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Massachusetts Institute of Technology

Organic Chemistry 5.13

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Notes for Lecture #17

Sigmatropic Rearrangments

Woodward-Hoffmann Rules for Sigmatropic Rearrangments

	Stereochemical Course	
# Electrons	**Thermal Mode**	**Photochemical Mode**
4n + 2	[s,s]	[s,a]
4n	[s,a]	[s,s]

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Summary of Unit 3

Molecular Orbital Theory, Pericyclic Reactions

A. **Molecular Orbital Theory**

1. Ethylene
2. Allyl cation, radical, anion
3. 1,3-Butadiene
4. Benzene
5. Cyclobutadiene – Frost's Circle (Polygon Rule)

B. **Cycloaddition Reactions**

1. Diels-Alder Reaction
    a. Basics – diene + dienophile (electron-poor)
    b. Only s-cis conformation of diene reacts.
    c. Cantharidin example
    d. Stereochemical course – part 1: Always suprafacial with respect to dienophile – stereospecific.
    e. Diels-Alder is a concerted reaction
    f. Frontier Molecular Orbital analysis of Diels-Alder reaction. HOMO of diene interacts with LUMO of dienophile. "HOMO/LUMO analysis".
    g. Stereochemical course – part 2: Always suprafacial with respect to diene. Disrotatory motion of orbitals.
    h. Woodward-Hoffman rules correctly predict the stereochemical course of the Diels-Alder reaction (and all other cycloaddition reactions): $\pi 4s + \pi 2s$.
    i. Regioselectivity – "ortho-para rule". Not governed by W-H rules, but a general trend.
    j. Diastereoselectivity – Alder endo rule.
    k. MO explanations: Coefficients of wavefunctions that represent orbitals vary with substitution. Secondary orbital interactions between dienophile and carbon(s) 2 and/or 3 of diene favor endo approach of dienophile.
2. Photochemical [2+2] Cycloaddition
    a. Review of 4 requirements of cycloaddition (concerted, pericyclic; cyclic T.S.; 2 separate arrays of orbitals; form 2 sigma bonds) and what W-H predicts for photo [2+2] ($\pi 2s + \pi 2s$)
    b. Explanation – HOMO/LUMO analysis. Excite electron to higher energy orbital, which becomes HOMO.
    c. Examples: cis-2-butene + maleic anhydride, thymidine dimmers
3. Thermal [2+2] Cycloaddition – Ketenes + Alkenes
    a. MO analysis and W-H rules predict $\pi 2s + \pi 2a$
    b. Side-on approach of diene and ketene ("+" sign)
4. Dipolar [4+2] Cycloaddition, Thermal
    a. Diene vs. Dipole – same # π electrons (4), different # atoms (4 vs. 3)

   b. Examples – azides, diazocompounds, nitrile oxides

5. Ozonolysis – Most important dipolar cycloaddition
   a. Mechanism – [4+2], retro-[4+2], [4+2]. (Then reduction or oxidation with additional reagent
   b. Zn or $(CH_3)_2S$ gives carbonyls in oxidation state as is (after hydrolysis)
   c. $NaBH_4$ reduces aldehydes, ketones to alcohols
   d. H_2CrO_4 (Jones) oxidizes aldehyde to acid (no effect on ketone)

C. Electrocyclic Reactions

1. Introductory Examples - (*E,Z*)-2,4-hexadiene and (*E,E*)-2,4-hexadiene
2. Definitions
   a. Concerted pericyclic process
   b. Cyclic transition state
   c. Intramolecular, i.e. **1** overlapping array of orbitals
   d. Formation/Breaking of **1** sigma bond
3. FMO Analysis of Stereochemical Results (see examples in A, above)
   a. (Thermal) (*E,Z*)-2,4-hexadiene –> ***cis***–3,4-dimethylcyclobutene (**conrotatory**) and (*E,E*)-2,4-hexadiene, thermal –> ***trans***–3,4-dimethylcyclobutene (**conrotatory**).
   b. (Photochemical) *(E,Z*)-2,4-hexadiene, –> ***trans***–3,4-dimethylcyclobutene - electron promoted to higher energy orbital; thus HOMO is different than in thermal reactions. (**disrotatory**) and (*E,E*)-2,4-hexadiene –> ***cis***–3,4-dimethylcyclobutene - electron promoted to higher energy orbital; thus HOMO is different than in thermal reactions. (**disrotatory**)
4. Electrocyclic Ring Opening – W-H rules still apply
   a. ***trans***–3,4-dimethylcyclobutene, thermal -> (*E,E*) -2,4-hexadiene (**conrotatory**)
   b. ***cis***–3,4-dimethylcyclobutene, thermal -> (*E,Z*) -2,4-hexadiene (**conrotatory**)
5. Electrocyclic Reactions Involving 6π Electrons
   a. (*E,Z,E*)-2,4,6-octatriene, thermal -> ***cis***–5,6-dimethyl-1,3-cyclohexadiene (**disrotatory**)
   b. (*E,Z,E*)-2,4,6-octatriene, photochemical -> ***trans***–5,6-dimethyl-1,3-cyclohexadiene - electron promoted to higher energy orbital; thus HOMO is different than in thermal reactions. (**conrotatory**)
   c. Found in Vitamin D synthesis

D. Sigmatropic Rearrangements

1. Definitions
   a. Concerted pericyclic process
   b. Cyclic transition state
   c. Intramolecular, i.e. **1** overlapping orbital array

    d. One sigma bond formed, one broken
    e. [i,j] – i + j = number of atoms in orbital array
       i, j = number of atoms on either side of sigma bond broken (or formed)
2. Cope Rearrangement, Thermal [3,3]
    a. Thermodynamically driven
        i. Alkene substitution
        ii. Ring strain
3. Claisen Rearrangement, Thermal [3,3]
4. Woodward-Hoffmann Rules
5. Thermal [1,5] H-Shift
6. Thermal [1,3] H-Shift
7. Thermal [1,7] H-Shift

Good Luck on the Exam!

– Tim Jamison –