

DIELS ALDER
nella sintesi di
STEROIDI
(vedi approfondimento)

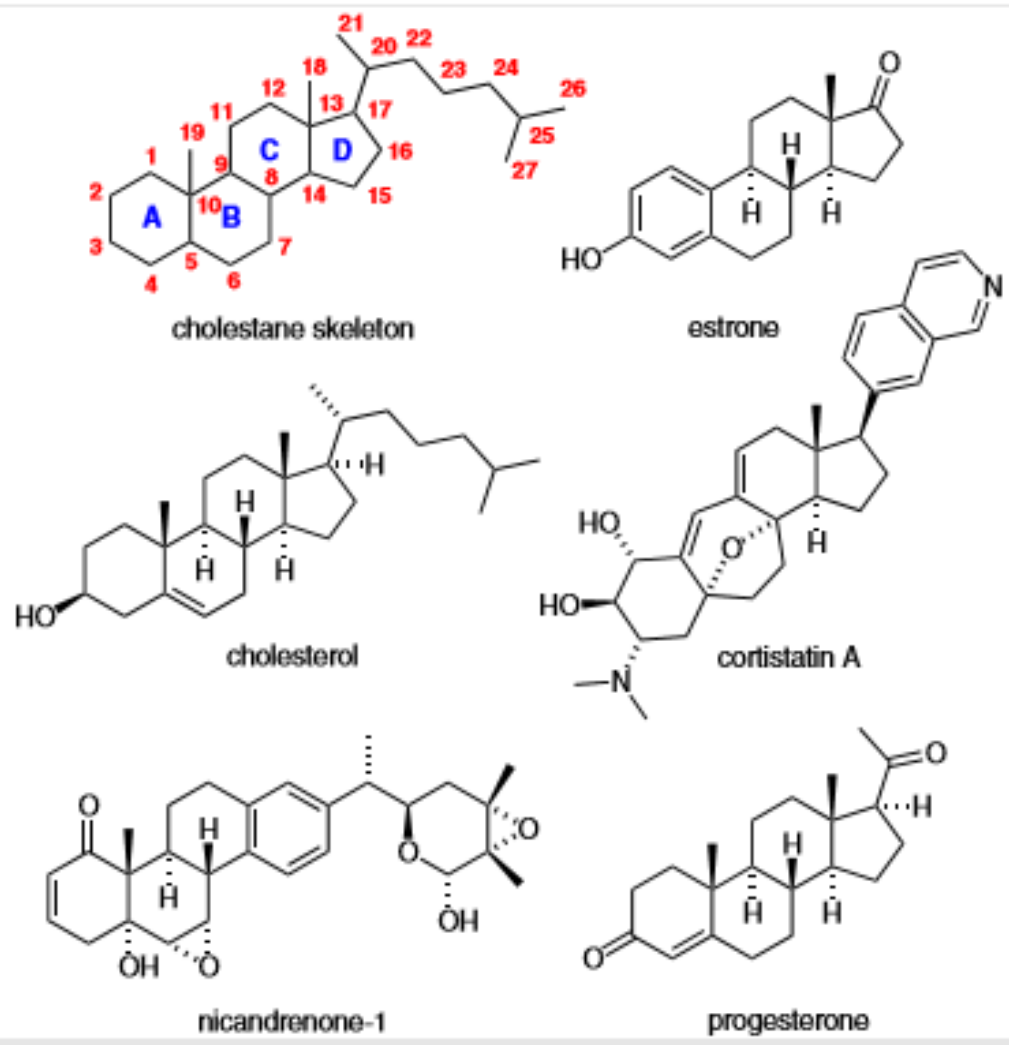
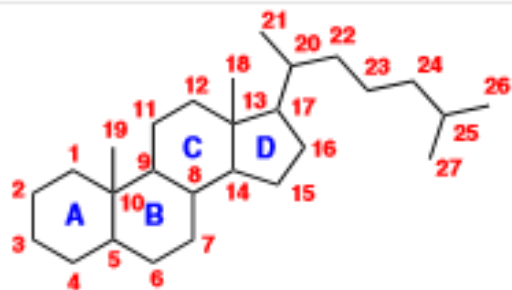
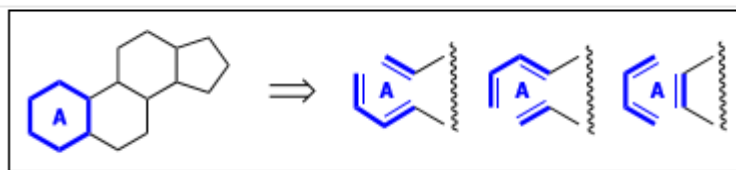


Figure 1 Selected steroid natural products



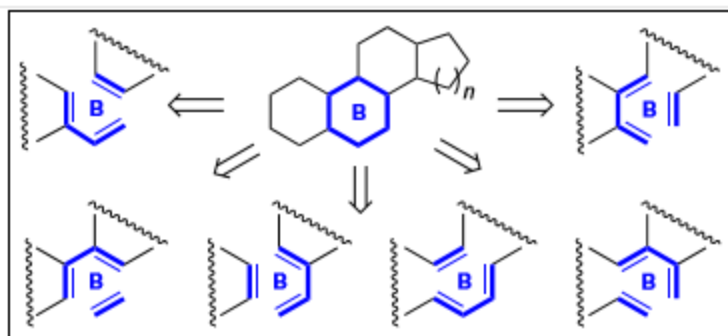
cholestane skeleton

2.2 Construction of the A-Ring



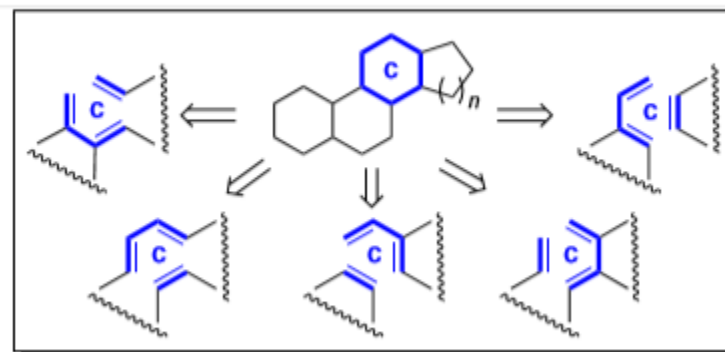
Scheme 8 A-ring disconnections reported so far

2.2 Construction of the B-Ring

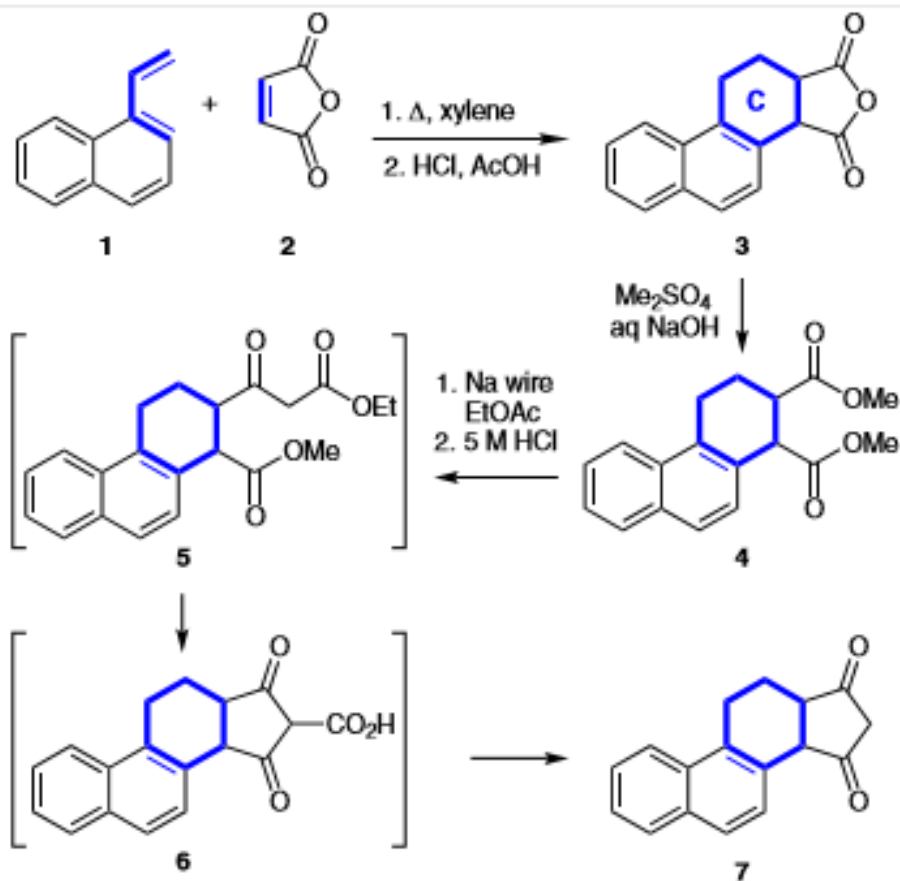


Scheme 13 B-ring disconnections reported so far

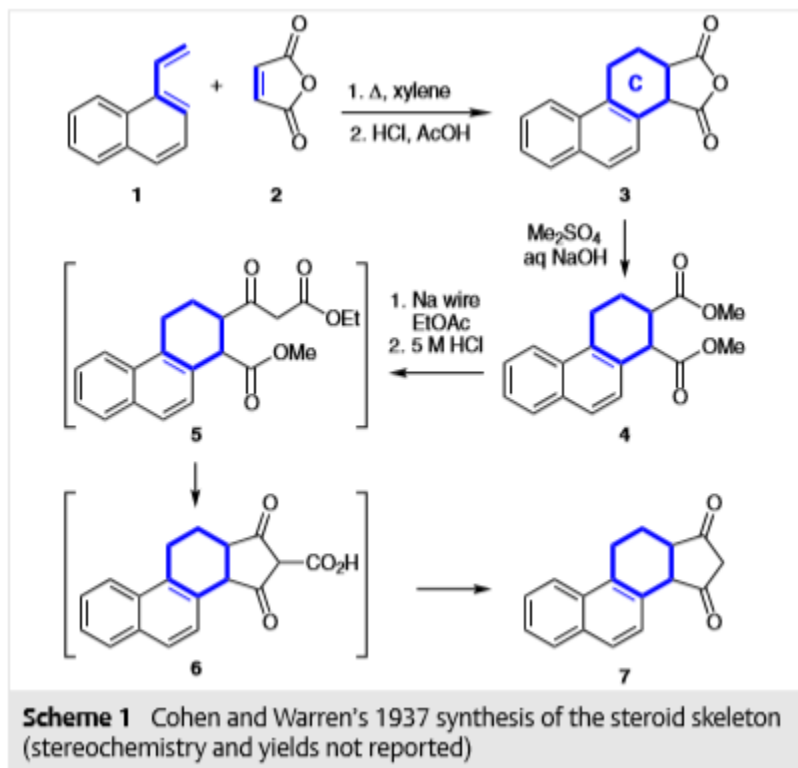
2.3 Construction of the C-Ring



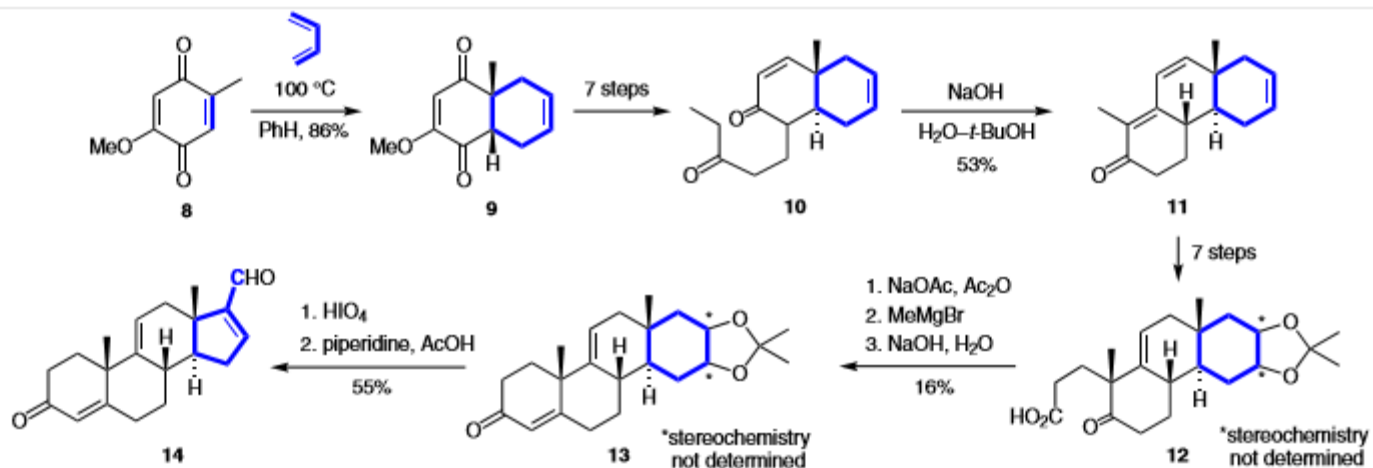
Scheme 27 C-ring disconnections reported so far



