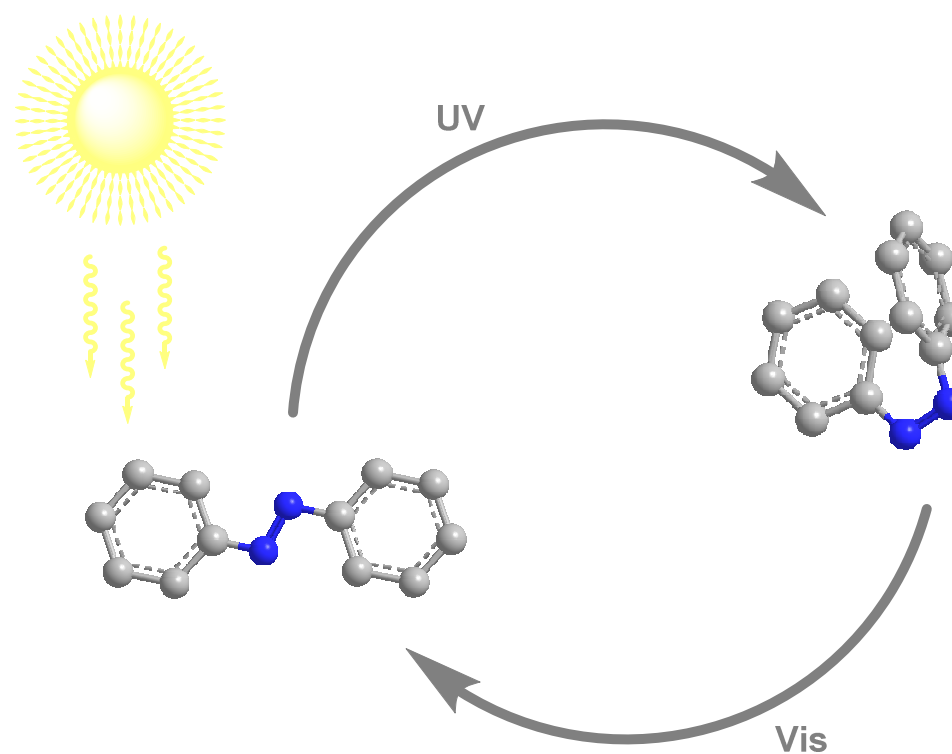


Organic Photochromic Compounds



Literature talk 11.07.2018

Lisa-Catherine Rosenbaum, Gaich group

Introduction

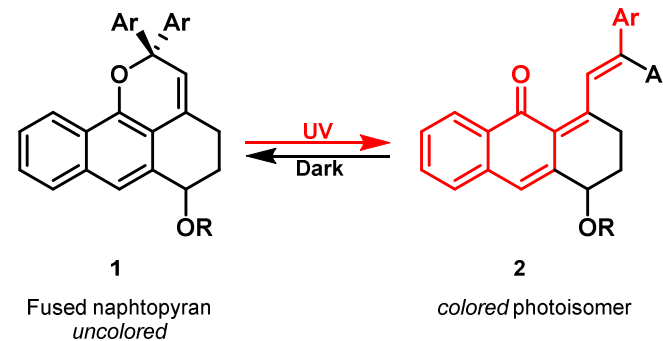
„**Photochromism**“ (from Greek *phos* = light, *chroma* = color; Hirshberg, 1950): light-induced reversible transformation of a chemical species between two forms with different absorption spectra



Photochromic action: • photo-induced darkening

• thermally induced reverse reaction which leads to initial transparent state

- from 1960s: glass lenses impregnated with silver halides and cuprous ions (photolytic decomposition of silver halide; reversible broad absorption band from UV to near IR)
- nowadays: organic photochromic lenses

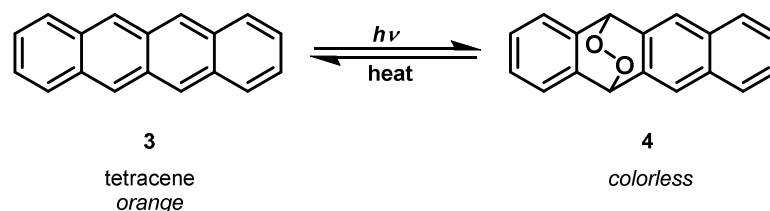


H. Dürr, H. Bouas-Laurent, *Photochromism: Molecules and Systems*, Elsevier Science, **2003**.

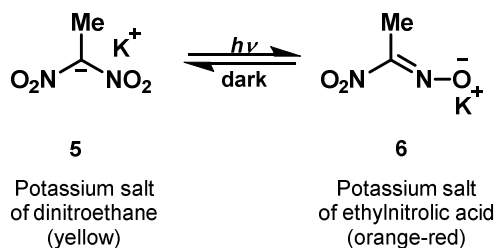
<https://www.zeiss.com/vision-care/int/better-vision/lifestyle-fashion/fast-dark-fast-clear-modern-self-tinting-lenses.html>, taken on 13.06.2018

Historical Survey

Photochromic phenomena first reported by **J. Fritsche (1867)**:



E. ter Meer (1876):



Chancel (1878), Hantzsch (1907): chromoisomerism (structure isomerism of "chromo-dinitro salts")

Fainzil'berg (1975): reversible formation of K-salt of ethylnitrolic acid

R. Hubbard, A. Kropf (1958): photoexcitation in the process of vision

1960s: development of physical methods (UV, IR, NMR, X-Ray, time-resolved and flash spectroscopy) and organic synthesis → mechanistic and synthetic studies;
limited potential applications (photodegradation), stagnation of research

1980s: fatigue-resistant photoswitches (spirooxazines and chromenes), fabrication and commercial application of photochromic lenses and other systems

J. Fritsche, *Comptes Rendus Acad. Sci.* **1867**, 69, 1035.

E. t. Meer, *Justus Liebigs Ann. Chem.* **1876**, 181, 1-22.

H. A., *Ber. Dt. Chem. Ges.* **1907**, 40, 1533-1555.

V. I. Slovetskii, V. P. Balykin, O. G. Strukov, Y. V. Salyn', A. A. Fainzil'berg, *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1975**, 24, 150-152.

Definition of Photochromism

reversible transformation between two forms:

- absorption of electromagnetic radiation (UV, Vis or IR)
- different absorption spectra & physical properties

- Most photochromic systems based on **unimolecular reactions**:
$$A \xrightleftharpoons[h\nu_2 \text{ or } \Delta]{h\nu_1} B$$
 e.g. rearrangements

thermodynamically stable form A transformed into form B by irradiation;
back reaction thermally activated (**photochromism of type T**) and/or photochemically (**photochromism of type P**)

positive photochromism: colorless or pale yellow form A and colored form B

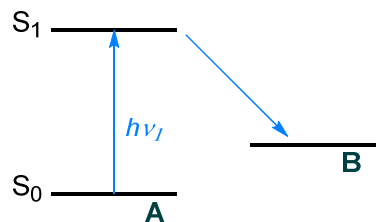
negative/inverse photochromism: $\lambda_{\max}(A) > \lambda_{\max}(B)$

- **bimolecular systems**:
$$A+B \xrightleftharpoons[h\nu_2 \text{ or } \Delta]{h\nu_1} P$$
 e.g. photocycloaddition reactions or electron transfer processes

- **Multiphotochromic systems**: more than two forms undergo photochemical and/or thermochemical interconversion

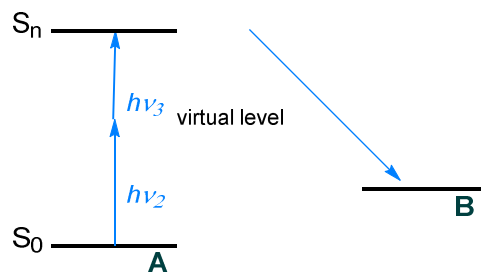
H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

One-Photon and Two-Photon Systems

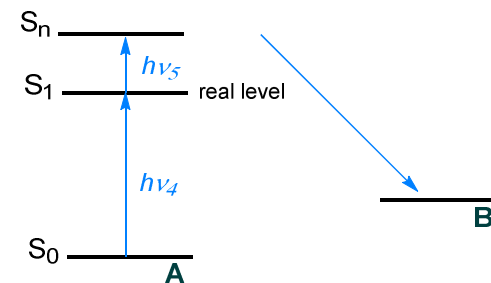


One-photon mechanism:

B formed from the singlet or triplet excited states of A

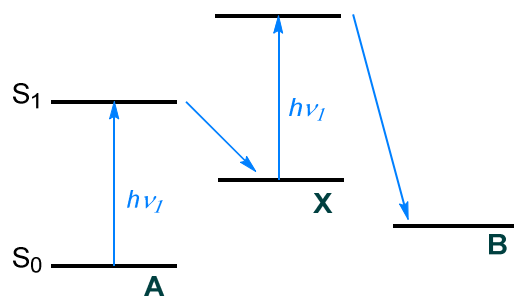


simultaneous two-photon absorption

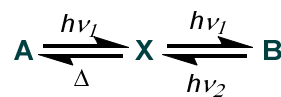


stepwise two-photon absorption

Absorption of two photons: B formed from an upper excited state of A
Excitation by subpicosecond laser pulses emitting high photon irradiance



stepwise two-photon process via a metastable intermediate

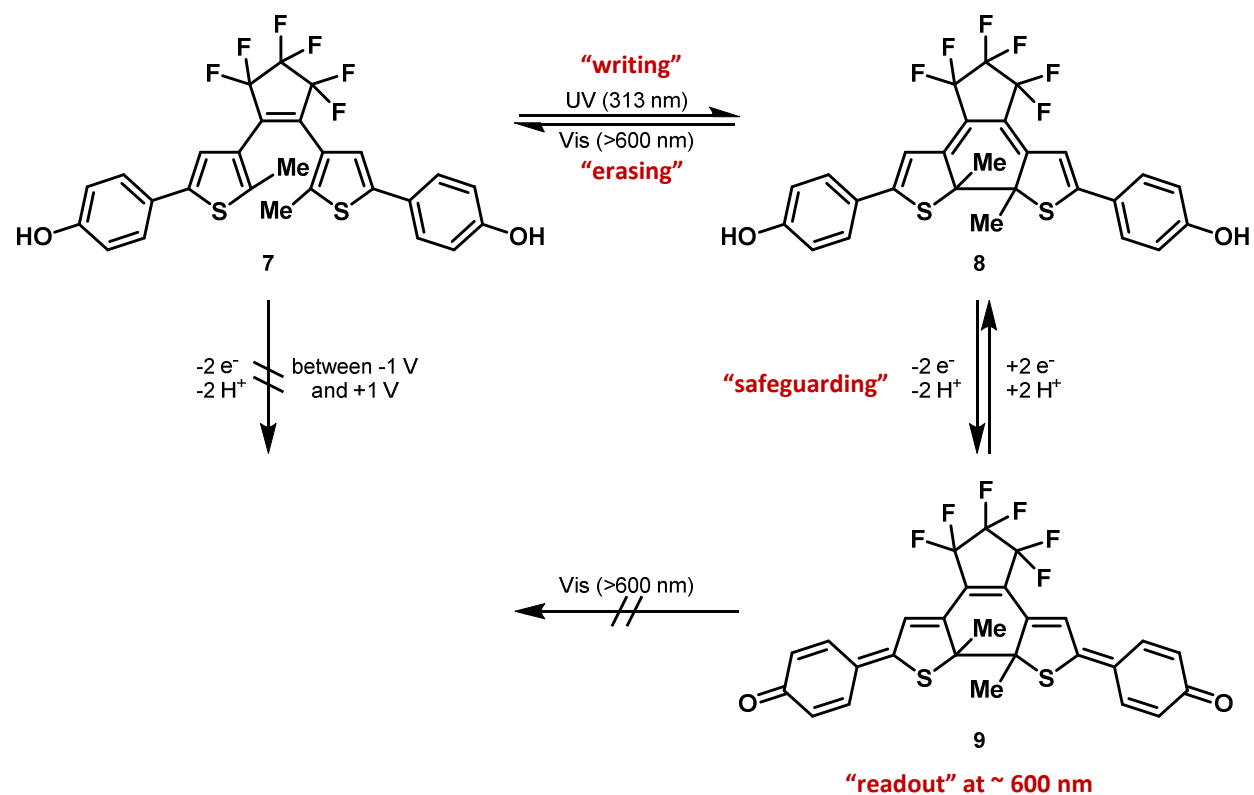


Excitation through **metastable intermediate**

Dual-Mode Photochromism

Excitation by two *different external stimuli* (e.g. light and electric current)

Dual-mode optoelectronic molecular switching device:

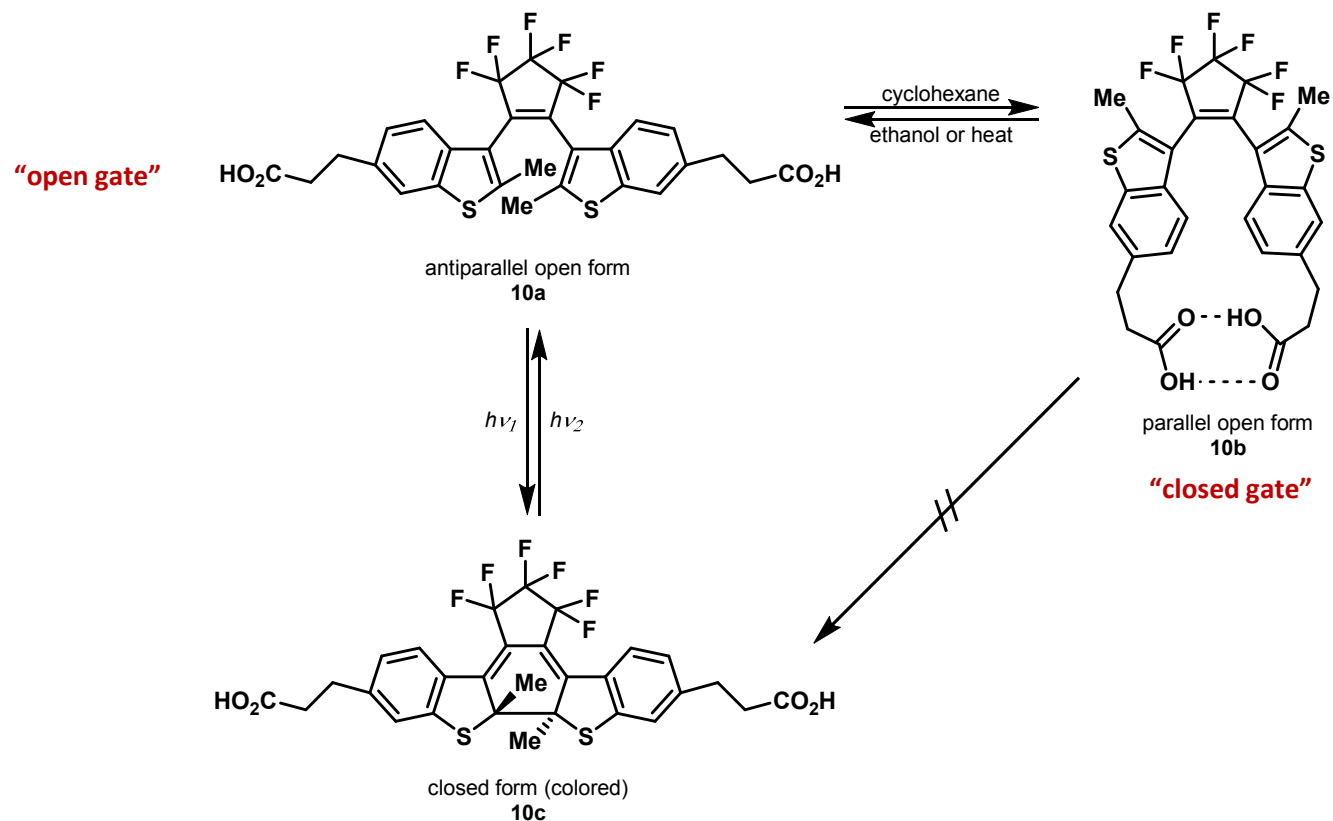


S. H. Kawai, S. L. Gilat, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1994**, 1011-1013.

Gated Photochromism

photochromic process depends on *inhibitory factor*:

Chemical or electrochemical, reversible transformation of one or both forms into non-photochromic form



M. Irie, O. Miyatake, K. Uchida, *J. Am. Chem. Soc.* **1992**, *114*, 8715-8716.

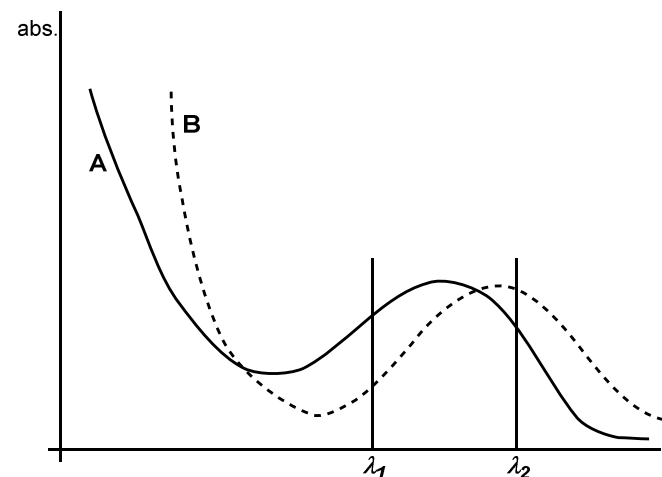
Chiral Switching Systems based on Photochromic Molecules

Diastereophotochromism: reversible *change of absorption spectra* between two diastereomers A and B

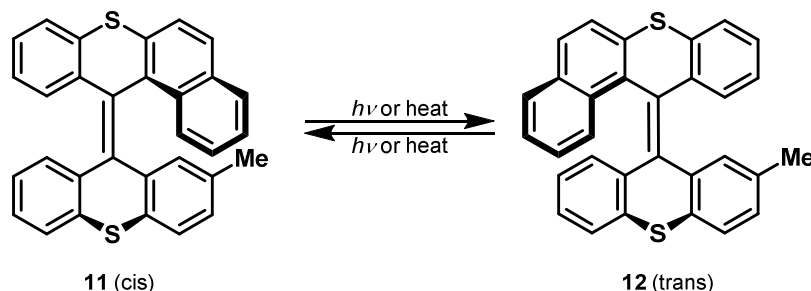
diastereomeric excess (E_{dia}) at photostationary state (PSS) depends on

- molar absorption coefficients (ϵ)
- interconversion quantum yields ($\Phi_{AB}(A \rightarrow B)$ & $\Phi_{BA}(B \rightarrow A)$):

$$[E_{dia}]_{pss} = \frac{[A] - [B]}{[A] + [B]} = \frac{(\epsilon_B \Phi_{BA} - \epsilon_A \Phi_{AB}) \lambda}{(\epsilon_B \Phi_{BA} + \epsilon_A \Phi_{AB}) \lambda}$$



Chirochromism: reversible *change of rotation of the plane of polarized light* between two chiral diastereomers of a photochromic system



- isomerization accompanied by simultaneous reversal of helicity
- **chiroptical molecular switch**

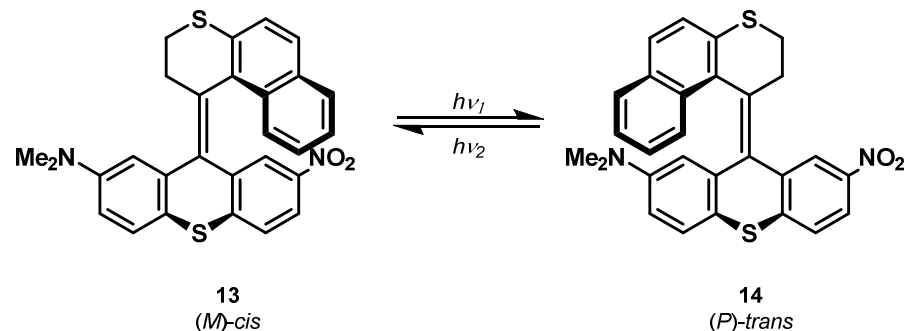
H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

B. L. Feringa, W. F. Jager, B. de Lange, *J. Chem. Soc., Chem. Commun.* 1993, 288-290.

Chiral Switching Systems based on Photochromic Molecules

Diastereomeric photobistable molecules:

photoisomerization by irradiation at two wavelengths λ_1 and λ_2



Enantiomeric photobistable molecules:

- interconversion of two enantiomers at single wavelength by changing handedness of light

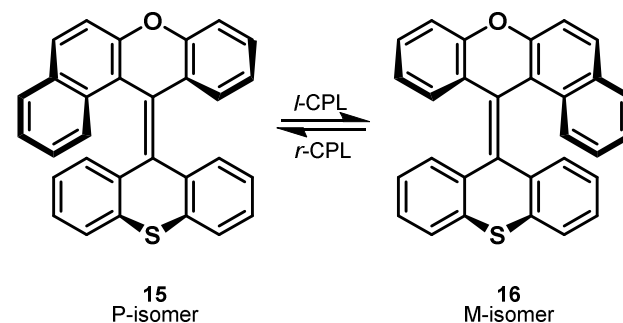
→ enantioselective switching in either direction

$$\text{enantiomeric excess in PSS: } ee_{PSS} = \frac{g}{2} = \frac{\Delta\epsilon}{2\epsilon}$$

g: Kuhn anisotropy factor

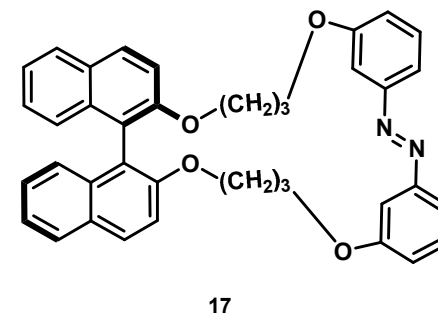
ϵ : molar absorption coefficient

- racemization of pure enantiomers by irradiation at specific wavelength



Achiral photobistable molecules in chiral assembly:

photoisomerization process induces changes in chirality of surrounding matrix



H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

B. L. Feringa, W. F. Jager, B. de Lange, *J. Chem. Soc., Chem. Commun.* 1993, 288-290.

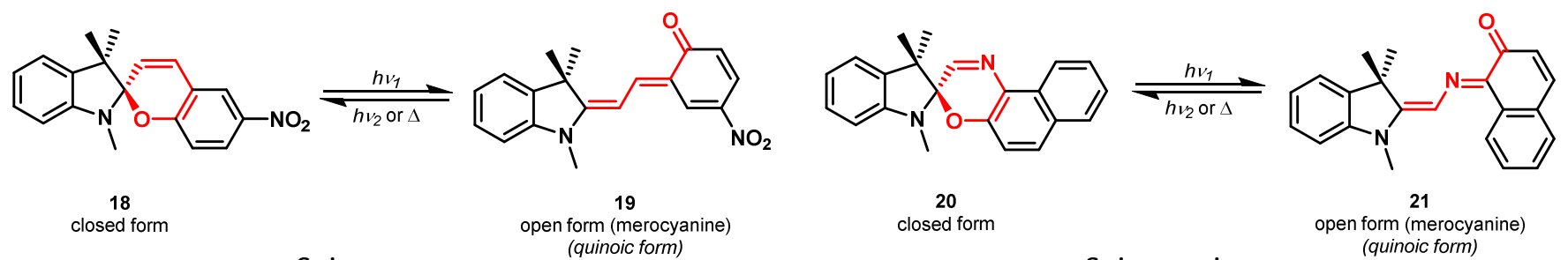
M. Mathews, R. S. Zola, S. Hurley, D.-K. Yang, T. J. White, T. J. Bunning, Q. Li, *J. Am. Chem. Soc.* 2010, 132, 18361-18366.

B. L. Feringa, W. R. Browne, *Molecular Switches*, Wiley, 2011.

Chemical Processes involved in Organic Photochromism

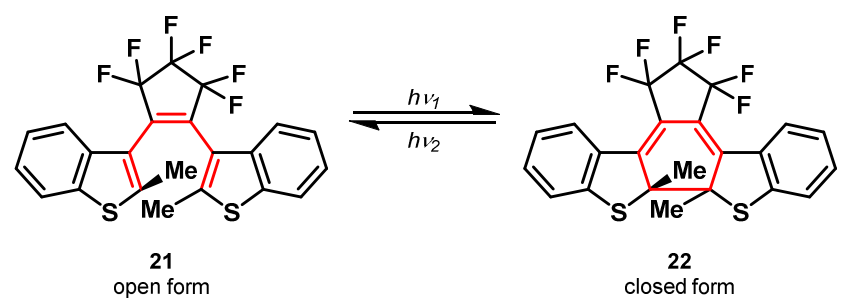
Pericyclic reactions

1) electrocyclizations, e.g. conrotatory 6π

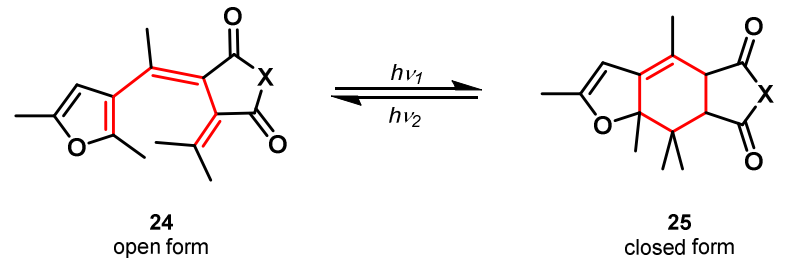


Spiropyrans

Spirooxazines



diarylethene derivatives



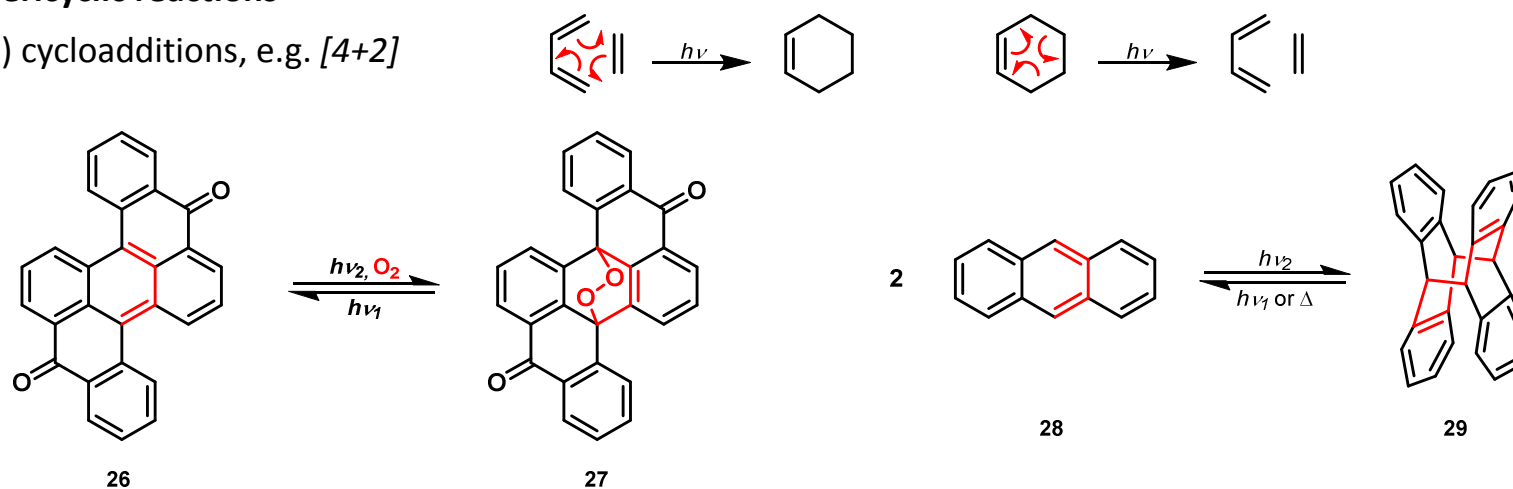
X=O (fulgides)
X=NR (fulgimides) Fulgides and fulgimides

H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

Chemical Processes involved in Organic Photochromism

Pericyclic reactions

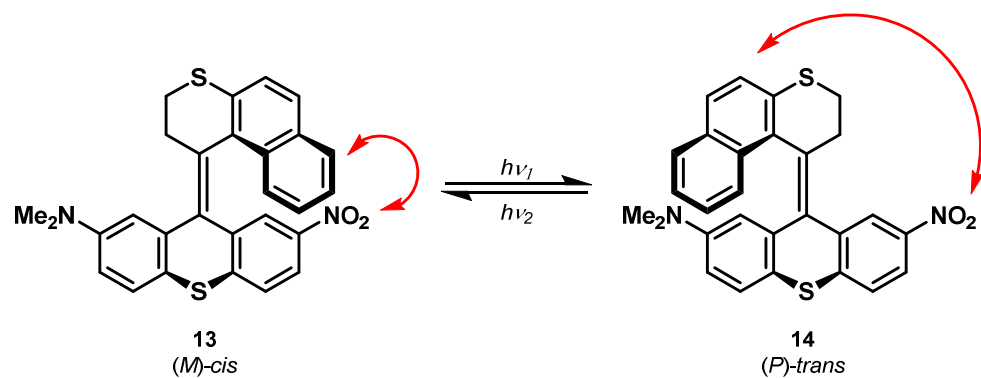
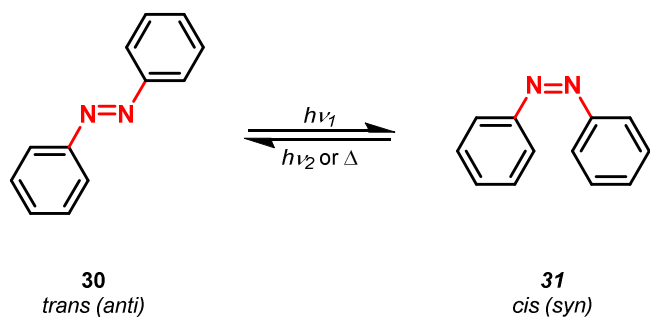
2) cycloadditions, e.g. [4+2]



Polycyclic aromatic compounds: [4+2] and [4+4] cycloadditions

Chemical Processes involved in Organic Photochromism

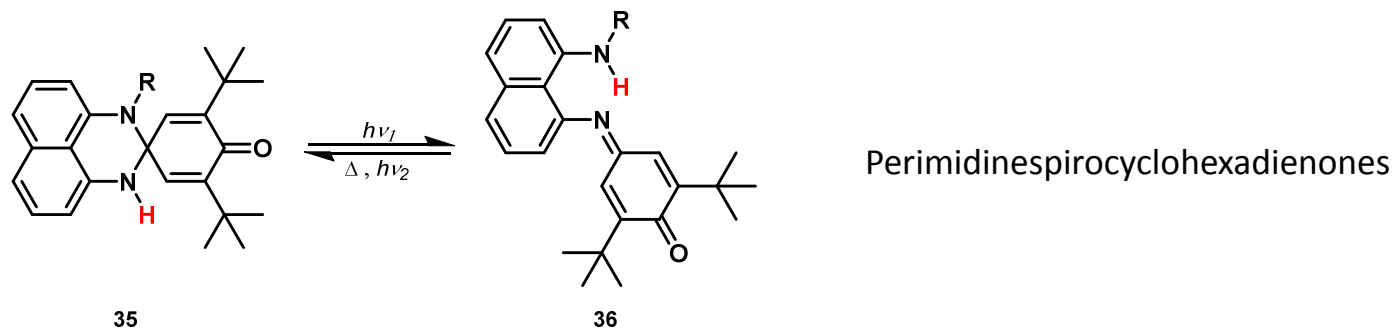
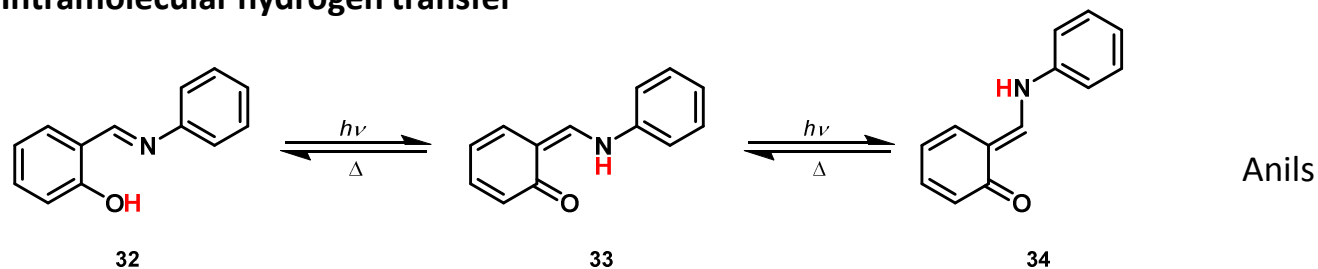
Cis-trans isomerizations of double bonds



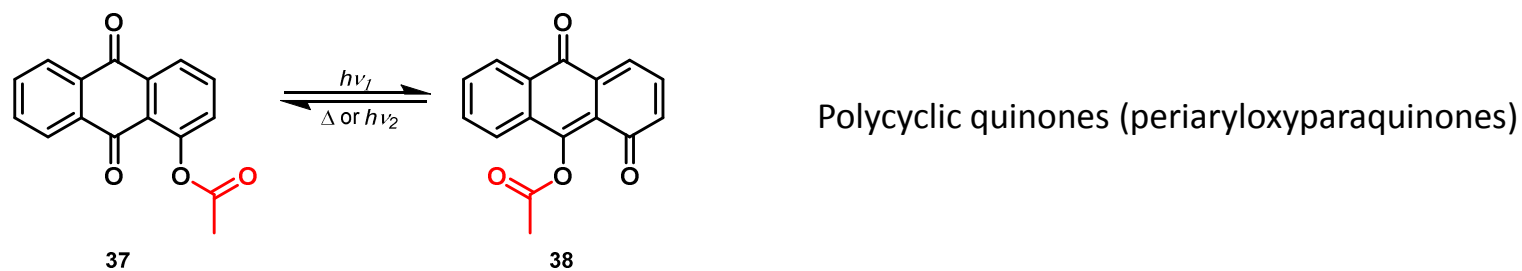
H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

Chemical Processes involved in Organic Photochromism

Intramolecular hydrogen transfer



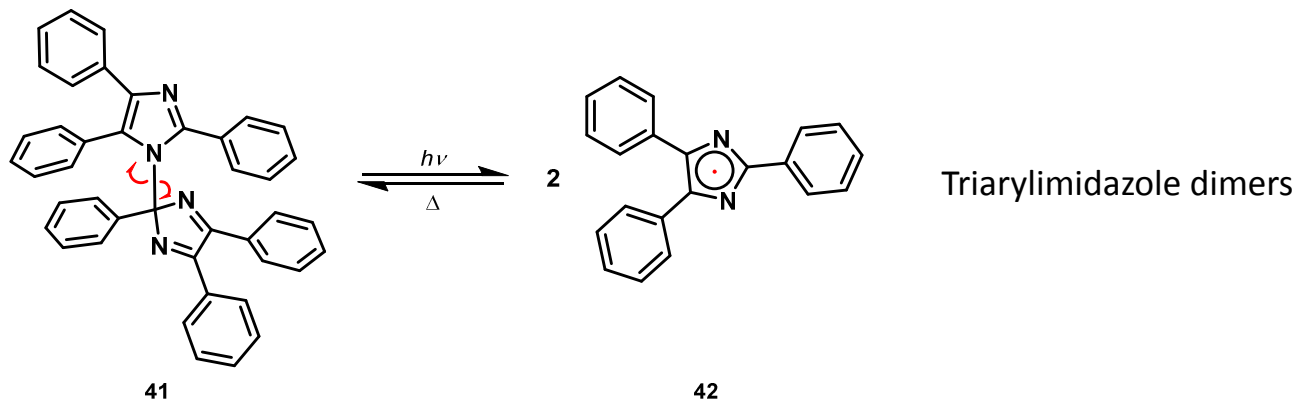
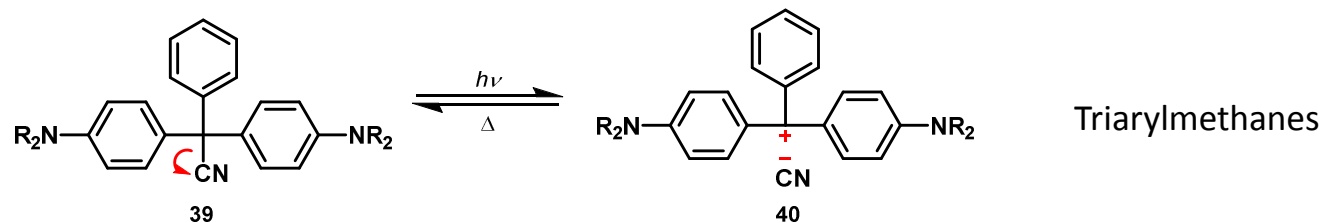
Intramolecular group transfer



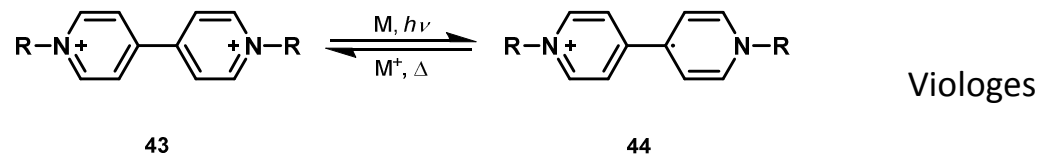
H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, 2001, p. 639.

Chemical Processes involved in Organic Photochromism

Dissociation processes (homolytic or heterolytic)



Electron transfers (oxido-reduction)



H. Yamashita, T. Ikezawa, Y. Kobayashi, J. Abe, *J. Am. Chem. Soc.* **2015**, *137*, 4952-4955
 H. Bouas-Laurent, H. Dürr, in *Pure Appl. Chem.*, Vol. 73, **2001**, p. 639.

Applications: Limitations

Colorability

ability of a photochromic material to color

follows Lambert-Beer in dilute solutions: $A_0(\lambda) = k\Phi_{col}\epsilon_B c_A$

$A_0(\lambda)$: initial absorbance at specific wavelength

K: proportionality constant

Φ_{col} : coloration quantum yield

ϵ_B : molar absorption coefficient of colored species

c_A : concentration of non-colored form

Fatigue

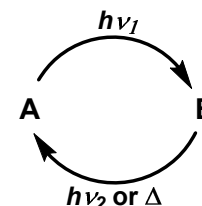
loss of performance over time: chemical degradation of material by photochemically activated oxidation processes/other photoinduced side reactions

Number of cycles & cyclability

$$y = (1 - x)^n$$

$$\approx 1 - nx$$

for very small x and very large n :



y : non-degraded fraction

x : degree of degradation

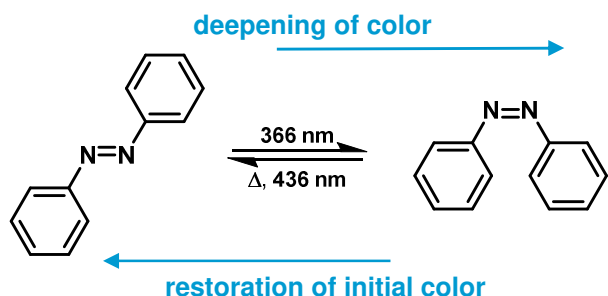
n : number of cycles

Z_{50} : number of cycles after which initial absorbance at specific wavelength is reduced by 50%

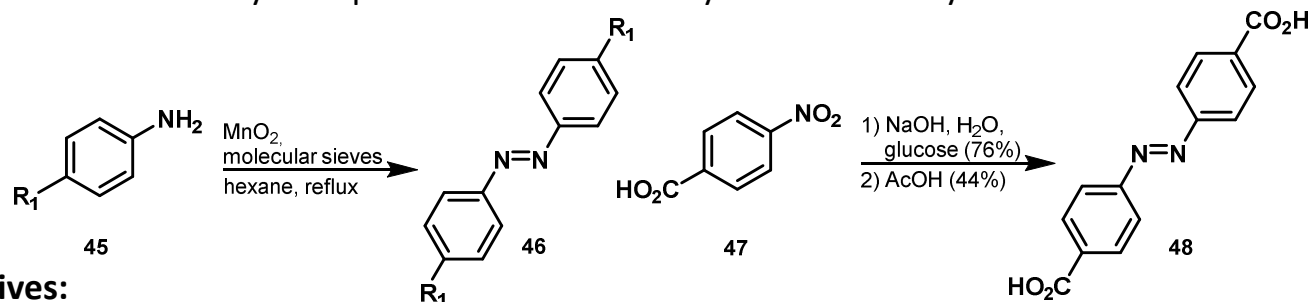
Half-life

$T_{1/2}$: time after which initial absorbance of colored form at specific wavelength during one cycle is reduced by 50% due to thermal bleaching

Applications: Azobenzene Photoswitches

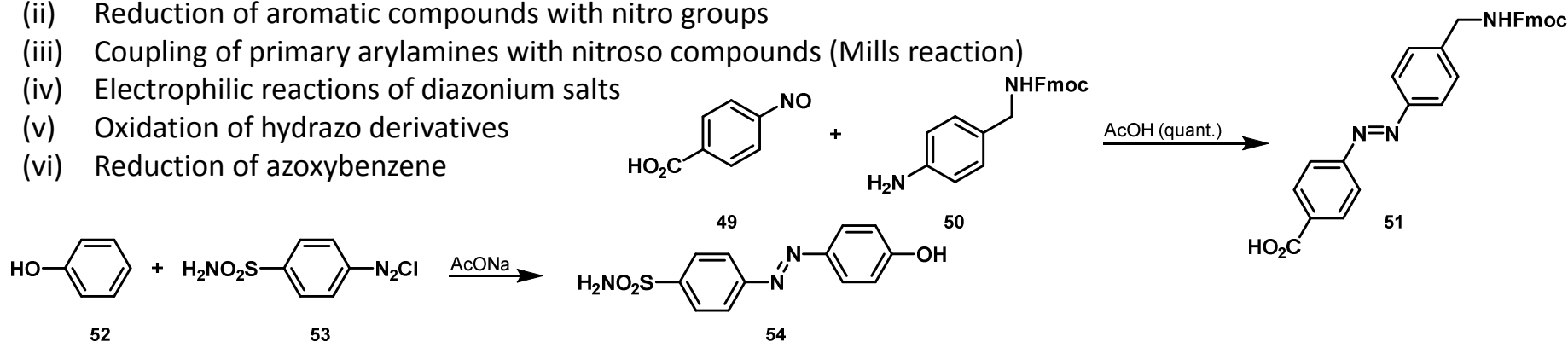


- photophysical and photochemical properties tunable by substituents
- E form thermodynamically more stable
- Z form kinetically stabilized
- very slow photooxidation to azoxybenzene as only side reaction



Synthesis of Azobenzene derivatives:

- Oxidation reaction of aromatic primary amines
- Reduction of aromatic compounds with nitro groups
- Coupling of primary arylamines with nitroso compounds (Mills reaction)
- Electrophilic reactions of diazonium salts
- Oxidation of hydrazo derivatives
- Reduction of azoxybenzene



F. Hamon, F. Djedaini-Pilard, F. Barbot, C. Len, *Tetrahedron* **2009**, *65*, 10105-10123.

H. Dürr, H. Bouas-Laurent, *Photochromism: Molecules and Systems*, Elsevier Science, **2003**.

M. Dong, A. Babalhavaeji, S. Samanta, A. A. Beharry, G. A. Woolley, *Acc. Chem. Res.* **2015**, *48*, 2662-2670.

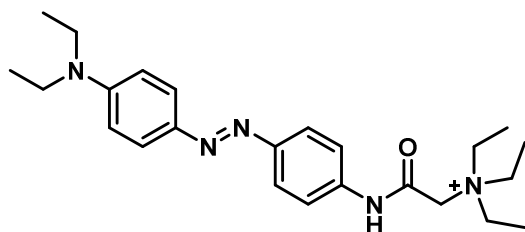
Applications: Azobenzene Photoswitches

Photoisomerization of azobenzene compounds to control specific biological targets *in vivo*:

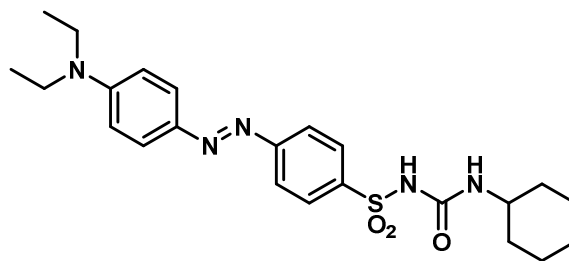
optically controlled drugs (“photopharmaceuticals”)

- nontoxic
- stable to hydrolysis and reduction of azo moiety
- absorption wavelengths in red, far-red or near infrared region required to pass through body tissue

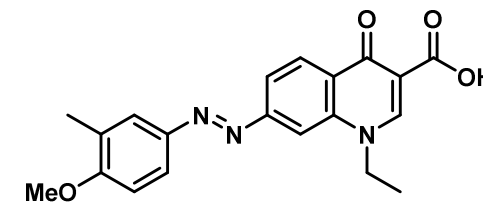
Site-directed mutagenesis or biorthogonal ligation methods to tether azobenzene derivatives to protein targets in living cells:



55
DENAQ
(ion channel photoswitch)



56
JB253
(sulfonyleurea receptor photoswitch)



57
azo-quinolone
photoswitchable antibiotic
“azologized” drugs

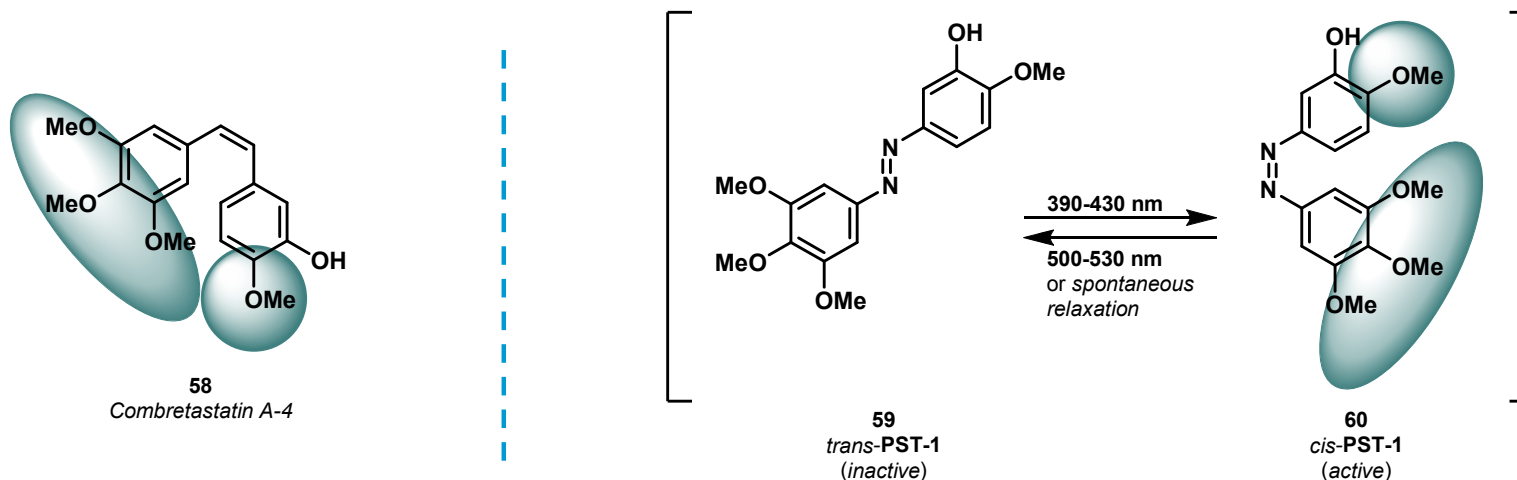
light-switchable receptors, K⁺-channels, kinases, transcription factors etc.

M. Dong, A. Babalhavaeji, S. Samanta, A. A. Beharry, G. A. Woolley, *Acc. Chem. Res.* **2015**, *48*, 2662-2670.

M. Borowiak, W. Nahaboo, M. Reynders, K. Nekolla, P. Jalinot, J. Hasserodt, M. Rehberg, M. Delattre, S. Zahler, A. Vollmar, D. Trauner, O. Thorn-Seshold, *Cell* **2015**, *162*, 403-411.

Applications: Azobenzene Photoswitches

Possibility of *in vivo* optical control of a drug:



nonspecific microtubule inhibitor
 • *cis*-stilbenoid binds to 'colchicine' site on tubulin

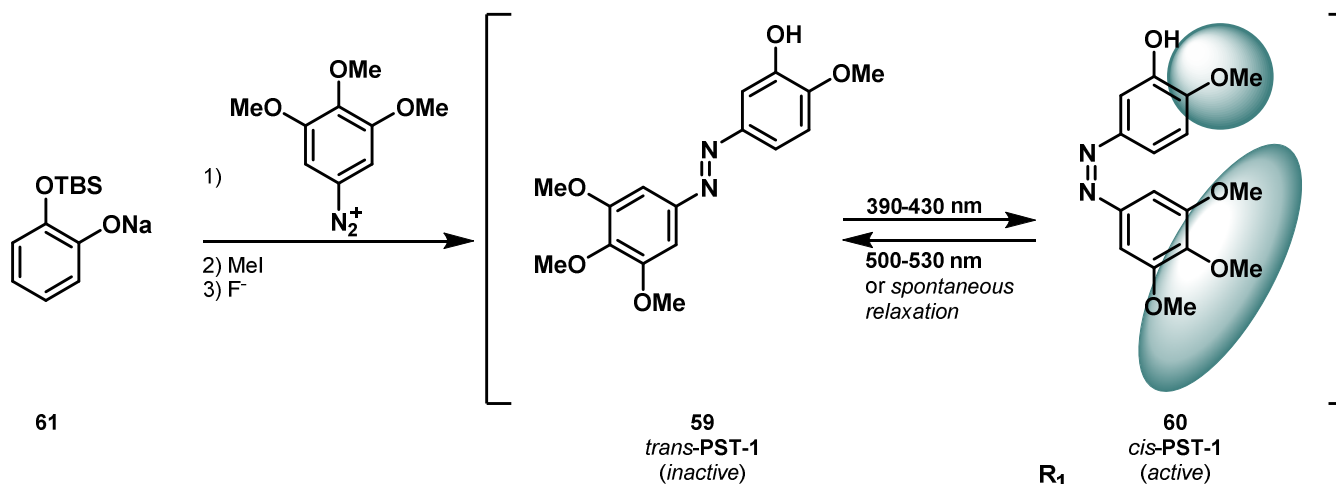
modified form of anti-cancer drug *Combretastatin A-4*

- less toxic to healthy cells by photoactivation
- reversible, *in situ* switching over many off/on cycles
- *cis*-PST-1 approx. 250 times more toxic than *trans* form
- spontaneous *cis-trans* relaxation in dark

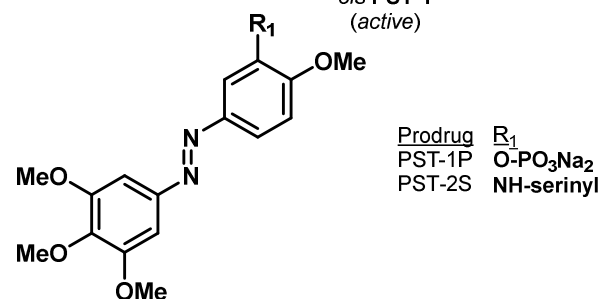
M. Borowiak, W. Nahaboo, M. Reynders, K. Nekolla, P. Jalinot, J. Hasserodt, M. Rehberg, M. Delattre, S. Zahler, A. Vollmar, D. Trauner, O. Thorn-Seshold, *Cell* **2015**, *162*, 403-411.
 G. R. Pettit, S. B. Singh, E. Hamel, C. M. Lin, D. S. Alberts, D. Garcia-Kendal, *Experientia* **1989**, *45*, 209-211.

Applications: Azobenzene Photoswitches

Synthesis of PSTs by diazonium coupling:



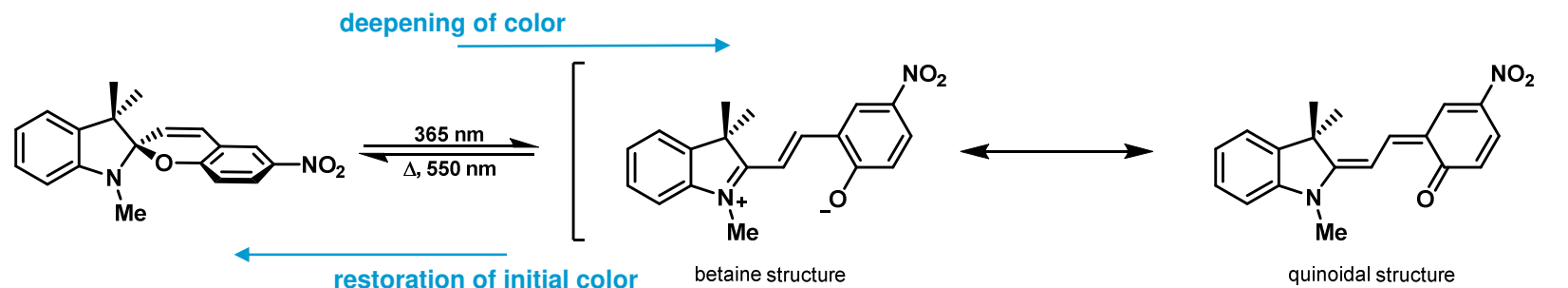
PST-1P and PST-2S as “azologues” of two nonspecific combretastatin prodrugs (Phase III clinical trials):



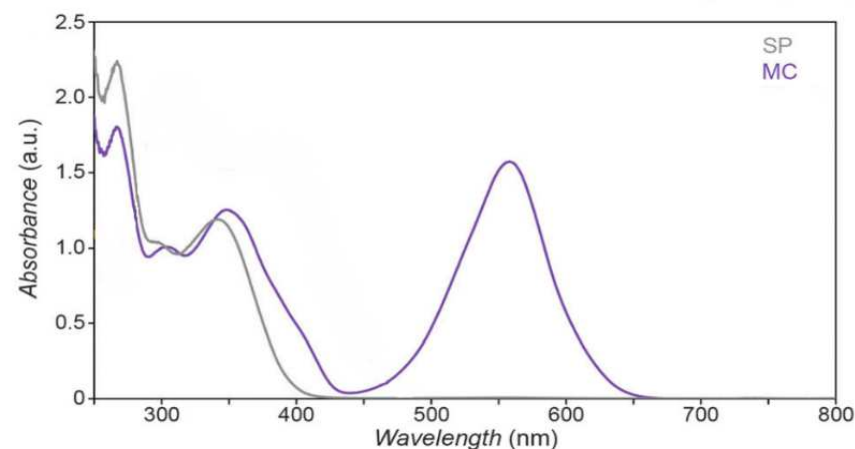
- PSTs reproduce microtubule disrupting, cytostatic and cytotoxic effects of CDIs (shown *in vitro*, *in cellulo* & *in vivo*)
- spatial and temporal targeting with full reversibility

M. Borowiak, W. Nahaboo, M. Reynders, K. Nekolla, P. Jalinot, J. Hasserodt, M. Rehberg, M. Delattre, S. Zahler, A. Vollmar, D. Trauner, O. Thorn-Seshold, *Cell* **2015**, *162*, 403-411.

Applications: Spiropyran Photoswitches



- photochromic isomers with vastly different properties (dipole moment, emission, basicity etc.)
 - subunits perpendicular
 - two localized transitions in absorption spectrum (π - π^* in indoline and chromene moieties)
 - reversible isomerization process triggered by different stimuli (light, solvent, metal ions, pH, temperature, redox potential, mechanical force)
 - in polar environments: negative photochromism (MC stabilized)
- hybrid of resonance forms (zwitterionic/quinoidal)
 - planar structure
 - single, delocalized transition shifted to visible region



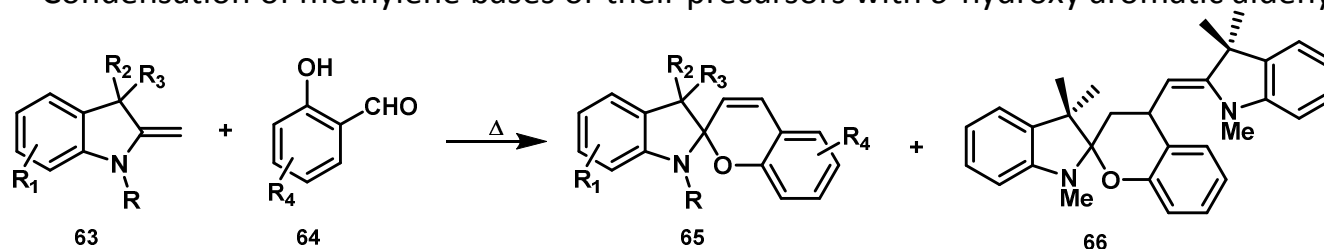
R. Klajn, *Chem. Soc. Rev.* **2014**, 43, 148-184.

B. S. Lukyanov, M. B. Lukyanova, *Chem. Heterocycl. Compd.* **2005**, 41, 281-311.

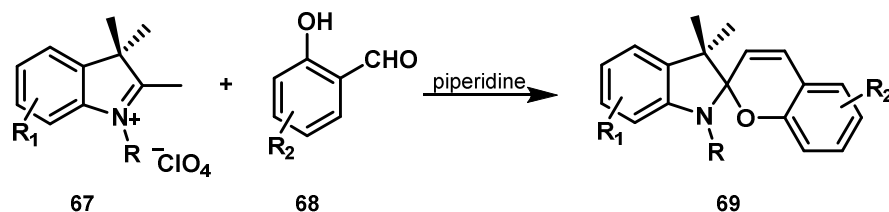
Applications: Spiropyran Photoswitches

Synthesis of Spiropyran derivatives:

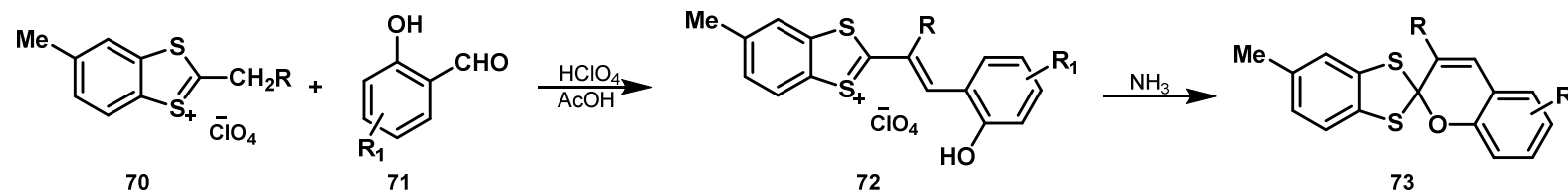
(i) Condensation of methylene bases or their precursors with *o*-hydroxy aromatic aldehydes



quaternary indolenylium salt + organic base:



(ii) Condensation of *o*-hydroxy aromatic aldehydes with salts of heterocyclic cations containing active methylene groups, isolation of intermediate styryl salts and base-mediated ring closure



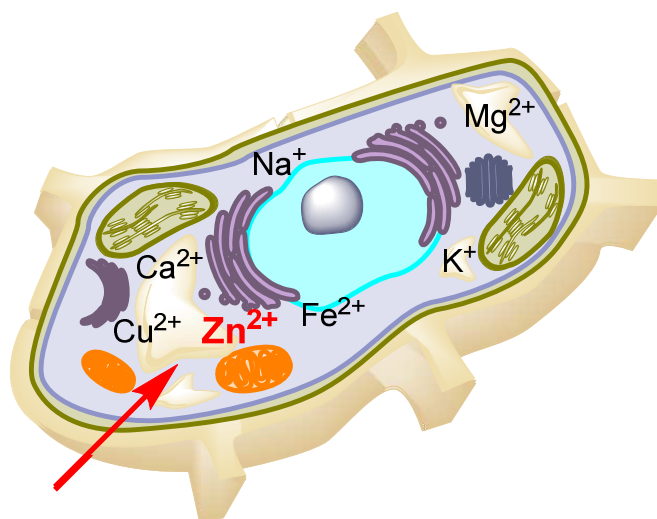
R. Klajn, *Chem. Soc. Rev.* **2014**, 43, 148-184.

B. S. Lukyanov, M. B. Lukyanova, *Chem. Heterocycl. Compd.* **2005**, 41, 281-311.

Applications: Spiropyran Photoswitches

Biologically compatible fluorescent Zn^{2+} ion sensors:

- insight into fundamental biological processes (e.g. osmotic regulation, catalysis, metabolism, biomineralization, signaling)
- extend knowledge of ion flux and associated ion fluctuations in various acute & chronic disease processes
- harmful & protective effects of intracellular Zn^{2+} during endothelial cell function and apoptosis

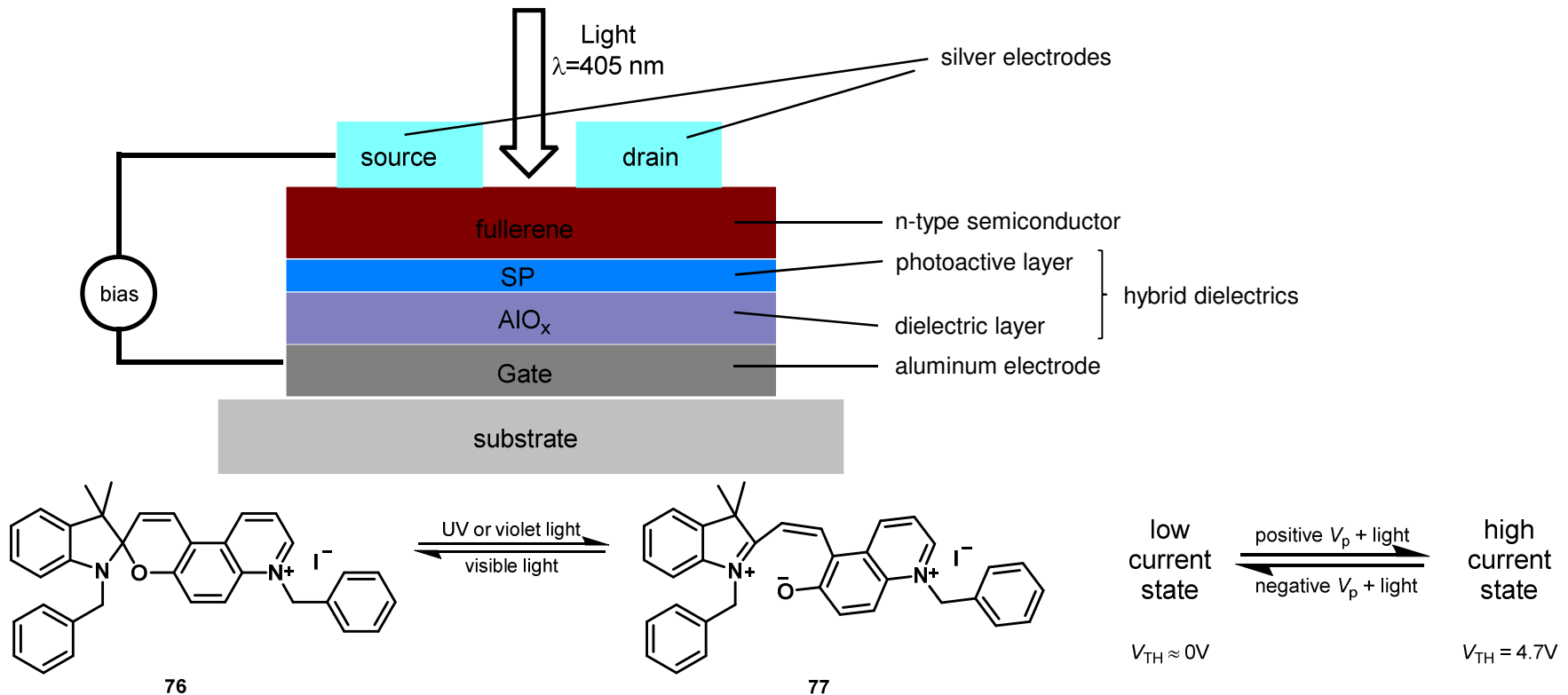


- low toxicity
- aqueous solubility & cell permeability
- reversible ion sensing
- fast photoswitching in aqueous solution
- high switching reliability & low fatigue
- high signal-to-background ratio
- high selectivity for Zn^{2+}

S. Heng, P. Reineck, A. K. Vidanapathirana, B. J. Pullen, D. W. Drumm, L. J. Ritter, N. Schwarz, C. S. Bonder, P. J. Psaltis, J. G. Thompson, B. C. Gibson, S. J. Nicholls, A. D. Abell, *ACS Omega* **2017**, 2, 6201-6210.

Applications: Spiropyran Photoswitches

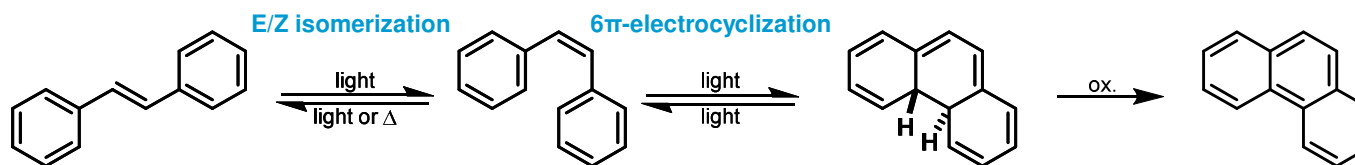
Transistor-type, rewritable optical memory elements using spiropyran-based salts as light-sensitive materials:
e.g. light-receiving organic field-effect transistor (OFET)



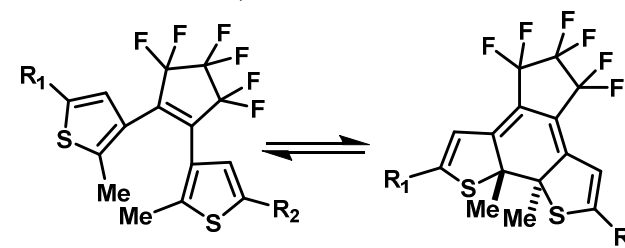
→ significant changes of electrical characteristics of conducting channel by photoinduced isomerization of photochromic compound at dielectric/semiconductor interface

L. A. Frolova, A. A. Rezvanova, B. S. Lukyanov, N. A. Sanina, P. A. Troshin, S. M. Aldoshin, *J. Mater. Chem. C* **2015**, *3*, 11675-11680.[1] Y.
Wakayama, R. Hayakawa, H.-S. Seo, *Sci. Technol. Adv. Mater.* **2014**, *15*, 024202.

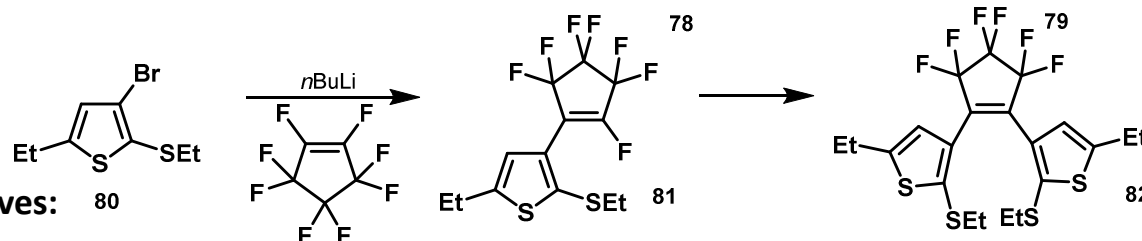
Applications: Diarylethene Photoswitches



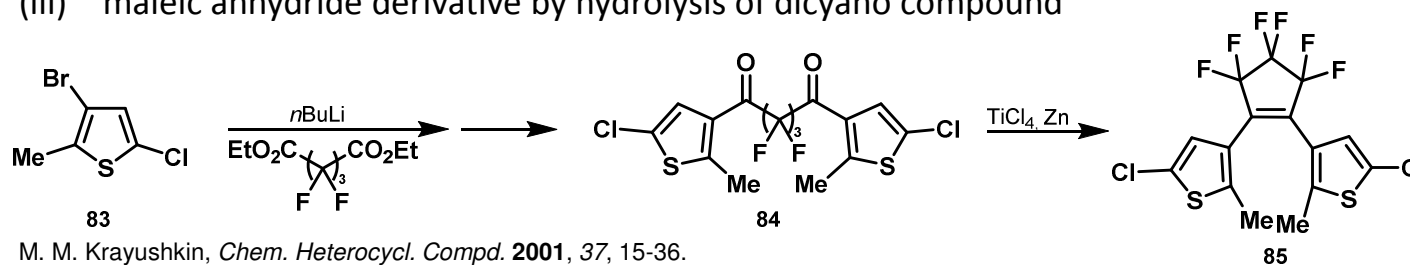
- prevention of *cis-trans* isomerization
- stabilization against oxidation
- elimination of low thermal stability
- improvement of thermal and chemical stability, stability to hydrolysis and fatigue resistance



Synthesis of Diarylethene derivatives:



- (i) lithium halogen exchange and addition to octafluorocyclopentene
- (ii) intramolecular McMurry coupling
- (iii) maleic anhydride derivative by hydrolysis of dicyano compound



M. M. Krayushkin, *Chem. Heterocycl. Compd.* **2001**, 37, 15-36.

B. L. Feringa, R. A. van Delden, N. Koumura, E. M. Geertsema, *Chem. Rev.* **2000**, 100, 1789-1816.

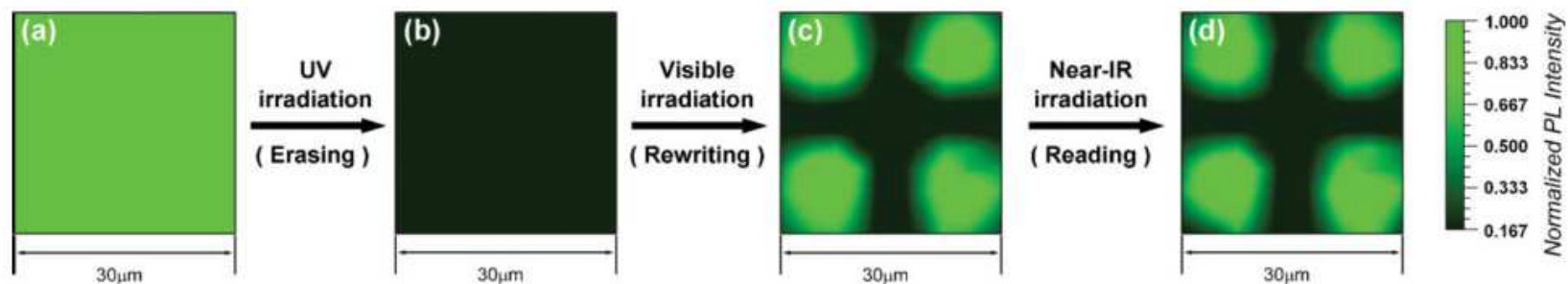
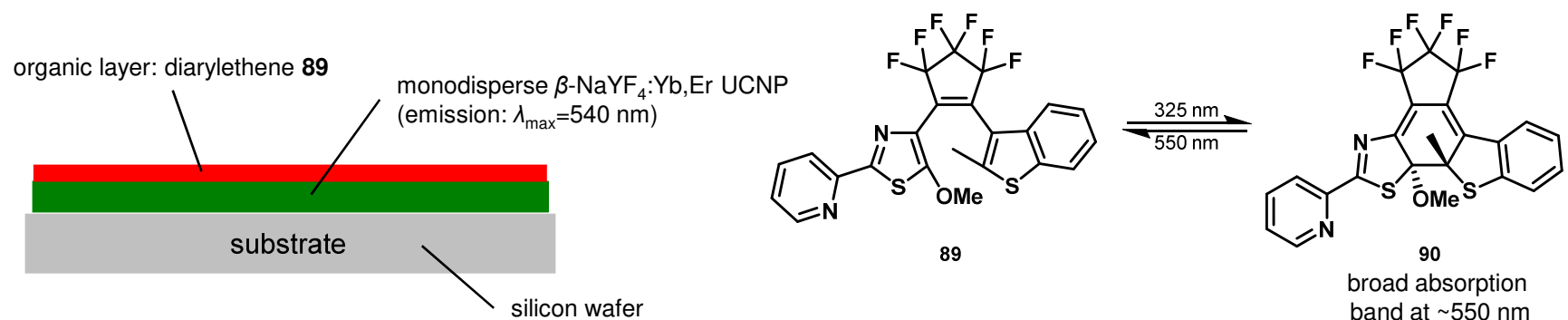
M. Irie, M. Mohri, *J. Org. Chem.* **1988**, 53, 803-808.

M. Irie, *Chem. Rev.* **2000**, 100, 1685-1716.

Applications: Diarylethene Photoswitches

Rewritable optical storage with nondestructive readout using photochromic diarylethenes:

- high uniformity & periodicity of recording material required → atomic or molecular lattices or superlattices
e.g. rare-earth-doped UCNPs (inorganic photoluminescent layer)
- robust diarylethene derivative as photoluminescence modulator → rewritable digital storage functionalities



→ Writing, erasing, reading under single beam irradiation: compatibility with current CD/DVD drivers

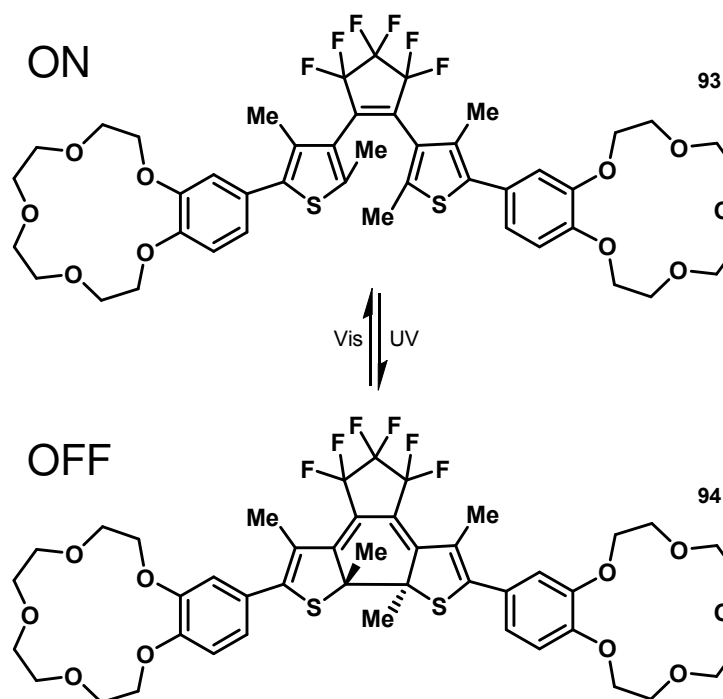
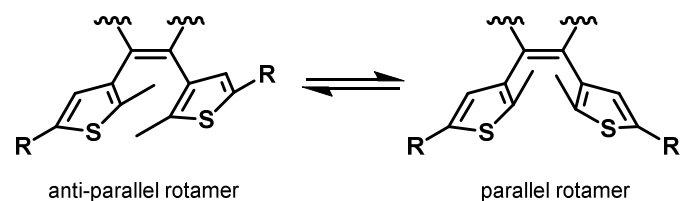
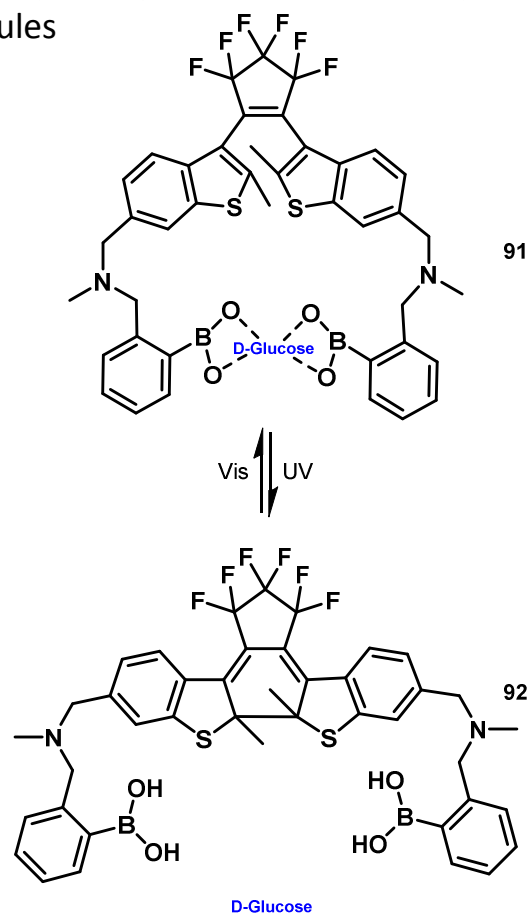
M. Irie, *Chem. Rev.* **2000**, *100*, 1685-1716.

Z. Chao, Z. Huan-Ping, L. Long-Yan, F. Wei, S. Wei, L. Zhan-Xian, X. Chun-Hu, F. Chen-Jie, S. Ling-Dong, Z. Ya-Wen, Y. Chun-Hua, *Adv. Mater.* **2010**, *22*, 633-637.

Applications: Diarylethene Photoswitches

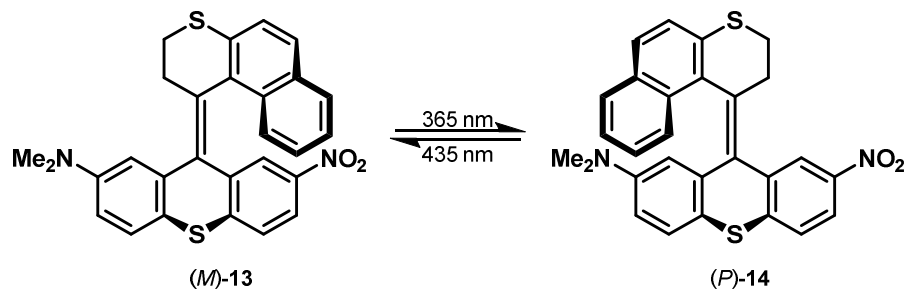
Photocontrollable “smart” receptors:

Switching host-guest interactions by photoirradiation enables substrate detection and active transport of guest molecules



M. Natali, S. Giordani, *Chem. Soc. Rev.* **2012**, 41, 4010-4029.
 M. Irie, *Chem. Rev.* **2000**, 100, 1685-1716.

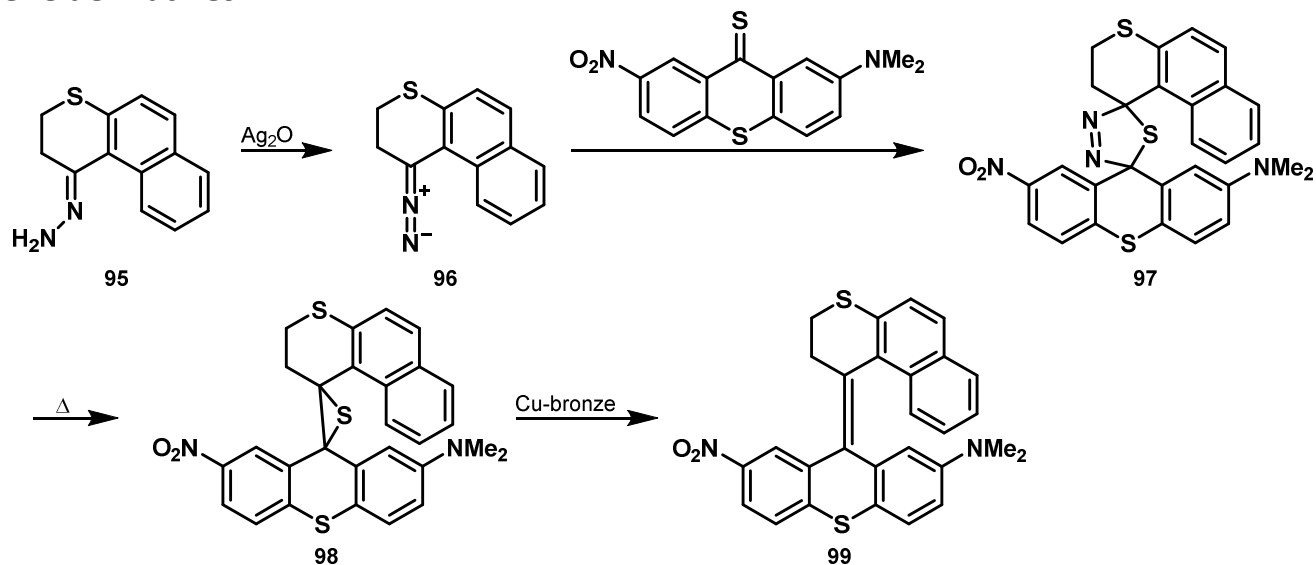
Applications: Overcrowded Alkene Photoswitches



- interconversion between enantiomers or diastereomers
- *cis-trans* isomerization accompanied by reversible change in helicity of molecules

Synthesis of overcrowded alkene derivatives:

via 1,3 dipolar cycloaddition

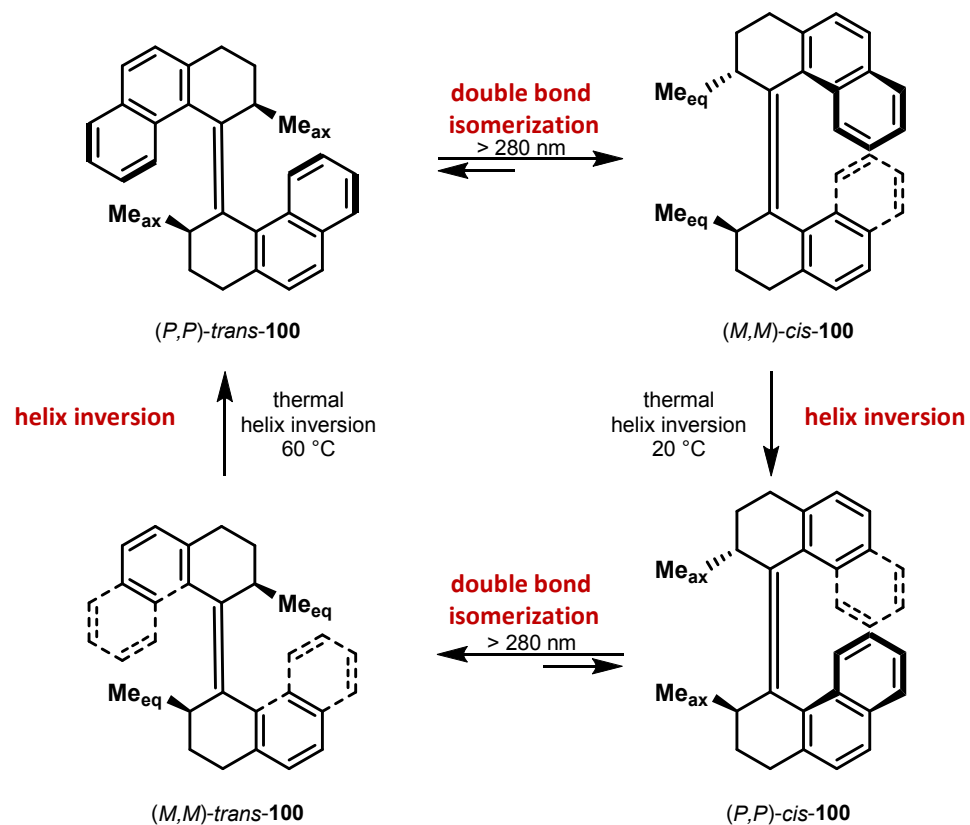


B. L. Feringa, *J. Org. Chem.* **2007**, 72, 6635-6652.

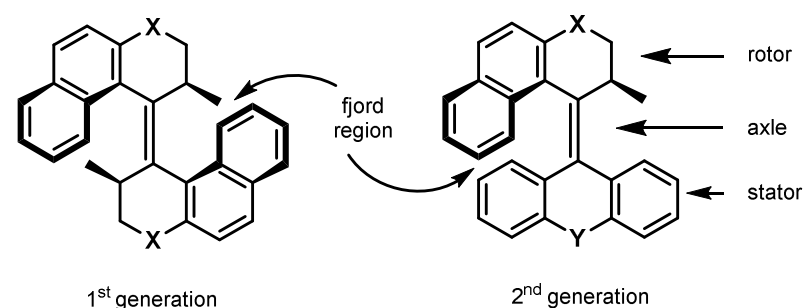
N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada, B. L. Feringa, *Nature* **1999**, 401, 152.

Applications: Overcrowded Alkene Photoswitches

Design of light-driven unidirectional molecular rotors:



- exploiting or overcoming of thermal motion
- detection of stimuli-induced motion and distinction above random thermal motions
- repetitive, unidirectional 360° motion
- light as energy source



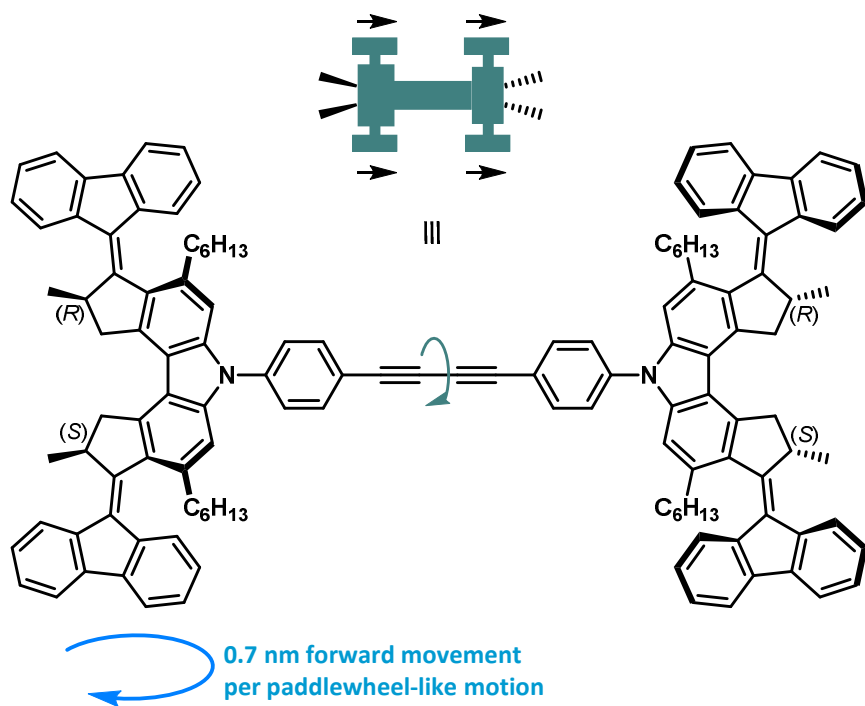
Advantages of 2nd generation switches:

- symmetric lower half for connection to other molecules/ surfaces
- acceleration of motor: reduced steric hindrance

B. L. Feringa, *J. Org. Chem.* **2007**, 72, 6635-6652.

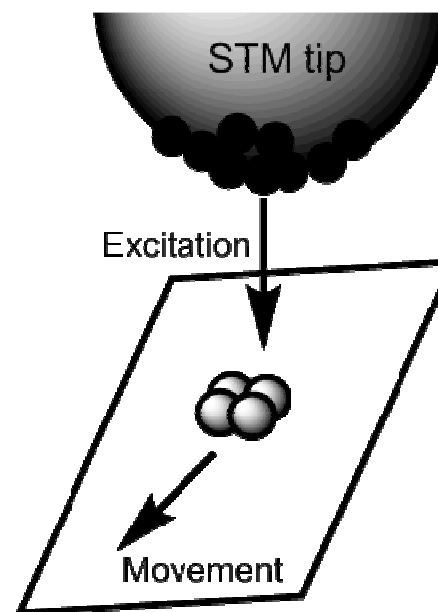
N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada, B. L. Feringa, *Nature* **1999**, 401, 152.

Applications: Overcrowded Alkene Photoswitches



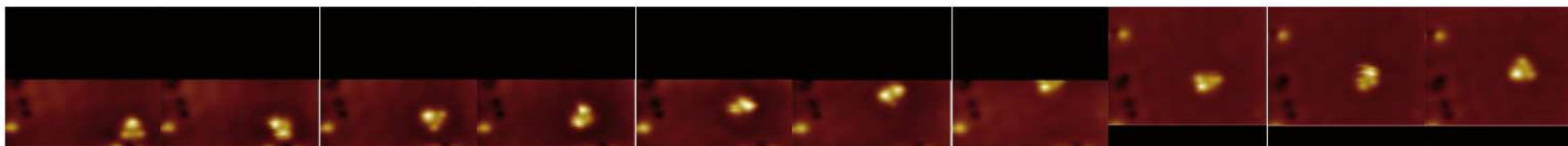
four-wheeled molecule: "nano car"

continuous & defined conformational changes upon sequential electronic and vibrational excitation



101

Linear movement of *meso*-(*R,S*-*R,S*) isomer:



T. Kudernac, N. Ruangsupapichat, M. Parschau, B. Maciá, N. Katsonis, S. R. Harutyunyan, K.-H. Ernst, B. L. Feringa, *Nature* **2011**, 479, 208.

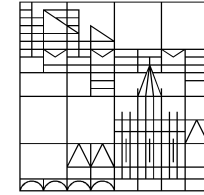
N. Koumura, R. W. J. Zijlstra, R. A. van Delden, N. Harada, B. L. Feringa, *Nature* **1999**, 401, 152.

N. Koumura, E. M. Geertsema, A. Meetsma, B. L. Feringa, *J. Am. Chem. Soc.* **2000**, 122, 12005-12006.

„Why does mankind need to fly? Why do we need molecular motors or machines? Nobody would have predicted that in the future one would build passenger planes each carrying several hundred people at close to the speed of sound between continents.“

B. Feringa, nobel lecture 2017

Universität
Konstanz



**Thanks for your
kind attention!**