

Ian Fleming's

Molecular Orbitals and Organic Chemical Reactions

Preface

1 Molecular Orbital Theory

2 The Structures of Organic Molecules

3 Chemical Reactions—How Far and How Fast

4 Ionic Reactions—Reactivity

5 Ionic Reactions—Stereochemistry

6 Thermal Pericyclic Reactions

7 Radical Reactions

8 Photochemical Reactions

The Effect of π Conjugation π 共役効果

Substituent 置換基

Substituent Effect 置換基効果

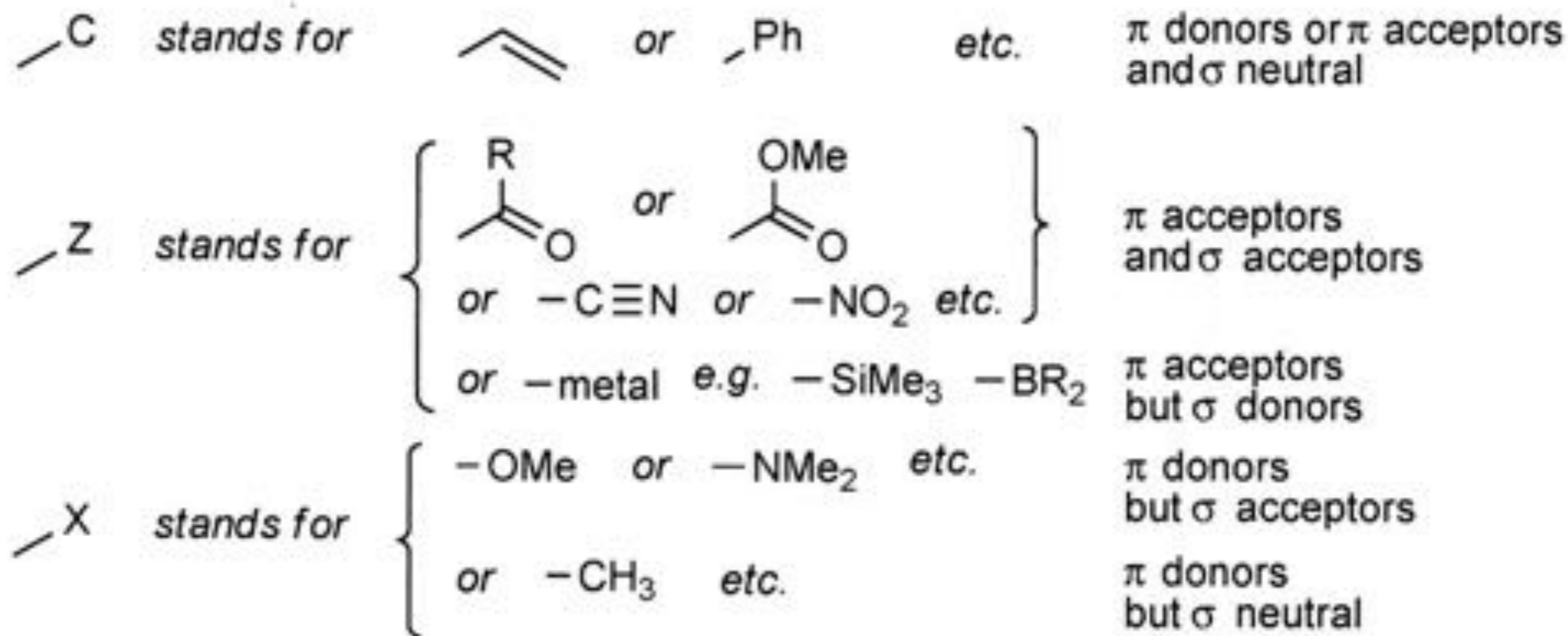
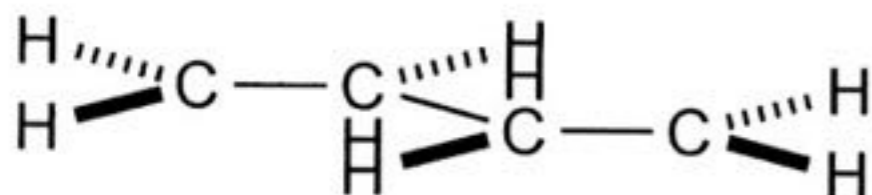
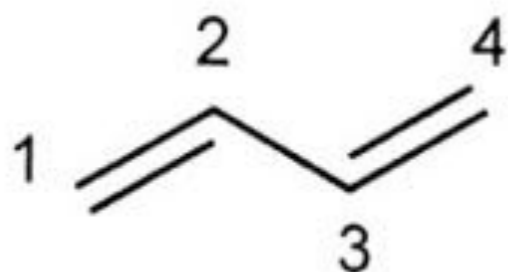


Fig. 2.1 Definitions and character of C-, Z- and X-substituents

Butadiene



$$c_{jr} = \sqrt{\frac{2}{n+1}} \sin \frac{rj\pi}{n+1}$$

Frontier Orbitals:

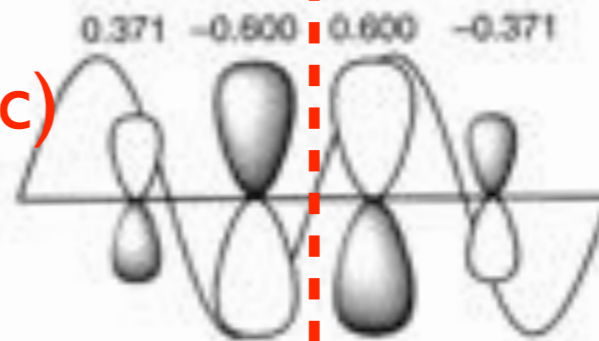
HOMO: Highest Occupied MO

LUMO: Lowest Unoccupied MO

A(Antisymmetric)

3 nodes

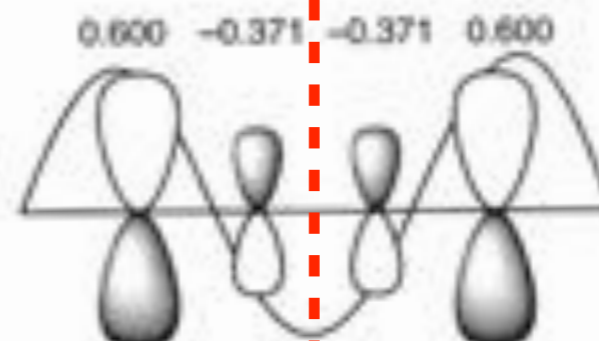
ψ_4^*



S(Symmetric)

2 nodes

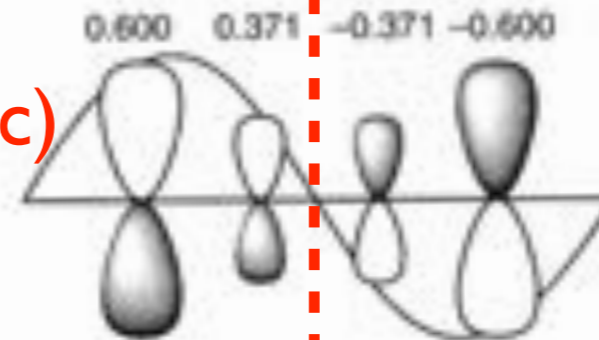
ψ_3^*



A(Antisymmetric)

1 node

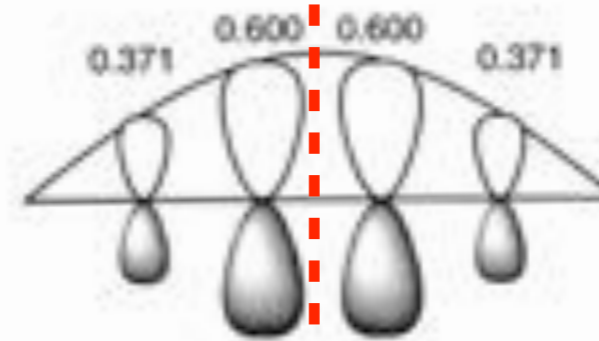
ψ_2



S(Symmetric)

0 nodes

ψ_1



—

—

LUMO

↑↓

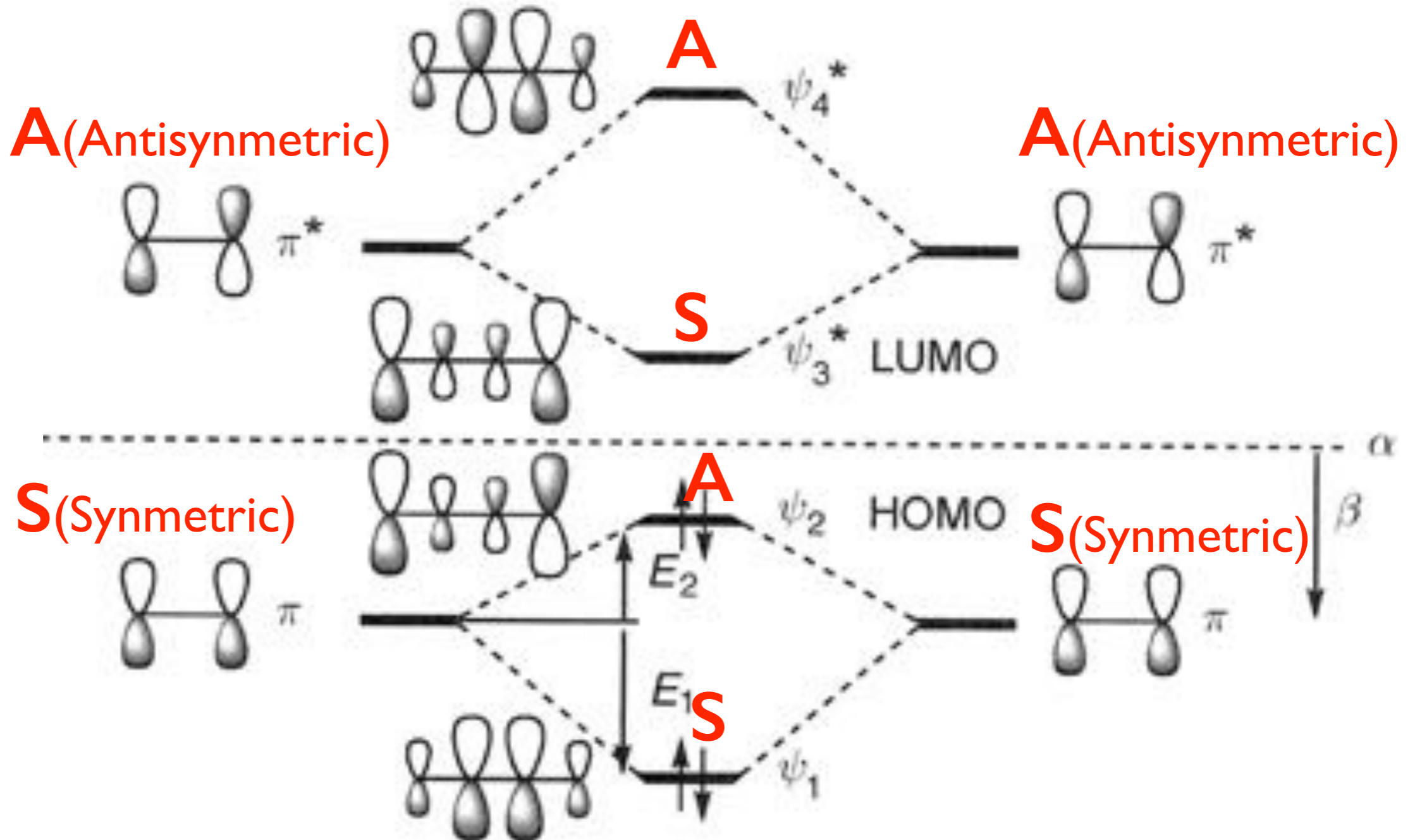
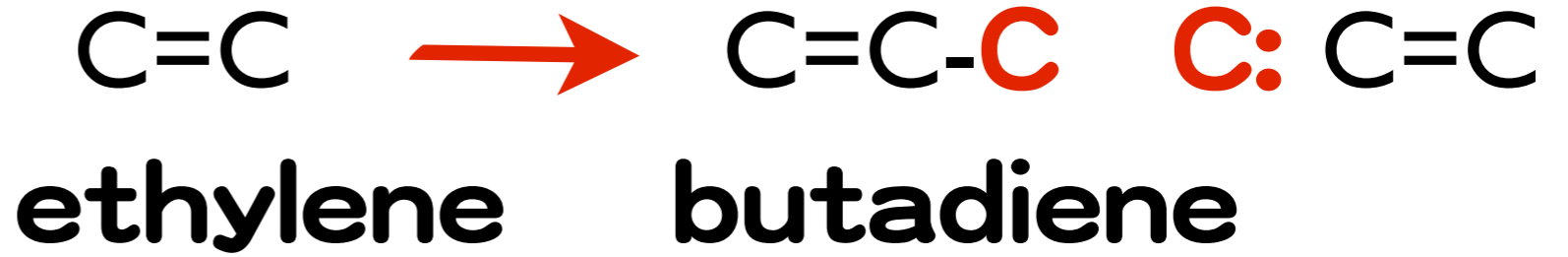
HOMO

↑↓

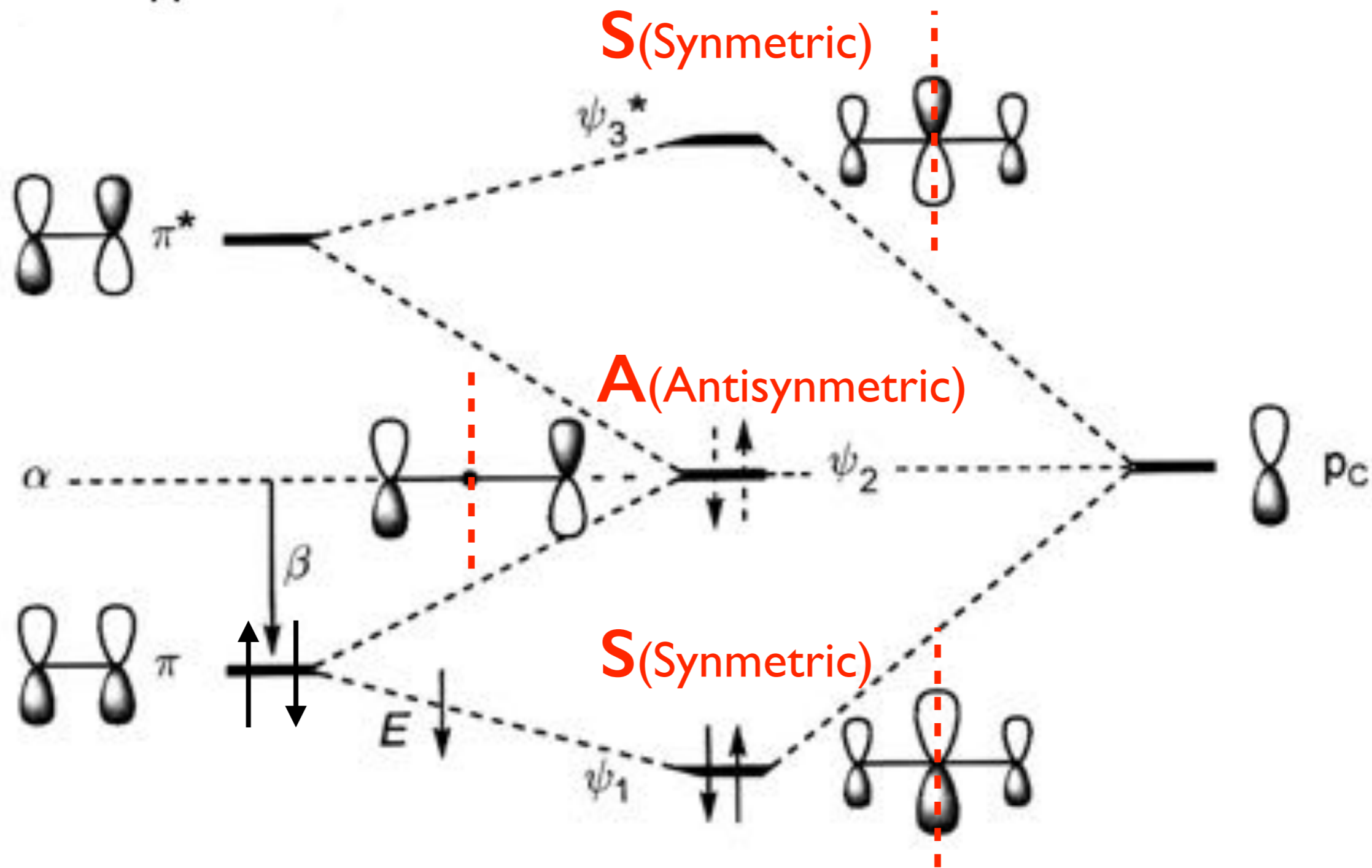
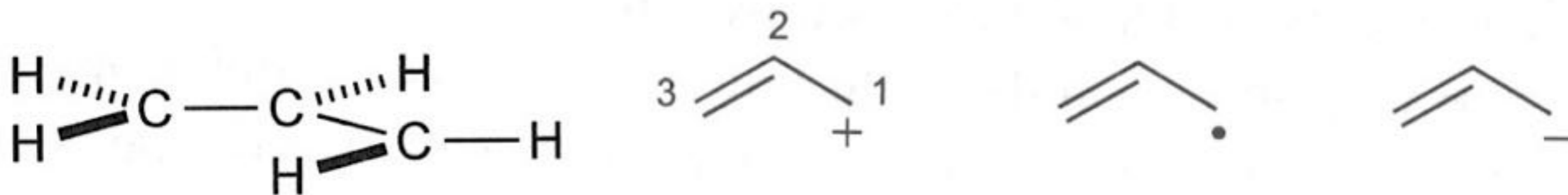
The Effect of Substituents on the Stability of Alkenes

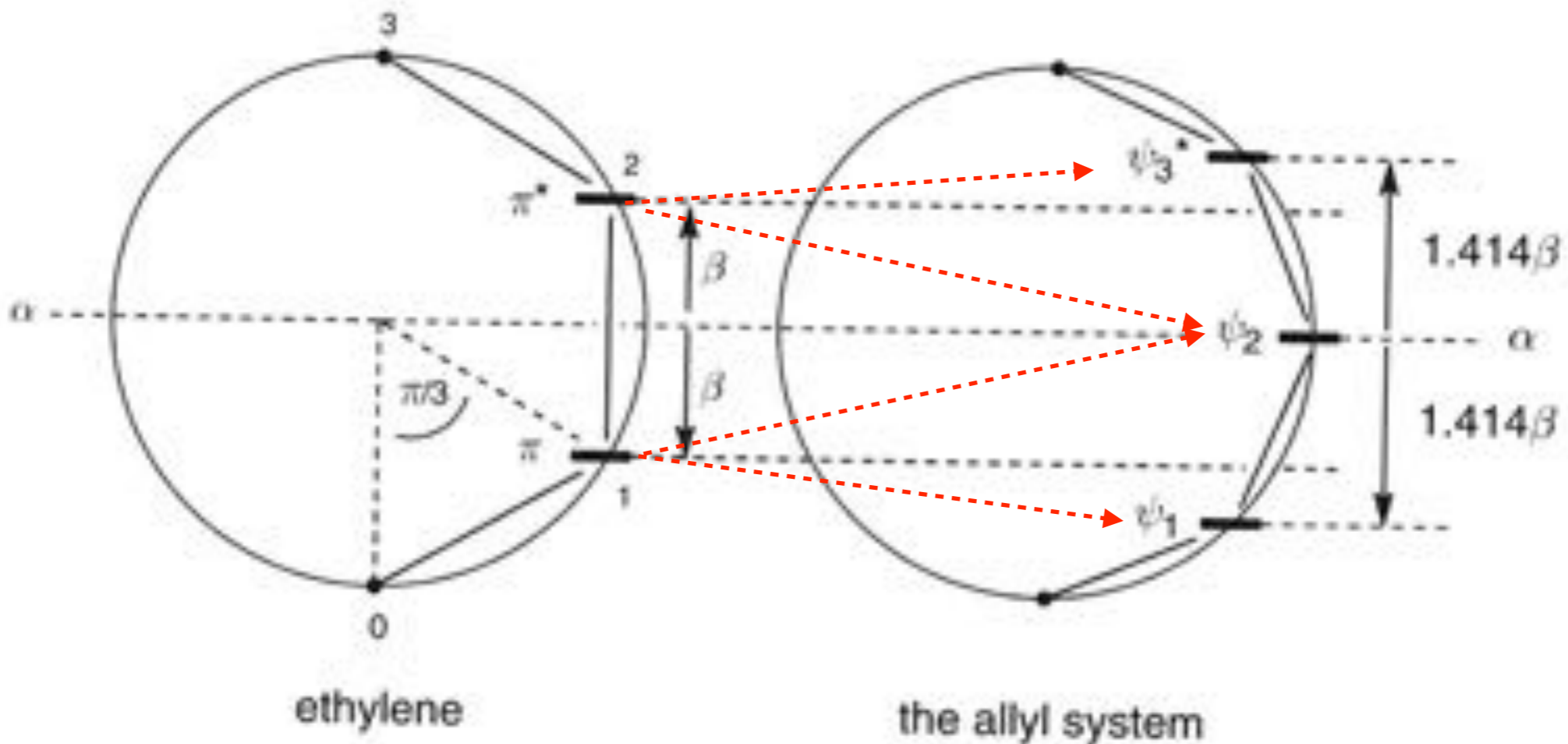
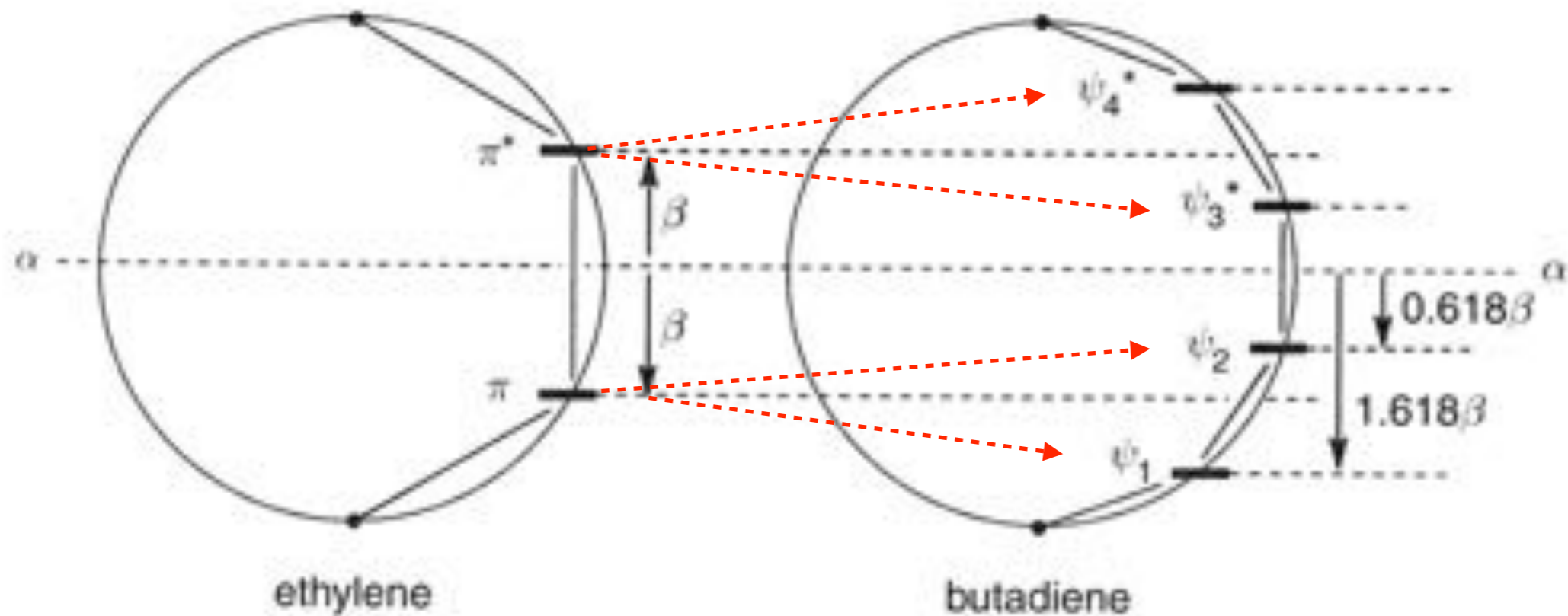
C-Substituents.

π donors or π acceptors
and σ neutral



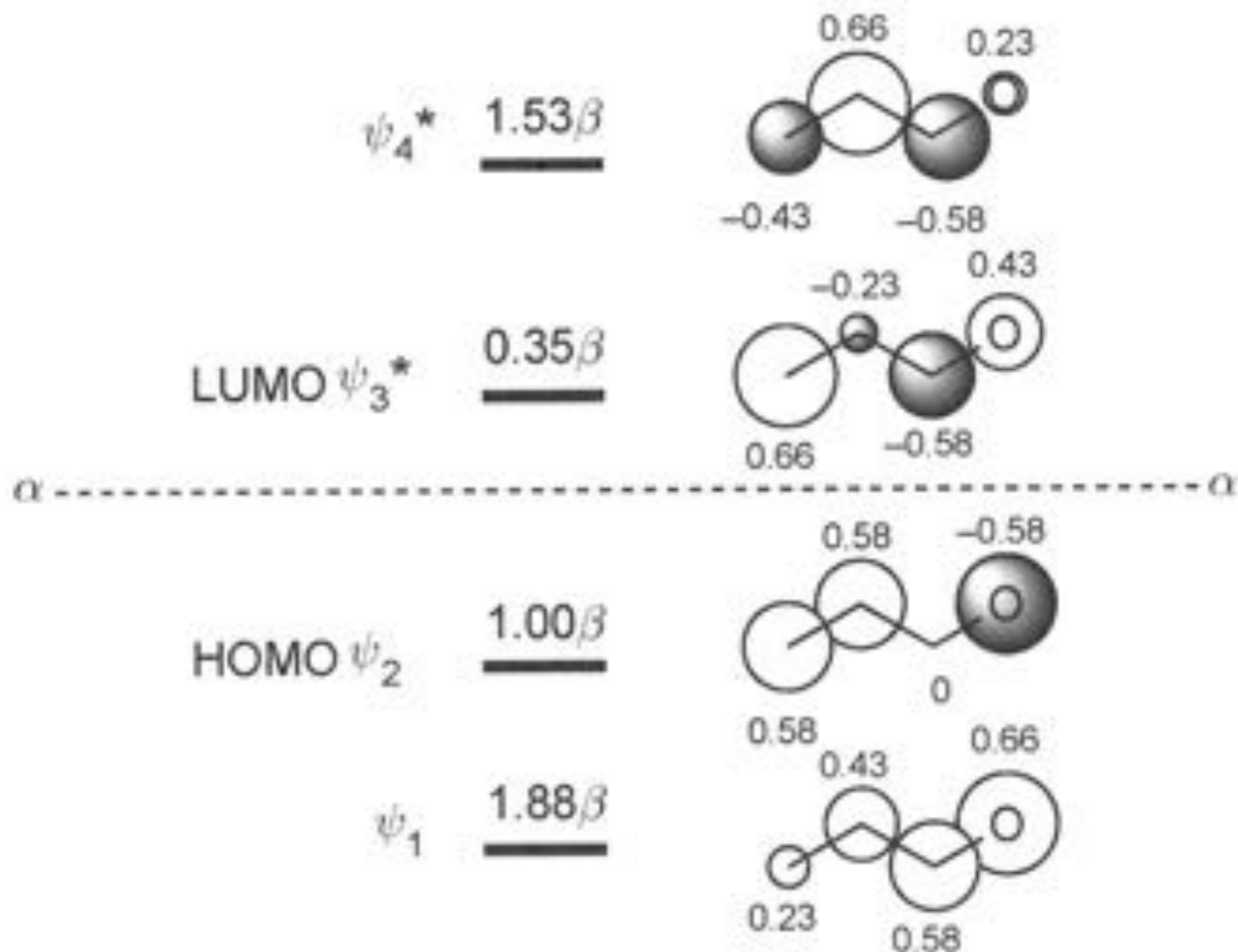
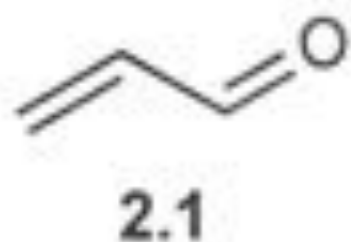
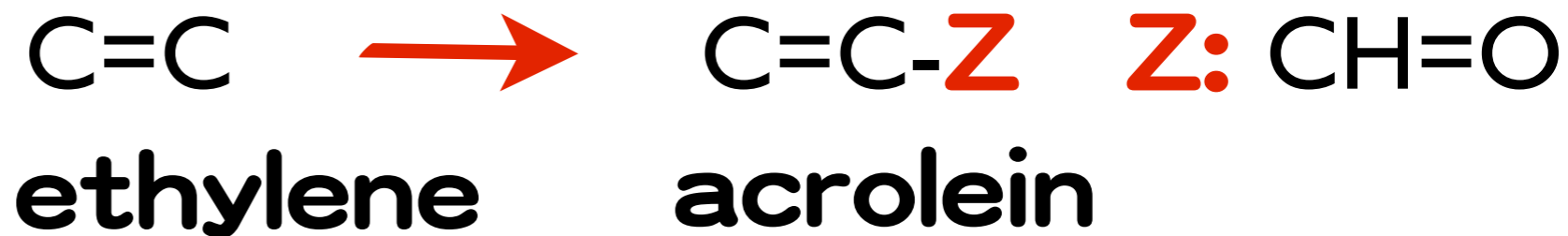
C-Substituents. allyl system





Z-Substituents.