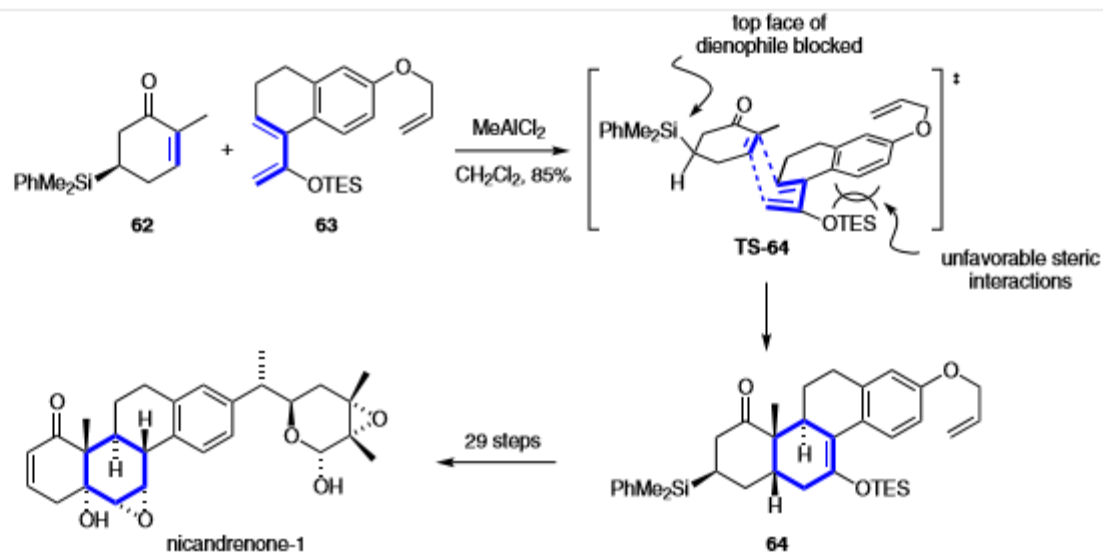
Scheme 1 Cohen and Warren's 1937 synthesis of the steroid skeleton (stereochemistry and yields not reported)



The utility of the DA reaction in the construction of the steroid skeleton dates back to 1937.⁴ In the first report, by Cohen and Warren, the C-ring was formed by way of a DA reaction between 1-vinylnaphthalene (**1**) and maleic anhydride (**2**), and an acid-catalyzed alkene isomerization to give naphthalene **3** (Scheme 1). On exposure to sodium hydroxide and dimethyl sulfate, the anhydride was converted into diester **4**, which in turn underwent a regioselective intermolecular Claisen condensation with ethyl acetate to give keto diester **5**. Dieckmann condensation and hydrolysis gave diketo acid **6**, which underwent decarboxylation in situ to give the tetracarbo-cyclic product **7**.



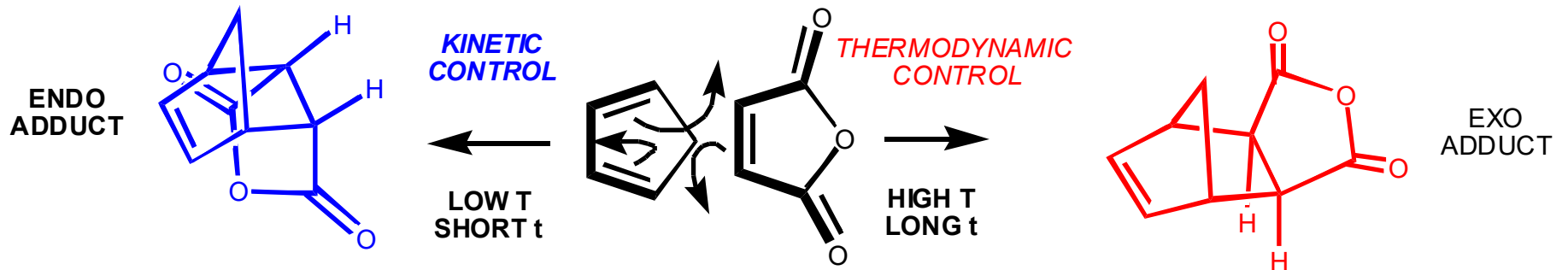
Scheme 2 Woodward's 1952 formal synthesis of steroids employing an early-stage DA reaction



Scheme 15 Corey and Stoltz's 2000 synthesis of the nicandrenones

An example of the use of this DA disconnection in total synthesis is the 2000 publication on the preparation of the nicandrenones by Corey and Stoltz,³⁸ which featured an unusual *exo*-selective DA reaction between enol ether **63** and enantiopure enone **62** (Scheme 15). The dienophile's bulky dimethylphenylsilyl substituent steers the diene away from its top face. Steric interactions between substituents on the diene in the *cisoid* form lead to a nonplanar conformation, which disfavors *endo*-mode transition states.³⁹ These features combine to favor **TS-64**, which leads to *exo* adduct **64**.

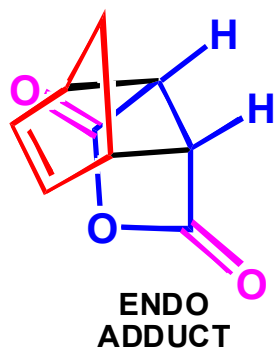
Esercizi su Pericicliche



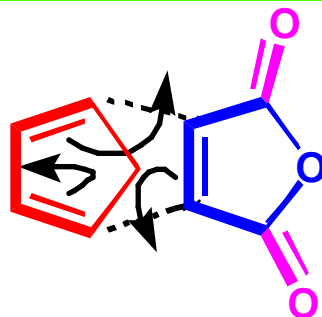
Interazioni secondarie di orbitali molecolari

Thermal $[\pi 4s + \pi 2s]^{\ddagger}$

KINETIC PRODUCT

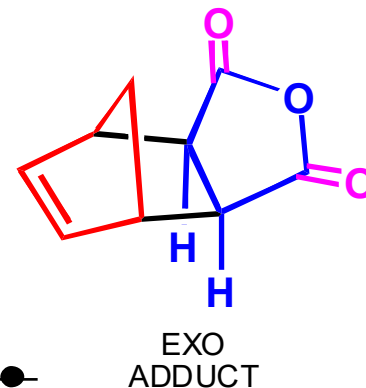


Low T
Short t

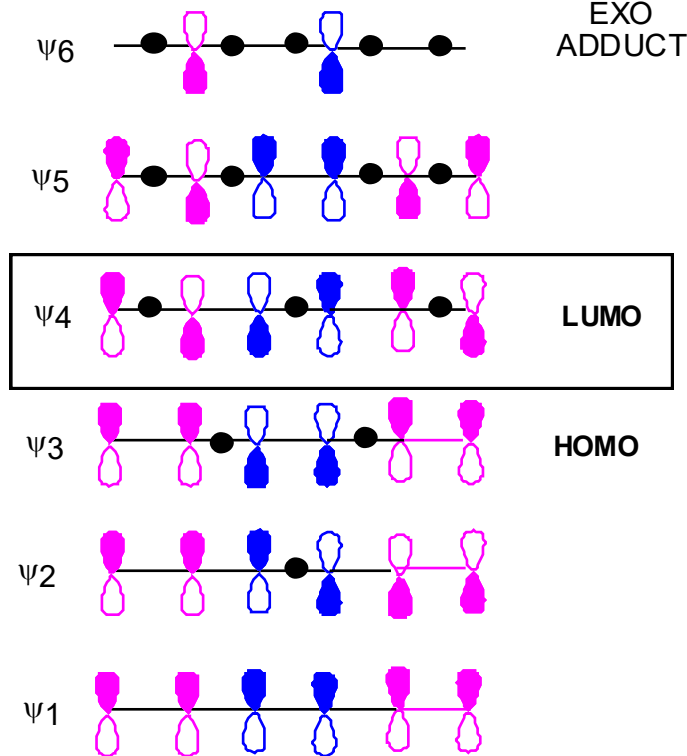
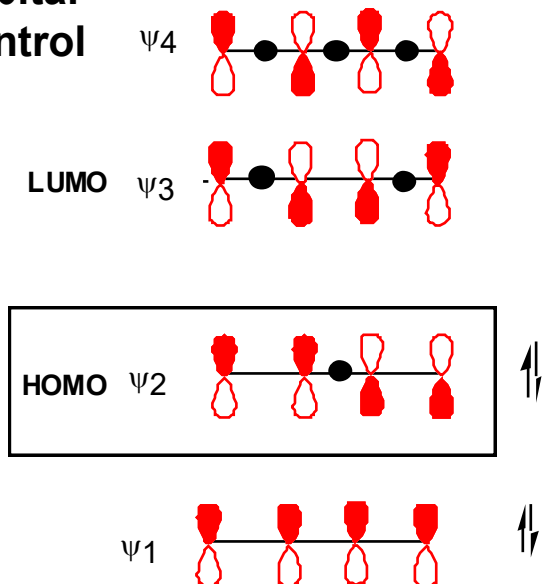


