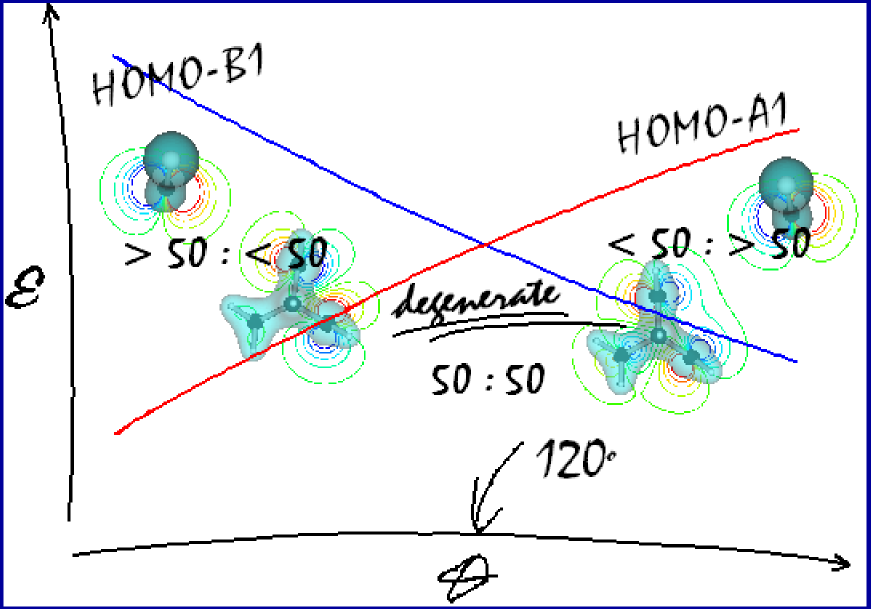
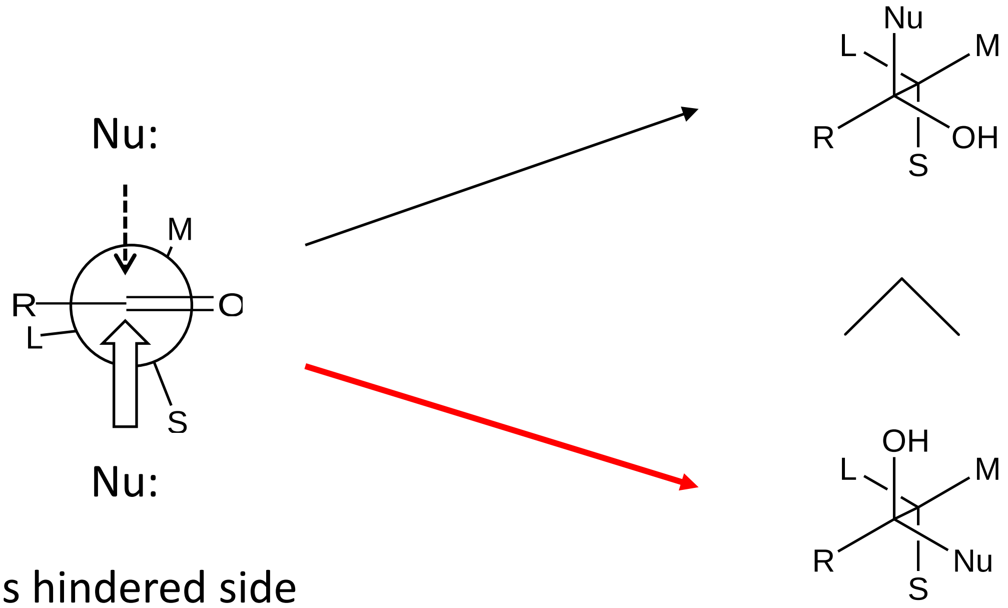
Geometrical Dependence of the Highest Occupied Molecular Orbital in Bicyclic Systems:

Origin of the π Facial Stereoselectivity of Bicyclic and Tricyclic Olefins



Motonori Tsuji
Institute of Molecular Function

Cram’s Rule



eclipsed

Less hindered side

Major Product

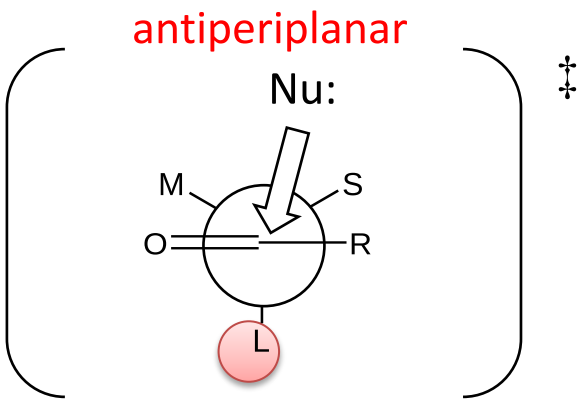
Ground State

S: small substituent

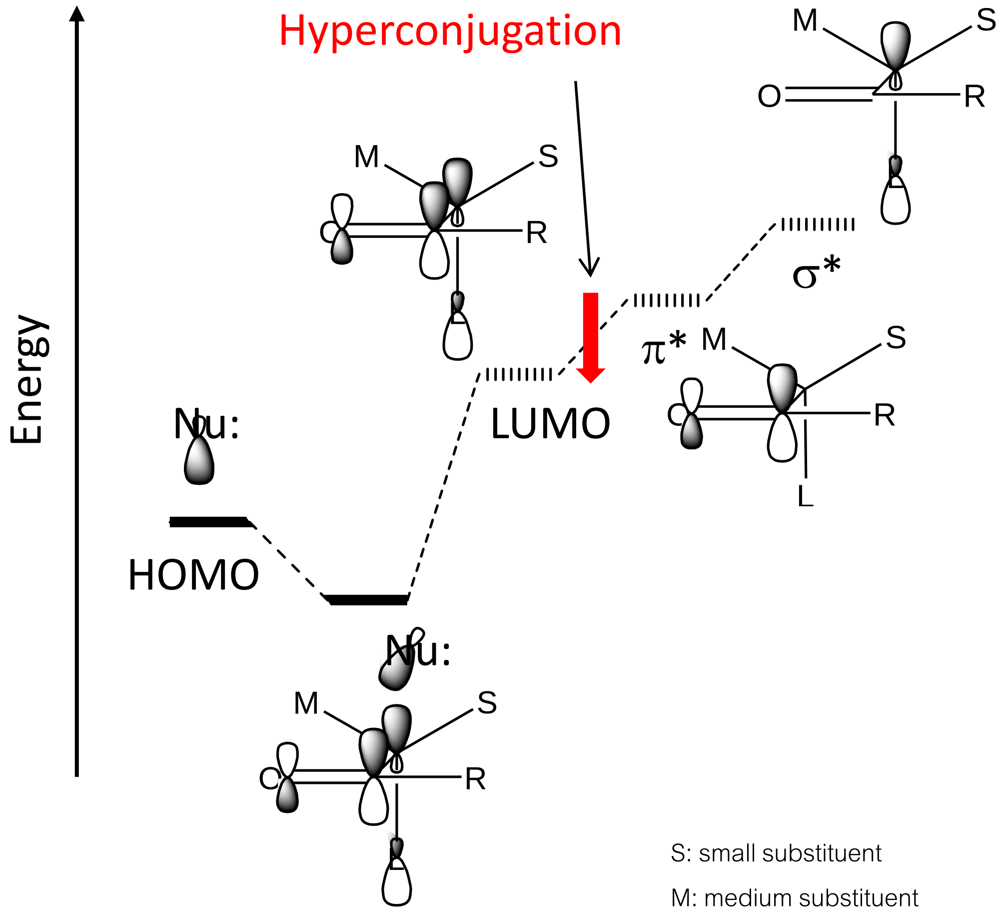
M: medium substituent

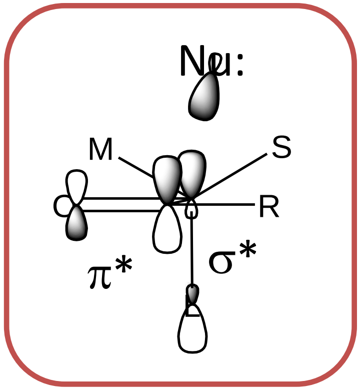
L: large substituent

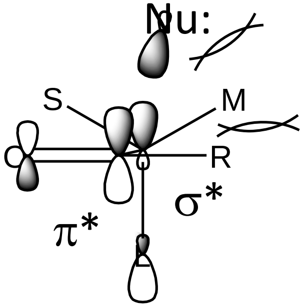
Felkin-Anh Model



Transition State







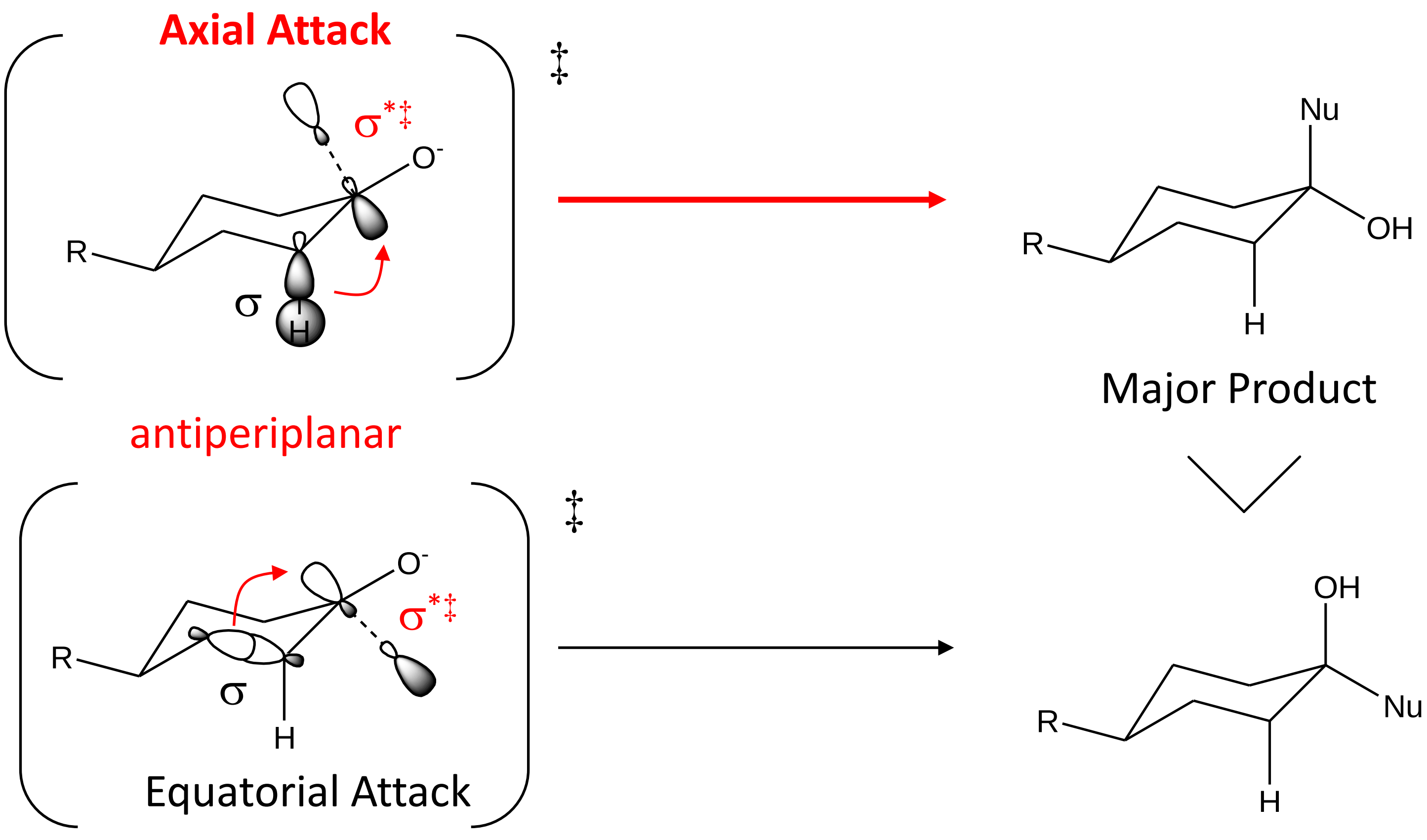
S: small substituent

M: medium substituent

L: large substituent

Cieplak Model

ASSUMPTION: ELECTRON DONOR NATURE: C-H > C-C



Axial Attack