π acceptors
and σ acceptors



X-substituents



π donors
but σ acceptors

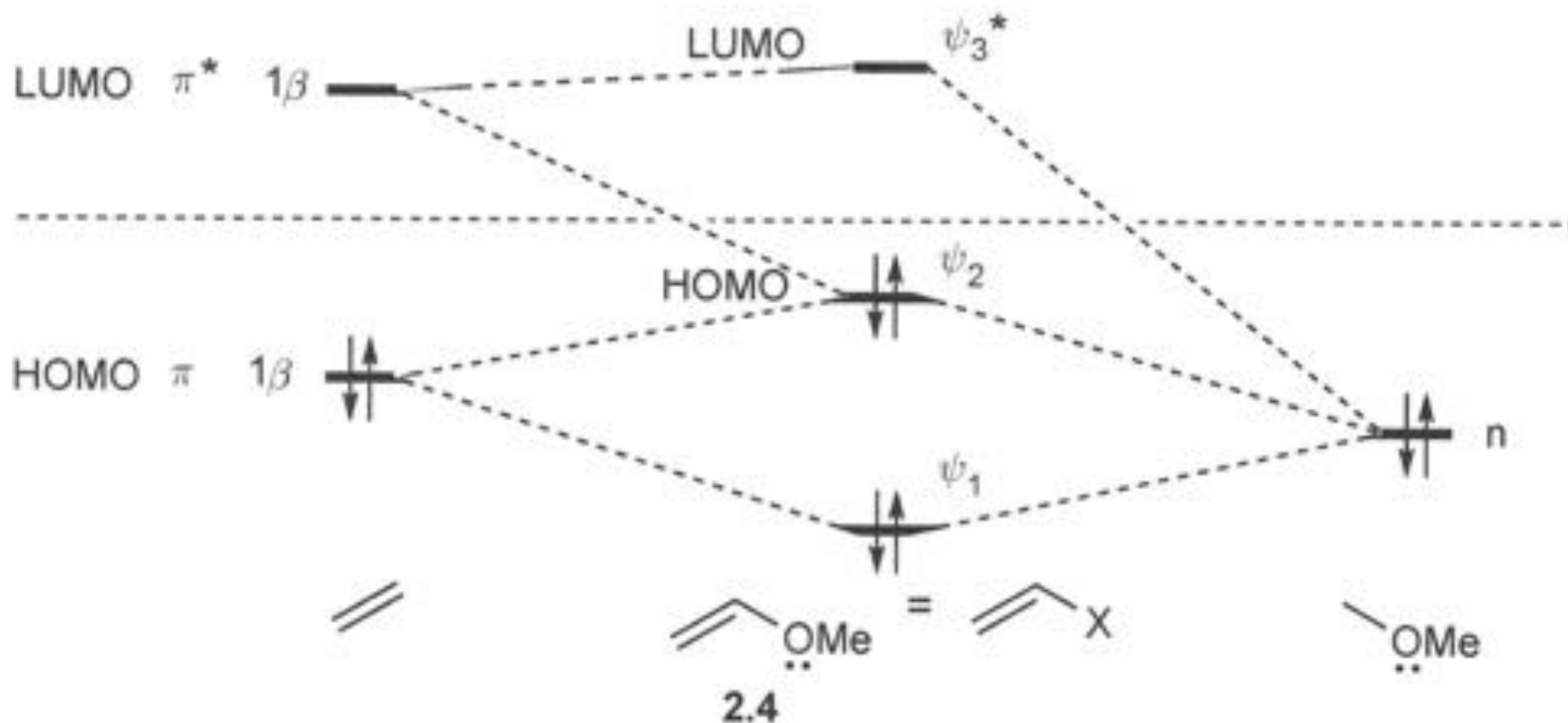
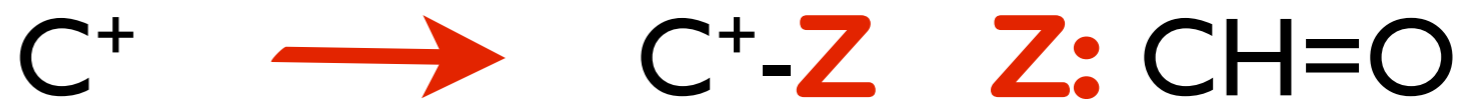


Fig. 2.5 Energies of the π orbitals of an X -substituted alkene

The Effect of Substituents on the Stability of Carbocations

Z-Substituents.



π acceptors
and σ acceptors

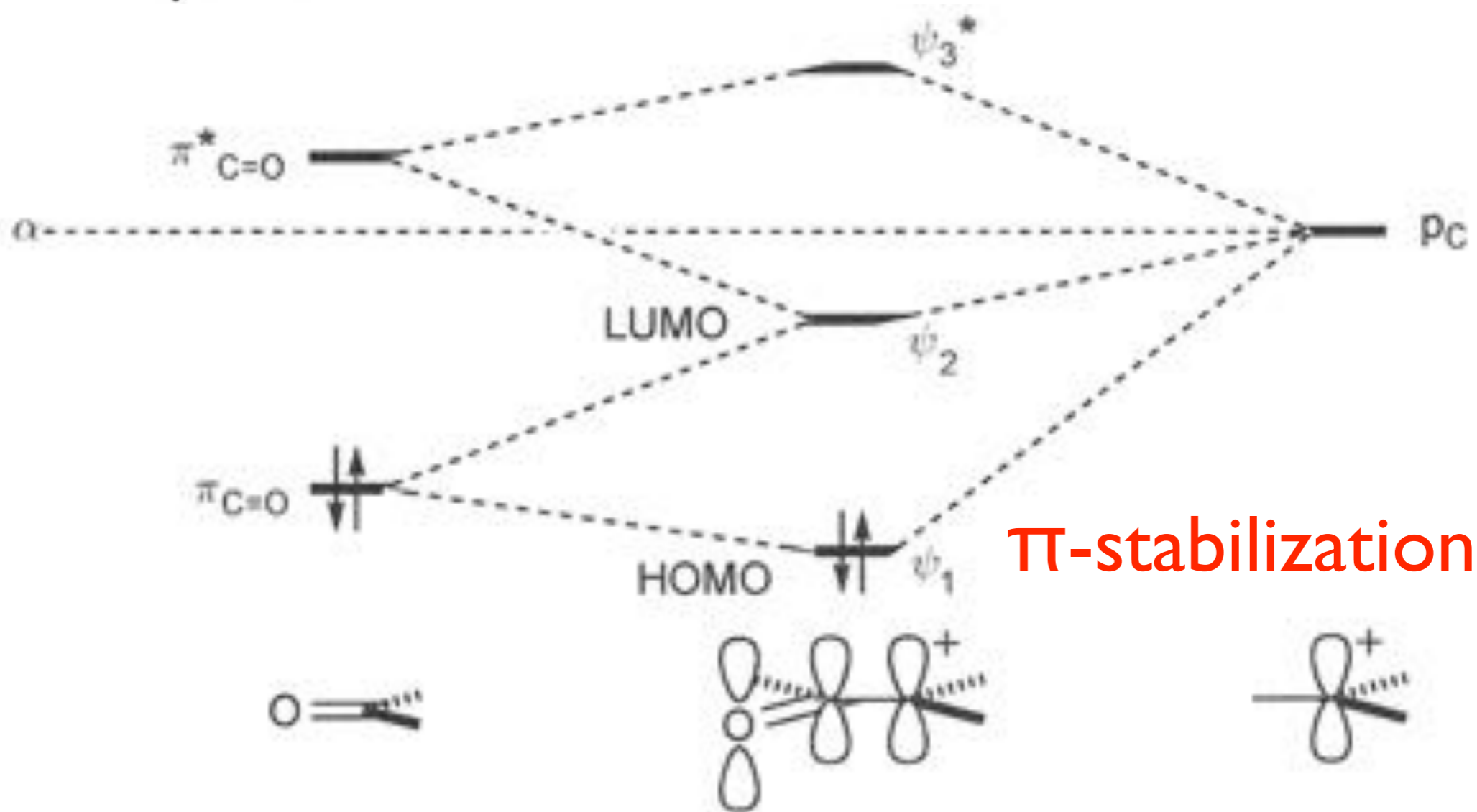


Fig. 2.7 The π orbitals of a carbocation conjugated to a Z-substituent

σ Conjugation—Hyperconjugation 超共役

C—H Hyperconjugation

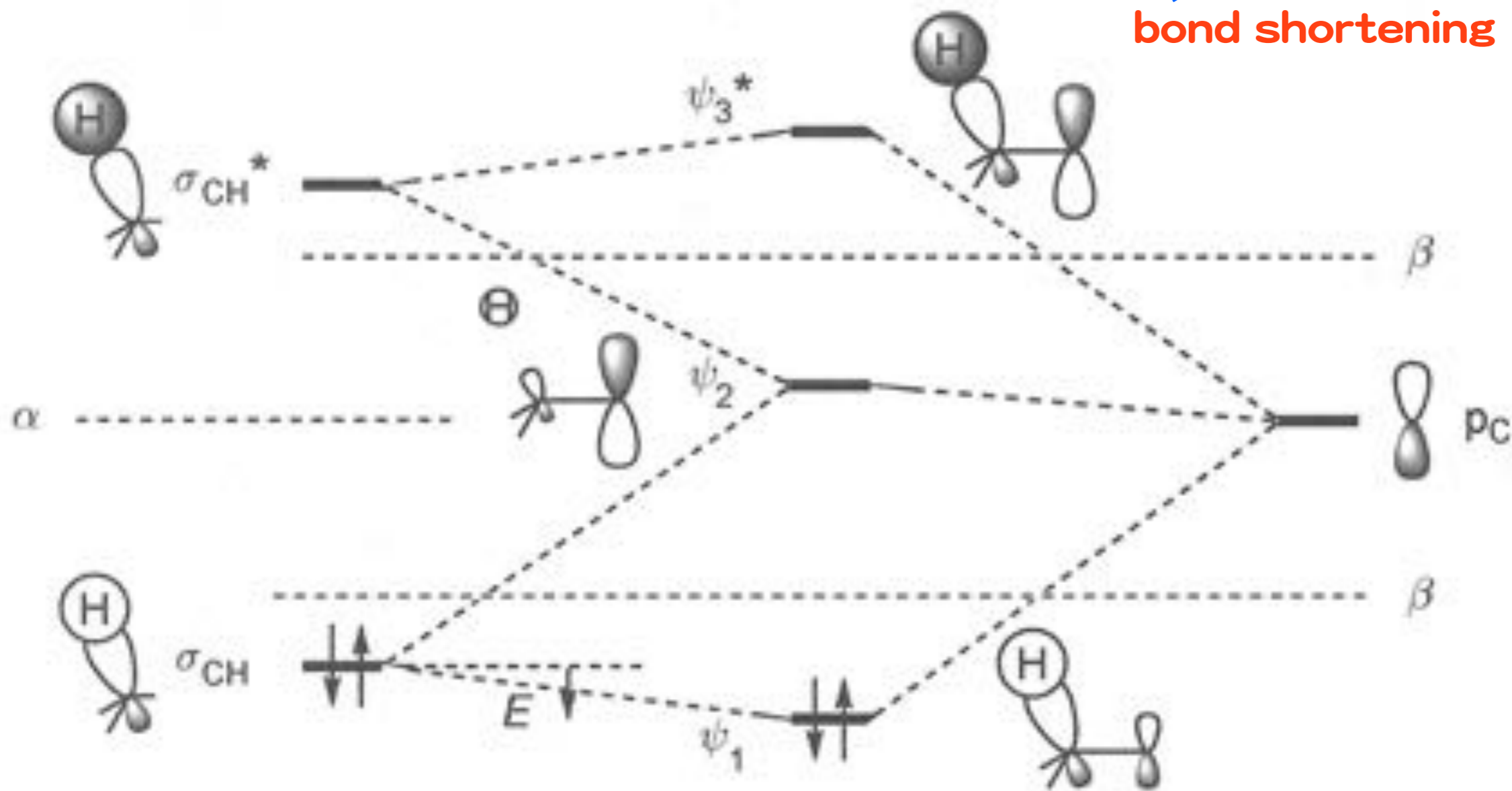
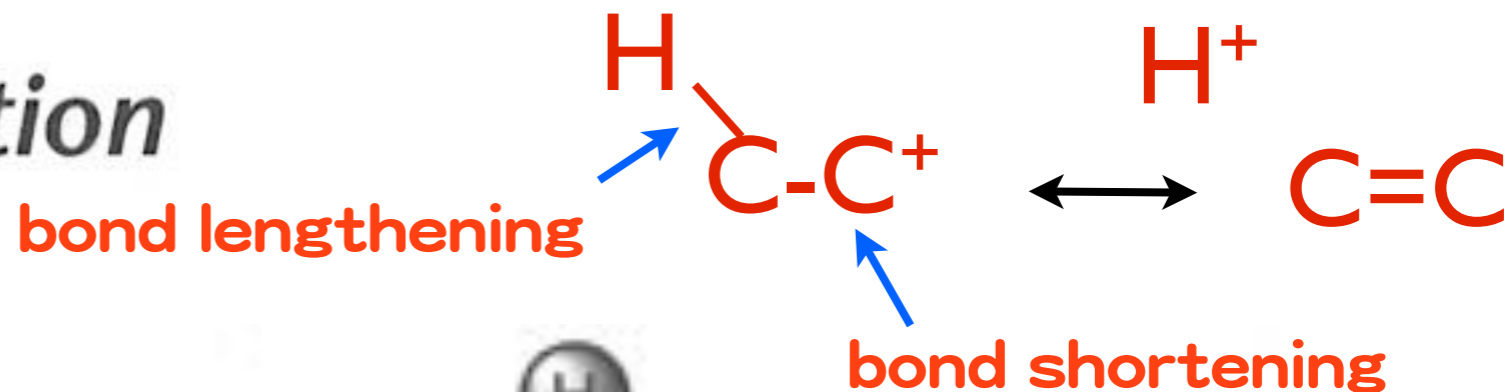


Fig. 2.9 Interaction of the orbitals of a σ C—H bond with an empty p orbital on carbon

C—H Hyperconjugation 超共役

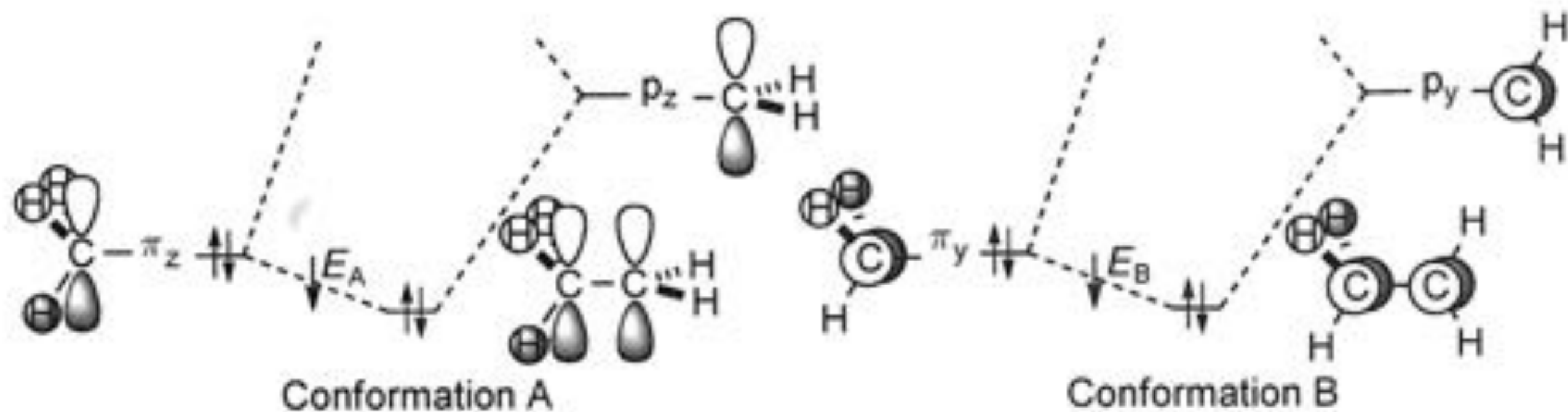
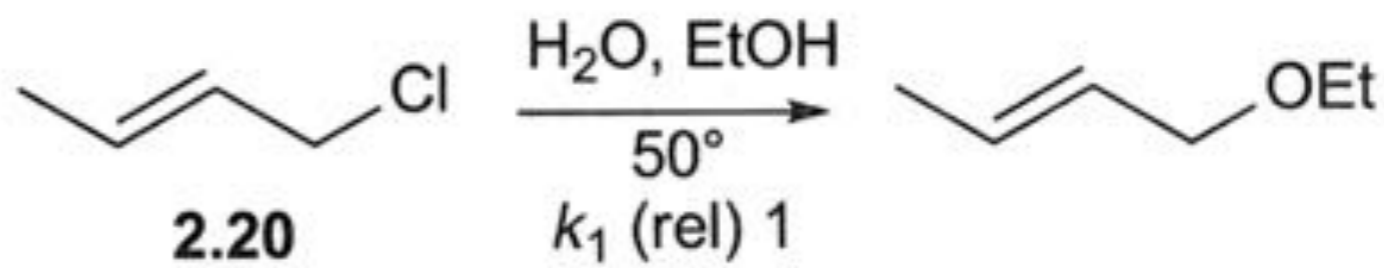
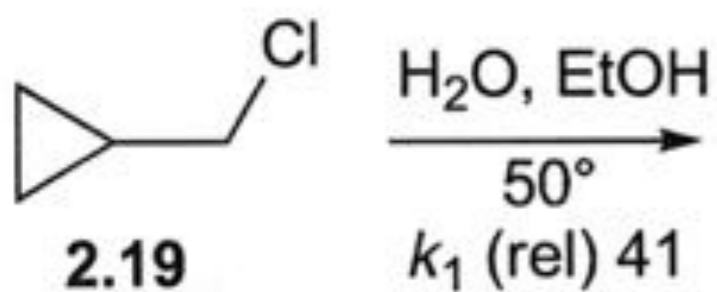
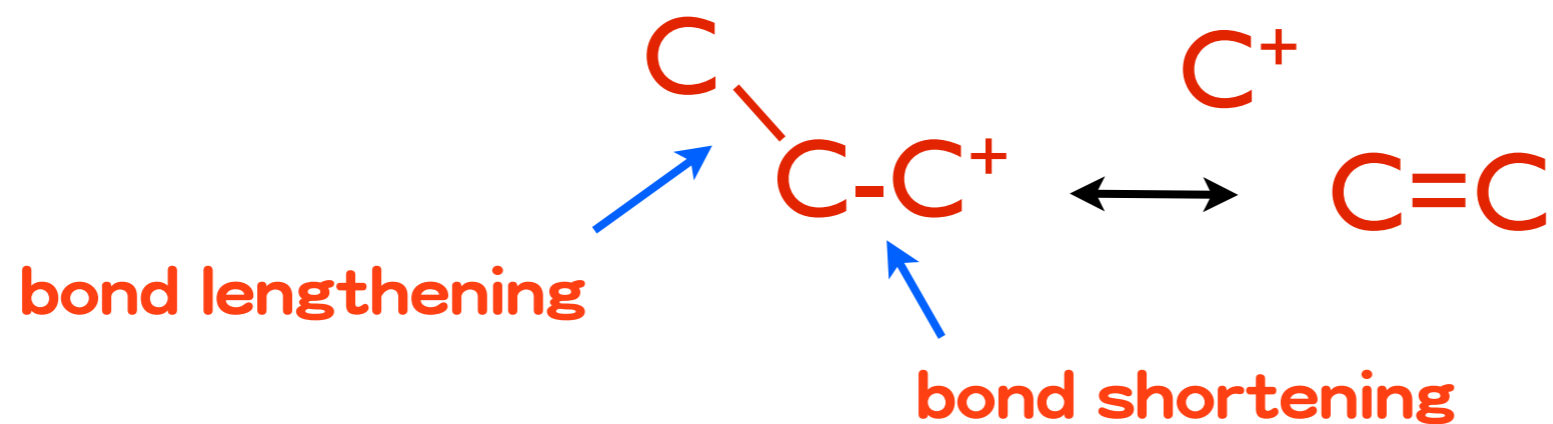


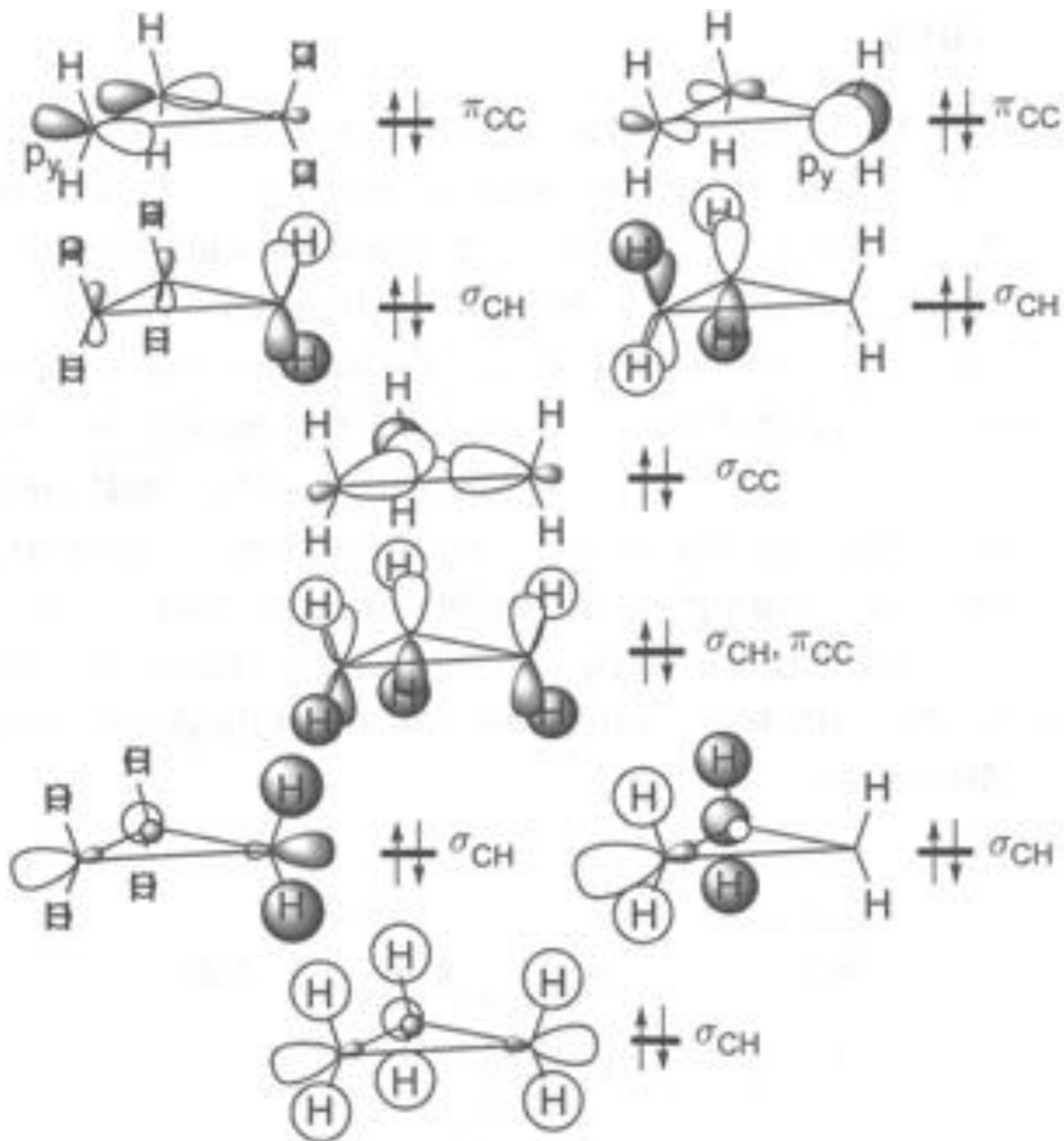
Fig. 2.10 Orbital interactions stabilising two conformations of the ethyl cation

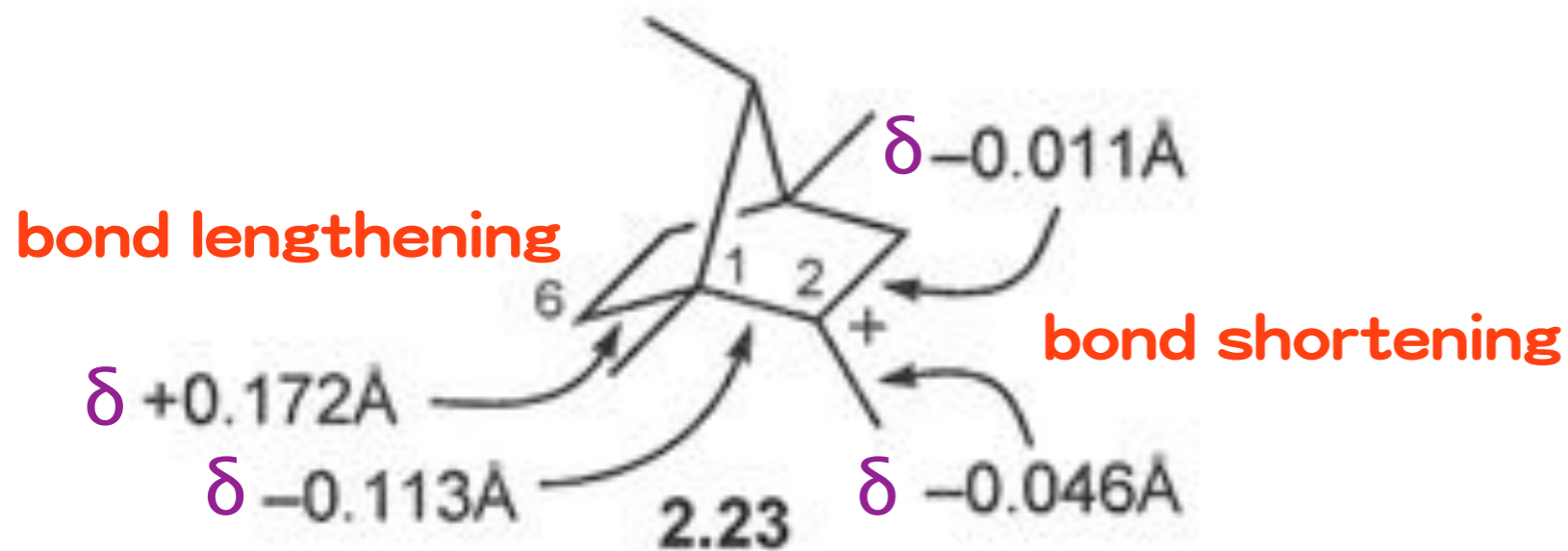
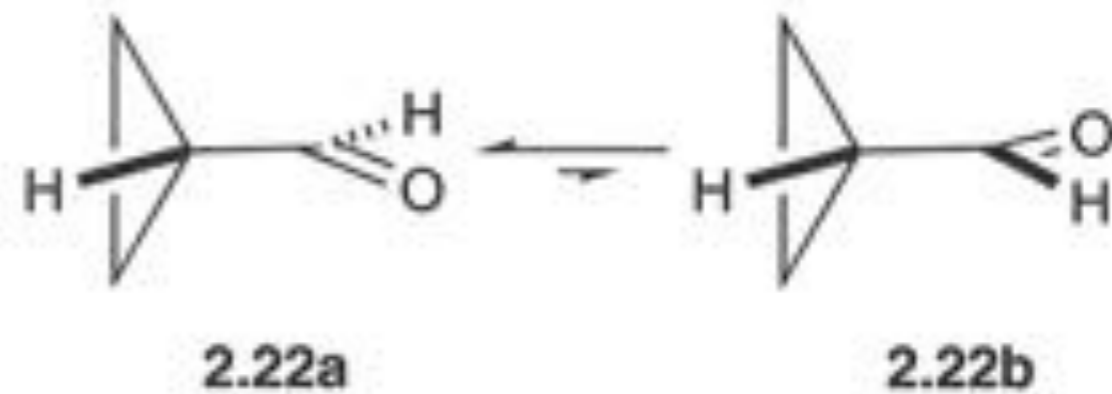
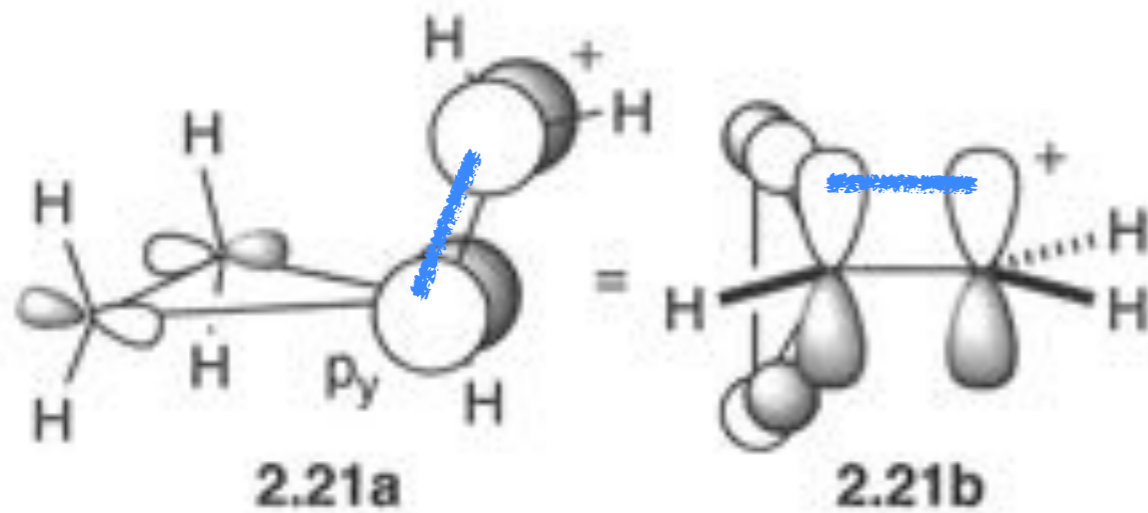
C—C Hyperconjugation