High T
Long t

THERMODYNAMIC PRODUCT

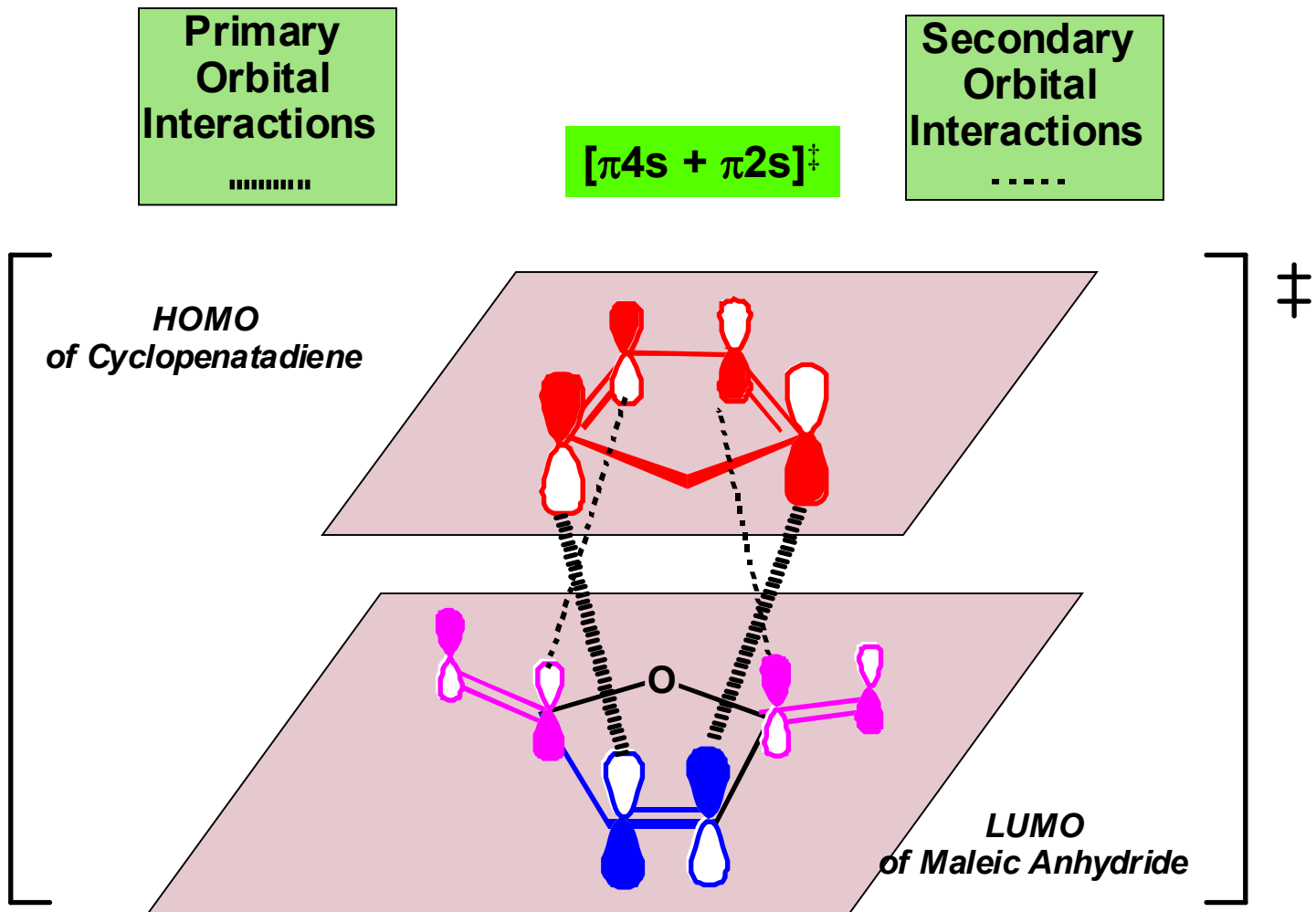


Secondary Orbital Interaction Control



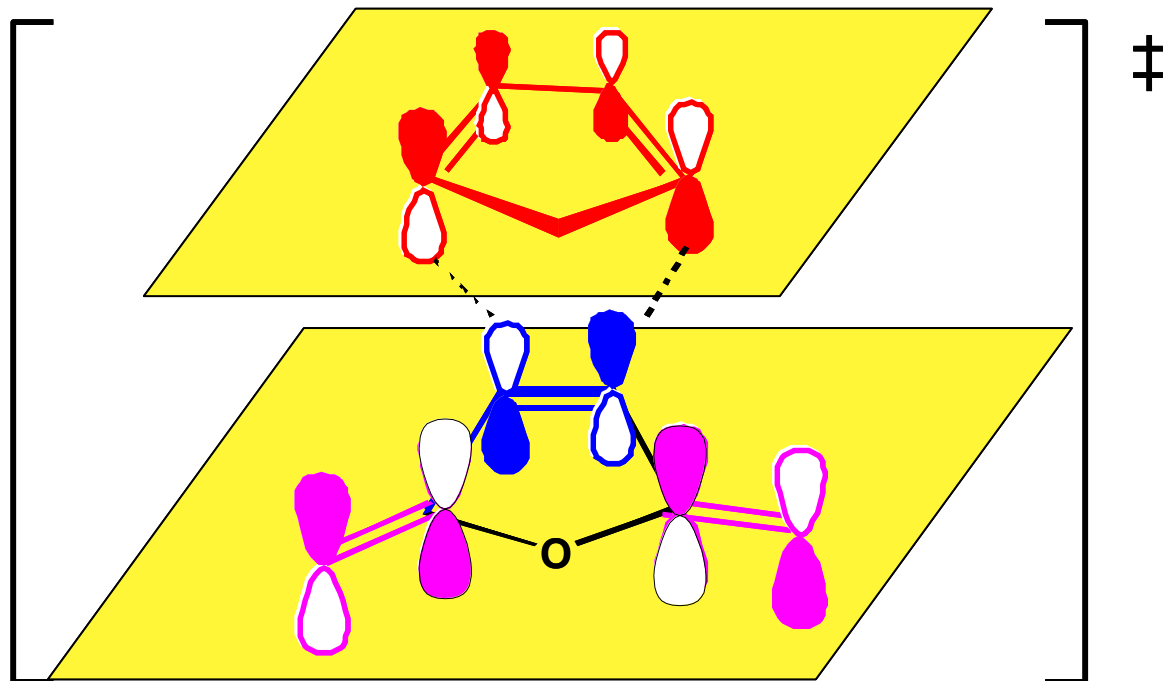
Interazioni secondarie di orbitali molecolari

ENDO

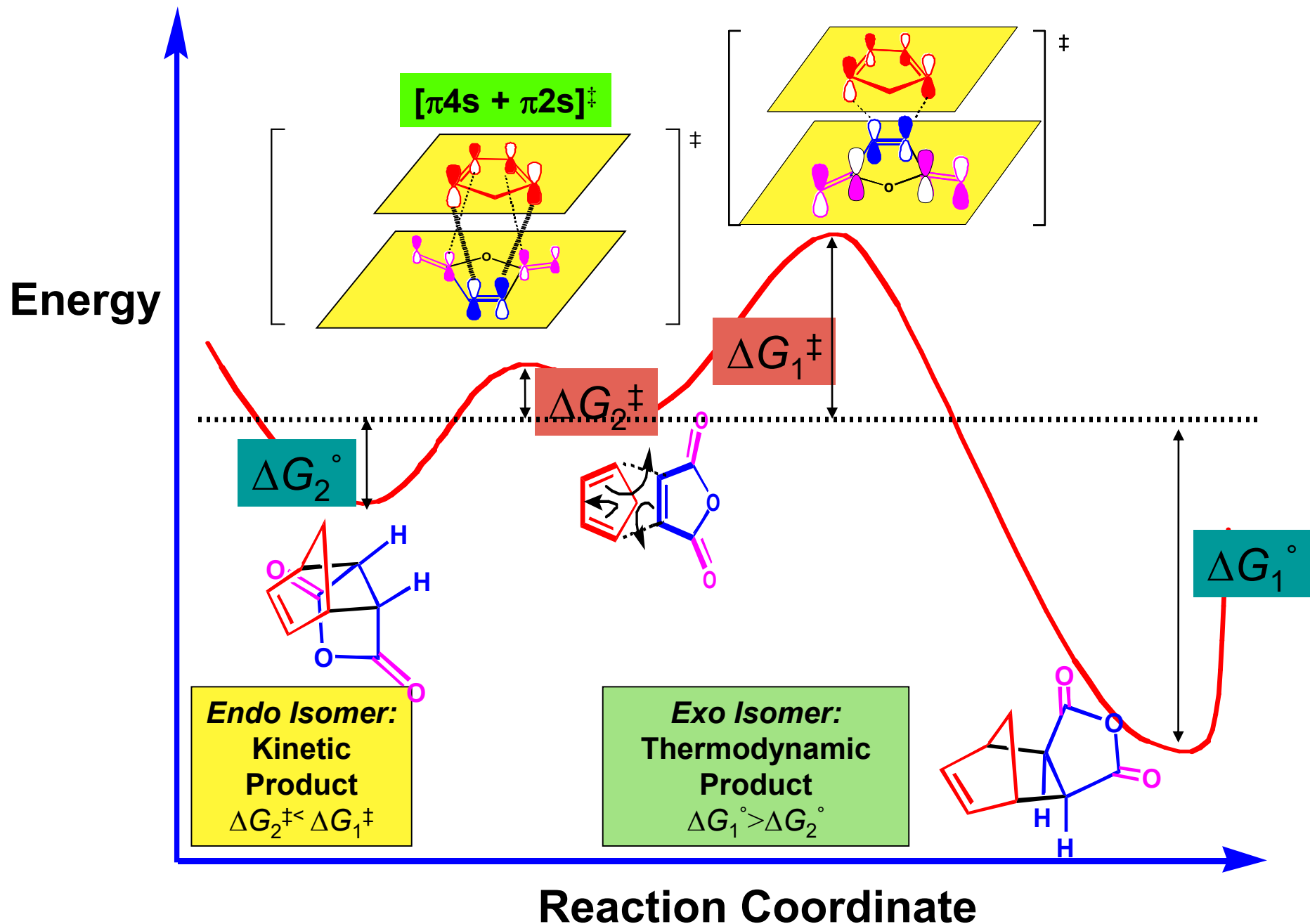


Interazioni secondarie di orbitali molecolari

ESO

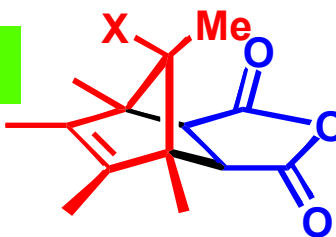
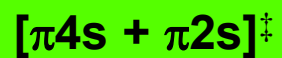
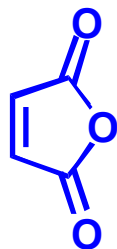
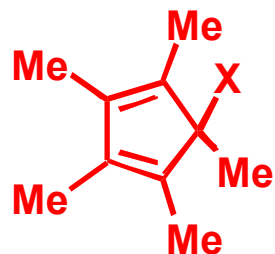


This orientation of reactants in the transition state does not facilitate any secondary orbital interactions.

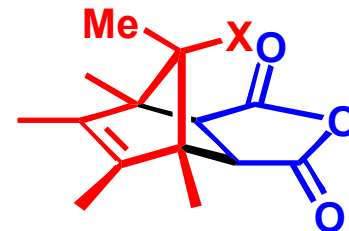


Qual è il prodotto TERMODINAMICO?

**Exo-Diels-Alder Adducts
(Thermodynamic Product)**



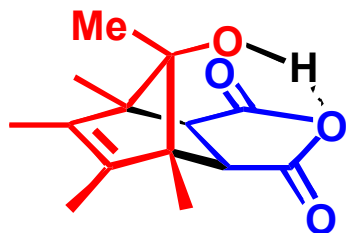
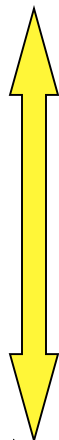
anti-Adduct

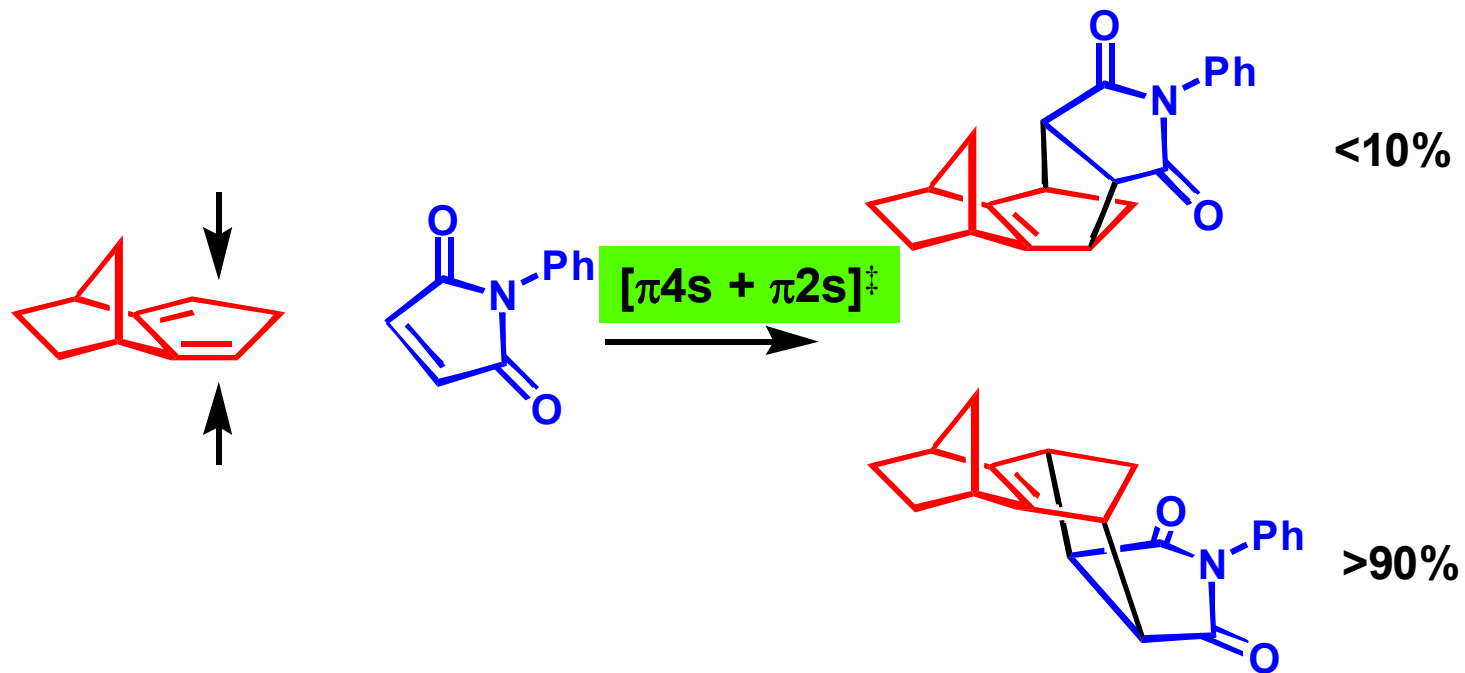
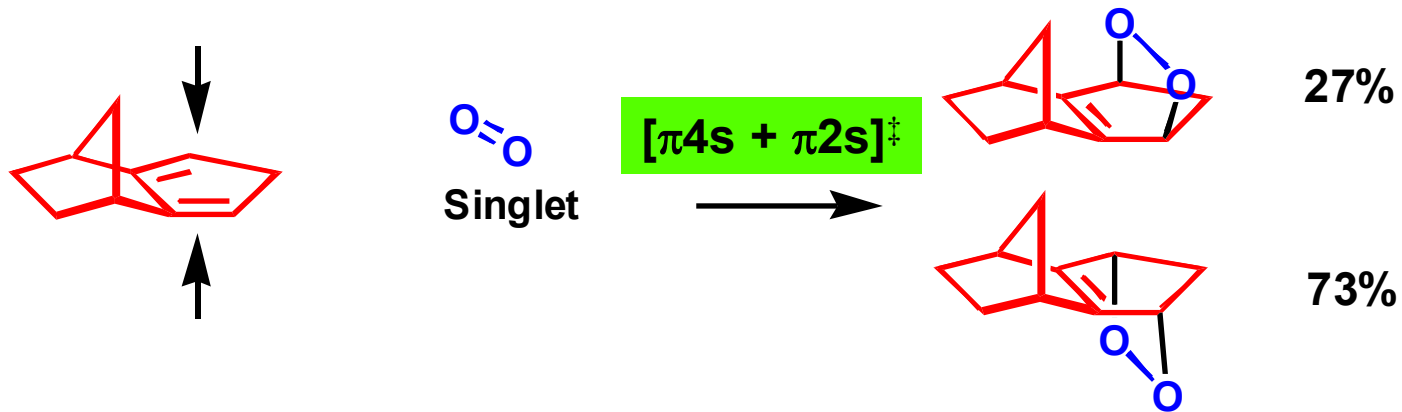


