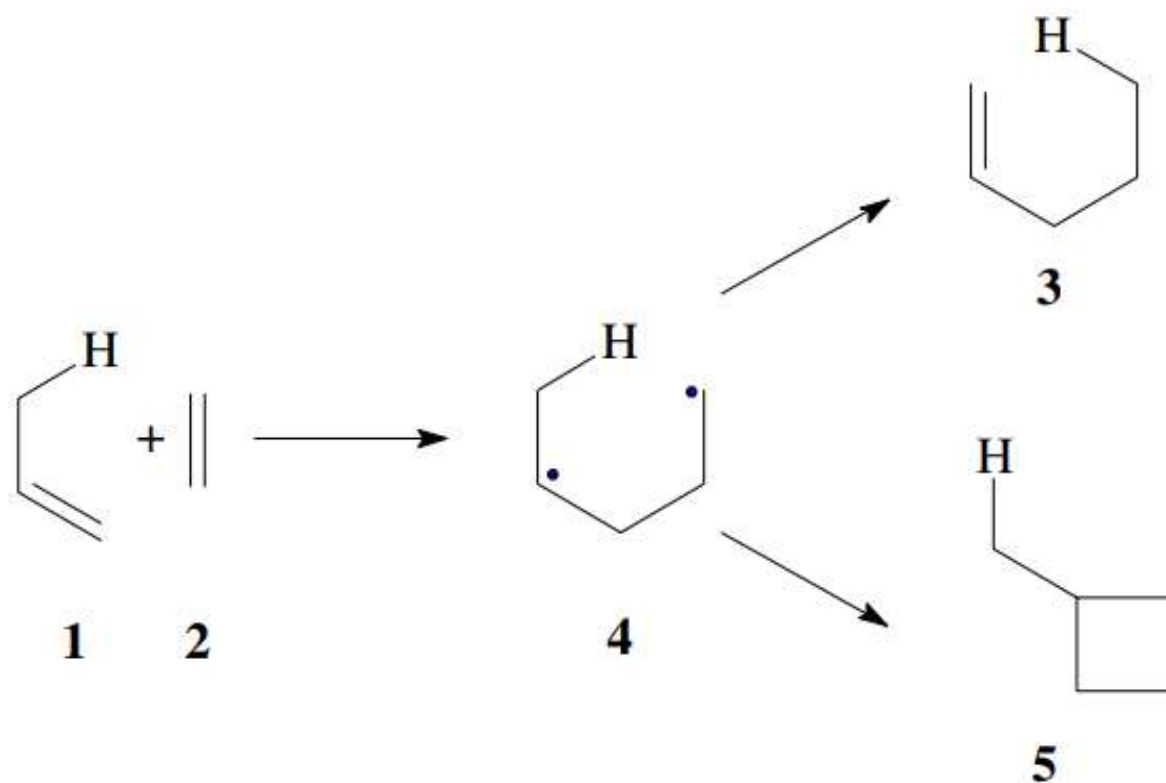


The *ene reaction* as a reaction principle has been first recognized and systematically investigated by *Alder*.¹ It is a thermal addition reaction of a double bond species **2**—the *enophile*—and an alkene **1**—the *ene*—that has at least one allylic hydrogen.² The intramolecular variant³ is of greater synthetic importance than is the intermolecular reaction.

