CHEM60001: Advanced Chemistry Topics 1 – Pericyclic Reactions

LECTURE 3

The Woodward-Hoffmann Rules & their Application

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Format & scope of lecture 3

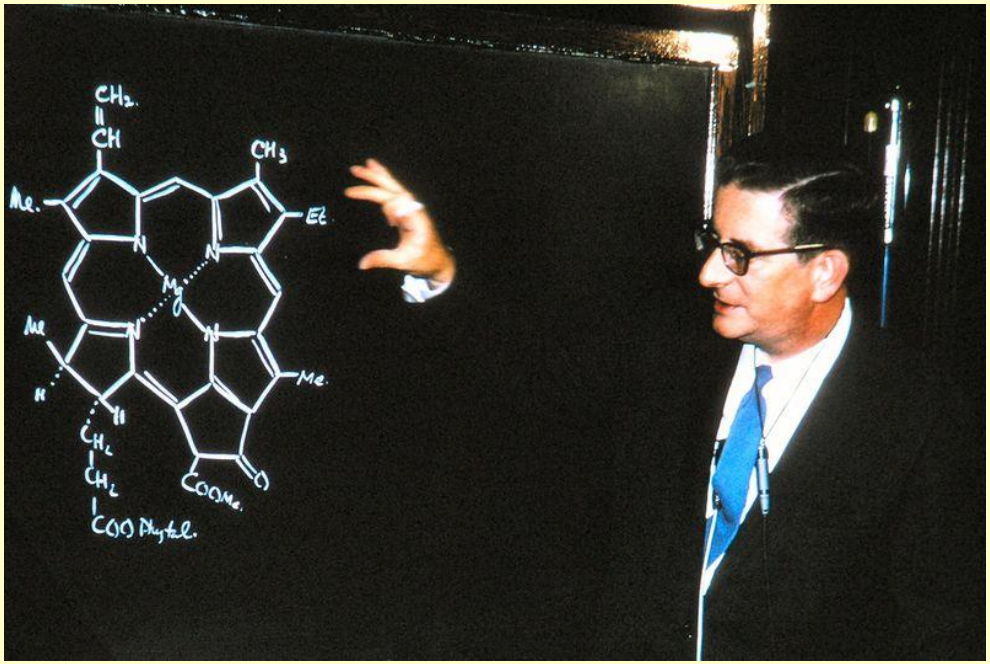
- ***The Woodward-Hoffmann Rules***
  - The rules
  - Suprafacial and antarafacial terminology
- ***Selected applications of the Woodward-Hoffmann Rules***
  - Diels-Alder reactions
  - [2+2]-cycloaddition reactions
  - [3,3]- and [2,3]-sigmatropic rearrangements
  - Electrocyclic ring-opening reactions
  - Violations of the rules!

Key further reading:

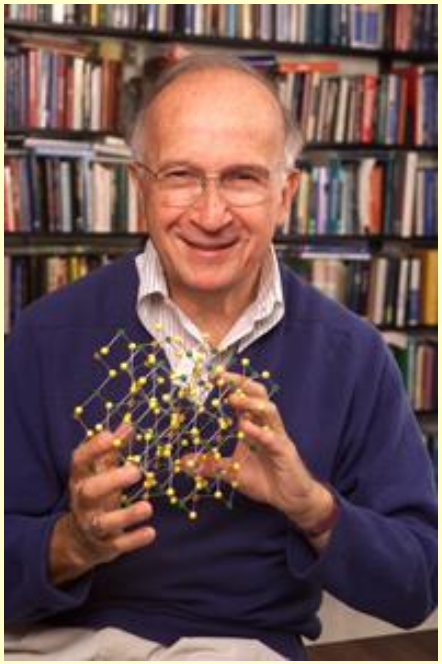
- BOOK: Clayden, Greeves & Warren, *Organic Chemistry*, 2nd Ed.,
  - *Chapter 34 – pericyclic reactions 1*

