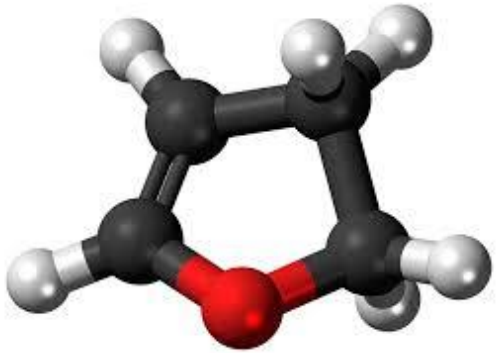
2302687 – Heterocyclic Compounds – Part I

Lecture 2-4

Heteroaromatic Synthesis via Pericyclic Reactions



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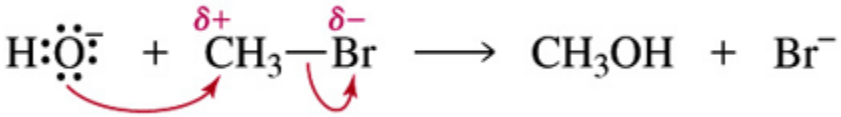
Recommended Textbook:

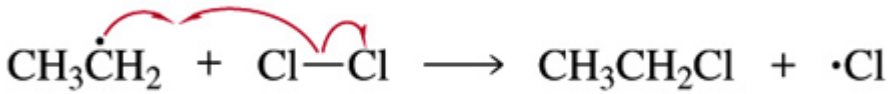
Heterocyclic Chemistry, 5th Edition, J. A. Joule, K. Mills, **2010**, Wiley

Types of Organic Reactions

Polar Reaction



Radical Reaction



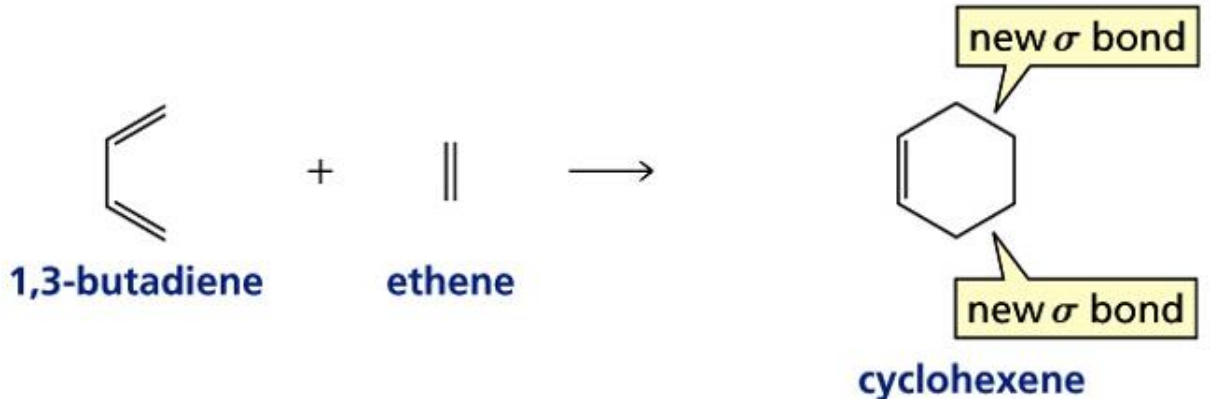
Pericyclic Reactions : a reaction that occurs as a result of reorganizing the electrons in the reactant(s)