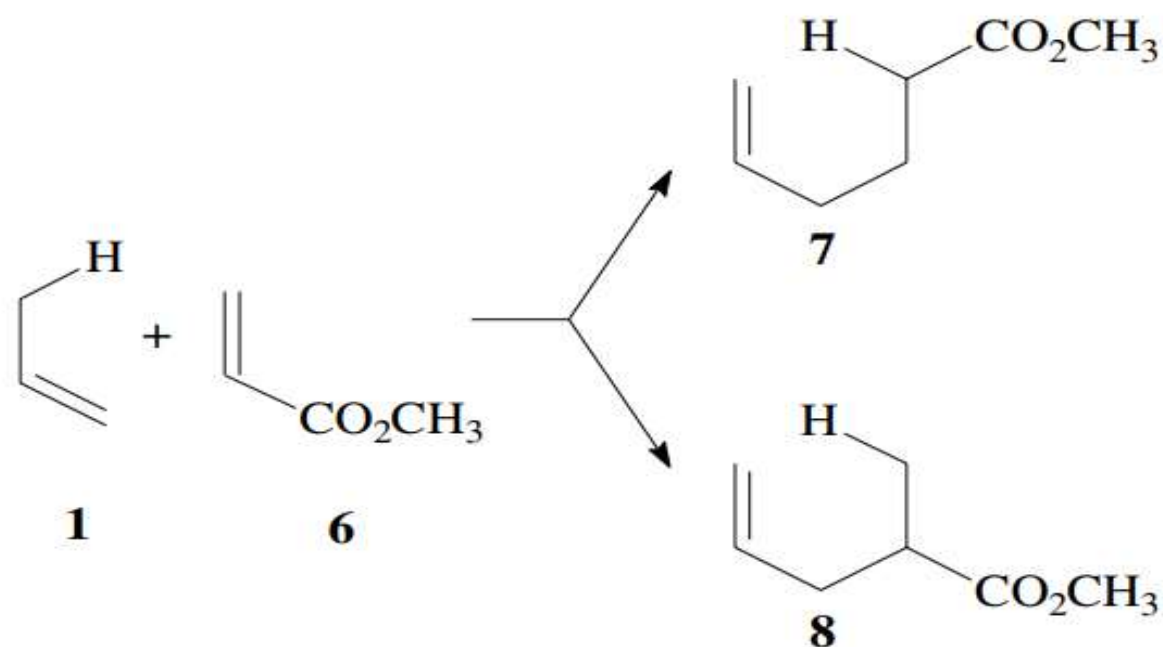
Just like the *Diels Alder reaction* or the 1,5-sigmatropic hydrogen shift, the ene reaction is believed to proceed *via* a six-membered aromatic transition state.



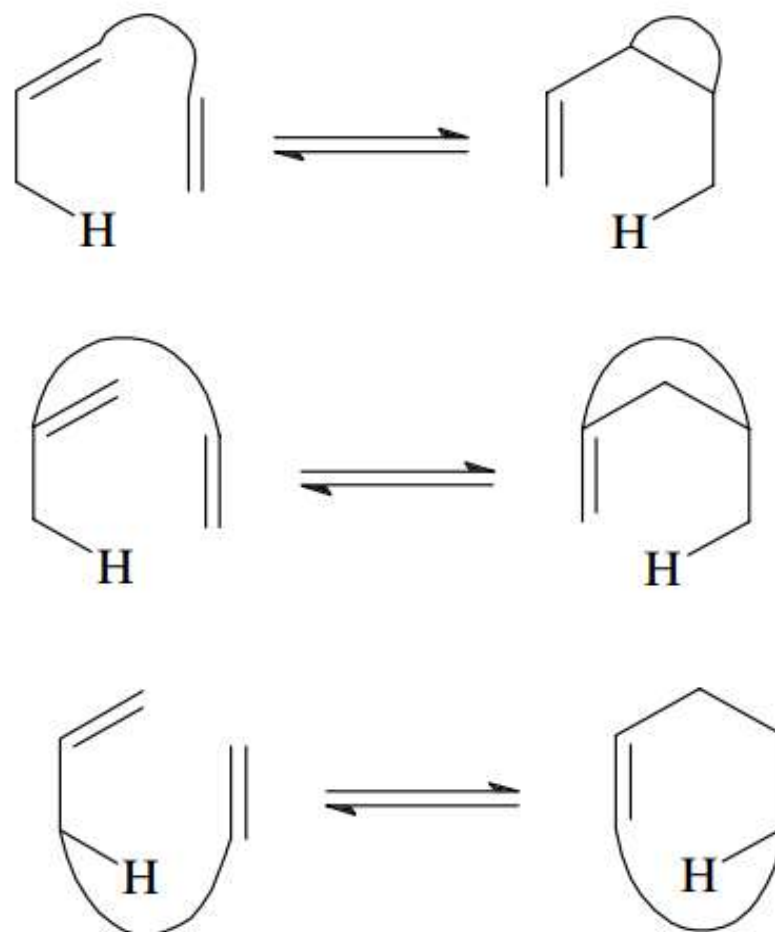
The overall reaction includes allylic transposition of a double bond, migration of the allylic hydrogen and formation of a bond between ene and enophile. Experimental findings suggest a concerted mechanism. Alternatively a diradical species **4** might be formed as intermediate; however such a species should also give rise to formation of a cyclobutane derivative **5** as a side-product. If such a by-product is not observed, one might exclude the diradical pathway:



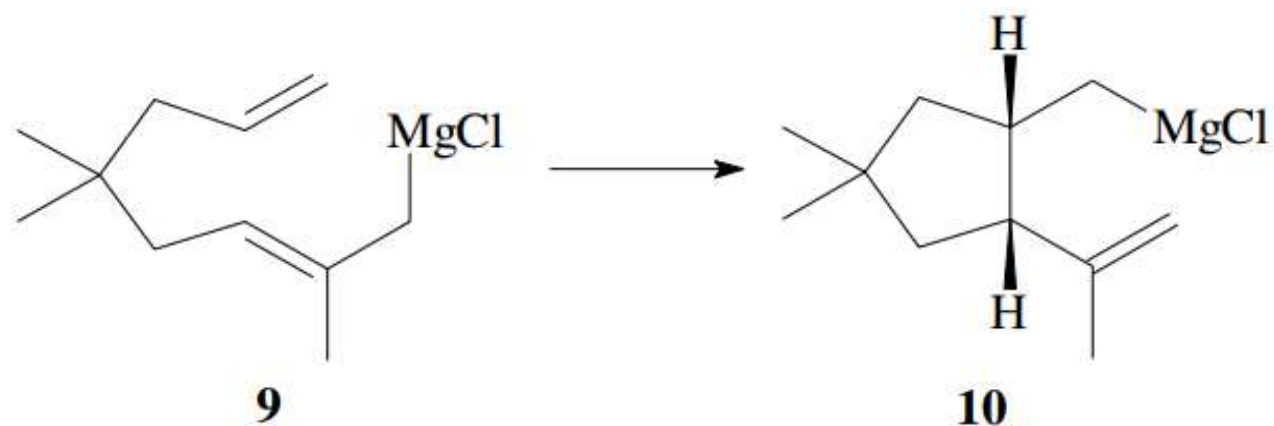
A primary allylic hydrogen at the ene **1** is especially reactive; a secondary hydrogen migrates less facile, and a tertiary one is even less reactive. The enophile unit should be of an electron-poor nature; it can consist of a carbon-carbon double or triple bond, a carbonyl group or an azo group. Mixtures of regioisomeric products may be obtained with substituted enophiles. The acrylic ester **6** reacts with propene **1** to give the regioisomers **7** (88%) and **8** (12%):