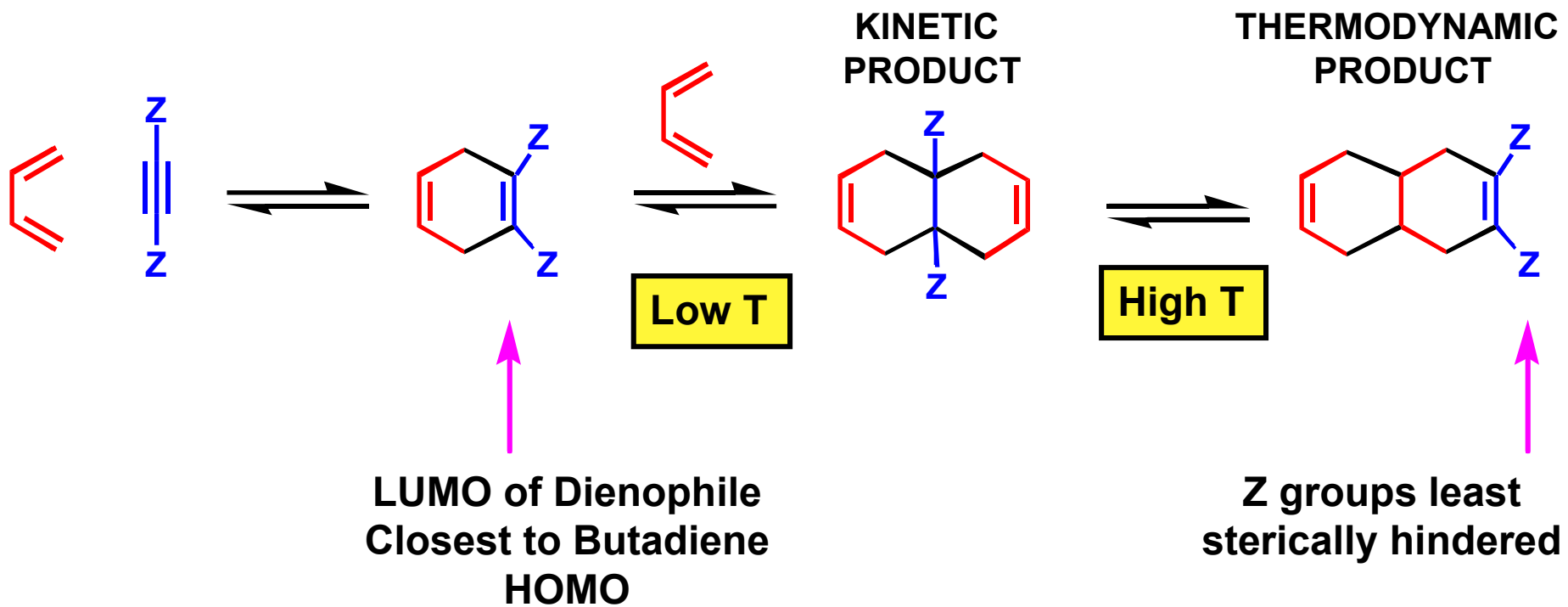
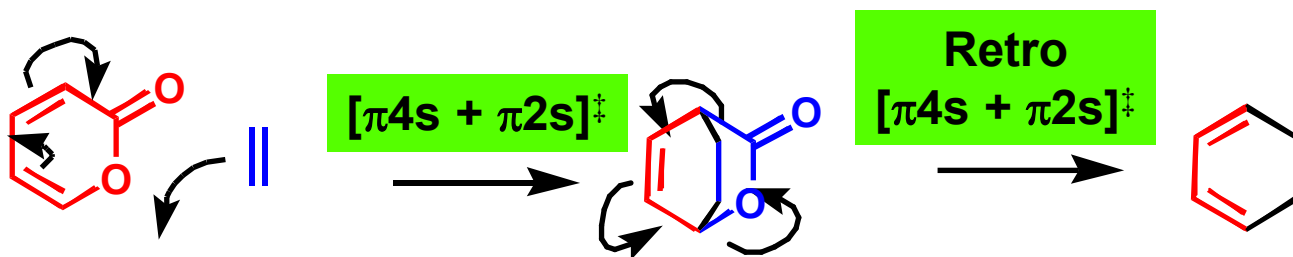
syn-Adduct

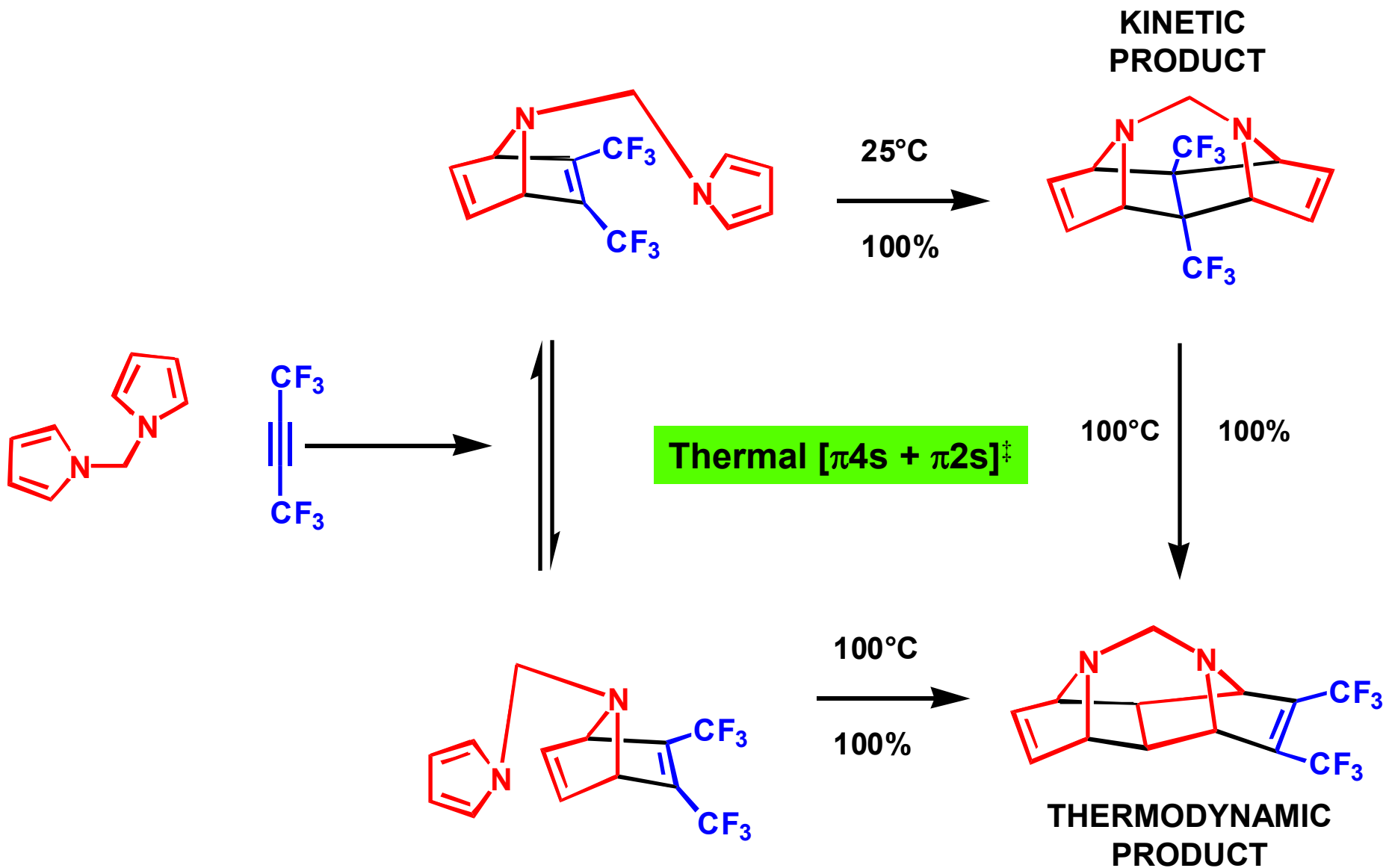
X	% <i>anti</i> -Adduct	% <i>syn</i> -Adduct
H	20	80
SMe	90	10
S(O)Me	>95	<5
S(O) ₂ ME	>95	<5
<i>i</i> Pr	>95	<5
Et	>95	<5
CHO	>95	<5
CH ₂ OH	>95	<5
OH	<5	>95

