

4th Lunch & Learn Session

November 5th - 13:00 CET/12:00 UK

Light-responsive Molecules: From the Fumehood to the Cell

Speakers:



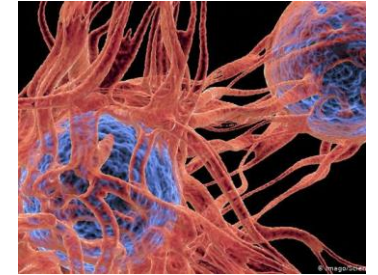
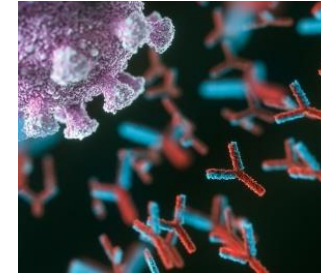
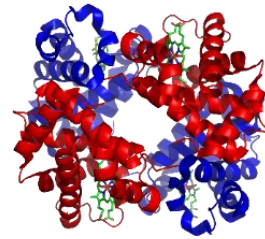
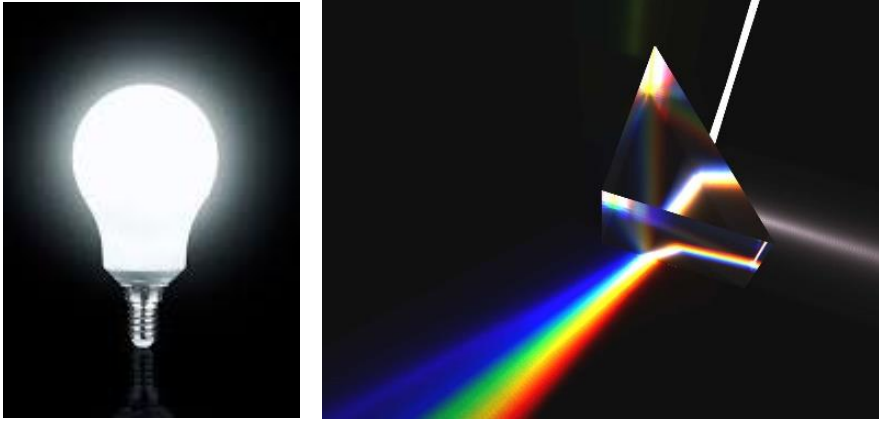
Dr. Jana Volarić
(Imperial College London, UK)



Dr. Davia Prischich
(University of Oxford, UK)



Dr. Markus Müller
(Dresden University of Technology, DE)

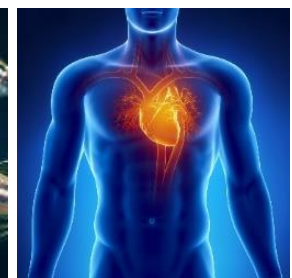
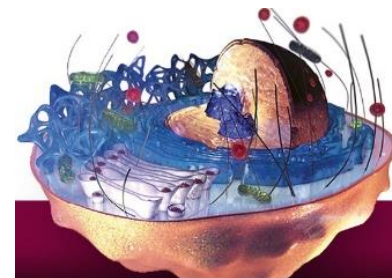


Light



**Understand, study and control
biological systems**

- non-invasive and bioorthogonal
- temporal control and spatial control



Optogenetics

Photodynamic therapy (PDT)

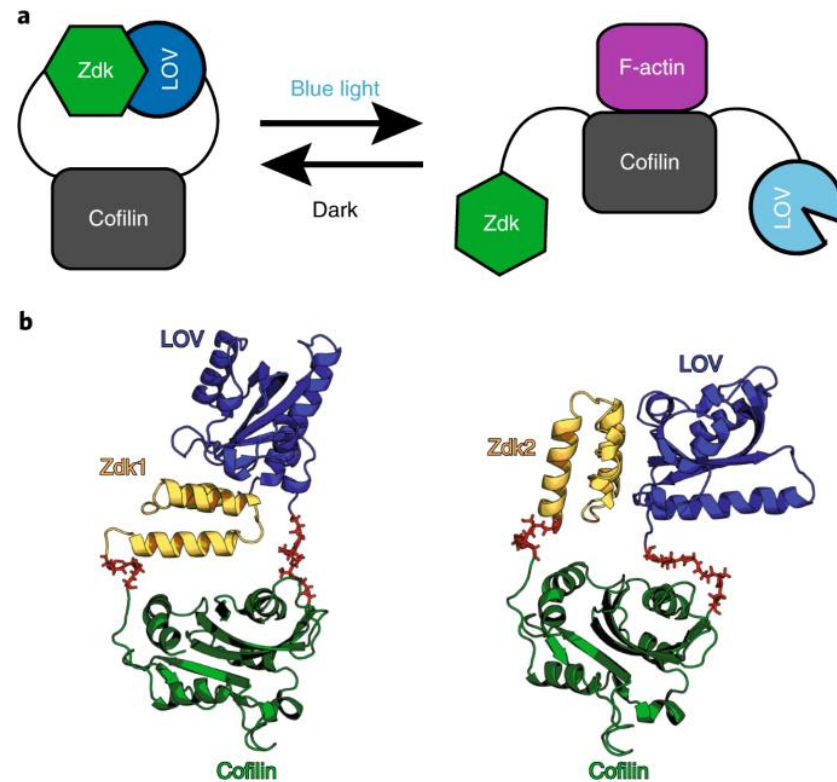
Photopharmacology

Optogenetics

Photodynamic therapy (PDT)

Photopharmacology

Genetically introduced protein
photoreceptors

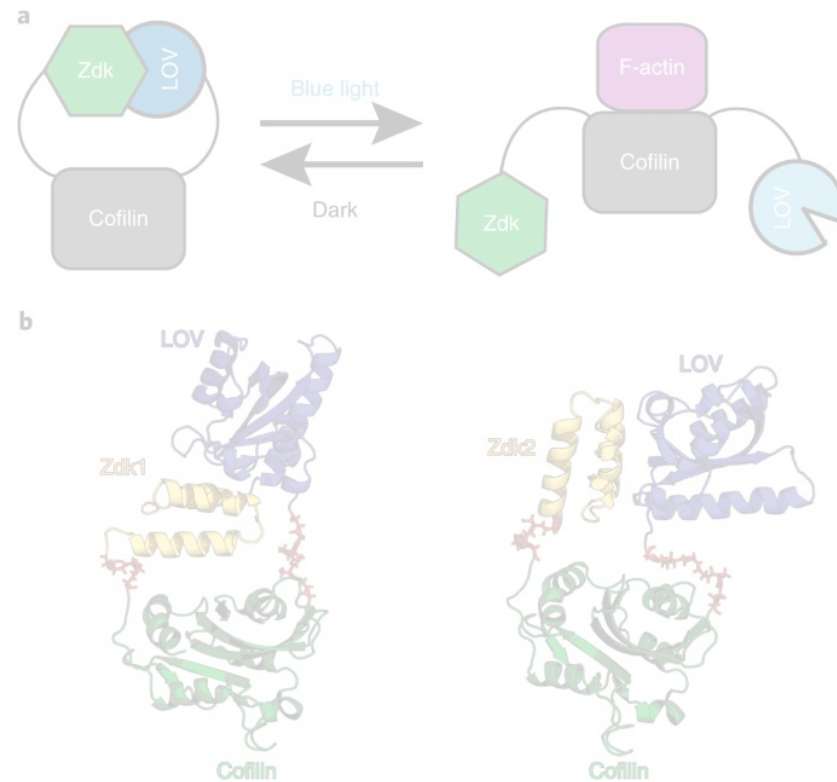


Optogenetics

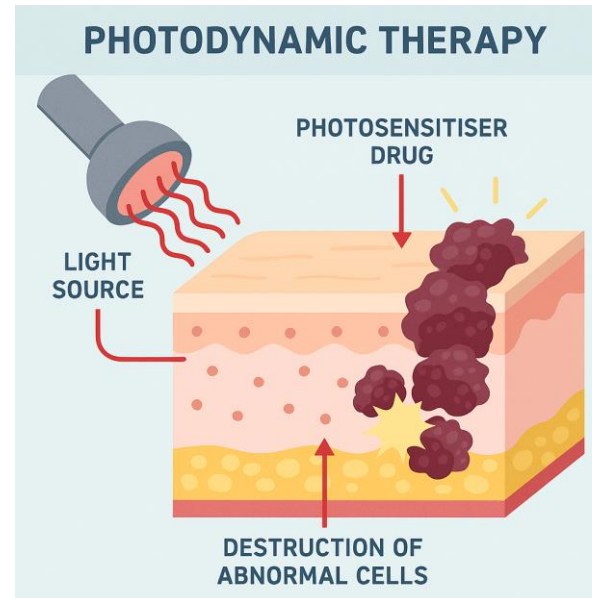
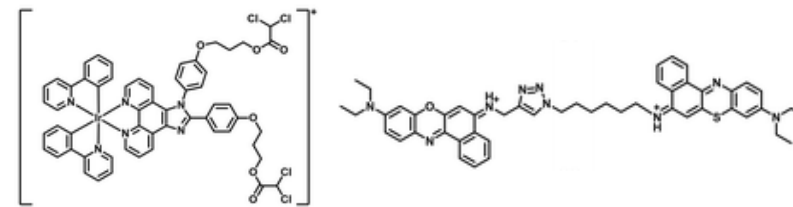
Photodynamic therapy (PDT)

Photopharmacology

Genetically introduced protein photoreceptors



Photosensitizers



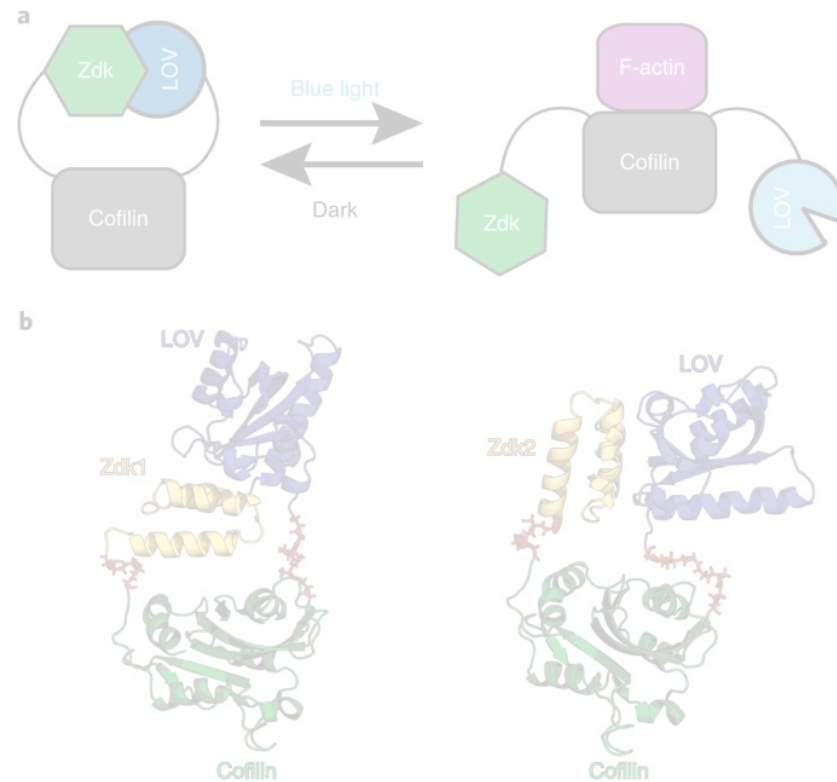
Chem. Soc. Rev., **50**, 4185 (2021)
www.skincarenetwork.co.uk/skin-cancer-news/the-science-behind-pdt-how-light-and-photosensitizers-target-skin-cancer-cells/

Optogenetics

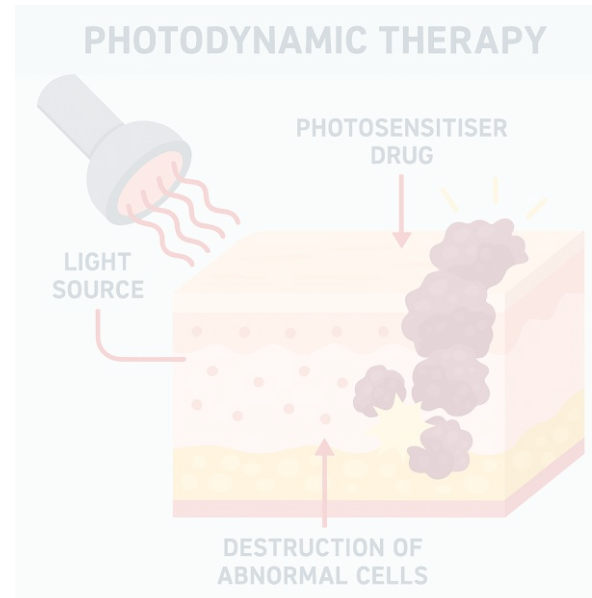
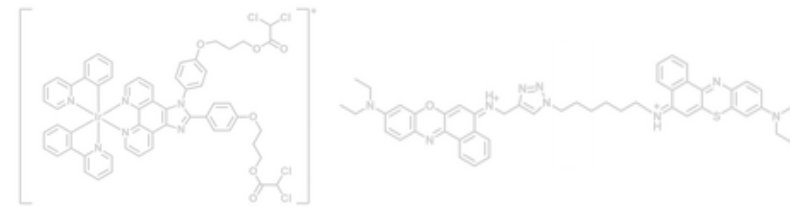
Photodynamic therapy (PDT)

Photopharmacology

Genetically introduced protein photoreceptors

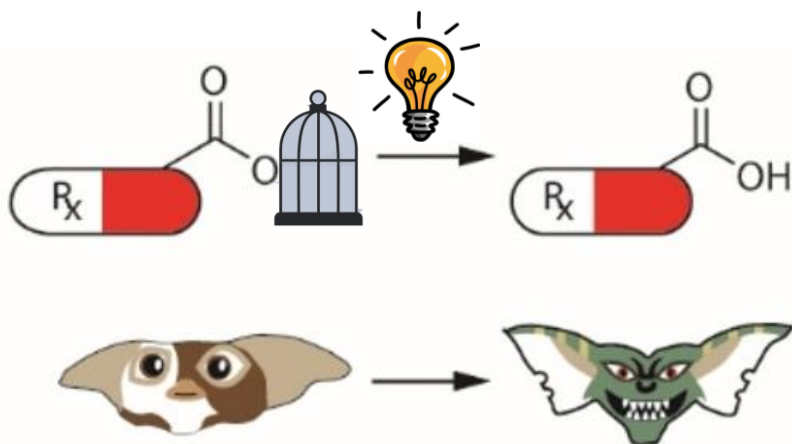


Photosensitizers



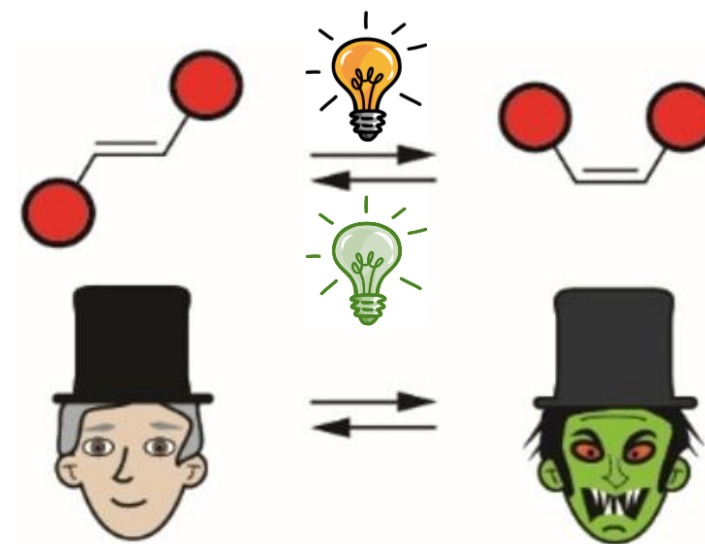
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www.skincarenetwork.co.uk/skin-cancer-news/the-science-behind-pdt-how-light-and-photosensitizers-target-skin-cancer-cells/

- Photocleavable protecting groups (PPGs)
= *Photocages*



irreversible

- Photoswitches

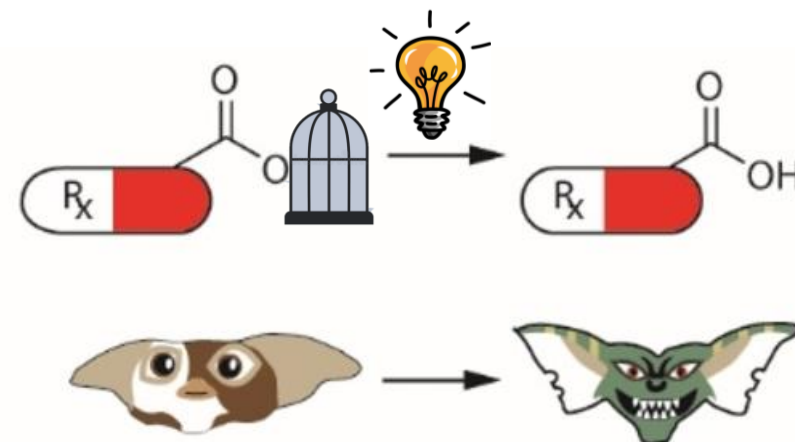


reversible

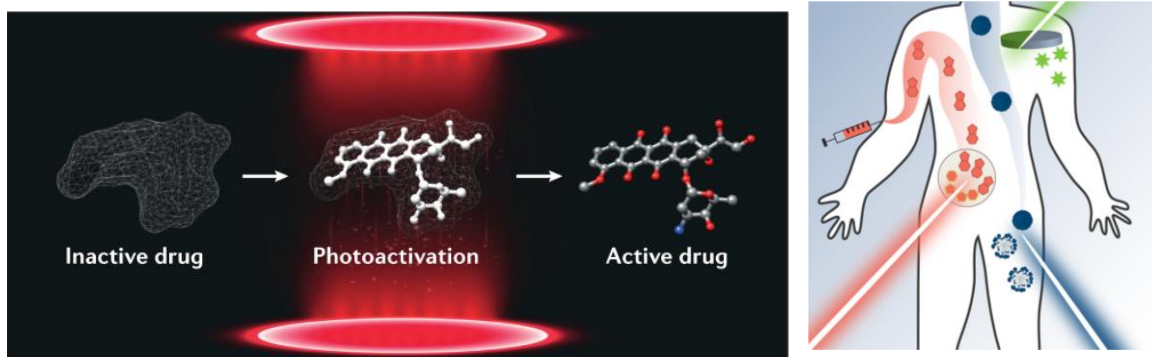


Important properties?

- Appropriate uncaging wavelength
- High photochemical efficiency
- Rate of release
- Byproducts biocompatible
- Caged compound inactive, stable and biocompatible



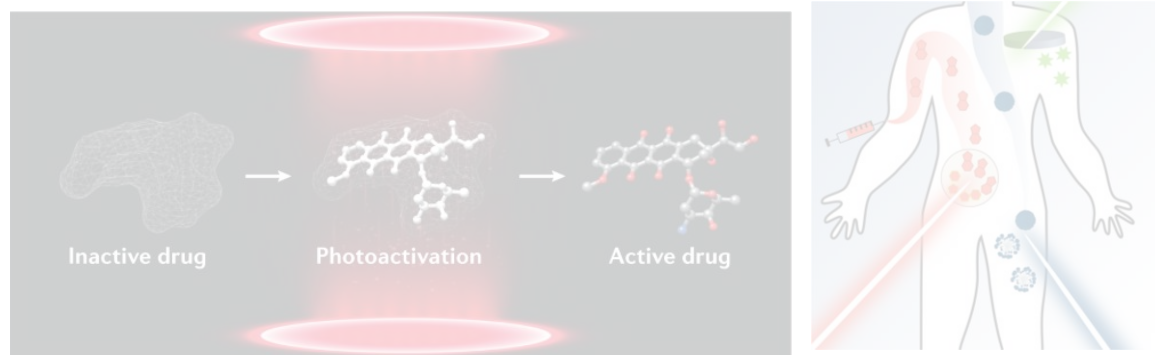
- **Control activity of a small molecules**
Activate drugs locally (targeted activation)



Nat. Rev. Chem., 5, 816. (2021); *Adv. Drug Deliv. Rev.* 171 (2021) 94.

- Control activity of a small molecules

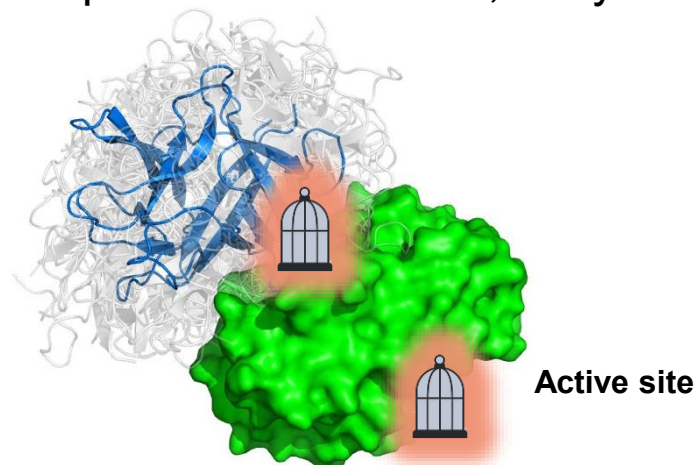
Activate drugs locally (targeted activation)



Nat. Rev. Chem., 5, 816. (2021); *Adv. Drug Deliv. Rev.* 171 (2021) 94.

- Control protein activity**

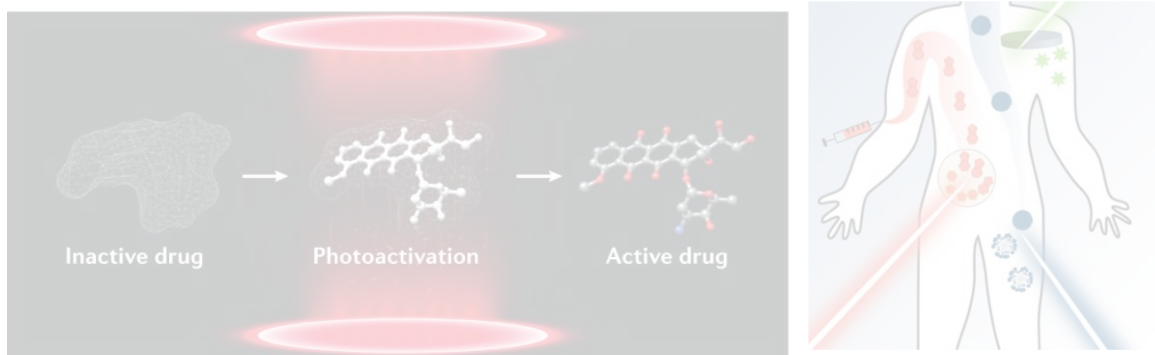
Protein-protein interactions, enzyme activity



Photocages: Application examples

- Control activity of a small molecules**

Activate drugs locally (targeted activation)



Nat. Rev. Chem., 5, 816. (2021); *Adv. Drug Deliv. Rev.* 171 (2021) 94.

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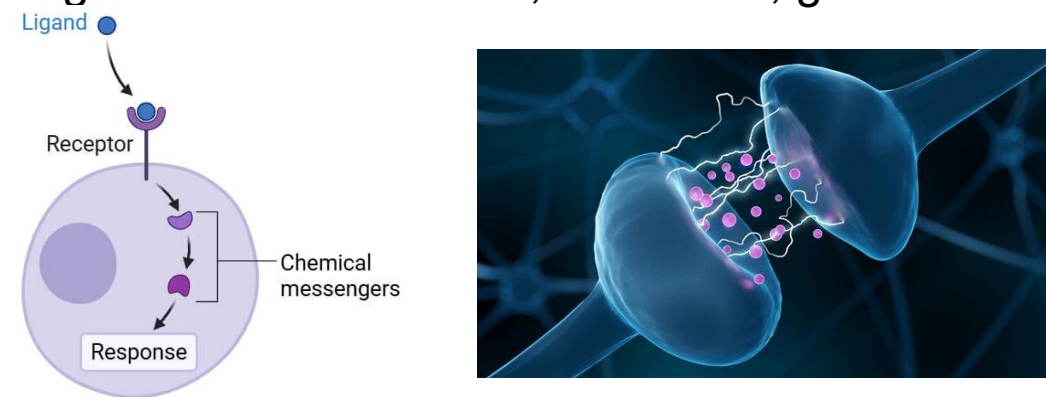
Protein-protein interactions, enzyme activity



Chem. Soc. Rev., 2021,50, 10403.

- Control cellular signalling**

Caged neurotransmitters, hormones, growth factors

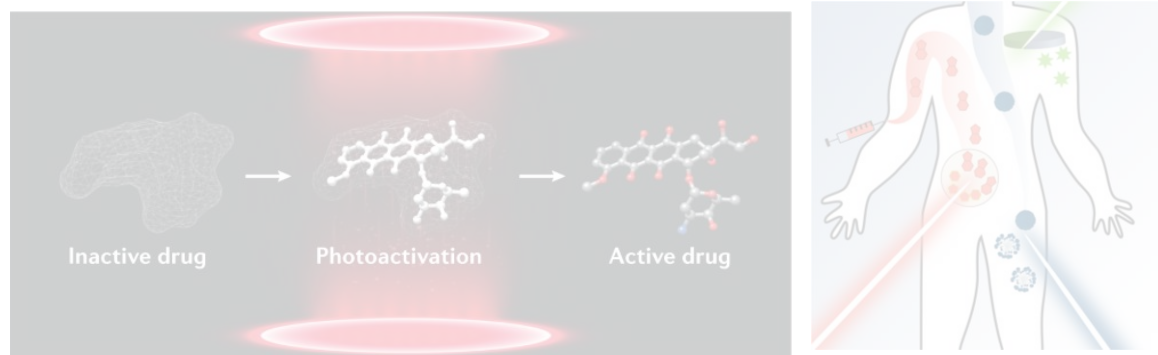


Curr. Opin. Struct. Biol. **2019**, 57, 164; *ChemBioChem* 2025, 26, e202500276

Photocages: Application examples

- Control activity of a small molecules**

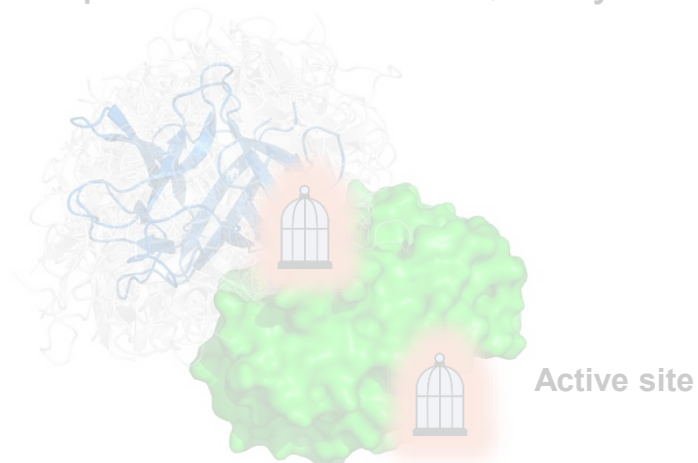
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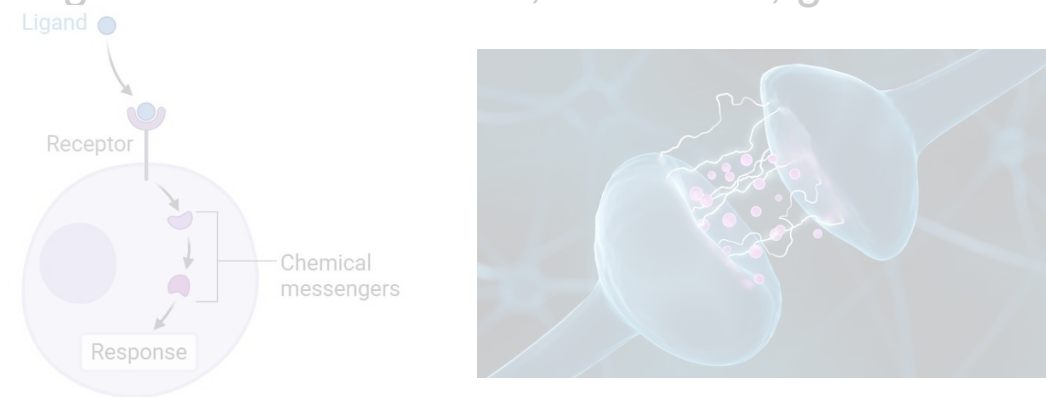
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- Control cellular signalling**

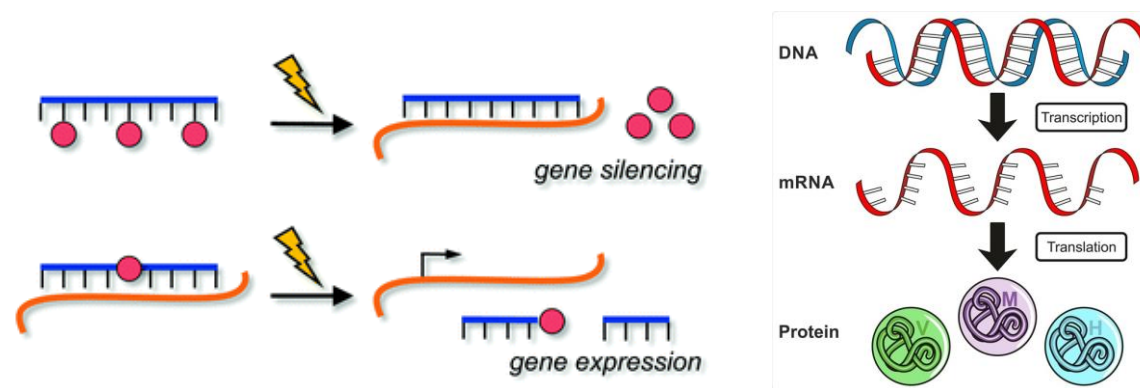
Caged neurotransmitters, hormones, growth factors



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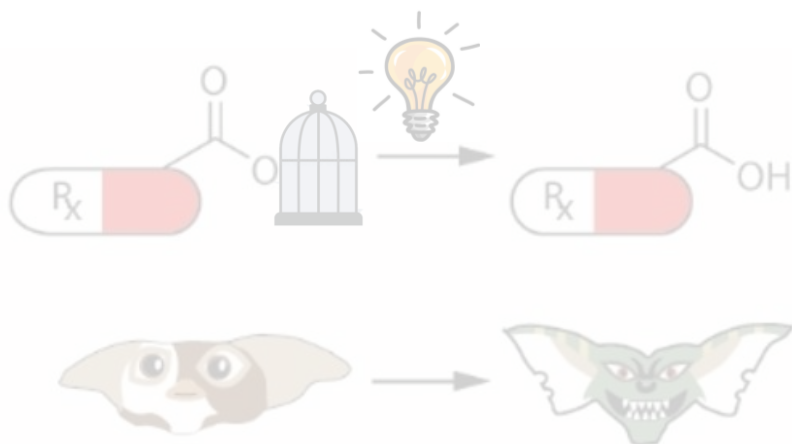
- Control nucleic acid activity**

Control gene expression and translation



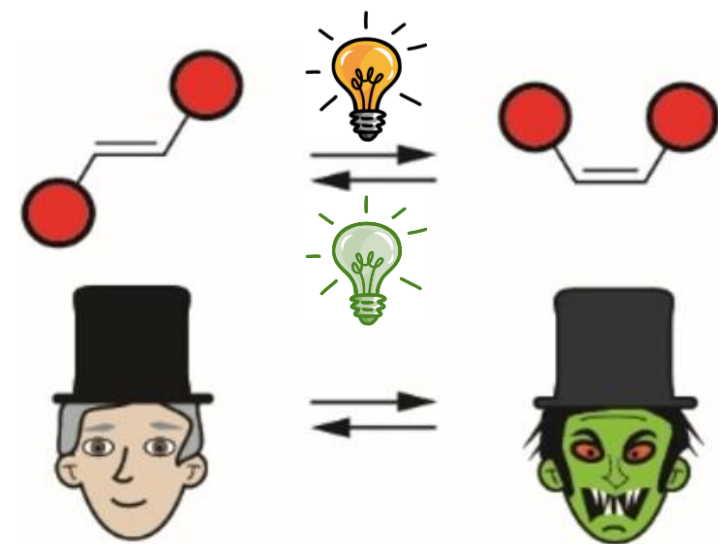
Chem. Soc. Rev., **2021**, 50, 13253; *ChemPhotoChem* **2025**, 9, e202500098

- Photocleavable protecting groups (PPGs)
= *Photocages*



irreversible

- Photoswitches

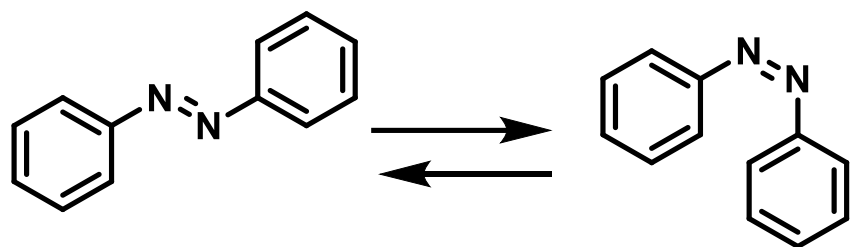


reversible

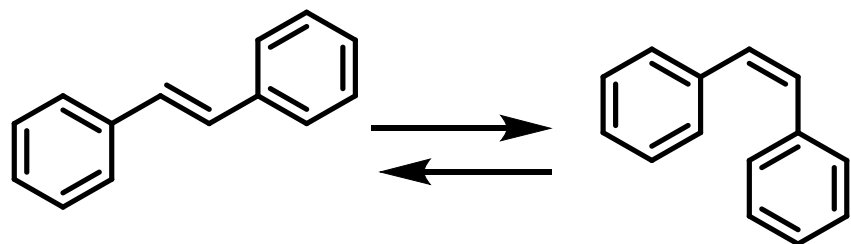
By mechanism type:

Trans/cis isomerization

Azobenzenes

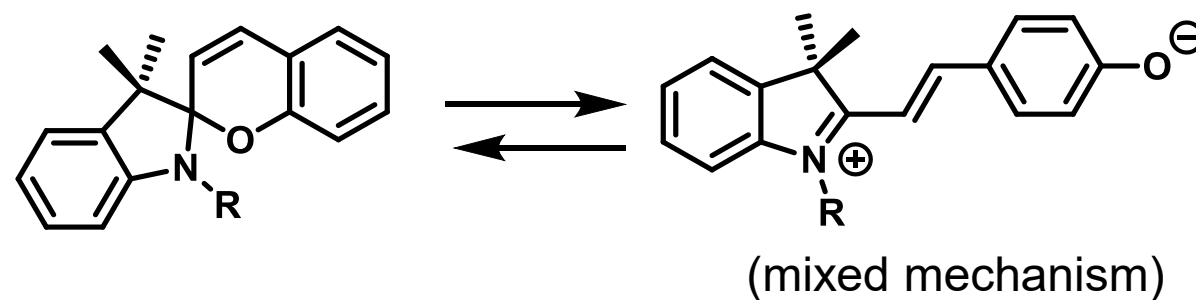


Stilbenes

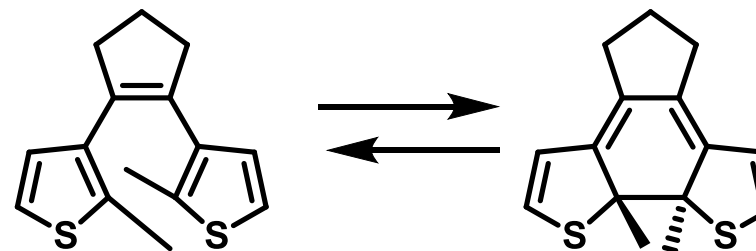


6π electrocyclization of triene system

Spiropyrans



Diarylethenes



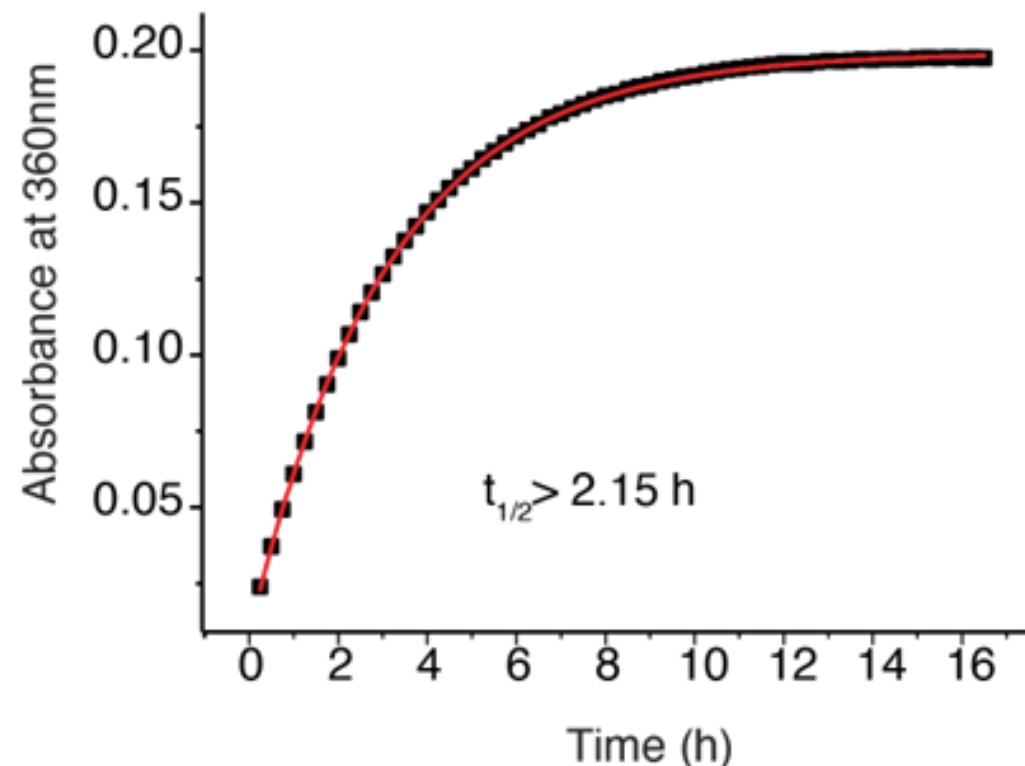
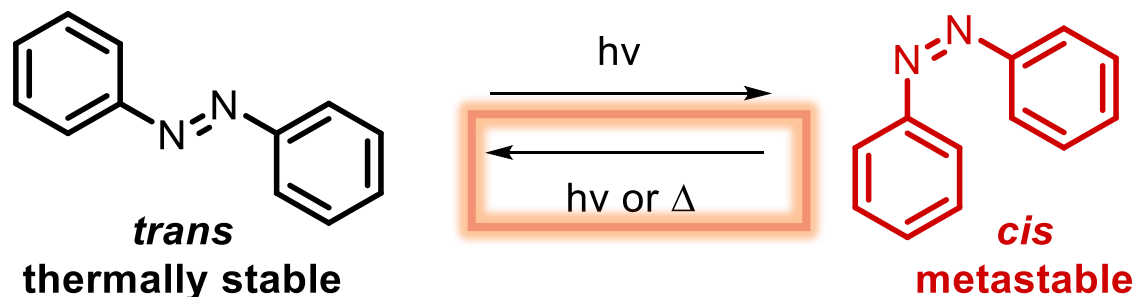
By thermal barrier for isomerization:

Thermal Type

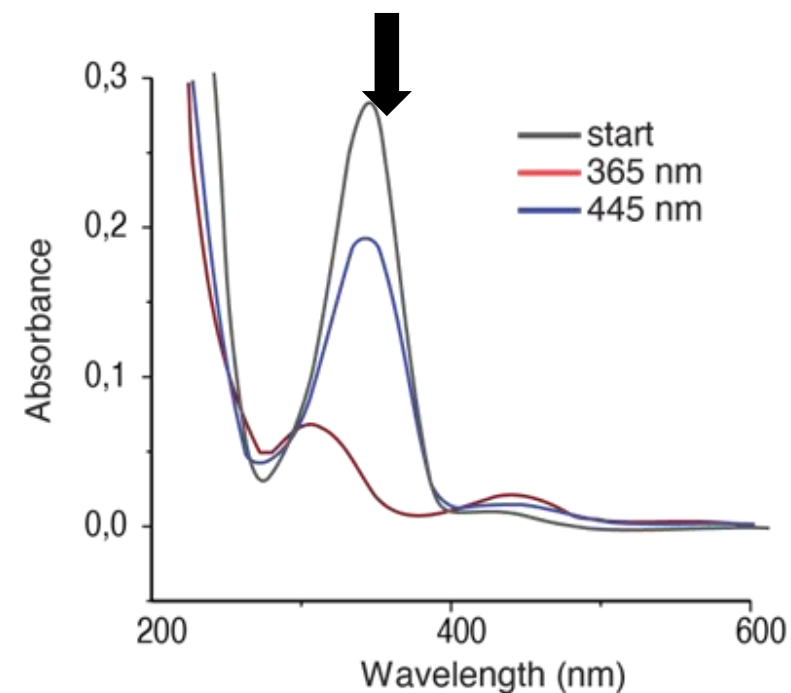
Photochemical Type

Photoswitch properties

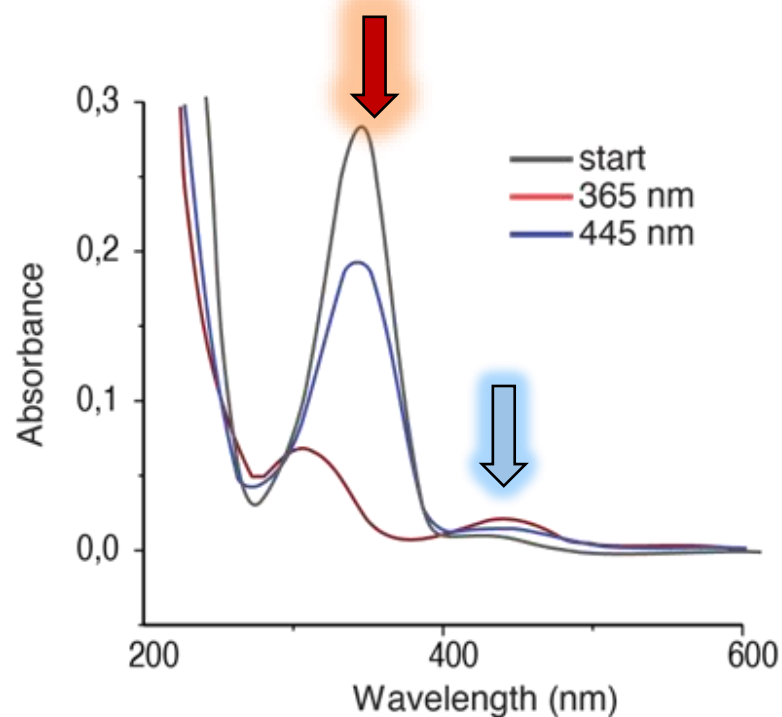
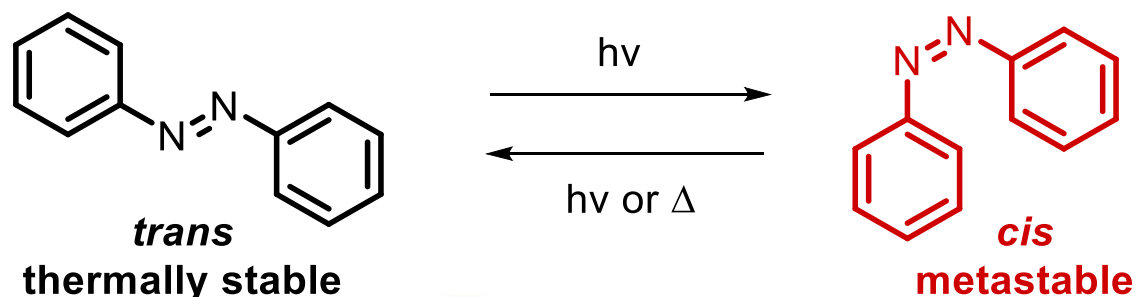
Thermal stability of metastable state (*half-life*)



*specific for compound, temperature, solvent

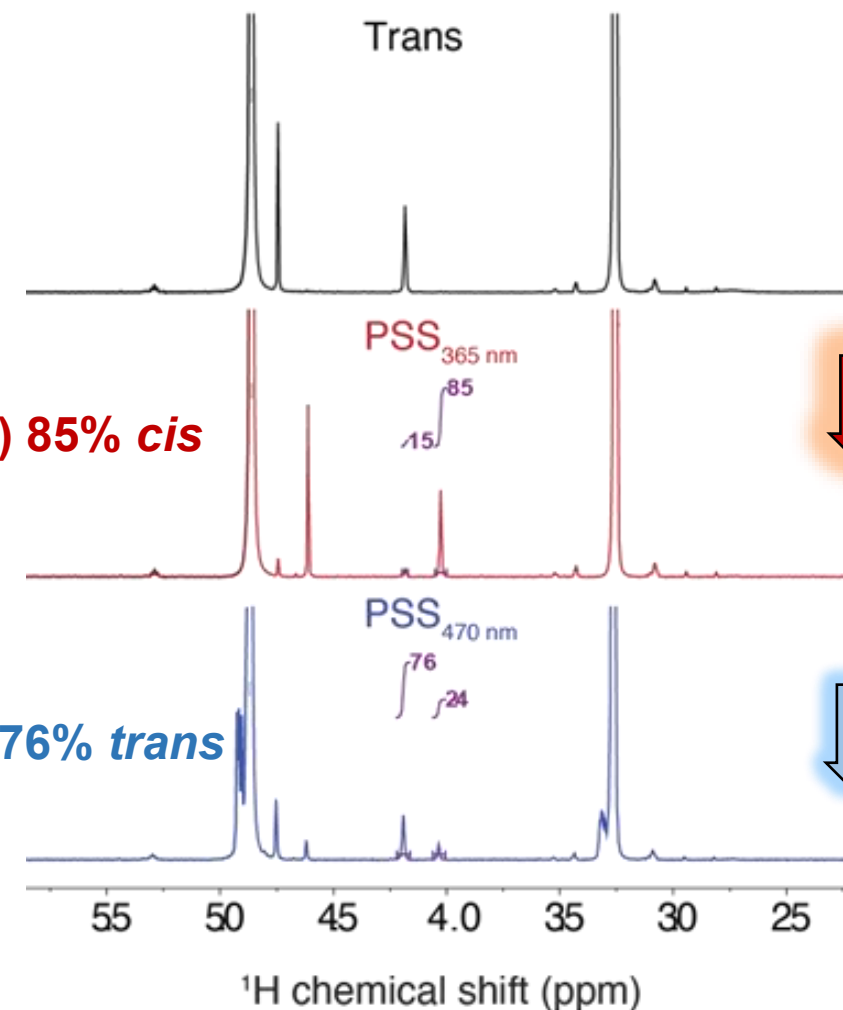


How much of each isomer? (*Photostationary state distribution (PSD/PSS)*)

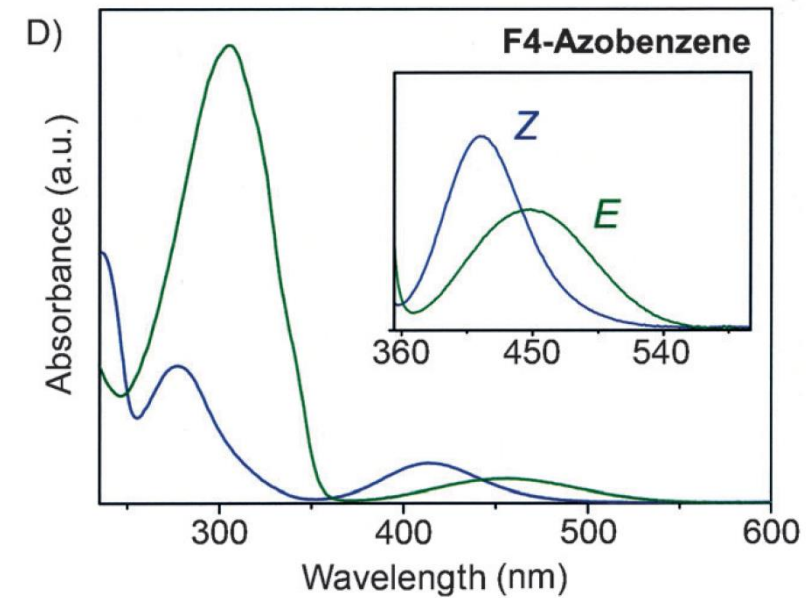
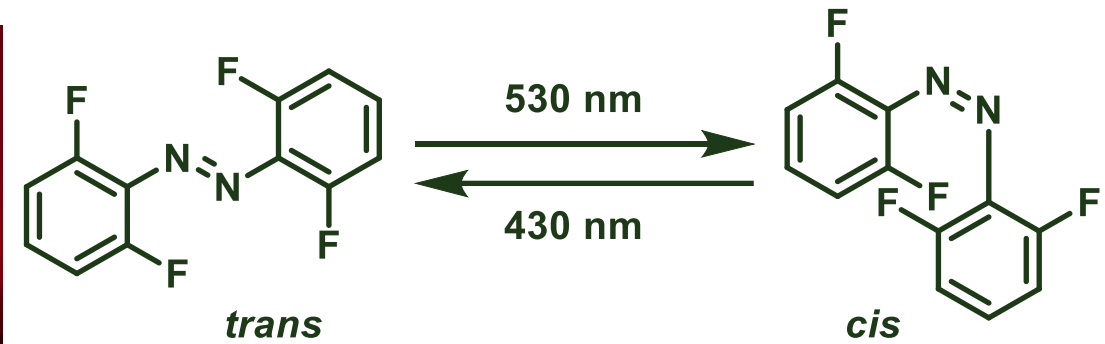


PSS(365 nm) 85% *cis*

PSS(445 nm) 76% *trans*



Wavelength(s)?



>possible to use visible light (530 and 430 nm)

Photoswitching efficiency? (*Quantum yield*)

- Time of irradiation
- Light/laser power



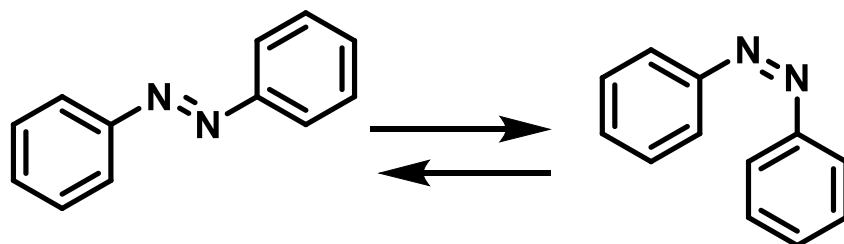
* dependent on switch, wavelength, solvent

Stability in physiological conditions

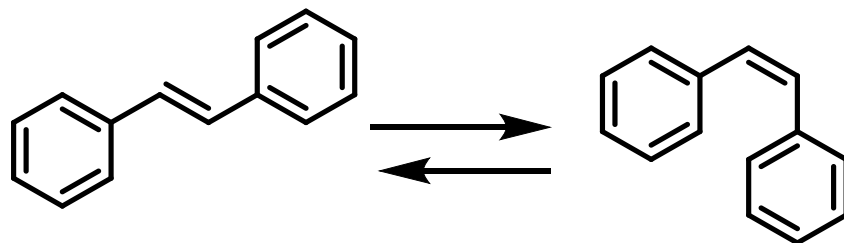
- Solubility



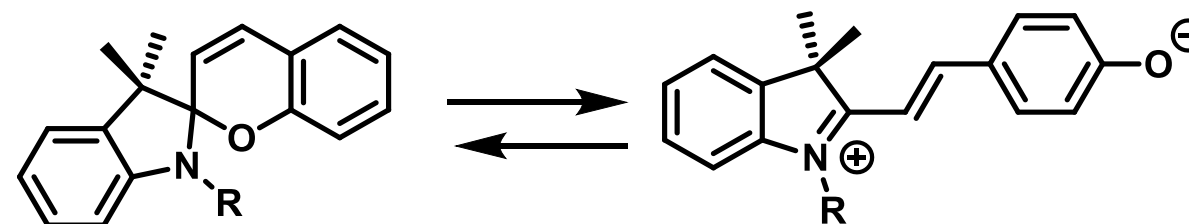
Azobenzenes



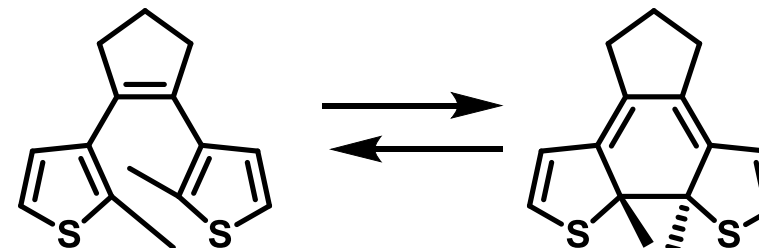
Stilbenes



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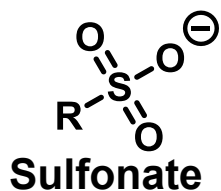
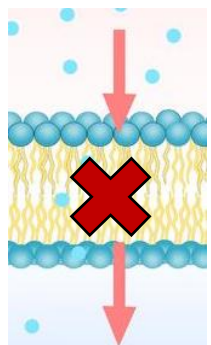


Diarylethenes

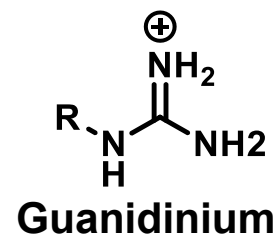
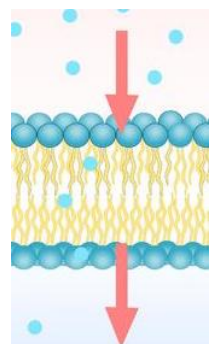


Stability in physiological conditions

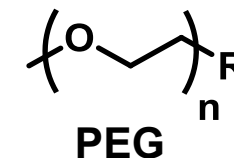
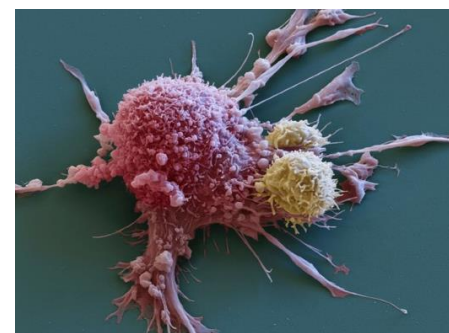
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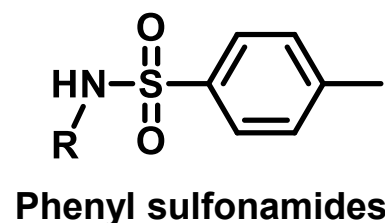
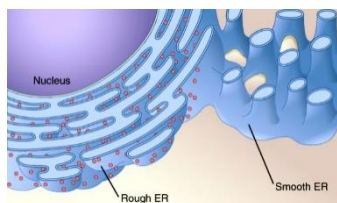
No passive uptake



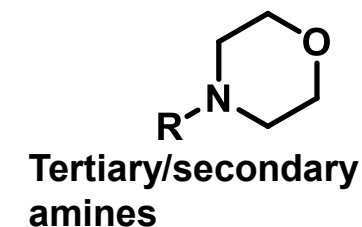
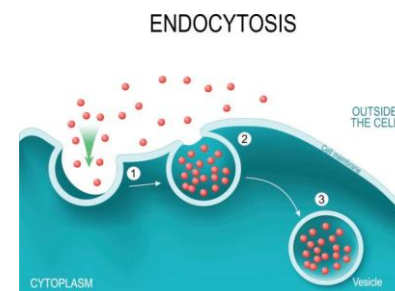
Great membrane permeability



accumulation in high-metabolism cells



Endoplasmic Reticulum (ER)

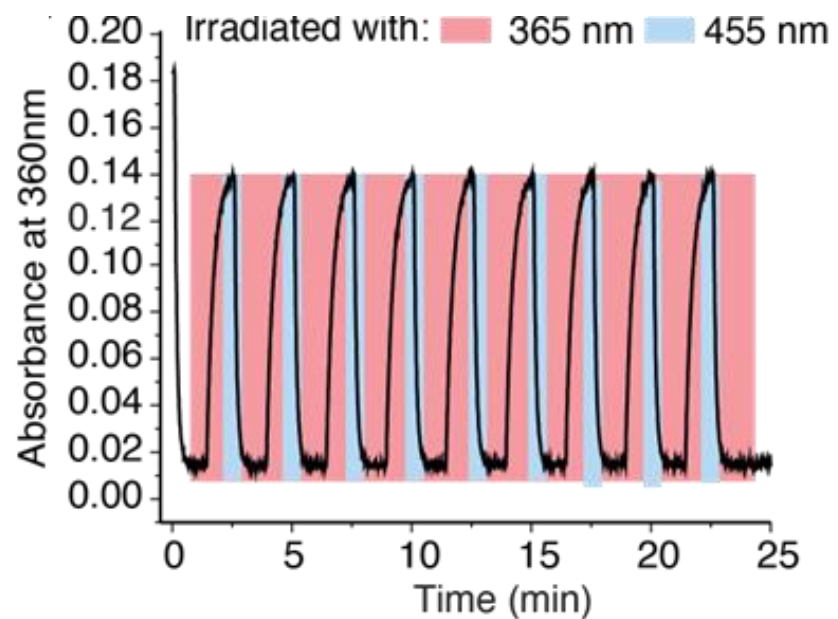


Lysosome/endosome



Stability in physiological conditions

- Stability + reversible photoswitching



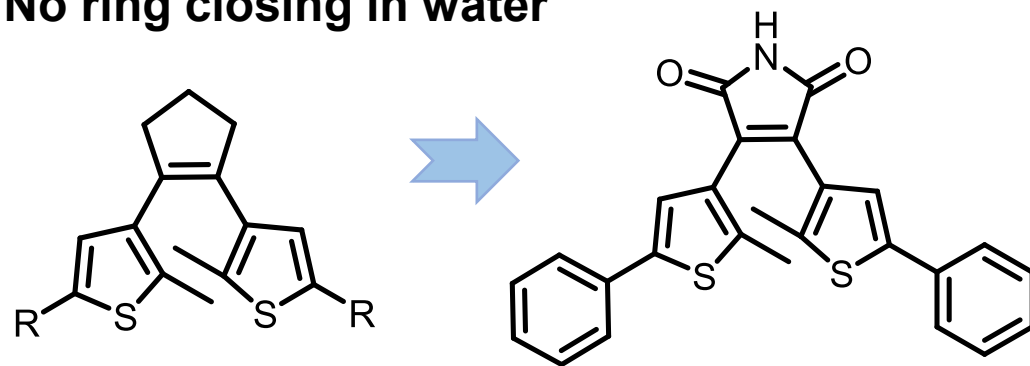


Photoswitch properties

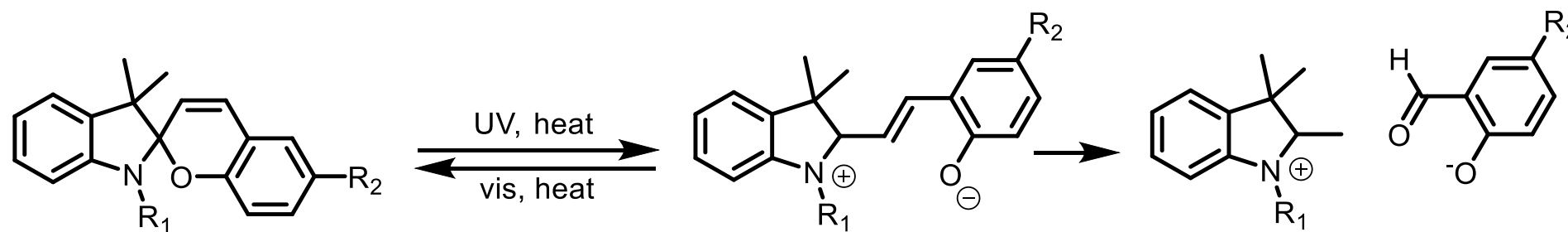
Stability in physiological conditions

- Stability + reversible photoswitching

No ring closing in water



Diarylethene (DTEs)



Spiropyran

hydrolysis of one isomer



- Thermal stability of metastable state (*half-life*)
- How much of each isomer? (*Photostationary state distribution (PSD/PSS)*)
- Wavelength?
- Photoswitching efficiency? (*Quantum yield*)
- Stability in physiological conditions