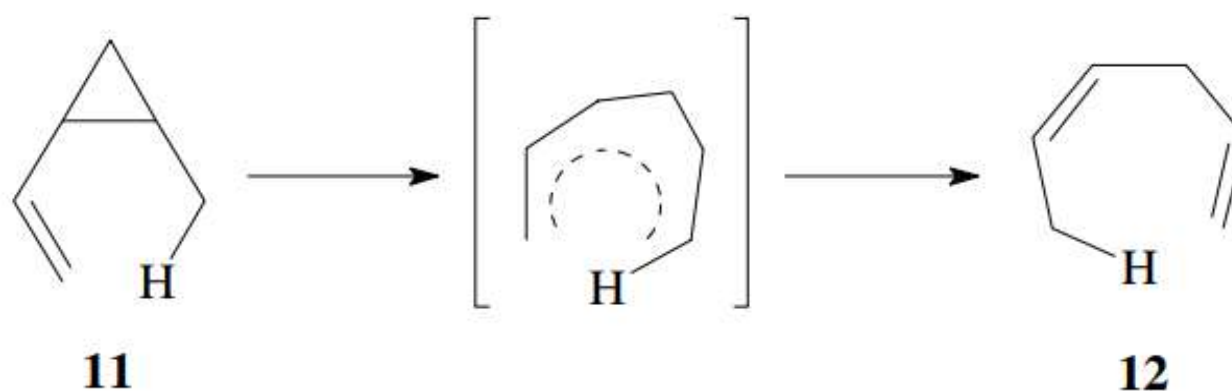
For the intramolecular variant, synthetically valuable applications have been developed during the last decade.⁴⁻⁶ Three types of intramolecular ene reactions are formulated—depending on the structure of the starting material:³



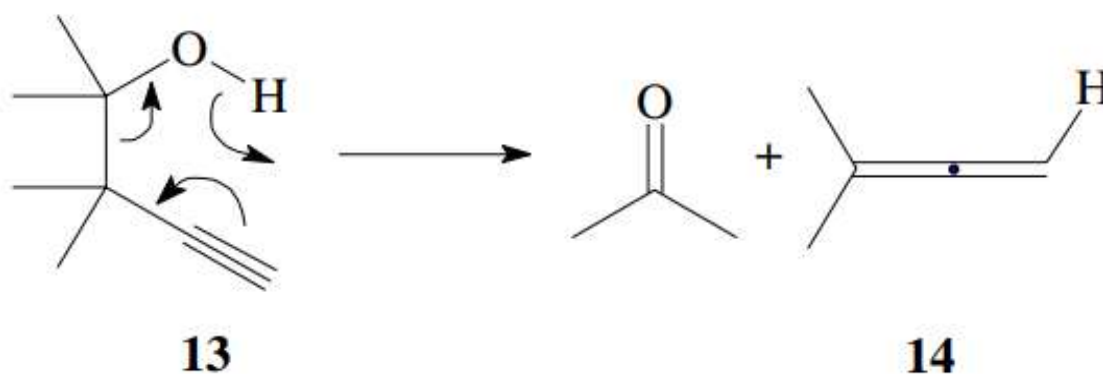
A modern variant is the intramolecular *magnesium-ene reaction*, e.g. the reaction of the alkene-allylic-Grignard compound **9** to give the five-membered ring product **10**. This reaction proceeds regio- and stereoselectively, and is a key step in a synthesis of the sesquiterpenoid 6-protoilludene:⁶



The *retro-ene reaction* also is of synthetic importance. While the application of high pressure facilitates the ene reaction, the retro-ene reaction is favored at higher temperatures.² Furthermore small-ring strain can shift the equilibrium towards the side of the dienes. The vinylcyclopropane **11** rearranges by a synchronous process to the open-chain diene **12**. Formally this process is the reverse of an intramolecular ene reaction:



β -Hydroxyalkenes are especially suitable starting materials for the retro-ene reaction; since a stable carbonyl compound is then released as product. The retro-ene reaction of β -hydroxyalkynes, e.g. **13** \rightarrow **14**, can be used for the preparation of allenes:^{7,8}



The reaction conditions for the ene reaction of simple starting materials are, for example, 220 °C for 20 h in an aromatic solvent like trichlorobenzene. Lewis acid-catalyzed intramolecular reactions have been described, e.g. with FeCl₃ in dichloromethane at -78 °C.⁴ Yields strongly depend on substrate structure.

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