超共役



Walsh Orbitals of Cyclopropane



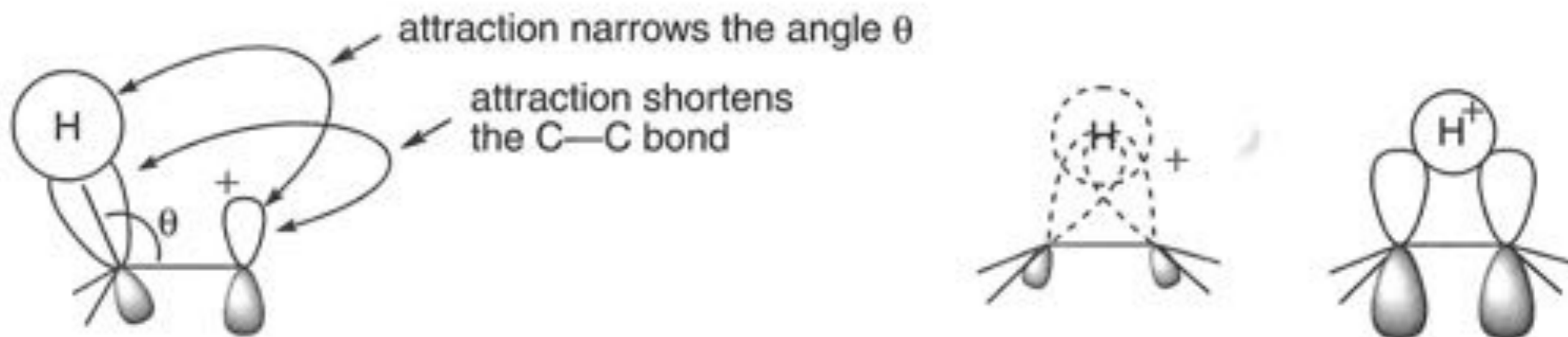


bicyclo[2.2.1]heptyl cation

typical $\text{C}(\text{sp}^3)\text{-C}(\text{sp}^2)$: 1.522\AA

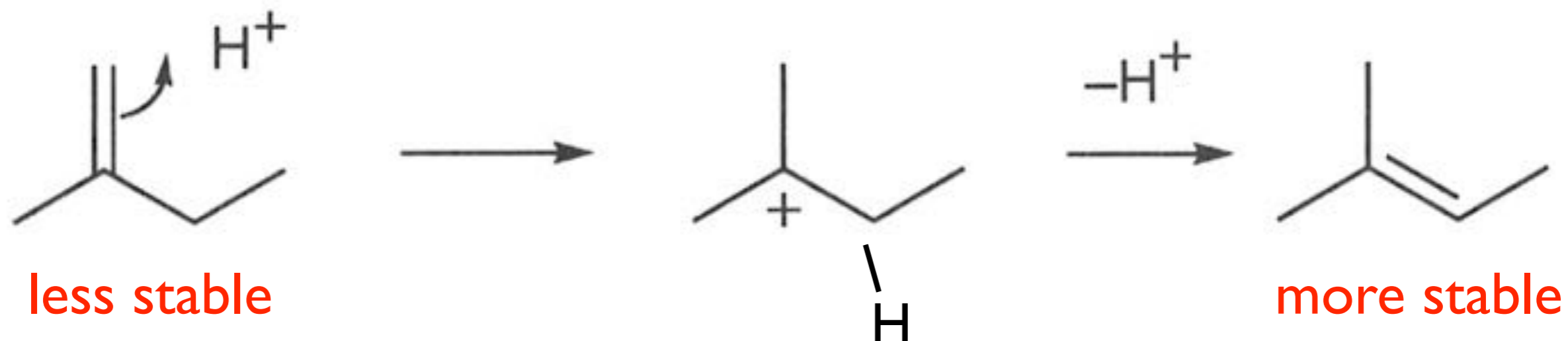
typical $\text{C}(\text{sp}^3)\text{-C}(\text{sp}^3)$: 1.538\AA

Structure of Carbocations



Cf: Transition State Structures of Carbocations in 1,2-Hydride shift and Wagner-Meerwein Type Rearrangement

Proton-catalysed Isomerisation of Olefins



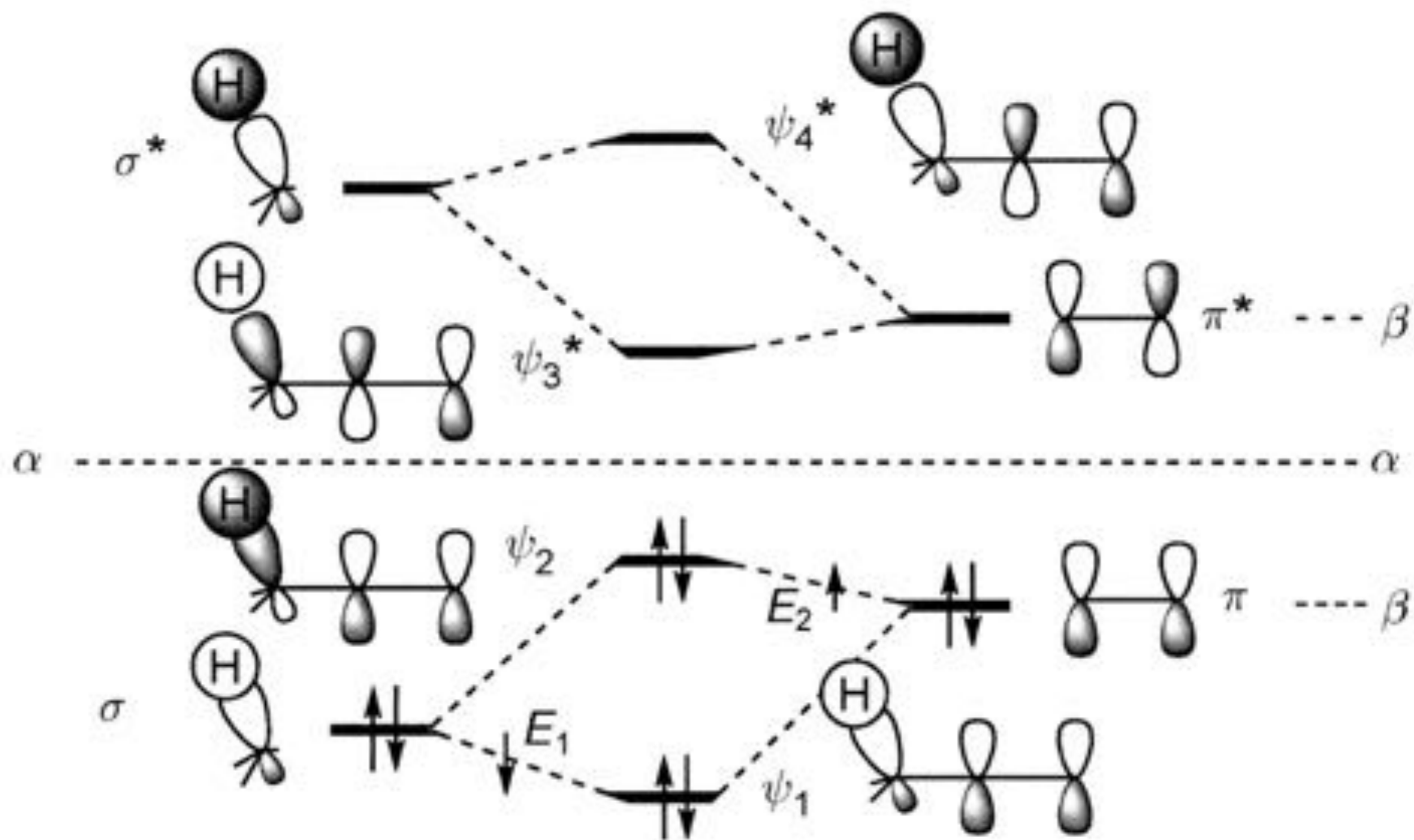


Fig. 2.11 Hyperconjugative stabilisation of a C=C π bond

C—M Hyperconjugation

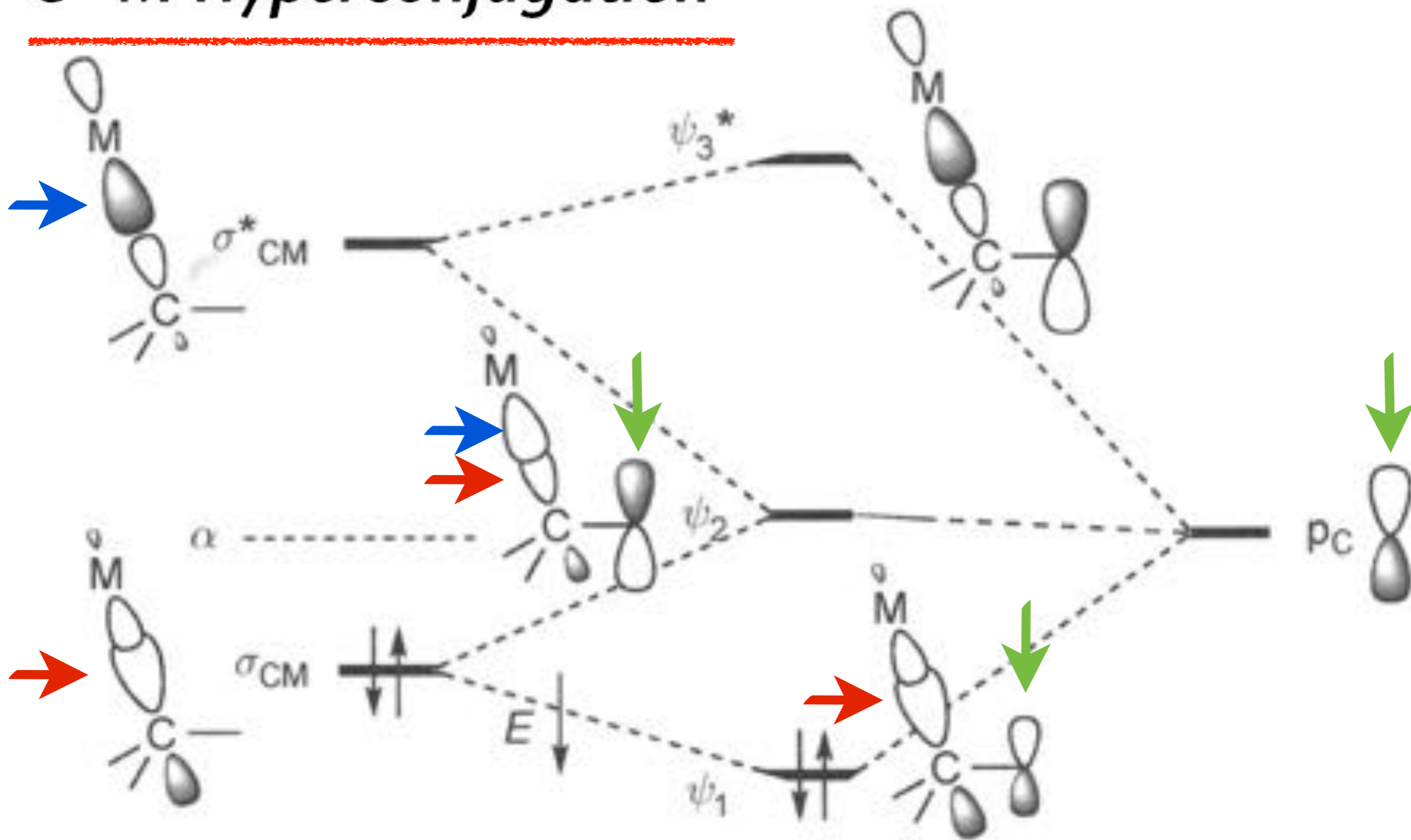
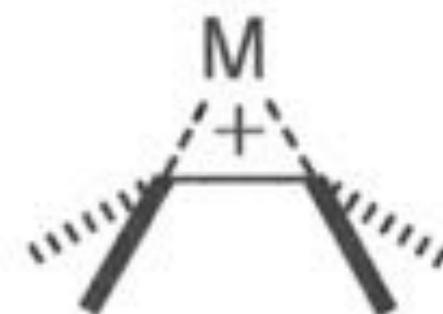
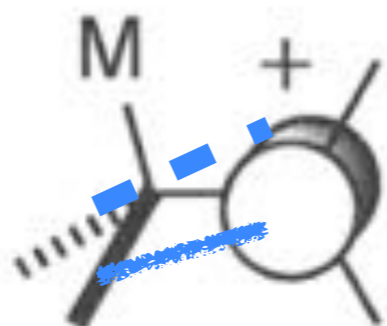
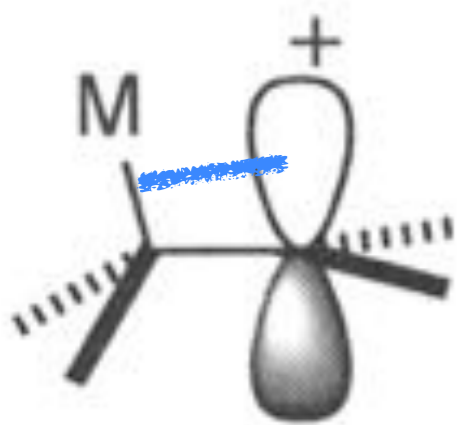


Fig. 2.13 Interaction of the orbitals of a carbon-metal bond with an empty p orbital on carbon

Interaction of carbocation with β -C-M bond is stronger than β -C-H and C-C bonds



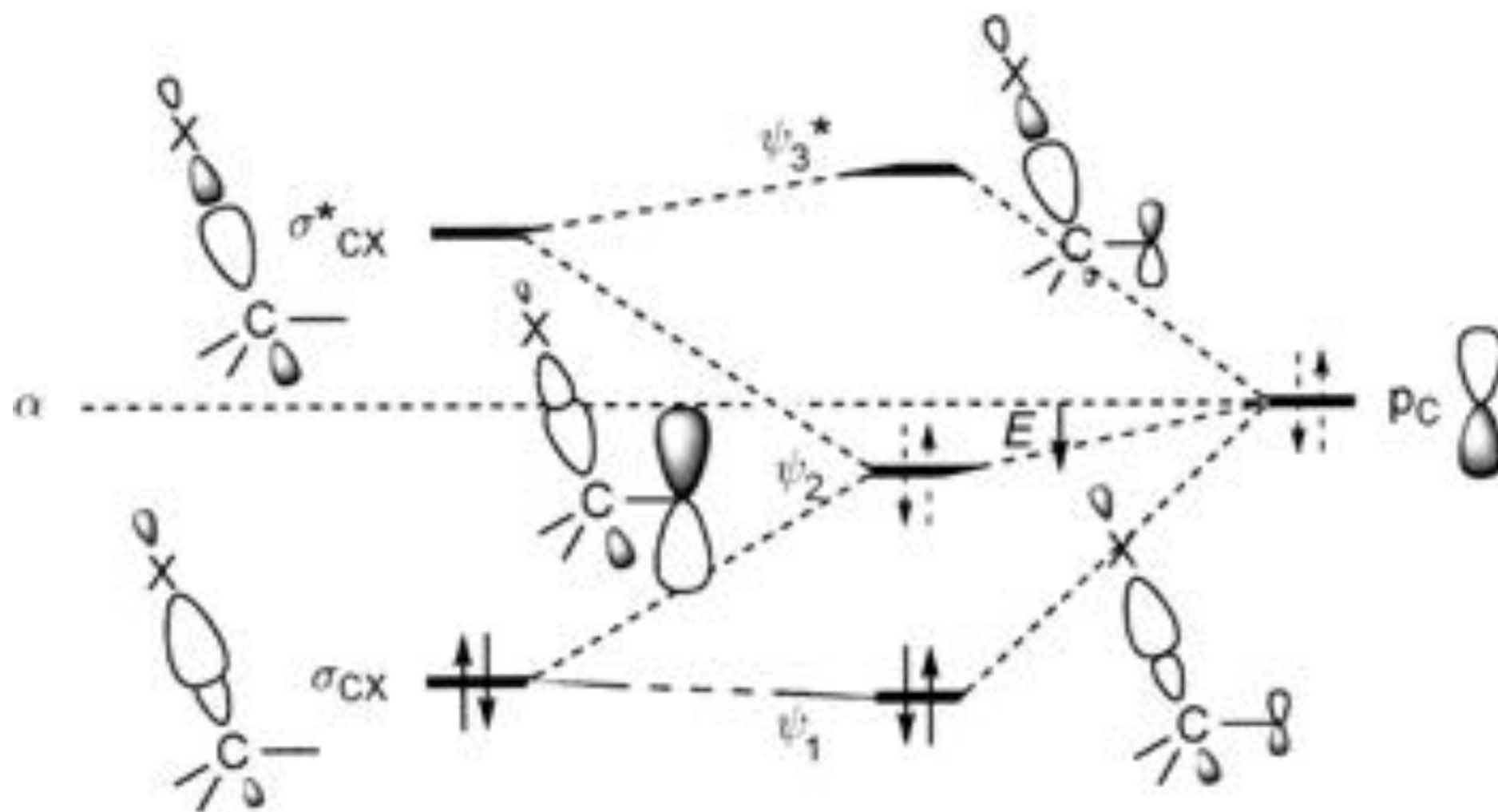
more stable

bridged structure
only with ethyl cation
substituted by SiMe_3

most of metal cations
bridged with olefins

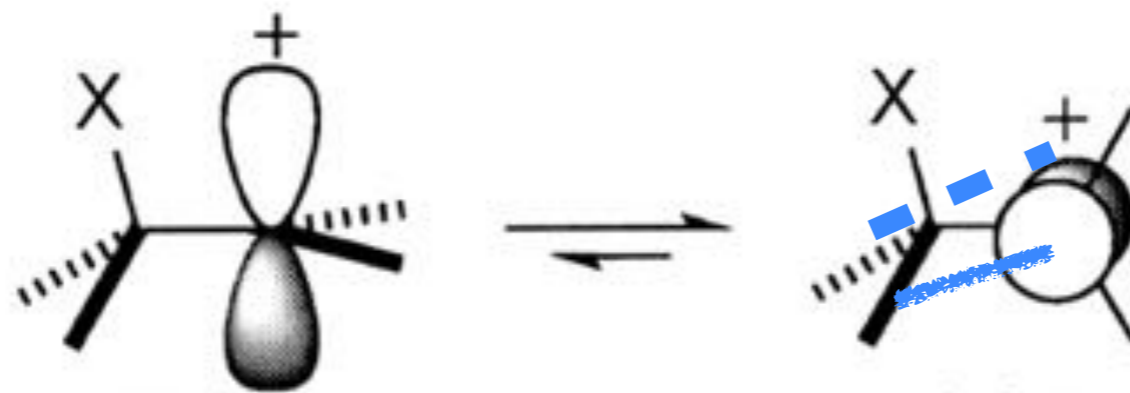
Negative Hyperconjugation

Negative Hyperconjugation with a Cation.



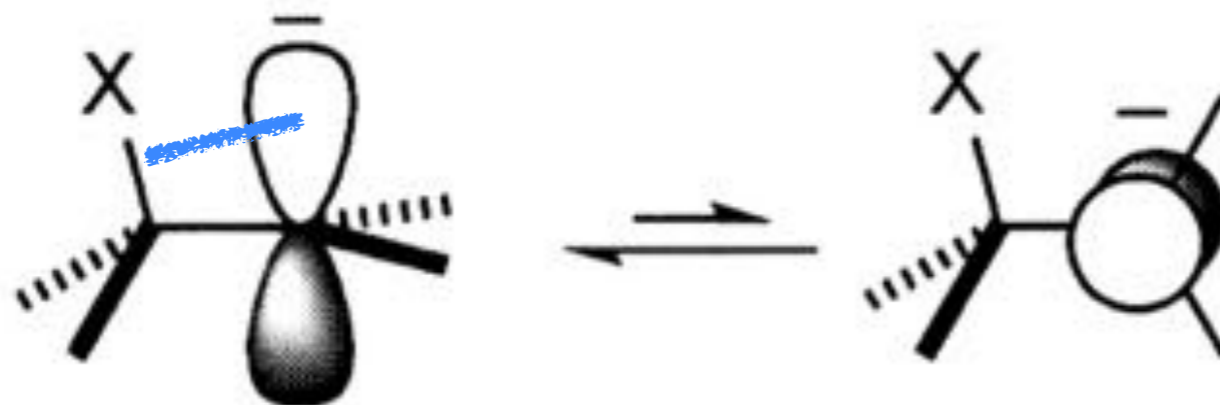
Interaction of the orbitals of a bond between carbon and an electronegative element X with a p orbital on carbon

little energy-lowering effect on a cation by low lying σ C-X bond

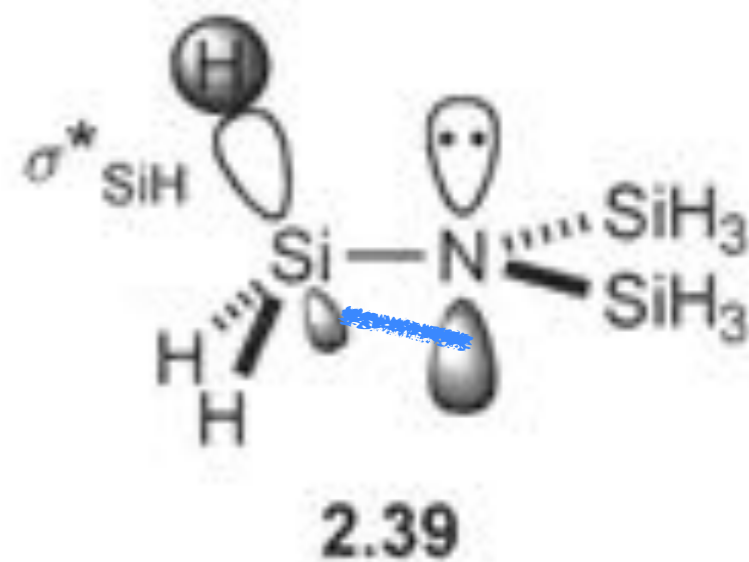
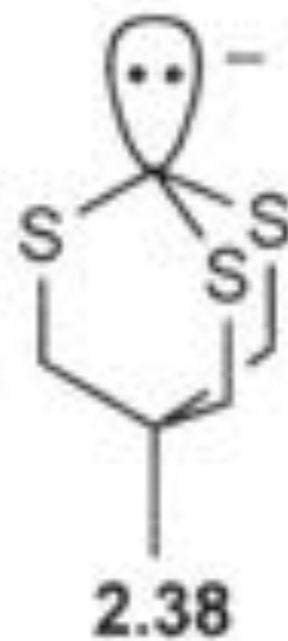
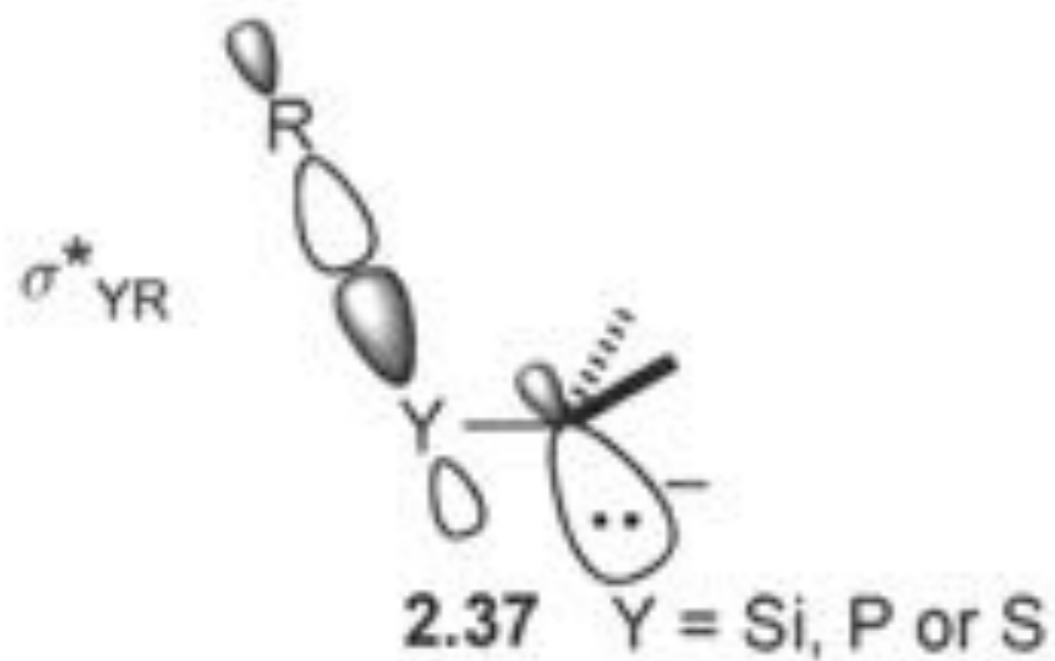


more stabilised by hyperconjugation
with β -C-H and/or C-C bonds

VS

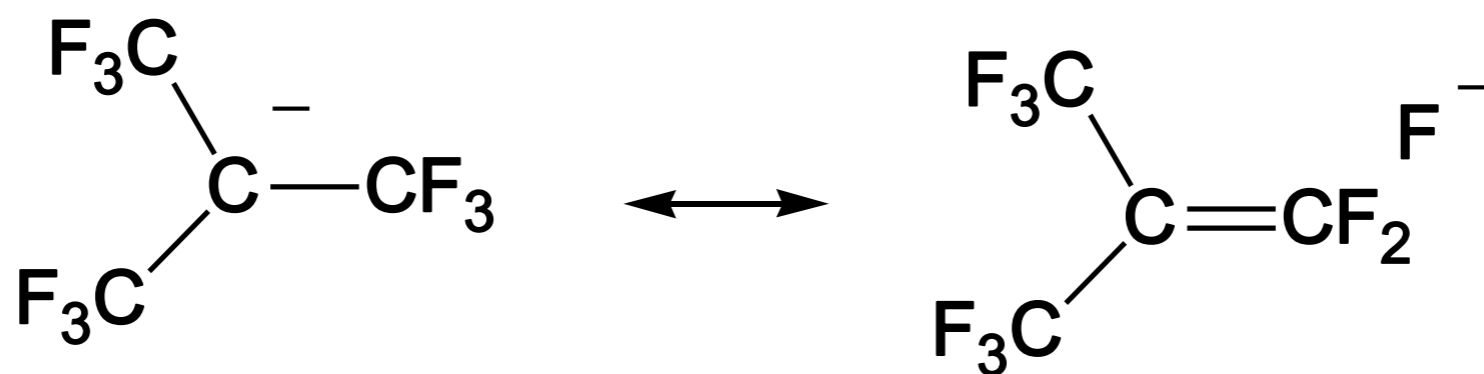


large energy-lowering effect on a carbanion by σ^* C-X bond



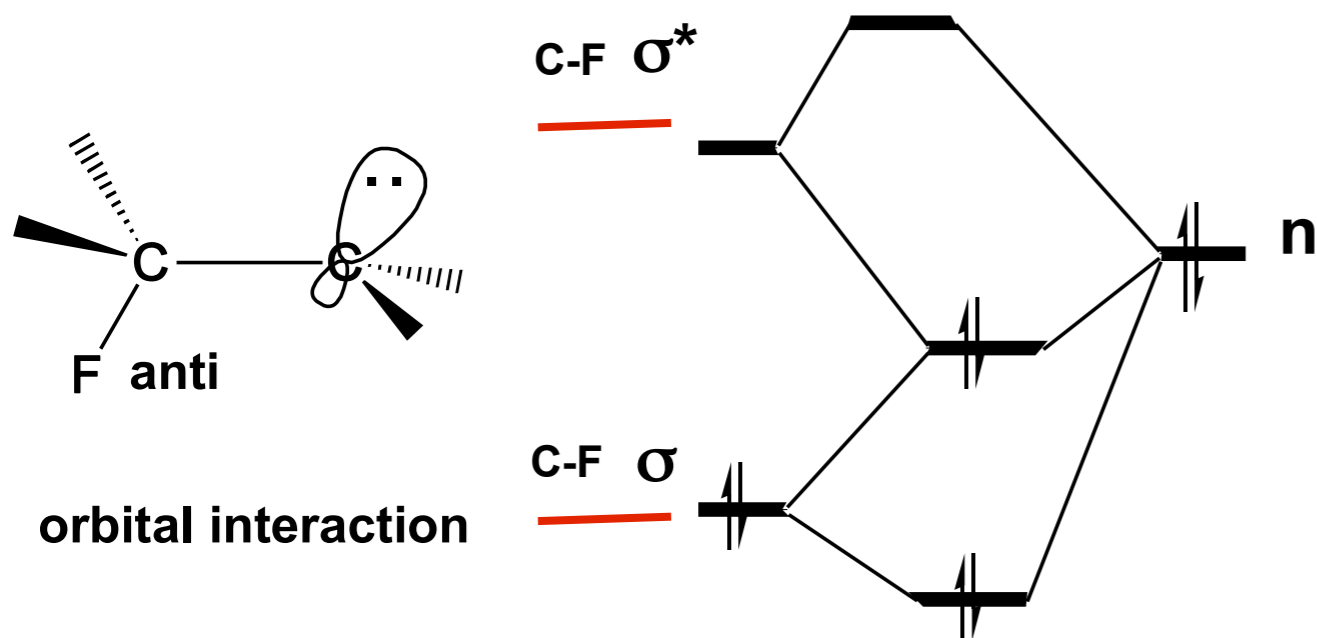
antiperiplanar

planar trigonal
nitrogen atom

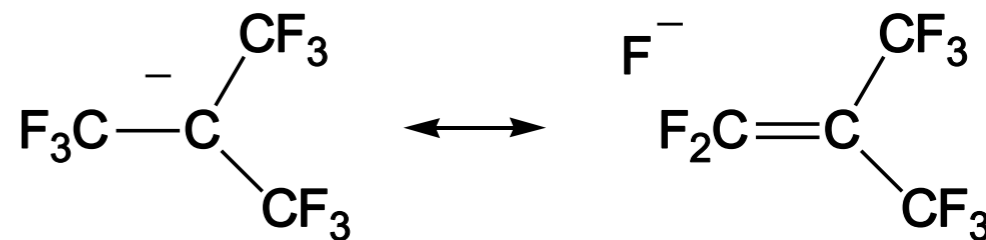


Anionic(Fluorine) Hyperconjugation
(Negative Hyperconjugation)

Anionic negative (Fluorine) hyperconjugative interaction between anionic center and C-F bonds at the β - position