- WEB: Pericyclic Reactions - https://www.stereoelectronics.org/webPR/PR_home.html
  - *Chapter 1 – introduction to pericyclic reactions*

The Woodward-Hoffmann rules



Robert Woodward (Harvard)

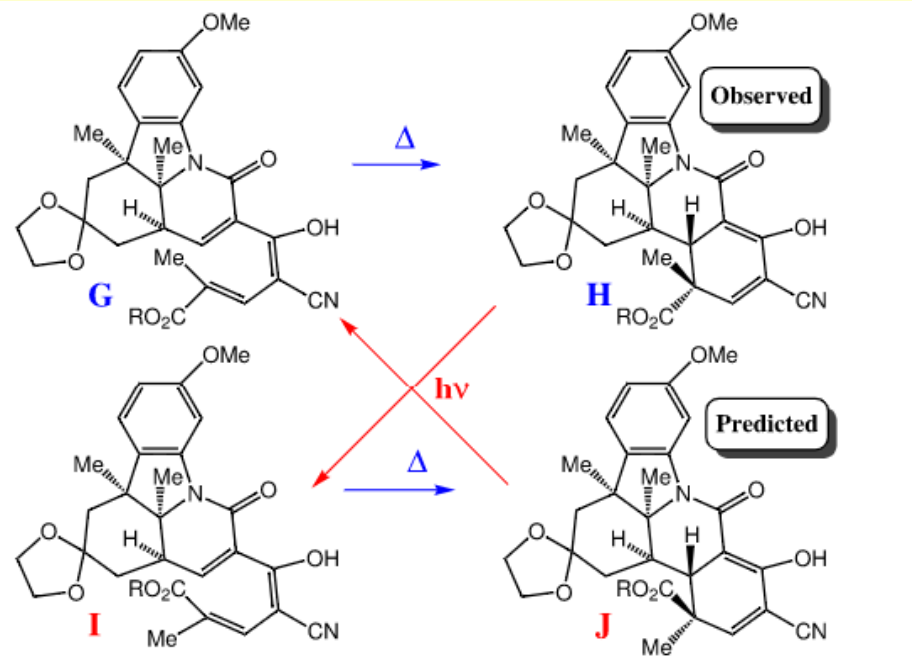


Roald Hoffmann (Cornell)

IMAGES: https://kids.kiddle.co/Image:Robert_Burns_Woodward_in_1965.jpg and https://www.nsf.gov/news/mmg/media/images/nsb_hoffmann_h.jpg

Vitamin B12 & the Woodward-Hoffmann Rules

In the mid 1960's Robert Woodward (Harvard) and Albert Eschenmoser (ETH, Zurich) were working on the total synthesis of vitamin B12. During this work, Woodward encountered the following electrocyclic ring-closure reaction:



- Woodward had anticipated that **G** ⇒ **J** was more likely than **G** ⇒ **H**, and so was considerably surprised when the thermal reaction actually gave the latter and not the former and that photolysis of the undesired **H** gave **I**, which then did give the desired **J** upon heating. What was going on?...

- For fascinating historical accounts see: Seeman *J. Org. Chem.* **2015**, *80*, 11632 [**DOI**], Seeman *Chem. Eur. J.* **2021**, *27*, 7000 [**DOI**], and Rzepa @https://www.ch.imperial.ac.uk/rzepa/blog/?p=8761

