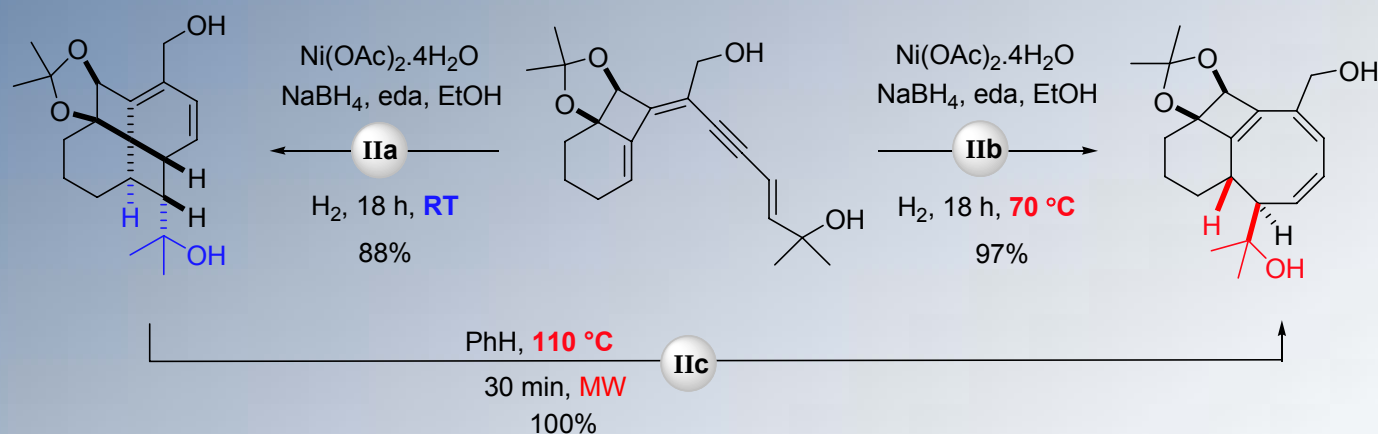


# Understanding the Torquoselectivity in 8 $\pi$ -Electrocyclic Cascade Reactions: Synthesis of Fenestradienes versus Cyclooctatrienes

Catherine Hulot, Shadi Amiri, Gaëlle Blond, Peter R. Schreiner,\* and Jean Suffert\*

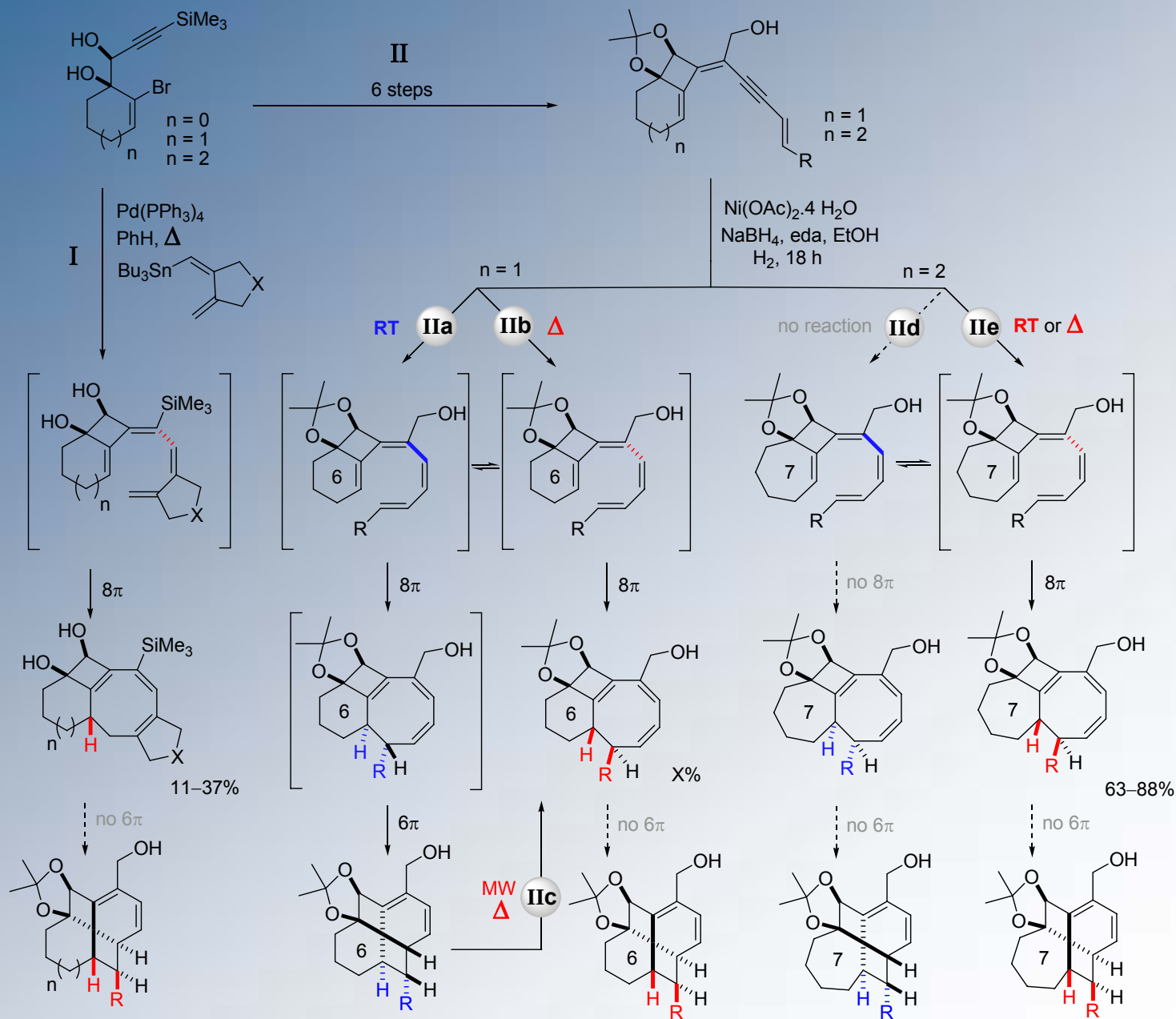


PRS Group Seminar

Shadi Amiri

JLU Giessen, 13.02.09

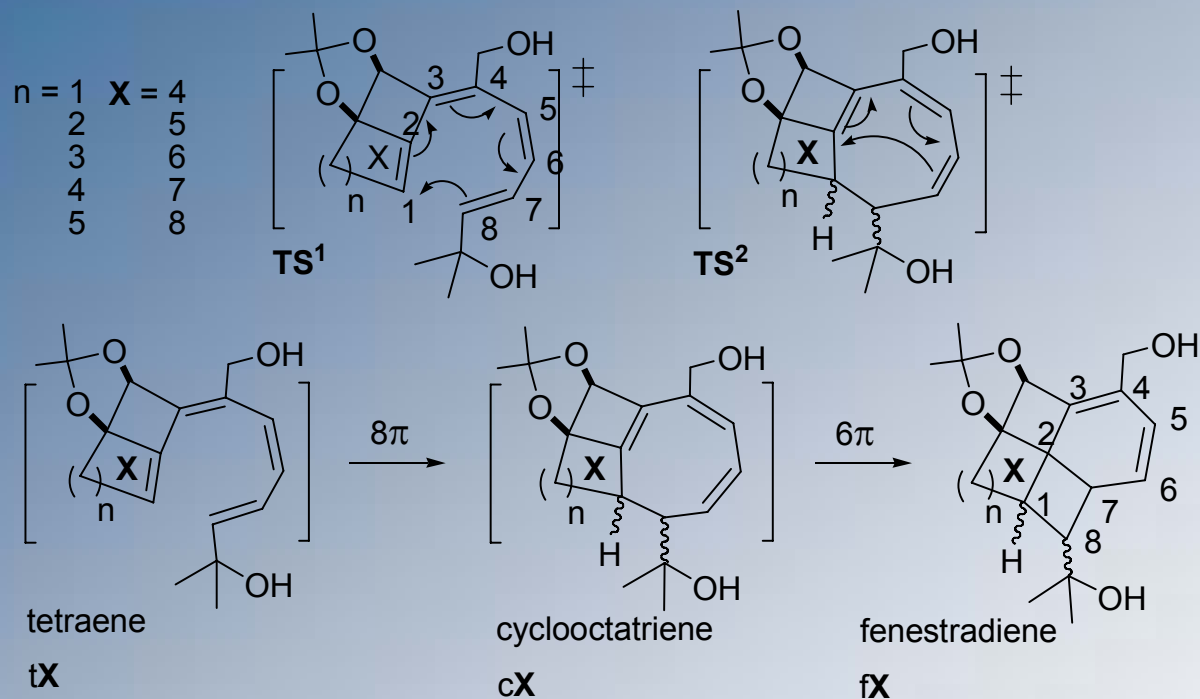
# Introduction



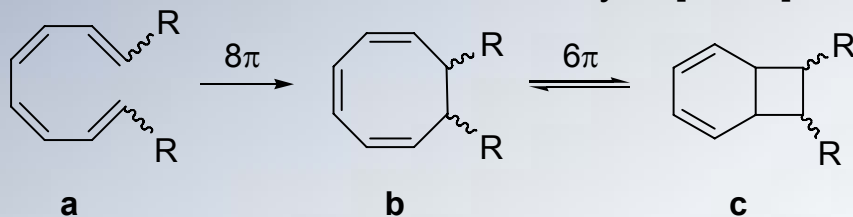
I. Salem, B.; Suffert, J. *Angew. Chem. Int. Ed.* **2004**, 43, 2826–2830.

**Ila.** Hulot, C.; Blond, G.; Suffert, J. *J. Am. Chem. Soc.* **2008**, *130*, 5046–5047.

# Introduction



Conversion of 1,3,5,7-tetraenes to bicyclo[4.2.0]octadienes



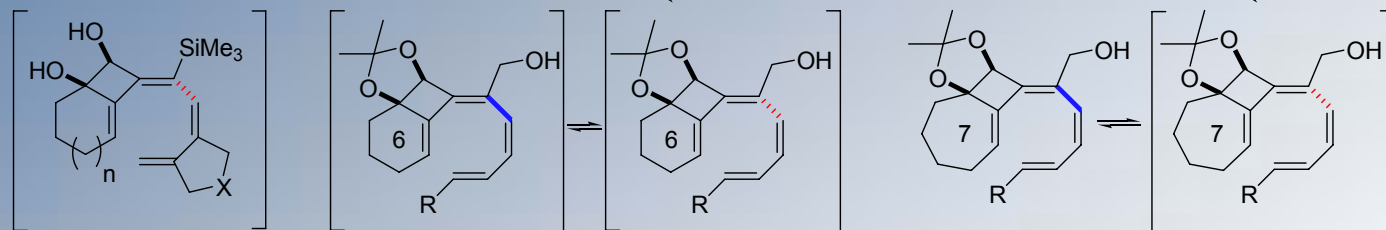
R = terminal substituents

# Introduction

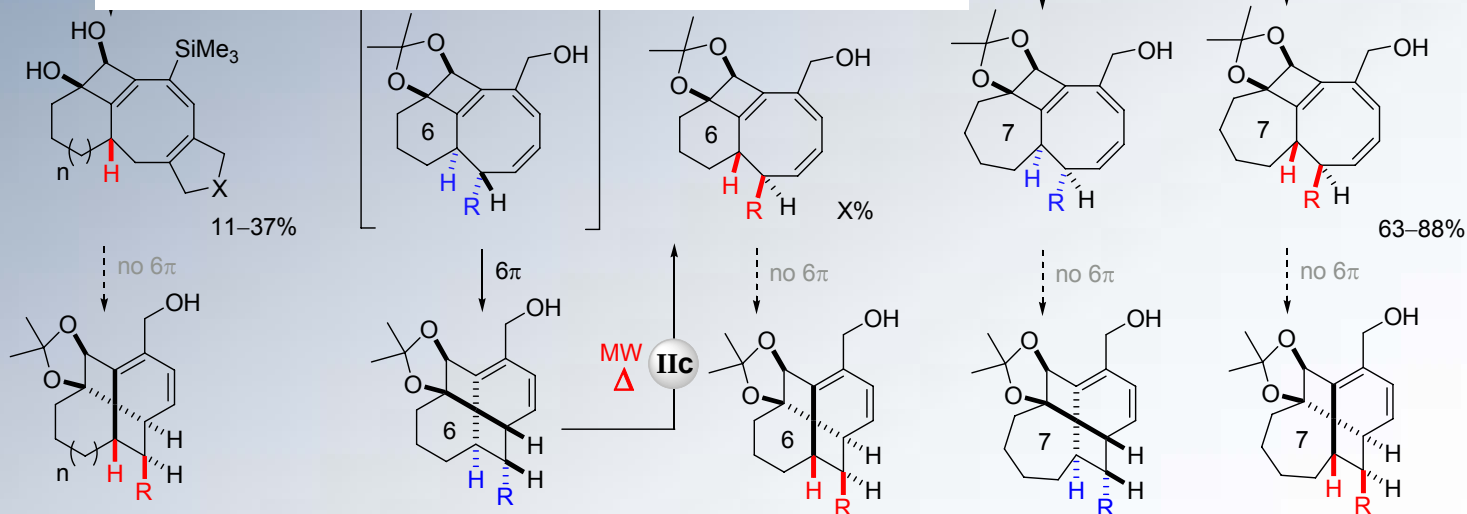
Questions:



## 1. Different stereochemistries observed in the reactions



## 2. Fenestradienes or Cyclooctatrienes?



I. Salem, B.; Suffert, J. *Angew. Chem. Int. Ed.* **2004**, 43, 2826–2830.

IIa. Hulot, C.; Blond, G.; Suffert, J. *J. Am. Chem. Soc.* **2008**, 130, 5046–5047.

