Photochemistry

- chemical reactions initiated by light
- energy is absorbed or emitted by matter in discrete quanta called photons

\[ E = h\nu = hc/\lambda \]

short \( \lambda \) light corresponds to high energy

-absorption of light leads to an electronic excitation (ground state \( \rightarrow \) excited state)

- promote an e\(^-\) like \( n \rightarrow \pi^* \) or \( \pi \rightarrow \pi^* \)

-most chemistry takes place from \( S_1 \) and \( T_1 \) excited states

\[ \begin{align*}
S_1 \text{ have a shorter lifetime and higher } E \text{ (10}^{-9} \text{ to 10}^{-5} \text{)} & \quad \downarrow \\
T_1 \text{ have a longer lifetime b/c spin flip req. (10}^{-5} \text{ to 10}^{-3} \text{)} & \quad \downarrow
\end{align*} \]
Photochemistry

-If a molecule absorbs energy, it can undergo a reaction or undergo loss of energy by two methods:
  • radiative processes-involve emission of a photon
    - phosphorescence-relaxation to a lower state with different multiplicity, such as \( T_1 \rightarrow S_0 \) (spin forbidden)
    - fluorescence-relaxation to lower state of same multiplicity, such as \( S_1 \rightarrow S_0 \) (spin allowed)
  • non-radiative processes-no emission
    - internal conversion-involves no spin change, such as \( S_1 \rightarrow S_0 \)
    - intersystem crossing-involves change in spin multiplicity
      • one way competes with phosphorescent decay of the lowest triplet state to the ground state
      • another way converts the lowest excited singlet state to the lowest triplet state (competes with fluorescence and IC)[gives access to triplet state]
- Excitation by E transfer is Sensitization (deactivation is Quenching)
- *cis/trans (E / Z)* isomerism under photochemical conditions commonly leads to thermodynamically less stable *cis*-isomer.
- *cis*-isomer typically absorbs at a lower λ due to decreased conjugation b/c of non-bonded interactions.
- Reactions come to photostationary state unless optical pumping is performed (irradiation of just 1 isomer to drive the equilibrium).

\[
R \begin{array}{c}
\text{R} \\
\text{hv}
\end{array} \longleftarrow \begin{array}{c}
\text{R} \\
\text{R}
\end{array}
\]

- w/o sensitizer photostationary state: \( E / Z : 8/92 \)
- w sensitizer photostationary state: \( E / Z : 50/50 \)
Geometrical Isomerism

Geometrical Isomerism

Electrocyclizations

-reactions generate a new $\sigma$-bond between the termini of the conjugated $\pi$-system
-concerted process-bond breaking occurs at the same time as bond formation
-reactions also come to photostationary state based on absorption coefficient at the $\lambda$ of irradiation

<table>
<thead>
<tr>
<th>Thermal Reactions</th>
<th>Photochemical Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>-occur via HOMO</td>
<td>-occur via LUMO</td>
</tr>
<tr>
<td>4n - conrotatory</td>
<td>4n - disrotatory</td>
</tr>
<tr>
<td>4n + 2 - disrotatory</td>
<td>4n + 2 - conrotatory</td>
</tr>
</tbody>
</table>
4π-Electrocyclizations

4π-electrocyclizations occur with disrotatory ring closure under photochemical conditions.

\[
\text{H}_2\text{C} = \text{C} - \text{H}_2\text{C} = \text{C} \xrightarrow{h\nu} \text{H}_2\text{C} - \text{H}_2\text{C} = \text{H}_2\text{C} = \text{C} = \text{H} \]

95% yield

\[
\text{H}_2\text{C} - \text{C} = \text{C} \xrightarrow{h\nu} \text{C} = \text{C} - \text{C} = \text{C} \]

59% yield

\[
\text{C} = \text{C} - \text{C} = \text{C} \xrightarrow{h\nu} \text{C} = \text{C} = \text{C} - \text{C} = \text{C} \]

\[
\text{C} = \text{C} - \text{C} = \text{C} \xrightarrow{\text{Fe(CO)}_5} \text{C} = \text{C} \]

254 nm

\[
\text{C} = \text{C} \xrightarrow{h\nu} \text{Fe} \quad \text{Fe(CO)}_5 \quad \text{CO} \]
8 and $6\pi$-Electrocyclizations

8$\pi$-electrocyclizations occur with disrotatory ring closure under photochemical conditions and $6\pi$-systems undergo conrotatory ring closure.