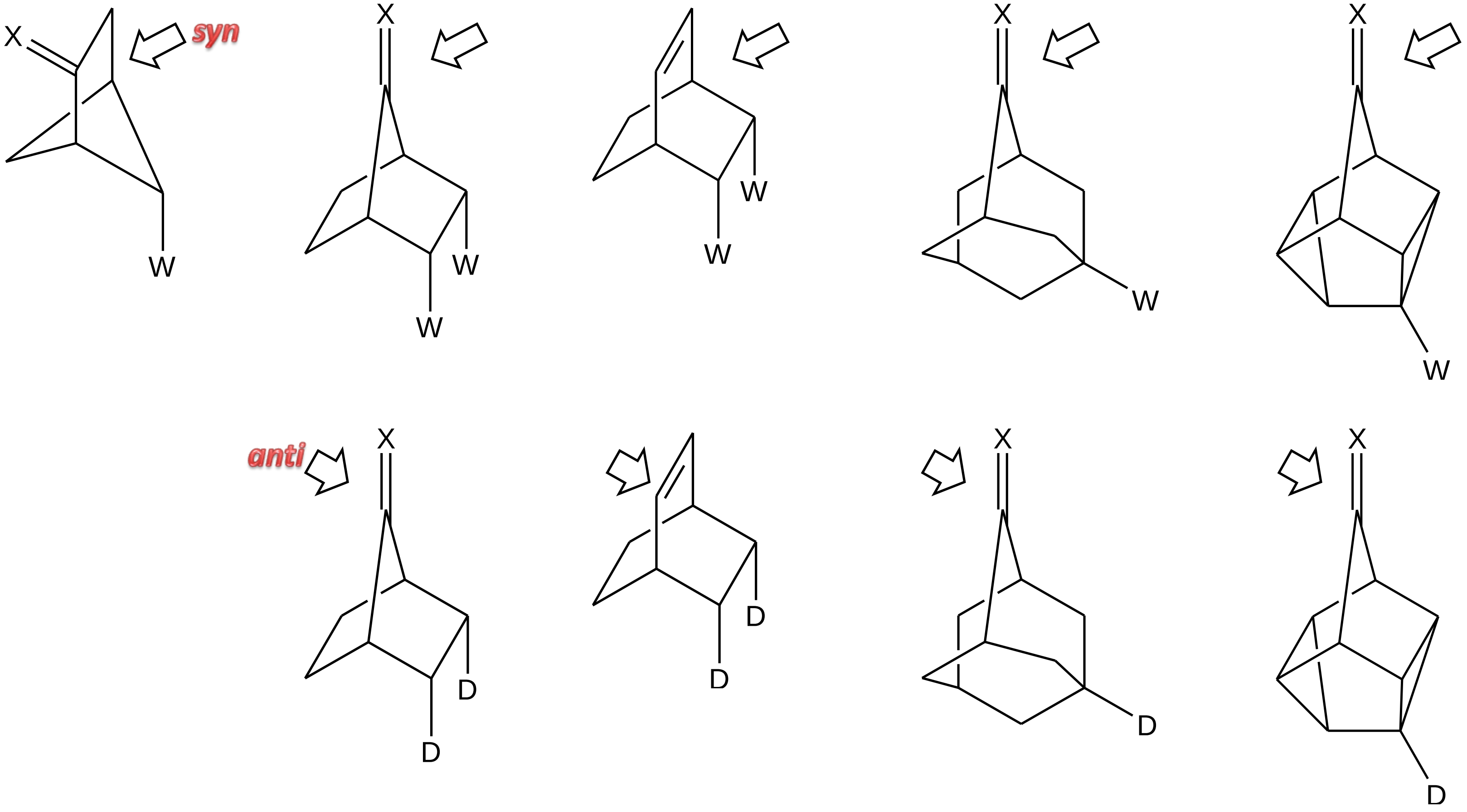
antiperiplanar

Major Product

Equatorial Attack

Transition State

Sterically Unbiased Systems for Facial Selectivity



X = O, CH_2

Electrophiles for Olefins
Nucleophiles for Carbonyls

```
W: Electron-withdrawing Group
D: Electron-donating Group
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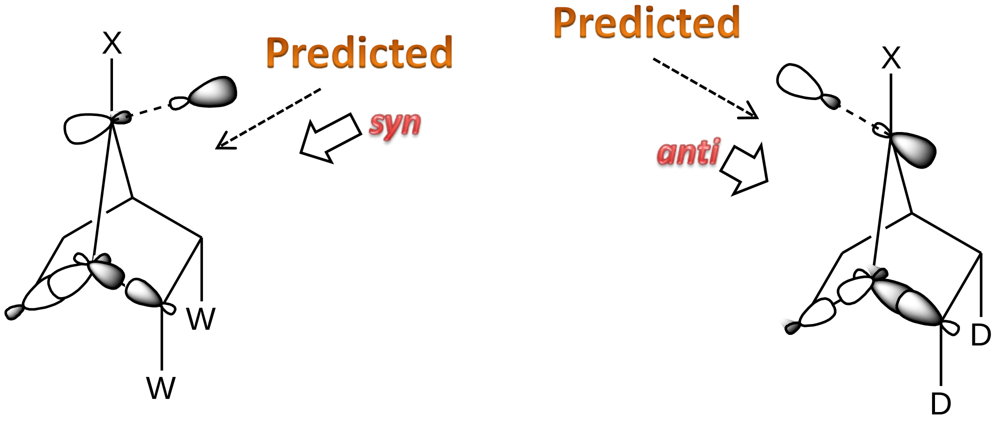
Explanation Using Cieplak Model

Steric, electrostatic, and torsional effects can ignore in these sterically unbiased systems.

Cieplak Model: Predictable

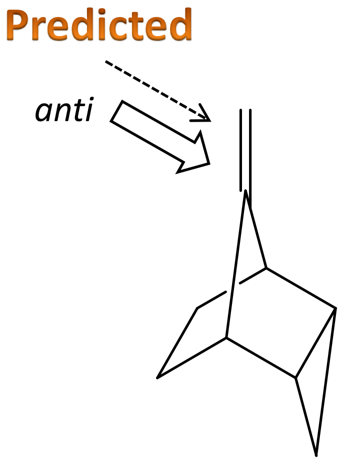


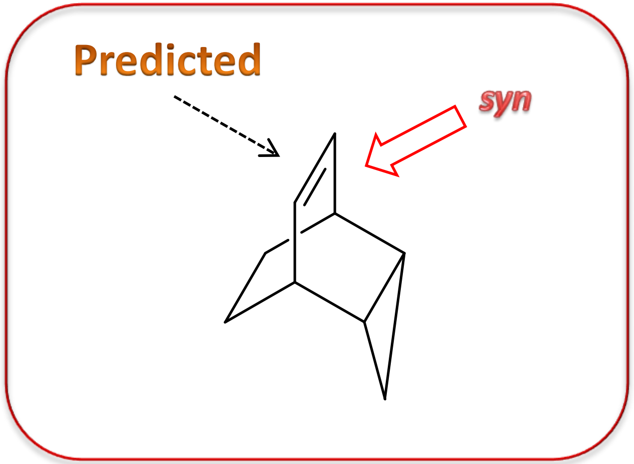
X = O, CH_2

Electrophiles for Olefins