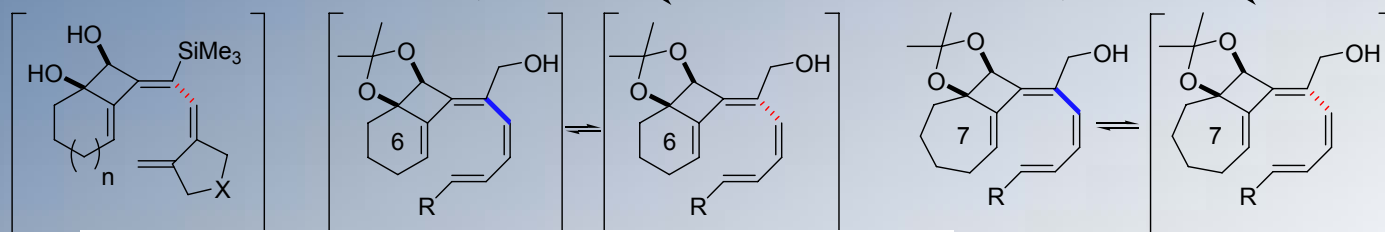
# Introduction

Questions:

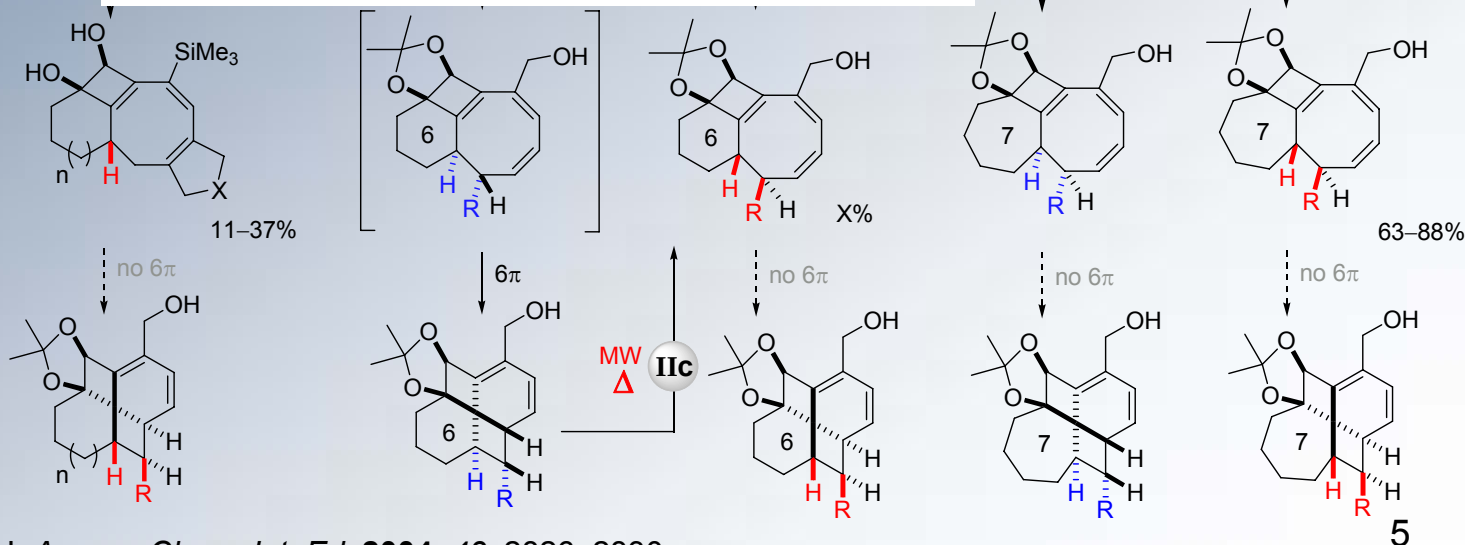


Here, the main effects are steric!

## 1. Different stereochemistries observed in the reactions



## 2. Fenestradienes or Cyclooctatrienes?



I. Salem, B.; Suffert, J. *Angew. Chem. Int. Ed.* **2004**, 43, 2826–2830.

IIa. Hulot, C.; Blond, G.; Suffert, J. *J. Am. Chem. Soc.* **2008**, 130, 5046–5047.

# Content

## 1. Different stereochemistries observed in the reactions

### Stereochemistries in Electrocyclic Reactions of polyenes

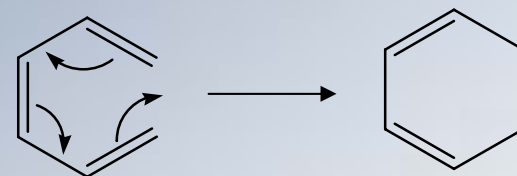
- Woodward-Hoffmann Rules
  - Conrotatory or disrotatory
- Torquoelectronic Theory
  - Ring opening of 3-substituted cyclobutenes (first studies)
  - Lone-pair conjugated in electrocyclic reactions
  - Ring closure of octatetraenes

## 2. Fenestradienes or Cyclooctatrienes?

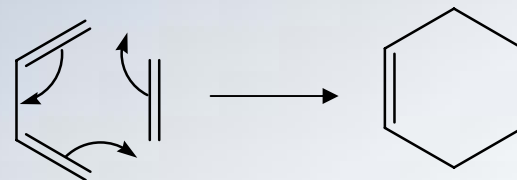
- Potential energy hypersurfaces
- Assessment of the aromaticities of the transition structures
  - (by using structural and magnetic criteria)
- Frontier molecular orbital analyses of the torquoselectivities
- Conformational interconversions of the olefinic ring moieties

## Pericyclic Reactions of Conjugated $\pi$ Systems:

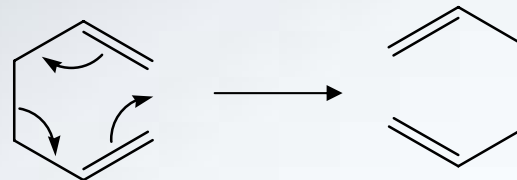
- Electrocyclic Reactions ( $\pi$  to  $\sigma$ )



- Cycloaddition Reactions ( $2\pi$  to  $2\sigma$ )



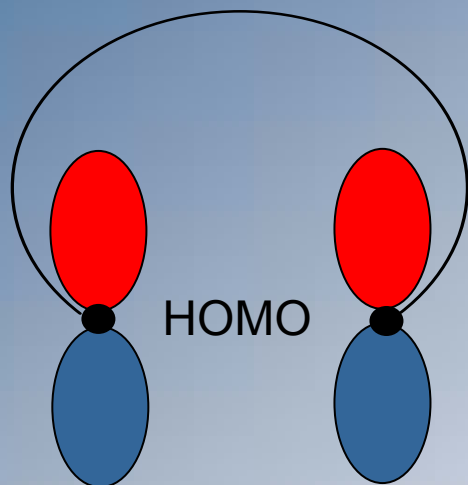
- Sigmatropic Reactions (no net change)



# Stereochemistries in Electrocyclic Reactions of polyenes

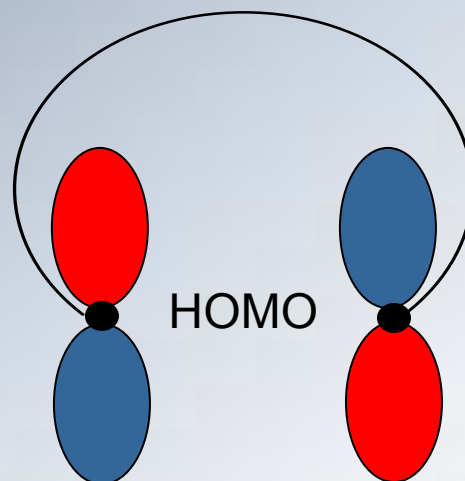
## FMO Theory

to explain stereochemistries in electrocyclic reactions



Like lobes on the same side  
 $(4n+2)\pi\bar{e}$

or



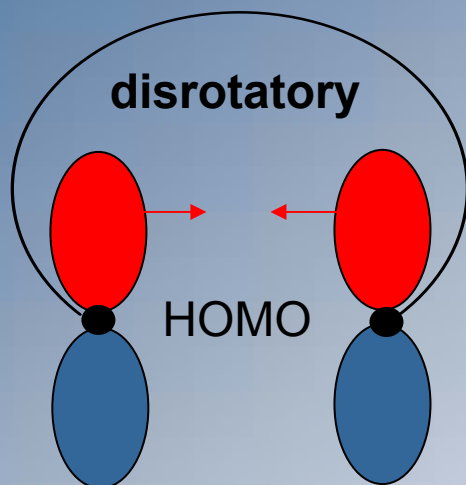
Like lobes on the opposite side  
 $(4n)\pi\bar{e}$

# Stereochemistries in Electrocyclic Reactions of polyenes

## FMO Theory

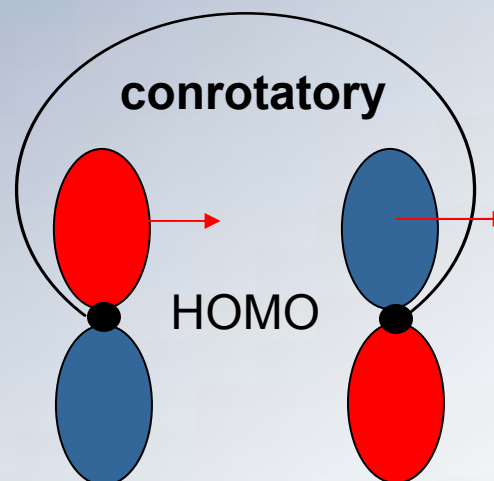
to explain stereochemistries in electrocyclic reactions

For a bond to form,  
the outermost  $\pi$  lobes must rotate so that favorable bonding interaction is achieved



Like lobes on the same side  
 $(4n+2)\pi\bar{e}$

or



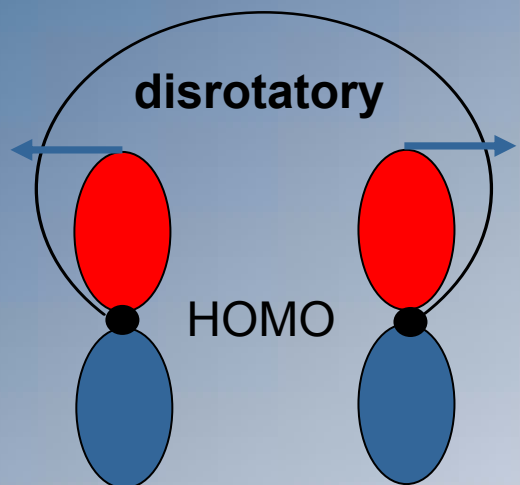
Like lobes on the opposite side  
 $(4n)\pi\bar{e}$

# Stereochemistries in Electrocyclic Reactions of polyenes

## FMO Theory

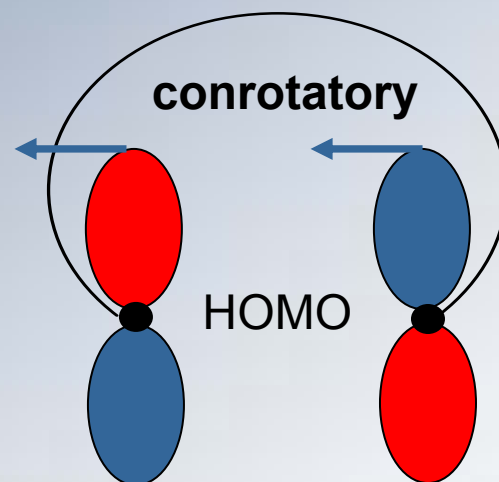
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For a bond to form,  
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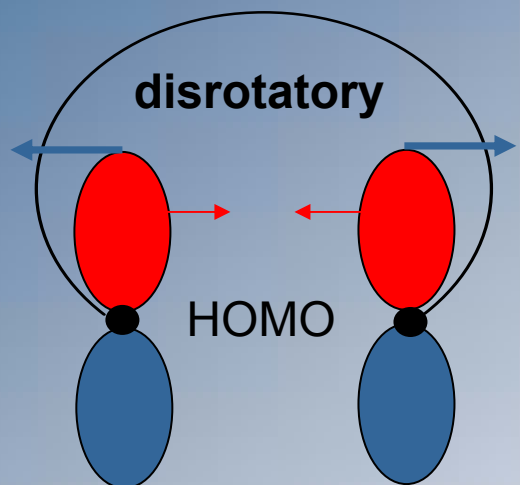
Like lobes on the opposite side  
 $(4n)\pi\bar{e}$

# Stereochemistries in Electrocyclic Reactions of polyenes

## FMO Theory

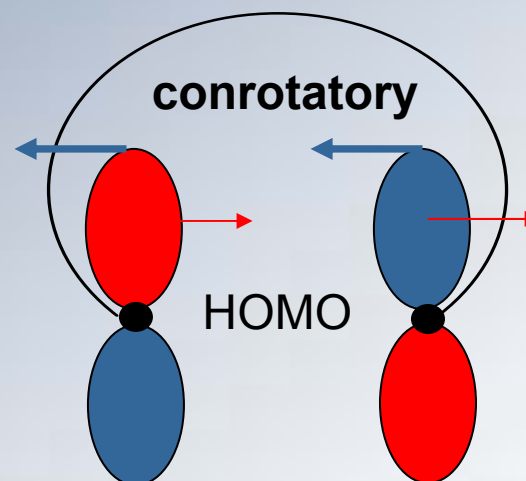
to explain stereochemistries in electrocyclic reactions

