Fonction et réaction organiques II

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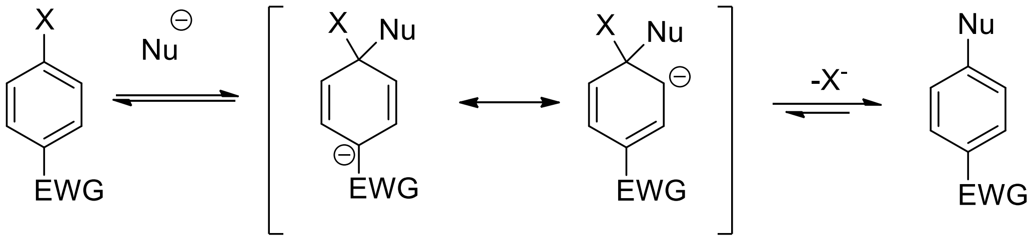
1.6. Nucleophilic Aromatic Substitution S_NAr



Meisenheimer complex

Criteria:

- X must be a leaving group with high electronegativity (F, Cl, OR…)
- EWG group (-NO_2, -CN, …)

→ The reaction proceeds by an addition/elimination mechanism.

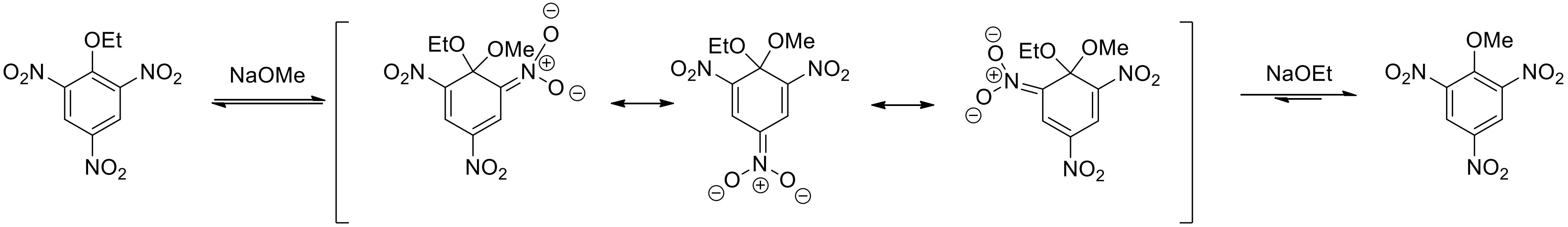
→ Obeys second order kinetics

→ EWG substituents must stabilize the negative charge of the Meisenheimer intermediate.

→ Therefore they must be in the ortho- or para- position.

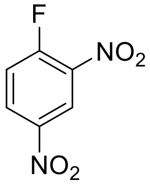
1.6. Nucleophilic Aromatic Substitution S_NAr

Prominent example of S_NAr

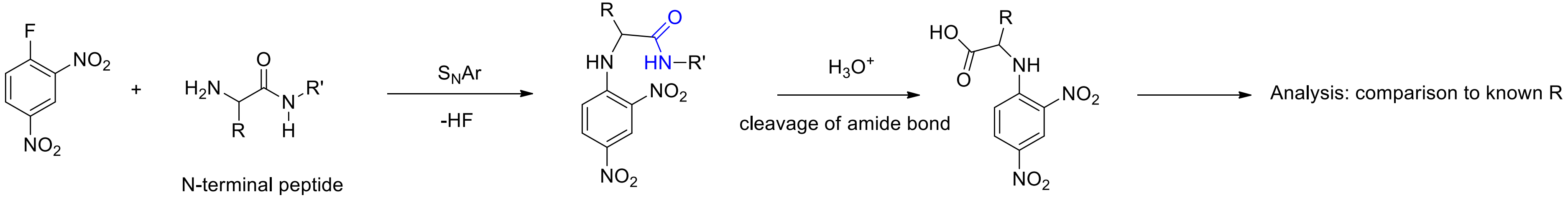


Meisenheimer-Complex

Historical very important application with Sanger’s reagent using S_NAr for amino acid sequence analysis