Ergosterol (provitamin D) $\xrightarrow{\text{hv}}$ Precalciferol (previtamin D) $\xrightarrow{6\pi}$ Vitamin D$_2$ (calciferol) $\xrightarrow{>20^\circ C}$ 1,7 H-shift

$\xrightarrow{\text{hv}}$ C$_9$H$_{17}$ HO C$_9$H$_{17}$ HO C$_9$H$_{17}$
6π-Electrocyclization in Synthesis

Ikarugamycin

Wittig Reaction

1. h\textsubscript{ν}, -78°C, hex.
2. HCl

retro-$6\pi$-Electrocyclization

Di-π-methane rearrangement

- Howard E. Zimmerman has studied this reaction extensively
- Reaction takes 1,4-dienes or 3-phenylalkenes to vinyl or phenyl cyclopropanes
**Oxa-di-π-methane rearrangement**

\[ \text{[Reaction Scheme]} \]

- **Pyrex** and \( t\)-BuOH (50%): 
  - [Reaction Structure]

- Acetone (70%): 
  - [Reaction Structure]
Di-$\pi$-methane rearrangement in Natural Products


![Diagram showing the transformation of erythrolide B to erythrolide A through di-$\pi$-methane rearrangement.]

- **Erythrolide B** transforms to **Erythrolide A** under the following conditions:
  - **Quartz PhH**: 87% conversion in 3 hr
  - **5% methanolic seawater (glass)**: 37% conversion in 8 days

The transformation is achieved through photochemical processes involving sunlight, with the use of quartz or methanolic seawater (glass).
Oxa-di-π-methane vs. 1,3-Acyl Migration

\[
\begin{align*}
\text{Keto} & \xrightarrow{h_\text{v}} \text{Keto, 300 nm, hexane, 50\%} \\
\text{MeO} & \xrightarrow{h_\text{v}} \text{MeO, 254 nm, acetone, 62\%}
\end{align*}
\]

\[
\begin{align*}
\text{X = O pinguisone} \\
\text{X = H}_2 \text{ deoxypinguisone}
\end{align*}
\]

1,3-Acyl Migration in Natural Products

[2 + 2] Cycloaddition

-[2+ 2] photocycloaddition is the cyclization of two olefinic units to provide a cyclobutane (generate 2 new C-C bonds and up to four new stereocenters)
-1908 Ciamician observed the first [2 + 2] reaction when exposure to Italian sunlight for 1 year generated carvone camphor from carvone

\[
\text{carvone} \quad \xrightarrow{hv} \quad \text{carvone camphor}
\]

-Photochemical conditions create charge like umpolung of enone (β-carbon is electron rich)
-Intermolecular variants also well known, but regioselect. can be highly dependent on both olefinic partners
-This [2 + 2] follows the "rule of 5" and none of the other regioisomer is observed

\[
\text{not observed}
\]
"Rule of 5"

\[ \text{[Chemical Structures]} \]

[Chemical Structures]
[2 + 2] Cycloaddition in Synthesis

de Mayo Reaction

-[2 + 2] cycloaddition involving double bond of an enol and another olefin and the retro-aldol reaction
Paterno-Büchi Reaction