For a bond to form,  
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Like lobes on the same side  
 $(4n+2)\pi\bar{e}$

or

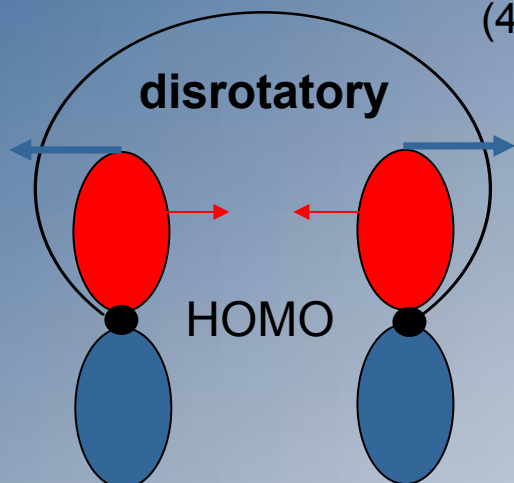


Like lobes on the opposite side  
 $(4n)\pi\bar{e}$

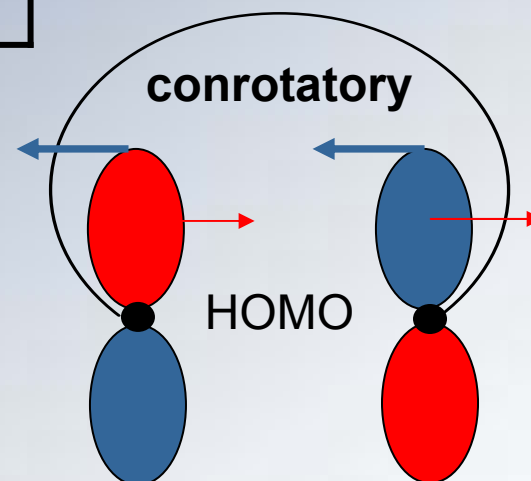
# Woodward-Hoffmann Rules for Electrocyclic Reactions (1965):

thermal                  photochemical

|                    |             |             |
|--------------------|-------------|-------------|
| $(4n+2)\pi\bar{e}$ | disrotatory | conrotatory |
| $(4n)\pi\bar{e}$   | conrotatory | disrotatory |

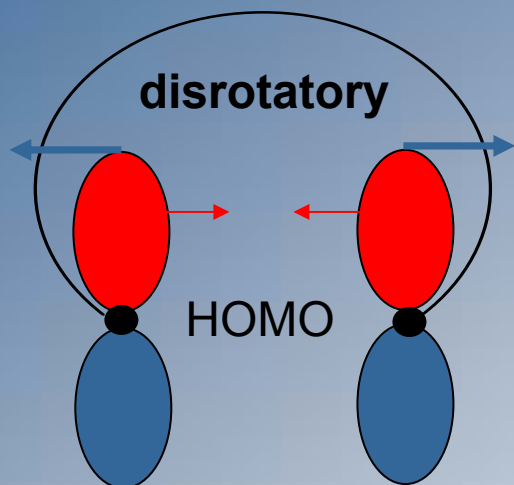


$(4n+2)\pi\bar{e}$



$(4n)\pi\bar{e}$

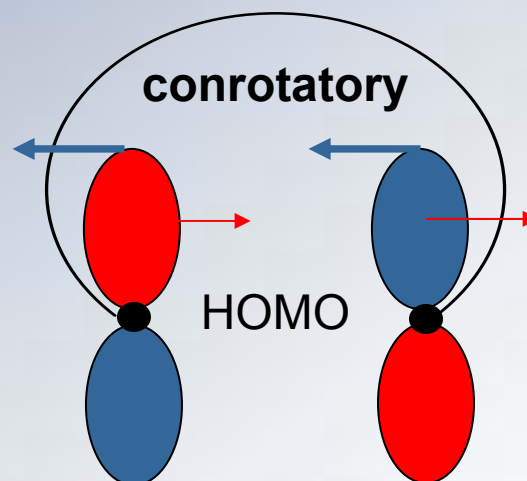
## Torquoselectivity (1996)!



$(4n+2)\pi\bar{e}$

The preference for '*inward*' or '*outward*' rotation of substituents in conrotatory or disrotatory electrocyclic ring opening reactions.

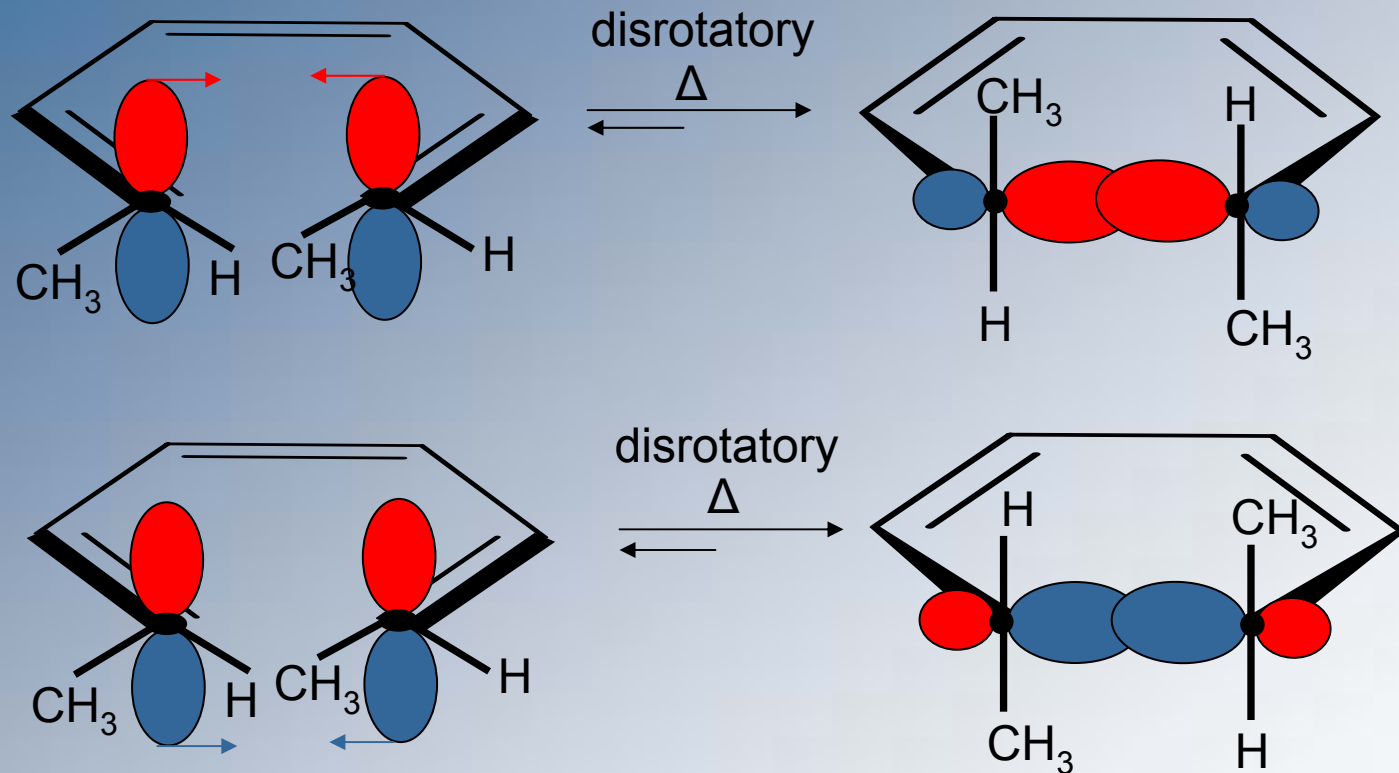
IUPAC 1997



$(4n)\pi\bar{e}$

Nicht nur in ring closure, sondern auch in ring opening!

## Different **Torquoselectivities** in Ring Closure of Conjugated Trienes:

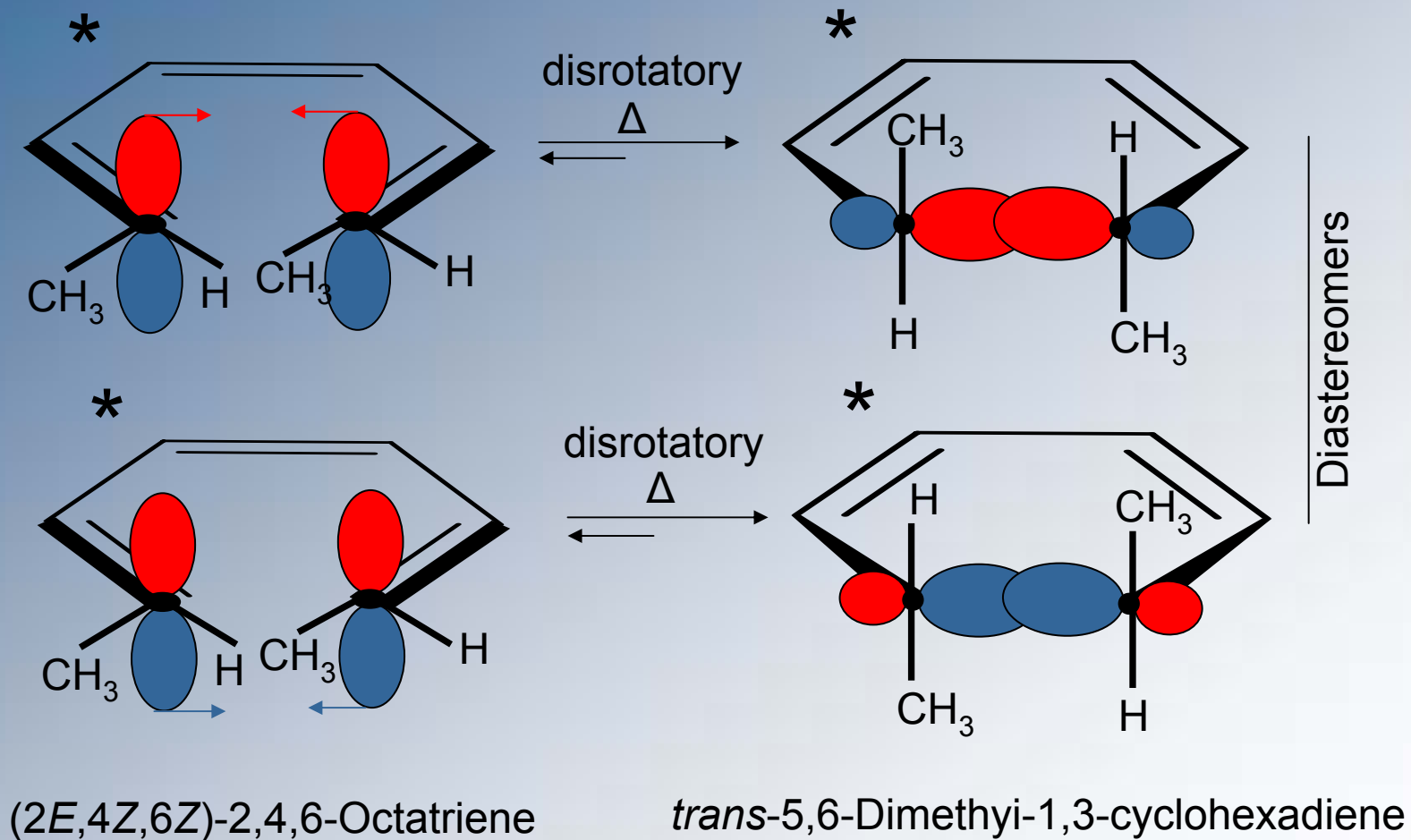


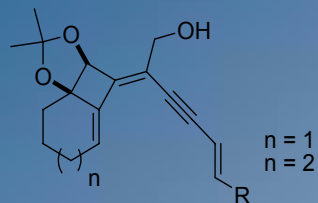
(2*E*,4*Z*,6*Z*)-2,4,6-Octatriene

*trans*-5,6-Dimethyl-1,3-cyclohexadiene

$$\Delta H^\circ = -14.7 \text{ kcal mol}^{-1}$$

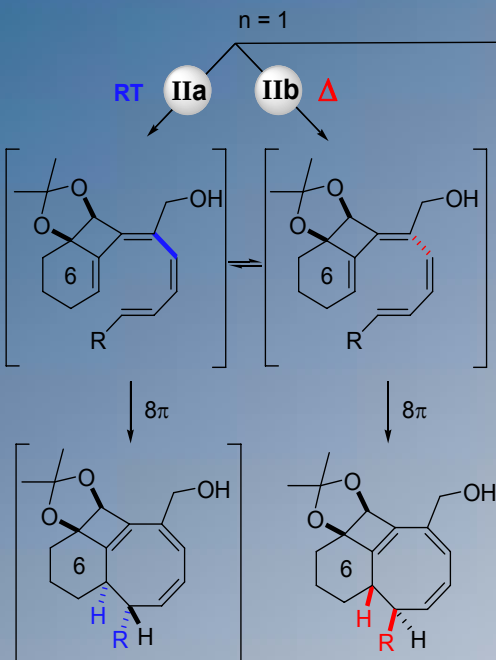
## Different **Torquoselectivities** in Ring Closure of Conjugated Trienes:



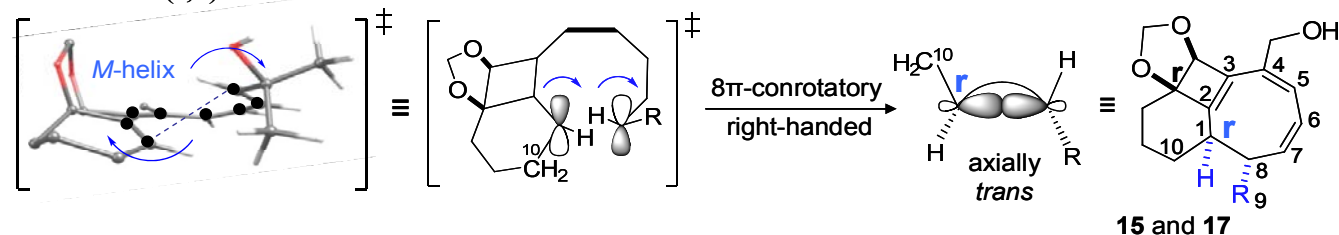


$\text{Ni}(\text{OAc})_2 \cdot 4 \text{H}_2\text{O}$   
 $\text{NaBH}_4$ , eda, EtOH  
 $\text{H}_2$ , 18 h

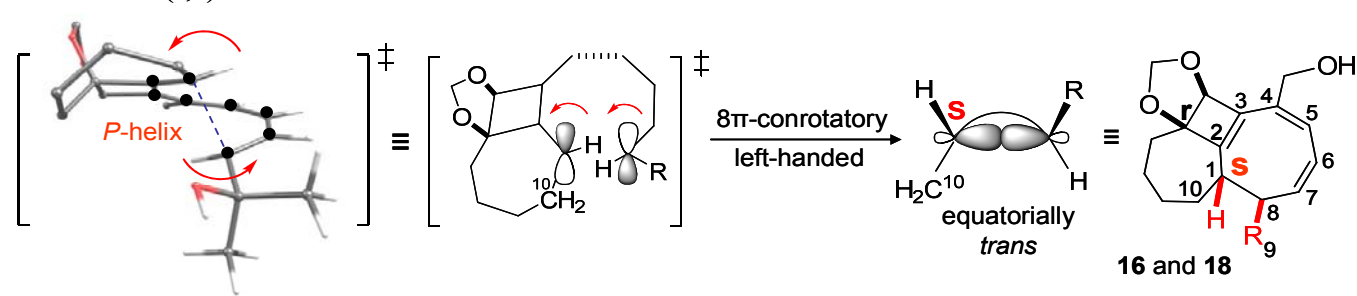
## Torquoselectivities in Investigated Electrocyclic Cascade Reactions