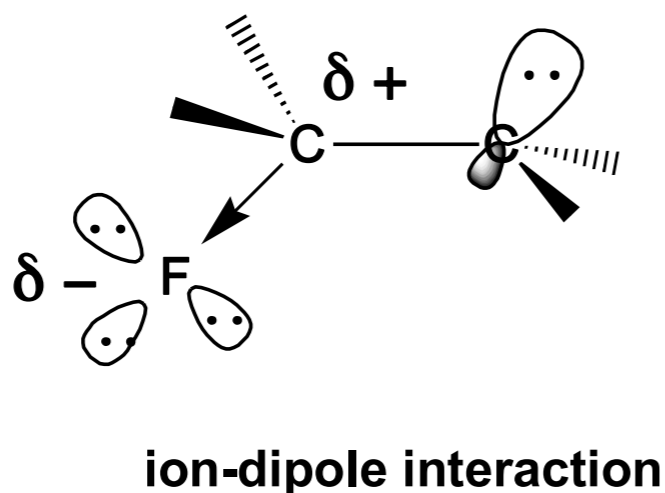


carbanion

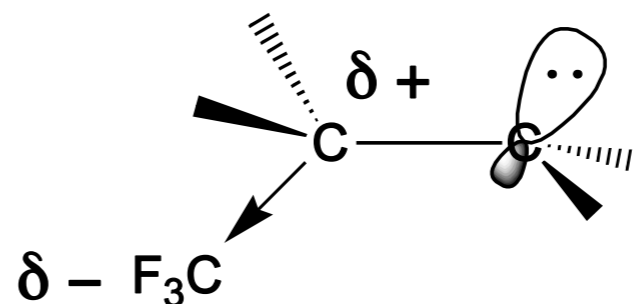


C-C bond shortening
C-F bond elongation
charge delocalization to F atom

Ion-dipole interaction between anionic center and C-F and CF₃ bonds (inductive and field effect)

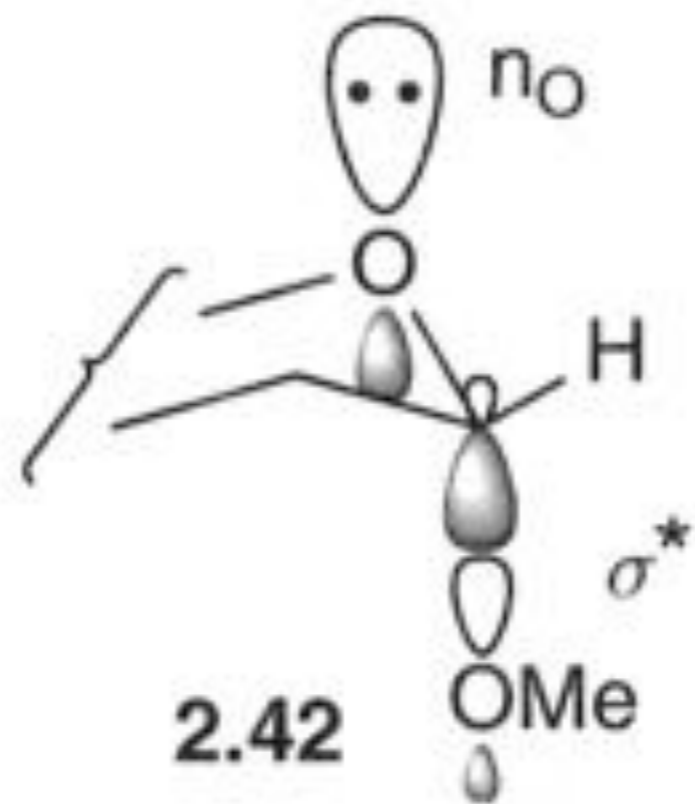
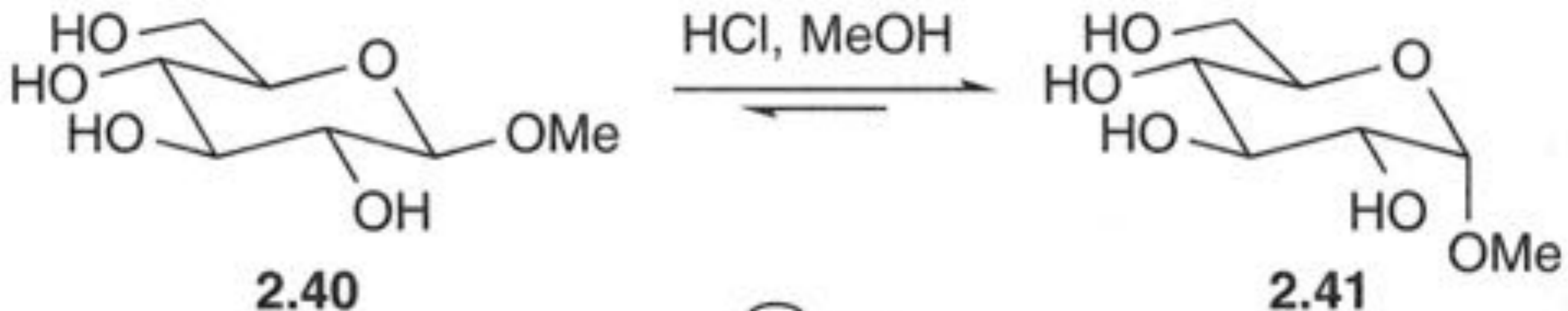


electrostatic interaction??



No C-CF₃ σ^* hyperconjugation??

The Anomeric Effect.

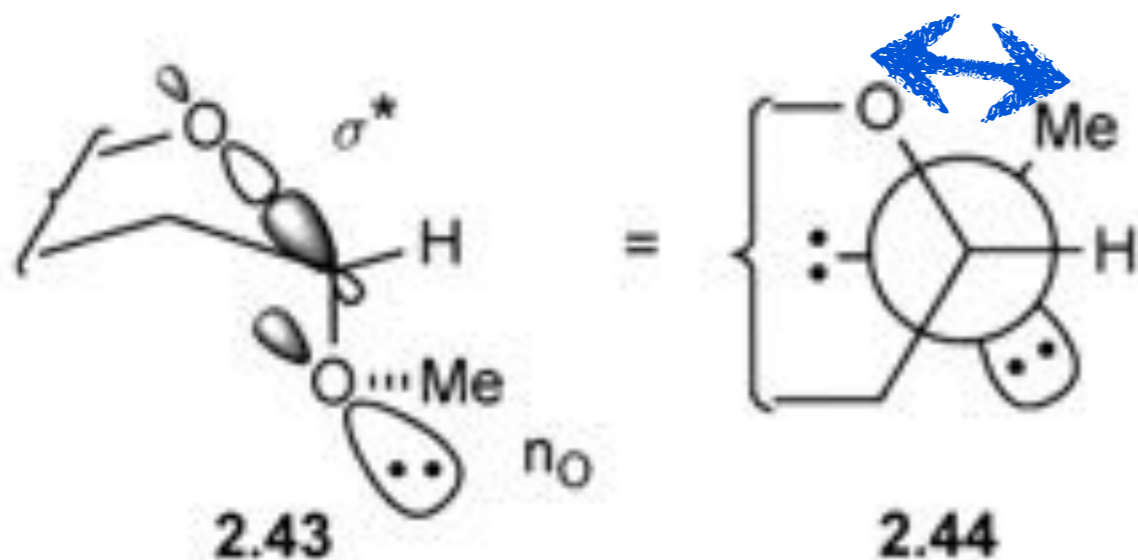


more stable

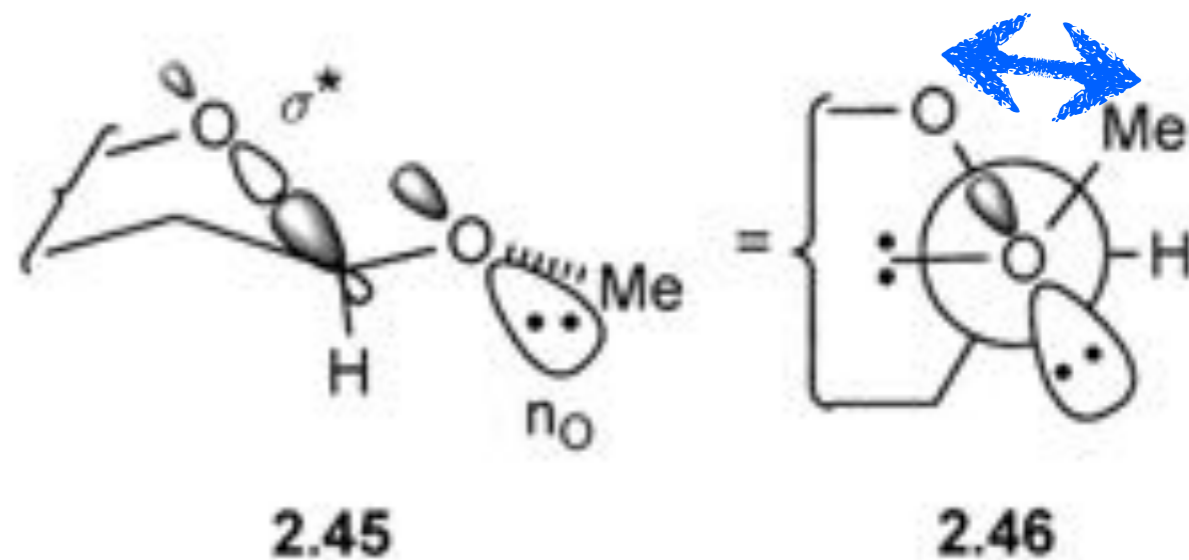
negative hyperconjugation of σ^* C-X bond with lone pair electrons

exo anomeric effect

preference for gauche orientation



axial conformer

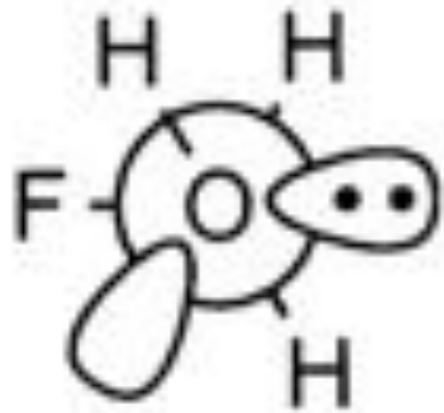


equatorial conformer

preferential orientation of exocyclic oxygen lone pair antiperiplanar to endocyclic σ^* C-O bond in both of axial and equatorial conformers

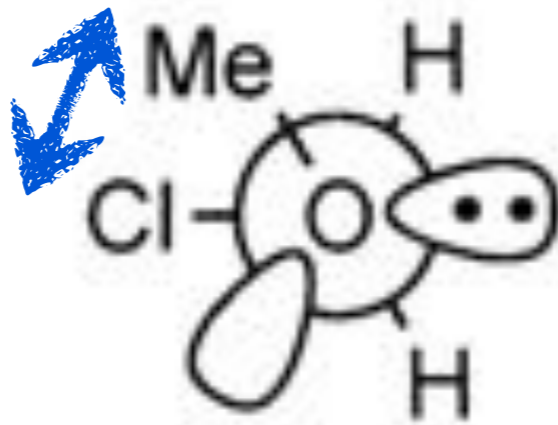
Most Stable Conformer with *anti-Periplanar Orientation*

gauche orientation



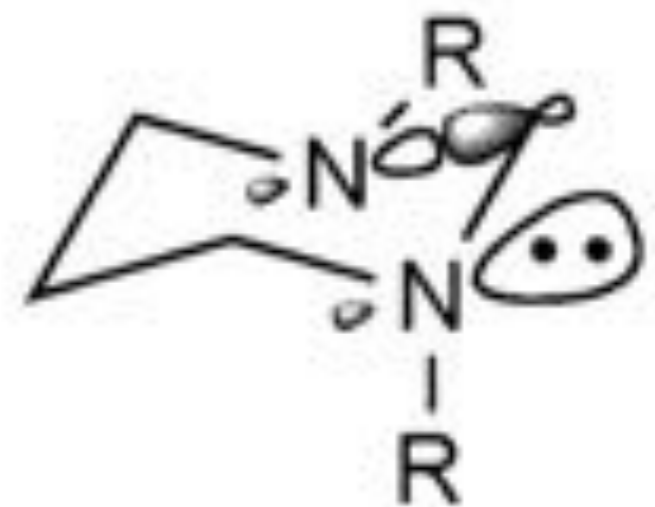
2.47

fluoromethanol



2.48

methoxymethyl chloride

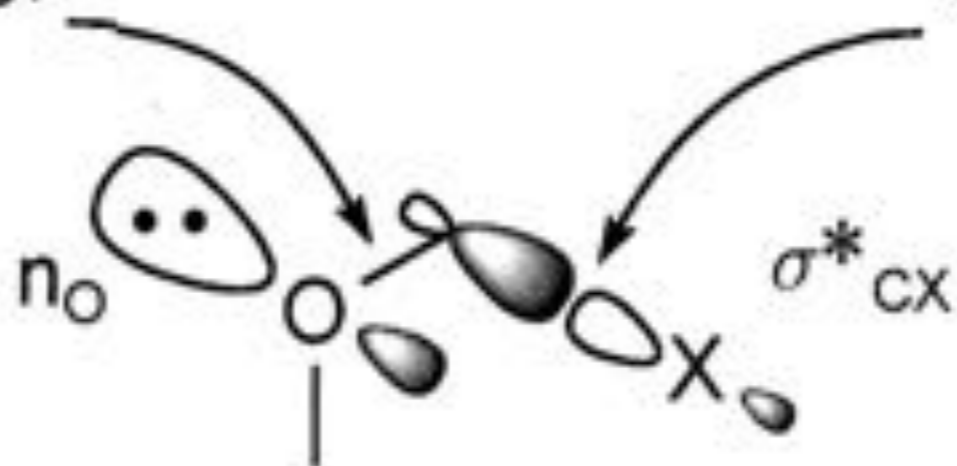


2.49

axial conformer

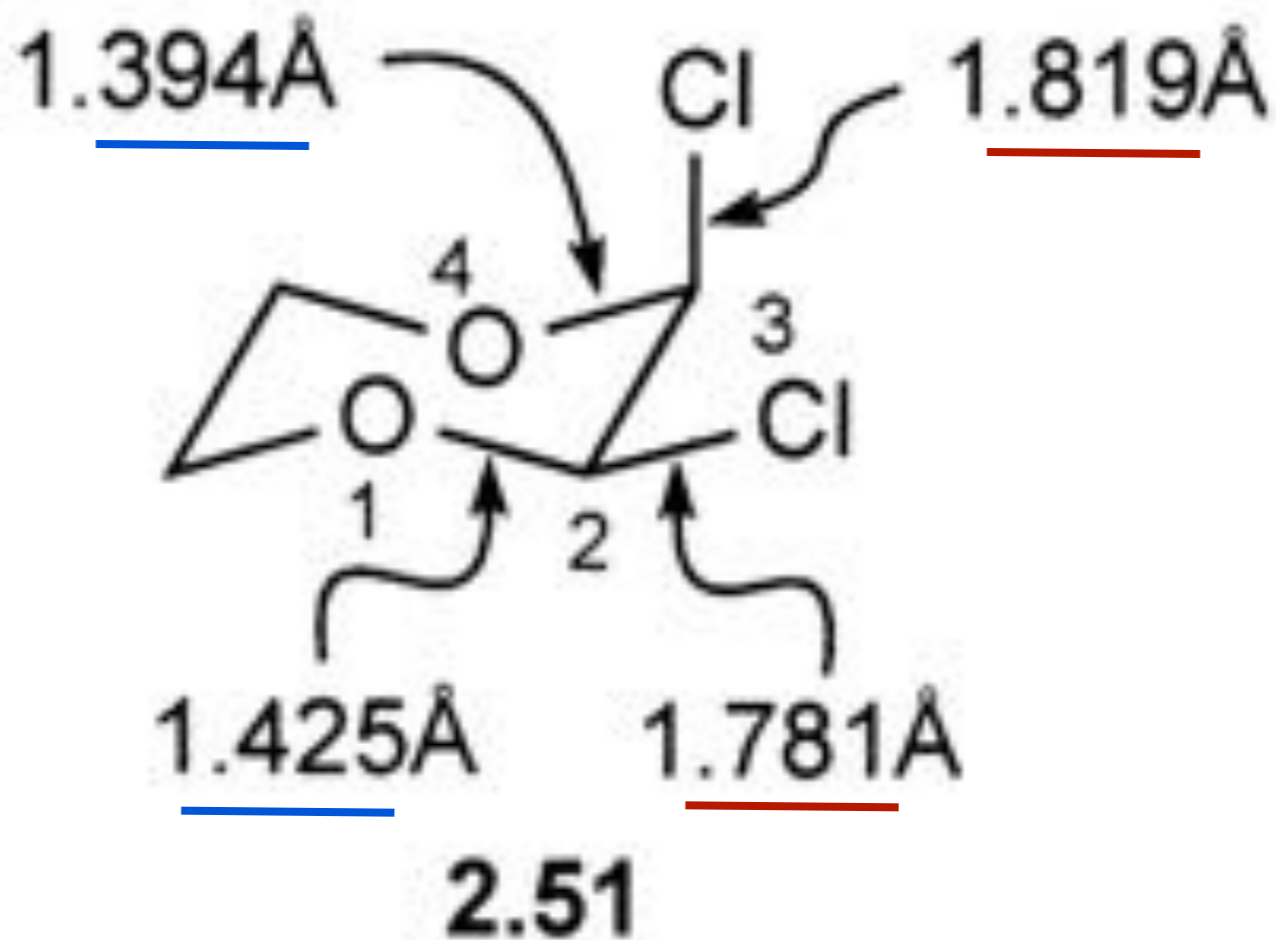
N,N-dialkyl-1,3-diazacyclohexane

increased bonding,
bond-shortening

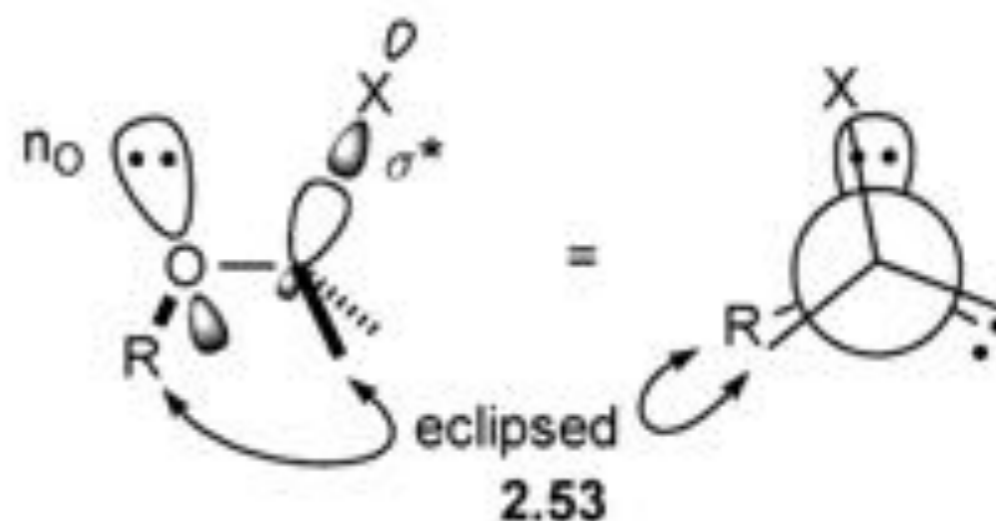
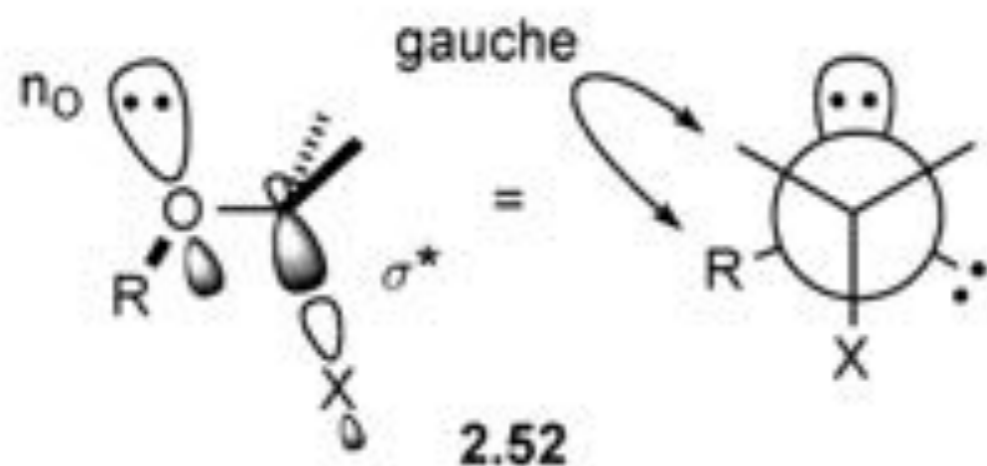


decreased bonding,
bond-lengthening

anti-periplanar



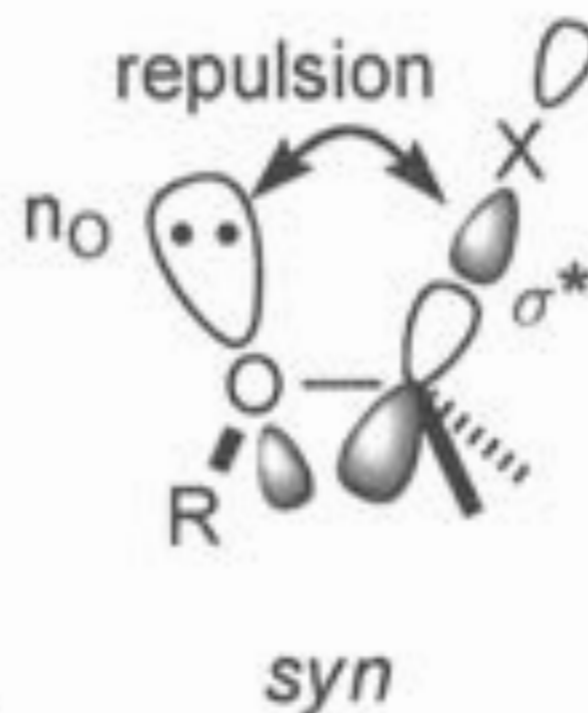
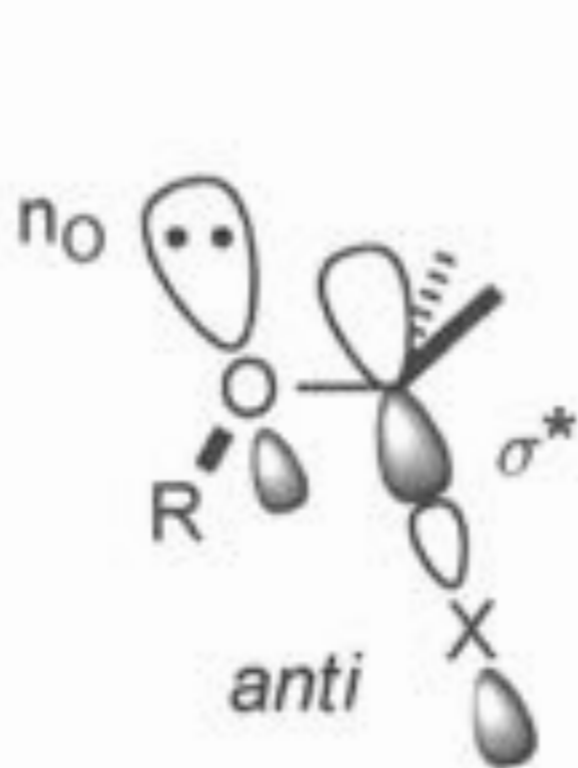
Syn-coplanar and Anti-Periplanar Overlap.

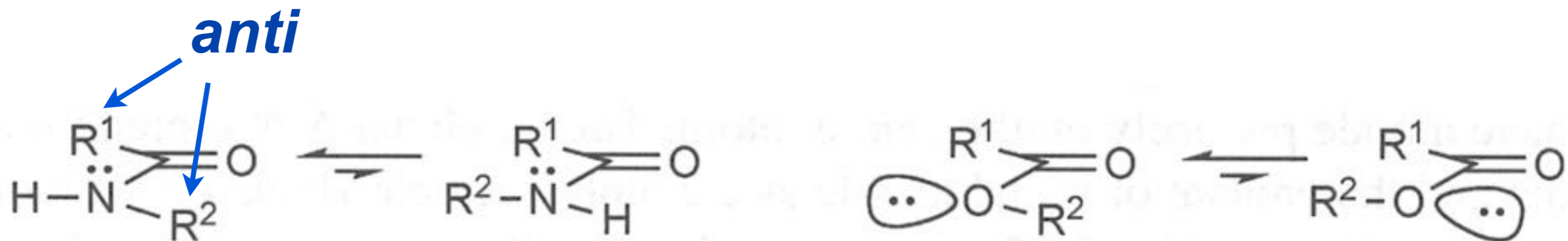


anti-periplanar

vs

syn-coplanar





Z-conformer

more stable

E-conformer

s-trans

more stable

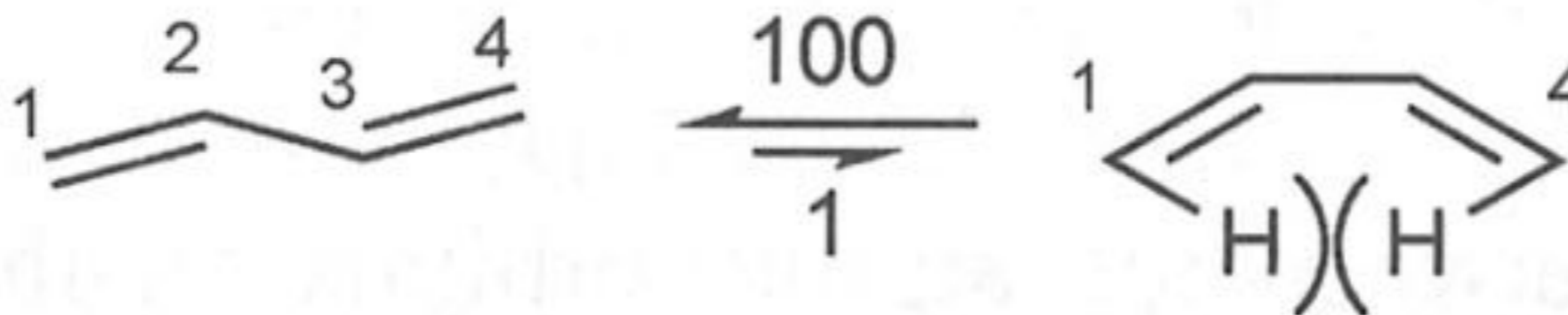
s-cis

anomeric effect :

A lone pair of oxygen atom is anti-periplanar to σ^* C-O bond of C=O group.

Cyclic lactones are more reactive compared with open-chain esters.