Sterically Favoured

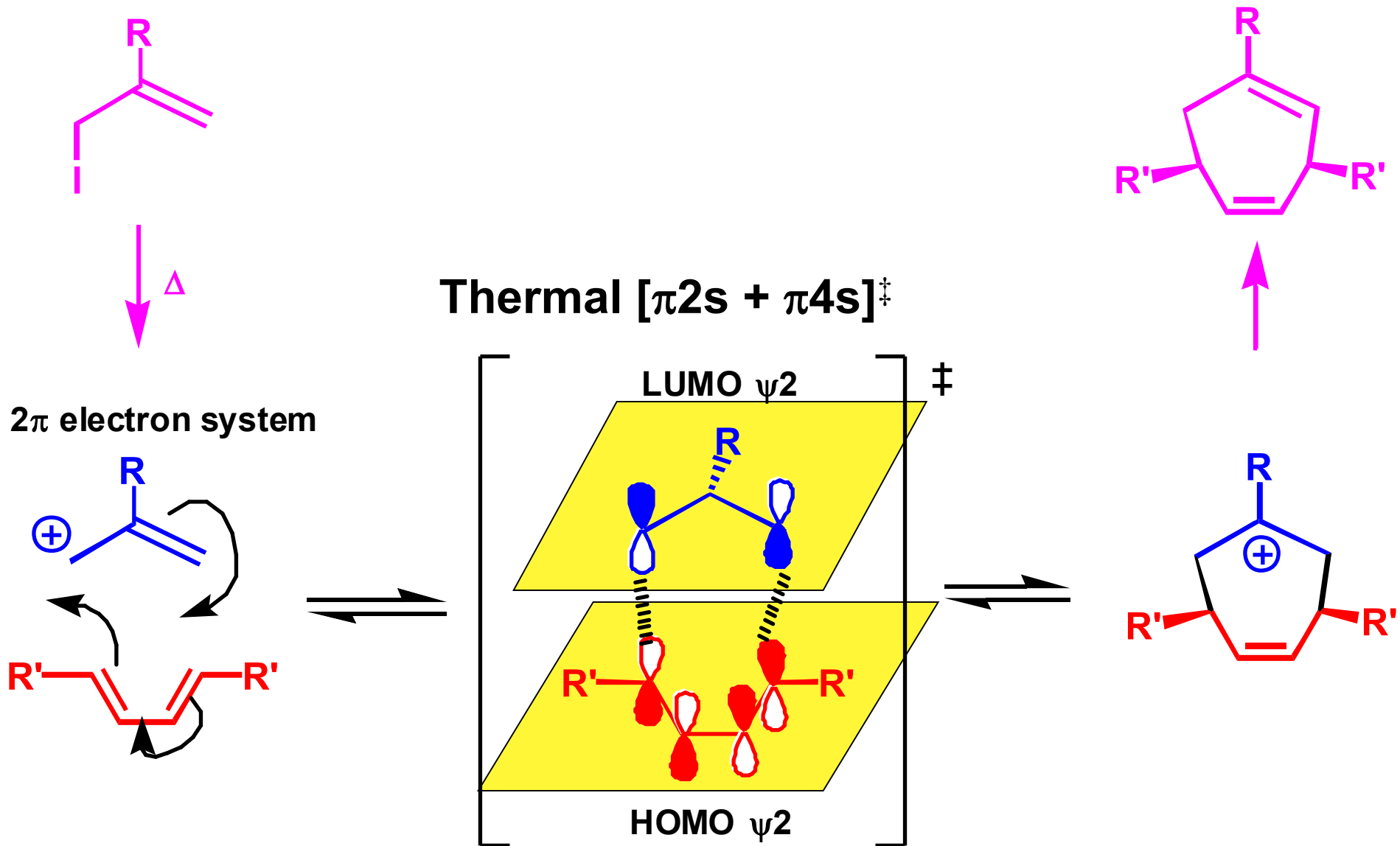




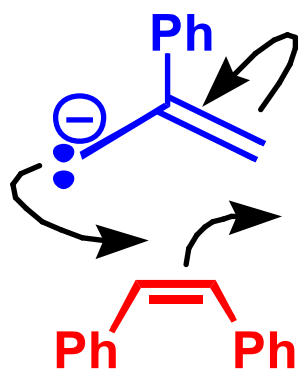
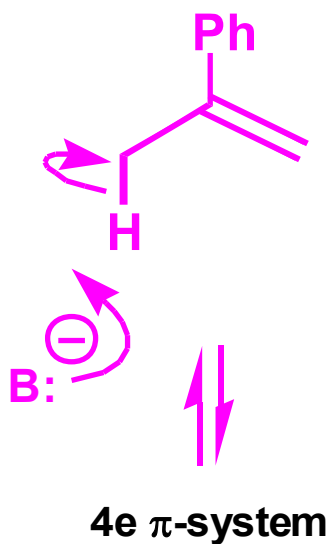




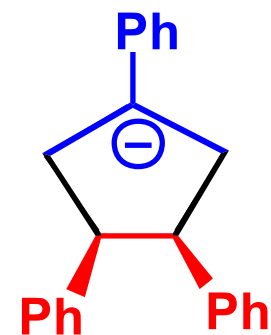
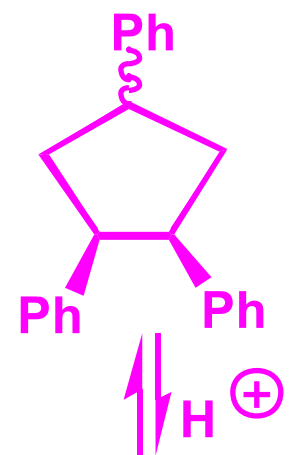
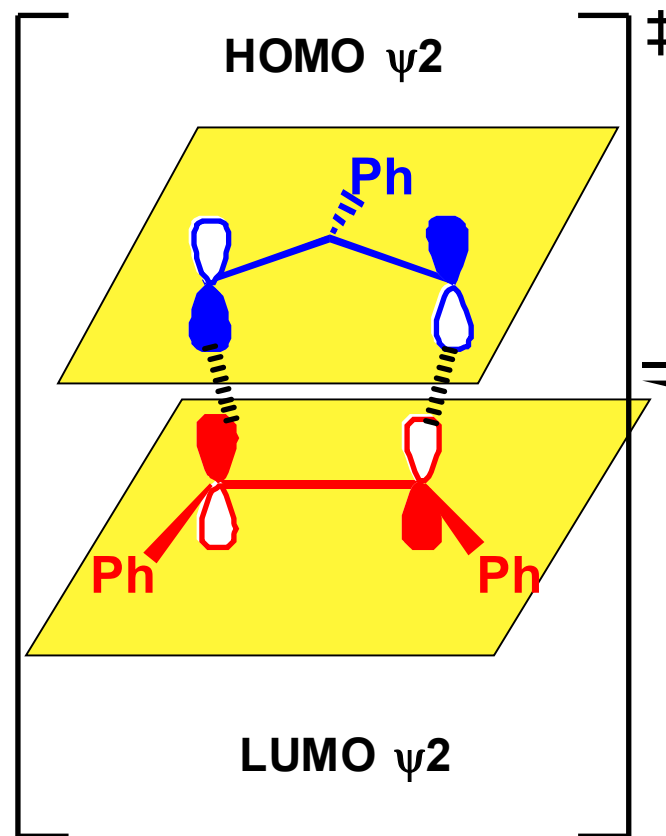
Cicloaddizione del CATIONE ALLILICO



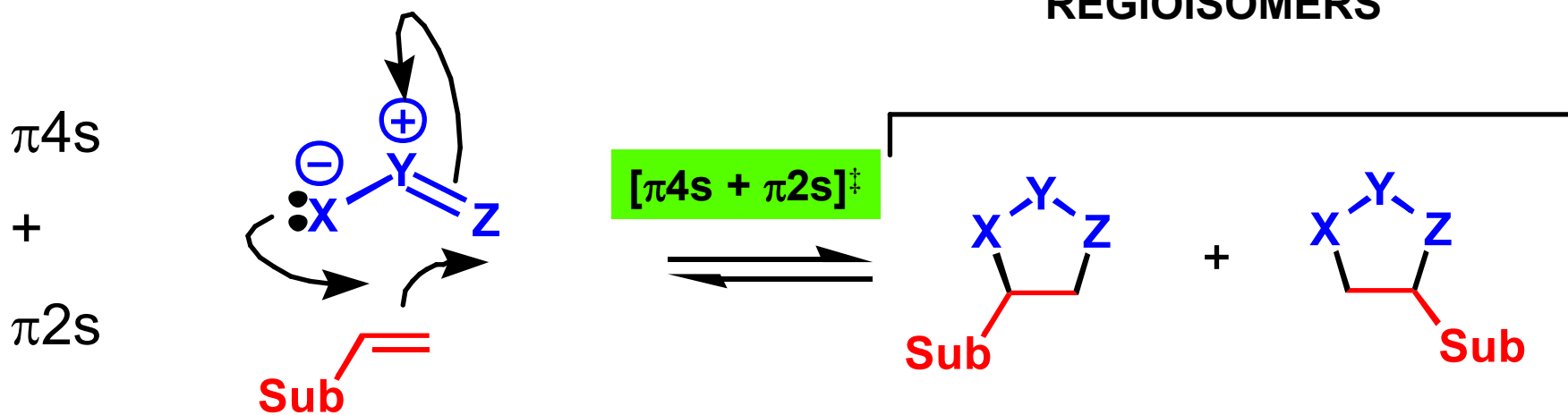
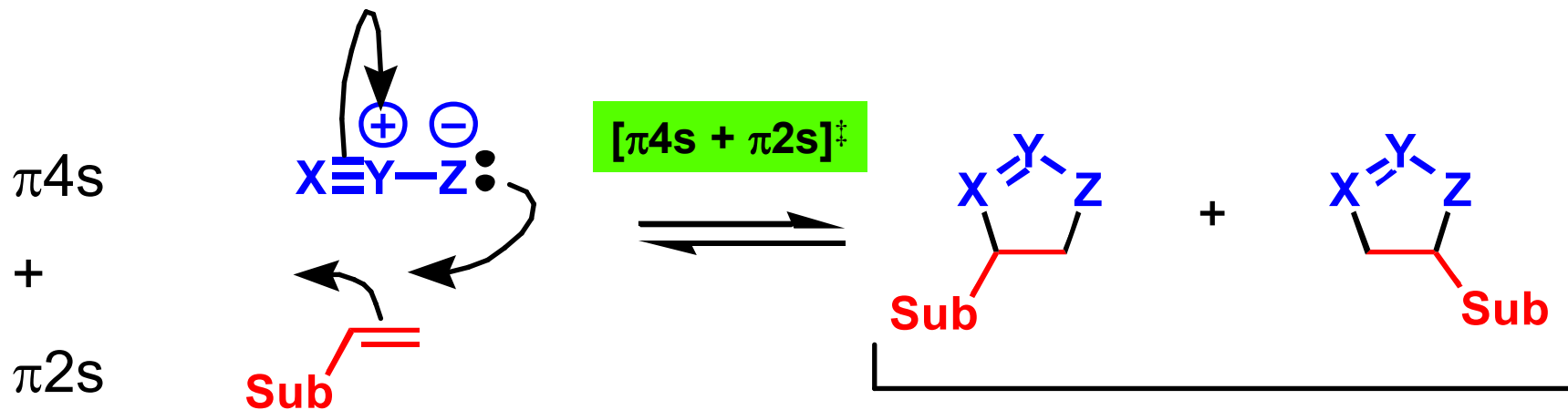
Cicloaddizione dell'ANIONE ALLILICO