Sanger’s reagent



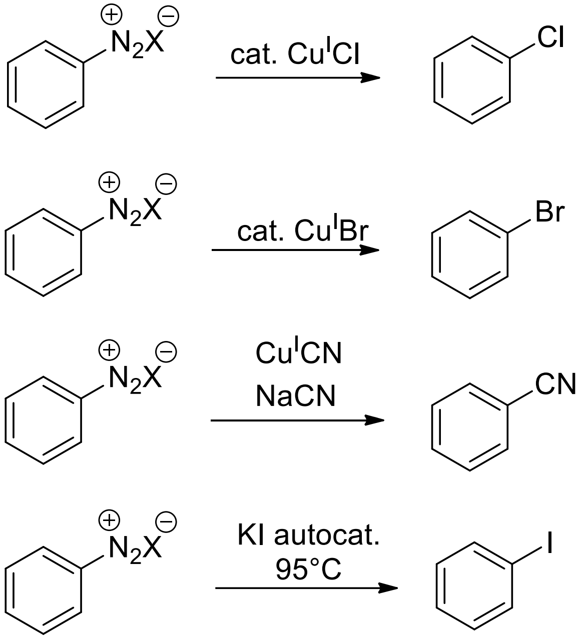
1.6. Nucleophilic Aromatic Substitution S_NAr

Comparaison between S_EAr and S_NAr : basic key facts

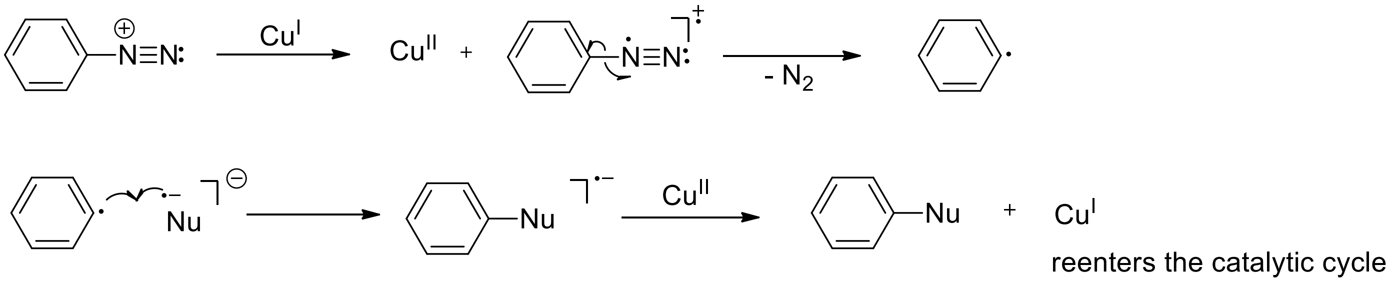
	S_EAr	**S_NAr**
Agent	E^+	Nu^-
Key Intermediate	Cationic, Wheland complex	Anionic, Meisenheimer Complex
Substituent that accelerate the reaction	+M/+I groups	strong -M groups
Leaving group	-H ($-SiR_3$; $-CR_3$)	-F, -Cl, -OR

1.7. Reaction of diazonium salts

- Sandmeyer reaction



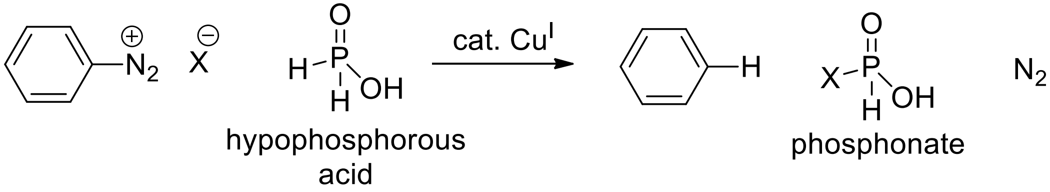
- General mechanism:



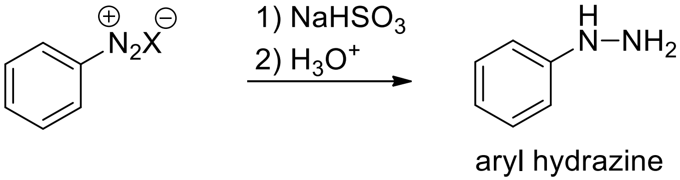
Exception: no copper needed with iodide, iodide act as a redox catalyst itself