Butadiene



more stable

repulsive

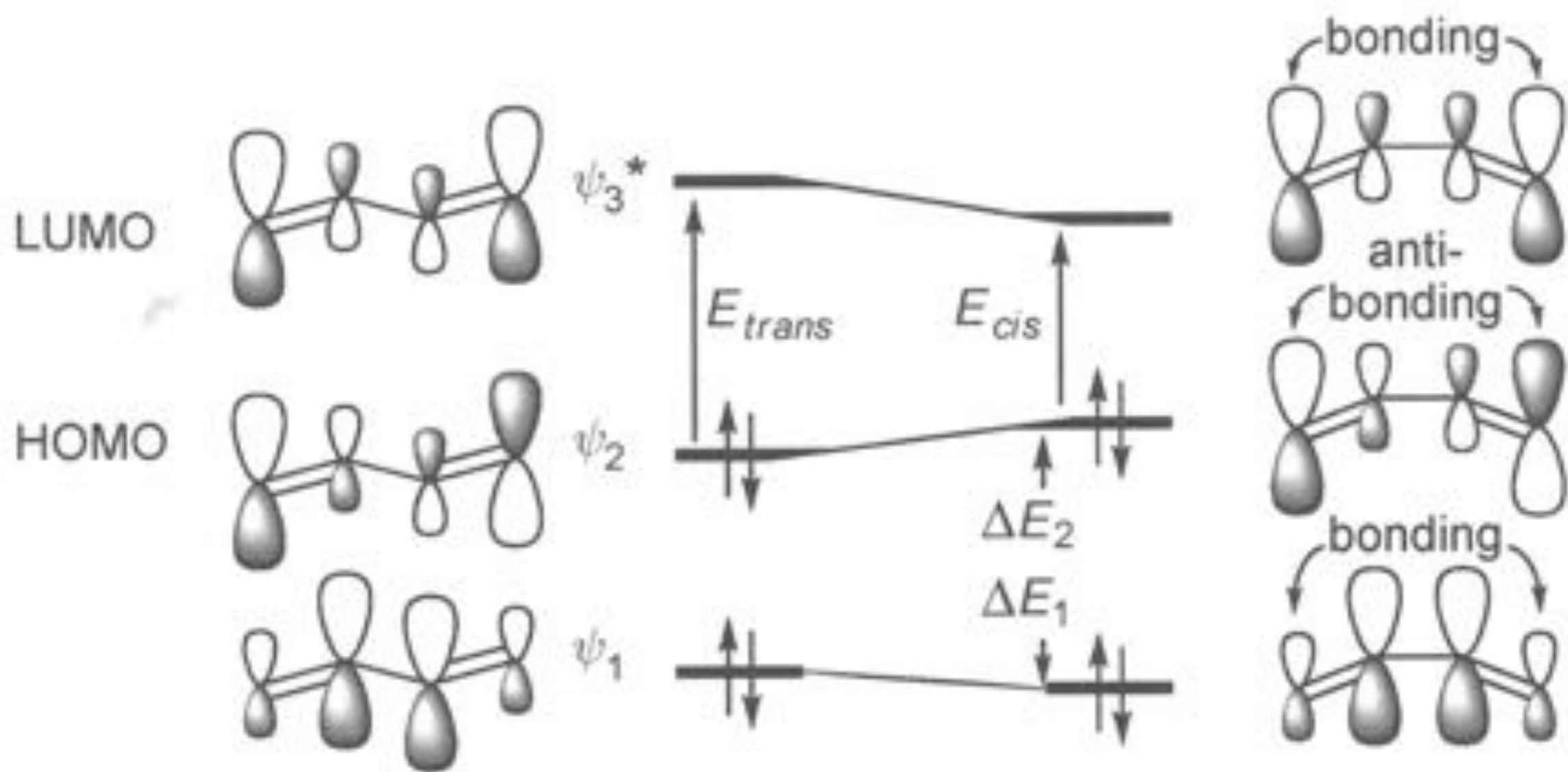
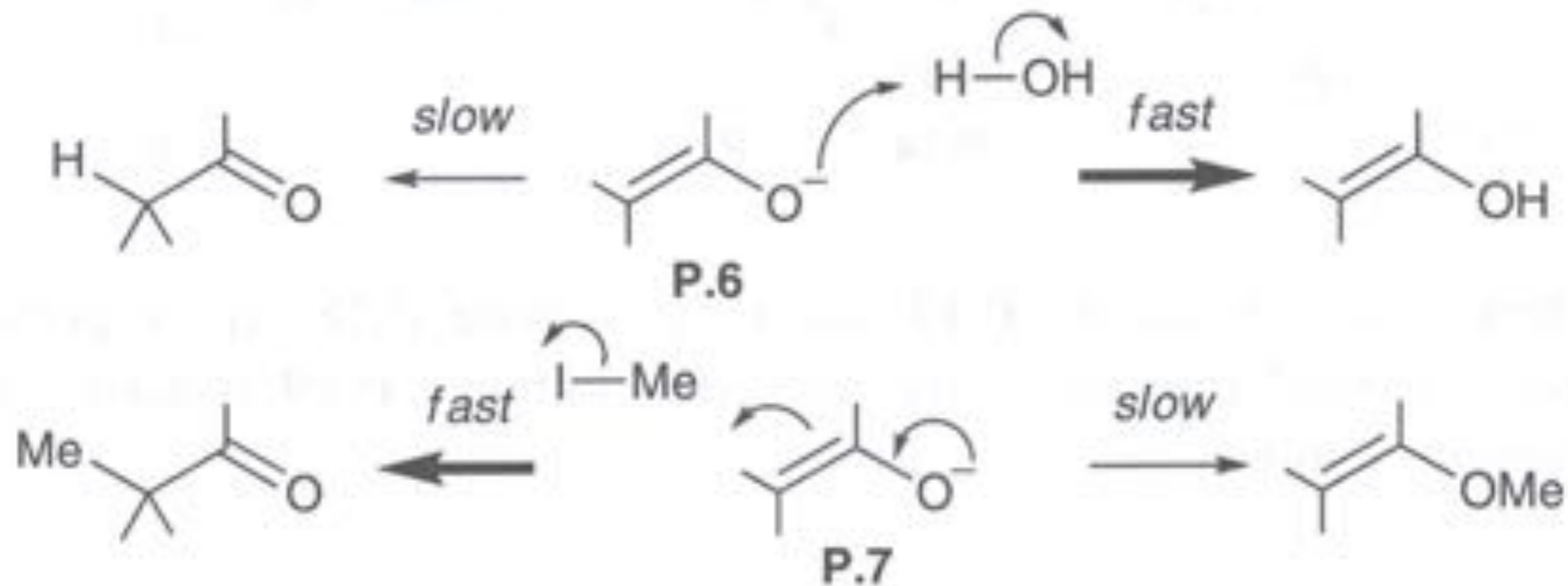
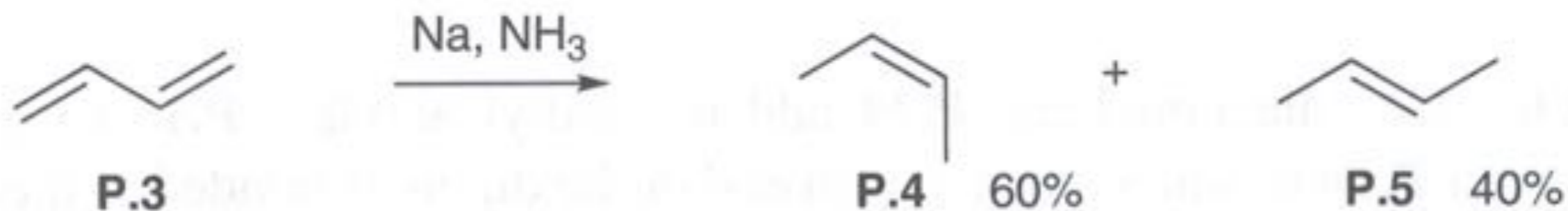


Fig. 2.16 Differences in π orbital energies for *s-trans* and *s-cis* butadiene

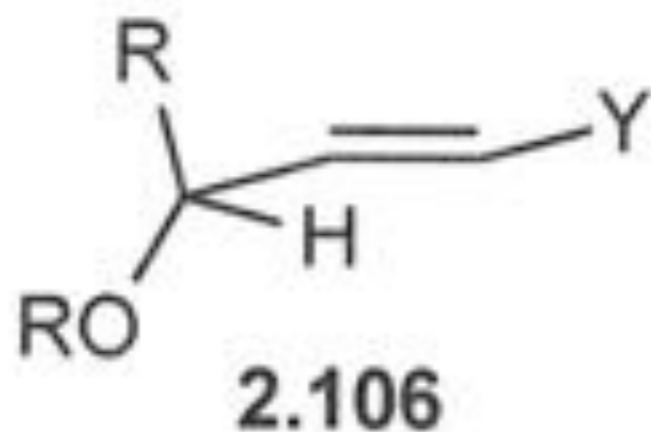


Exercises

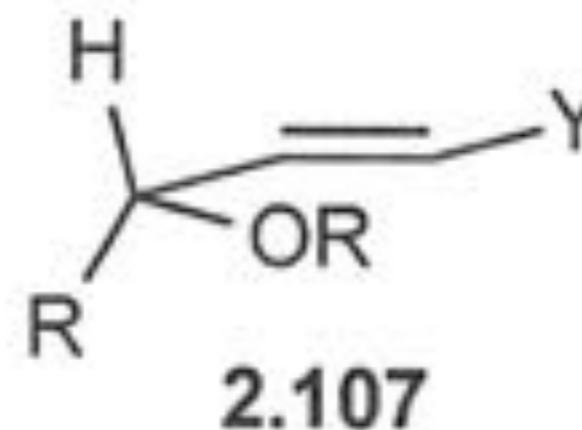
- 1) Explain why $B(OMe)_3$ is much less Lewis acidic than BX_3 by considering the energies of the interacting p orbitals.



- 2) Explain the substituent effects on the following conformation equilibrium.



preferred for Y = alkyl



preferred for Y = CO_2Et or $C\equiv N$

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Molecular Orbitals and Organic Chemical Reactions

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1 Molecular Orbital Theory

2 The Structures of Organic Molecules

3 Chemical Reactions—How Far and How Fast

4 Ionic Reactions—Reactivity

5 Ionic Reactions—Stereochemistry

6 Thermal Pericyclic Reactions

7 Radical Reactions

8 Photochemical Reactions

Physical Organic Chemistry 物理有機化学

物理有機化学においては、有機化学の諸現象を**物理化学的概念**を用いて理解する。

有機化合物の**分子構造**から、その化合物の**物性**や**反応性**を論じ、**反応中間体**や**反応機構**を予測する。

化学結合の基本原則や**有機反応論**を理解すると、**反応速度の予測**や**選択的合成反応**を実現するための**反応条件の予測**が自ずから可能となる。

物理有機化学における研究対象は、有機分子の構造と物性反応相関に関する基礎研究から、機能分子の合成設計研究や、生体分子系の生命現象の機構解析まで、広い研究範囲におよんでいる。

参考書:



基本有機反応機構
Peter Sykes (著)
奥山 格 (翻訳)

東京化学同人
(1996/03)



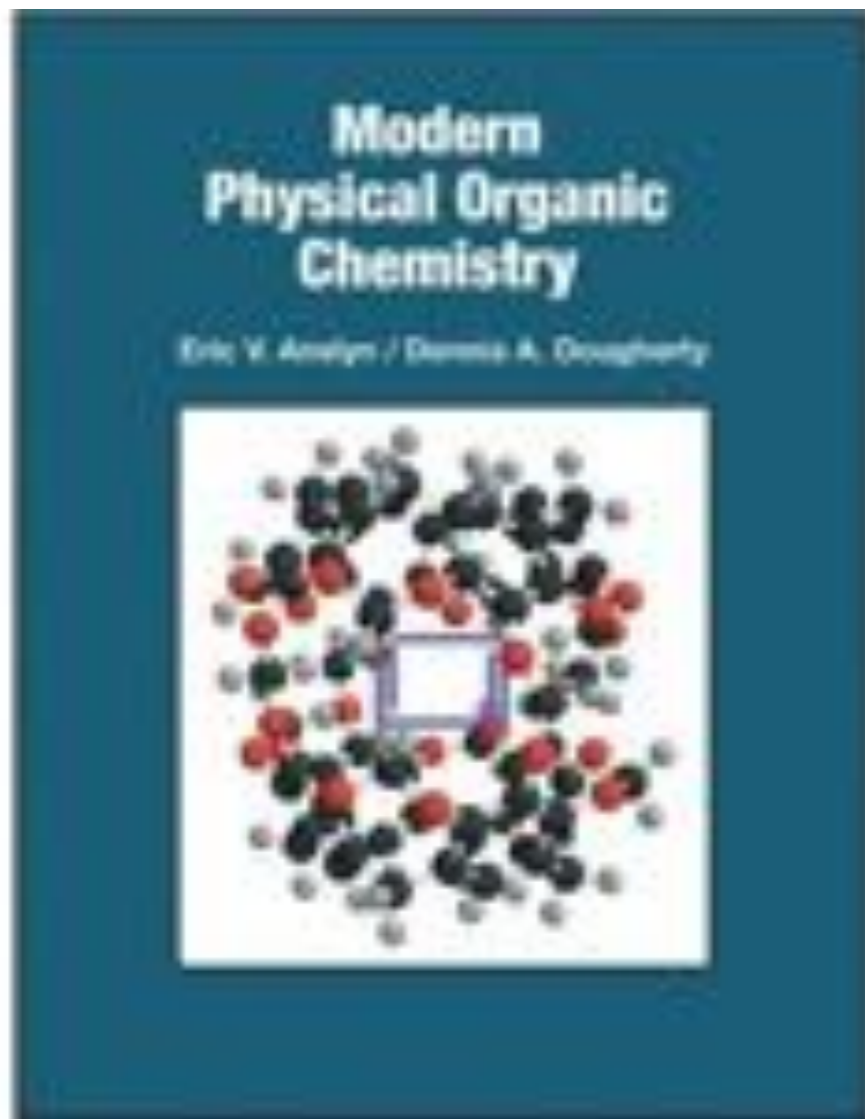
有機反応機構
Peter Sykes (著),
久保田 尚志 (翻訳)

東京化学同人;
第5版 (1984/01)



有機反応機構の書き方
基礎から有機金属反応
Robert B. Grossman (著),
奥山 格 (翻訳)

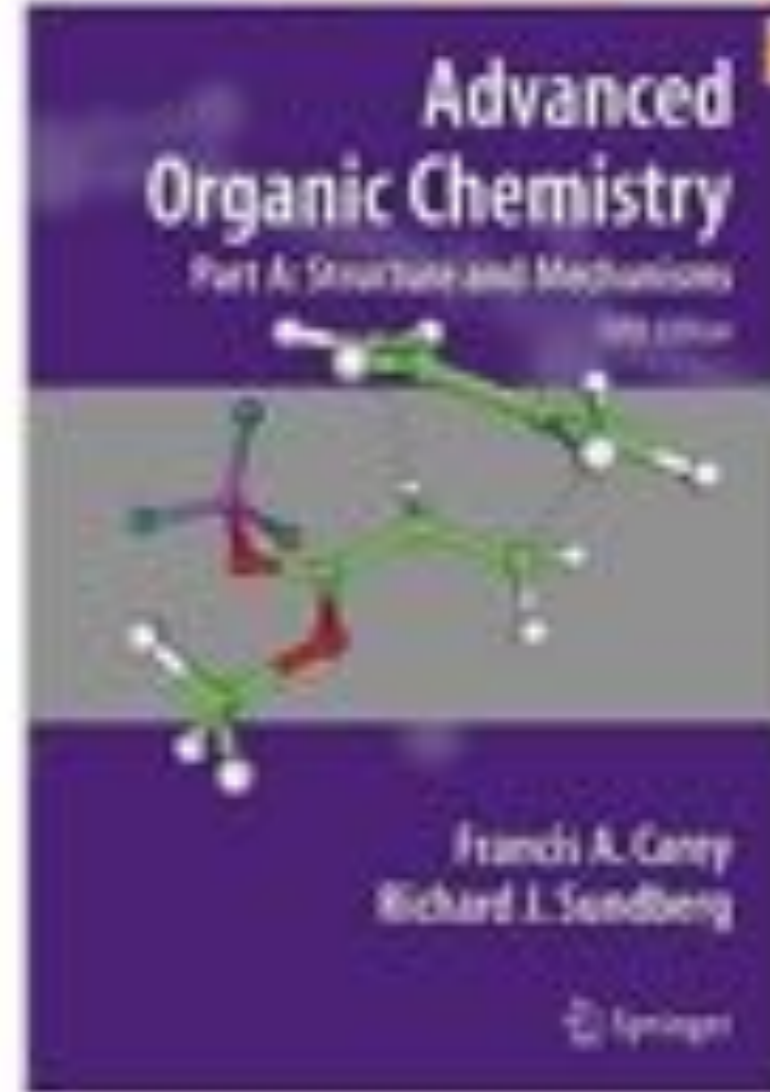
丸善 (2010/1/22)



Modern Physical Organic Chemistry

Eric V. Anslyn (著),
Dennis A. Dougherty (著)
ハードカバー: 1104ページ (¥ 10,786)

Univ Science Books;
illustrated edition版 (2005/07)



Advanced Organic Chemistry: Part A: Structure and Mechanisms

Francis A. Carey (著),
Richard J. Sundberg (著)
ペーパーバック: 1199ページ (¥ 5,678)
Springer; 5th ed. 2007.
Corr. 2nd printing版 (2007/6/13)

化学反応における結合開裂様式

1.ヘテロリシス(heterolysis) hetero(不均一)+lysis(分解)

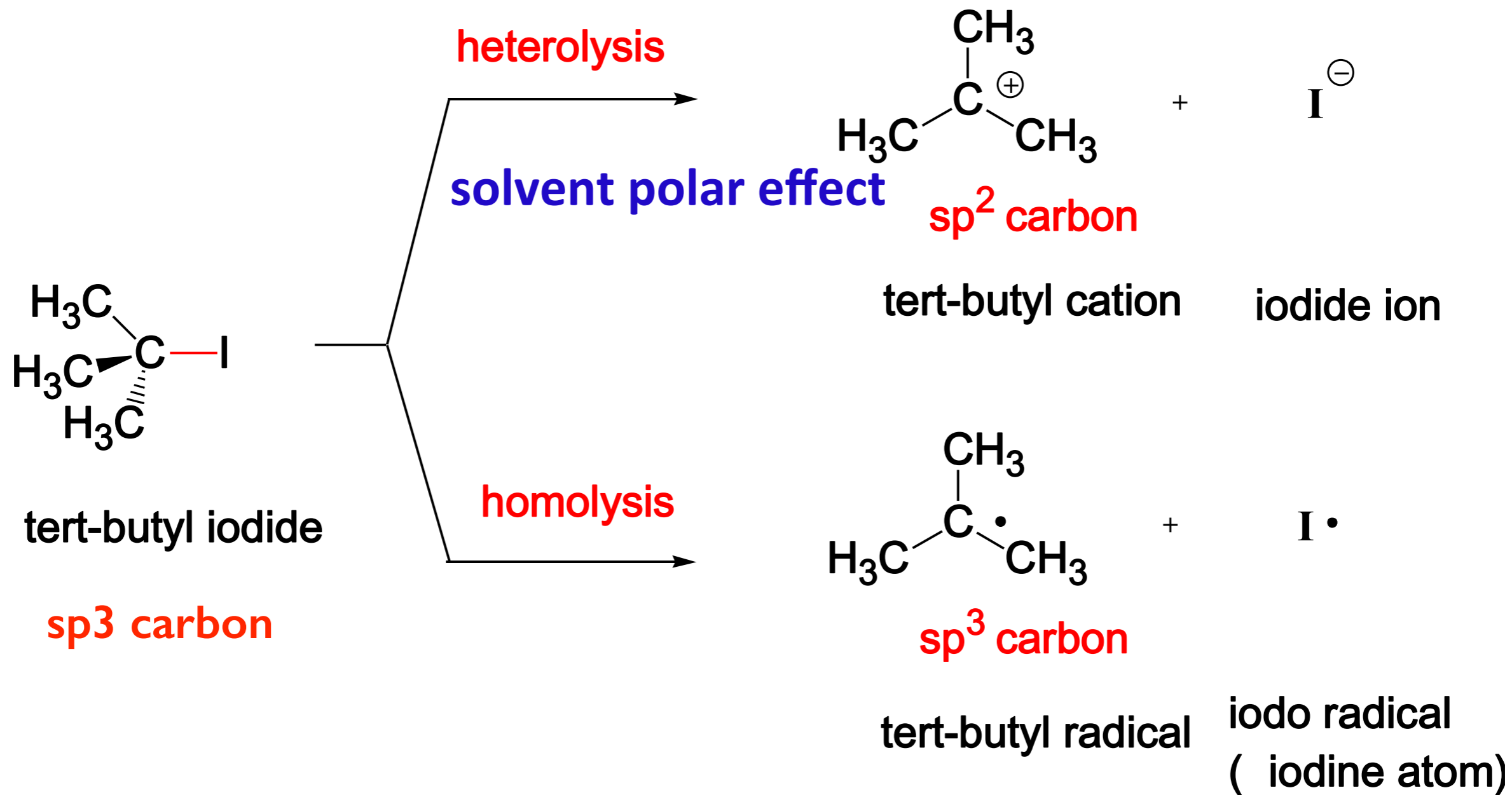


2.ホモリシス(homolysis) homo(均一)+lysis(分解)

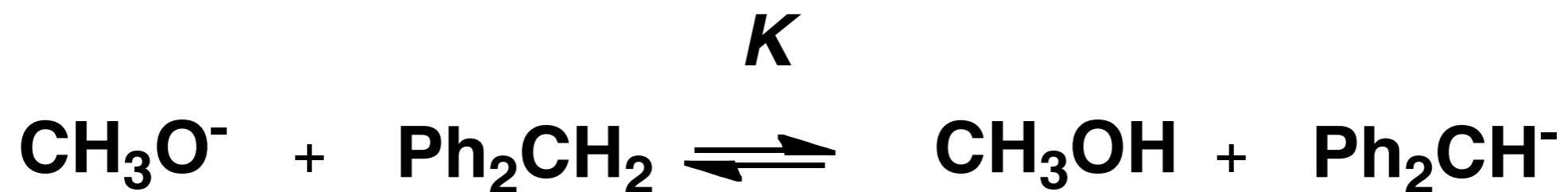


結合解離エネルギー(Bond Dissociation Energy)





酸性度におよぼす溶媒効果 Solvent Effect on Acidity



Solvent	K
H_2O	10^{-18}
gas-phase	10^{11}

**CH₃O⁻アニオンは水和によって大きく安定化するが、
非局在安定化したPh₂CH⁻アニオンはほとんど水和されない！**

CH₃-OH

291 kJ mol⁻¹

CH₃-Br

291 kJ mol⁻¹

H-Br

366 kJ mol⁻¹

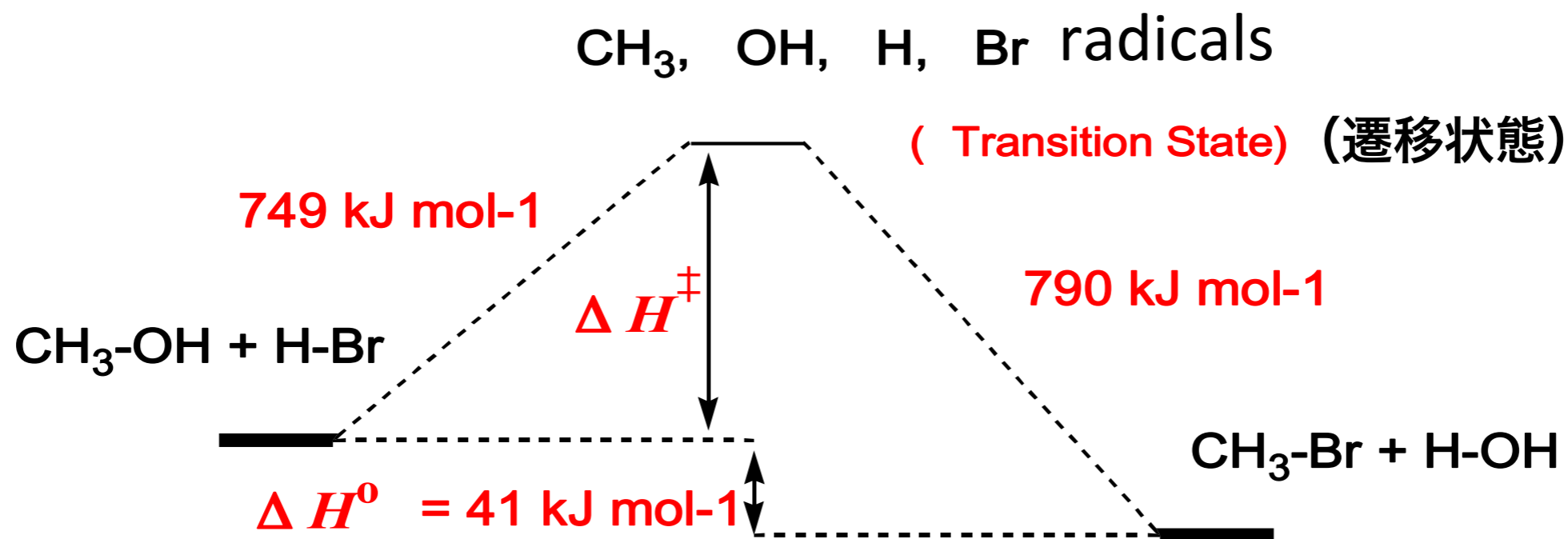
H-OH

499 kJ mol⁻¹

開裂する結合エネルギー 749 kJ mol⁻¹

生成する結合エネルギー 790 kJ mol⁻¹

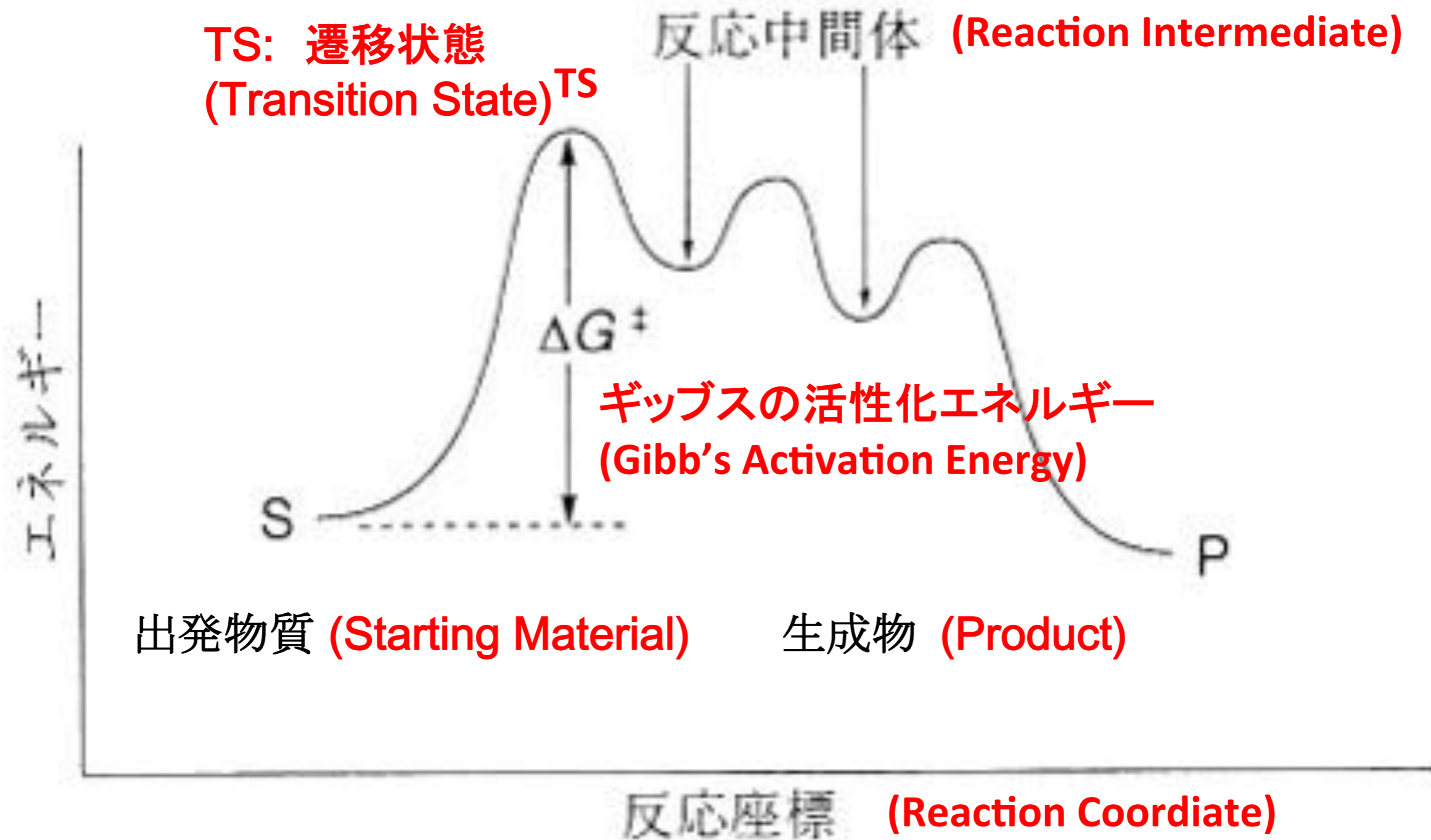
反応熱(Heat of Reaction) $\Delta H^\circ = 749 - 790 = -41 \text{ kJ mol}^{-1}$



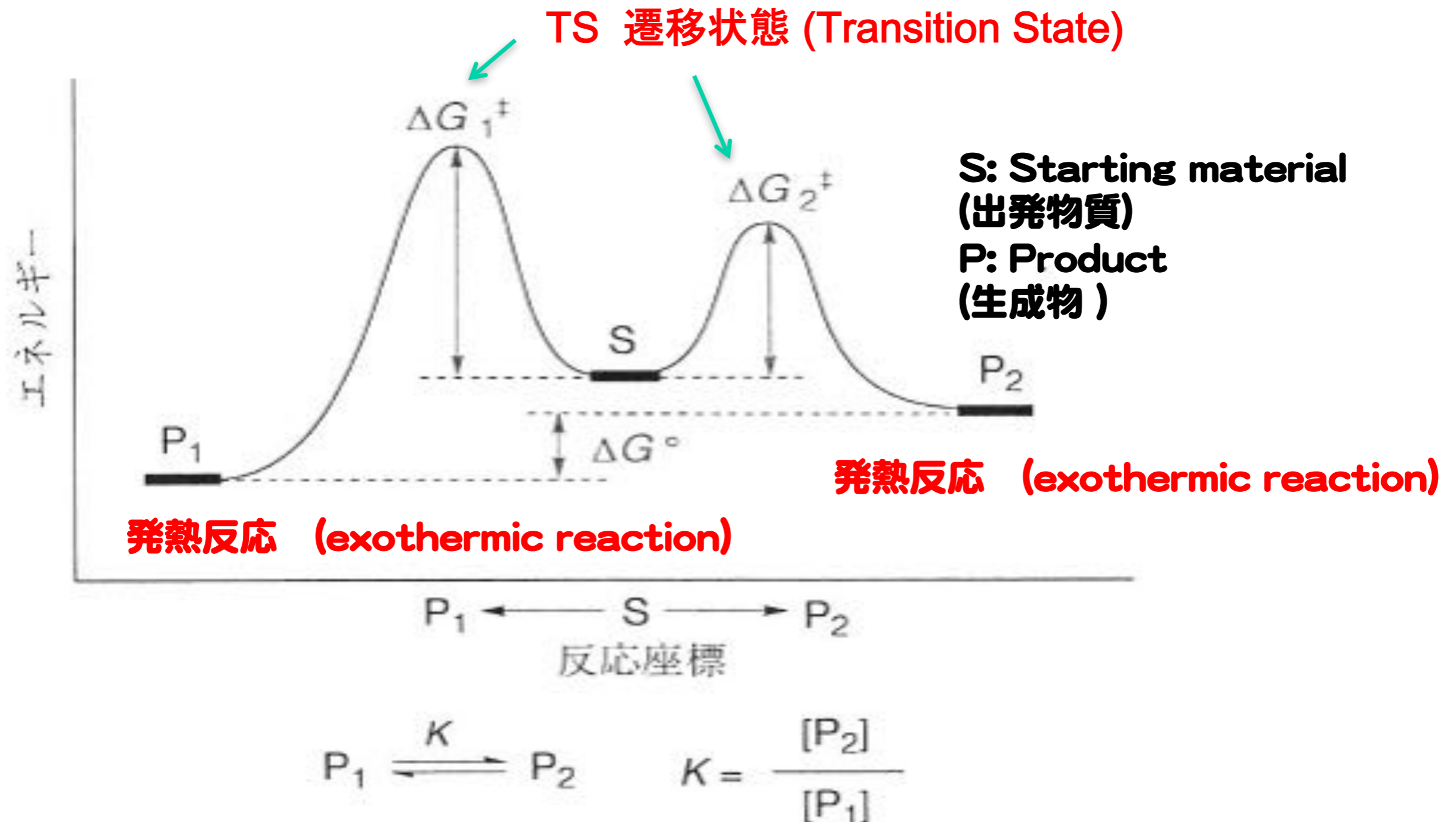
$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