Oxidation/Reduction

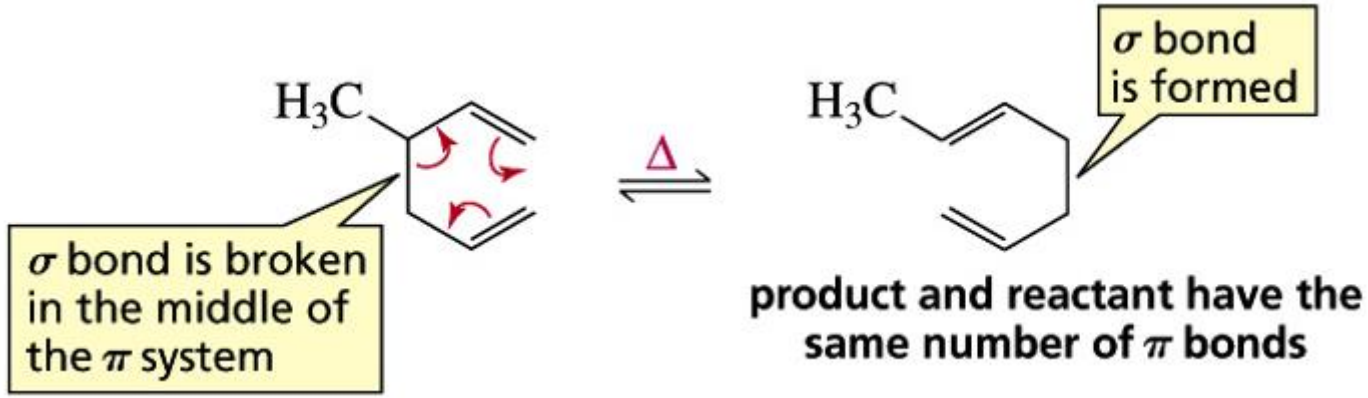
Types of Pericyclic Reactions

1) Electrocyclic

2) Cycloaddition



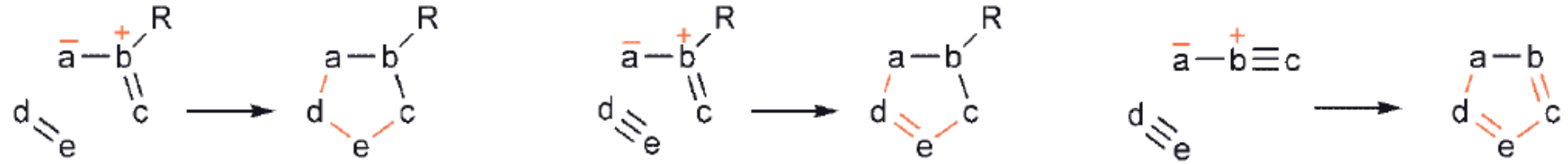
3) Sigmatropic rearrangements



Synthesis – Pericyclic Reactions

- **1,3-Dipolar cycloadditions** produce 5-membered heterocycles

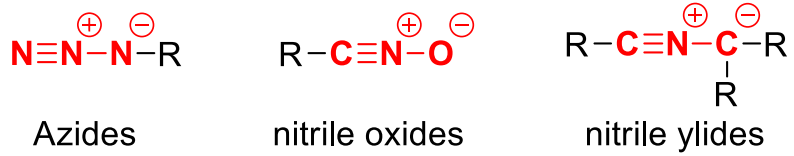
1,3-Dipoles



Dipolarophiles

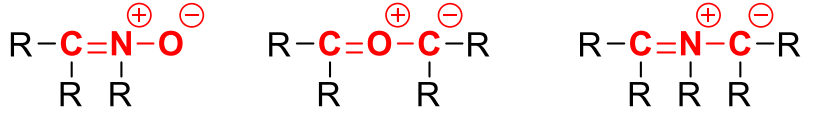
- **1,3-Dipoles** always contain a **heteroatom as the central atom** of the trio, either sp or sp^2 hybridised; for examples

sp :



Azides | nitrile oxides | nitrile ylides

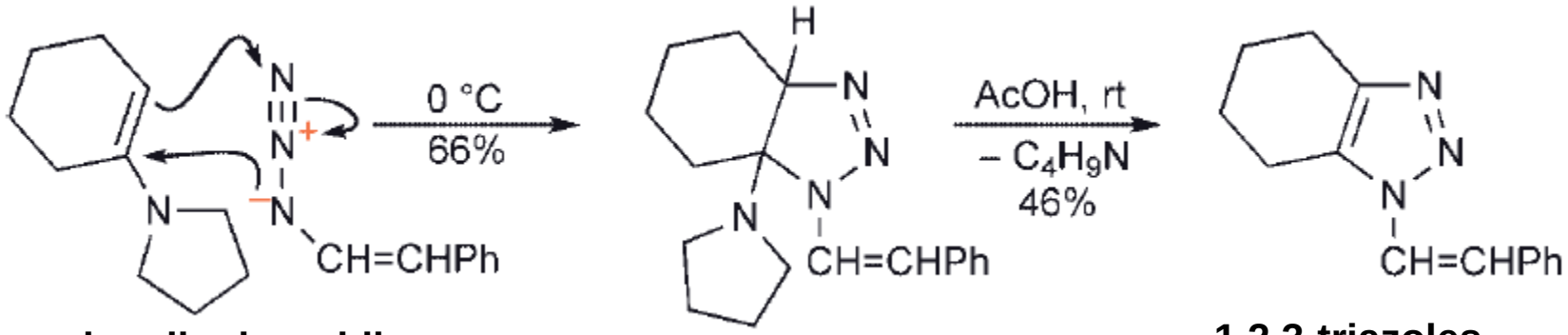
sp^2 :