1.7. Reaction of diazonium salts

- Meerwein reduction: removal of the diazonium group



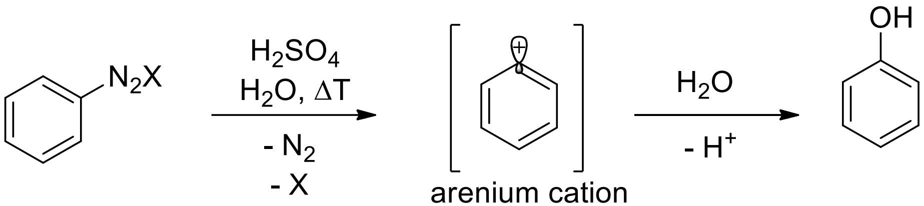
- Reduction of a diazonium salt maintaining the N-N single bond: preparation of aromatic hydrazines



1.7. Reactions proceeding by arenium cations

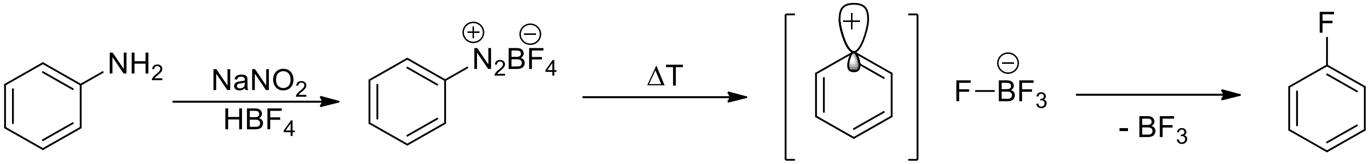
Only possible with the very best leaving group: N_2

- Generation of arene cations: “Phenol cooking”



arenium cation
orthogonal to π-system
unstabilized and very reactive

- Balz-Schiemann reaction: introduction of a fluorine substituent

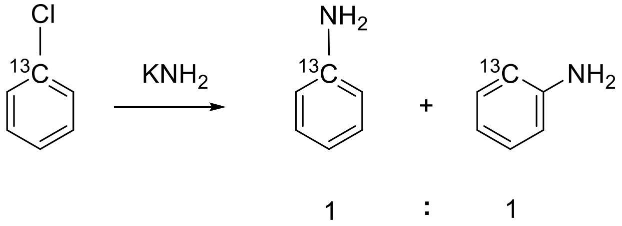


isolated salt

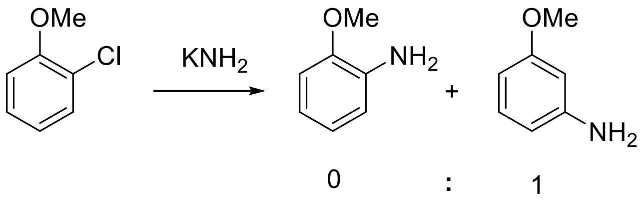
1.8. Substitution by the aryne mechanism

Experimental observations:

A)

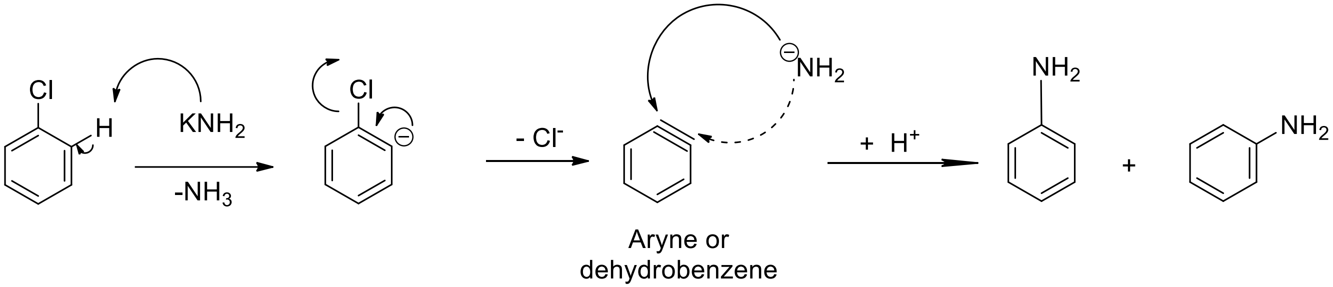


B)