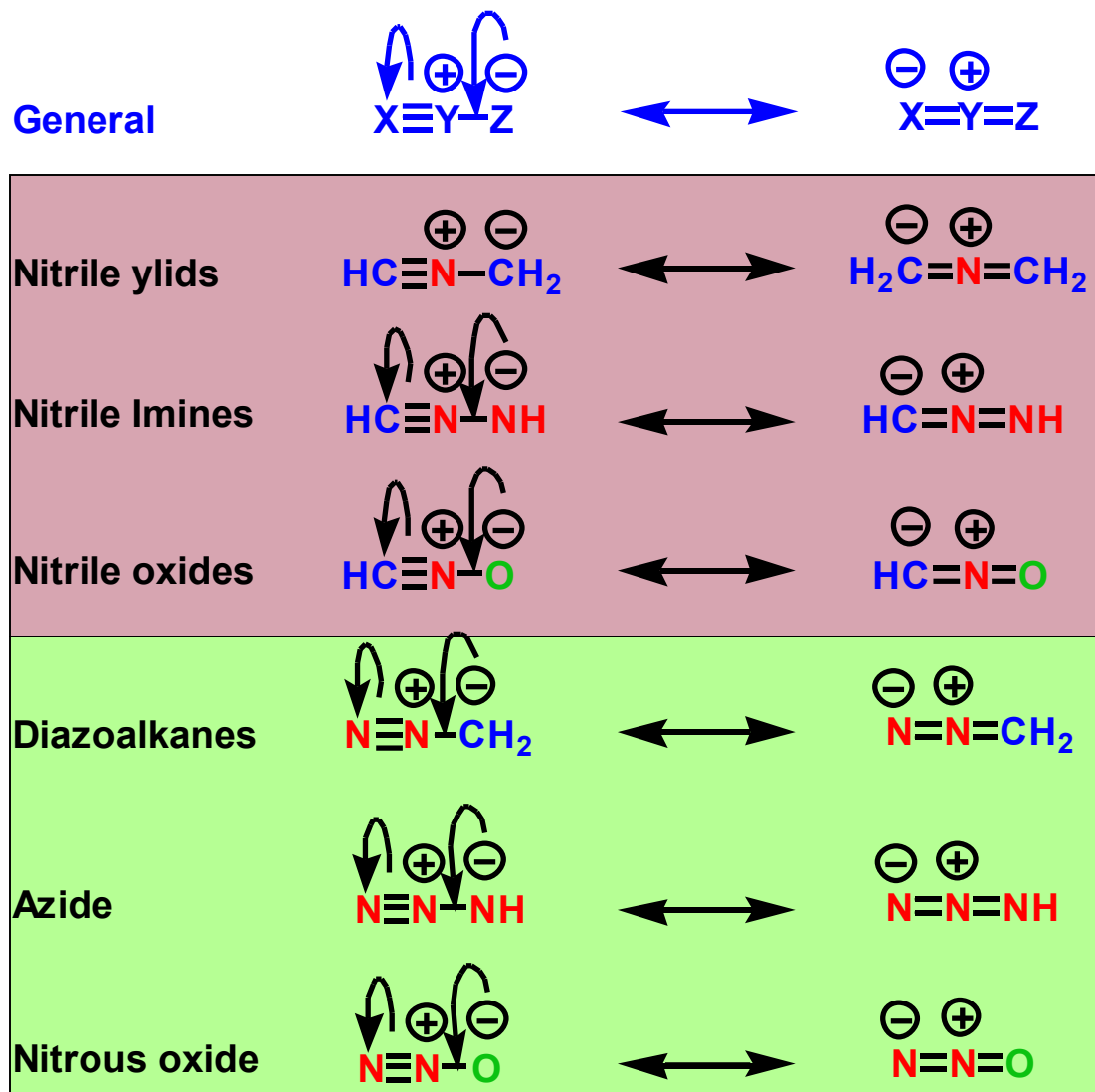
Thermal $[\pi 4s + \pi 2s]^{\ddagger}$



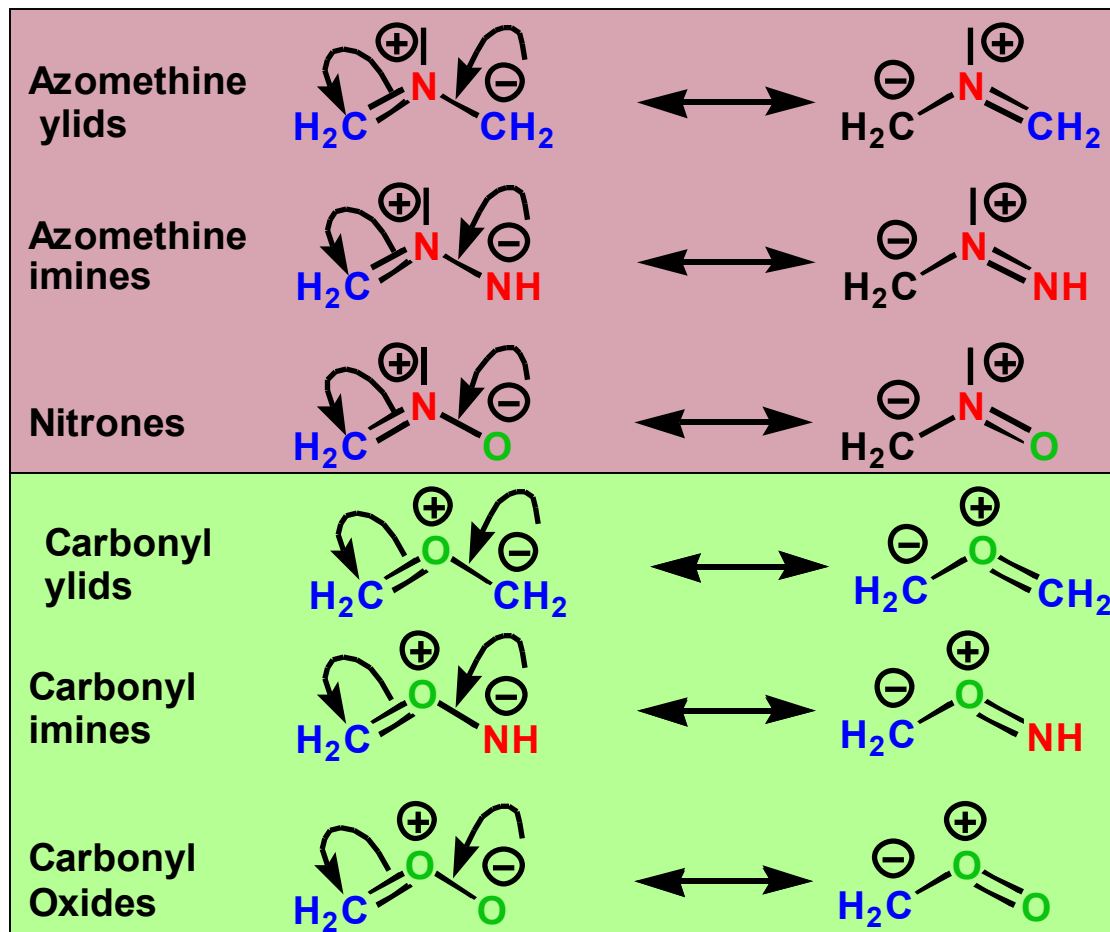
Cicloaddizioni 1,3-DIPOLARI



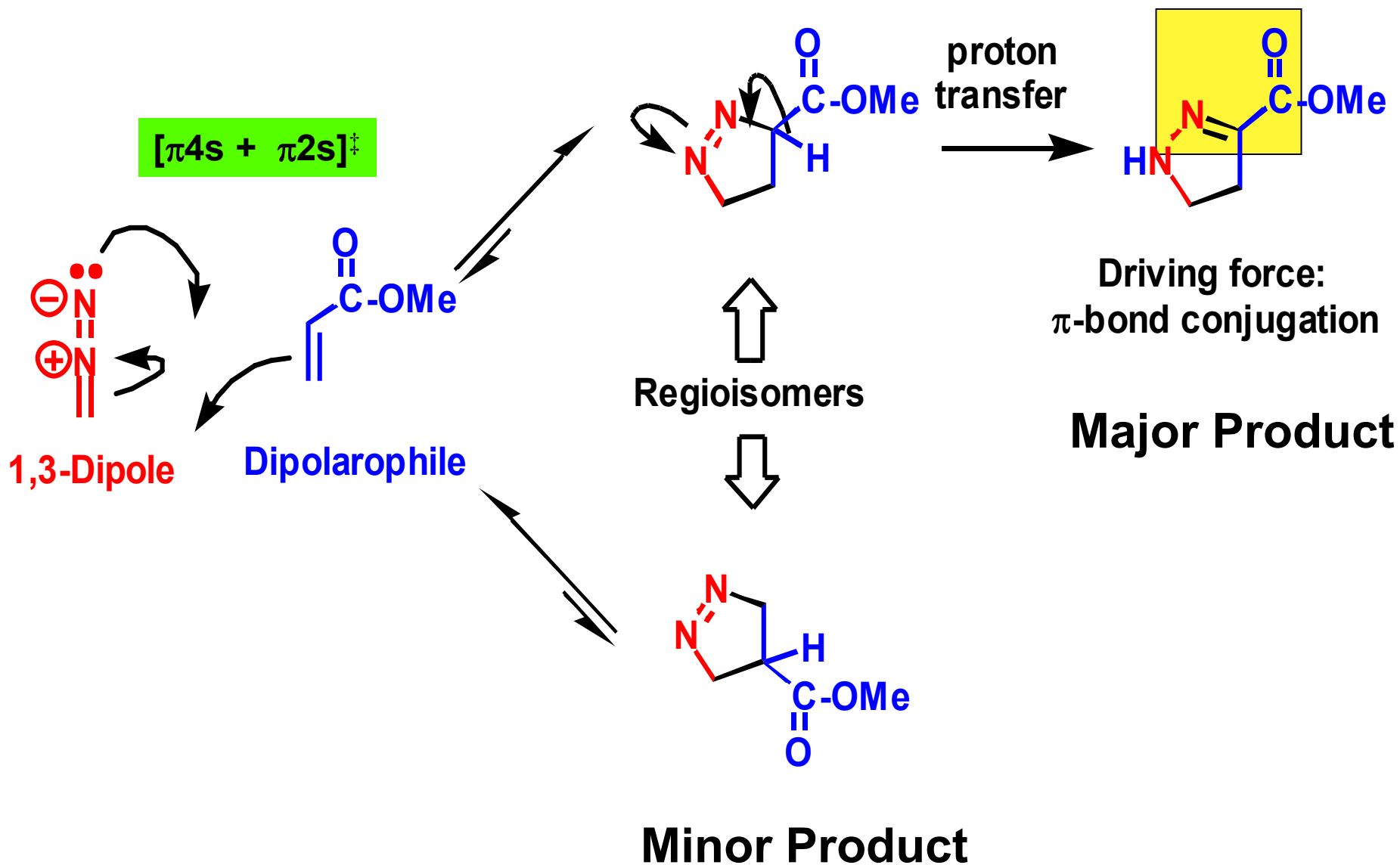
1,3-DIPOLI lineari



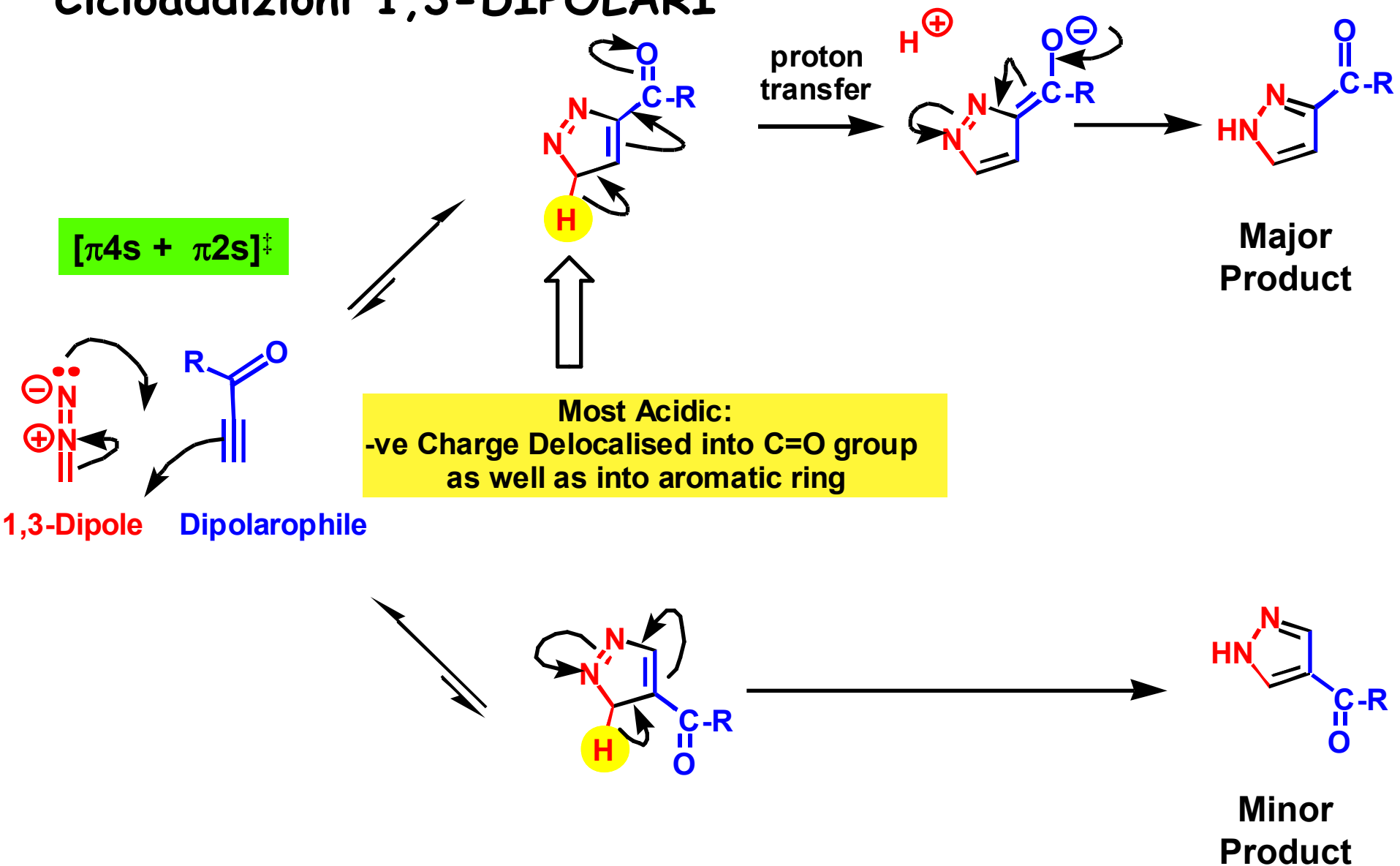
1,3-DIPOLI non lineari



Cicloaddizioni 1,3-DIPOLARI

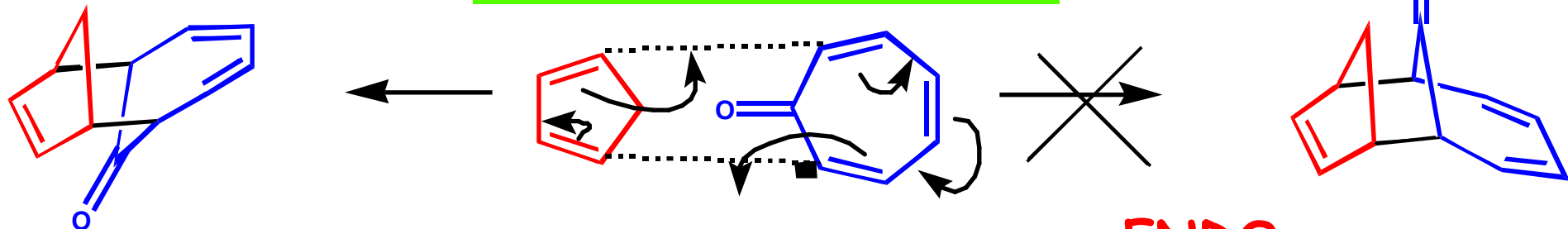


Cicloaddizioni 1,3-DIPOLARI



Interazioni secondarie di orbitali molecolari

Thermal 10 ($4n+2$, $n=2$) e D-A

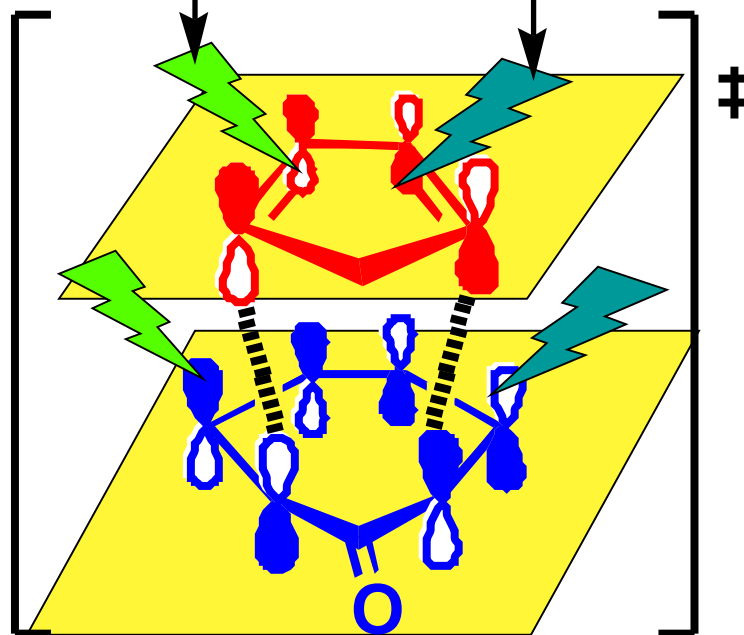
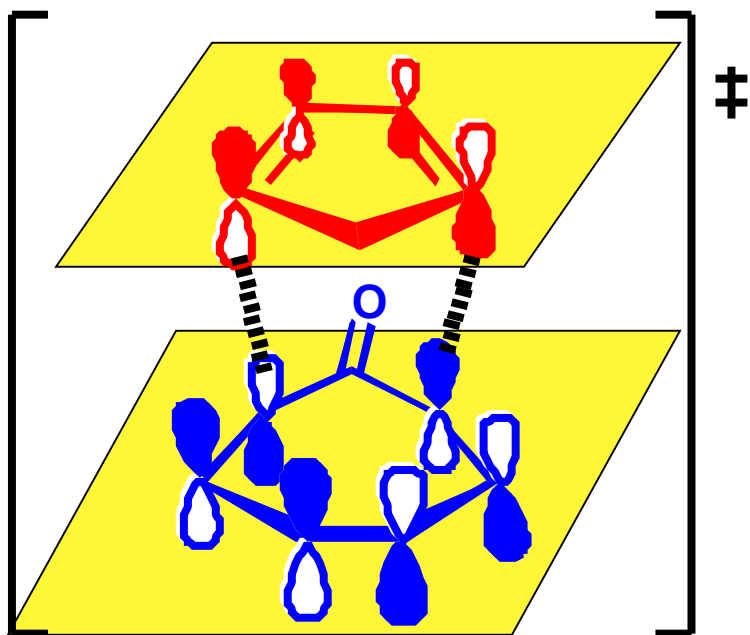


ENDO

Thermal $[\pi 4s + \pi 6s]^{\ddagger}$

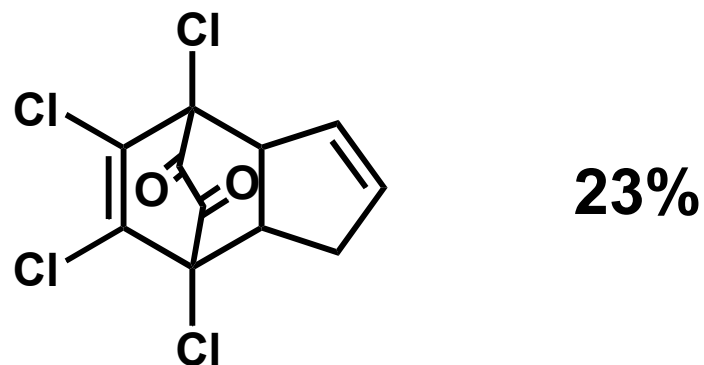
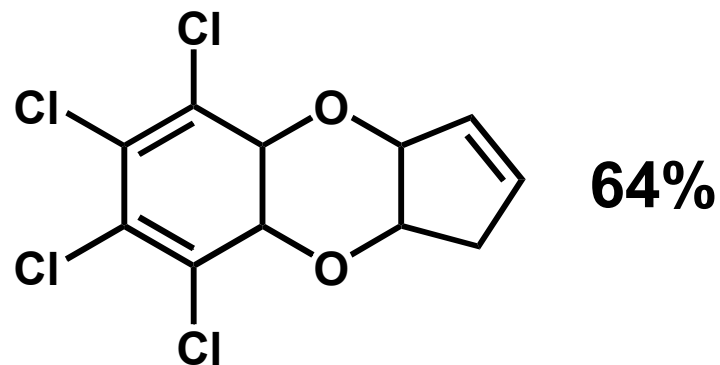
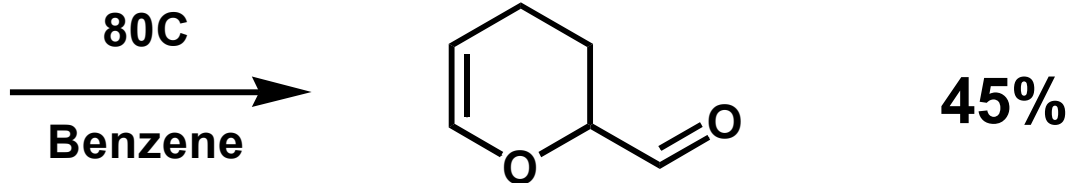
ESO

Antibonding Secondary
Orbital Interactions



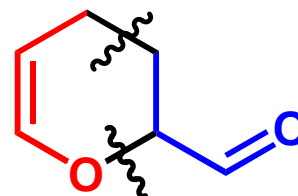
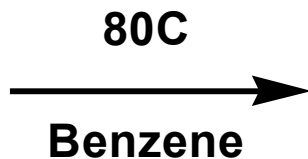
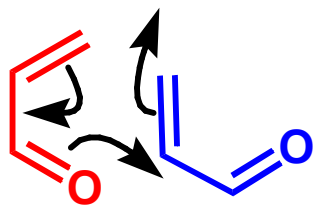
ESERCIZI

Identify the starting materials and propose arrow pushing mechanisms for the formation of the following products

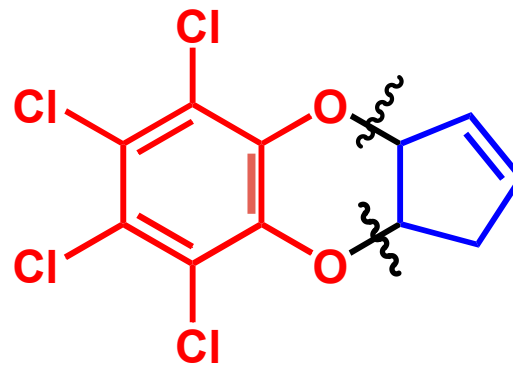
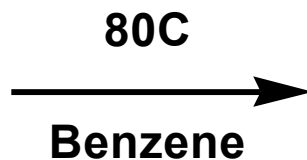
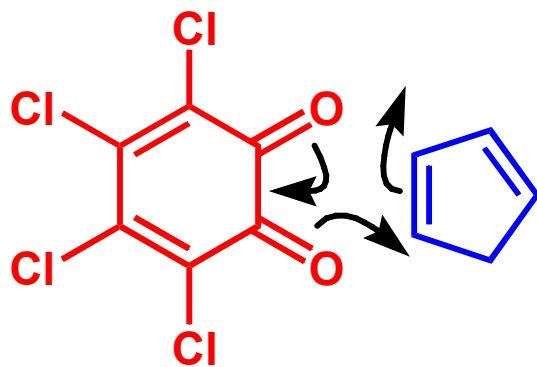


RISPOSTE

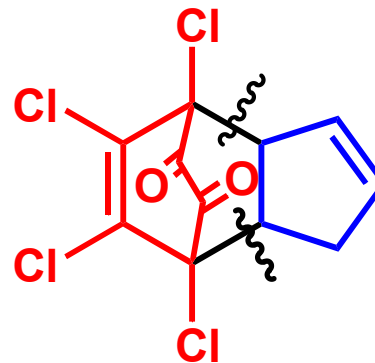
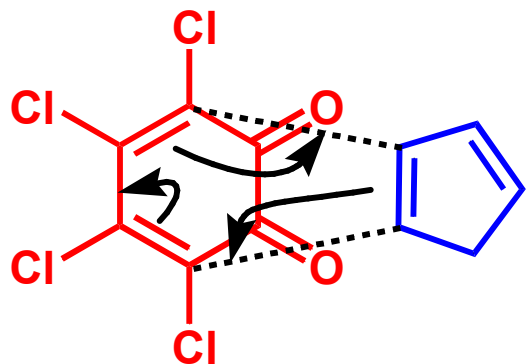
Identify the starting materials and propose arrow pushing mechanisms for the formation of the following products



45%



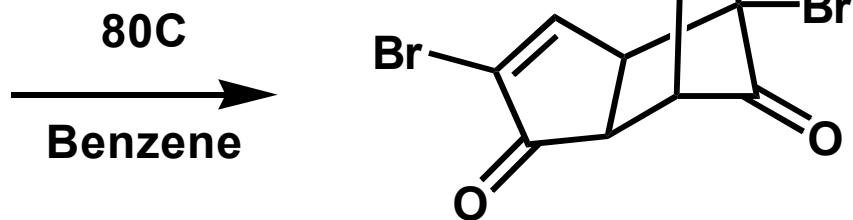
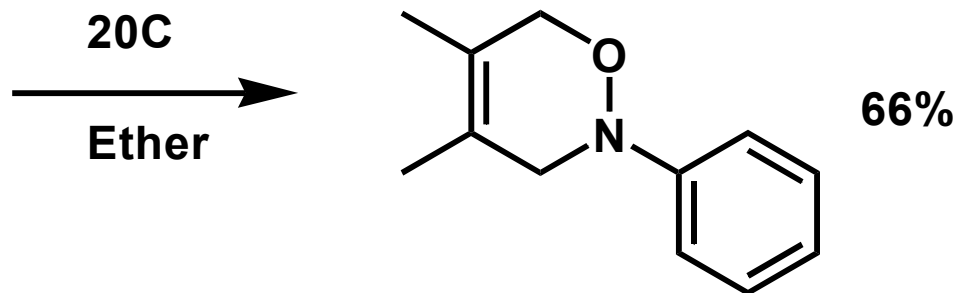
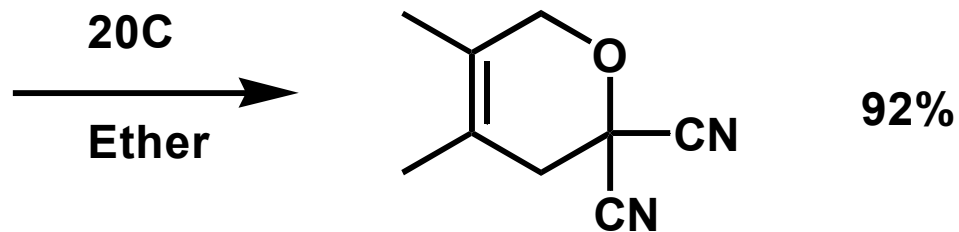
64%



23%

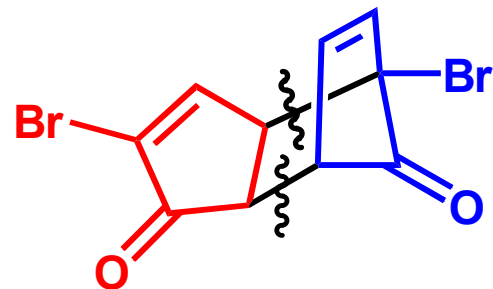
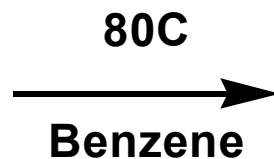
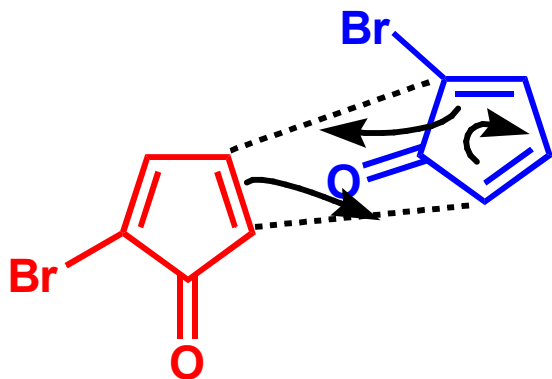
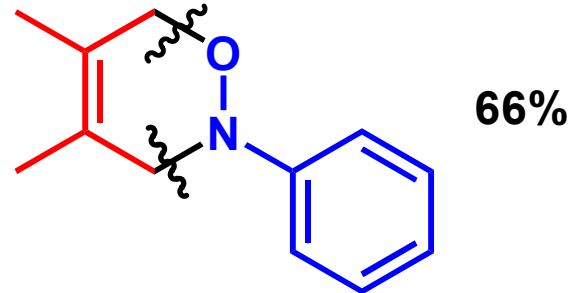
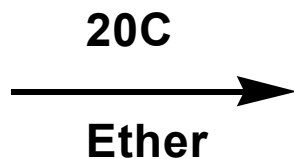
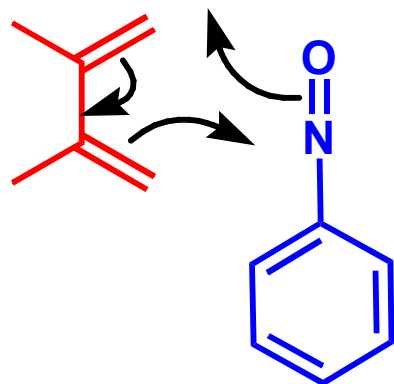
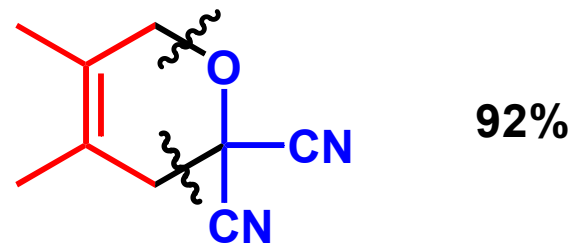
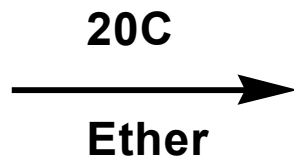
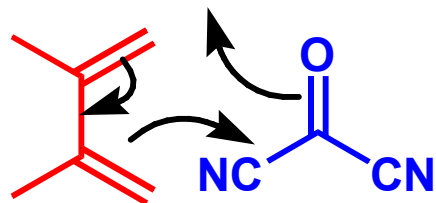
ESERCIZI

Identify the starting materials and propose arrow pushing mechanisms for the formation of the following products



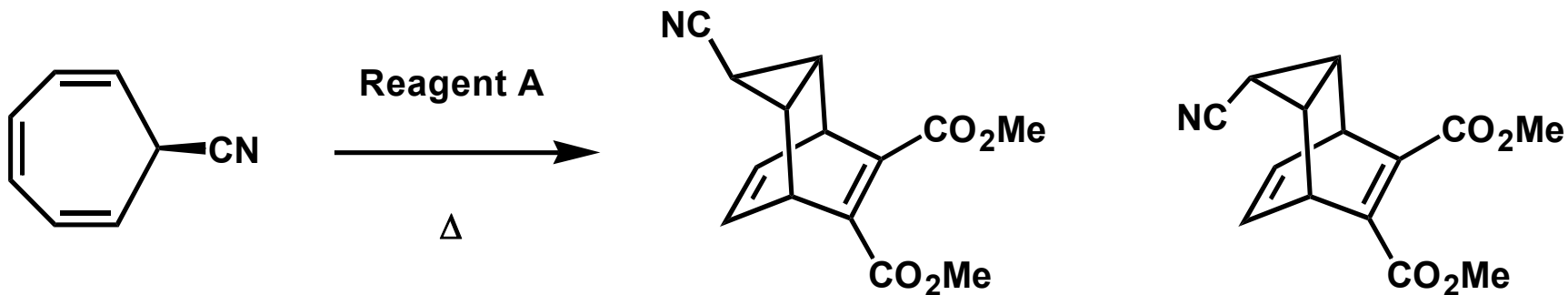
RISPOSTE

Identify the starting materials and propose arrow pushing mechanisms for the formation of the following products



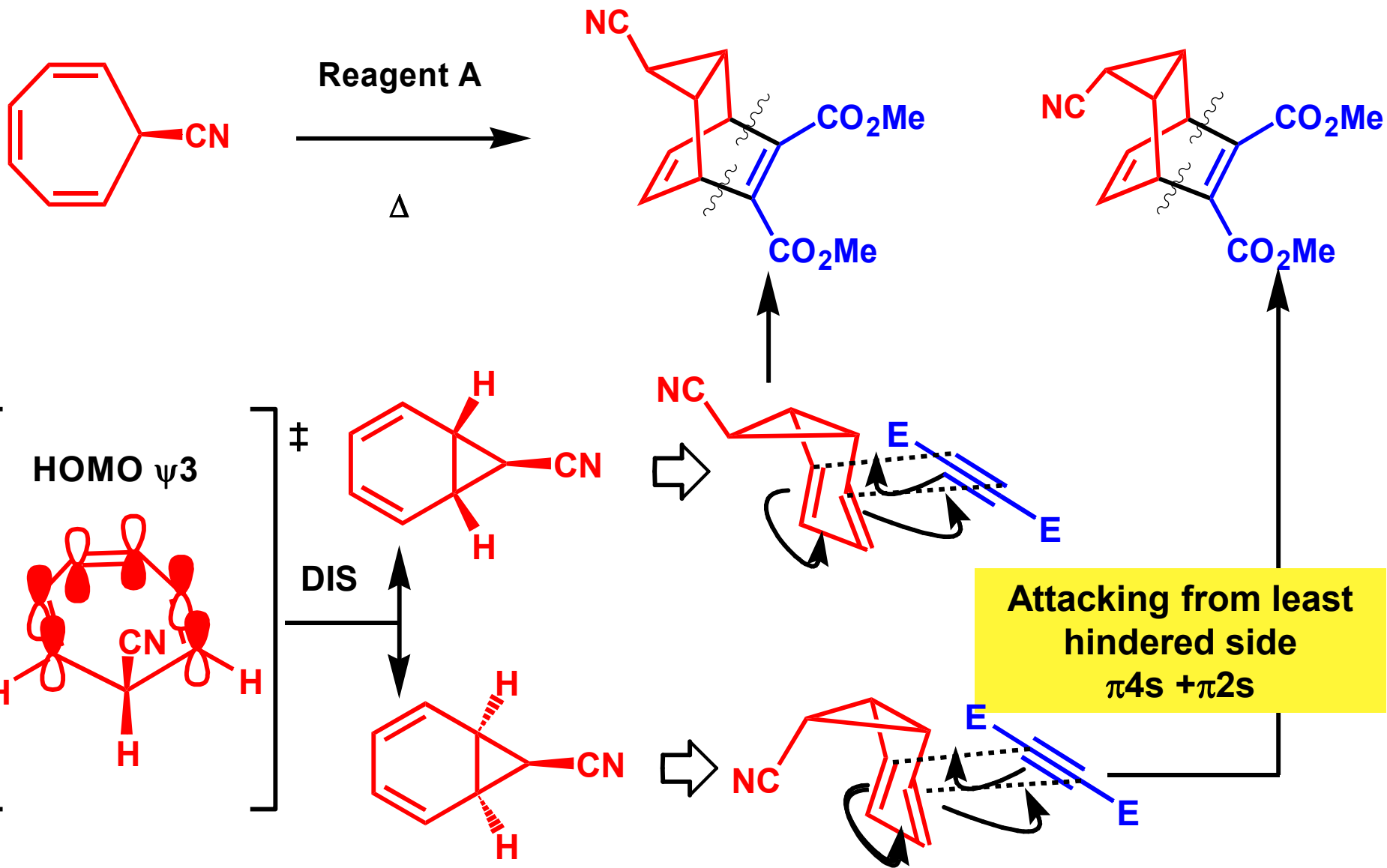
ESERCIZI

Rationalise the following reaction scheme utilising frontier molecular orbitals and identify reagent A.



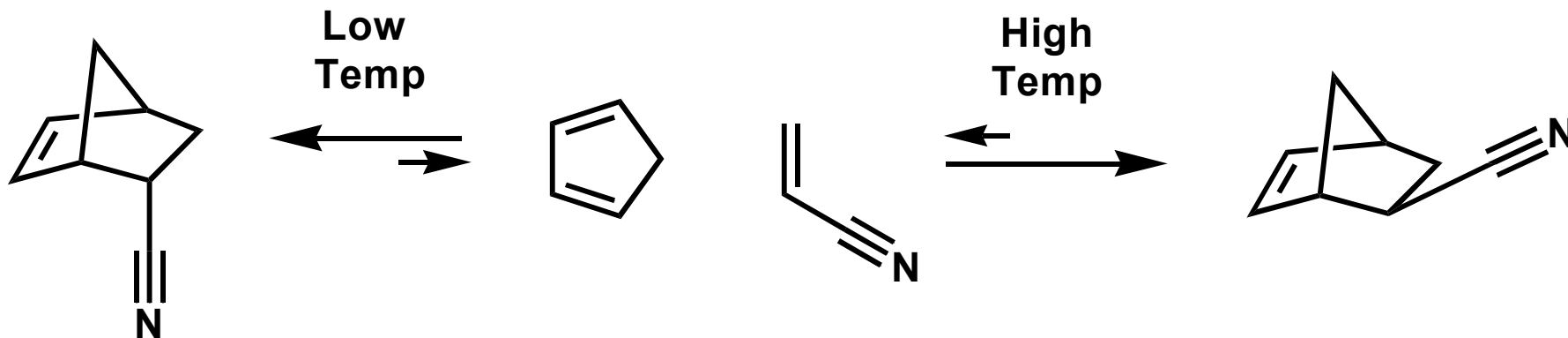
RISPOSTE

Rationalise the following reaction scheme utilising frontier molecular orbitals and identify reagent A.



ESERCIZI

Rationalise the following reaction scheme utilising secondary orbital interactions.



RISPOSTE

Rationalise the following reaction scheme utilising secondary orbital interactions.