Isocyanates | carbonyl ylides | azomethine ylides

Synthesis – Pericyclic Reactions

- **Alkene dipolarophiles**, with a group that can be eliminated following cycloaddition, give the same result as equivalent alkyne dipolarophiles

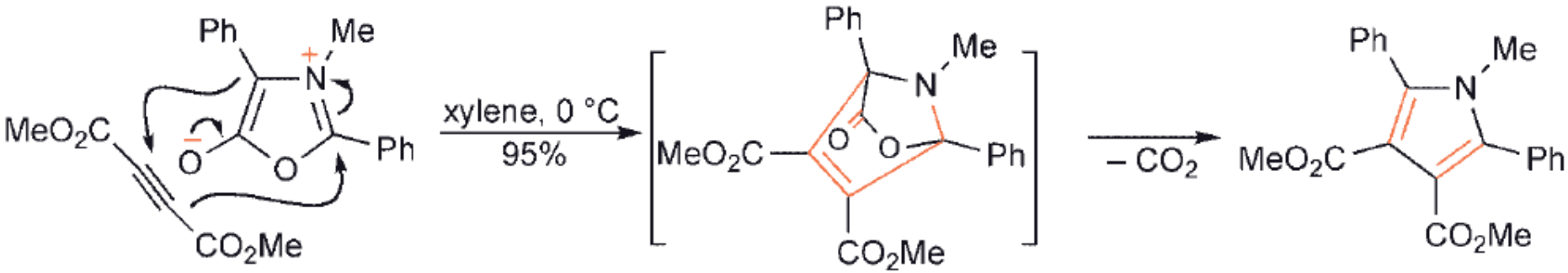


Enamine dipolarophile

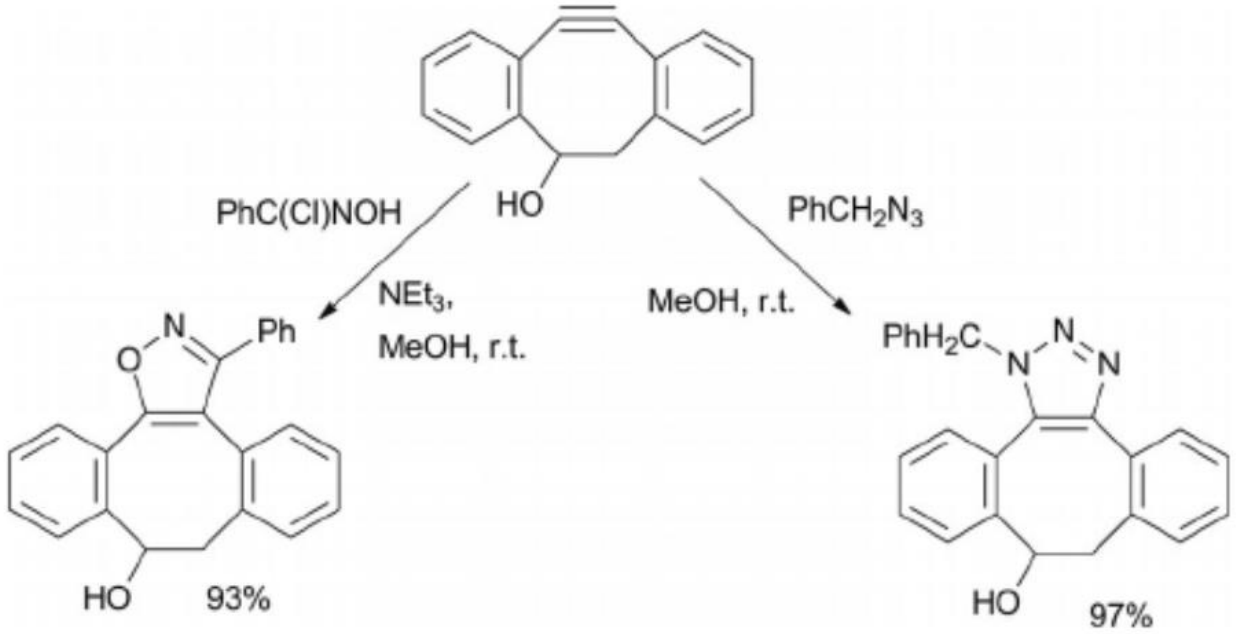
1,2,3-triazoles

Synthesis – Pericyclic Reactions

- Many **mesoionic substances** can act as 1,3-dipoles, and, after *elimination of a small molecule* – carbon dioxide in the example shown – produce aromatic heterocycles



Example:


PhC(Cl)NOH
NEt3,
MeOH, r.t.
HO
PhCH2N3
MeOH, r.t.
N
O
Ph
HO
93%
PhH2C
N
N
N
HO
97%