Nucleophiles for Carbonyls

`W: Electron-withdrawing Group`
`D: Electron-donating Group`

A Reverse Facial Stereoselectivity with the Electron-donating Cyclopropane Ring





All models can not explain the facial stereoselectivity

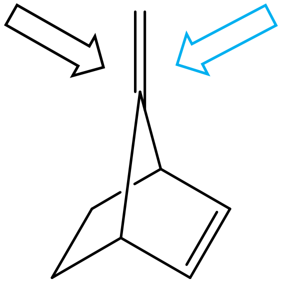
Cram’s Rule, Felkin-Anh Model, Cieplak Model
Steric Effect, Electrostatic Effect, Torsional Effect,
Ruled Out

Model Systems in Which the π Nature of Cyclopropane Is Maximized

Three-center Geometry

Weak
Elecrophiles
anti

Strong
Electrophiles
syn



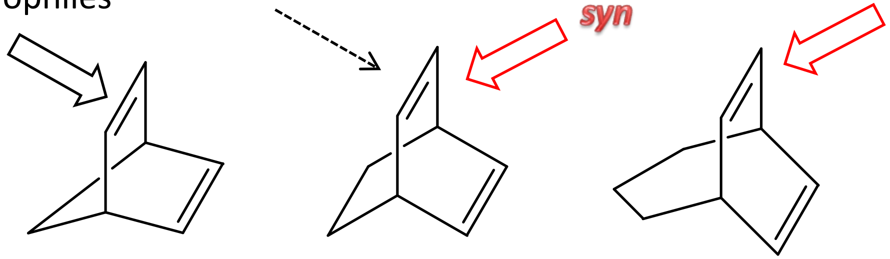
Four-center Geometry

Both
Electrophiles
anti

Predicted

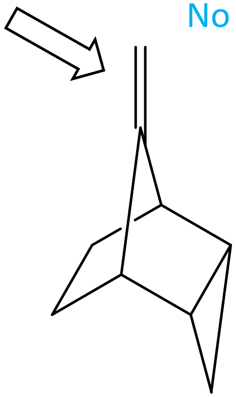
syn

syn