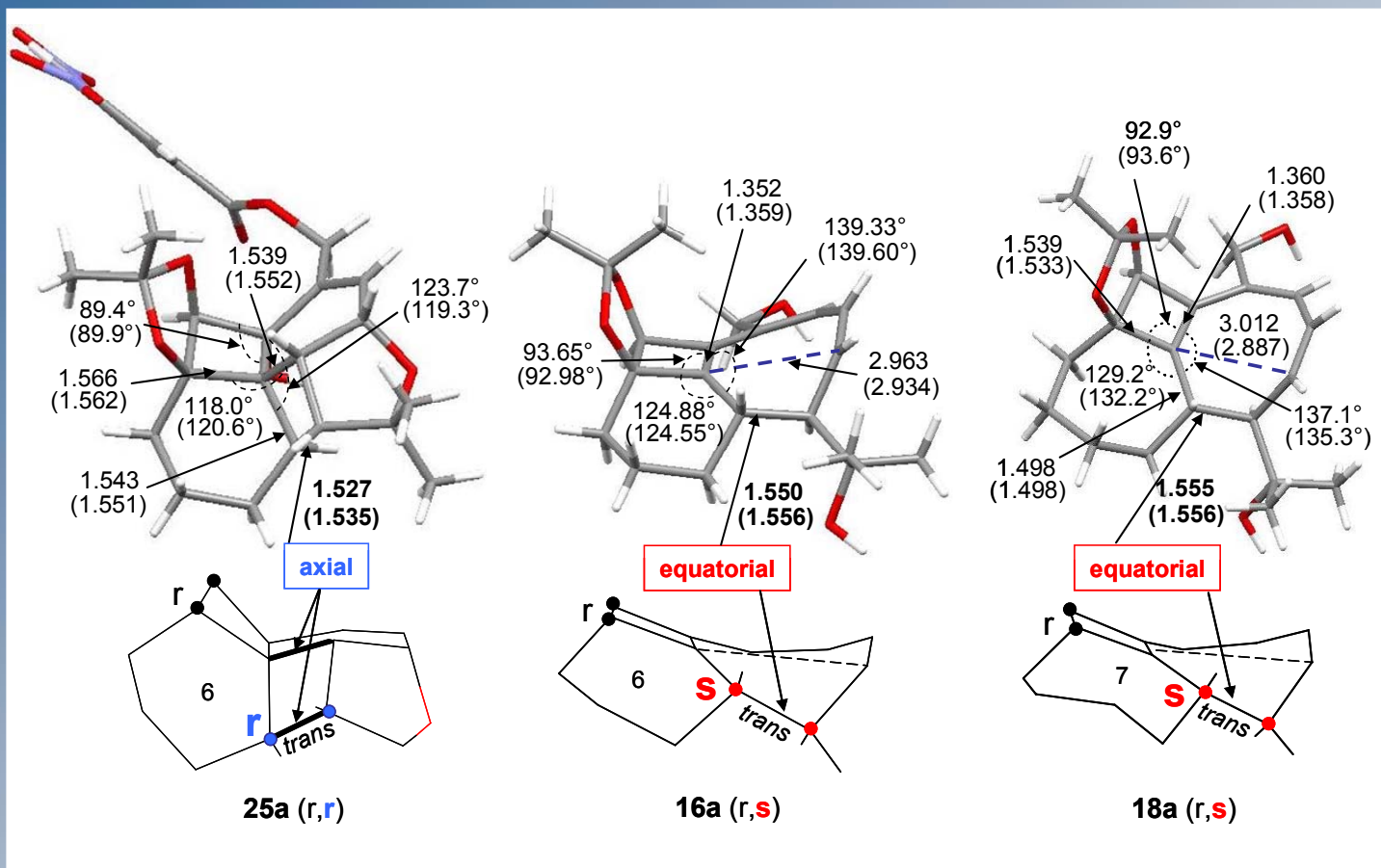


**IIa and IIc: (r,r)**



**IIb and IIe: (r,s)**



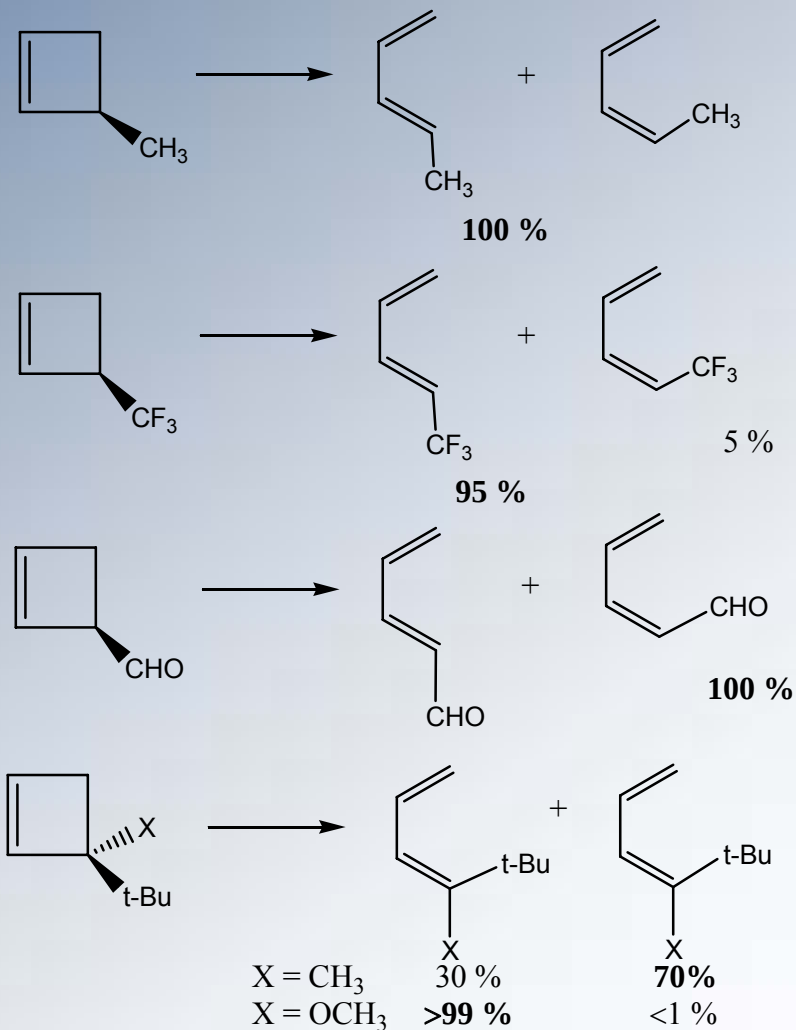


X-ray structural analyses of the nitrobenzoate derivate of fenestrene **25a** and cyclooctatrienes **16a** and **18a**. Selected B3PW91/6-31G(d,p) computed parameters in parentheses; bond lengths in Å. The simplified X-ray structures beneath show the different stereochemistries for the new single bonds formed by the  $8\pi$ -conrotatory ring closures. The relative configurations of the stereogenic centers are shown by (r,r) and (r,s) symbols.

## Torquoselectivity!

1. Conrotatory opening of cyclobutenes have been extensively investigated, leading to a novel theory that nicely illustrates some qualitative MO reasoning.

- EWGs prefer to occupy the *inward* position
- ERGs prefer to occupy the *outward* position

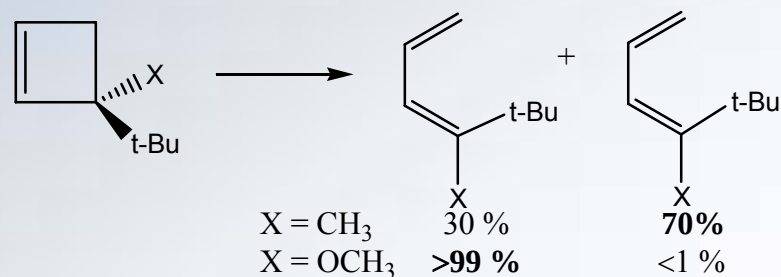
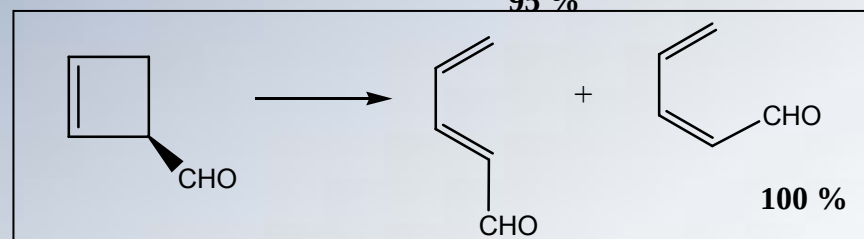
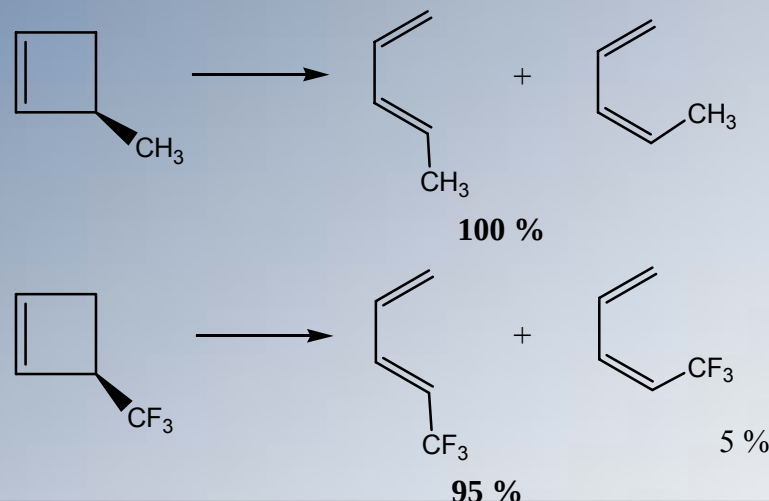


(a) Dolbier, W. R., Jr.; Koroniak, H.; Burton, D. J.; Bailey, A. R.; Shaw, G. S.; Hansen, S. W. *J. Am. Chem. Soc.* **1984**, *106*, 1871-1872. (b) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989-7991. (c) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099-2111.

## Torquoselectivity!

1. Conrotatory opening of cyclobutenes have been extensively investigated, leading to a novel theory that nicely illustrates some qualitative MO reasoning.

more reactive than parent hydrocarbon!

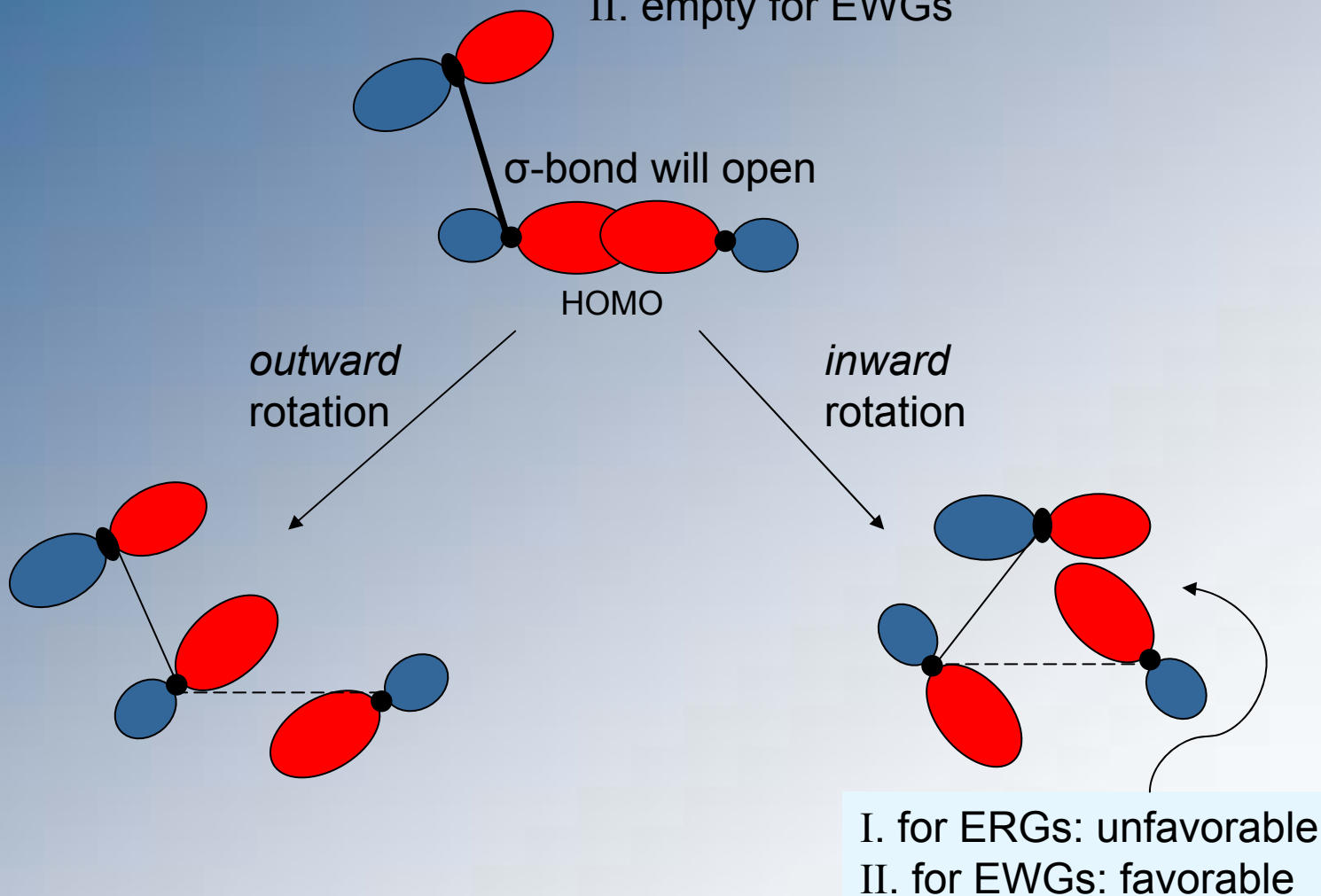


(a) Dolbier, W. R., Jr.; Koroniak, H.; Burton, D. J.; Bailey, A. R.; Shaw, G. S.; Hansen, S. W. *J. Am. Chem. Soc.* **1984**, *106*, 1871-1872. (b) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989-7991. (c) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099-2111.