-Paterno and Chieffi observed the first example of a [2 + 2] cycloaddition between a carbonyl and an olefin to make an oxetane

\[
\text{AcO} \xrightarrow{h\nu} \left[ \begin{array}{c} \text{O}^* \\ T_1 \end{array} \right] + \xrightarrow{\text{acetone} 42\%} \xrightarrow{\text{HI} \text{ AcOH} 82\%} \text{OH}
\]

Paterno-Büchi Reaction in Synthesis

1. i-Pr₂NMgl, Δ
2. PDC, DMF
65%

LDBB
THF
-78°C
66%

NaBH₄
TFA

endo-hirsutene

-this variant of the [2 + 2] offers a photochemical variant of the aldol reaction through transformations of the photoadduct

Furan-Carbonyl Variant of the Paterno-Büchi Reaction

\[
\text{Furan} + \text{Benzyl Acetate} \xrightarrow{h_v} \text{Product} (63\%)
\]

establishes 2 stereocenters present in asteltoxin (architecture used to install remaining stereocenters in next few steps)

asteltoxin

Arene-Olefin Cycloadditions

- Cycloadditions between arenes and an olefin
  - Ortho cycloadditions - [2 + 2]
  - Para cycloadditions - [4 + 2]
  - Meta cycloadditions - [3 + 2]

Ortho Cycloadditions

\[
\text{R}_1 \quad \text{h} \quad \text{ν} \quad \text{R}_2 \quad \text{hv} \quad \text{R}_1 = \text{OMe} \quad \text{R}_2 = \text{CN} \\
\text{R}_1 = \text{CN} \quad \text{R}_2 = \text{OAc} \\
\text{R}_1 = \text{H} \quad \text{R}_2 = \text{CN}
\]
Para Cycloadditions

\[
\text{benzene} + \text{ethyne} \xrightleftharpoons{h\nu} \text{product}
\]

\[
\text{anthracene} + \text{acrylonitrile} \xrightleftharpoons{h\nu} \text{product}
\]
Bryce-Smith and Blair dispelled the long standing myth that arenes are photochemically inert.

In 1966, Wilzbach and Kaplan and Bryce-Smith, Gilber and Orger codiscovered the meta arene olefin cycloaddition.
Meta Cycloadditions in Synthesis

Wender pioneered the use of [3 + 2] arene/olefin cycloadditions in synthesis.

P. Wender, J. Howbert J. Am. Chem. Soc. 1981, 103, 688
Meta Cycloadditions in Synthesis

P. Wender, G. Dreyer *Tetrahedron* 1981, 37, 4445
Photoinduced Electron Transfer

Acceptor + Donor $\xrightarrow{h\nu} A^- + D^{++}$ → chemistry

polar solvents facilitate the generation of radical ions and subsequent chemical reactions

Witkop Cyclization

Witkop Cyclization in Synthesis

A. Burgett, Q. Li, Q. Wei, P. Harran Angew. Chem. Int. Ed. 2003, 42, 4961

TeocHN₂

(hv (300nm))

CH₃CN/ aq. LiOH 72%

steps

(32-40% in initial synthesis of the nominal diazonamides)

diazonamide A
Additional Photochemical Reactions

- Norrish Type I and II (\(\alpha\)-cleavage of carbonyl and H-abstraction and fragmentation)
- Nitrogen extrusion (generate carbenes such as the Wolff rearrangement or to give diradical)
- Sigmatropic rearrangements such as (1,3), (1,5), and (1,7)
- \(^{1}O\) reactions
- Deprotections (such as cleavage of nitroarenes)
- Many other PET reactions
  - Isomerizations
  - Rearrangements
  - Fragmentations
  - Arene substitutions and reductions
  - Photooxygenations
  - And many more reactions
either substrate can be used
to generate the product and
both give essentially the same
yield of tricycle

reaction sequence used
in Danheiser's synthesis
of salvilenone

Problem 1 Solution

Problem 2

Problem 2 Solution

1. $h\nu$, 87%
2. EtOH, reflux
3. cat. PPTS
   EtOH
   87% 2 steps