Weak
Elecrophiles
anti

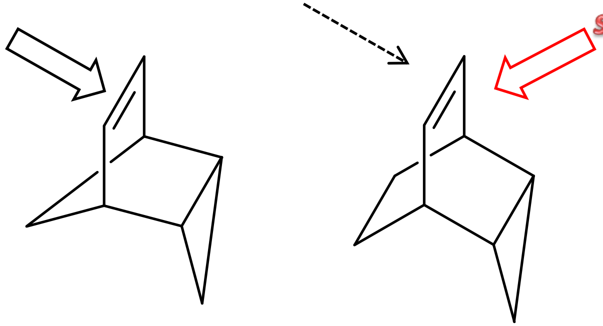
Strong
Electrophiles
No Selectivity



anti

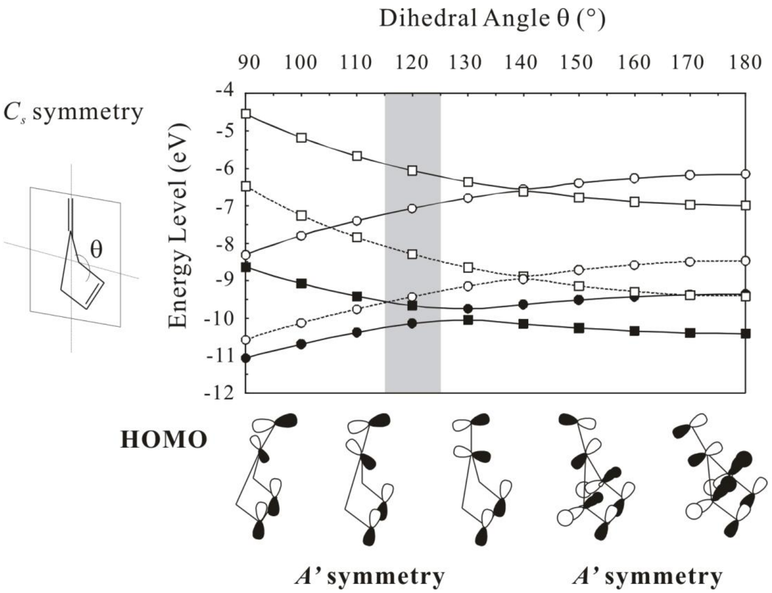
Predicted

syn



Geometrical Dependence of the HOMO in the Non-Conjugated Dienes

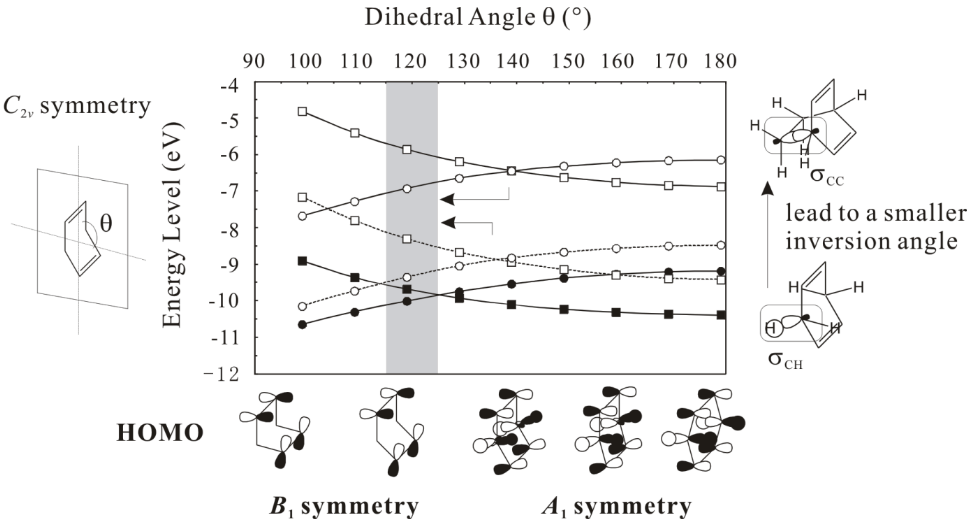
Three-center Geometry



Though-space

Though-bond
(Hyperconjugation)

Four-center Geometry

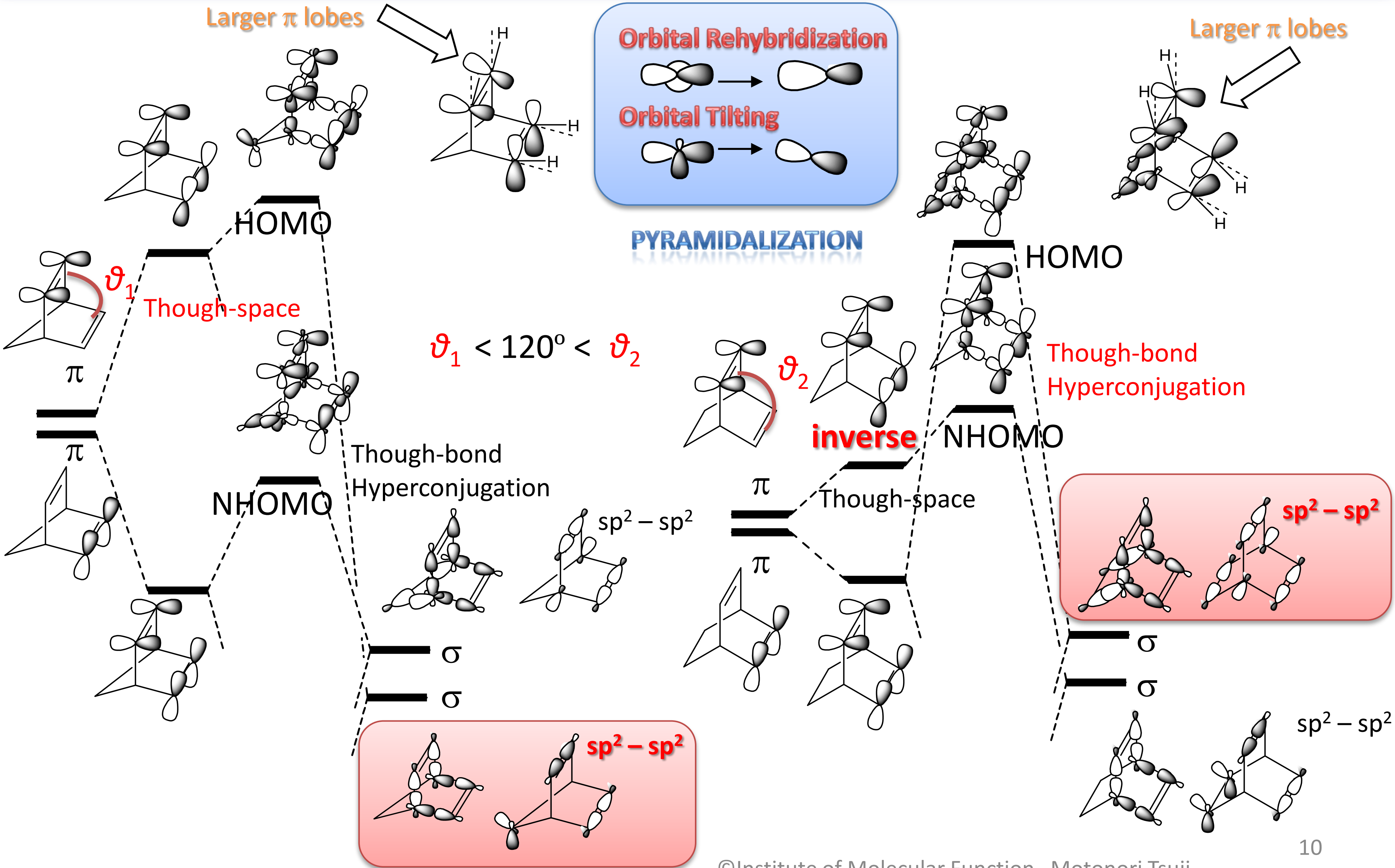


Though-space

Though-bond
(Hyperconjugation)

A1-symmetry orbitals (circles) and *B1*-symmetry orbitals (squares) were obtained at the RPM3 (solid), RB3LYP/6-31G* (open), and ROVGF/6-31G*//HF/6-31G* (dotted line) methods.

Origin of the Facial Stereoselectivity in the Four-center Geometry



Larger π lobes

Orbital Rehybridization

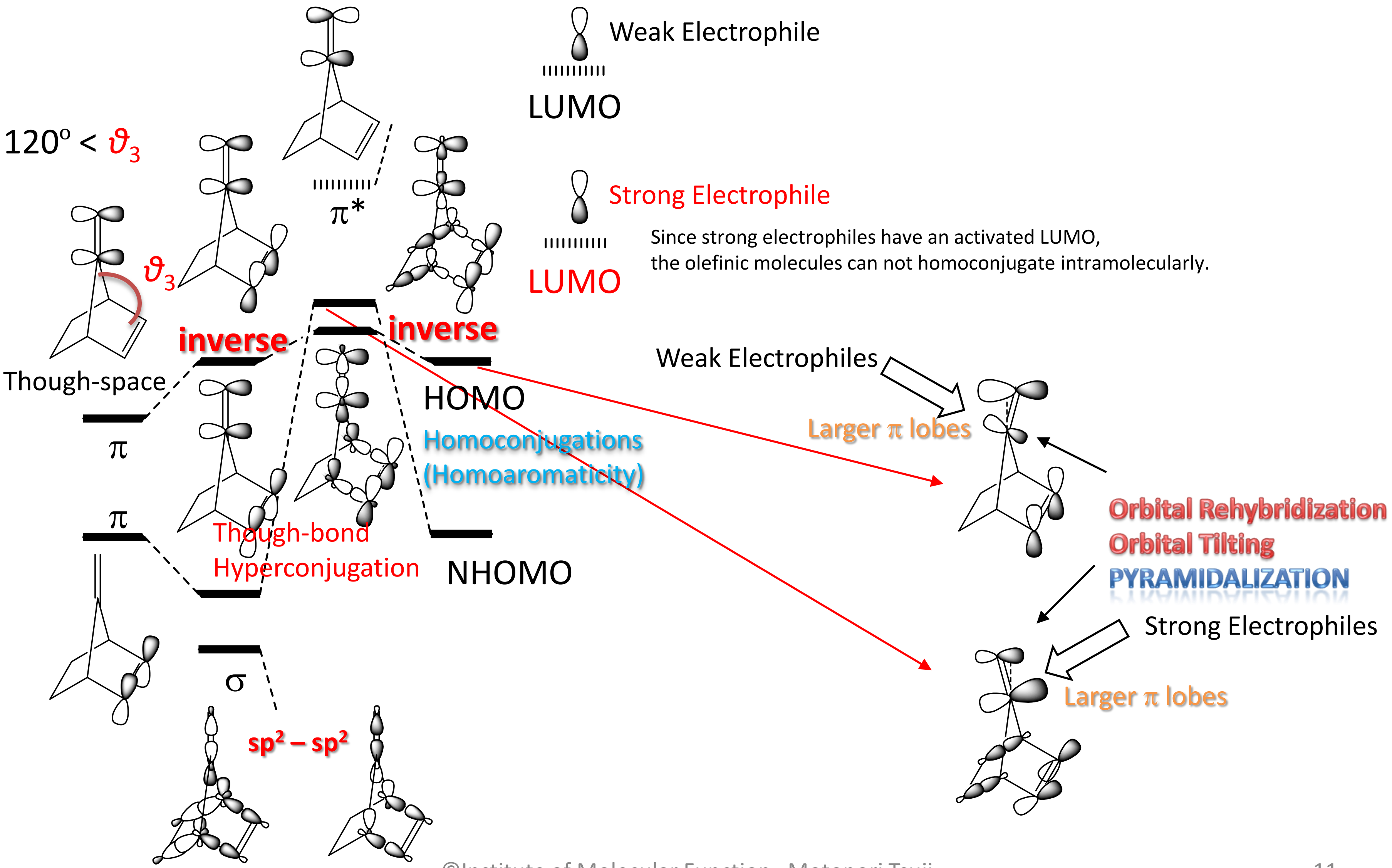
Orbital Tilting

PYRAMIDALIZATION

Larger π lobes

$\vartheta_1 < 120^o < \vartheta_2$

Origin of the Facial Stereoselectivity in the Three-center Geometry



$120^{o} < \vartheta_3$

ϑ_3

Though-space

π

π

inverse

inverse

π^*

Though-bond Hyperconjugation

σ

$sp^2 - sp^2$

HOMO

Homoconjugations (Homoaromaticity)

NHOMO

Weak Electrophile

LUMO

Strong Electrophile

LUMO

Since strong electrophiles have an activated LUMO, the olefinic molecules can not homoconjugate intramolecularly.

Weak Electrophiles

Larger π lobes

Orbital Rehybridization

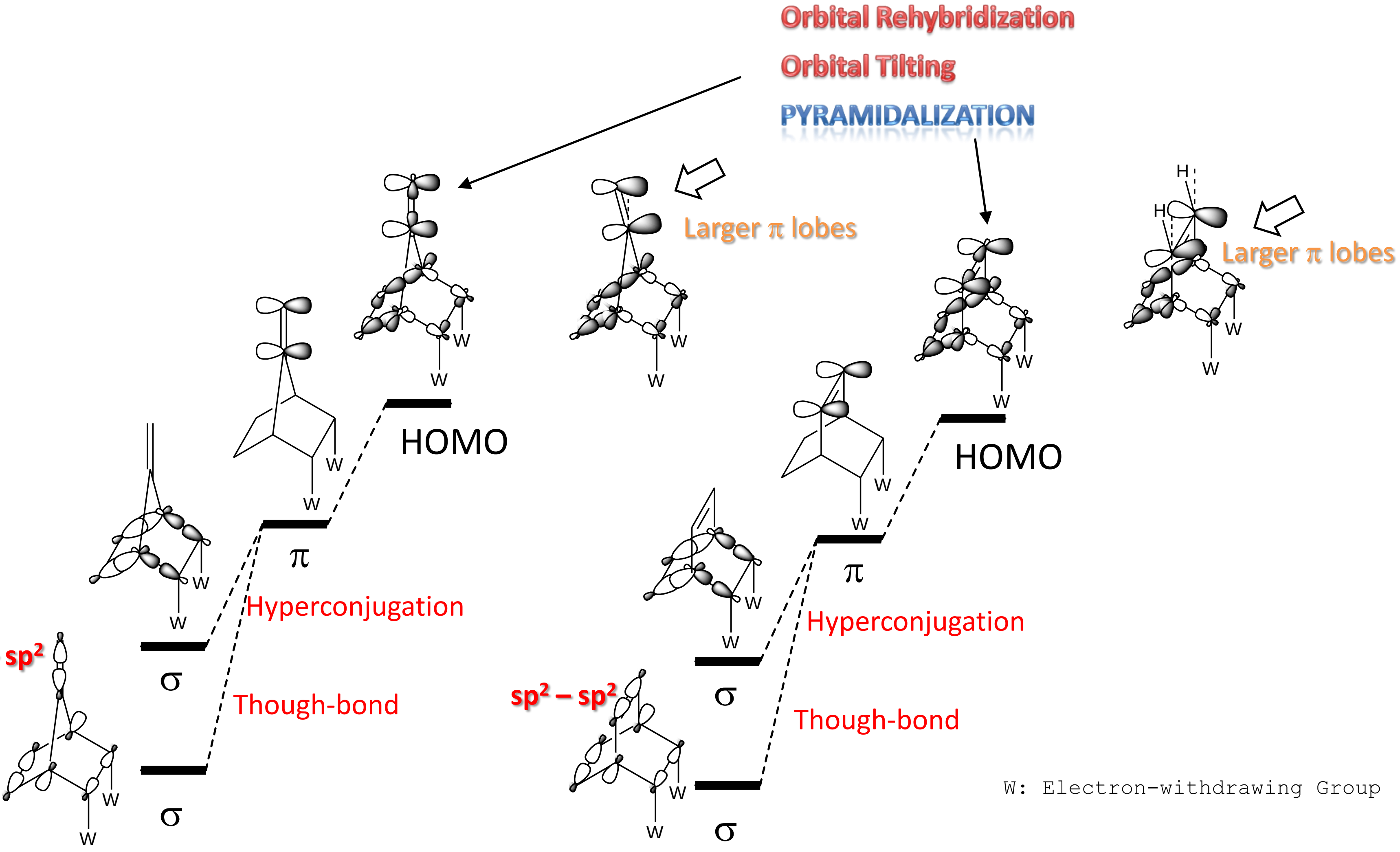
Orbital Tilting

PYRAMIDALIZATION

Strong Electrophiles

Larger π lobes

Effect of the Electron-withdrawing Group on the Facial Stereoselectivity



Orbital Rehybridization

Orbital Tilting

PYRAMIDALIZATION

Larger π lobes

Larger π lobes

Hyperconjugation

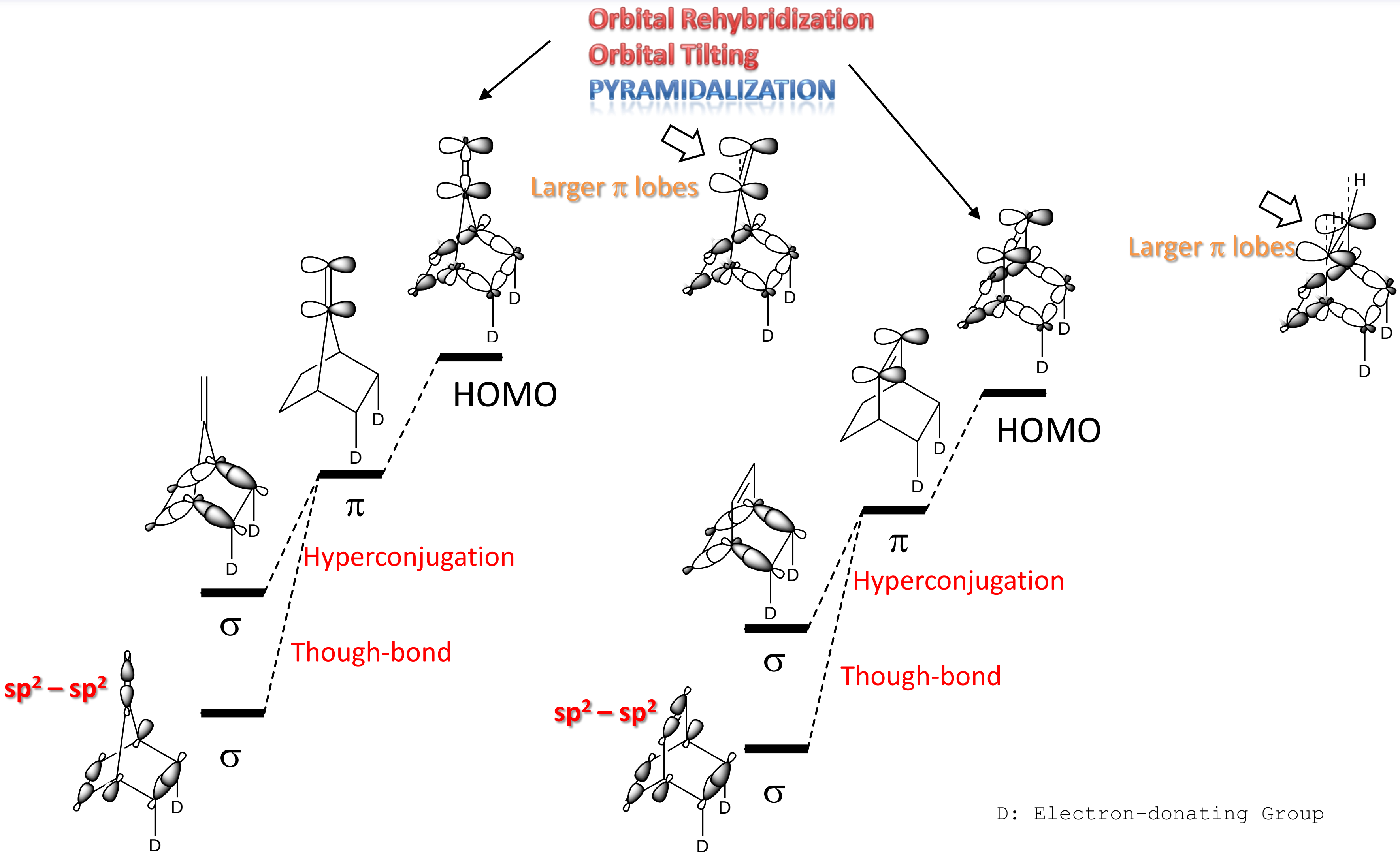
Though-bond

Hyperconjugation

Though-bond

W: Electron-withdrawing Group

Effect of the Electron-donating Group on the Facial Stereoselectivity



D: Electron-donating Group

Conclusions

HOMO of molecule depends on the geometry.

This HOMO determines the facial stereoselectivity.

Depending on the molecular geometry, the symmetrical π orbital is mixed with the different types of σ orbitals.

These σ orbitals are mixed with π orbital via through-bond interactions.

As a result, through-bond interactions, such as hyperconjugation, bring about the orbital rehybridization (pyramidalization) and tilting, leading to the desired transition structure.

The magnitude of through-space interaction affects on the orbital sequence, thus leading to the reverse selectivity.

In the three center geometry, homoconjugation (homoaromaticity) strongly affects on the orbital sequence, thus giving the ambident selectivity.

M. TSUJI. *ASIAN JOURNAL OF ORGANIC CHEMISTRY*, 2015, 4, 659-673.