## Stereochemistries in Electrocyclic Reactions of polyenes

FMO interactions in the transition states:

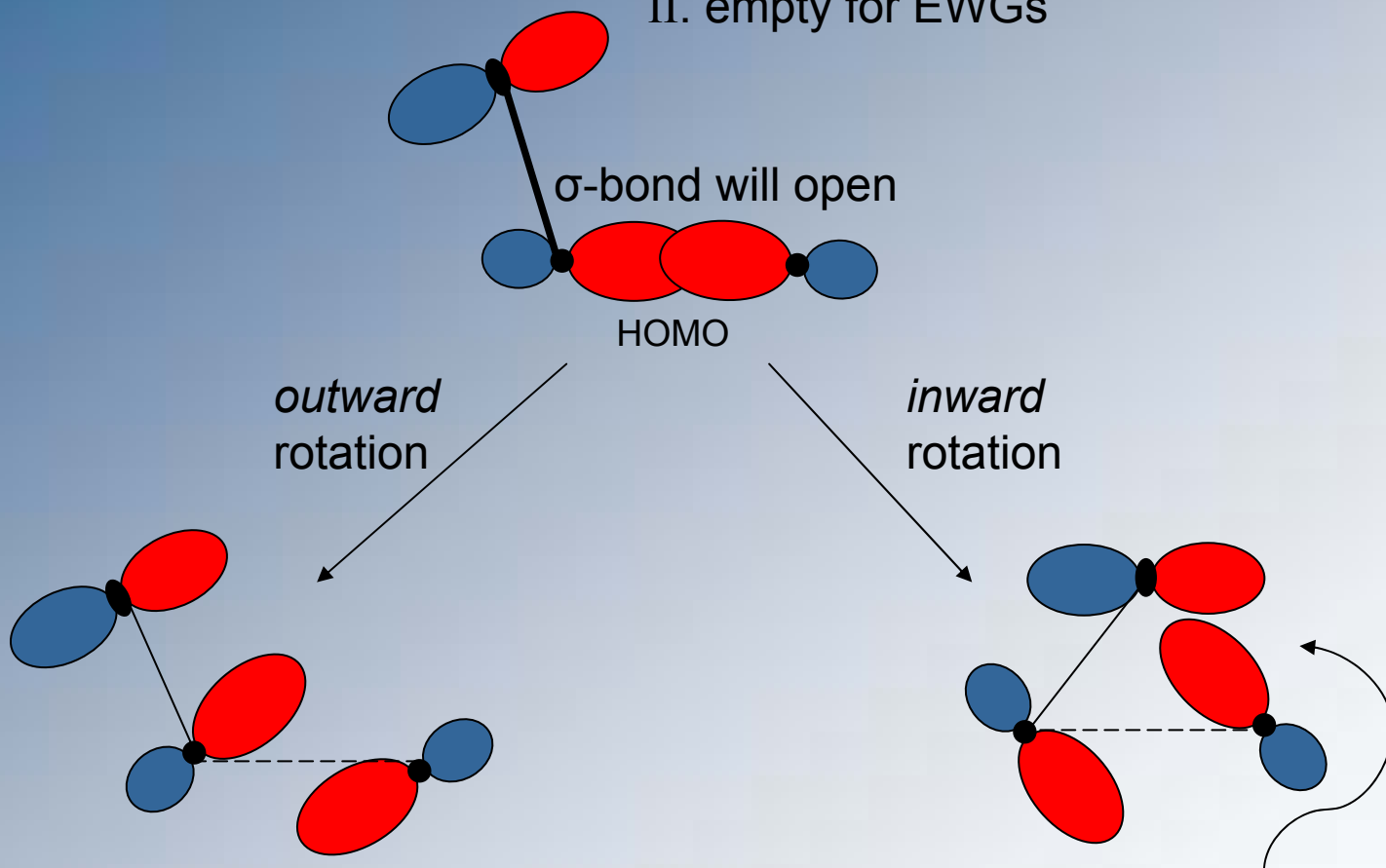
substituent orbital: I. filled for ERGs  
II. empty for EWGs



## Stereochemistries in Electrocyclic Reactions of polyenes

FMO interactions in the transition states:

substituent orbital: I. filled for ERGs  
II. empty for EWGs



- ERGs prefer to occupy the *outward* position
- EWGs prefer to occupy the *inward* position

I. for ERGs: unfavorable  
II. for EWGs: favorable

Torquoselectivity first described in the ring openings of 3-substituted cyclobutenes, further it has been examined in systems with

2. heterosubstitution (conjugated lone-pair),
3. differing ring sizes,
4. charges,
5. cumulated  $\pi$  bonds in the  $\pi$ -system.

(a) Evanseck, J. D.; Thomas, B. E., IV; Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1995**, *60*, 7134-7141. (b) Thomas, B. E., IV; Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 4165. (c) Cossi'o, F. P.; Arrieta, A.; Lecea, B.; Ugalde, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 2085. (d) Kallel, E. A.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 6006. (e) Niwayama, S.; Kallel, E. A.; Sheu, C.; Houk, K. N. *J. Org. Chem.* **1996**, *61*, 2517. (f) Lo'pez, S.; Rodr'iguez, J.; Rey, J. G.; de Lera, A. R. *J. Am. Chem. Soc.* **1996**, *118*, 1881. (g) Luo, L.; Bartberger, M. D.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 12366. (h) Iglesias, B.; de Lera, A. R.; Rodr'iguez-Otero, J.; Lo'pez, S. *Chem. Eur. J.* **2000**, *6*, 4021.

## 2. Conjugated lone-pair

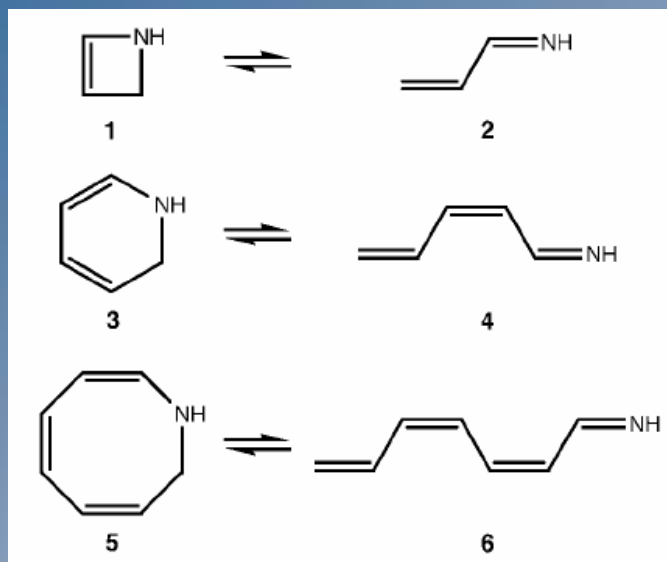
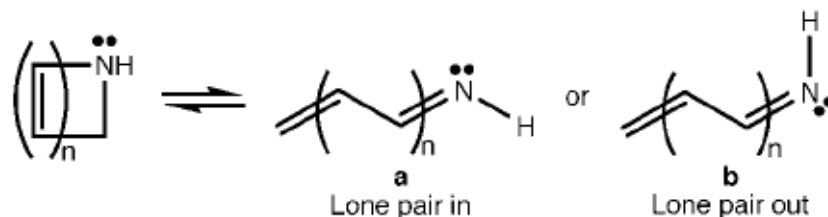
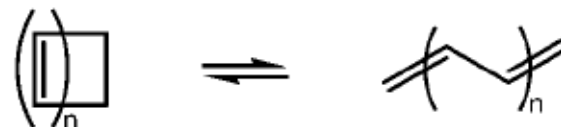


Table 1. Ring-Opening Energetics for Equations 1–3 (Energies in kcal/mol)



| product | n | lone pair | $\Delta E^\ddagger$ | $\Delta E$ |
|---------|---|-----------|---------------------|------------|
| 2a      | 1 | in        | +26.4               | −23.5      |
| 2b      | 1 | out       | +35.0               | −23.0      |
| 4a      | 2 | in        | +27.7               | +7.1       |
| 4b      | 2 | out       | +44.7               | +7.3       |
| 6a      | 3 | in        | +19.4               | +0.4       |
| 6b      | 3 | out       | +20.0               | +0.7       |

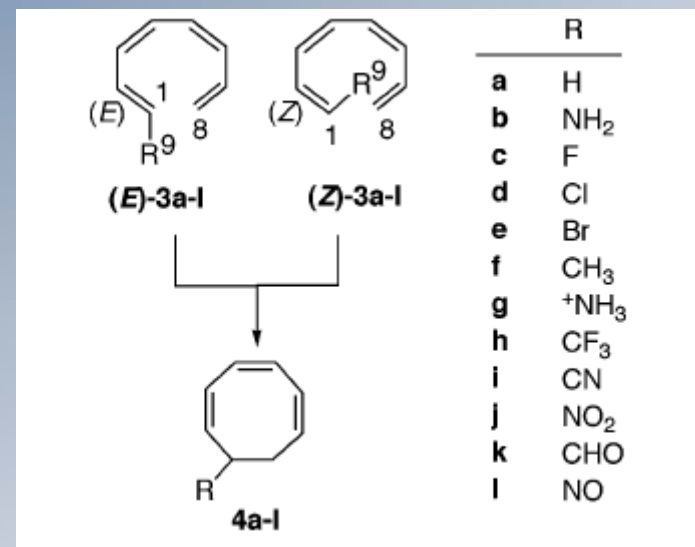
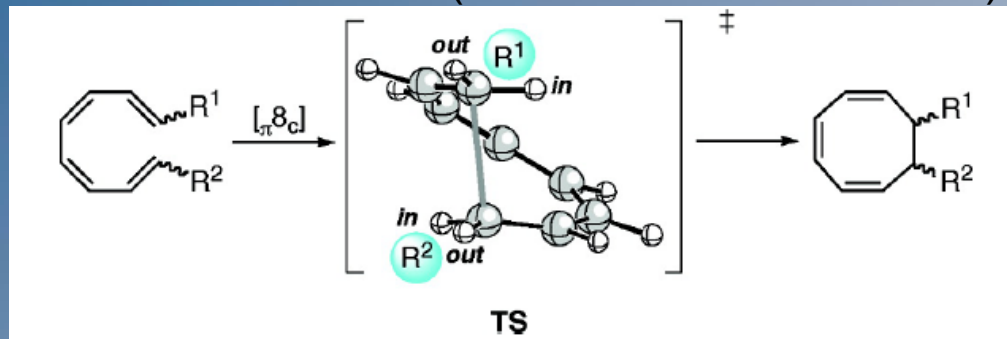
Table 2. Ring-Opening Energetics for the Hydrocarbon Parent Reactions of Equations 1–3 (Energies in kcal/mol)



| n | $\Delta E^\ddagger$ | $\Delta E$ | ref |
|---|---------------------|------------|-----|
| 1 | +29.6               | −15.1      | 16  |
| 2 | +42.9               | +12.6      | 31  |
| 3 | +16.5               | +0.9       | 16  |

## 3. Different ring sizes:

$$\Delta E^\ddagger = +8 \text{ kcal mol}^{-1} \text{ (MP2/6-31G}^*//\text{HF/6-31G}^*)^b$$



1. The  $8\pi$ -electron conrotatory electrocyclization via **Möbius** aromatic transition structure of helical conformation.
2. In general, transition structures having **outward** substituents are preferred with respect to the inward transition structures, irrespective of the  $\pi$ -donor or  $\pi$ -acceptor character of the substituent.
3. In contrast with  $4\pi$ -electron conrotatory electrocyclic reactions, torquoelectronic effects are not relevant, the stereochemical outcome being the result of **secondary orbital interactions**, **electrostatic interactions**, and **steric effects**.

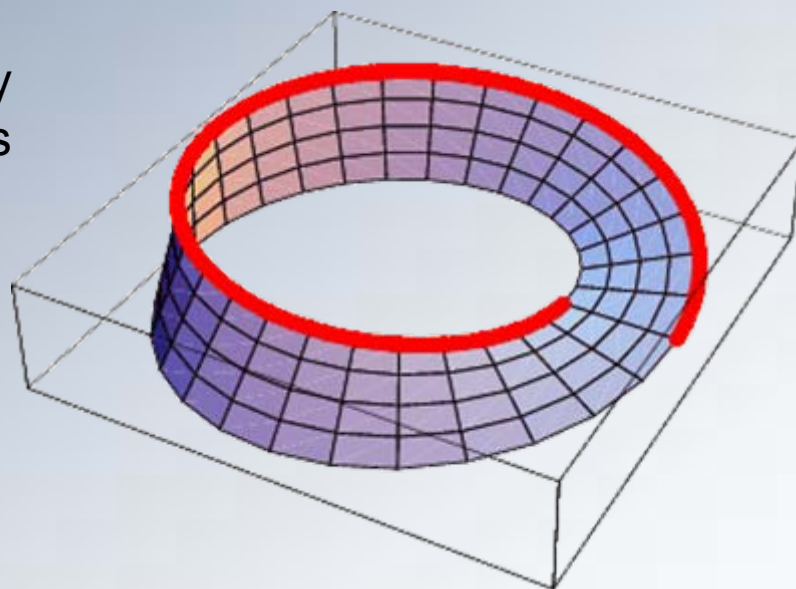
(a) Lecea, B.; Arrieta, A.; Cosso, F. P. *J. Org. Chem.* **2005**, 70, 1035.

(b) Thomas, B. E.; IV; Evanseck, J. D.; Houk, K. N. *J. Am. Chem. Soc.* **1993**, 115, 4165.

### Möbius strip

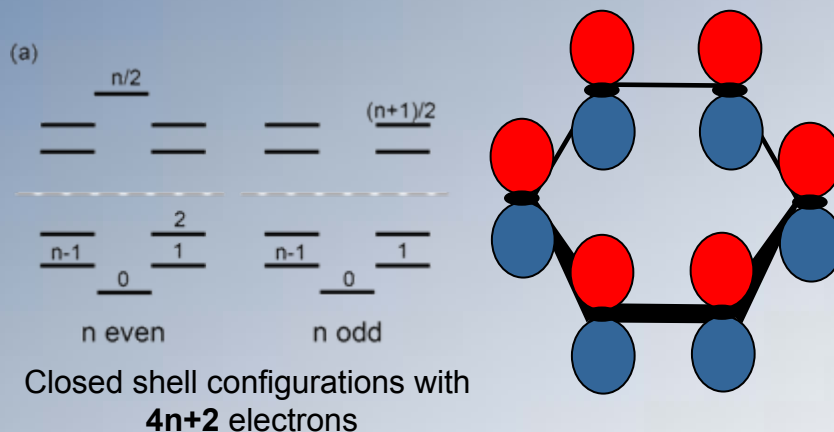
The ***Möbius strip*** (twisted cylinder) is a ***one-sided nonorientable surface***.

It was invented by Möbius in 1858, although it was discovered independently by Listing, who published it, while Möbius did not. Like the cylinder, it is not a true surface, but rather a surface with boundary.

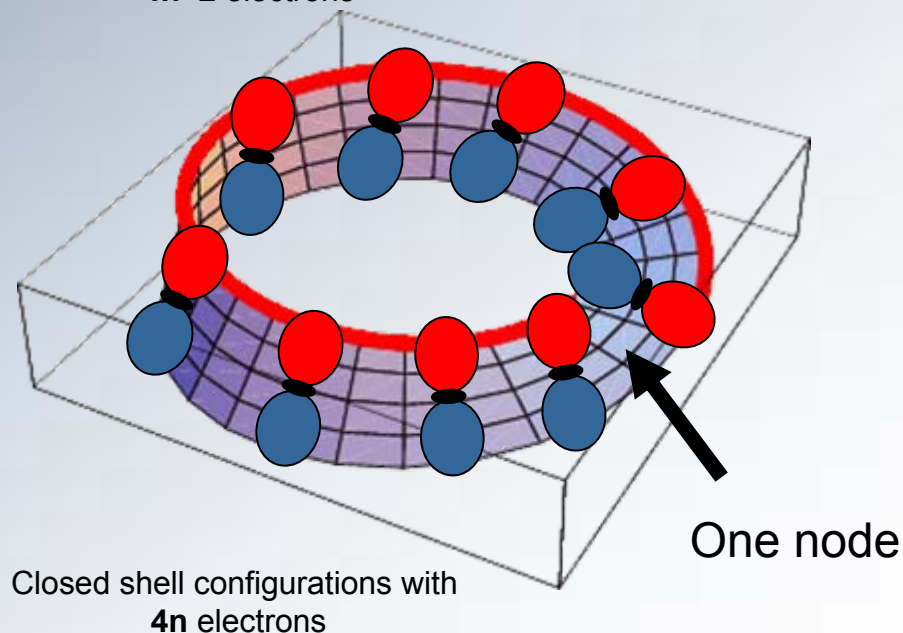
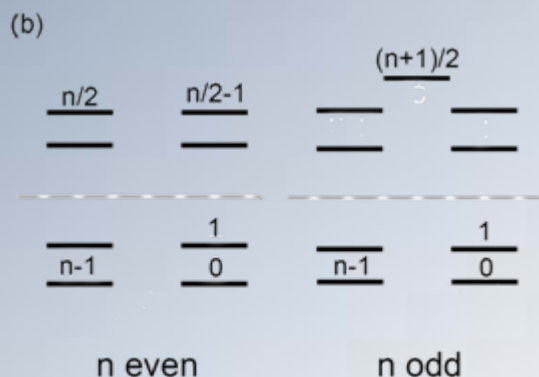


## Möbius aromaticity (E. Heilbronner, 1964)

- a) The  $\pi$ -system of benzene (Huckel system: coplanar, aromatic with  $4n+2$   $\pi$ -electrons).

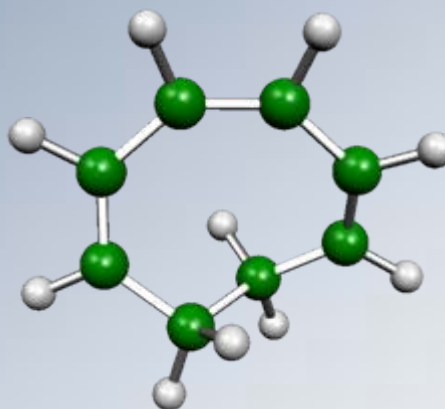
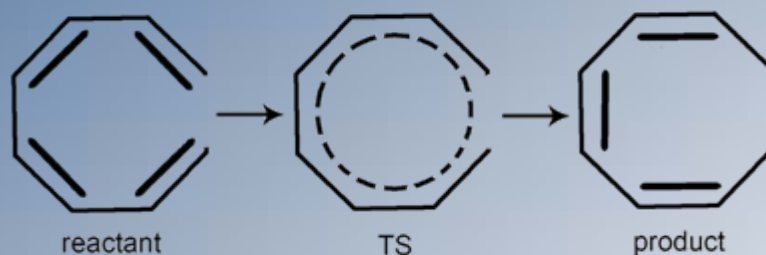


- b) The higher members of annulenes might adopt Möbius geometries without any apparent strain ( $\pi$ -system has Möbius topology; aromatic with  $4n$  electrons).

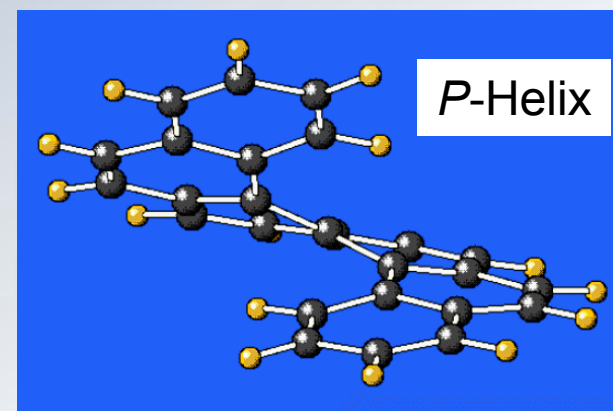
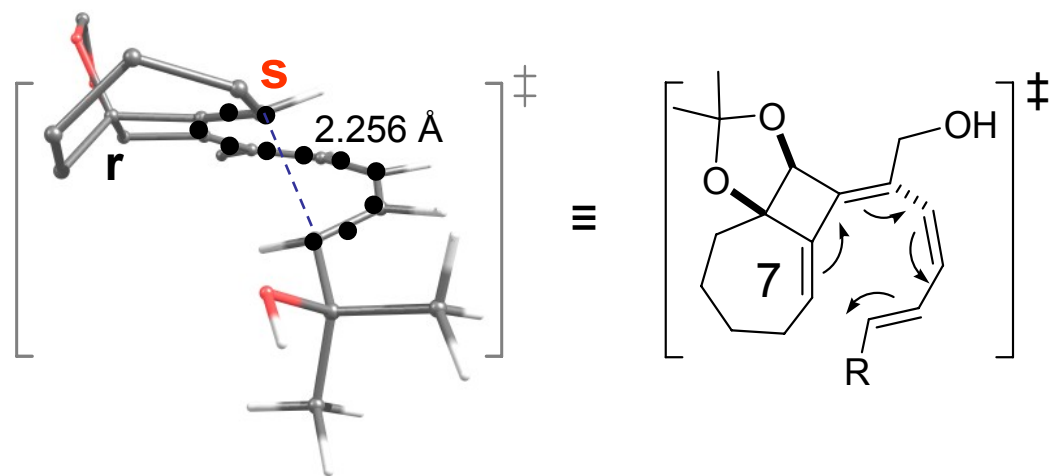
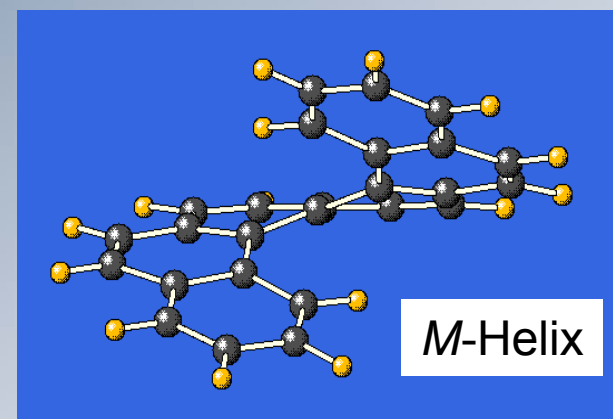
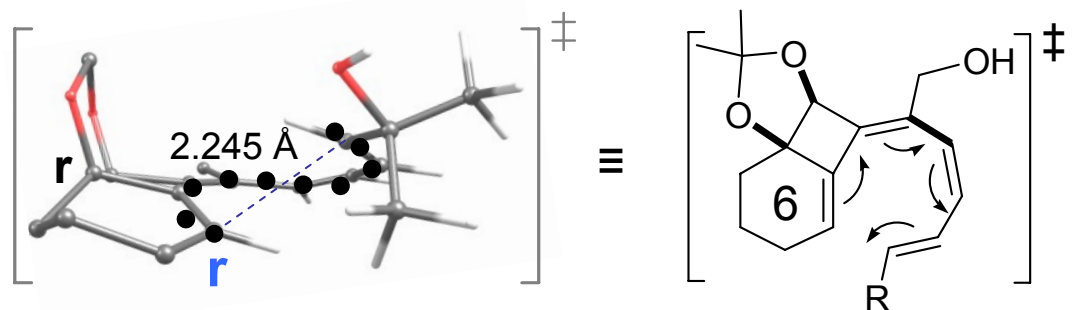


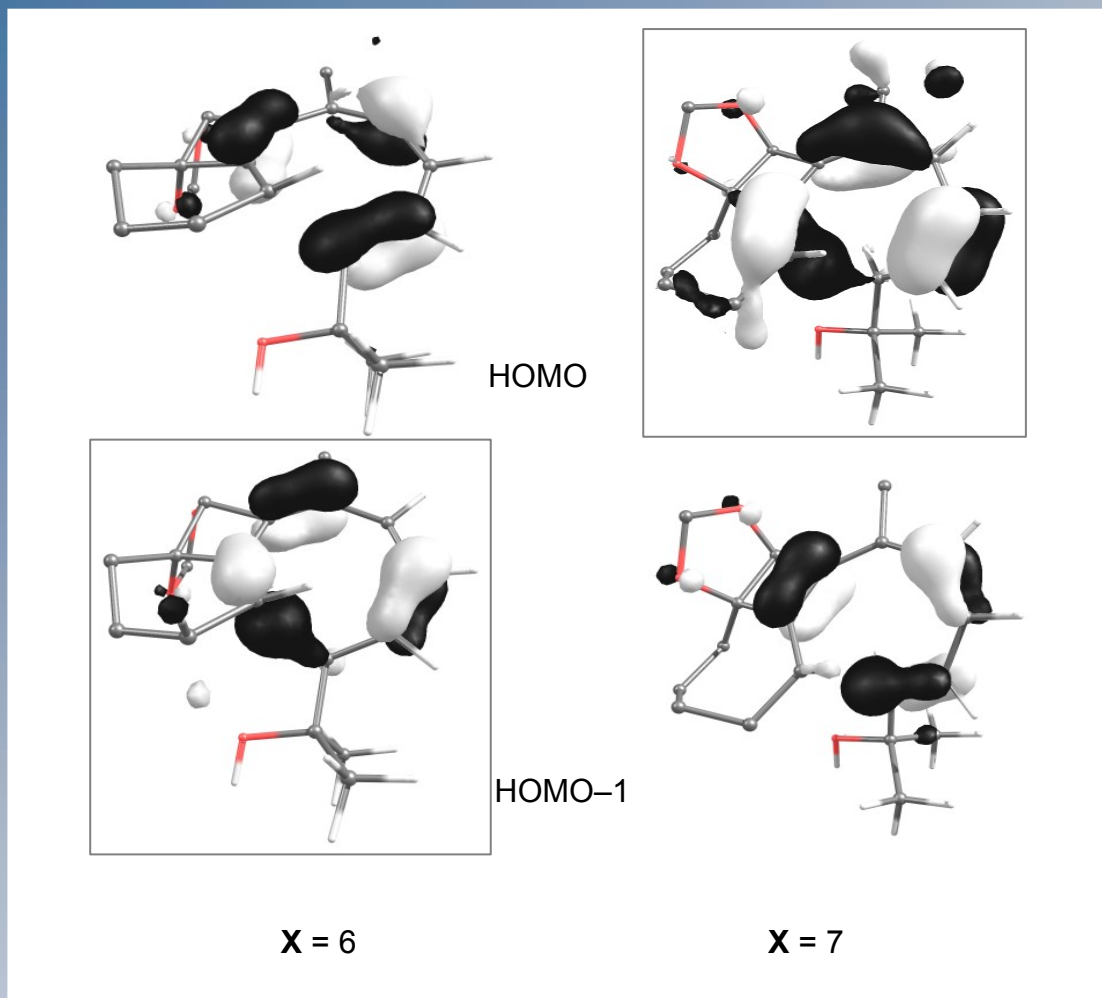
Can Heilbronner's original suggestion be realized in any stable molecule?

Conversion of (Z,Z)-octa-1,3,5,7-tetraen into (Z,Z,Z)-cycloocta-1,3,5-triene



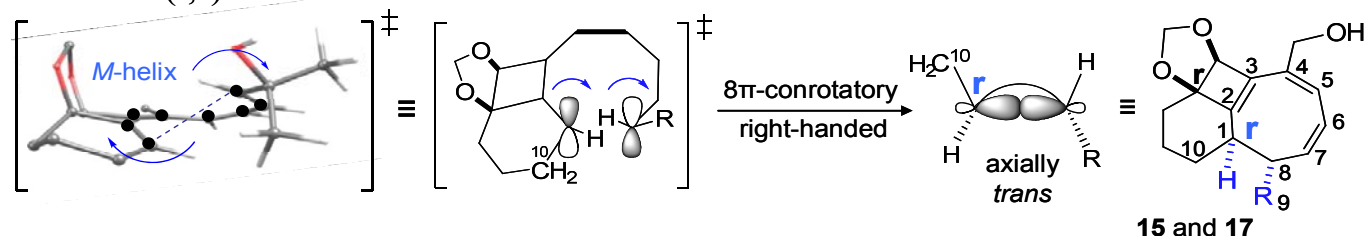
The aromaticity of the TS for the 8-electron conrotatory electrocyclic process involving only carbon centers was analyzed by *Schleyer et. al.* (1994)



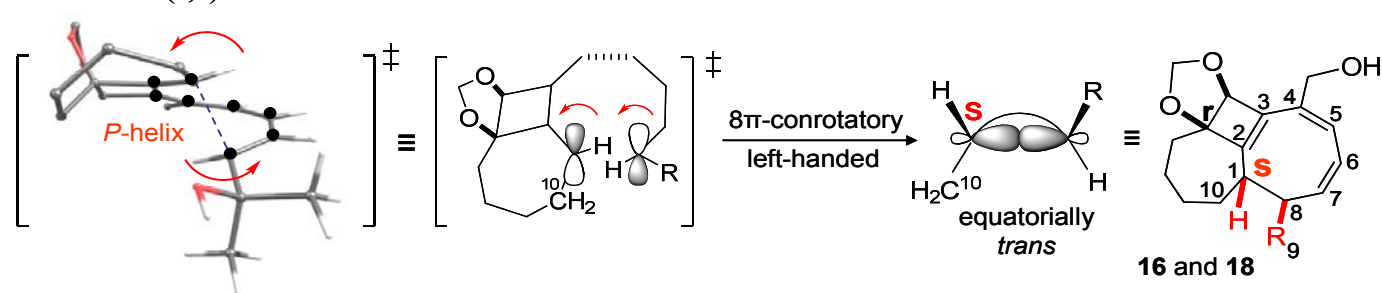


B3PW91/6-31G(d,p) Contour plots for the bonding molecular orbitals of the two TS<sup>1</sup> **X** = 6 and 7. The HOMO-1 and HOMO for **X** = 6 and 7, respectively, show favorable overlap for the 8 $\pi$ -conrotatory process. The contour value was chosen  $\pm 0.05$  a.u. for the HOMO (**X** = 7) and for the other orbitals it is  $\pm 0.06$  a.u. Some hydrogens have been omitted for clarity.

IIa and IIc: (r,r)



IIb and IIe: (r,s)

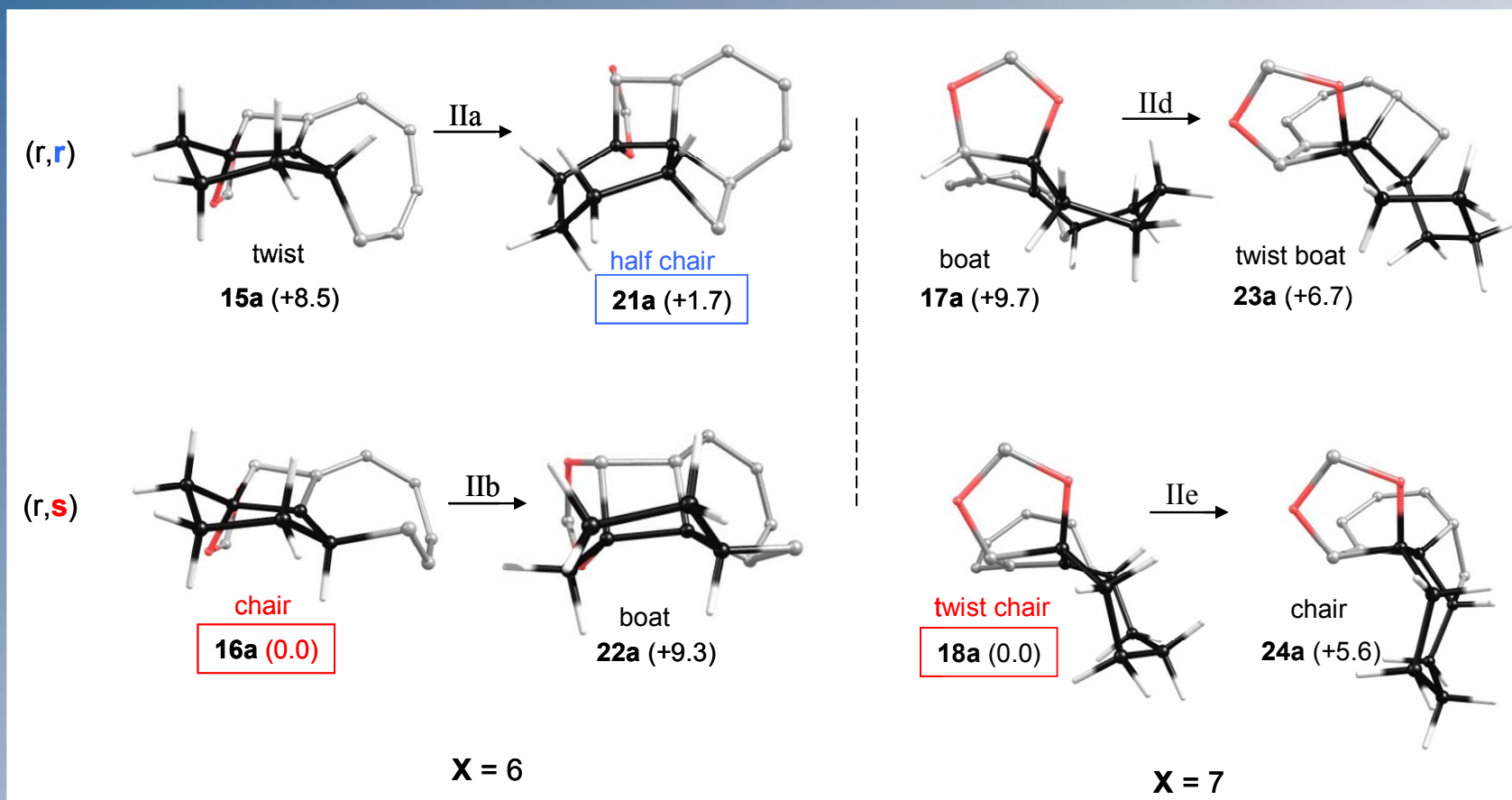


B3PW91/6-31G(d,p) Geometric analysis for TS1 with different ring sizes and B3LYP/6-311G(d,p) //B3PW91/6-31G(d,p) total NICS(0) values [ppm] in the ring center

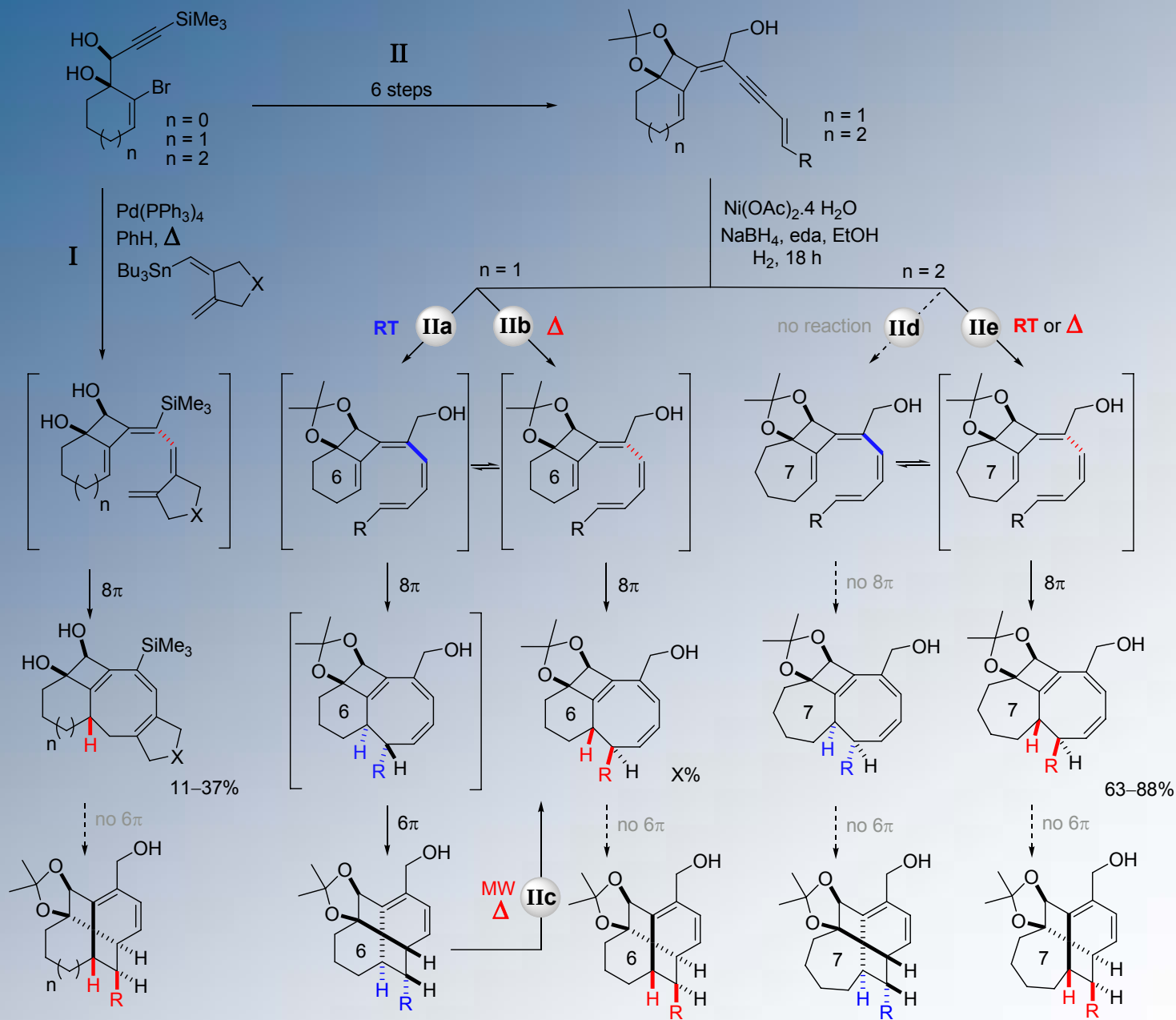
| X | $(C^1C^8)_{\text{termini}}$ | $(C^2C^3)$ | $r^{-a}$ | $\Delta r_m^b$ | $\angle (C^1C^2C^3)$ | $\phi(C^{10}C^1C^8C^9)$ | NICS(0) <sup>c</sup> |
|---|-----------------------------|------------|----------|----------------|----------------------|-------------------------|----------------------|
| 4 | 2.191                       | 1.386      | 1.399    | 0.010          | 150.1                | +60.8                   | -11.2                |
| 5 | 2.258                       | 1.395      | 1.397    | 0.009          | 149.8                | +35.7                   | -10.6                |
| 6 | 2.245                       | 1.402      | 1.398    | 0.007          | 140.2                | +9.7                    | -11.1                |
| 7 | 2.256                       | 1.403      | 1.400    | 0.004          | 135.5                | -0.4                    | -10.9                |
| 8 | 2.220                       | 1.404      | 1.401    | 0.002          | 131.4                | -14.3                   | -10.1                |

<sup>a</sup>The mean bond length for the delocalized chain including  $C^1$  to  $C^8$  [Å]. <sup>b</sup>The maximum deviation from the mean bond length [Å]; per definition the amount smaller than 0.06 Å indicates an aromatic character. <sup>c</sup>The NICS(0) for the benzene as the reference system at the same level of chemistry is -8.9 ppm.

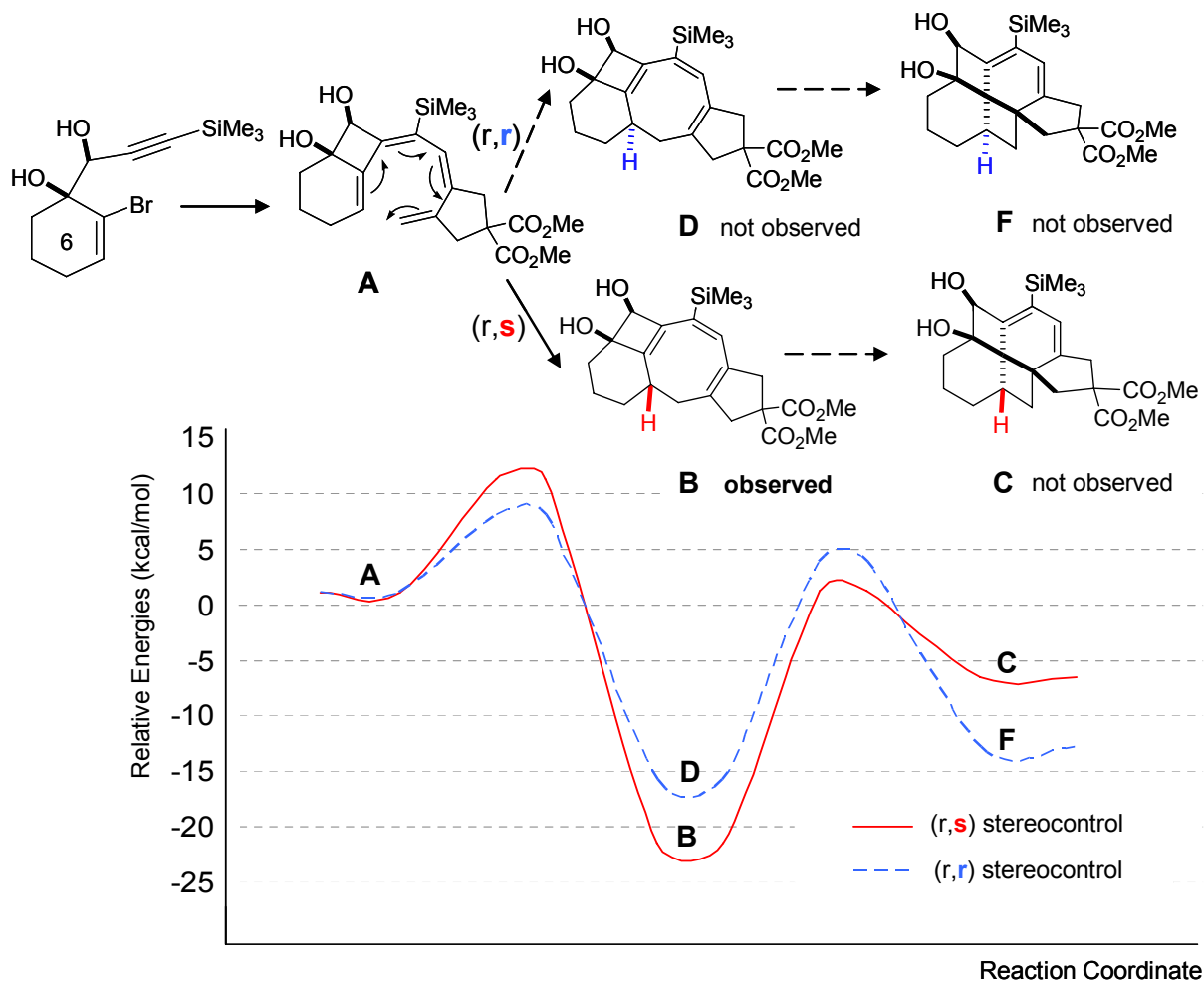
# Conformational Analyses of the Aliphatic Moieties

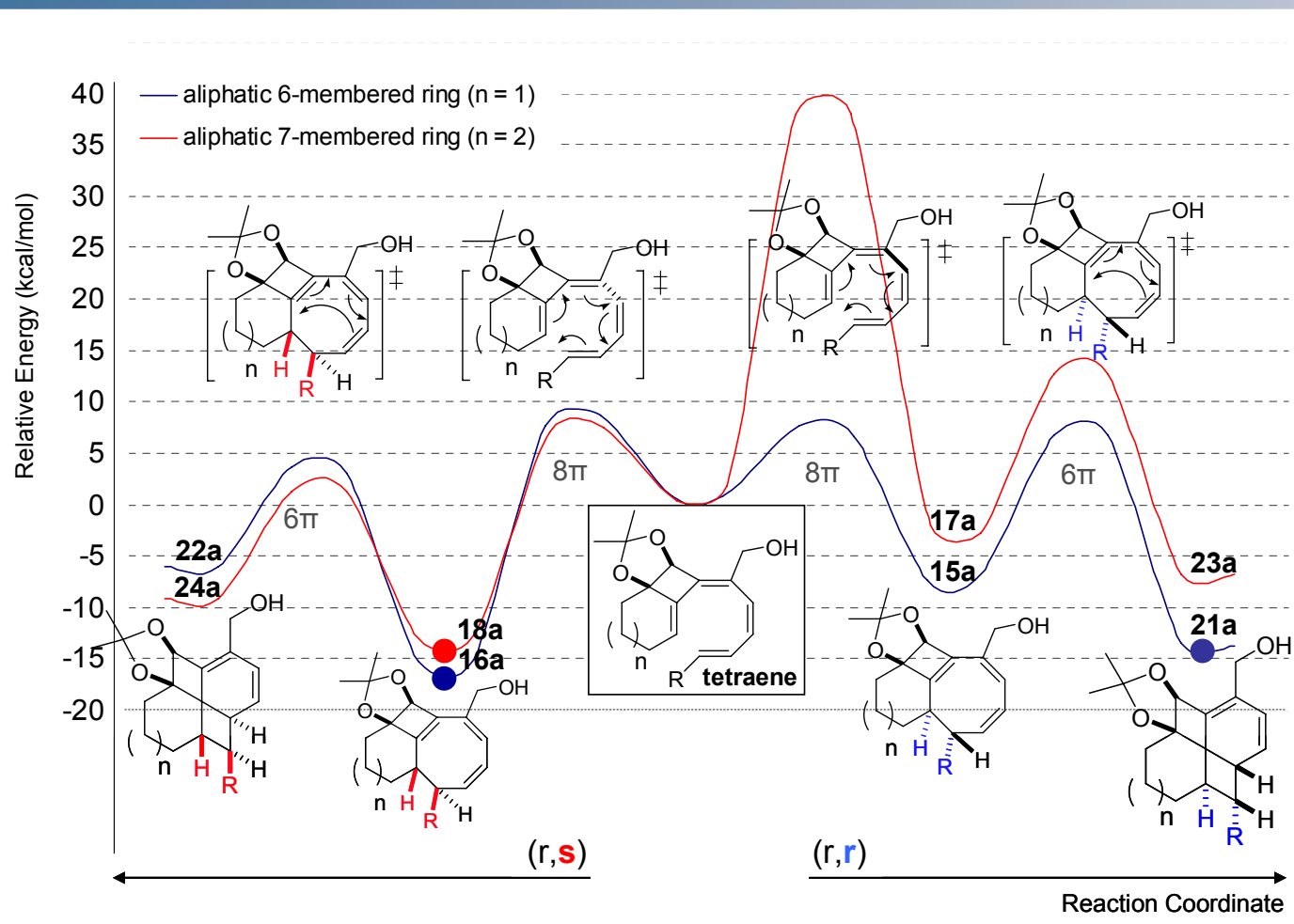


Conformational interconversions of the two six- and seven-membered ring moieties in cyclooctatrienes and fenestradienes. The experimentally observed structures are been shown in boxes.

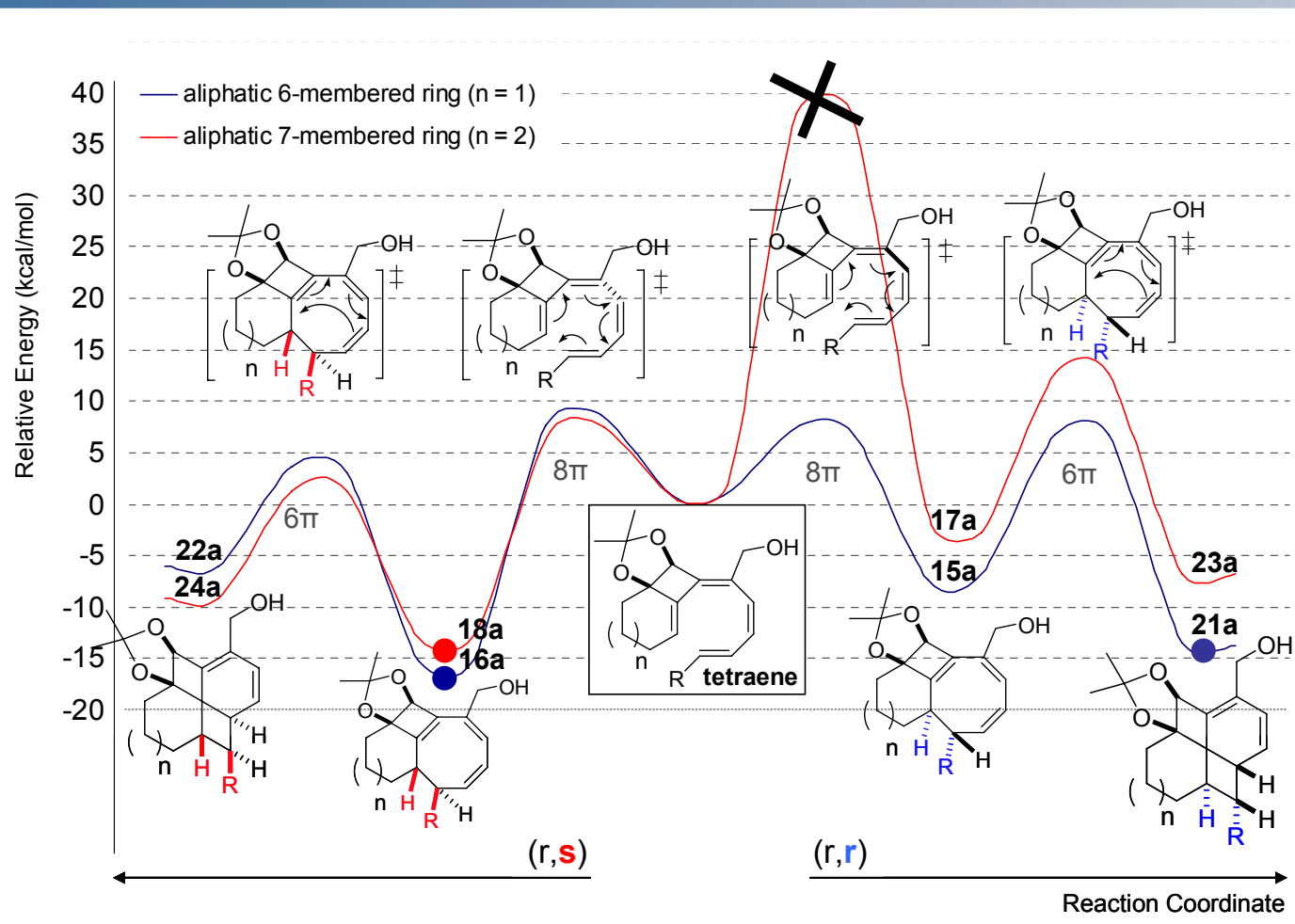


# Potential energy hypersurfaces for the two stereochemical controls in pathway I.



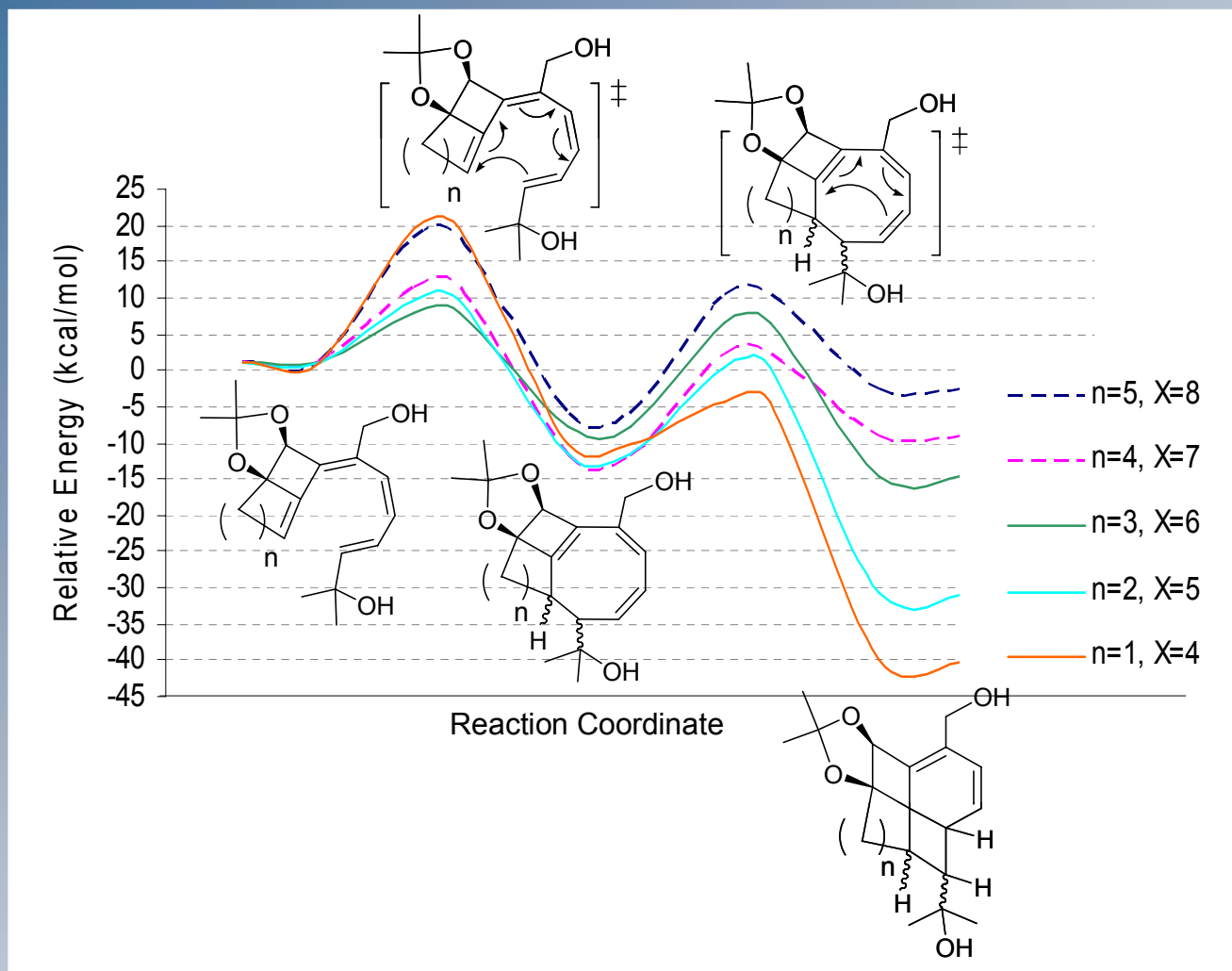


The potential energy hypersurfaces for the two possible stereochemical outcomes for  $\mathbf{X} = 6$  and 7. The right part of the surface is responsible for the (r,r) and the left part for the (r,s) stereoisomers. The experimentally observed structures are boxed.



The potential energy hypersurfaces for the two possible stereochemical outcomes for  $X = 6$  and 7. The right part of the surface is responsible for the (r,r) and the left part for the (r,s) stereoisomers. The experimentally observed structures are boxed.

## Synthesis [4.X.4.6]Fenestradienes versus Cyclooctatrienes



The surface energy potentials of the [4.X.4.6]fenestrenes for  $X = 4-8$

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**DAAD**