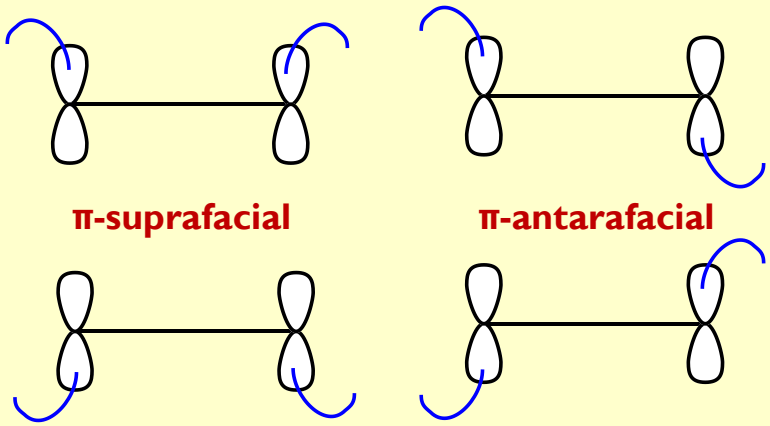
The Woodward-Hoffmann Rules

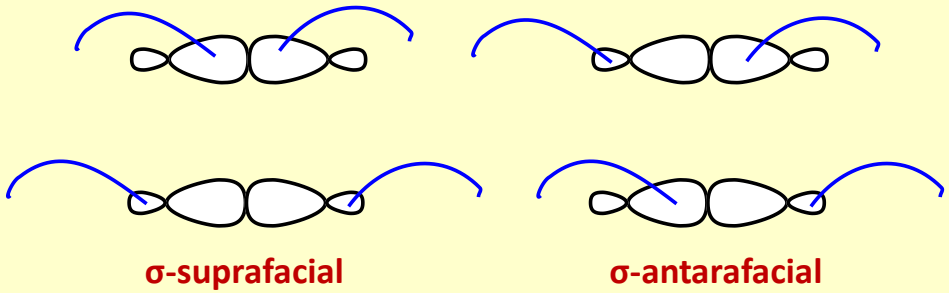
Correlation diagrams are useful for predicting which pericyclic reactions are allowed but are not easy to construct. Happily, they can be distilled into a simple rule:

A ground state (*i.e.* **thermal**) pericyclic reaction is symmetry allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is **odd** (where q and r must be integers).

A first electronically excited state (*i.e.* **photochemical**) pericyclic reaction is symmetry allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is **even** (where q and r must be integers).

's' = **suprafacial** [bond formation on the 'same' faces of a molecular 'component']
'a' = **antarafacial** [bond formation on the 'opposite' faces of a molecular 'component']





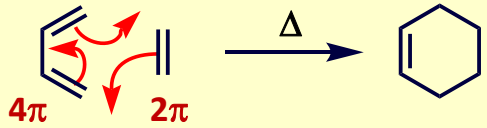
Selected applications of the W-H Rules

‘Orbital Symmetry’
(Robin Moline, 2017)

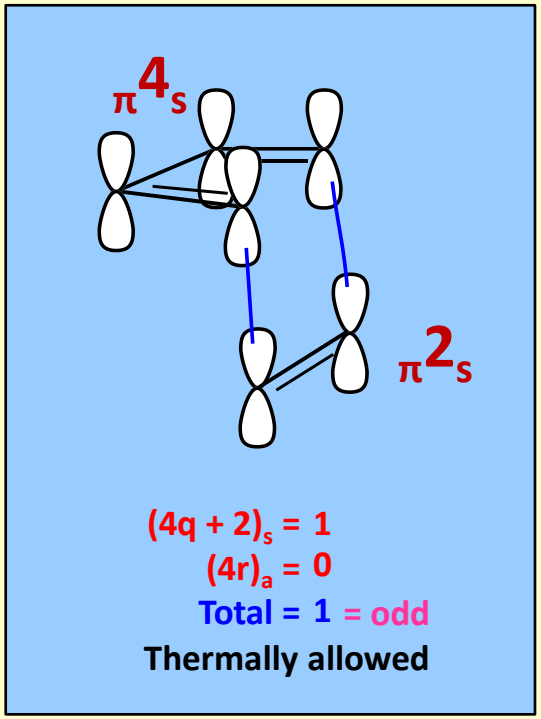
IMAGE: https://pixels.com/featured/orbital-symmetry-robin-moline.html

The W-H Rules: *a Diels-Alder reaction*

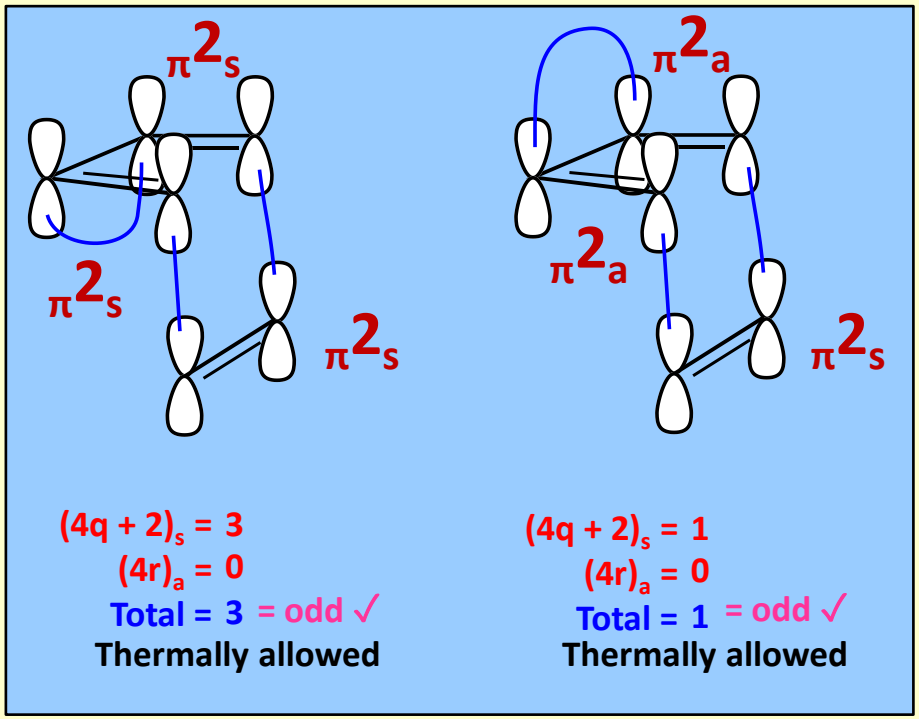
- 1. draw a ‘curly arrow’ mechanism
- 2. identify ‘components’ (how many p/s electrons in each component)
- 3. draw 3D orbital diagram to show approach and overlap of components
- 4. label **components** as suprafacial or antarafacial
- 5. sum components according to W-H rule and decide whether thermally or photochemically allowed



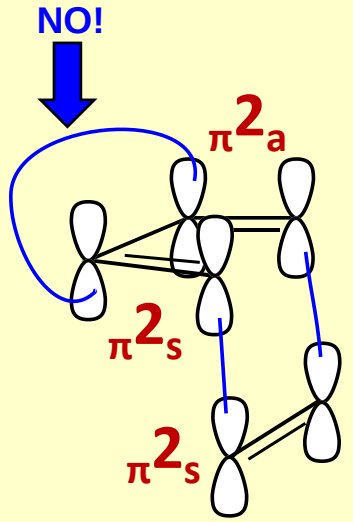
Diels-Alder [$_{\pi}4_{s}$+$_{\pi}2_{s}$]-cycloaddition



Recommended method



Alternative valid methods

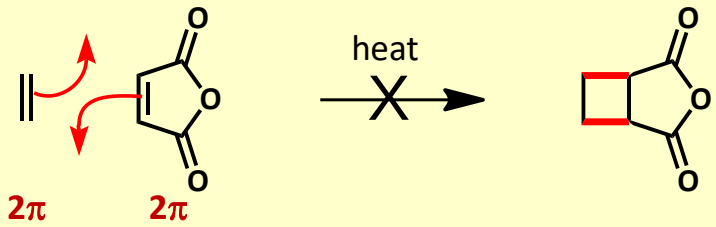


Blue line representing impossible developing orbital overlap

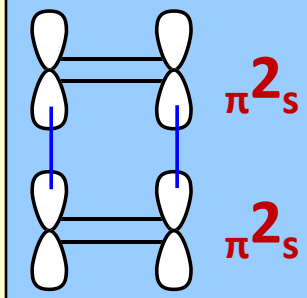
Invalid method

The W-H Rules: *a [2+2] cycloaddition*

- 1. draw 'curly arrow' mechanism and identify 'components'
- 2. draw 3D orbital diagram to show approach and overlap of components
- 3. label **components** as suprafacial or antarafacial
- 4. sum components according to W-H rule and decide whether allowed or forbidden

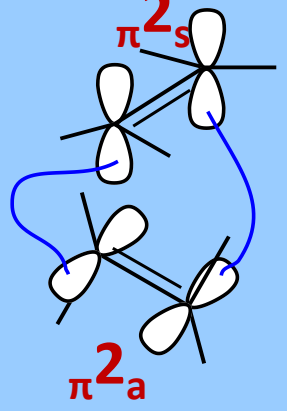


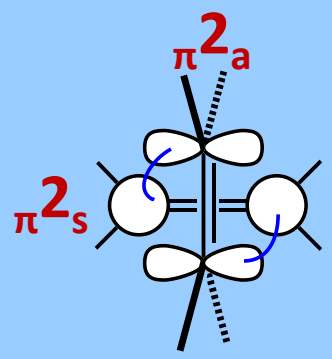
[$_{\pi}2_{s}$+$_{\pi}2_{s}$]-cycloaddition



$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✗
forbidden (thermally)

$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✓
allowed – photochemically





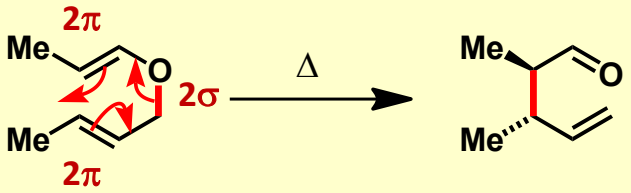
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed (thermally)

but geometrically unreasonable, therefore does **not** *occur*

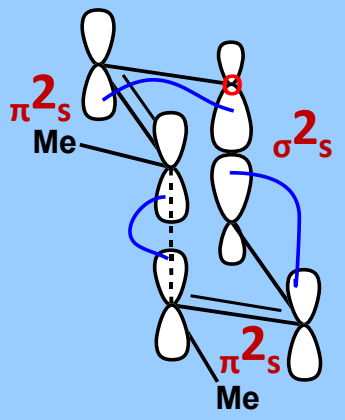
The Woodward-Hoffmann rule gives you the symmetry allowed orbital overlap but *you* have to decide whether the overlap *you* have drawn is geometrically reasonable.

The W-H Rules: *a [3,3]-sigmatropic rearrangement*

- 1. draw 'curly arrow' mechanism and identify 'components'
- 2. draw 3D orbital diagram to show approach and overlap of components
- 3. label **components** as suprafacial or antarafacial
- 4. sum components according to W-H rule and decide whether thermally or photochemically allowed

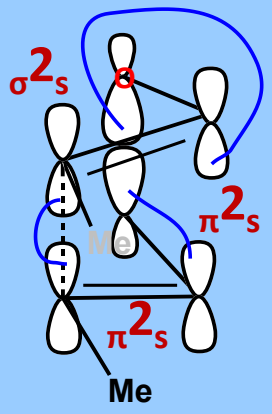


Claisen [3,3]-rearrangement



$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3 = odd
Thermally allowed

Claisen rearrangement *via* ***chair*** TS is allowed.



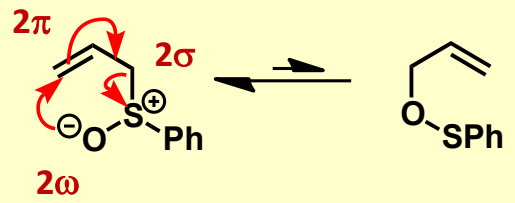
$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3 = odd
Thermally allowed

Claisen rearrangement *via* ***boat*** TS is allowed.

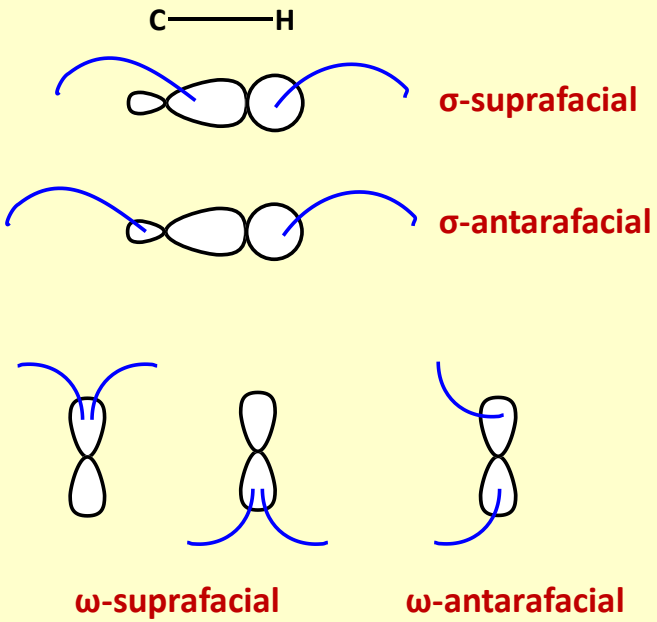
The Woodward-Hoffmann rule does **not** tell us that the chair TS is lower in energy than the boat TS - you need to use your knowledge/intuition to decide this.

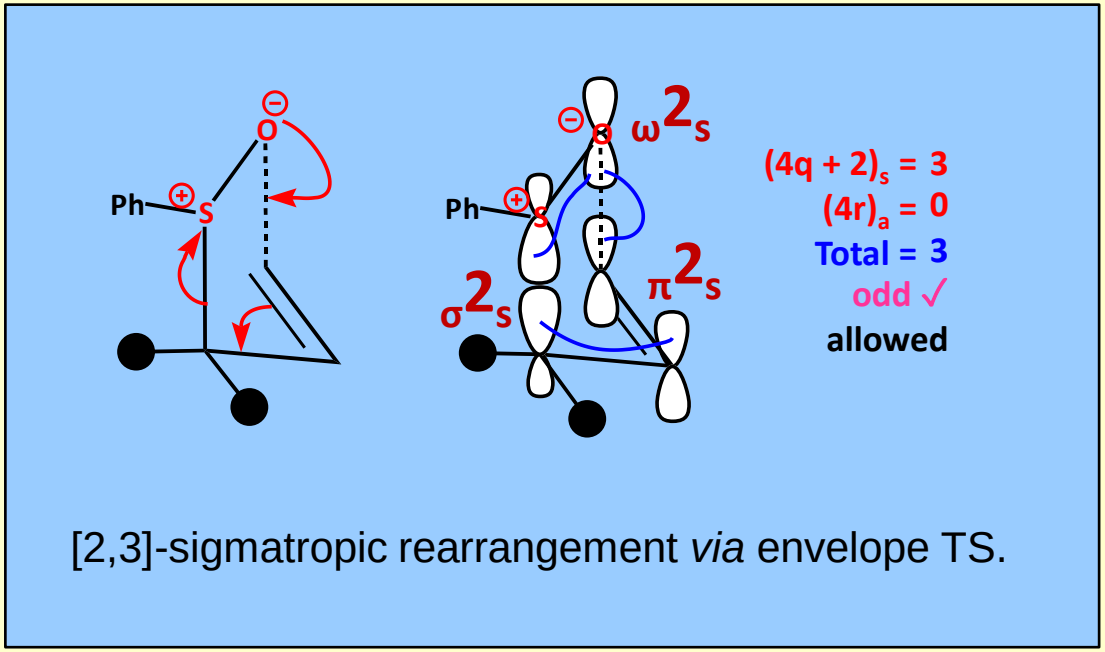
The W-H Rules: *a [2,3]-sigmatropic rearrangement*

- 1. draw ‘curly arrow’ mechanism and identify ‘components’
- 2. draw 3D orbital diagram to show approach and overlap of components
- 3. label **components** as suprafacial or antarafacial
- 4. sum components according to W-H rule and decide whether allowed or forbidden



Allyl sulfoxide [2,3]-rearrangement

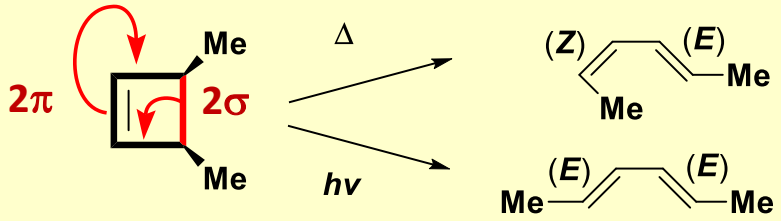




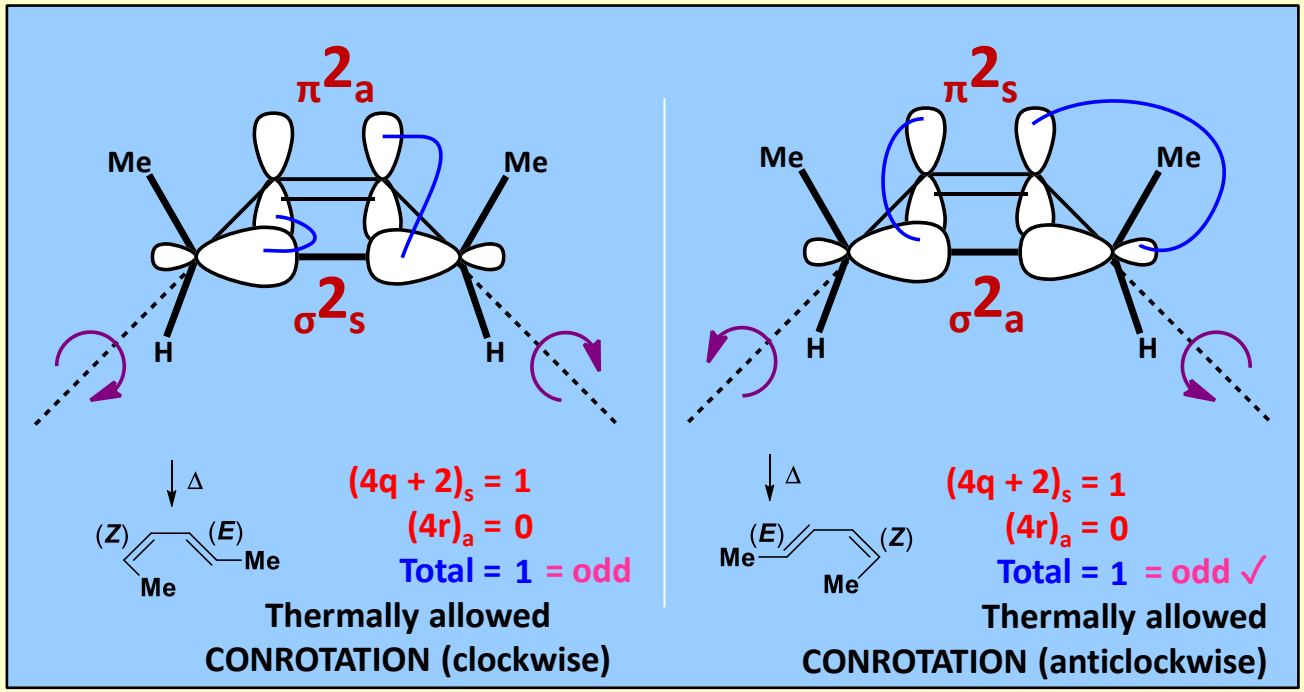
[2,3]-sigmatropic rearrangement *via* envelope TS.

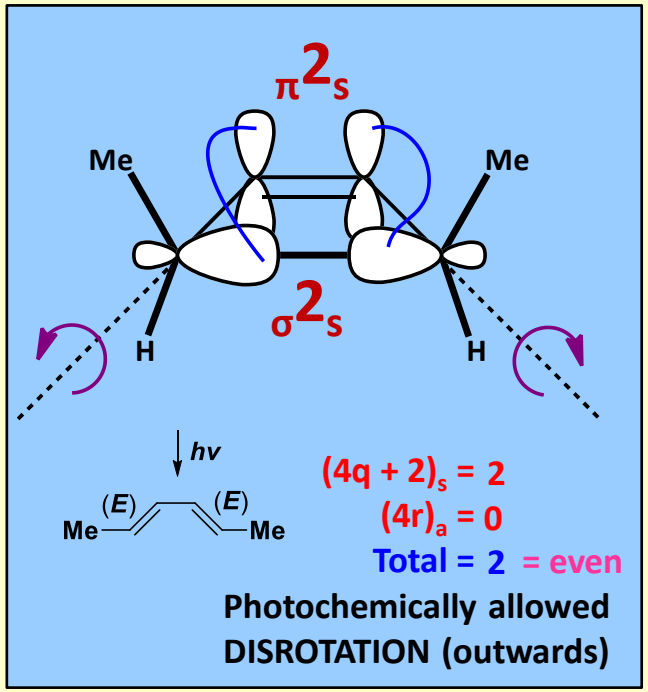
The W-H Rules: *electrocyclic ring-opening*

- 1. draw ‘curly arrow’ mechanism and identify ‘components’
- 2. draw 3D orbital diagram to show approach and overlap of components
- 3. label **components** as suprafacial or antarafacial
- 4. sum components according to W-H rule and decide whether thermally or photochemically allowed



Cyclobutene ring-opening



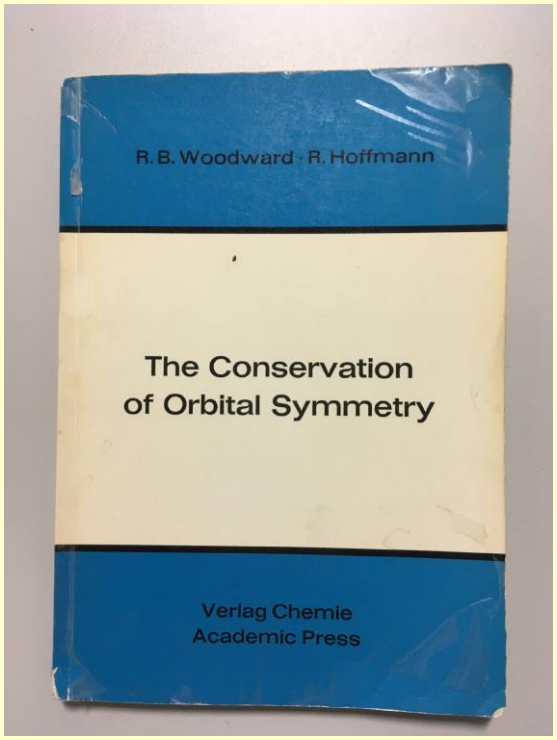


Both equally valid methods for this *thermal* case (products identical)

Thermal ring-opening is ***conrotatory***; ***Photochemical*** ring-opening is ***disrotatory***.

“Violations”

- There is an entire chapter in “The Conservation of Orbital Symmetry” given over to violations of the Woodward-Hoffmann rules



12. Violations

There are none!

Nor can violations be expected of so fundamental a principle of maximum bonding. All the more is it then important to give consideration to some reactions which might appear on casual inspection to contravene orbital symmetry conservation.

- It’s great to be able to be so confident – but remember the rules only tell us whether there is a symmetry imposed barrier to a reaction – not what the mechanism actually is.