Gibb's Free Energy Change for Transition State of Reaction

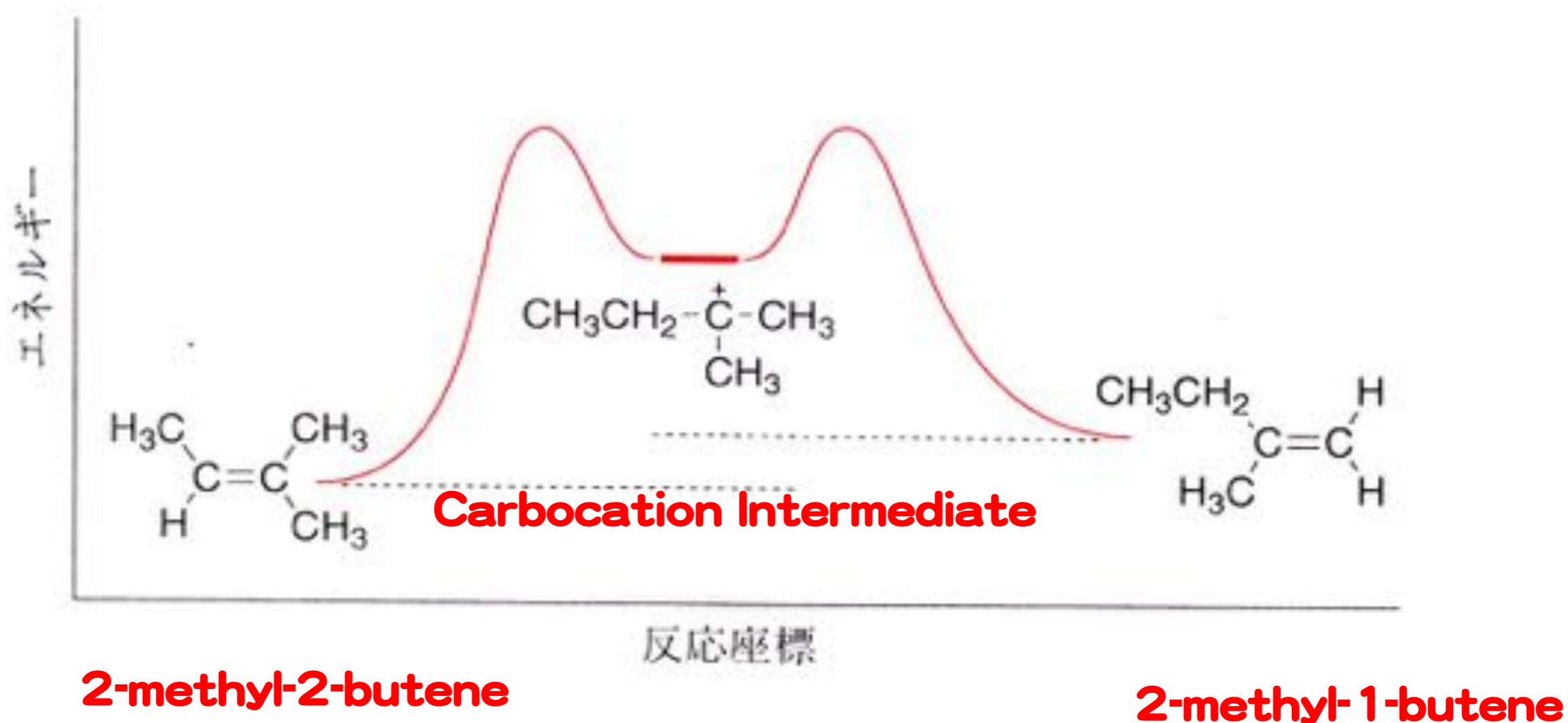
有機反応機構 (Organic Reaction Mechanism)



速度支配と熱力学支配 (Kinetic Control and Thermodynamic Control)



熱力学的に支配された反応 (Thermodynamically Controlled Reaction)

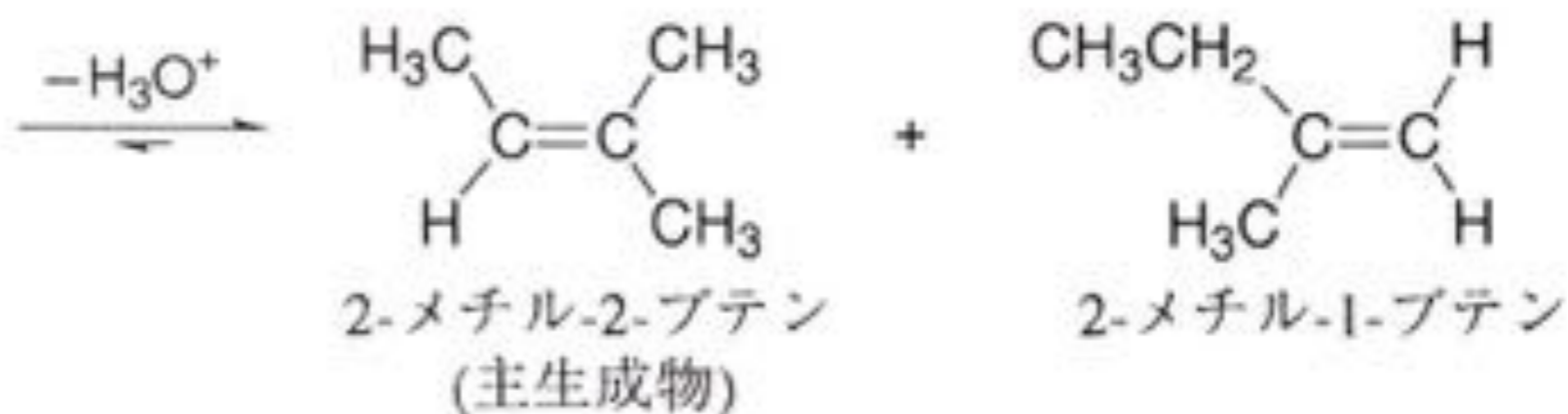
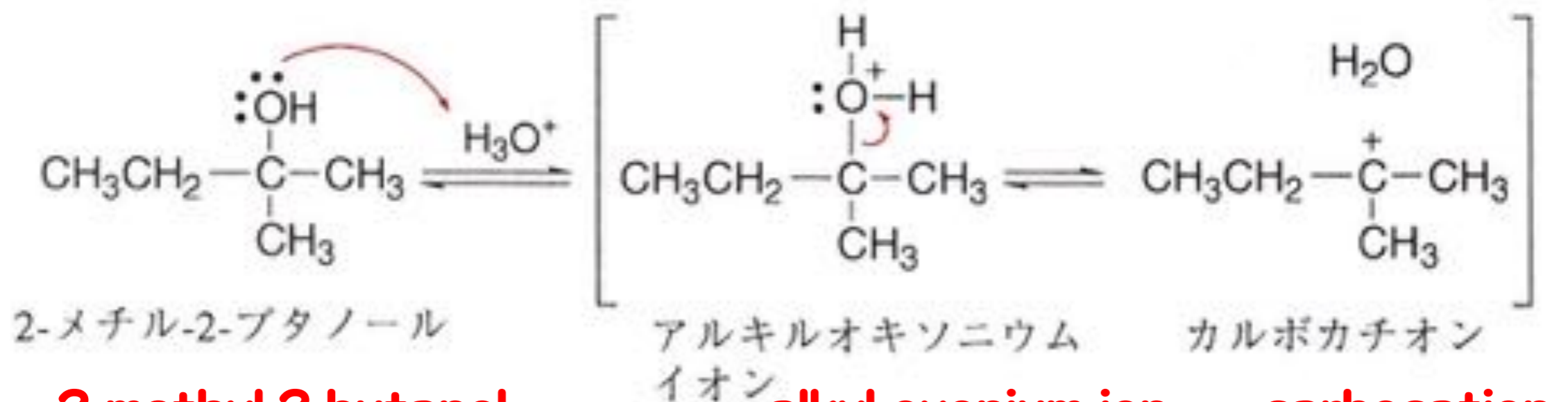


Saytzeff則 :
脱離反応では多置換アルケンがより優先して生成する。

2-methyl-1-butene に比べて **2-methyl-2-butene**の方がより安定なのは何故か？

Alkene Formation by Dehydration(脱水によるアルケンの生成)

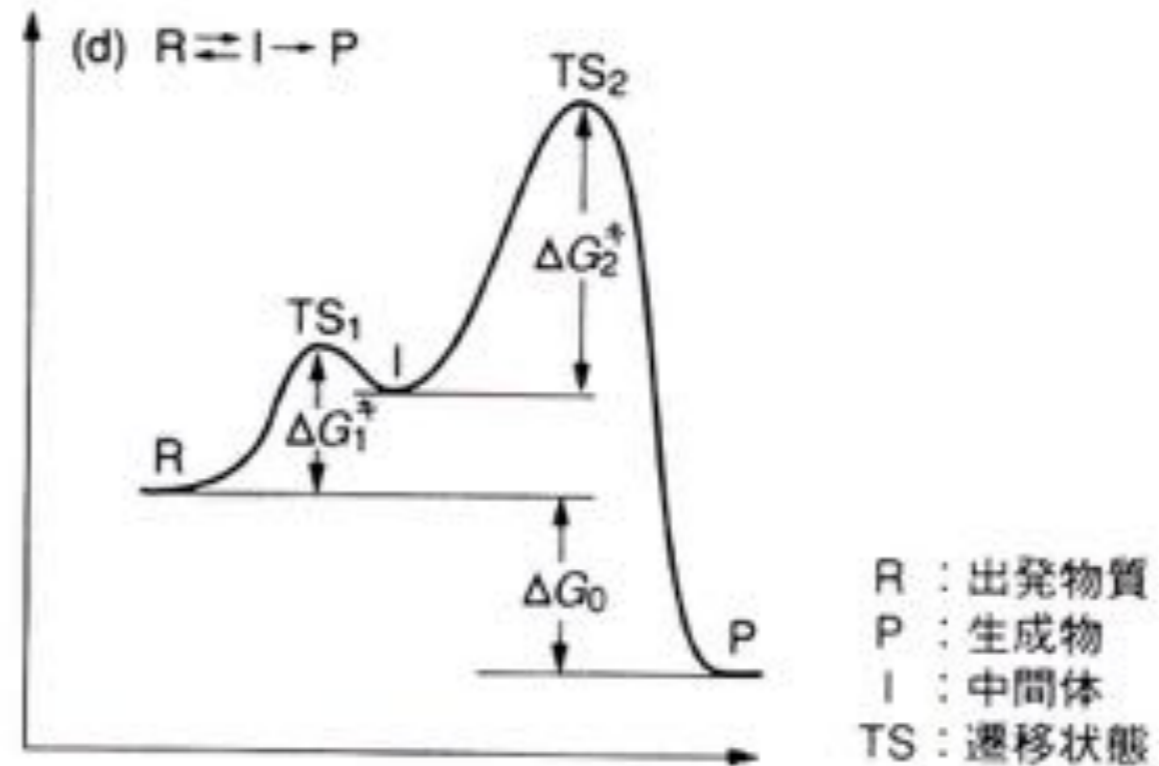
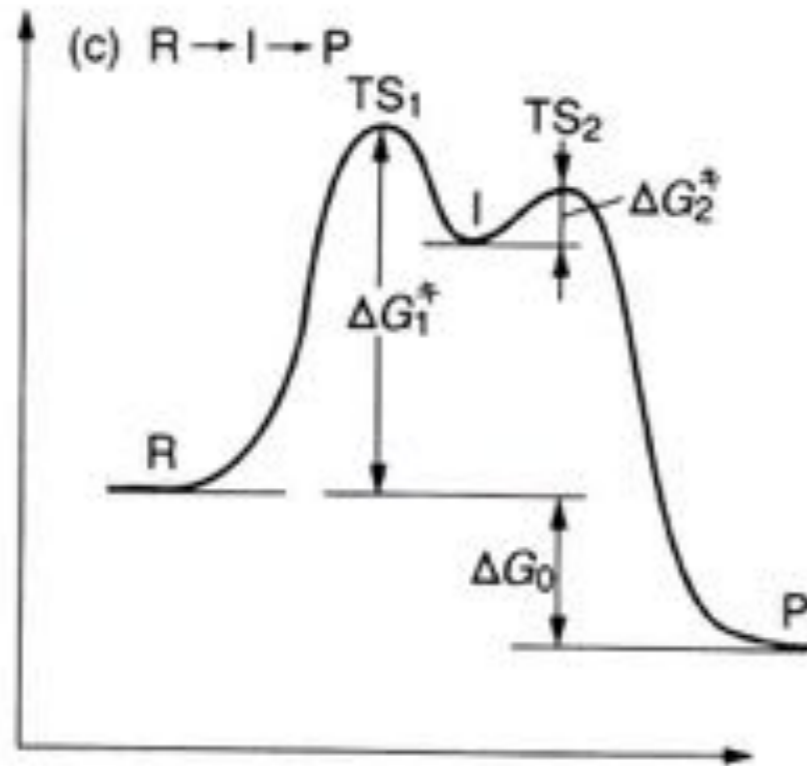
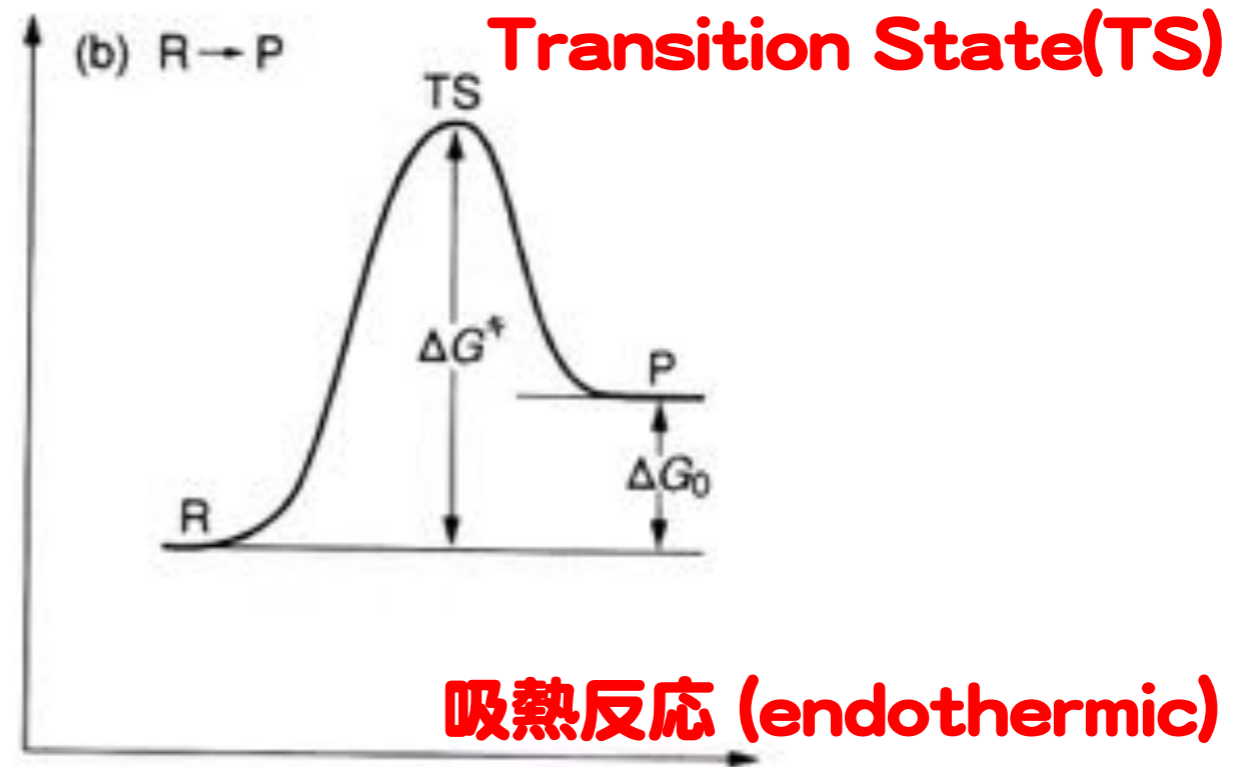
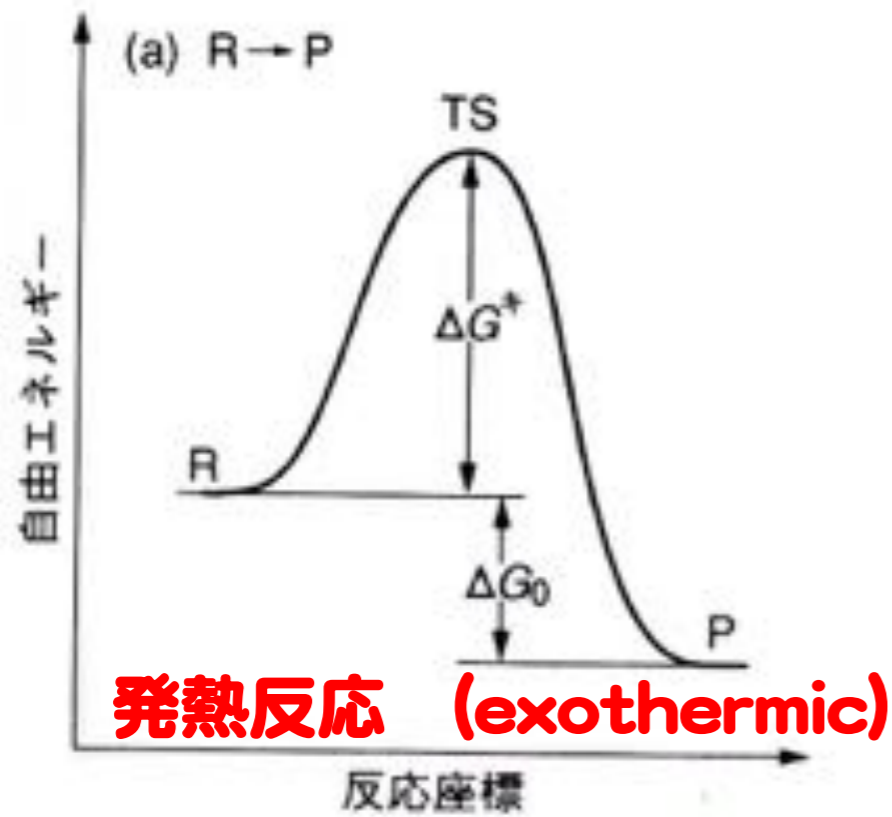
Dehydration (脱水)



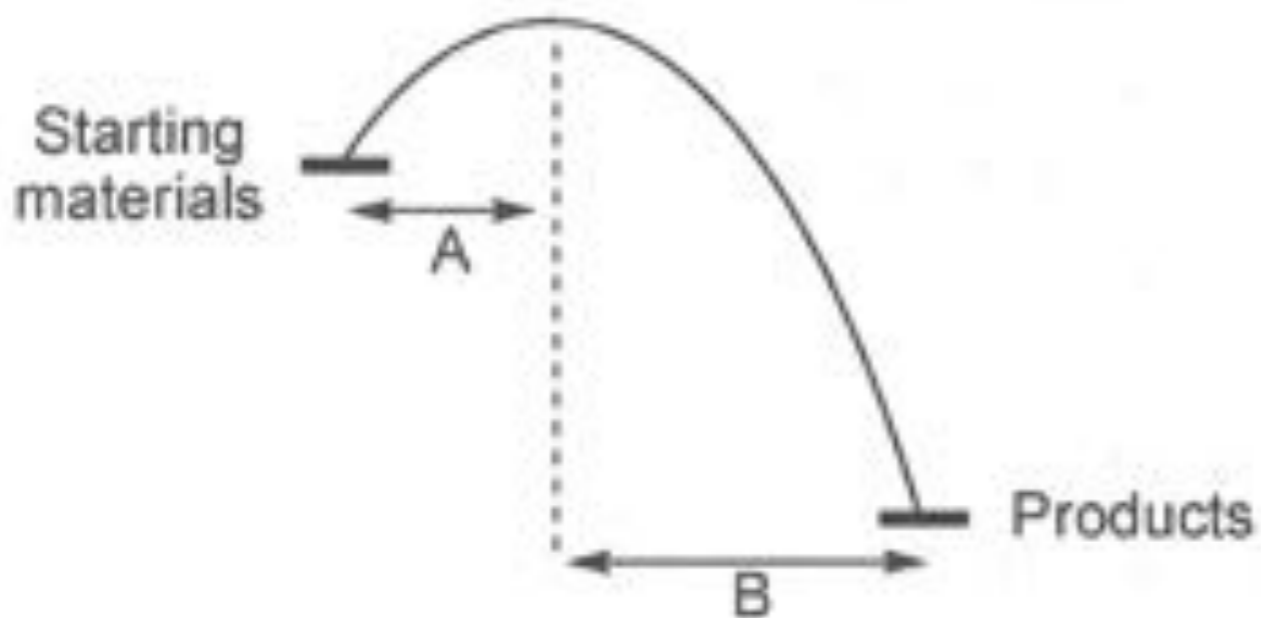
2-methyl-2-butene
(main product)

2-methyl-1-butene

Transition State(TS) and Intermediate(I) (遷移状態と中間体)

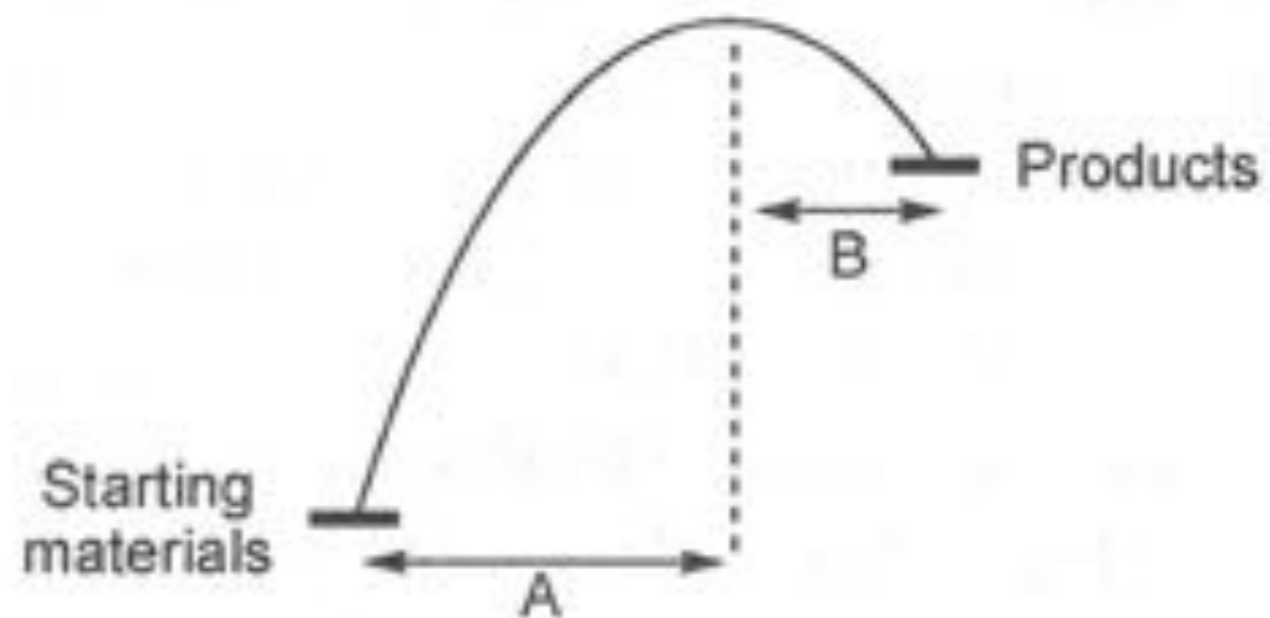


early TS



(a) An exothermic reaction, with a reactant-like transition structure

late TS



(b) An endothermic reaction, with a product-like transition structure

The Hammond postulate (仮説)

Lewis 酸(A) :電子対を受け取るもの (電子対受容体 **electron-pair Acceptor**)

Lewis 塩基(B) :電子対を与えるもの (電子対供与体 **electron-pair Donor**)



電荷移動相互作用 : Charge-Transfer(CT) Interaction

ドナー・アクセプター相互作用 : Donor-Acceptor(DA) Interaction

Lewisの酸塩基相互作用 (1923)

金属錯体の配位結合(Coordinate Bond of Metal Complex)

超共役相互作用(Hyperconjugation Interaction)

アンチペリプラナー効果 ((anti-periplanar Effect, 超共役の一種)

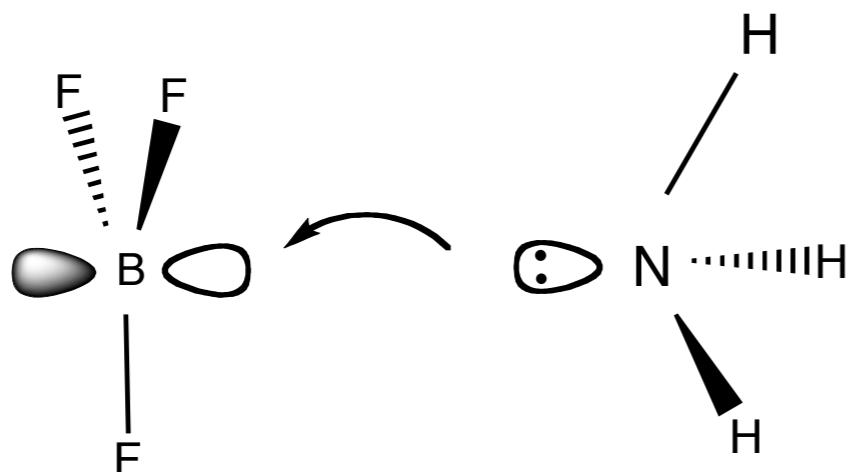
π -錯体(π -complex)の形成

水素結合(Hydrogen Bond)

化学反応の初期状態 (pre-association complexes in chemical reactions)

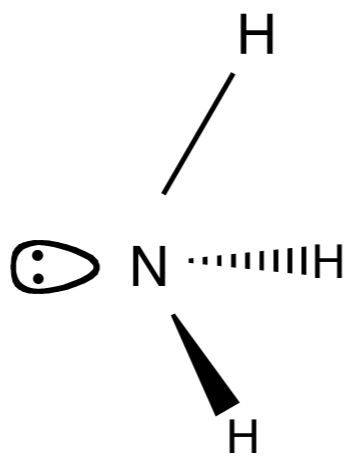
etc.

分子の世界で普遍的に働く安定化相互作用であり、電子の非局在化機構の一種として非常に重要な役割を果たしている。

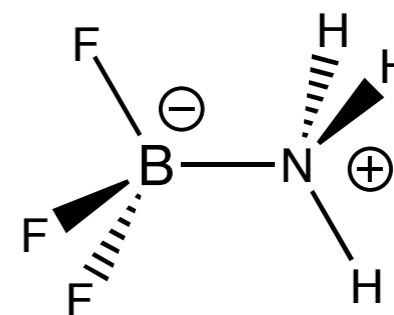


sp^2 boron

trifluoroborane BF_3

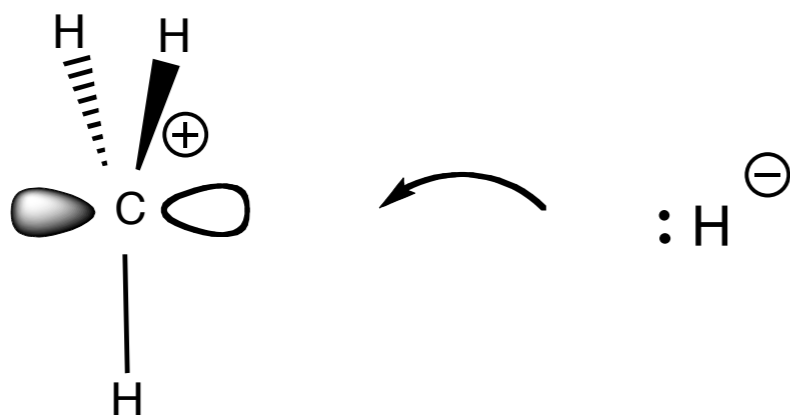


ammonia NH_3



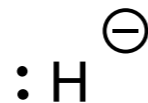
sp^3 boron

Lewis acid-base complex

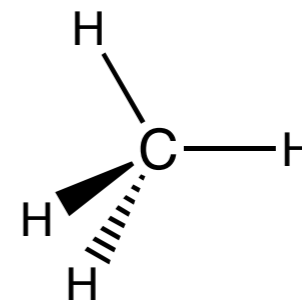


sp^2 carbon

methyl cation CH_3^+



hydride



sp^3 carbon

methane

(isoelectronic to BF_3)

The Perturbation Theory of Reactivity

反応性の摂動理論

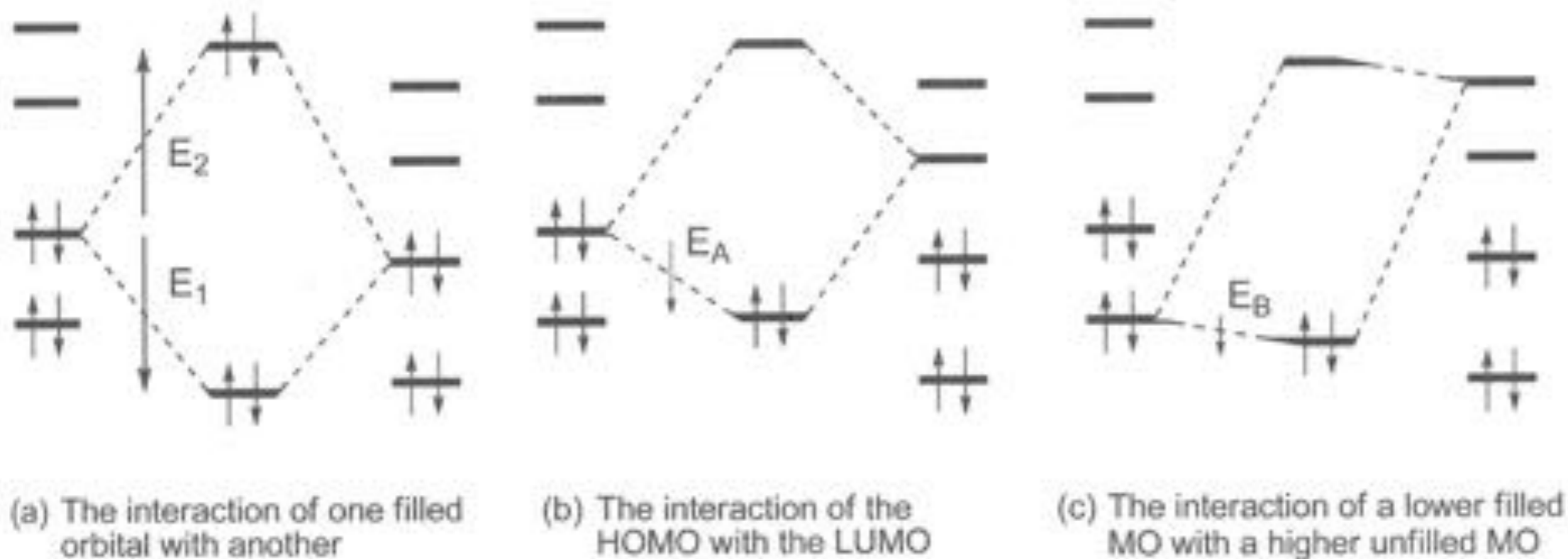


Fig. 3.3 The interactions of the molecular orbitals of one molecule with the molecular orbitals of another

The Salem-Klopman Equation

$$\Delta E = \underbrace{-\sum_{ab} (q_a + q_b) \beta_{ab} S_{ab}}_{\text{first term}} + \underbrace{\sum_{k < l} \frac{Q_k Q_l}{\epsilon R_{kl}}}_{\text{second term}} + \underbrace{\sum_r^{\text{occ.}} \sum_s^{\text{unocc.}} - \sum_s^{\text{occ.}} \sum_r^{\text{unocc.}} \frac{2(\sum_{ab} c_{ra} c_{sb} \beta_{ab})^2}{E_r - E_s}}_{\text{third term}}$$

各原子の
内核電子間反発部分

静電力
相互作用部分

占有軌道-非占有軌道
相互作用部分

The first term is the first-order, closed-shell repulsion term (Fig. 3.3a).

The second term is simply the Coulombic repulsion or attraction.

The third term represents the interaction of all the filled orbitals with all the unfilled of correct symmetry (Fig. 3.3b and 3.3c).

The Salem-Klopman Equation

$$\Delta E = \underbrace{-\sum_{ab} (q_a + q_b) \beta_{ab} S_{ab}}_{\text{first term}} + \underbrace{\sum_{k < l} \frac{Q_k Q_l}{\epsilon R_{kl}}}_{\text{second term}} + \underbrace{\sum_r^{\text{occ.}} \sum_s^{\text{unocc.}} - \sum_s^{\text{occ.}} \sum_r^{\text{unocc.}} \frac{2(\sum_{ab} c_{ra} c_{sb} \beta_{ab})^2}{E_r - E_s}}_{\text{third term}}$$

各原子の
内核電子間反発部分

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相互作用部分

As two molecules collide, three major forces operate.

- (i) *The occupied orbitals of one repel the occupied orbitals of the other.*
- (ii) *Any positive charge on one attracts any negative charge on the other (and repels any positive).*
- (iii) *The occupied orbitals (especially the HOMOs) of each interact with the unoccupied orbitals (especially the LUMOs) of the other, causing an attraction between the molecules.*

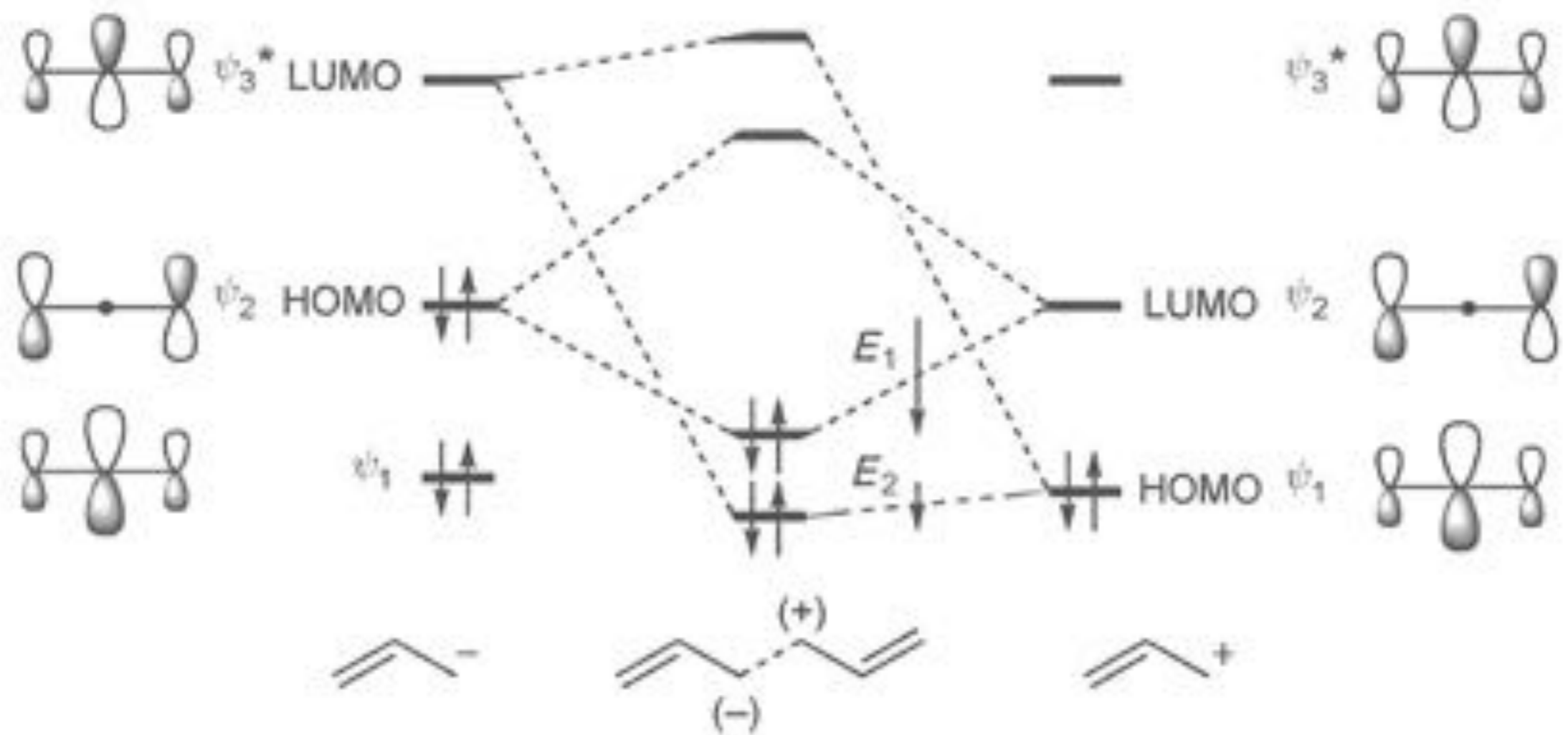


Fig. 3.4 Orbital interactions in the reaction of the allyl anion with the allyl cation

Hard and Soft Nucleophiles and Electrophiles



hard base and hard acid

hard base and soft acid



soft base and soft acid

soft base and hard acid

Hard nucleophiles have a low-energy HOMO and usually have a negative charge.

Soft nucleophiles have a high-energy HOMO but do not necessarily have a negative charge.

Hard electrophiles have a high-energy LUMO and usually have a positive charge.

Soft electrophiles have a low-energy LUMO but do not necessarily have a positive charge.

(i) *A hard-hard reaction is fast because of a large Coulombic attraction.*

hard-hard 相互作用は静電相互作用が主要因

(ii) *A soft-soft reaction is fast because of a large interaction between the HOMO of the nucleophile and the LUMO of the electrophile.*

soft-soft 相互作用はHOMO(求核種)-LUMO(親電子種)相互作用が主要因

(iii) *The larger the coefficient in the appropriate frontier orbital (of the atomic orbital at the reaction centre), the softer the reagent.*

Frontier軌道係数が大きくなるほど試薬はよりsoftになる

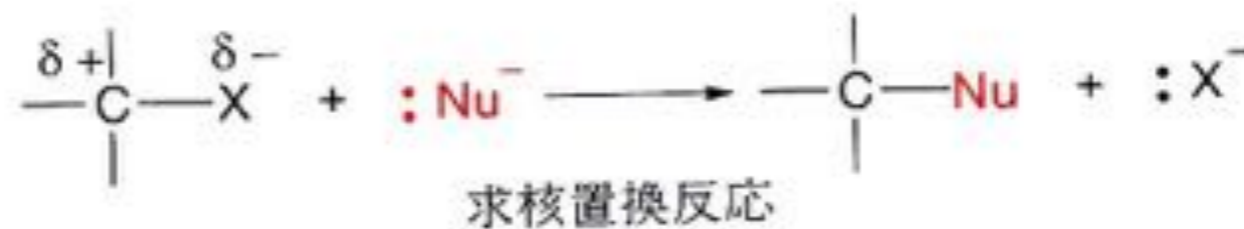
Other Factors Affecting Chemical Reactivity

Strain in the σ framework **σ 骨格の歪み**

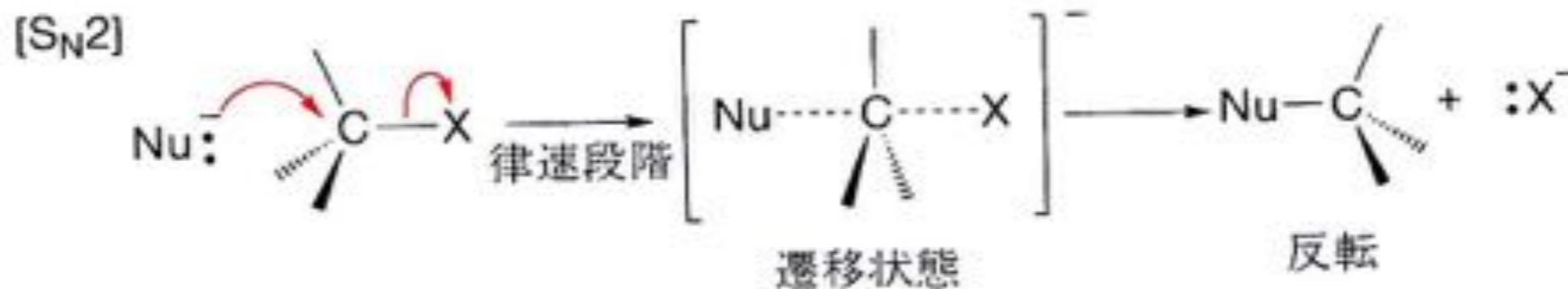
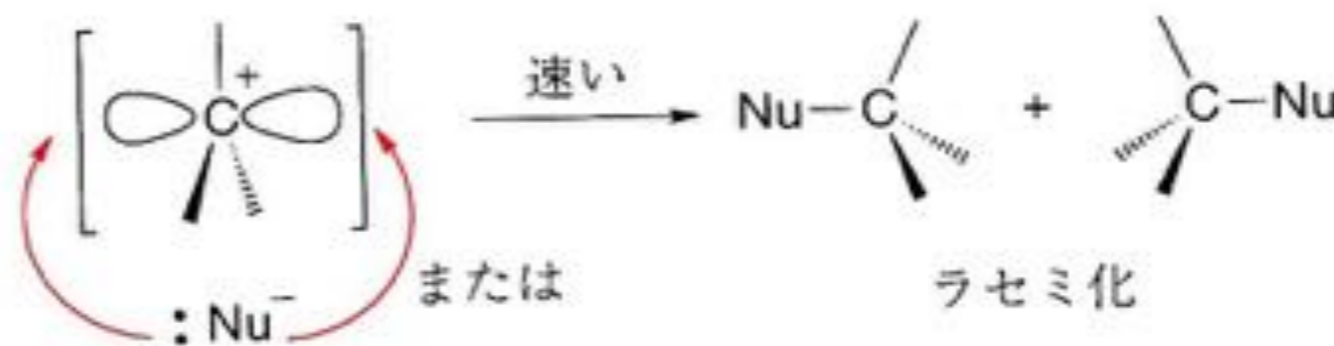
Factors which affect the *entropy* of activation **活性化エントロピー**

solvent effects **溶媒効果 (分子間相互作用)**

Nucleophilic Substitution Reactions of Alkyl Halide (アルキルハライドの求核置換反応)



Substitution
Nucleophilic
Unimolecular
(two-step reaction)



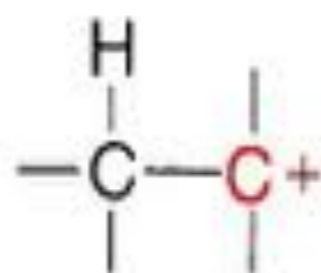
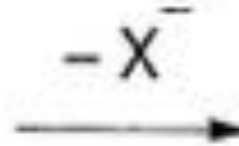
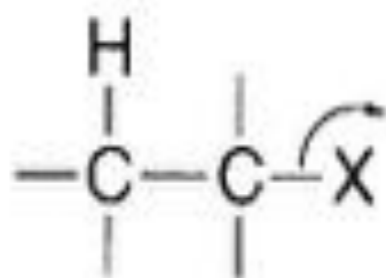
Substitution
Nucleophilic
Bimolecular
(one-step reaction)

Transition State

S_N1 (Substitution Nucleophilic Unimolecular) Reaction vs $E1$ (Elimination Unimolecular) Reaction

S_N1 反応と $E1$ 反応は競争的に起こる

S_N1 反応と $E1$ 反応



Carbocation
Intermediate

求核性の低い試薬
第三級ハロゲン化アルキル
プロトン性極性溶媒

Substitution

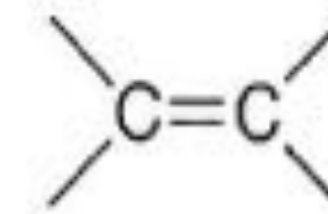
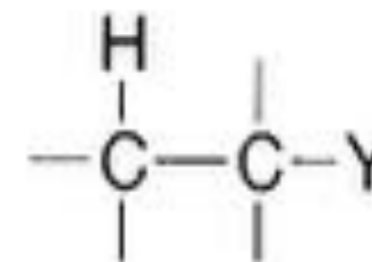
S_N1

Y^-

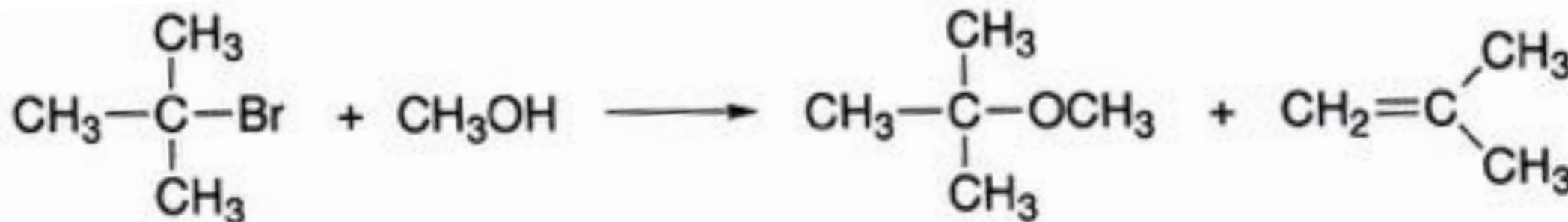
$-H^+$

$E1$

Elimination



Example: S_N1 vs E1

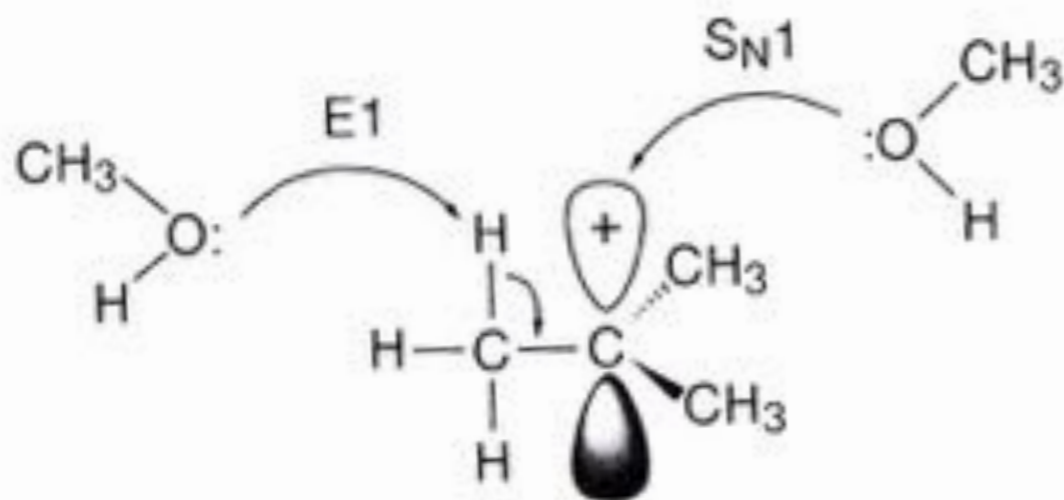


2-ブromo-2-メチル
プロパン

2-bromo-2-methylpropane

S_N1 生成物

E1 生成物



カルボカチオン中間体

炭素陽イオンはルイス酸として働く

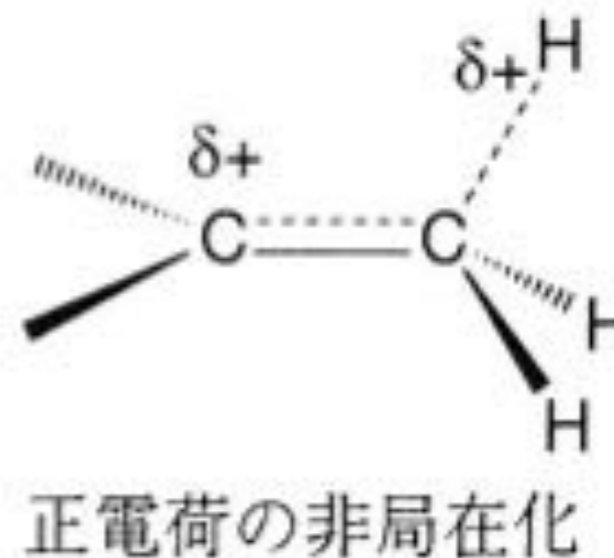
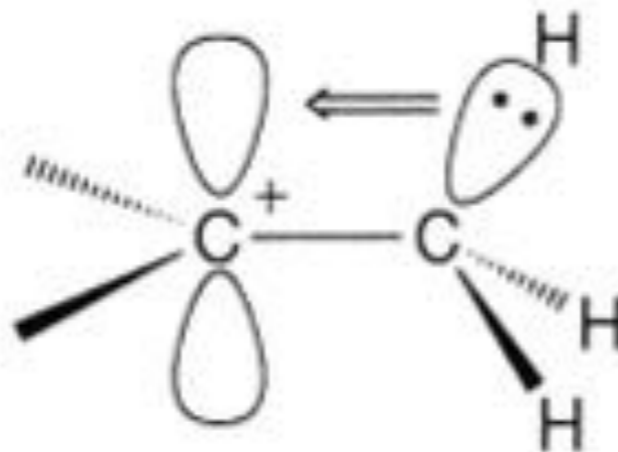
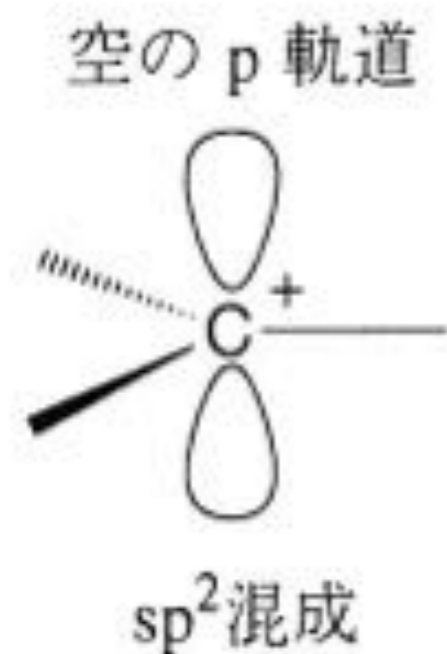
S_N1: メタノールのOの非共有電子対が求核的攻撃

E1: メタノールのOの非共有電子対が塩基として作用してプロトンを引き抜く

炭素陽イオンはブレンスツテッド酸として働く

Hyperconjugative Stabilization in tert-Butyl Cation

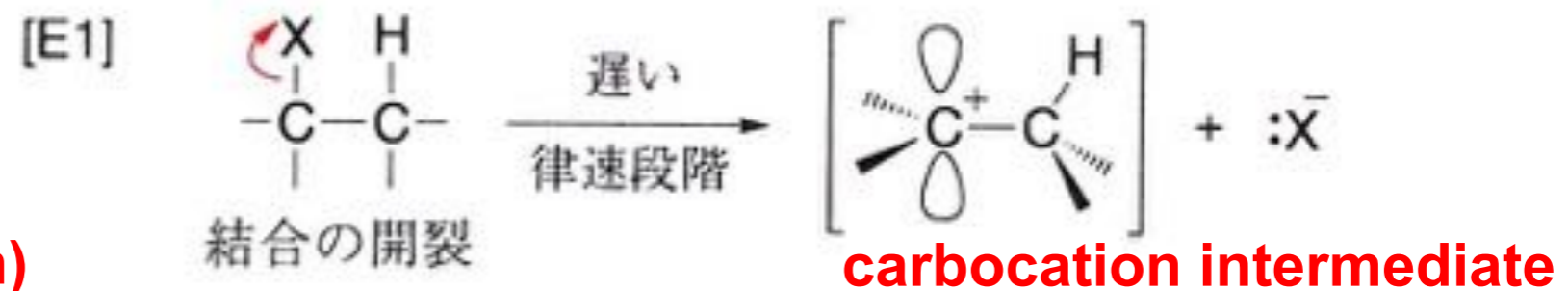
(3級ブチルカチオンにおける超共役安定化)



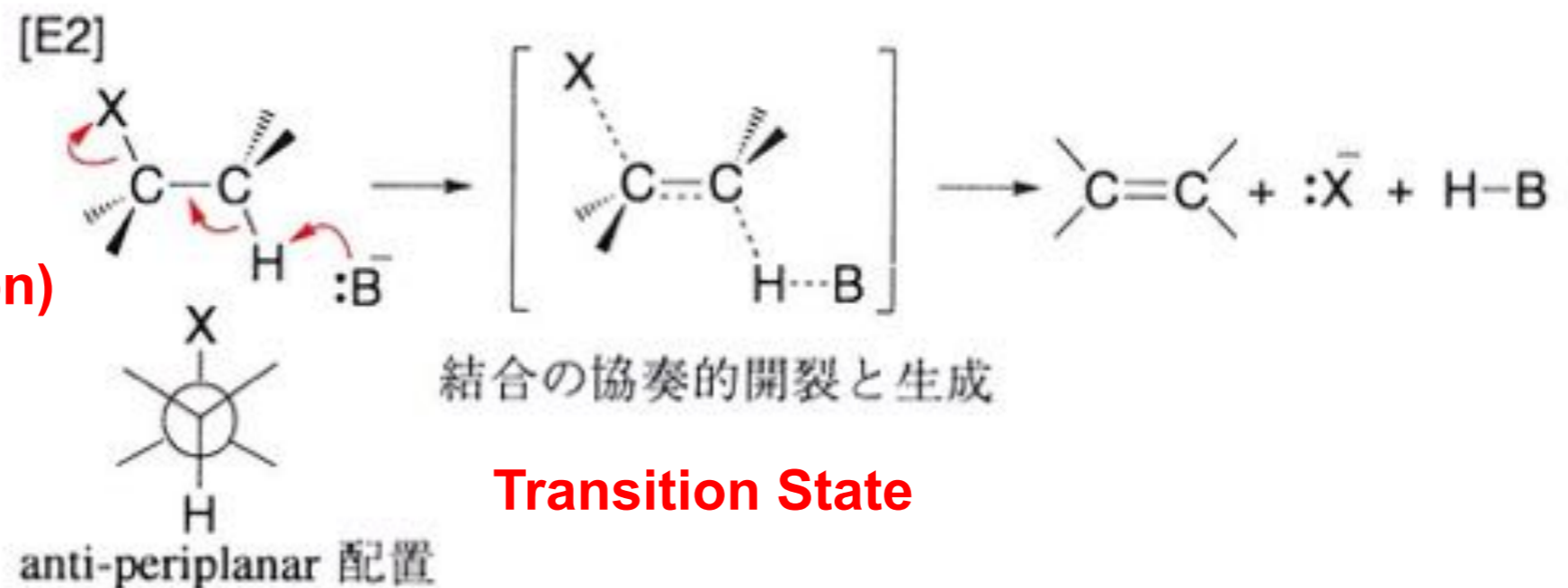
Hyperconjugative Stabilization
超共役安定化

Elimination Reactions of Alkyl Halide (アルキルハライドの脱離反応)

**Elimination
Unimolecular
(two-step reaction)**

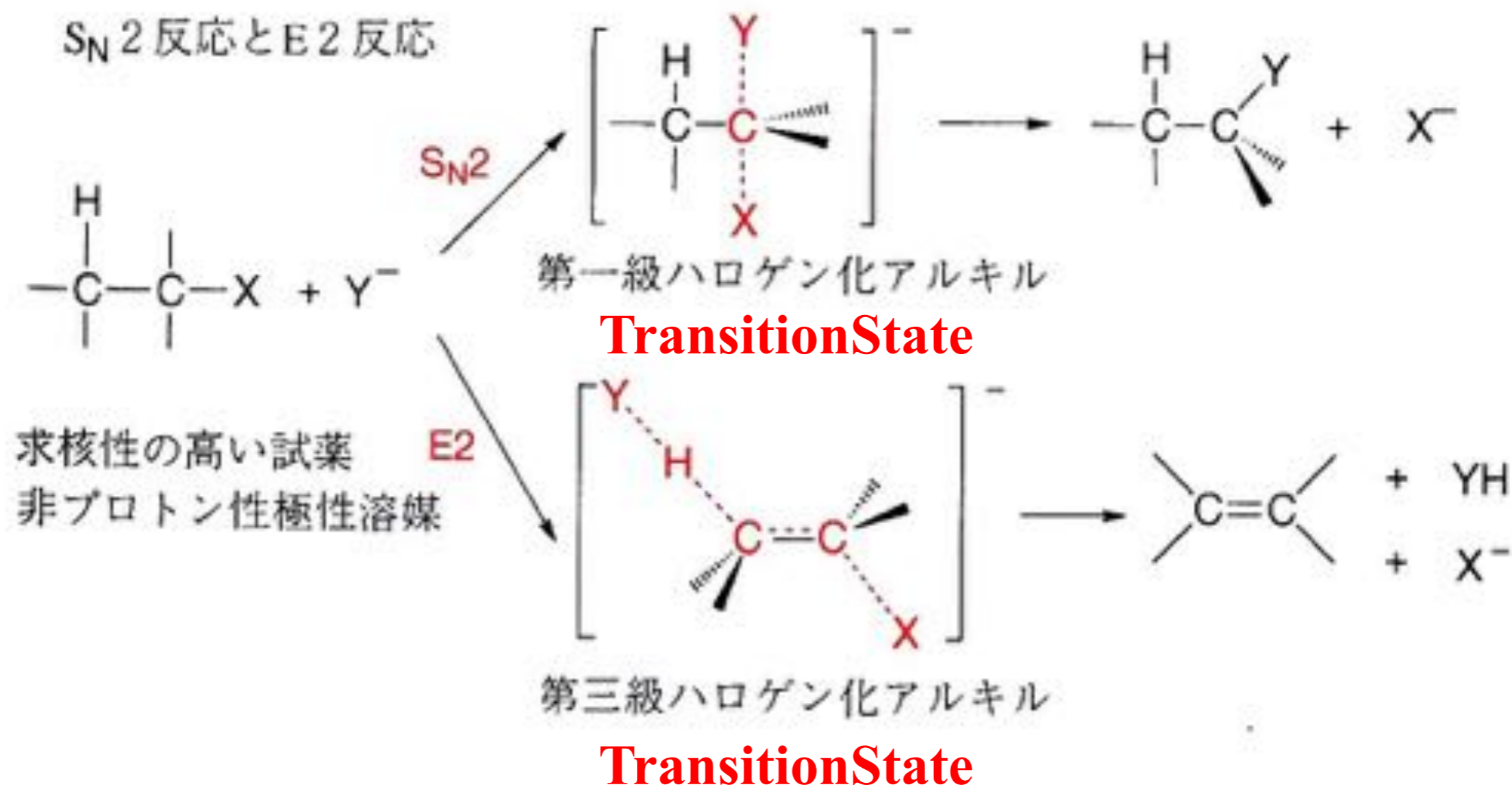


**Elimination
Bimolecular
(one-step reaction)**

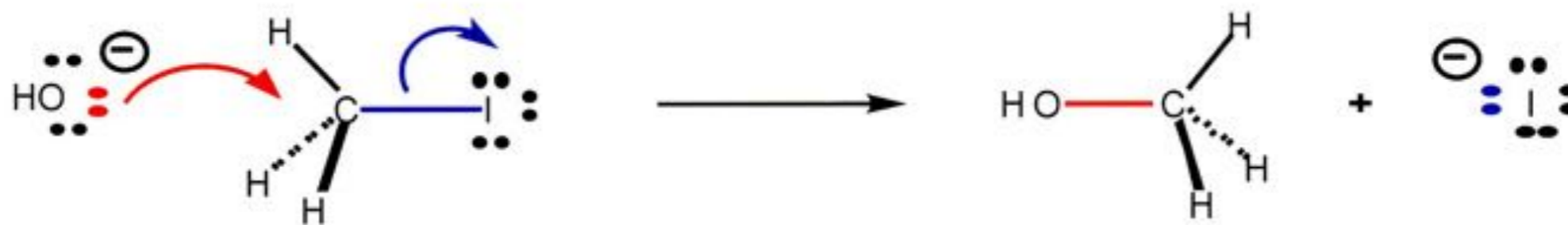


S_N2 (Substitution Nucleophilic Bimolecular) Reaction vs $E2$ (Elimination Bimolecular) Reaction

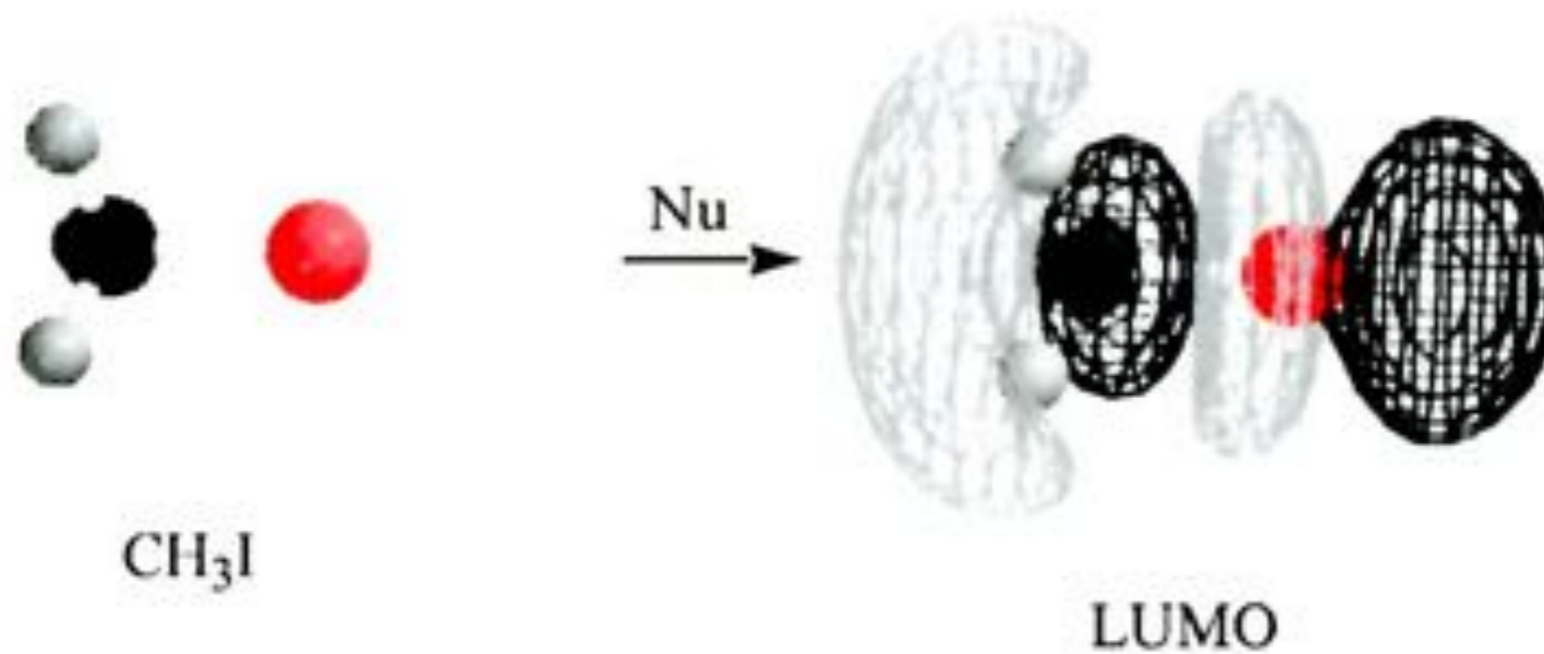
S_N2 反応と $E2$ 反応は競争的に起こる



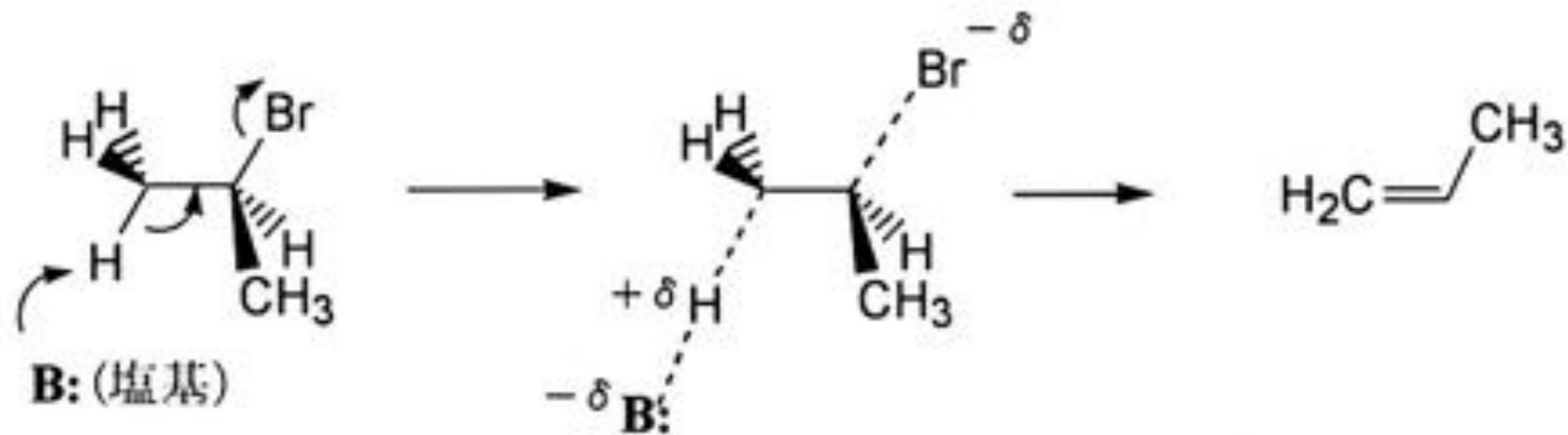
有機電子論による S_N2 反応の説明



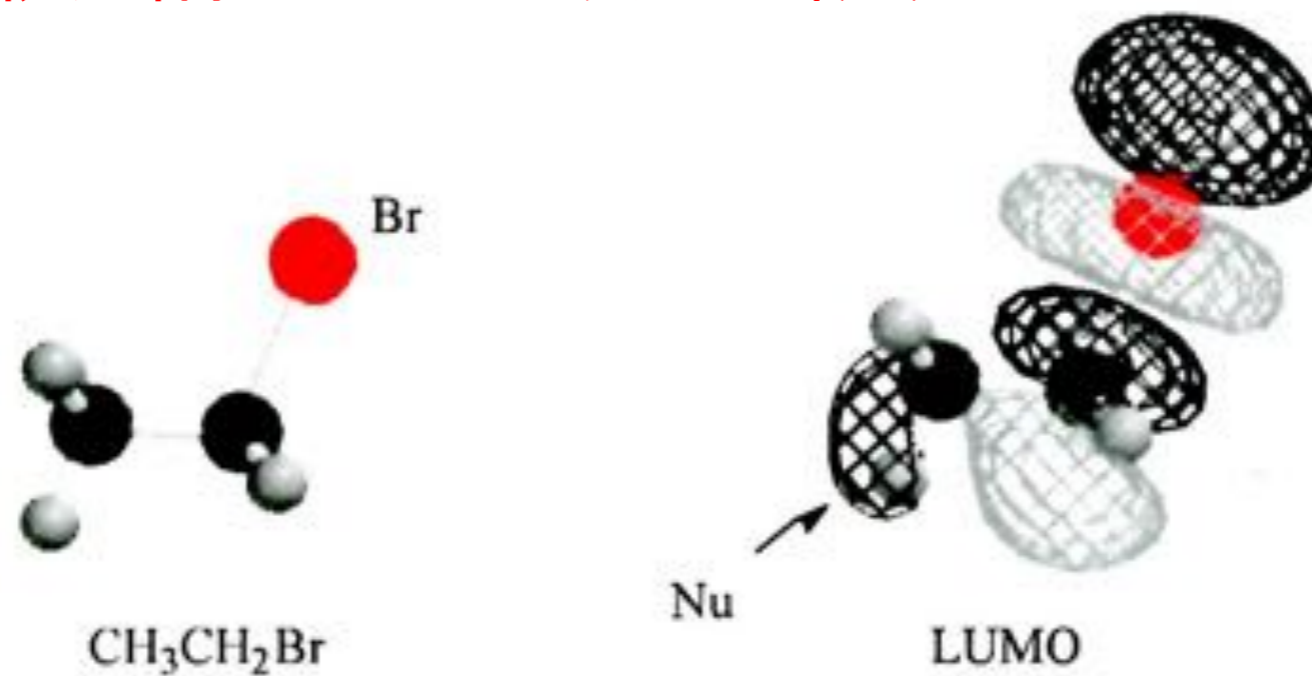
フロンティア軌道論による S_N2 反応の説明



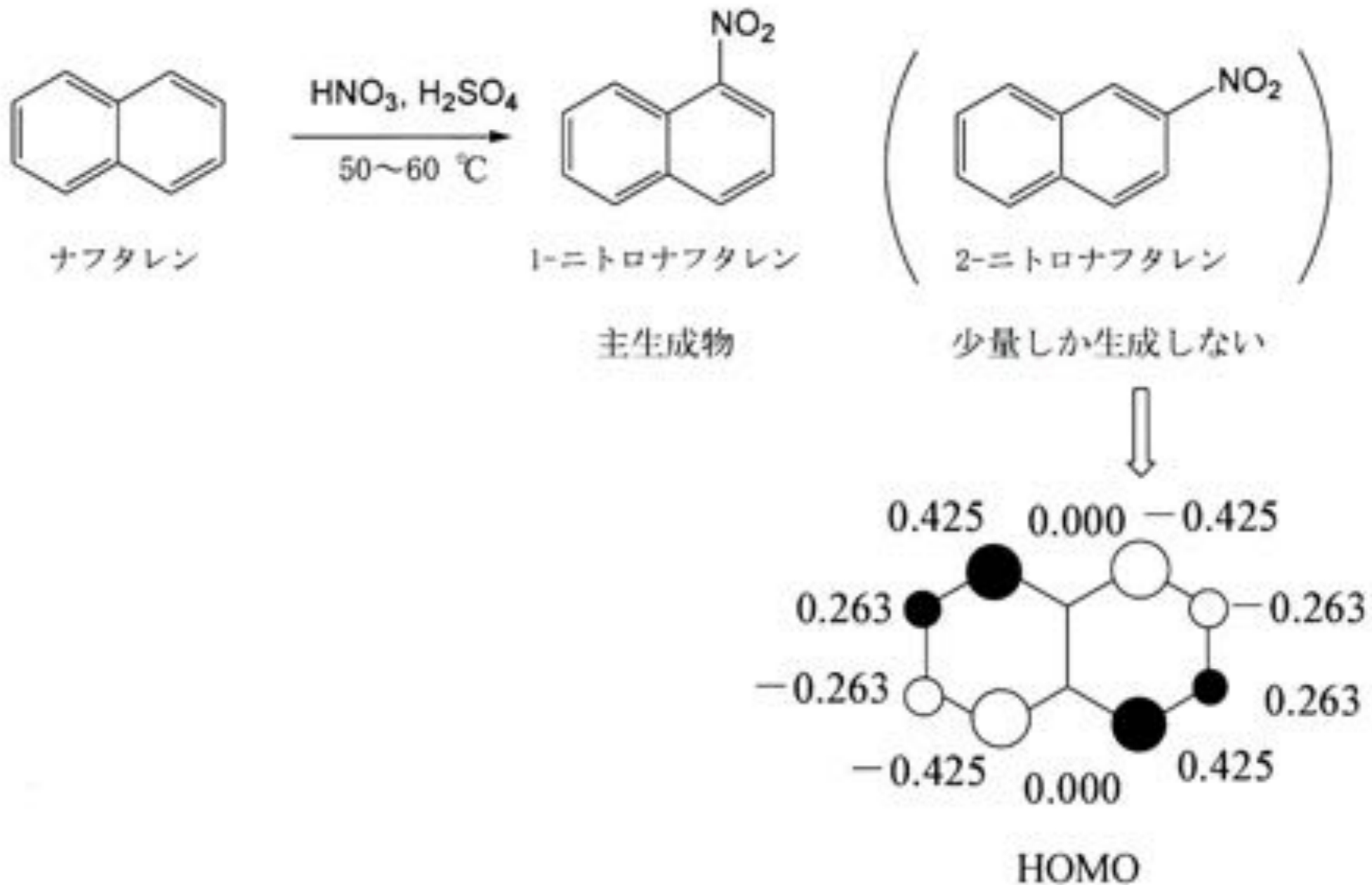
有機電子論によるE2 反応の説明



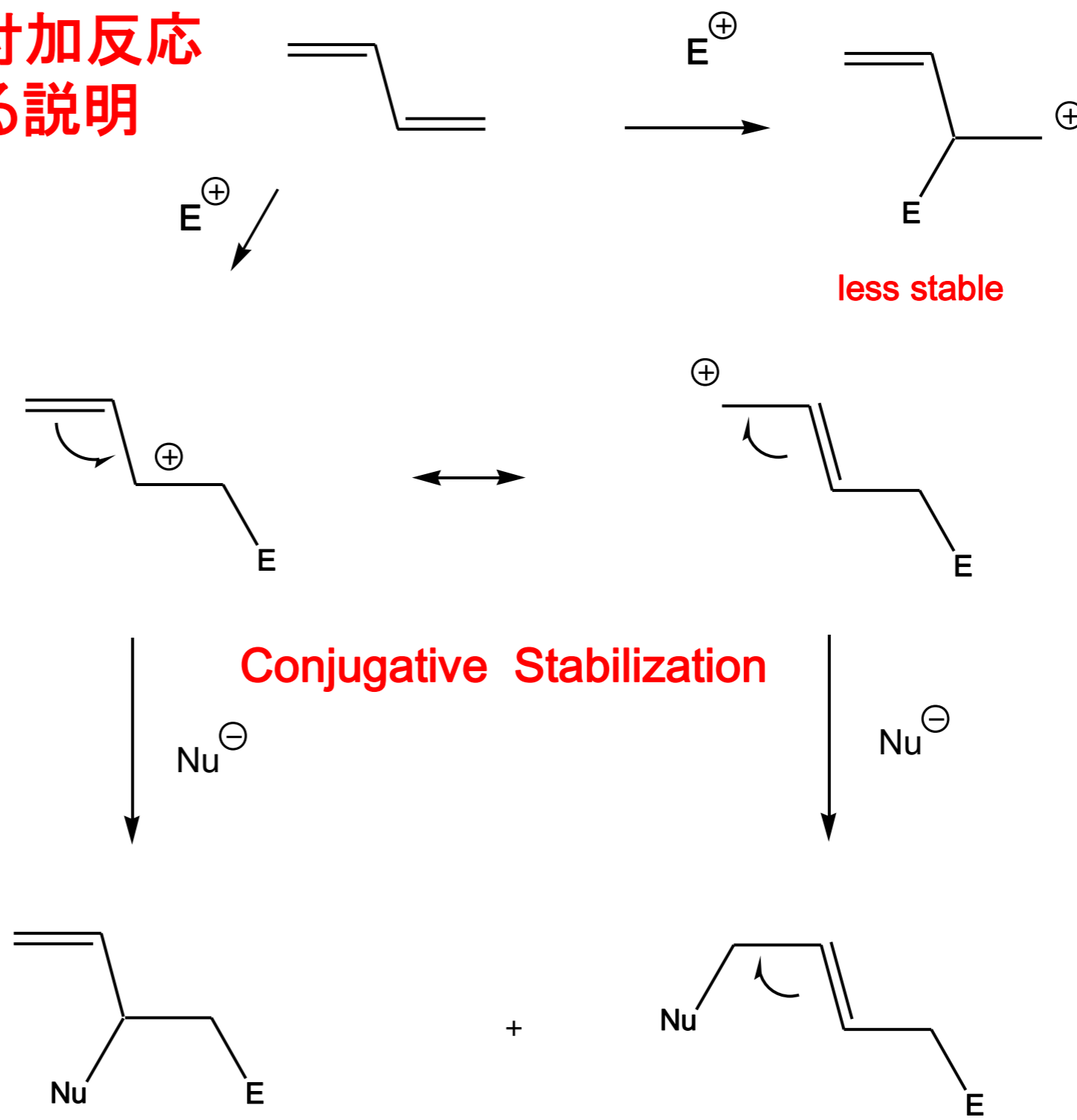
フロンティア軌道論によるE2 反応の説明



ナフタレンの親電子ニトロ化反応のフロンティア理論による解釈

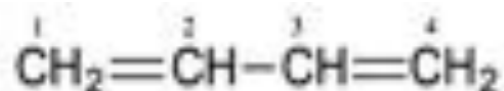


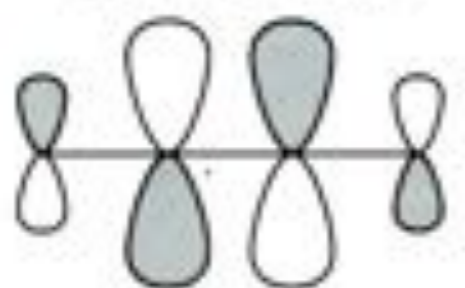
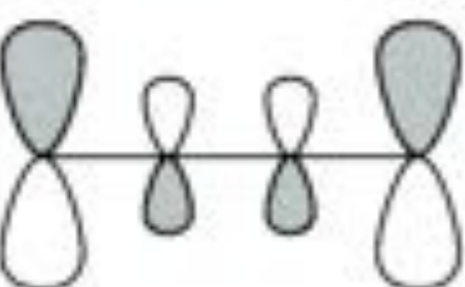
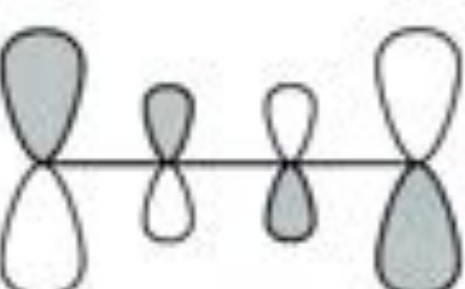
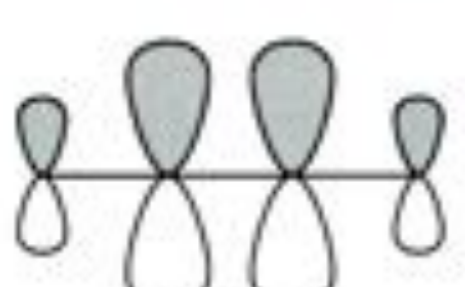
親電子種(E⁺)の付加反応 有機電子論による説明



1,2- and 1,4-adducts

ブタジエンの分子軌道と軌道エネルギー

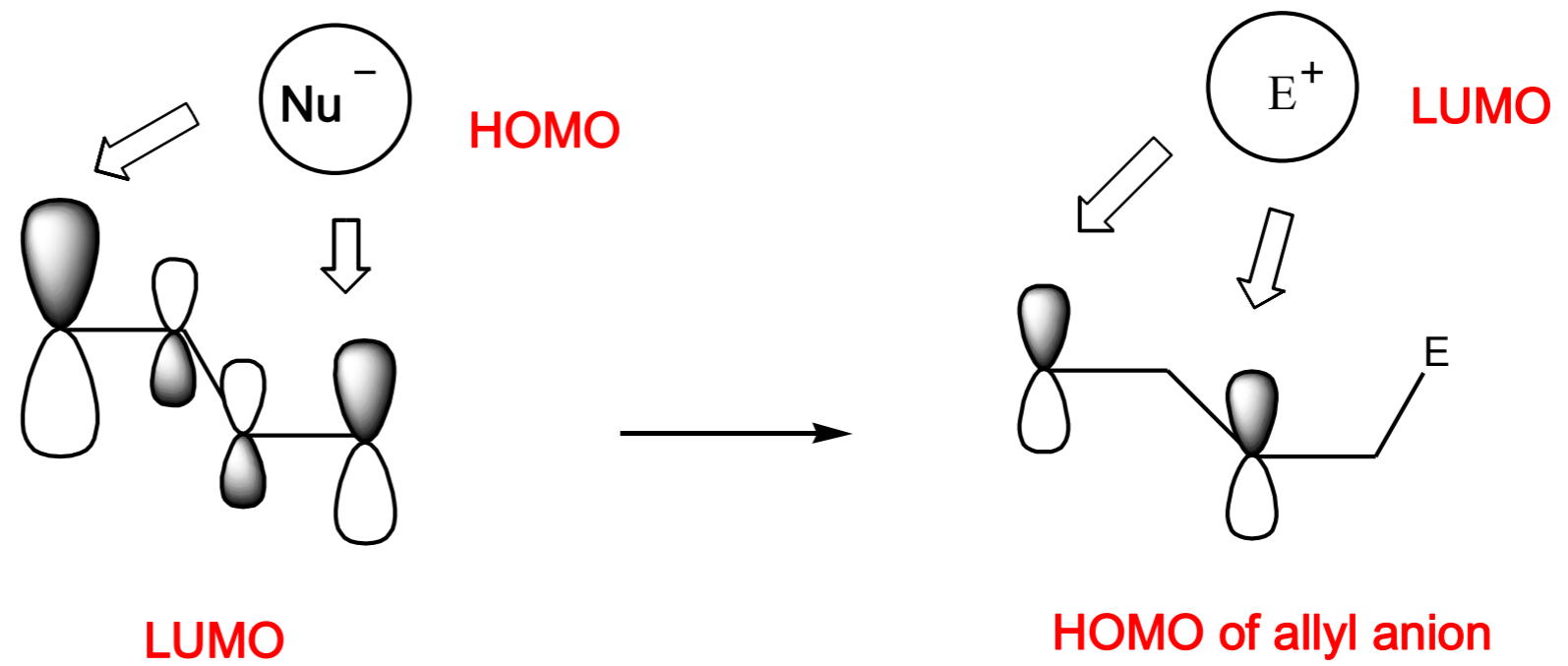
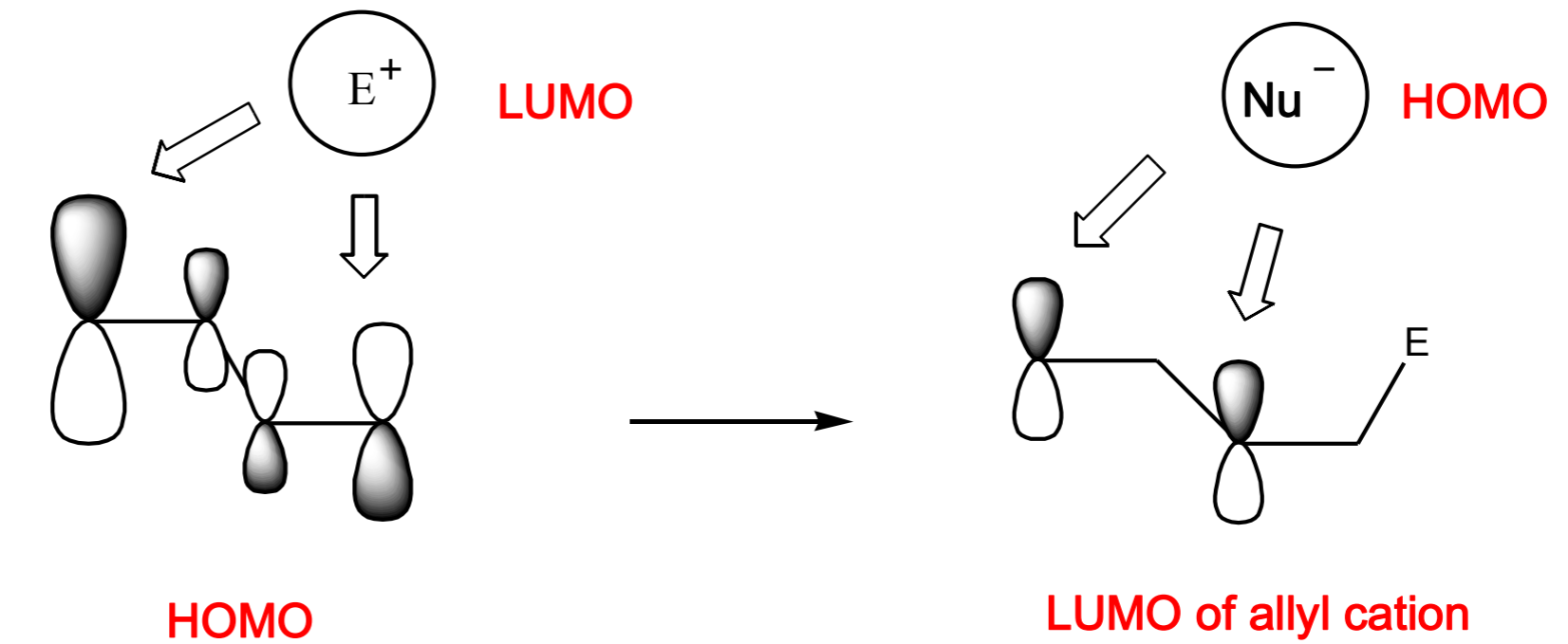


分子軌道の概形	分子軌道関数	軌道エネルギー	基底電子配置
	$\psi_4 = 0.372\chi_1 - 0.602\chi_2 + 0.602\chi_3 - 0.372\chi_4$	$\epsilon_4 = \alpha - 1.618\beta$	—
	$\psi_3 = 0.602\chi_1 - 0.372\chi_2 - 0.372\chi_3 + 0.602\chi_4$	$\epsilon_3 = \alpha - 0.618\beta$	—
	$\psi_2 = 0.602\chi_1 + 0.372\chi_2 - 0.372\chi_3 - 0.602\chi_4$	$\epsilon_2 = \alpha + 0.618\beta$	↑↓
	$\psi_1 = 0.372\chi_1 + 0.602\chi_2 + 0.602\chi_3 + 0.372\chi_4$	$\epsilon_1 = \alpha + 1.618\beta$	↑↓

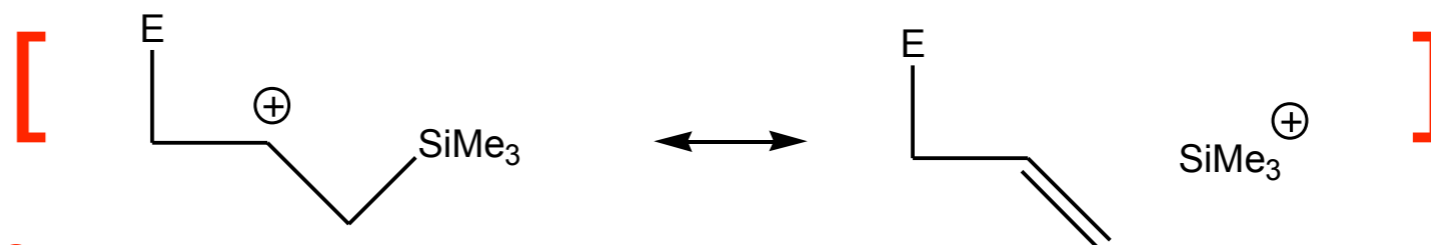
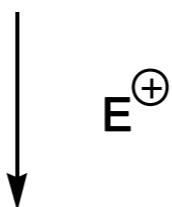
最低空軌道 Lowest Unoccupied Molecular Orbital (LUMO)

最高被占軌道 Highest Occupied Molecular Orbital (HOMO)

フロンティア軌道論による説明

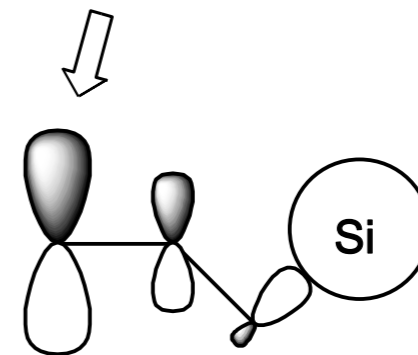
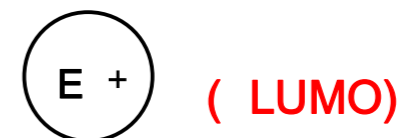


Reaction of Allyl Silane with Electrophile

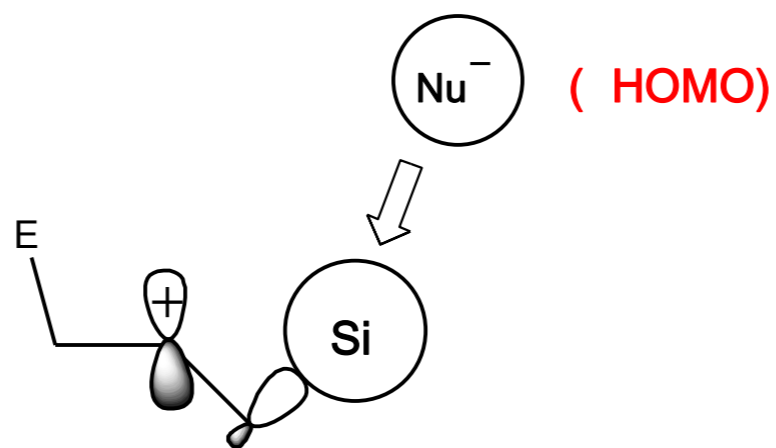


hyperconjugation of β -C-Si σ bond

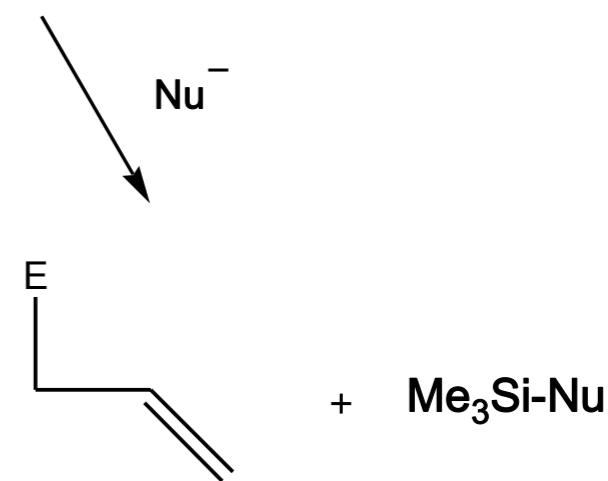
Frontier MO interaction



HOMO of Allyl Silane



LUMO of carbocation with β -C-Si σ bond



Hyperconjugative Stabilization of Carbocation by C-Si σ Bond vs C-C σ Bond