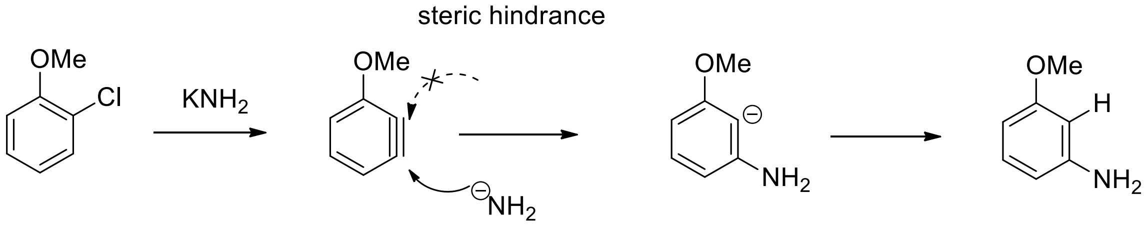


Explanation by a new mechanism:

A)



B)



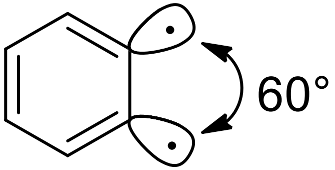
- σ- acceptor stabilizes the negative charge
- Attack on meta position due to less steric hindrance

1.8. Substitution by the aryne mechanism

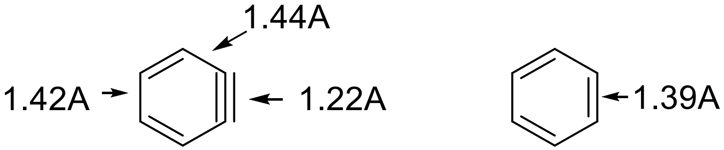
General properties of the arynes

- Are not real/normal triple bond with two sp-hybridized carbon atoms
- Only a partial orbital overlap possible, remain mostly sp^2-hybridized

- Arynes are reactive singulett species

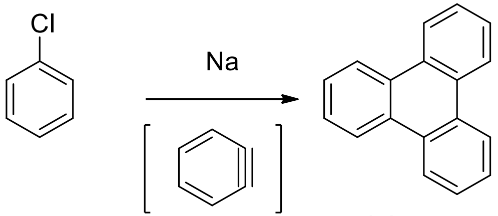


- Bond lengths in comparison to benzene



1.8. Substitution by the aryne mechanism

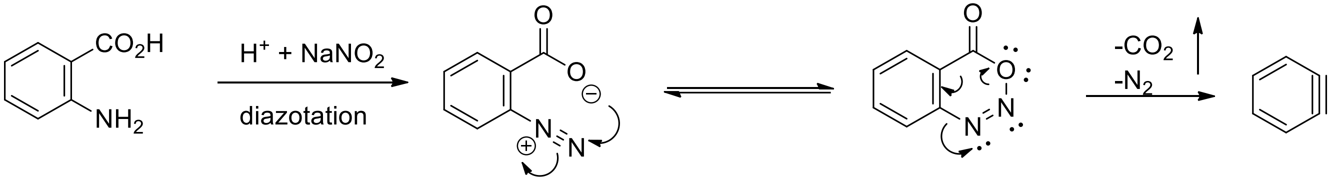
Other reactions of arynes:



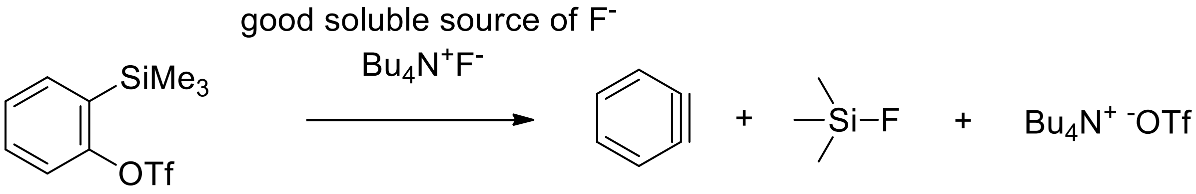
triphenylene

Trimerization in higher concentration and absence of reaction partner

Additional methods for their preparation:



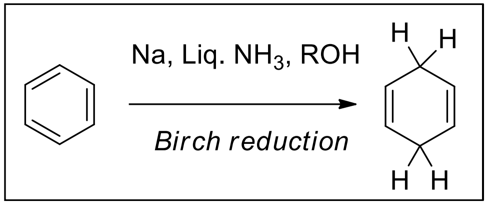
Modern method:



Tf= Triflat, Trifluoromethane sulfonyl $^{-}O_3SCF_3$

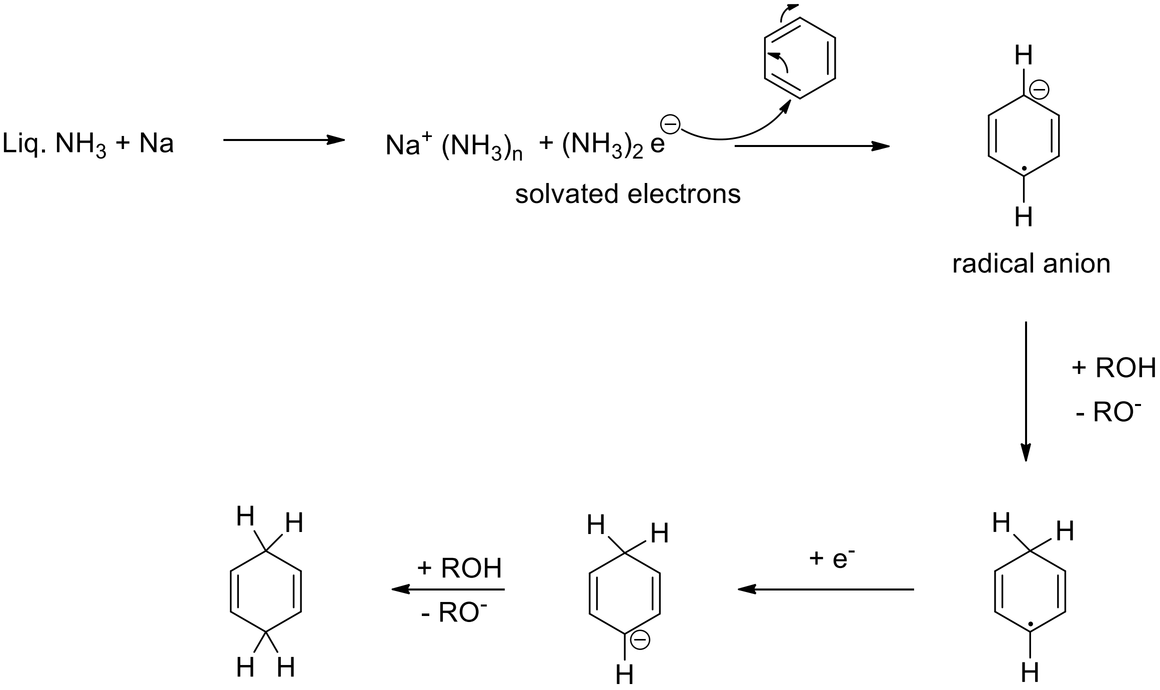
1.9. Reduction of the aromatic ring

Birch reduction: reduction of the aromatic ring to give 1,4-cyclohexadienes



Solvent: liquid ammonia
Reaction below -31°C

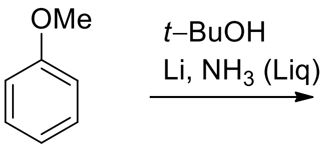
Mechanism:

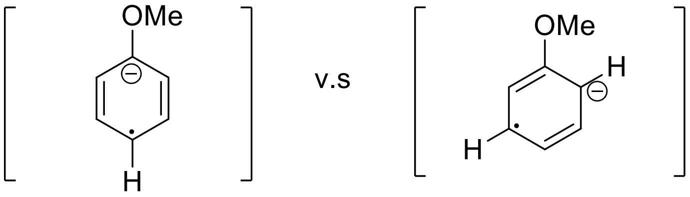


1.9. Reduction of the aromatic ring

Regioselectivity of the reduction:

Case 1: Electron-donating substituents

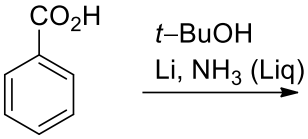


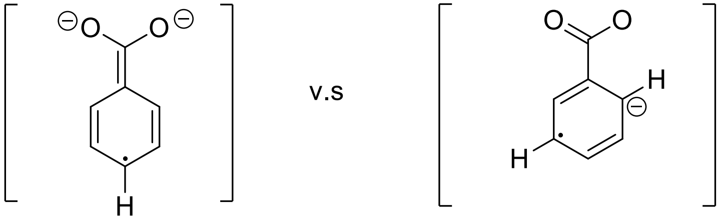


less stable intermediate
not formed

more stable intermediate
preferred

Case 2: Electron-withdrawing substituents





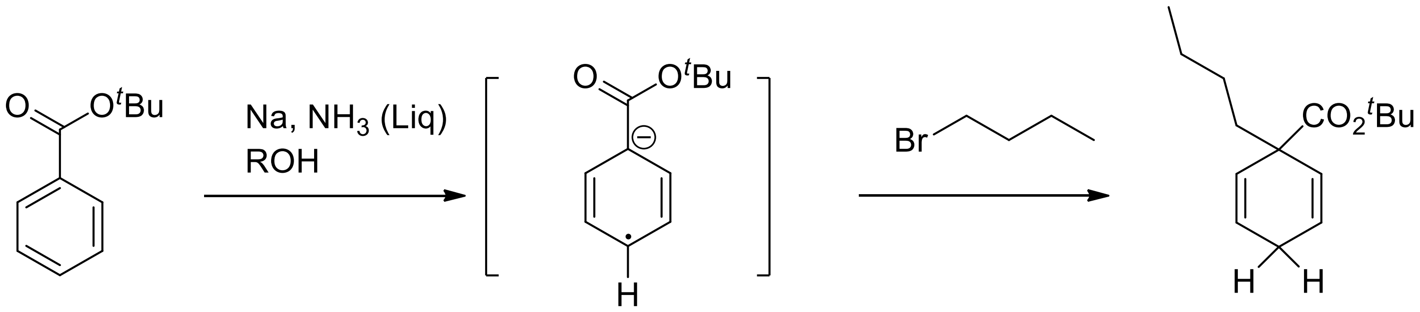
better stabilization of
the negative charge

not formed

1.9. Reduction of the aromatic ring

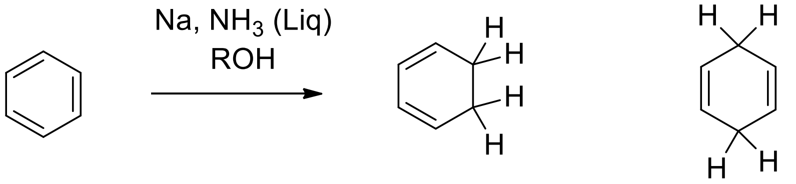
Example for a Birch alkylation:

interception of the carbanion by an electrophile, e.g. alkylhalide instead of proton



1.9. Reduction of the aromatic ring

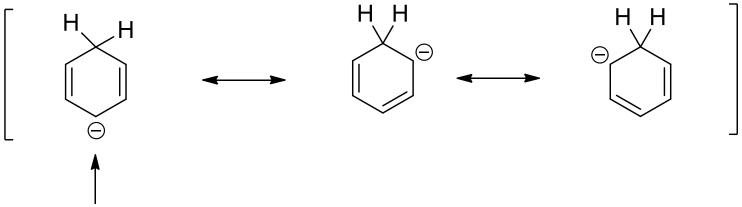
The Birch reduction yields selectively 1,4-Cyclohexadienes.
Why are 1,3-Cyclohexadienes not formed?



1,3-Cyclohexadiene
not formed

1,4-Cyclohexadiene
observed

Explanation by the electron densities of the pentadienyl anion



highest electron density
most reactive position

Relevant HOMO: the electron density is highest at central carbon atom C3

MO scheme: