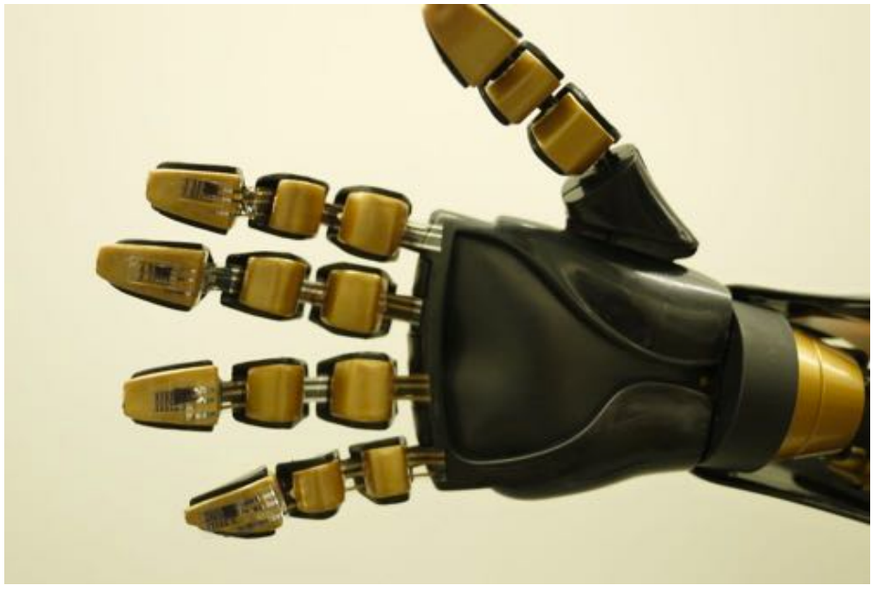
Smart Materials: Design and Applications

Yong Yao Loh
MacMillan Group Meeting
24 January 2018

Introduction to Smart Materials

Smart materials: *Materials that are designed to have one or more properties that can be significantly changed in a controlled fashion by external stimuli*



Outline

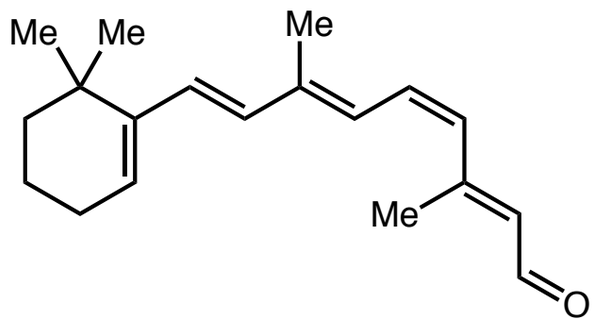
Light Responsive Systems

Chemo Responsive Systems

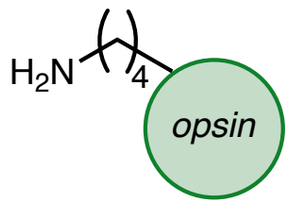
Electrically Responsive Systems

Applications of molecular motors to organic synthesis

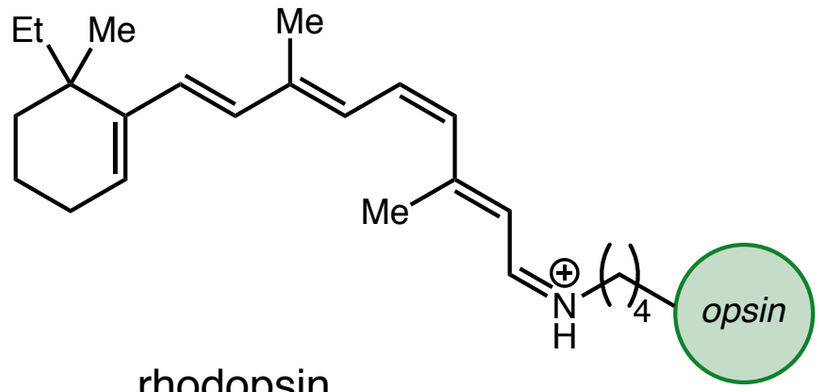
Photo-responsive Materials: Retinal



11-*cis*-Retinal



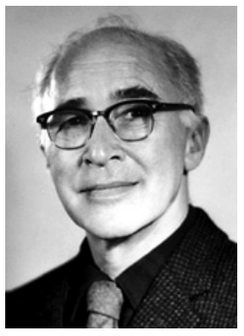
$-H_2O$



rhodopsin

Ragnar Granit

Haldan Hartline

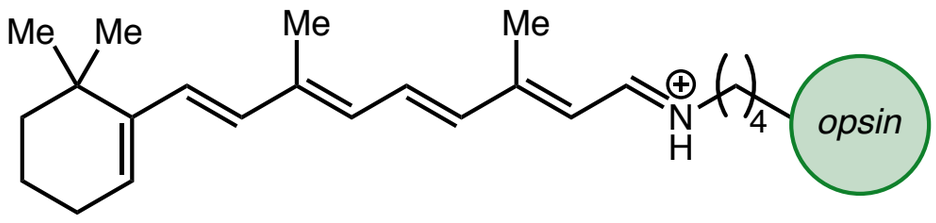


George Wald

1967 Nobel Prize in Physiology or Medicine

hv

photoisomerization event



trans-Retinal

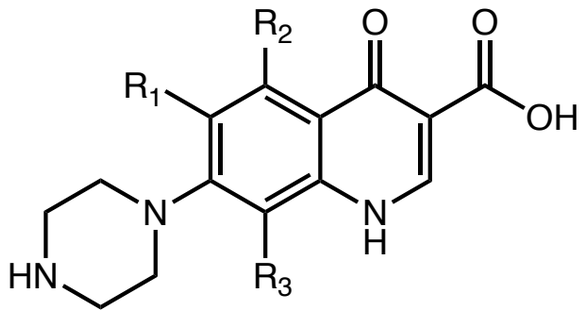
cellular response cascade

vision

Up to 8 different opsins differing in few amino acid side chains modulate λ_{max} to enable colour vision

Rando, R. R. *Chem. Rev.* **2001**, *101*, 1881–1896.

Use of Photoswitches in Antibiotics



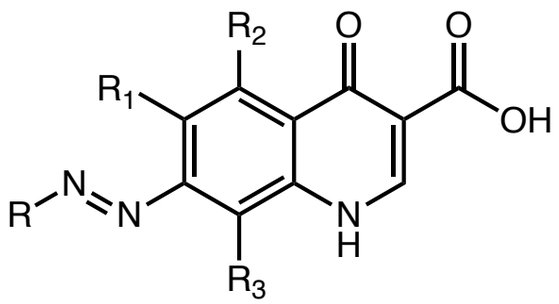
quinolones

broad spectrum anti-bacterial agents

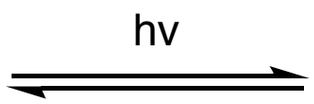
R_1, R_2, R_3 = H or F

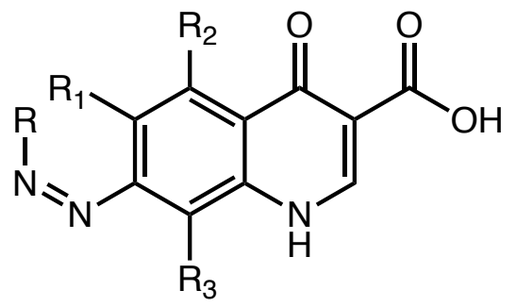
binds to DNA gyrase, blocking DNA replication

can we control the antibacterial activity of the molecule using light?



***trans*-isomer**
no anti-bacterial activity

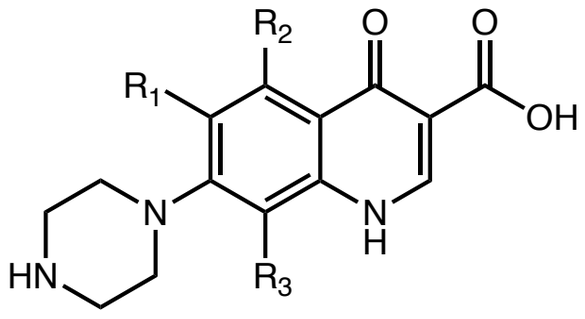




***cis*-isomer**
inhibits bacterial growth

Velema, W. A.; Van Der Berg, J. P.; Hansen, M. J.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *Nat. Chem.* **2013**, *5*, 924–928.

Use of Photoswitches in Antibiotics



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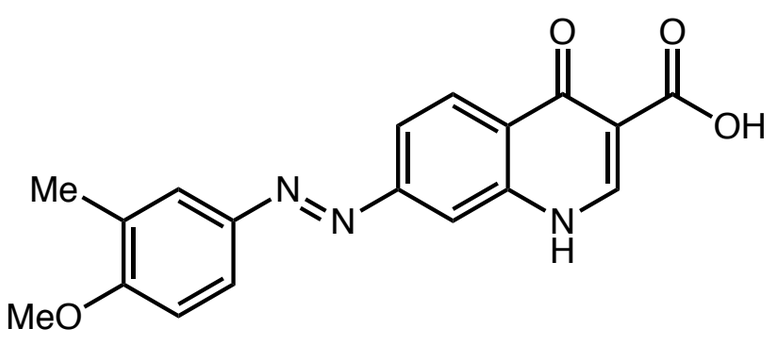

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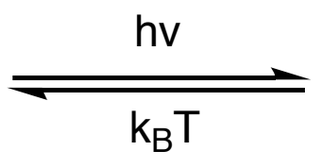

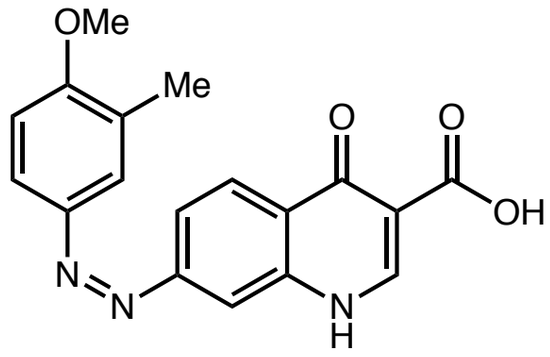

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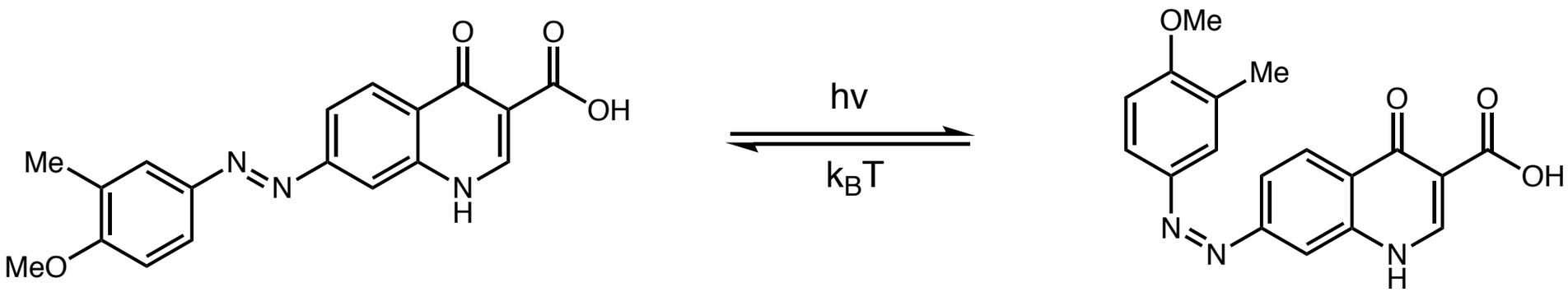

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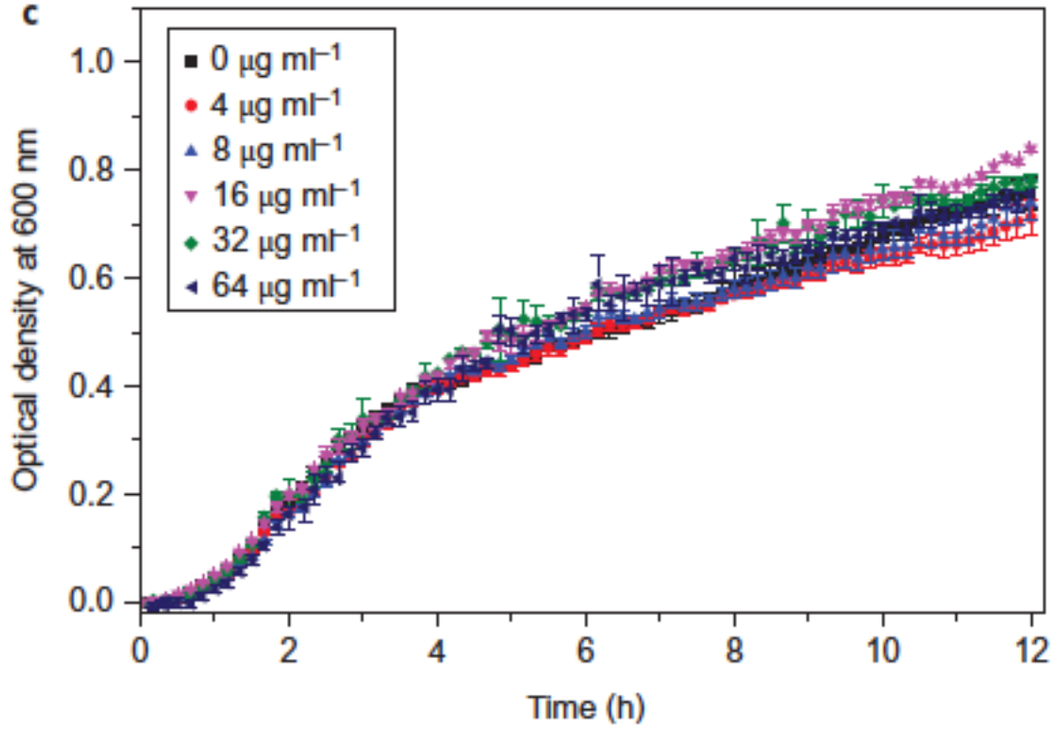
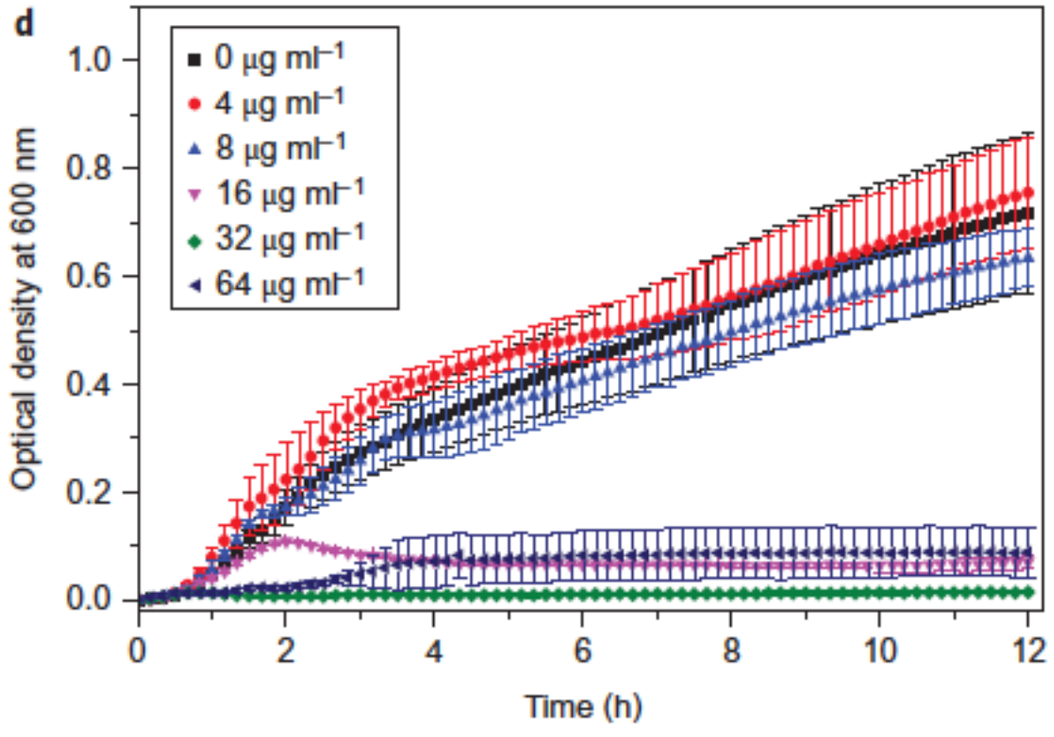


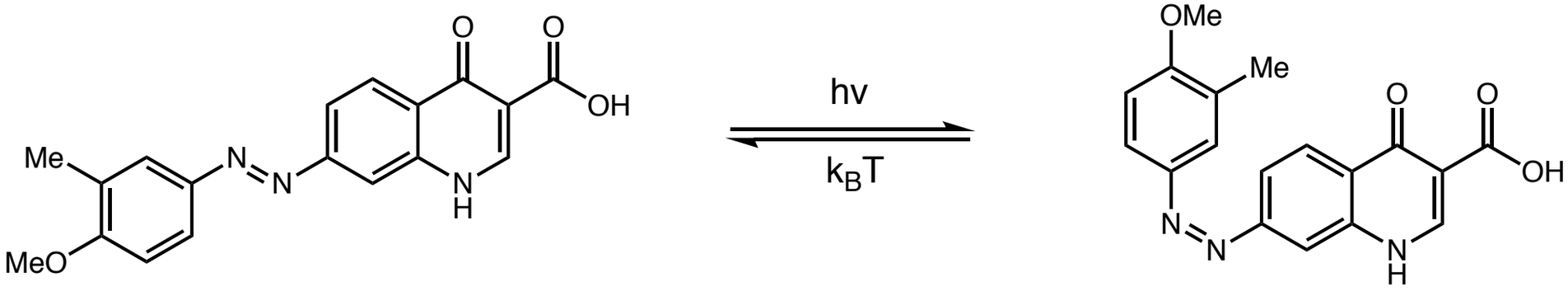
exposure of *E. coli* to non-irradiated *trans*-isomer



exposure of *E. coli* to irradiated (365 nm) *trans*-isomer

Velema, W. A.; Van Der Berg, J. P.; Hansen, M. J.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *Nat. Chem.* **2013**, *5*, 924–928.

Use of Photoswitches in Antibiotics



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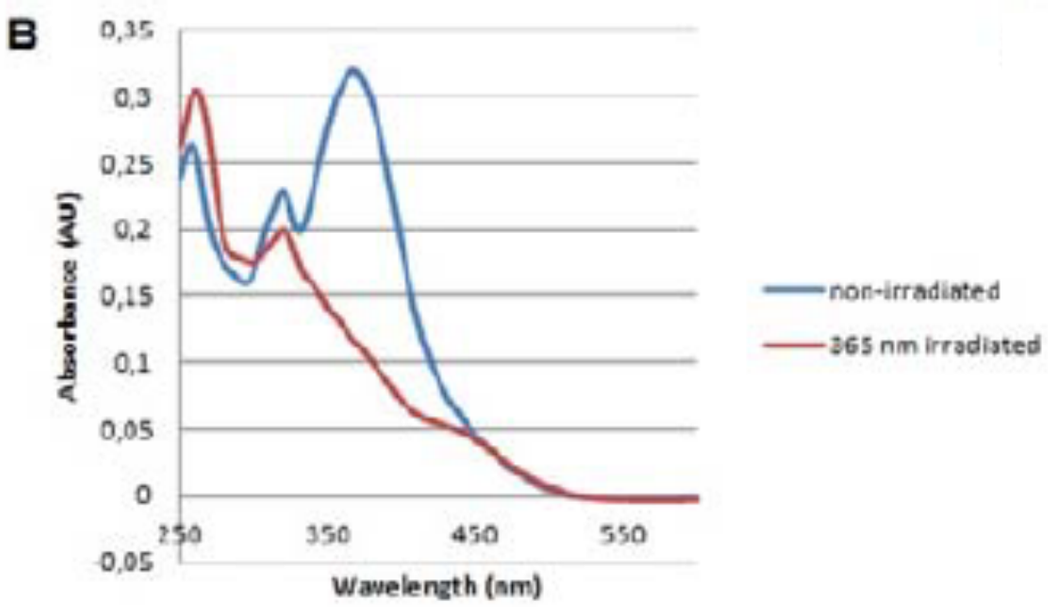
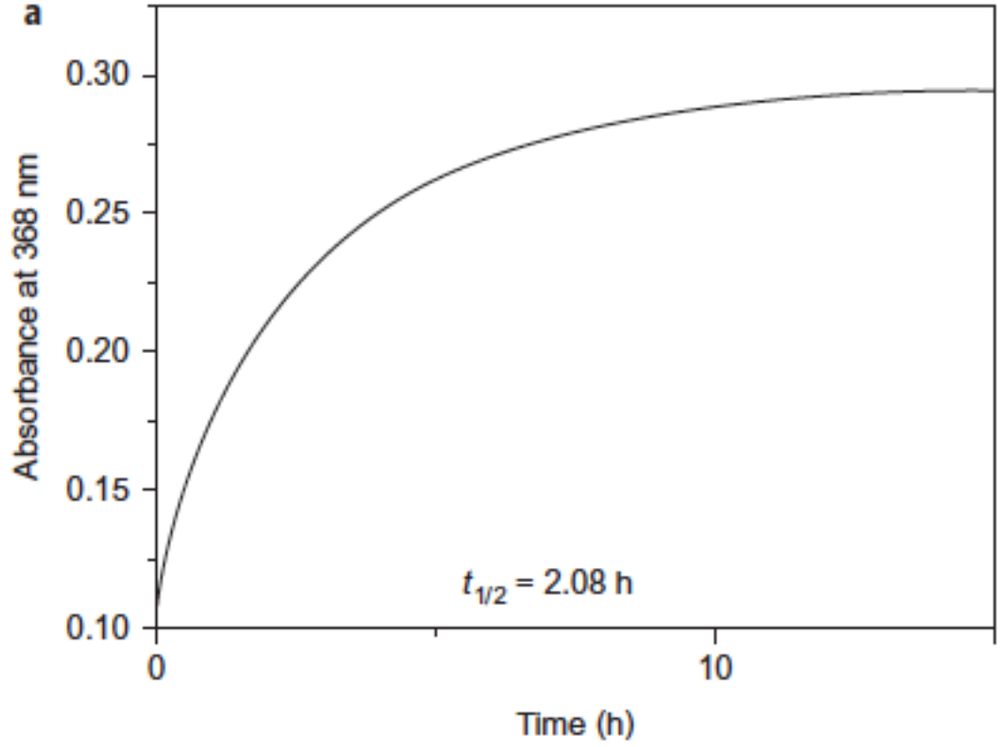


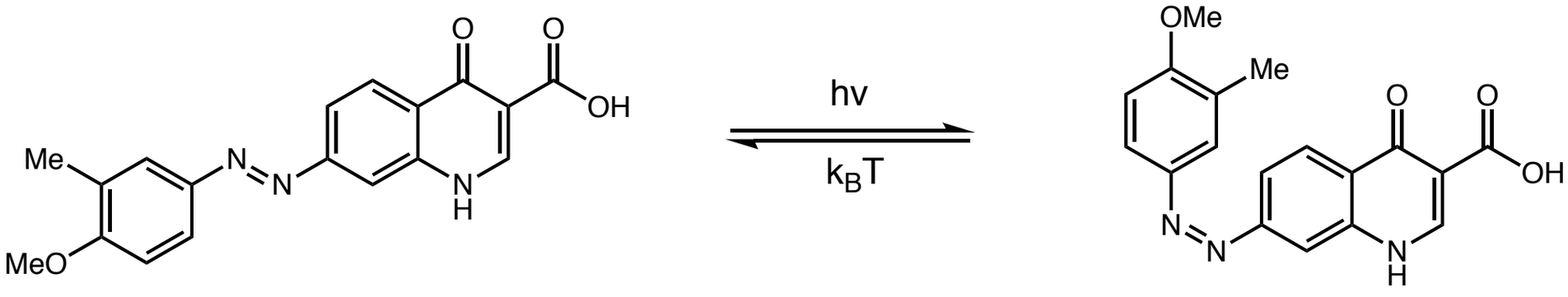
UV-Vis of compound before and after irradiation



thermal cis-trans isomerization at 37 °C

Velema, W. A.; Van Der Berg, J. P.; Hansen, M. J.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *Nat. Chem.* **2013**, *5*, 924–928.

Use of Photoswitches in Antibiotics



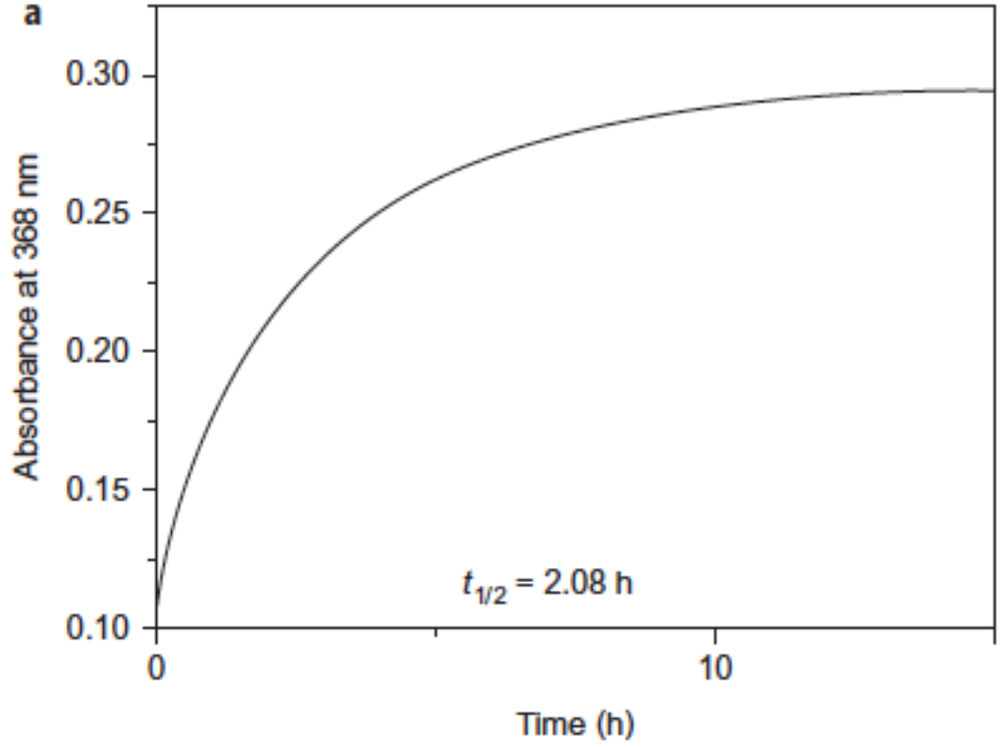
***trans*-isomer**
no anti-bacterial activity

***cis*-isomer**
inhibits bacterial growth

antibiotics are often excreted unmetabolized

build up in environment leads to bacterial resistance

auto-deactivation can help to combat this



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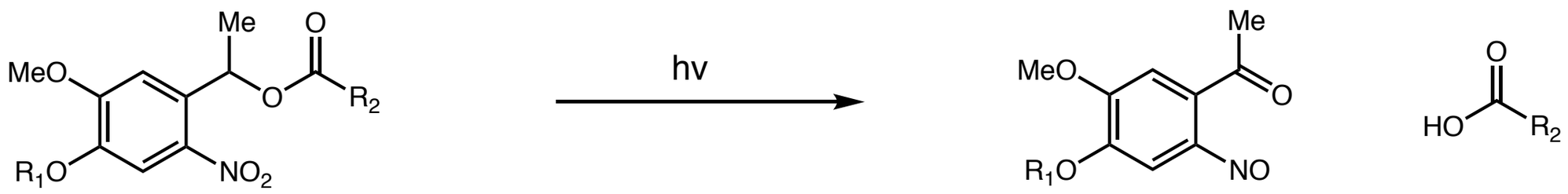
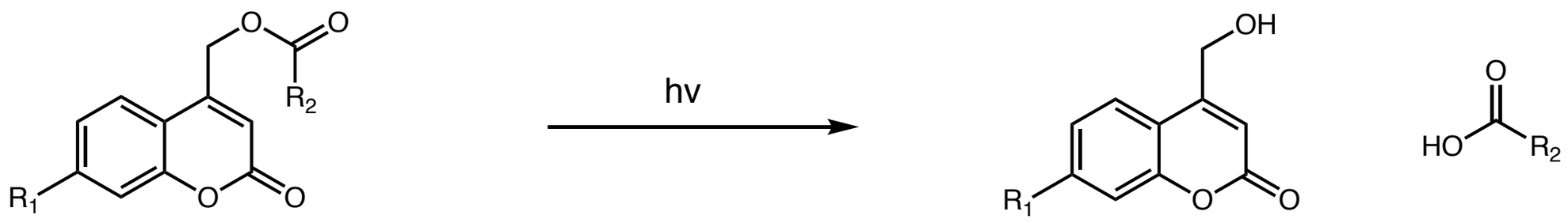
Photocleavage

ortho-nitrobenzyl esters



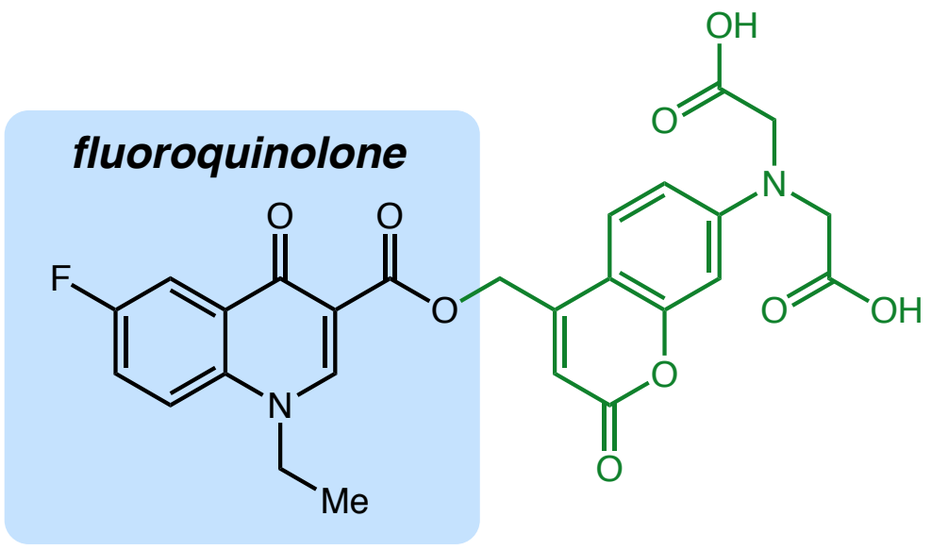
courmarine esters



- offers a modular approach
- rapid response
- non-reversible

Ruskowitz, E. R.; DeForest, C. A. *Nat. Rev. Mater.* **2018**, *3*, 17087.

Photocleavage

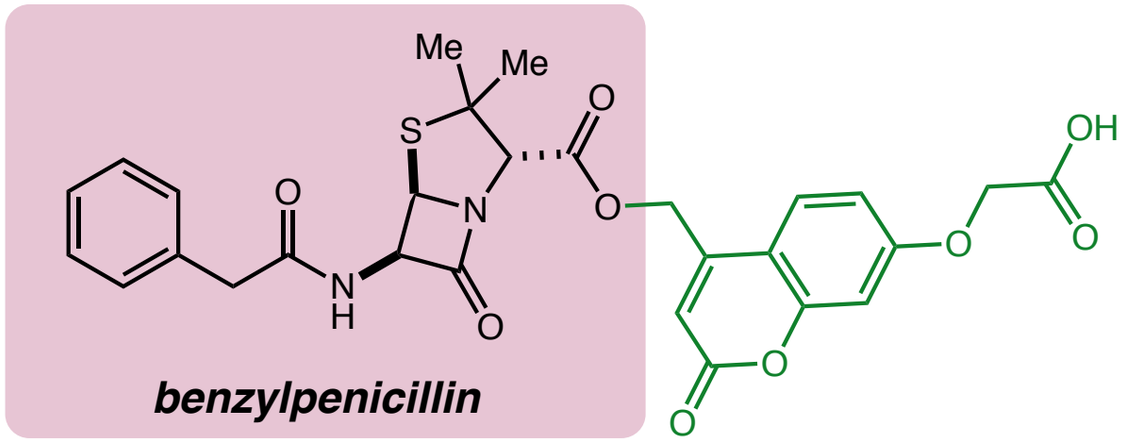


active for *E. coli*

masked carboxylic acid

essential for binding to DNA

undergoes photocleavage at 312 nm

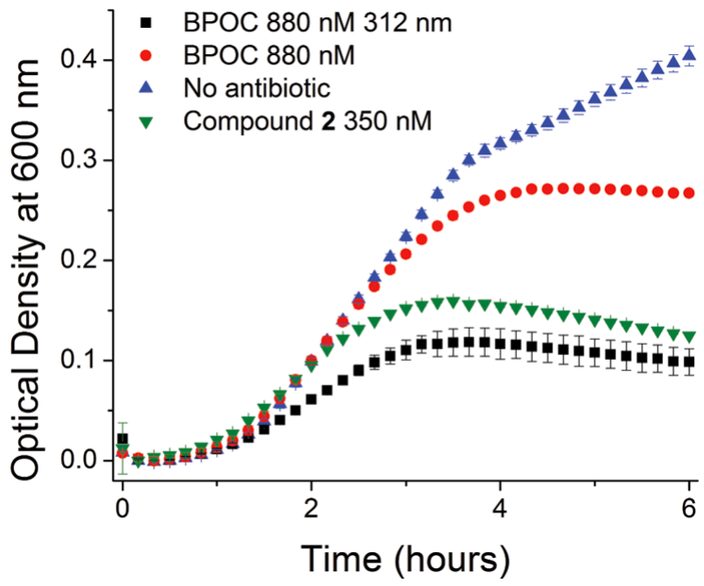


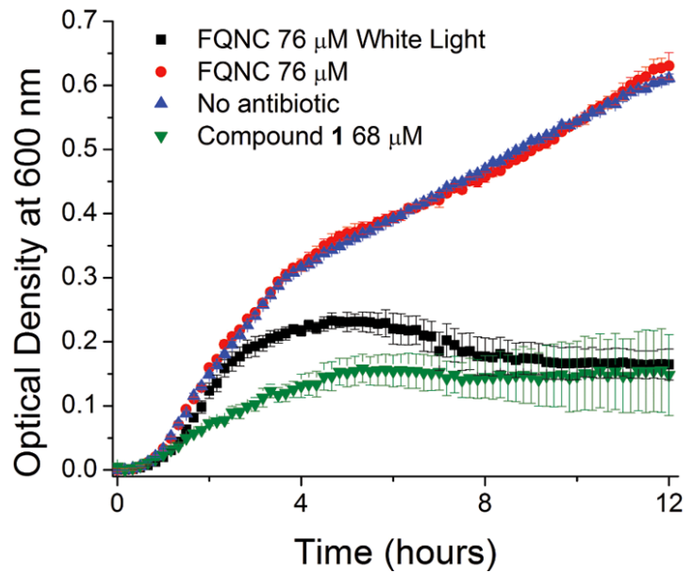
active for *S. aureus*

masked carboxylic acid

interacts with transpeptidase

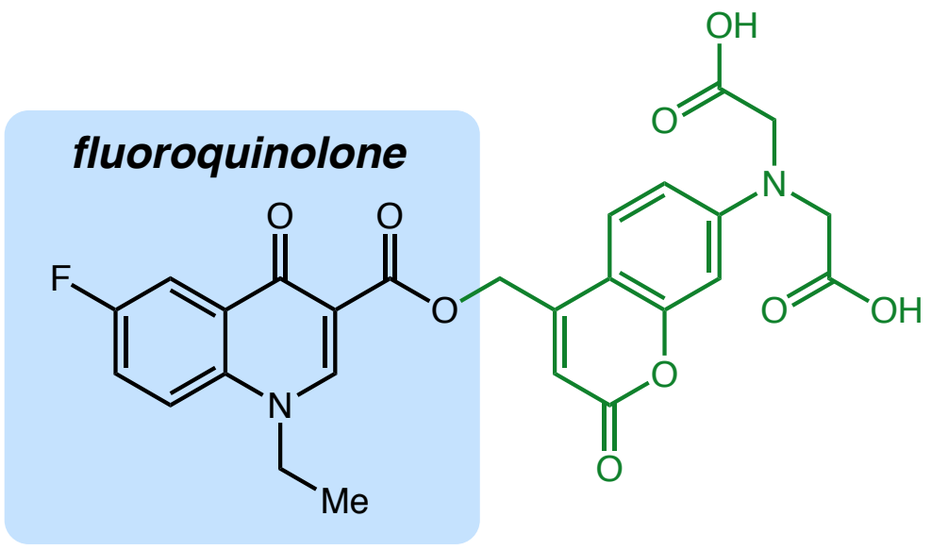
undergoes photocleavage under visible light





Velema, W. A.; Van Der Berg, J. P.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *ACS Chem. Biol.* **2014**, *9*, 1969–1974.

Photocleavage



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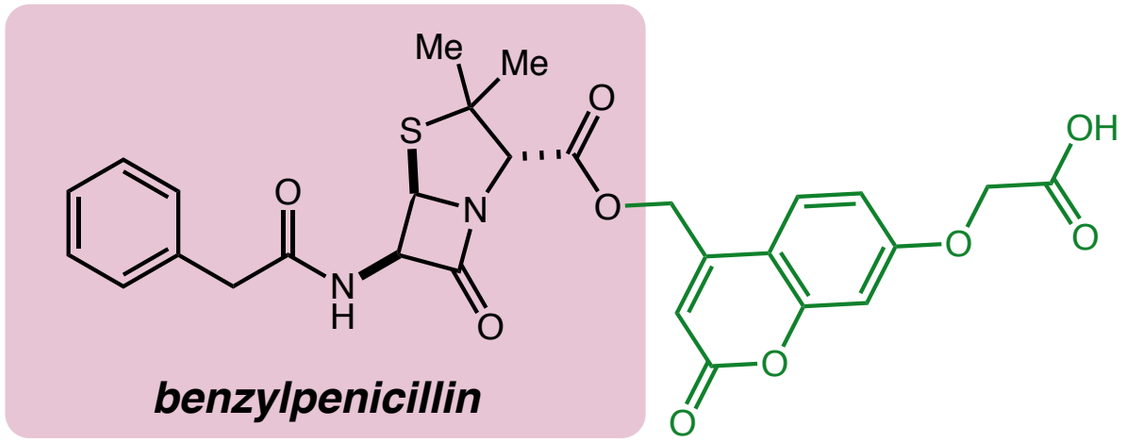


active for *S. aureus*

masked carboxylic acid

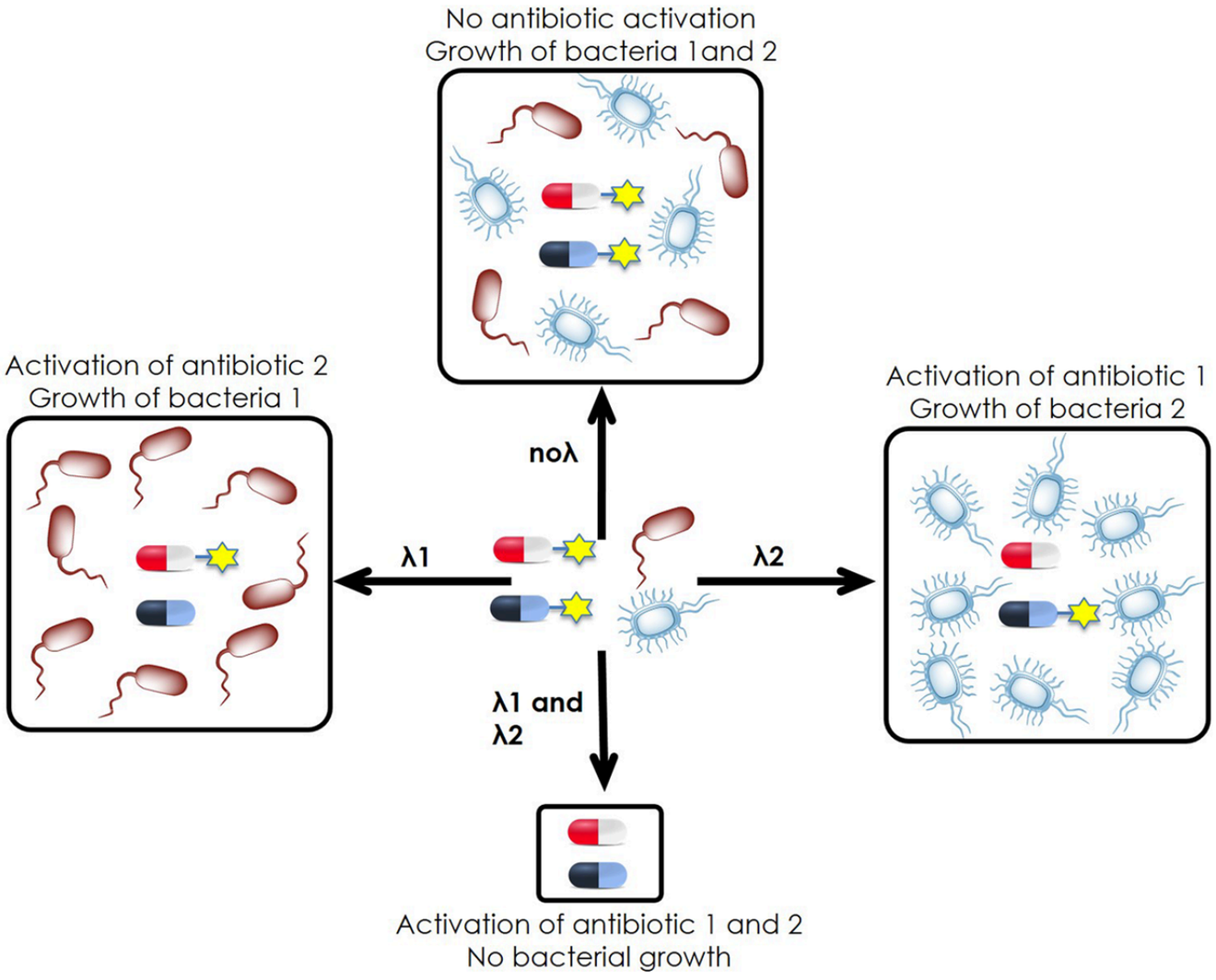
interacts with transpeptidase

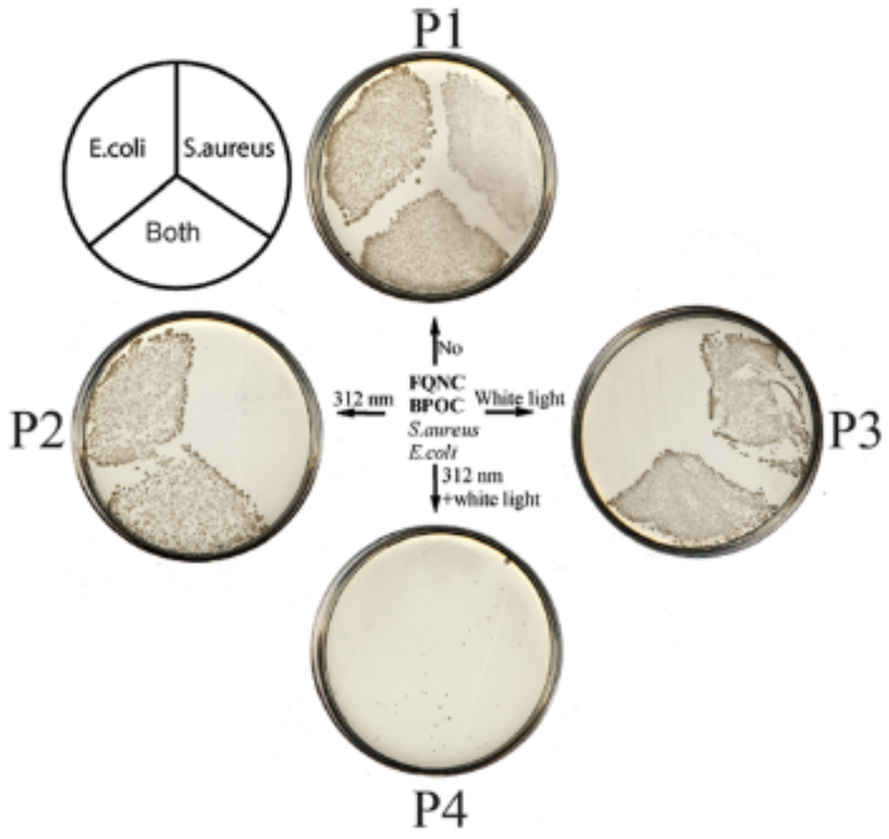
undergoes photocleavage under visible light

Compound	MIC *E. coli* (μM)	MIC *S. aureus* (μM)
1	68	>1700
2	288	0.35

Velema, W. A.; Van Der Berg, J. P.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *ACS Chem. Biol.* **2014**, *9*, 1969–1974.

Photocleavage



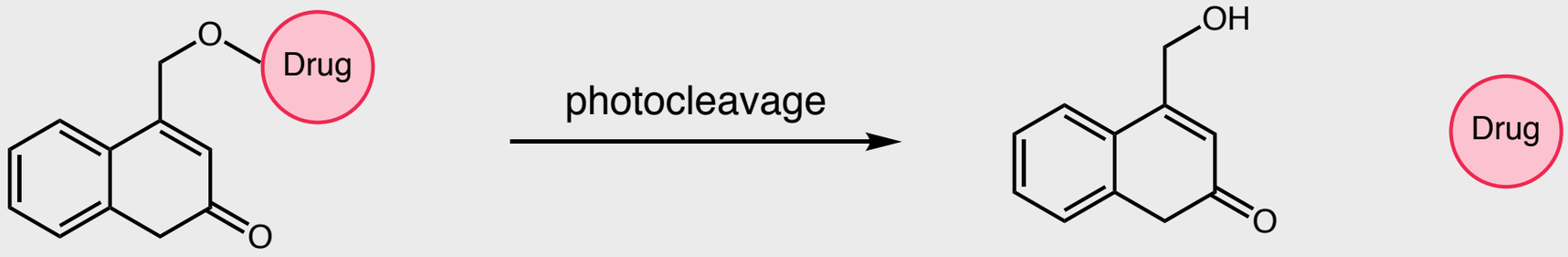


- ***orthogonally addressable photocleavable groups***
- ***allows complex mixtures of bacterial strains to be analyzed***
- ***enables control of composition of microbial populations***

Velema, W. A.; Van Der Berg, J. P.; Szymanski, W.; Driessen, A. J. M.; Feringa, B. L. *ACS Chem. Biol.* **2014**, *9*, 1969–1974.

Photocleavage: Targeted Drug Delivery to Cancer Cells

Light as a control element for drug delivery

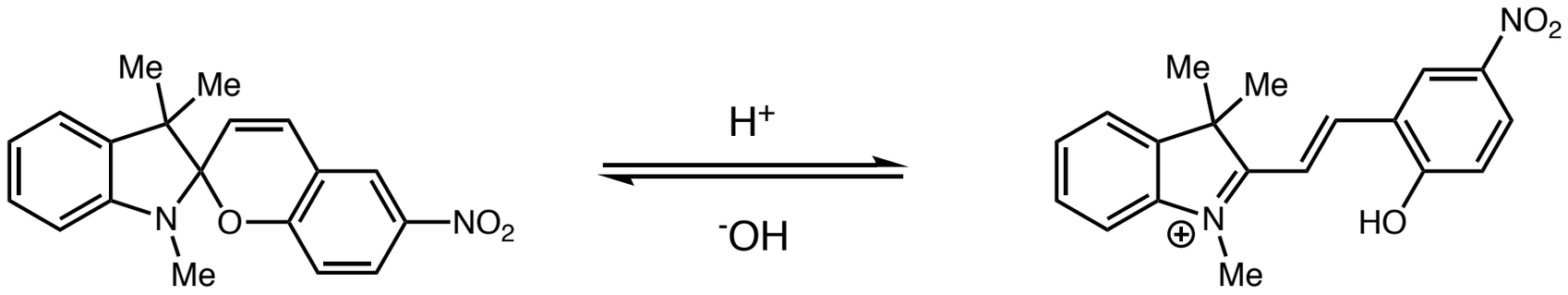


easily tuned and highly specific trigger

spatial and temporal control

Can we further increase the specficity of drug delivery to discriminate between cancer cells and healthy cells?

acid-chromism of spiropyrans



absorbs in UV

absorbs visible light

cancer cells have a low pH microenvironment; pH responsiveness can be exploited

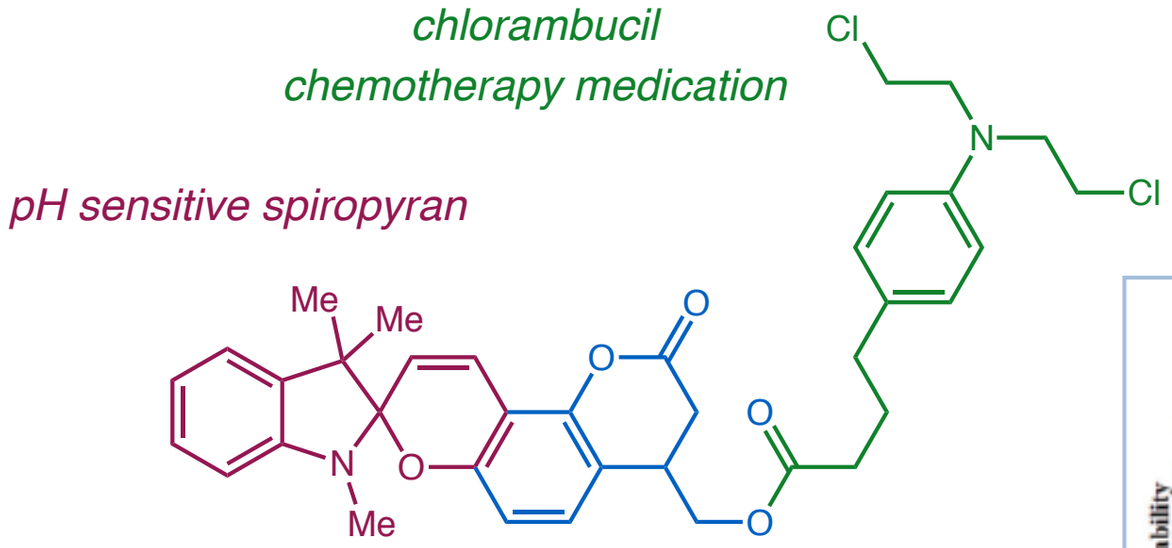
Barman, S.; Das, J.; Biswas, S.; Maiti, T. K.; Pradeep Singh, N. D. *J. Mater. Chem. B* **2017**, *5*, 3940–3944

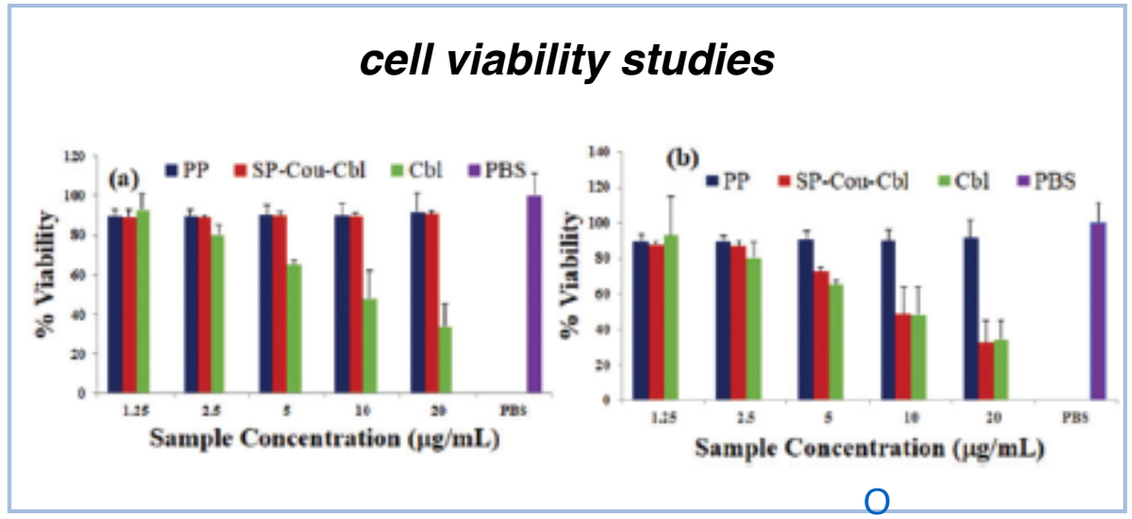
Photocleavage: Targeted Drug Delivery to Cancer Cells

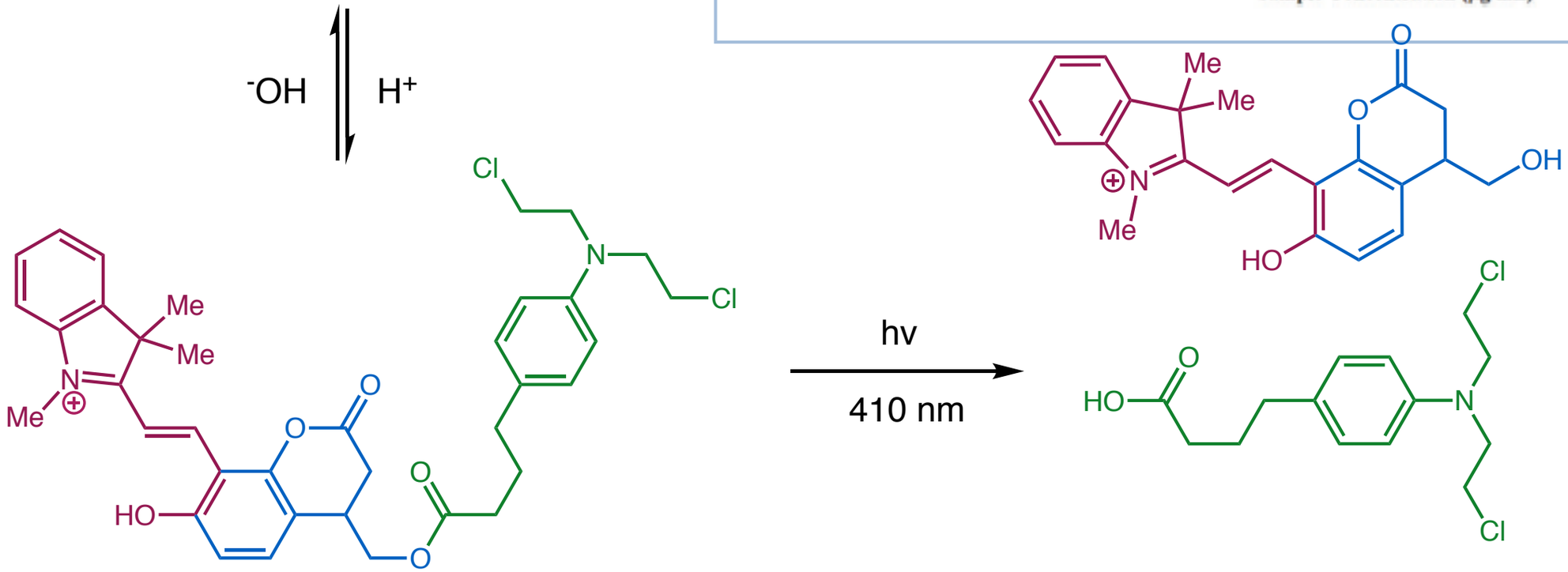
chlorambucil
chemotherapy medication

pH sensitive spiropyran

photocleavable
coumarin ester







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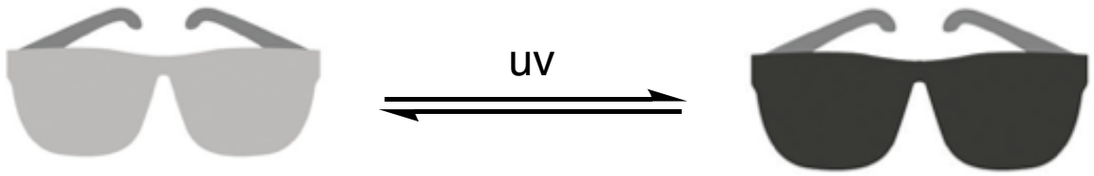
Photochromic Lenses



1960s technology: glass photochromic lenses

silver chloride — silver atom — chlorine atom

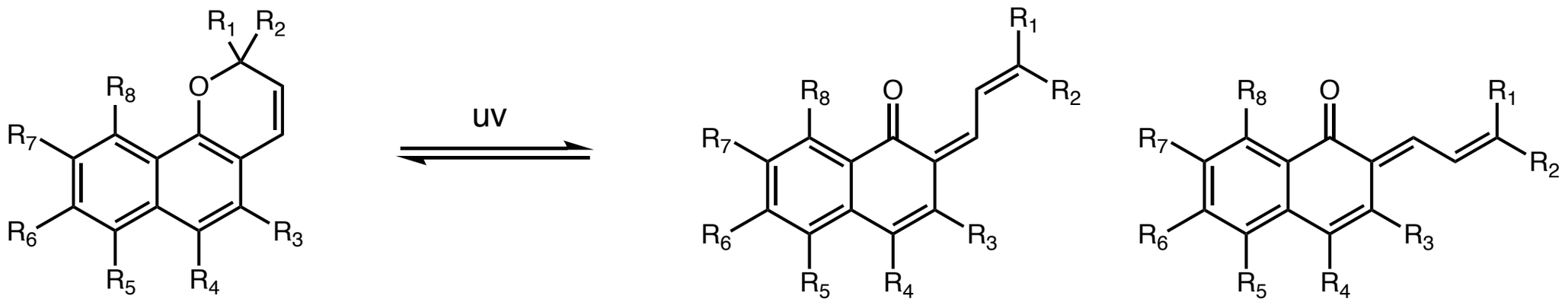
aggregation of silver atoms into nanoparticles confers colour

products are metastable; revert to AgCl salt upon removal of light

Cu-doped AgCl is usually used to prevent loss of chlorine

Armistead, W. H.; Stookey, S. D. *Science* **1964**, *144*, 14–16.

modern day: plastic photochromic lenses



napthopyran — *transoid-cis* (TC) isomer — *transoid-trans* (TT) isomer

Sousa, C. M.; Berthet, J.; Delbaere, S.; Polónia, A.; Coelho, P. J. *J. Org. Chem.* **2015**, *80*, 12177–12181.

Photochromic Lenses

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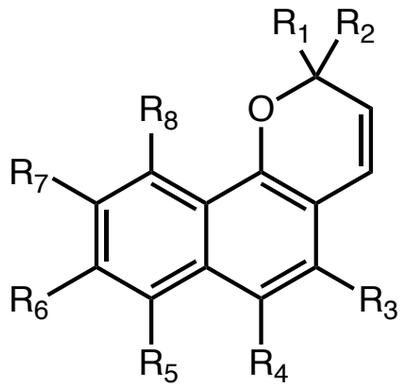
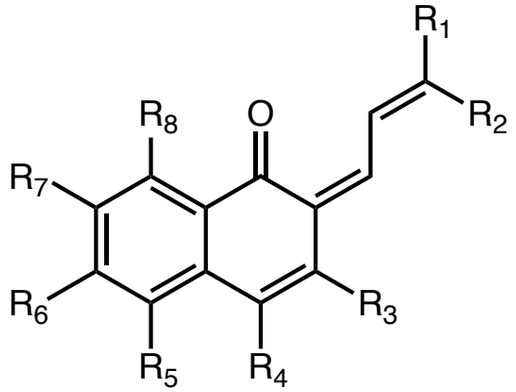
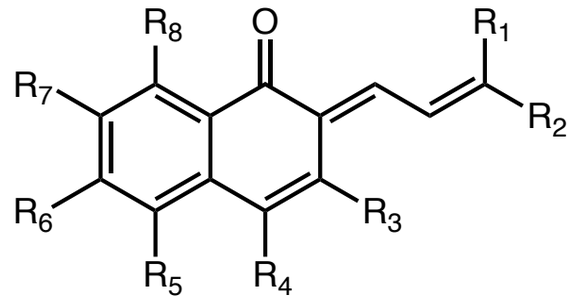


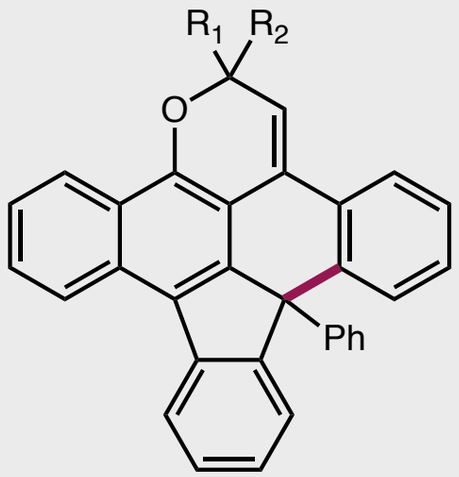
napthopyran



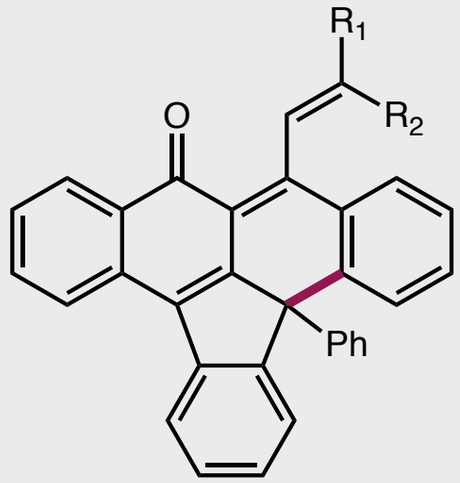
transoid-cis (TC) isomer
fast transition



transoid-trans (TT) isomer
slow transition



fused napthopyran isomer
colourless



transoid-cis (TC) isomer
fast transition

only photocleavage product

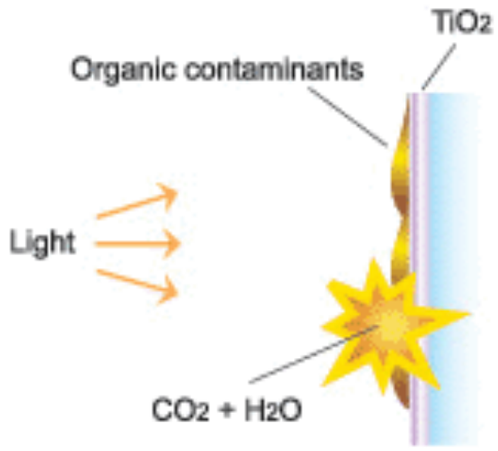
$t_{1/2}$ = 63 ms at 20 ºC

Sousa, C. M.; Berthet, J.; Delbaere, S.; Polónia, A.; Coelho, P. J. *J. Org. Chem.* **2015**, *80*, 12177–12181.

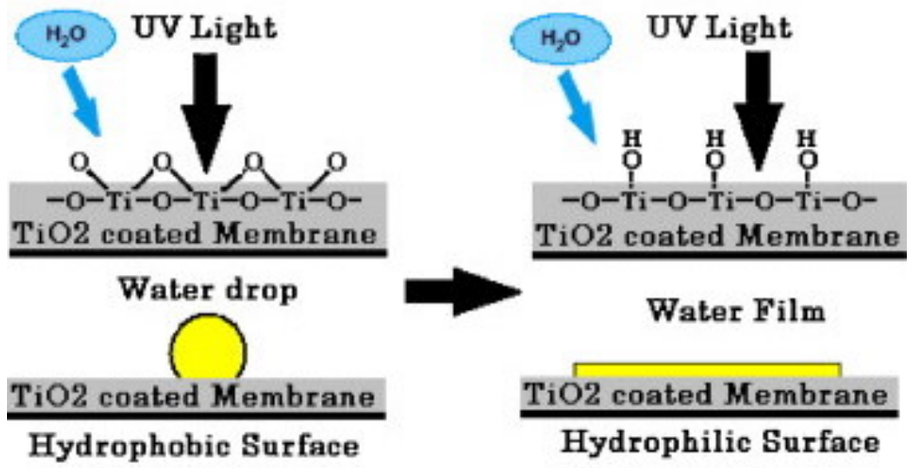
Photocatalysts in Smart Materials

- TiO_2 has long been known to exhibit self-cleaning properties via two photocatalytic pathways

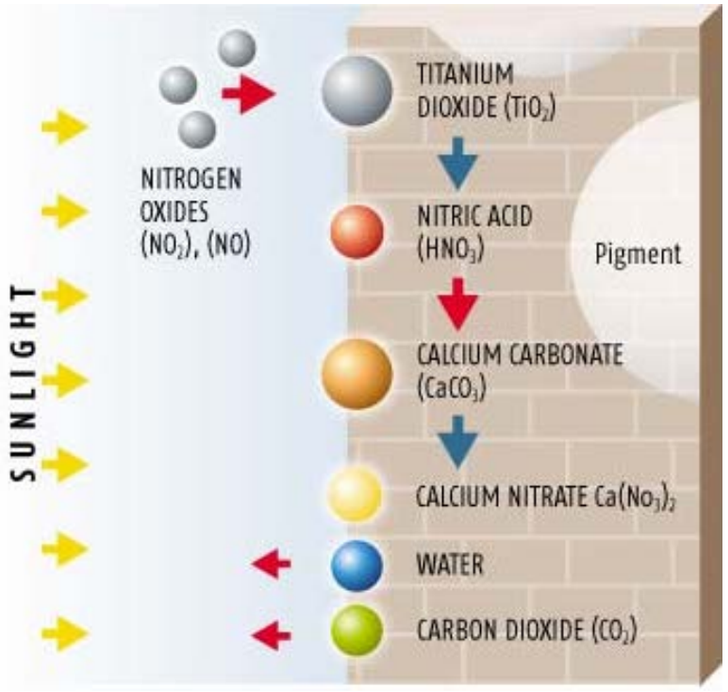
Mechanism 1: Photodecomposition of contaminants



Mechanism 2: Formation of superhydrophilic surface



- More recently, TiO_2 has been found to react with fossil fuel pollutants such as NO_2



NO_x molecules react photocatalytically with TiO_2 to give nitric acid

nitric acid reacts with $CaCO_3$ to give $Ca(NO_3)_2$

eco-friendly paint called EcoPaint

technology has also been adapted to for cement, named TioCem

Bedjanian, Y.; El Zein, A. *J. Phys. Chem. A* **2012**, *116*, 1758–1764.

Outline

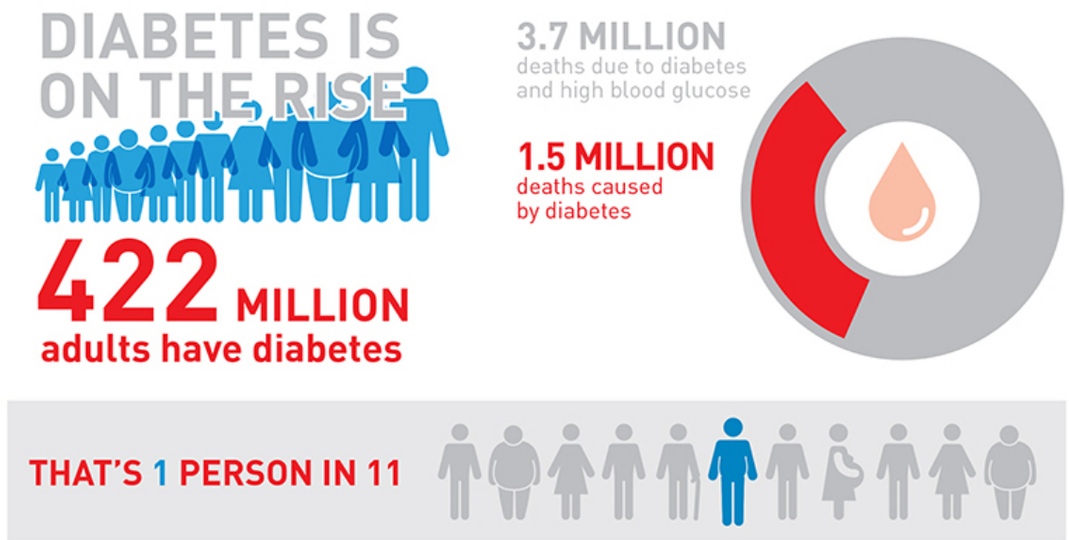
Light Responsive Systems

Chemo Responsive Systems

Electrically Responsive Systems

Applications of molecular motors to organic synthesis

Smart Gel for Glucose-Responsive Insulin Delivery



Current treatments for diabetes

- ***"open-loop" insulin delivery based on patient self-administration***
- ***suffers from inaccuracy of dose control***
- ***overdose can lead to fatal hypoglycemia***
- ***increasing interest in "closed-loop" delivery e.g. "artificial pancreas***
- ***typically involve electronic sensors which suffer from high costs***

current attempts to implement non-electronic closed-loop insulin delivery

centred around the use of glucose oxidase (GOD) or Concanavalin A (a sugar binding lectin)

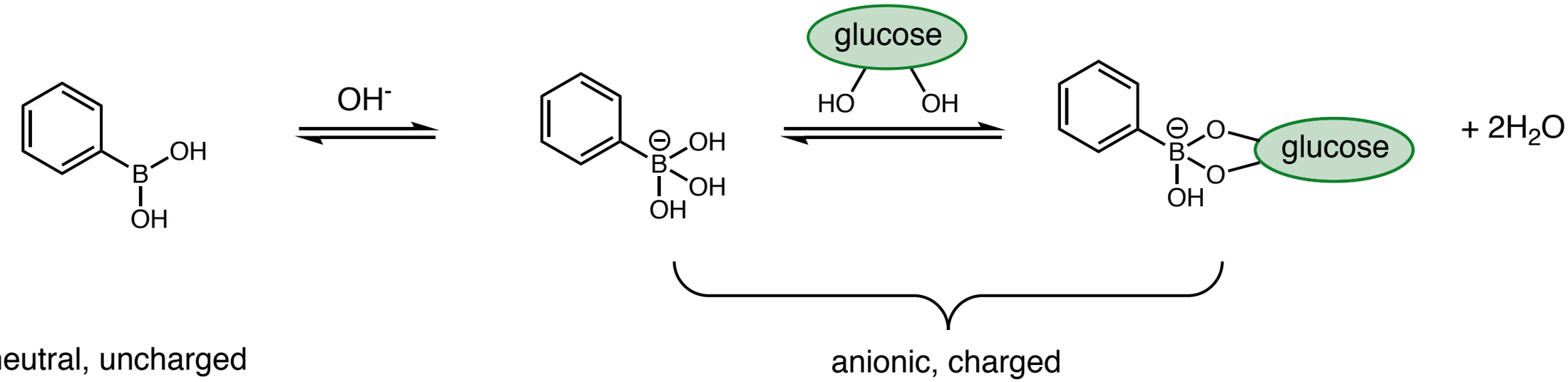
protein-based materials are not amenable for long-term use due to denaturation and cytotoxcity

can we design an artifical pancreas that circumvents electronic sensors and proteinaceous materials?

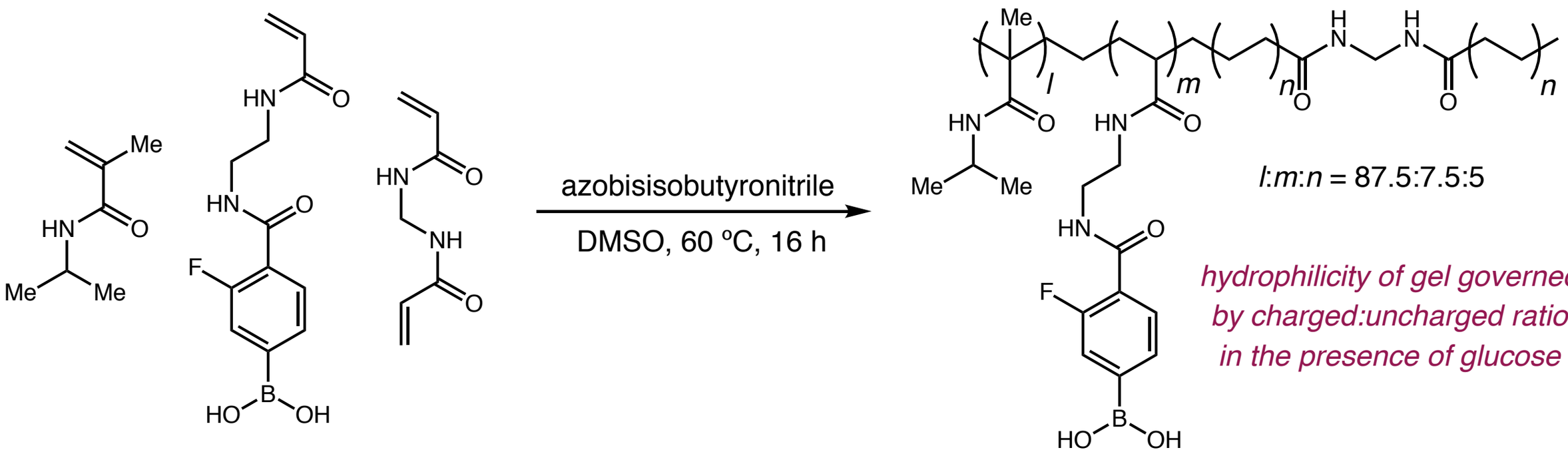
Matsumoto, A.; Tanaka, M.; Suganami et al. *Sci. Adv.* **2017**, 10.1126/sciadv.aaq0723

Smart Gel for Glucose-Responsive Insulin Delivery

- Phenylboronic acid (PBA) derivatives readily complex with 1,2- and 1,3-*cis*-diols



- PBA derivatives can be incorporated into a polymer gel with an amphiphilic acylamide backbone

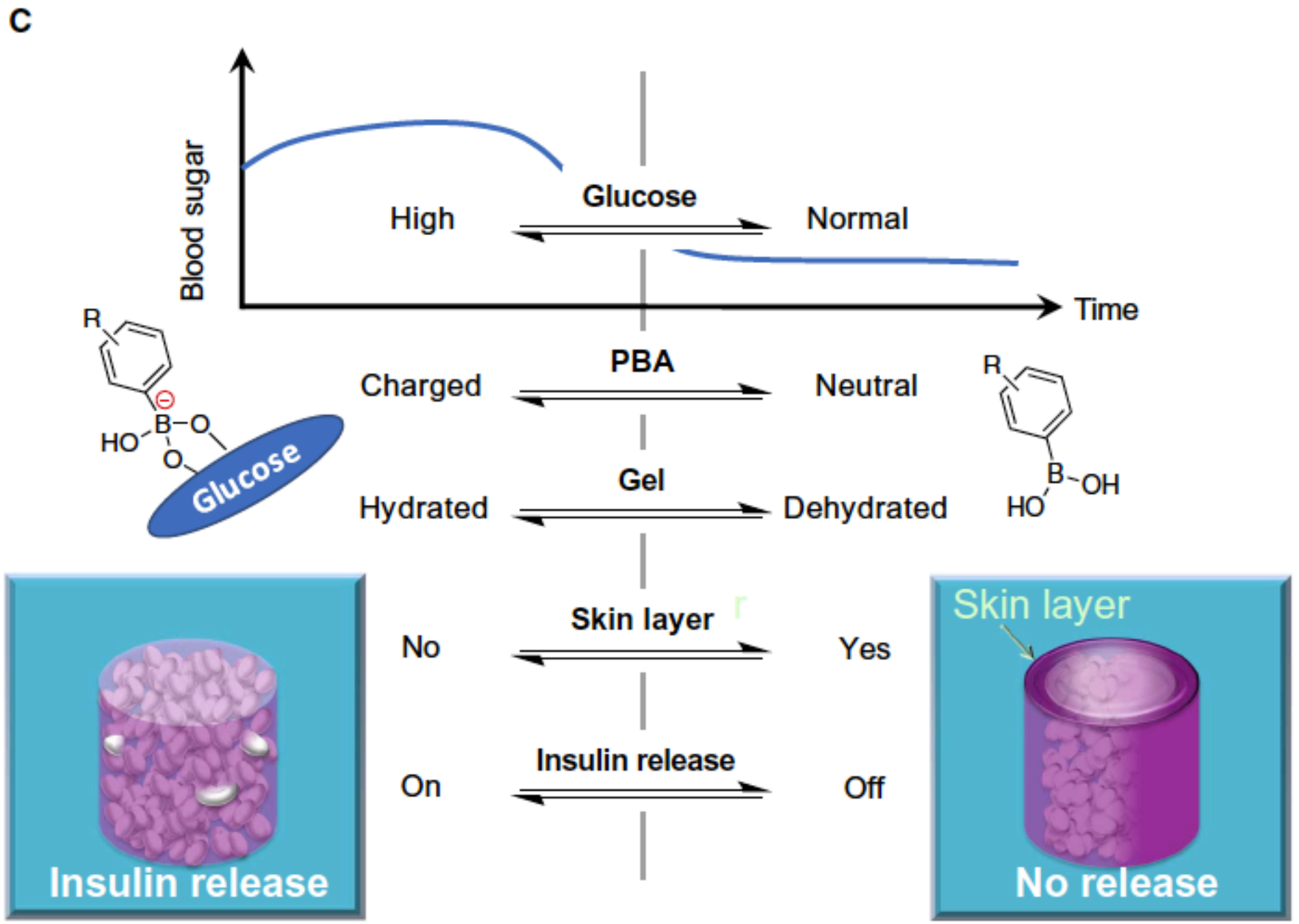


hydrophilicity of gel governed by charged:uncharged ratio in the presence of glucose

Matsumoto, A.; Tanaka, M.; Suganami et al. *Sci. Adv.* **2017**, 10.1126/sciadv.aaq0723

Smart Gel for Glucose-Responsive Insulin Delivery

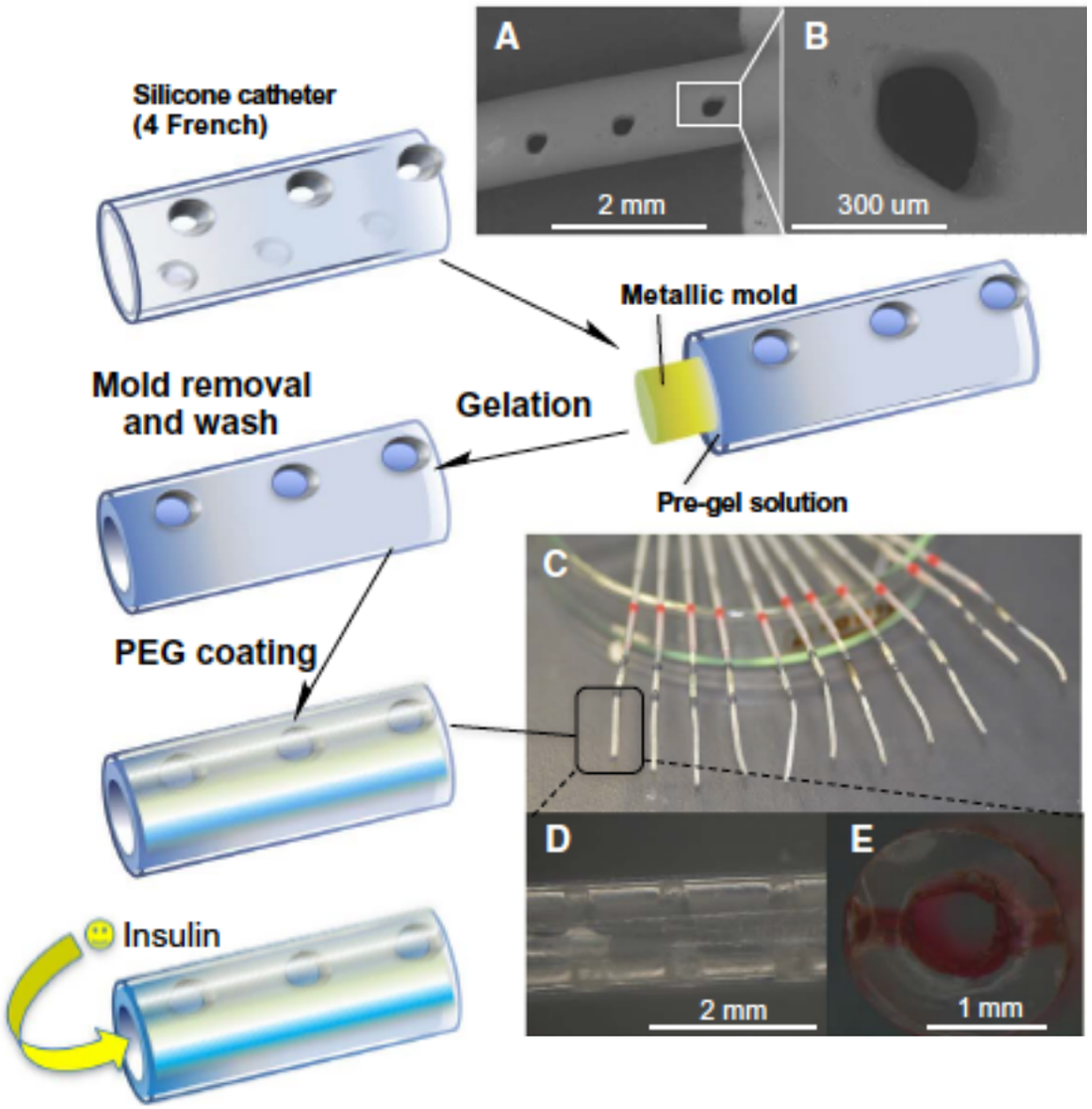
■ Mechanism of glucose-responsive smart gel

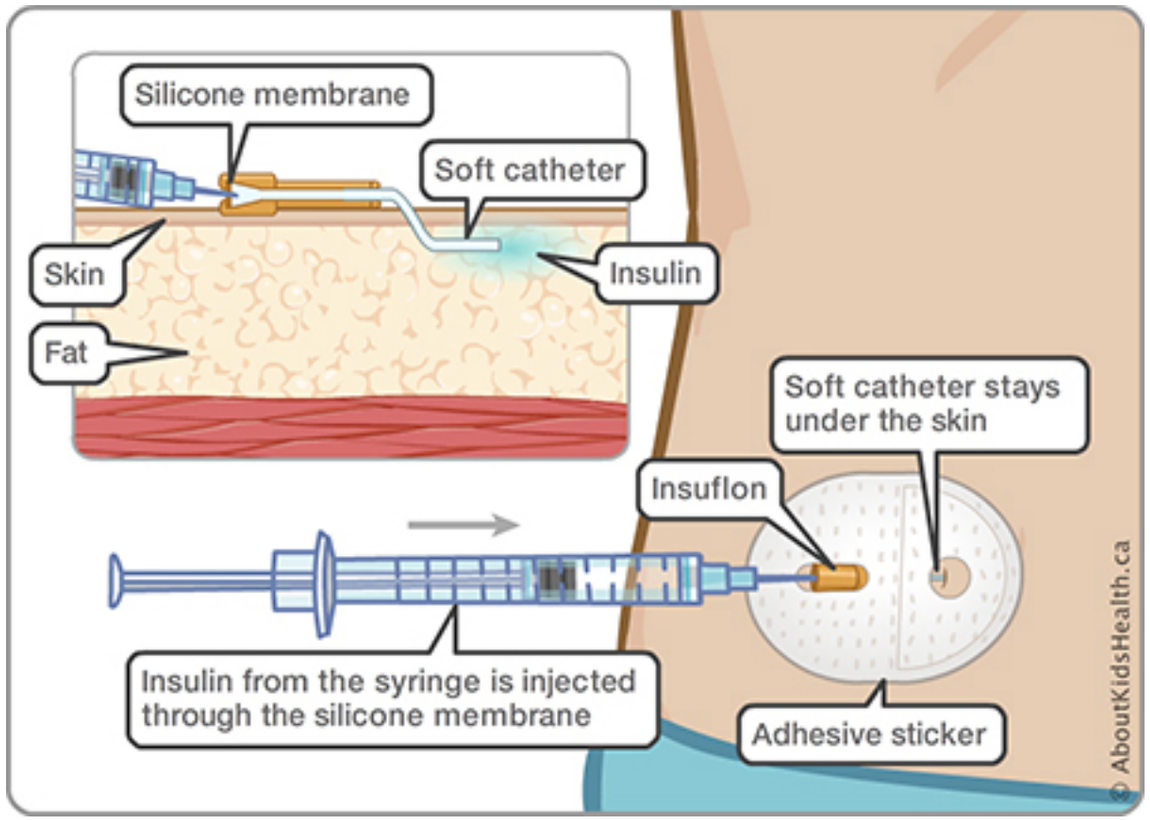


Matsumoto, A.; Tanaka, M.; Suganami et al. *Sci. Adv.* **2017**, 10.1126/sciadv.aaq0723

Smart Gel for Glucose-Responsive Insulin Delivery

■ Device structure



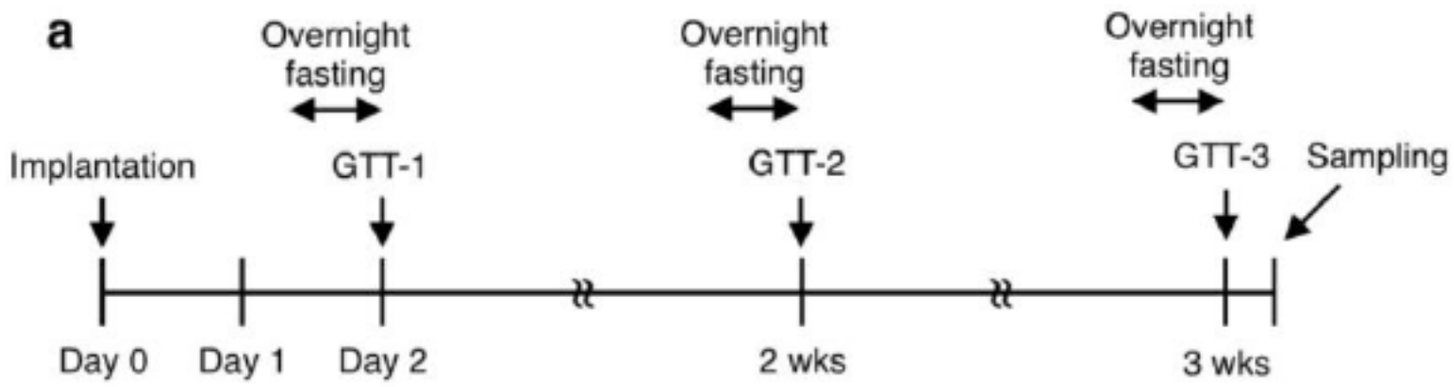


no electronics and no proteinaceous materials involved

Matsumoto, A.; Tanaka, M.; Suganami et al. *Sci. Adv.* **2017**, 10.1126/sciadv.aaq0723

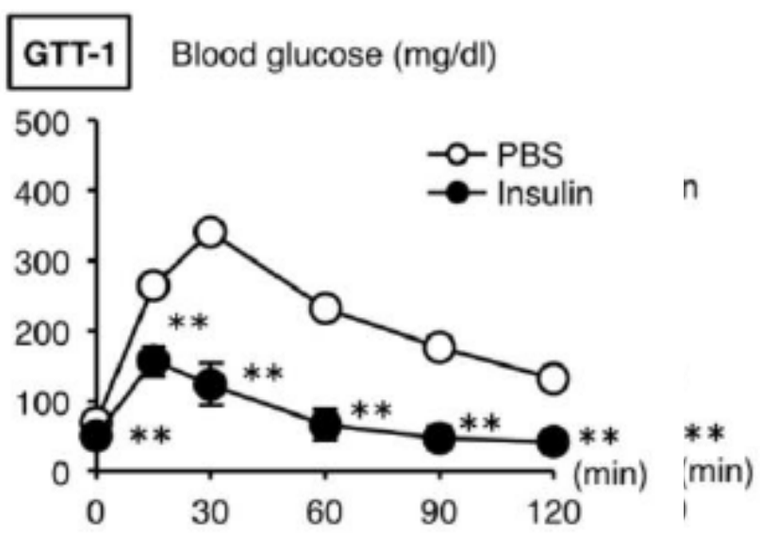
Smart Gel for Glucose-Responsive Insulin Delivery

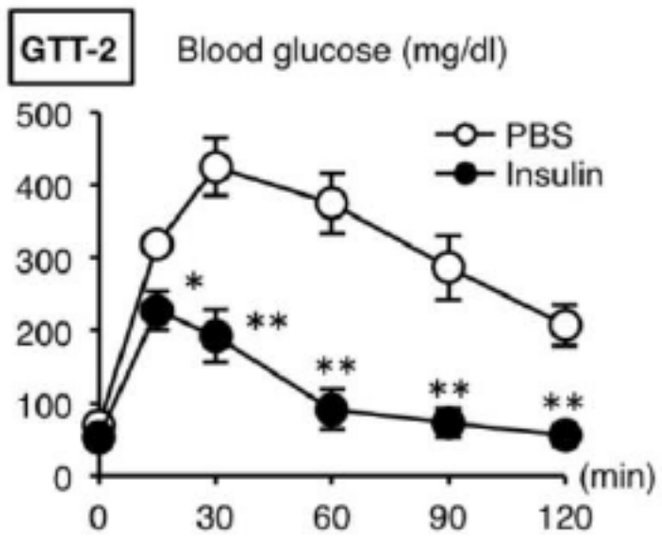
■ Efficacy of glucose-responsive smart gel

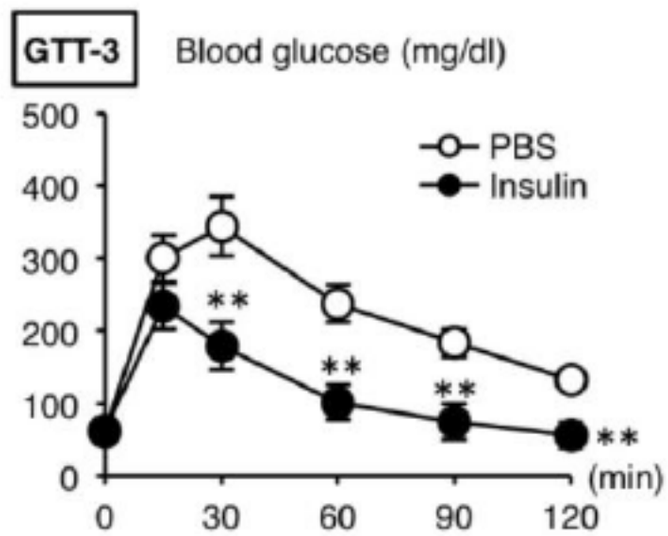


GTT = glucose tolerance test

3g / kg body weight of glucose was injected







Efficacy of insulin delivery in response to blood glucose levels is maintained over 3 weeks

Matsumoto, A.; Tanaka, M.; Suganami et al. *Sci. Adv.* **2017**, 10.1126/sciadv.aaq0723

Sea Cucumber Inspired Intracortical Implants

what are intracortical implants?

implants that replace neural circuitry in that brain that no longer functions appropriately

contain microelectrodes which act as electrical contacts to bridge neural cells

wide variety of potential uses, ranging from the restoration of vision to the treatment of dementia

current challenges

functionality of current electrodes decrease over time

attributed to neuron degradation and foreign body encapsulation

due to mismatch between mechanical properties of electrode and brain tissue

proposed solution

development of mechanically adaptive implants

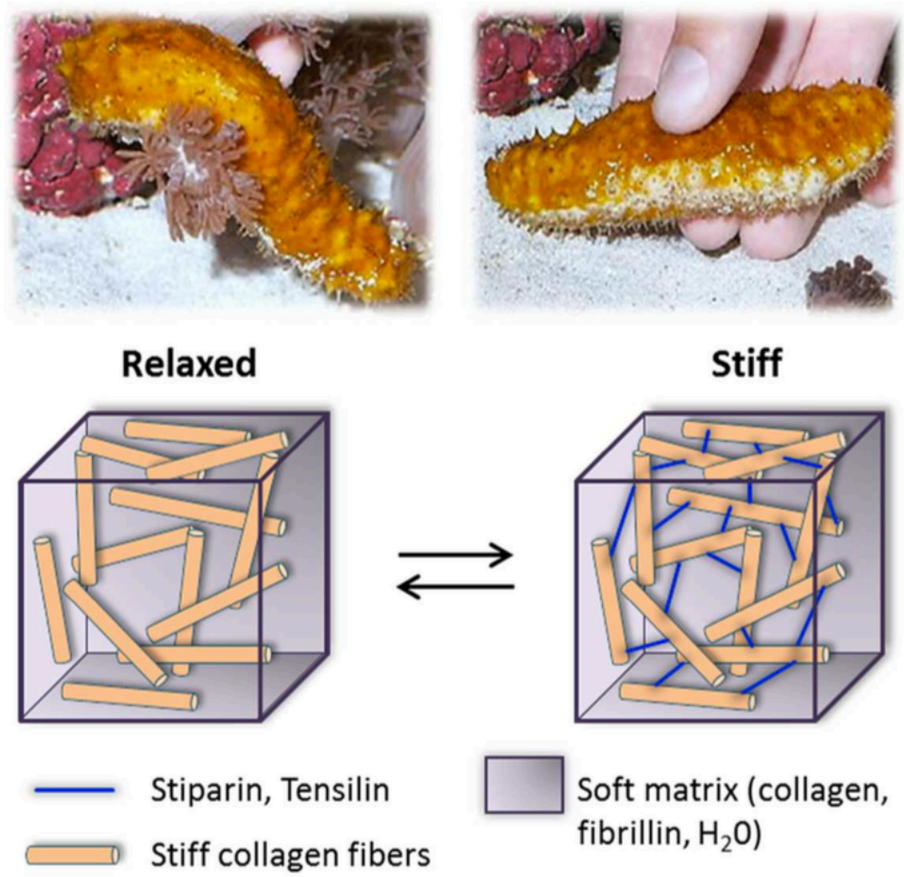
rigid to facilitate implantation; soften upon exposure to physiological conditions

aim to reduce inflammatory response of surrounding tissue

Montero De Espinosa, L.; Meesorn, W.; Moatsou, D.; Weder, C. *Chem. Rev.* **2017**, *117*, 12851–12892.

Sea Cucumber Inspired Intracortical Implants

- Sea cucumber defends itself by stiffening its usually flexible dermis



in the presence of predators, glycoprotein stiparin, a stiffening agent is absorbed from extracellular matrix

↓

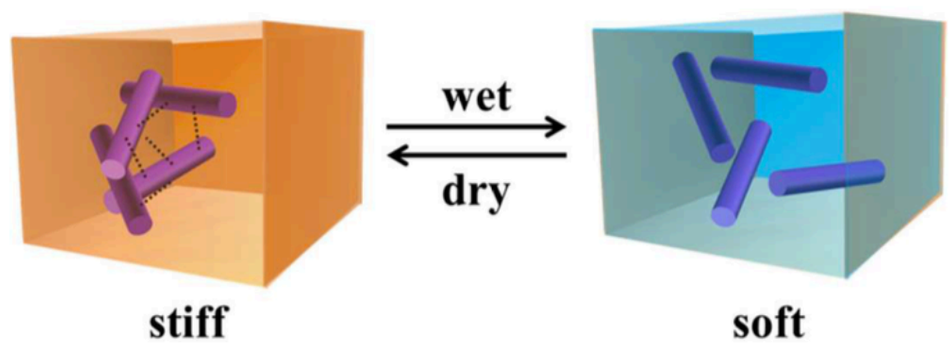
stiparin bridges the collagen fibers, causing rapid aggregation

↓

elastic modulus of dermis increases from 5 MPa to 50 MPa

H-bonding between surface hydroxyl groups of cellulose nanocrystals can be disrupted by water molecules

can we harness this mechanical adaptiveness towards intracotical implants?



Capadona, J. R.; Shanmuganathan, K.; Tyler, D. J.; Rowan, S. J.; Weder, C. *Science* **2008**, *319*, 1370–1374.

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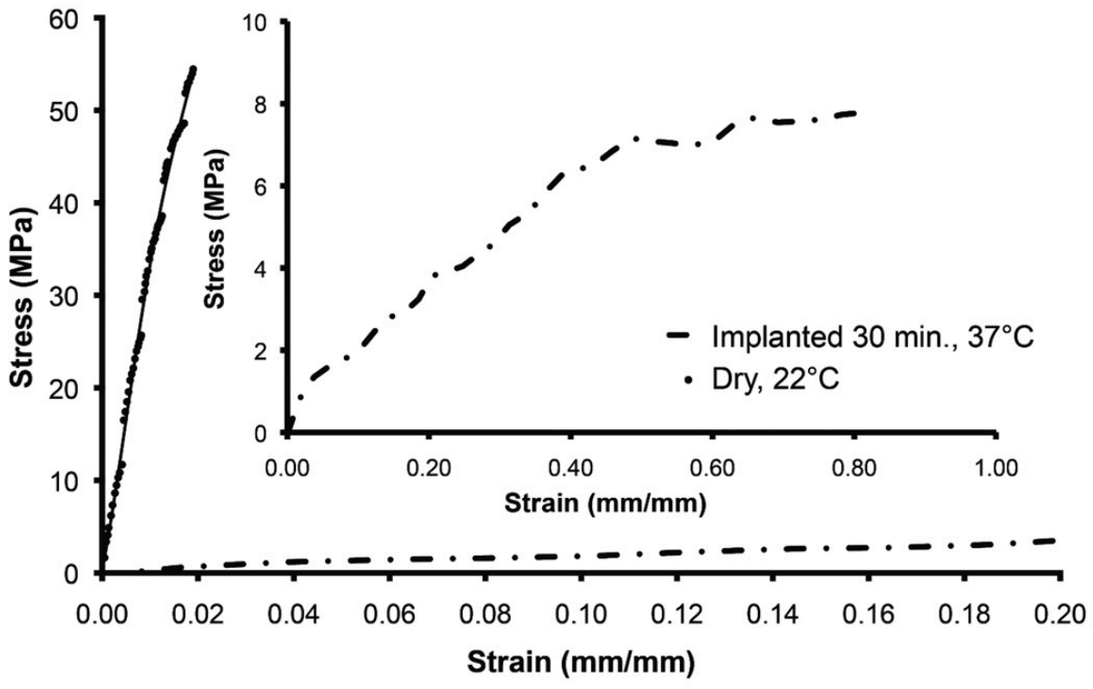
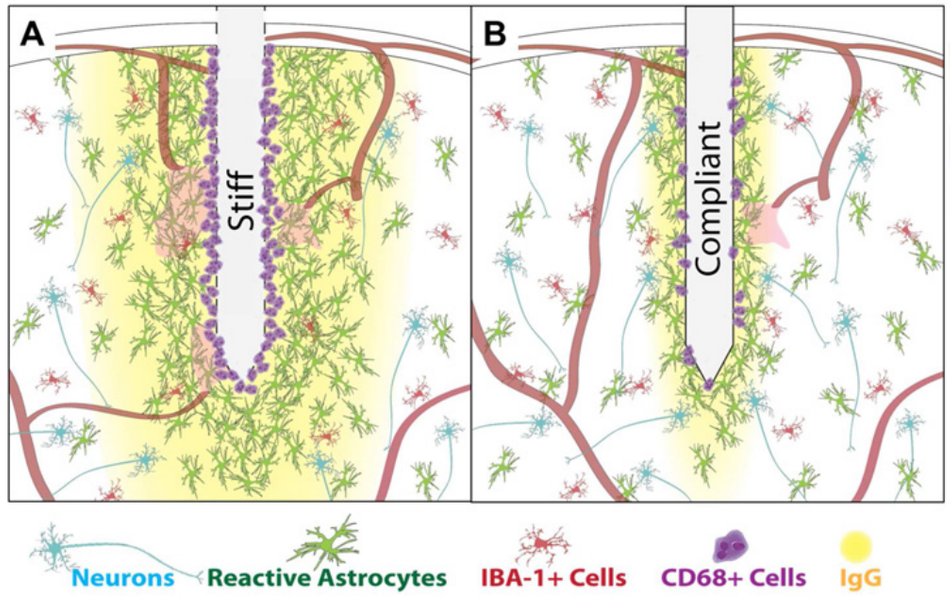
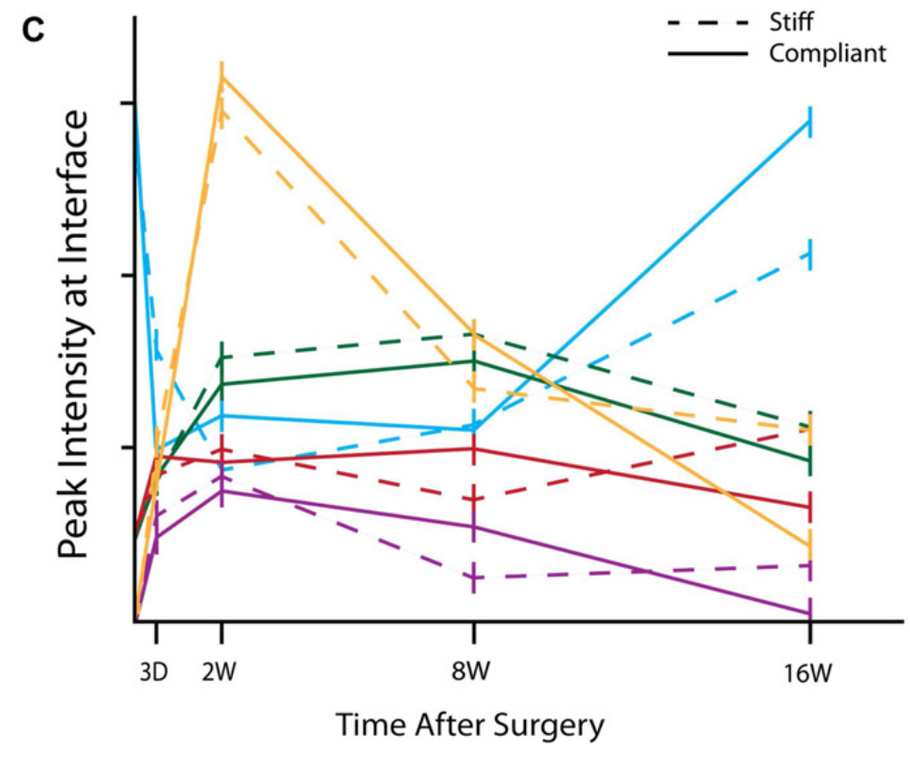


elastic modulus of cellulose nanocrystal containing implants (in a PVAc matrix) decreased 100x upon implantation in artificial cerebral spinal fluid





Nguyen, J. K.; Park, D. J.; Skousen, J. L.; Hess-Dunning, A. E.; Tyler, D. J.; Rowan, S. J.; Weder, C.; Capadona, J. R. *J. Neural Eng.* **2014**, *11*, 56014.

Outline

Light Responsive Systems

Chemo Responsive Systems

Electrically Responsive Systems

Applications of molecular motors to organic synthesis

Electrochromic Smart Windows

Electrochomic windows: windows that change colour in response to applied potential difference

why electrochromic windows?

71% of electricity consumed in the US is from buildings

more than 30% of this load comes from indoor heating/cooling

darkening of windows can help to block heat transfer

environmentally friendly; up to 40% cost savings

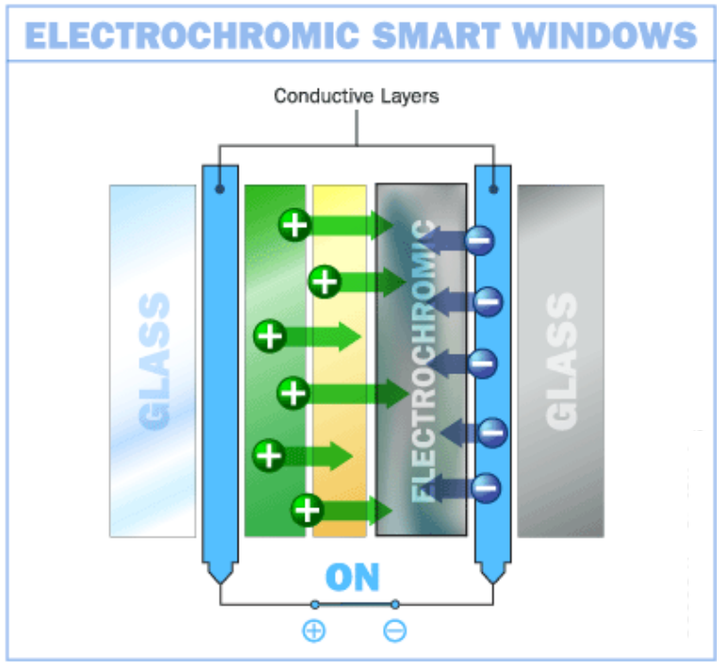
Desirable Properties

fast switching speed

high cycling stability

mid-cycle stability

low manufacturing cost



current technologies and limitations

metal oxides	→	slow switching
viologens	→	sensitivity to UV
polymer dispersed liquid crystals	→	“on” state requires applied voltage
conjugated conducting polymers	→	mostly coloured in both states

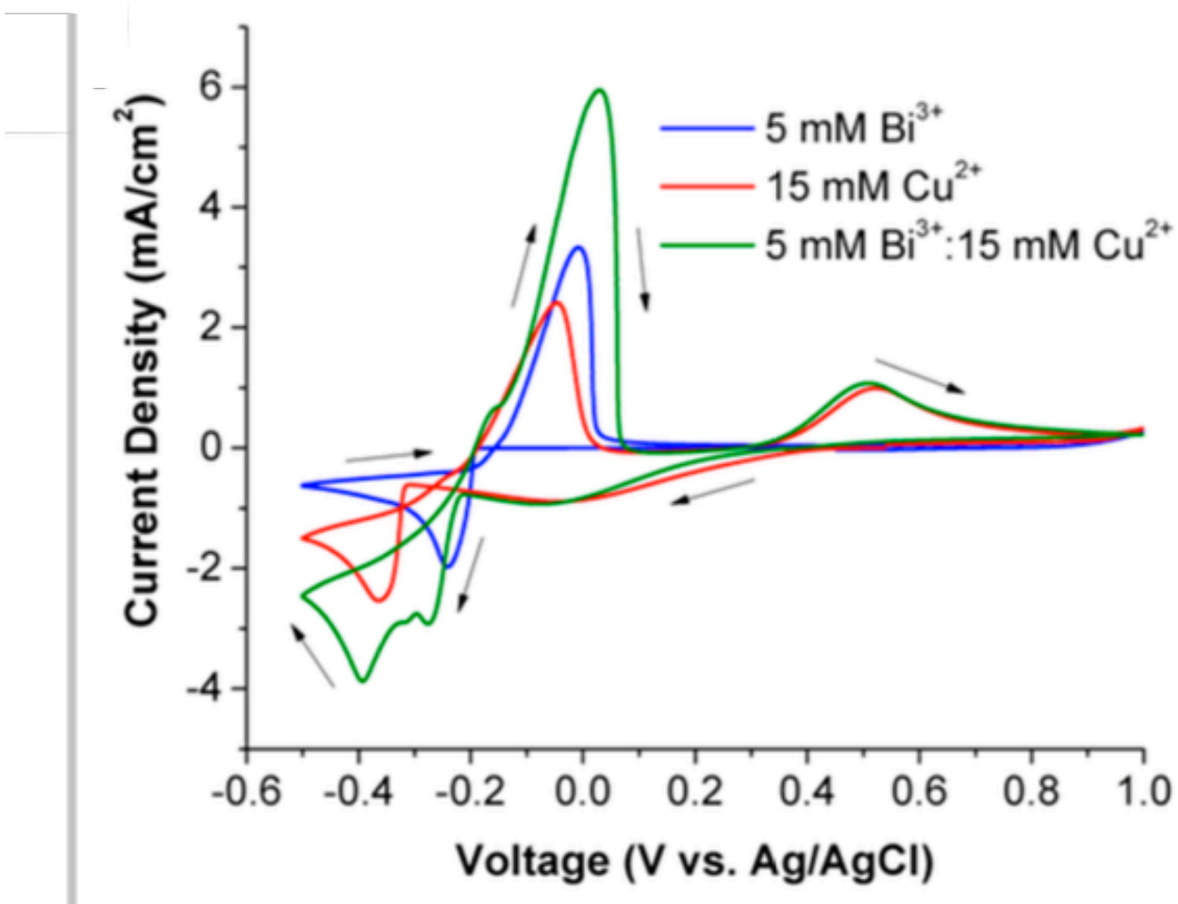
Mortimer, R. J. Annu. Rev. Mater. Res. **2011**, 41, 241–268.

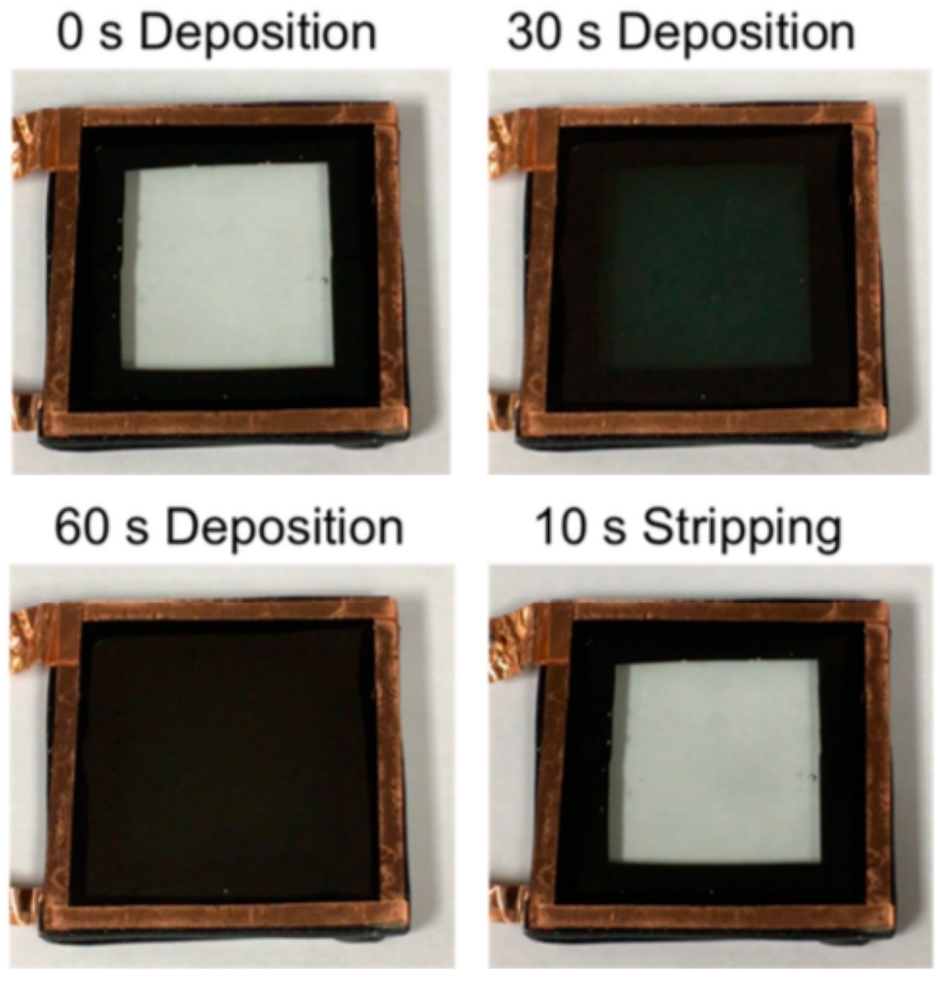
Electrochromic Smart Windows: Recent Advances

■ Reversible Metal Electrodeposition of Bi and Cu

Electrodeposition of Cu is well understood, very uniform, but Cu is red in colour

Bi is black and opaque, aesthetically desirable for smart windows





Hernandez, T. S.; Barile, C. J.; Strand, M. T.; Dayrit, T. E.; Slotcavage, D. J.; McGehee, M. D. *ACS Energy Lett.* **2017**, 104–111.

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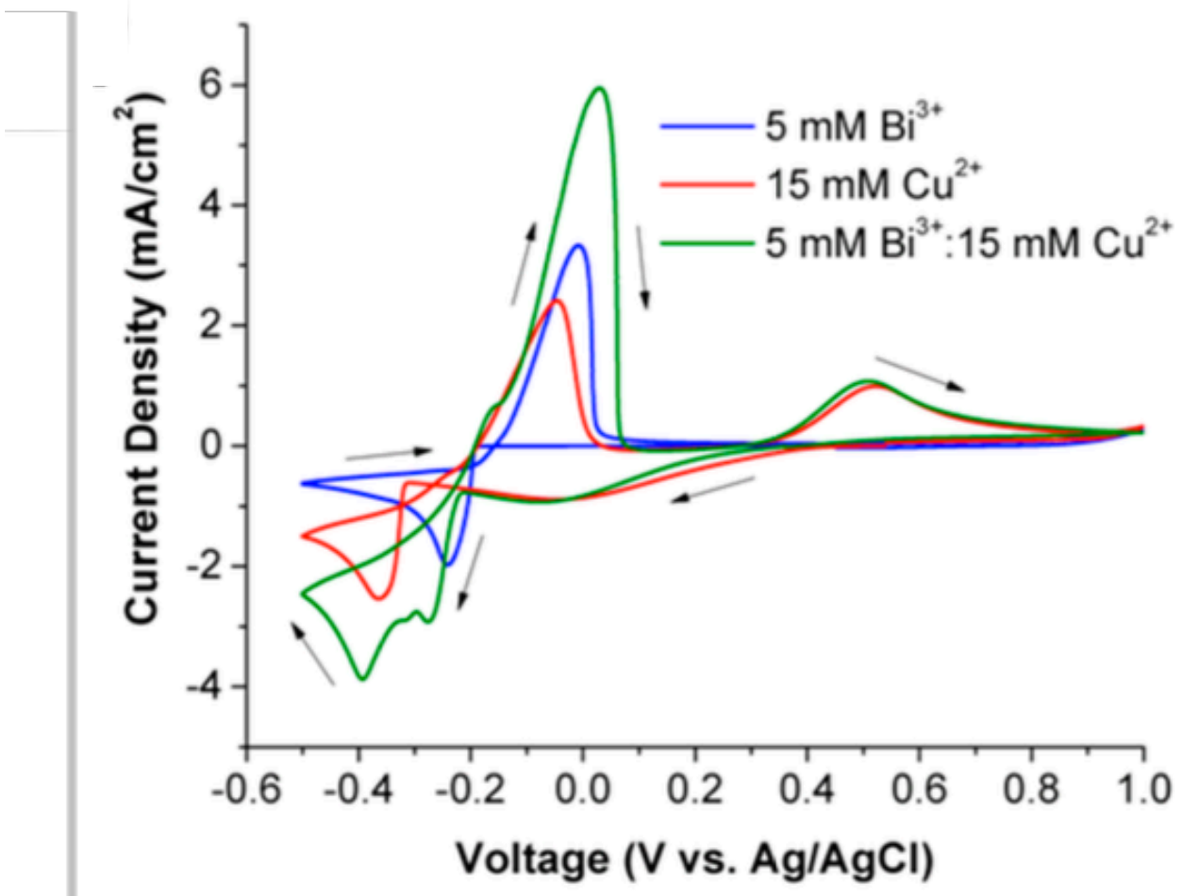

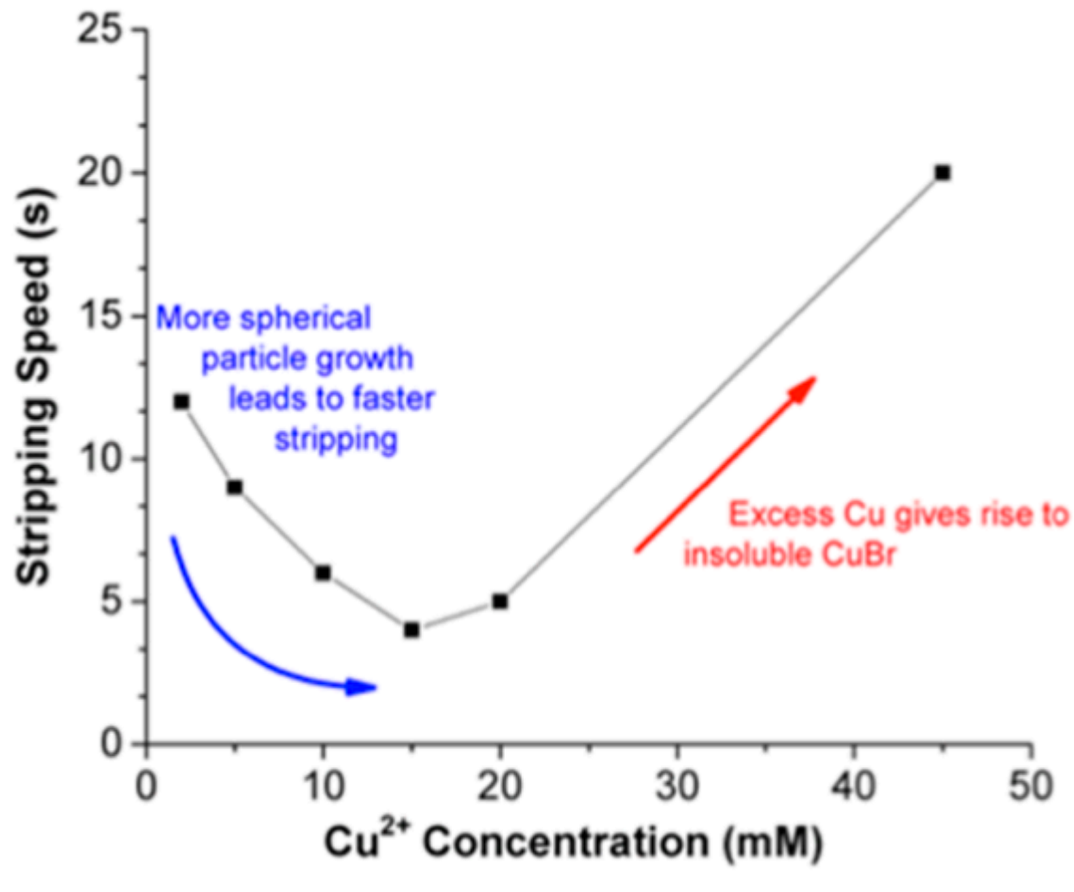

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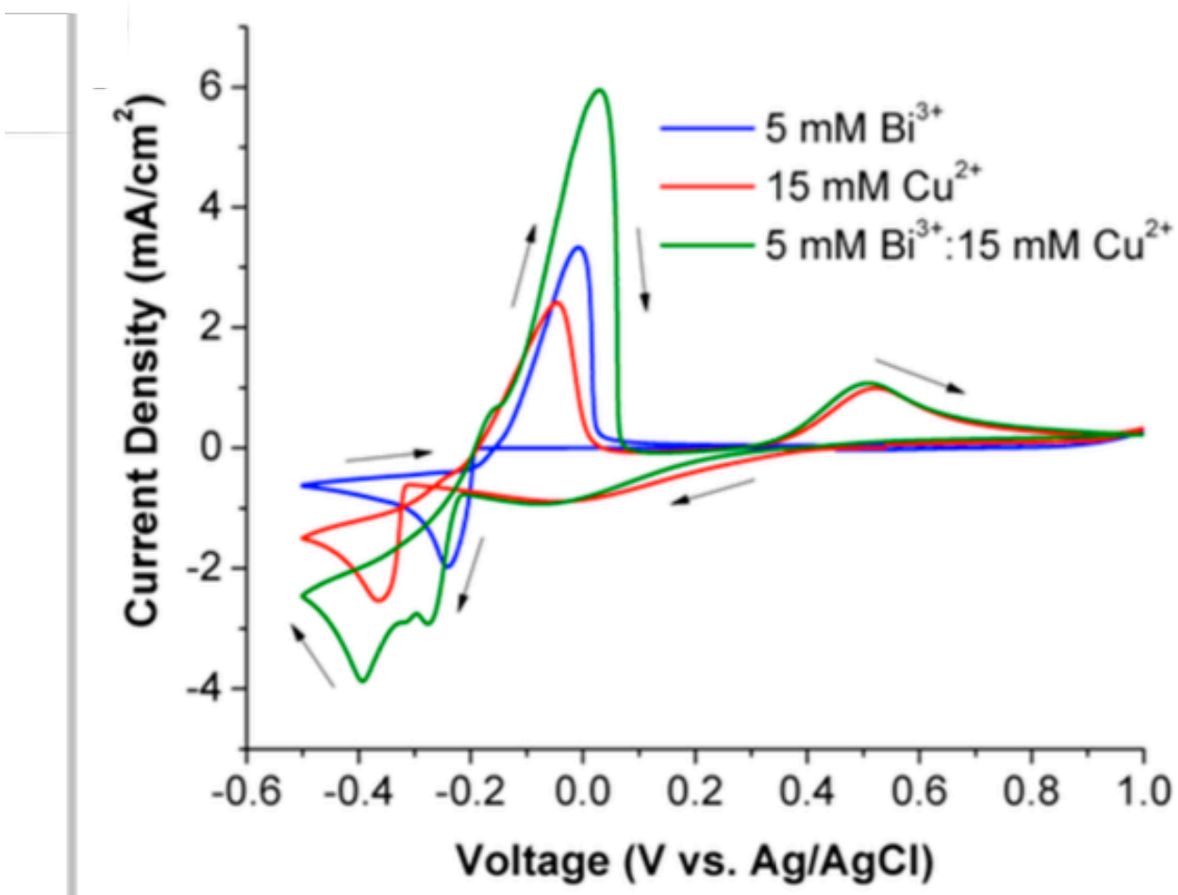

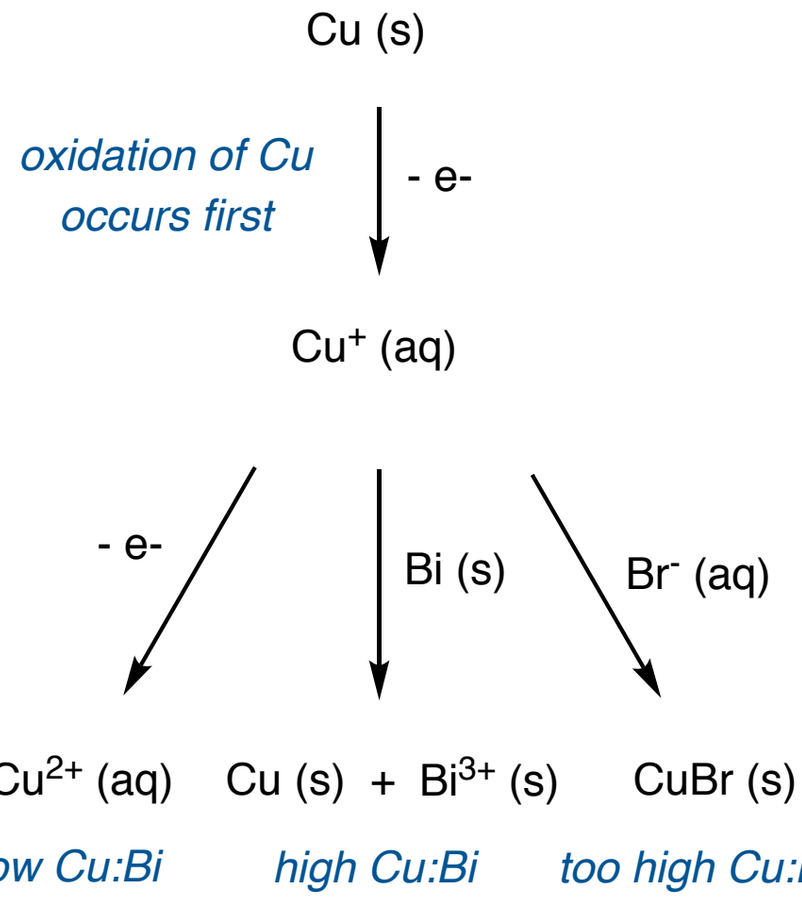

control of Cu:Bi ratio is critical for rapid stripping

Hernandez, T. S.; Barile, C. J.; Strand, M. T.; Dayrit, T. E.; Slotcavage, D. J.; McGehee, M. D. *ACS Energy Lett.* **2017**, 104–111.

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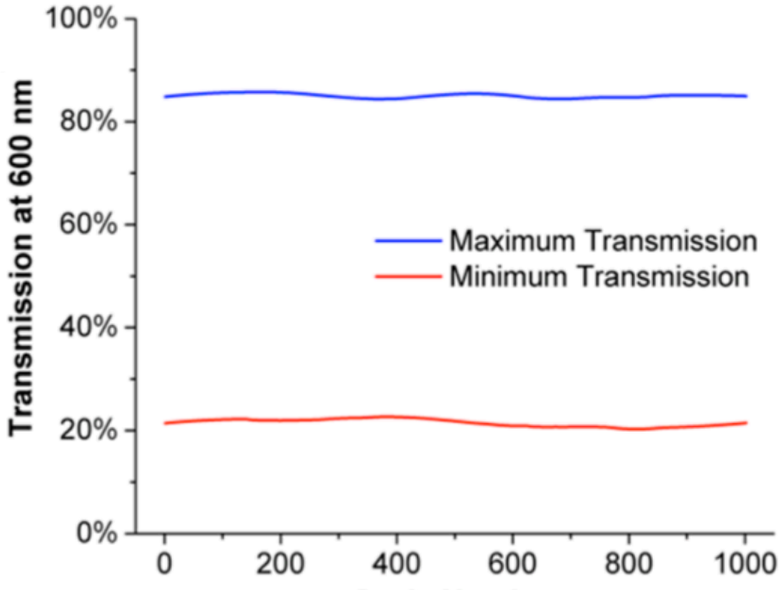
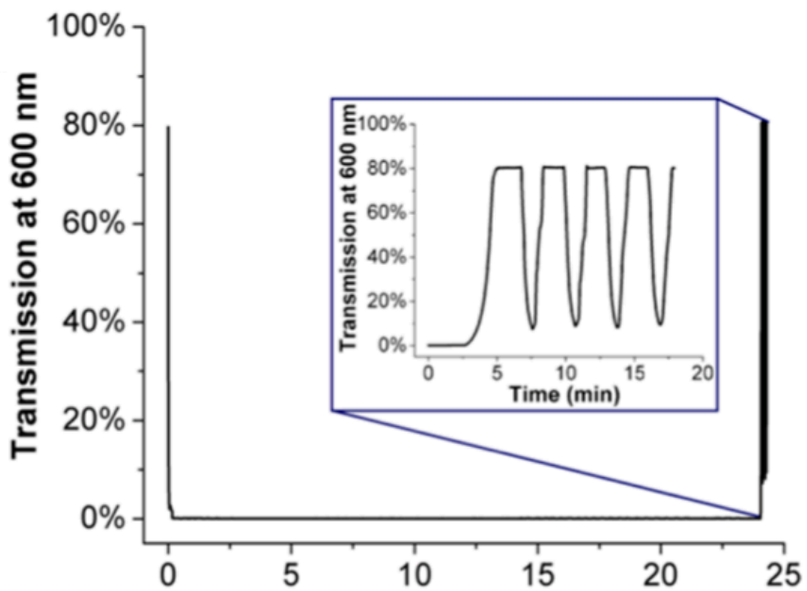
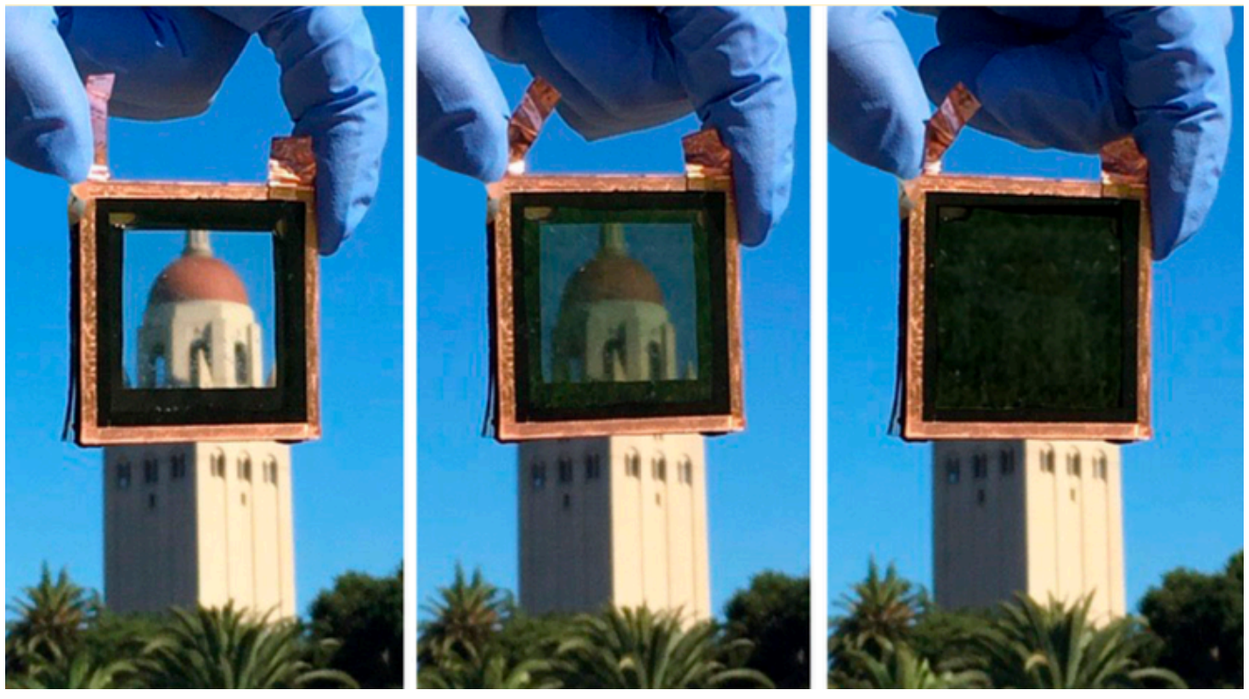






5cm x 5cm prototype

60 s deposition

10 s stripping

transmission easily controlled

Hernandez, T. S.; Barile, C. J.; Strand, M. T.; Dayrit, T. E.; Slotcavage, D. J.; McGehee, M. D. *ACS Energy Lett.* **2017**, 104–111.

Dynamic Camouflage via Plamonic Tuning

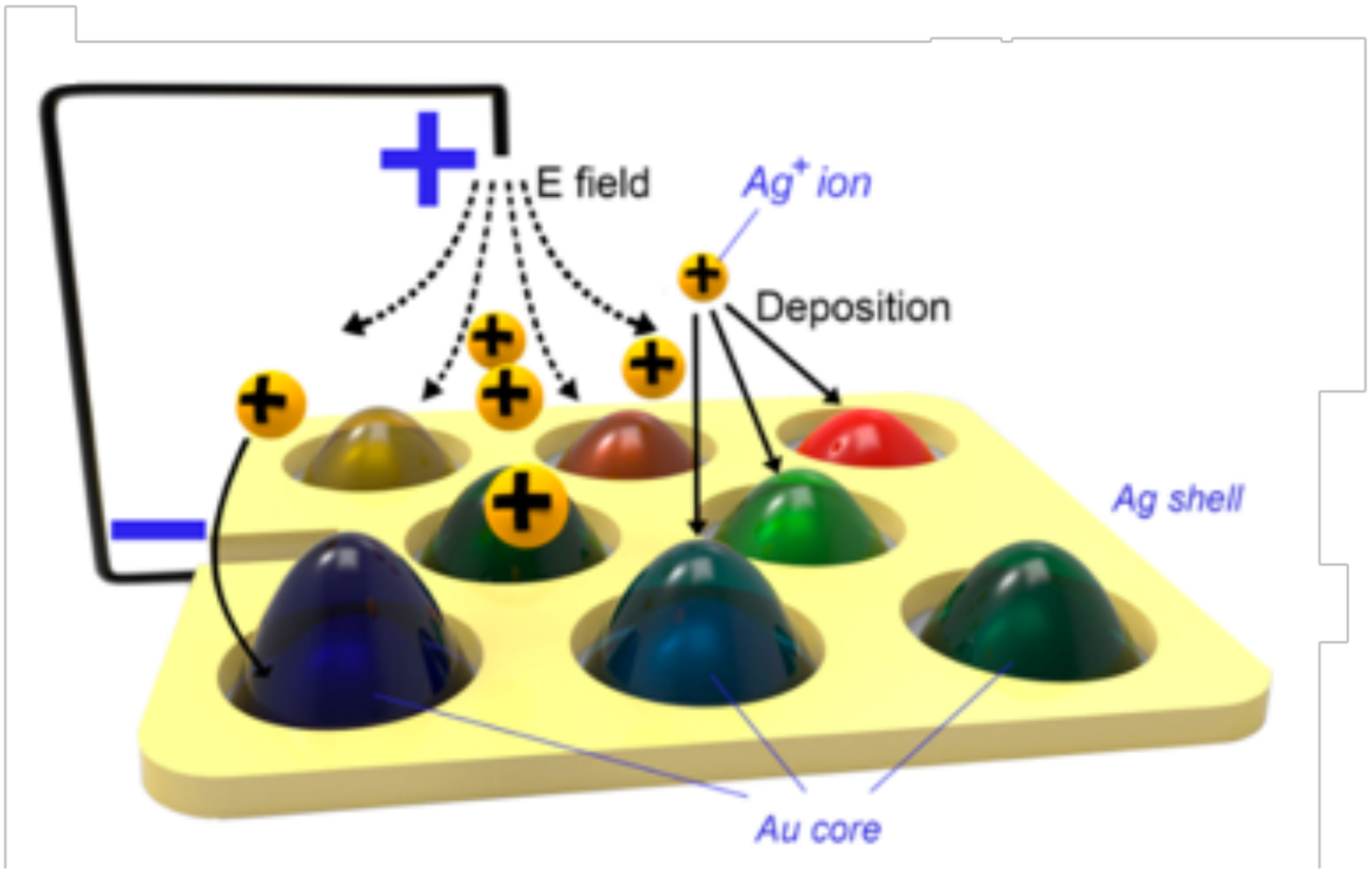
Plasmon: a quanta of plasma oscillations

Plasma oscillations: rapid oscillations of electron density in conducting media like metals

optical properties of plasmonic metal-nanostructures are highly sensitive to material thickness

can we exploit reversible electrodeposition to control optical properties in real time?

Device Synthesis & Design



1. nanoholes are etched into SiO_2/ITO glass by complete etching of SiO_2

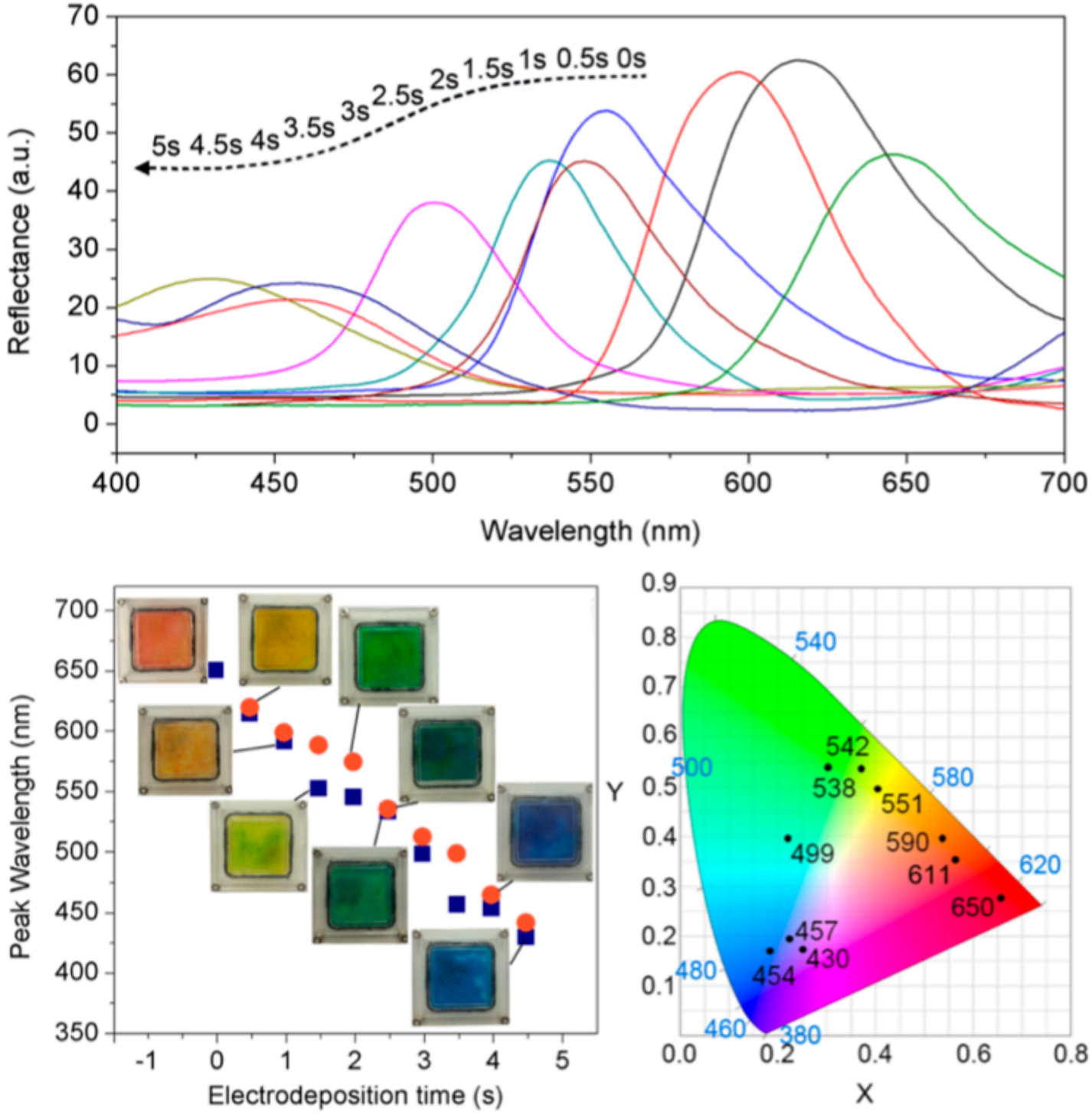
2. Au core is deposited, creating an array of Au nanodomes

3. Au nanodomes are filled with gel electrolyte containing Ag^+ ions

Wang, G.; Chen, X.; Liu, S.; Wong, C.; Chu, S. *ACS Nano* **2016**, *10*, 1788–1794.

Dynamic Camouflage via Plamonic Tuning

Optical properties of device as a function of electrodeposition time



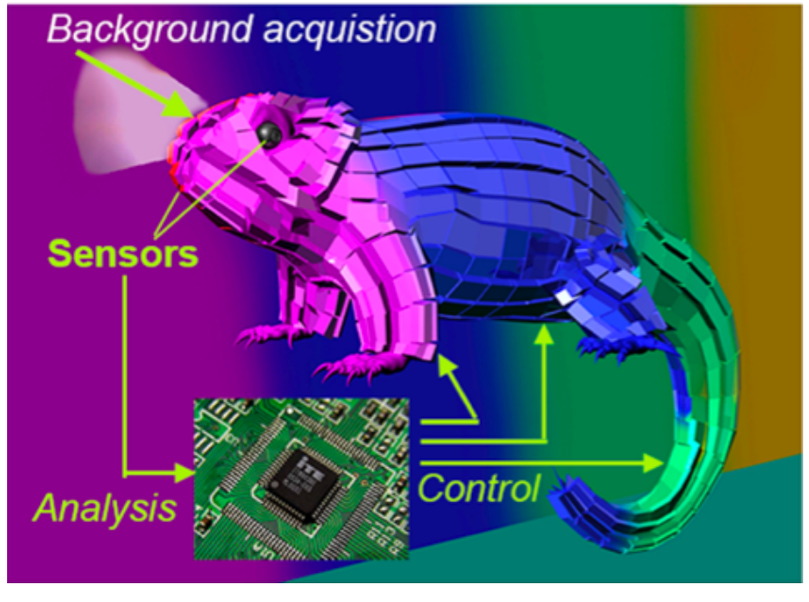
Wang, G.; Chen, X.; Liu, S.; Wong, C.; Chu, S. *ACS Nano* **2016**, *10*, 1788–1794.

Dynamic Camouflage via Plamonic Tuning

Application to artificial chameleon

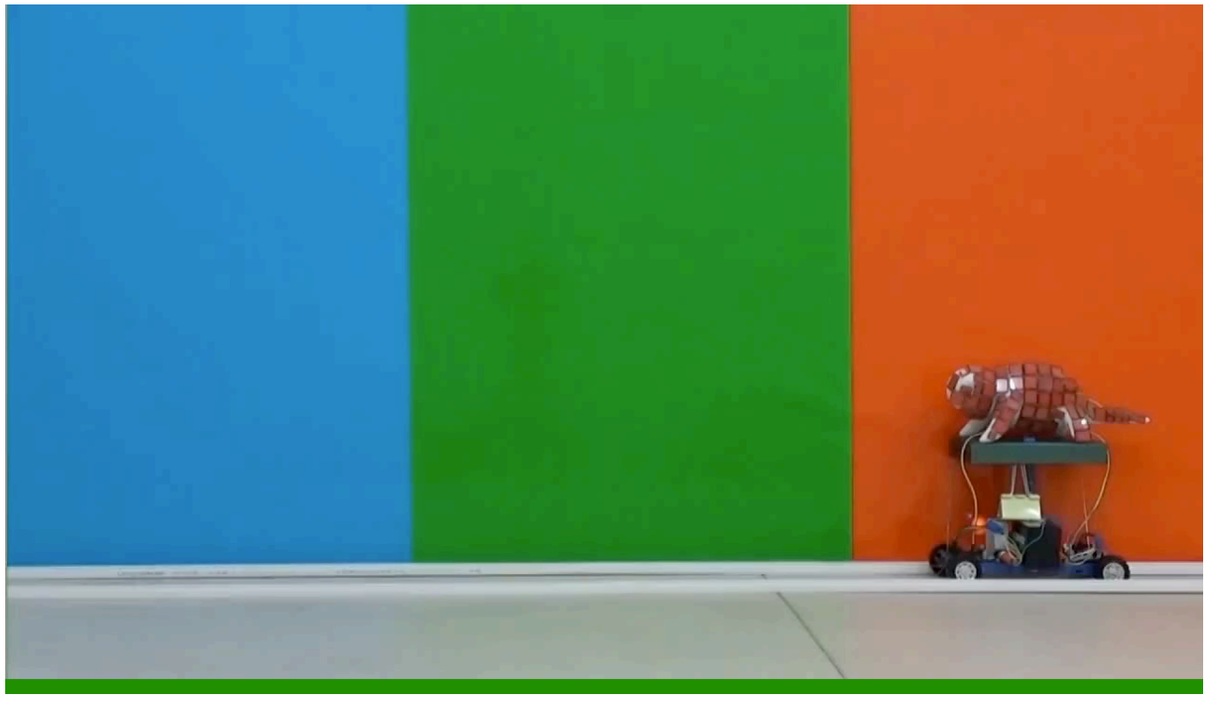
whole body is covered with plasmonic cell device

sensors are capable of detecting red, green and blue



computer chip will output voltage signals based on sensor

plasmonic cell will adjust colour accordingly



video available at: http://pubs.acs.org/doi/suppl/10.1021/acsnano.5b07472

Wang, G.; Chen, X.; Liu, S.; Wong, C.; Chu, S. *ACS Nano* **2016**, *10*, 1788–1794.

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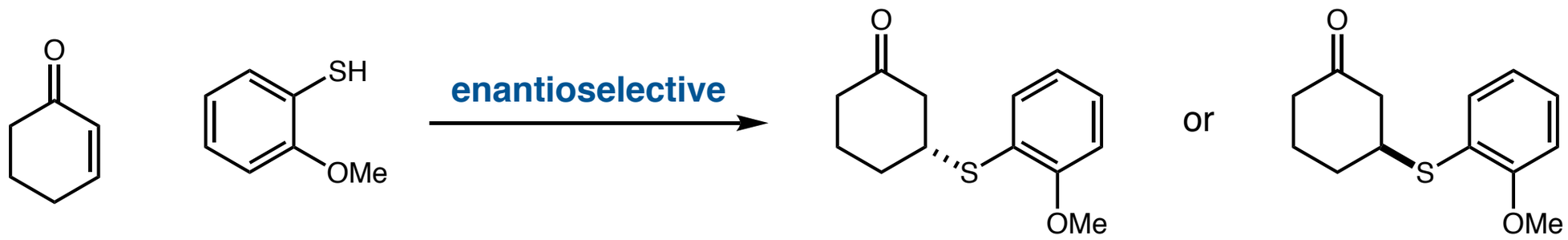
Chiral Catalysis Using Molecular Machines

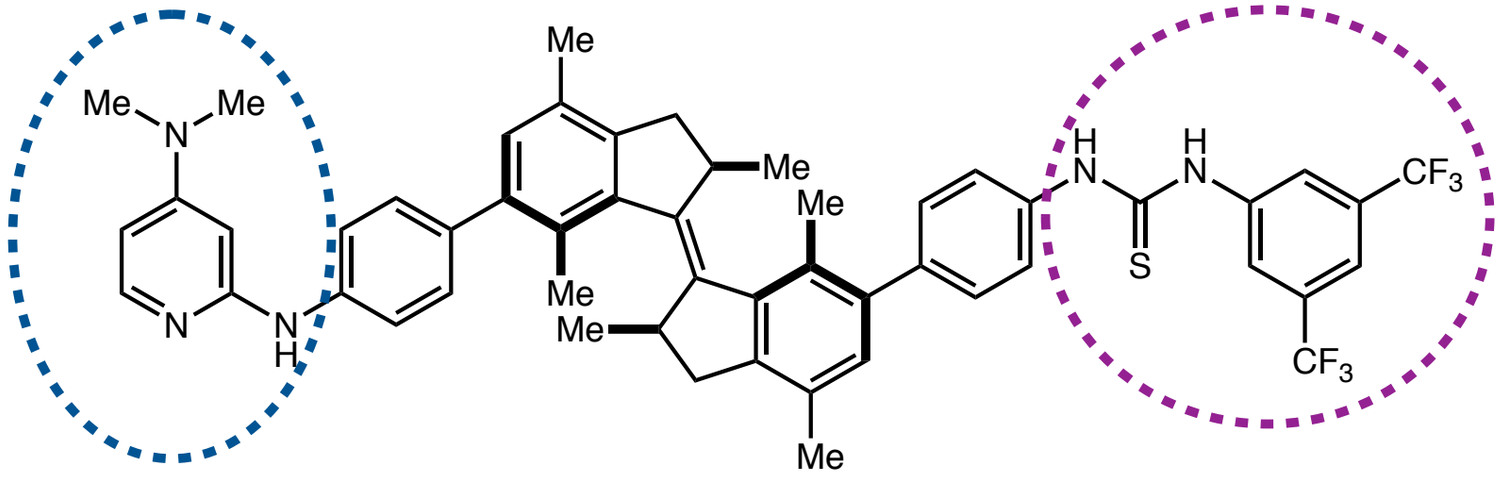
Proof of concept: stimuli-responsive chiral catalysis using molecular machines



A

DMAP

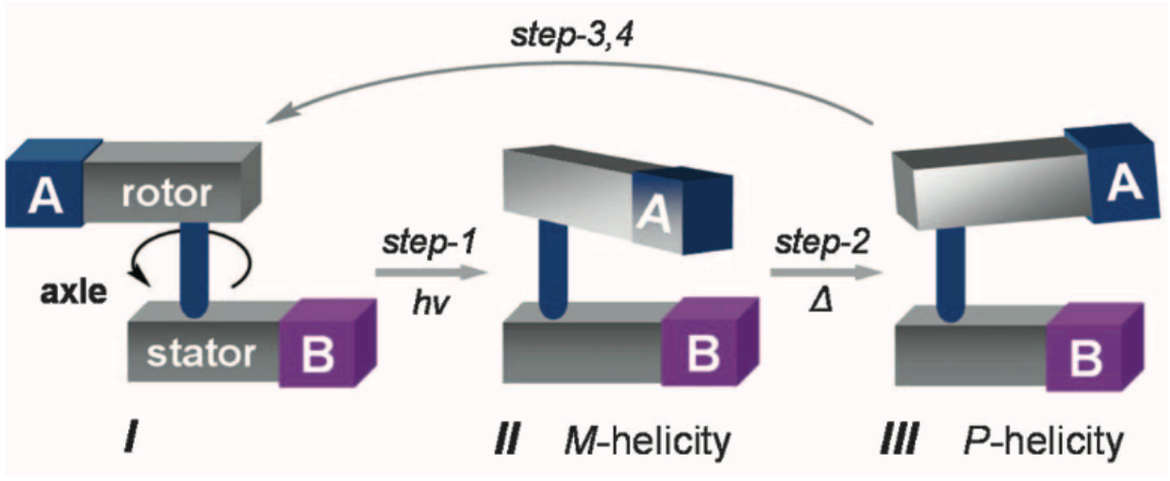
co-catalyst



B

H-bonding

thiourea catalyst



(2*R*,2'*R*)-(*P*,*P*)-*trans* catalyst

(2*R*,2'*R*)-(*M*,*M*)-*cis* catalyst

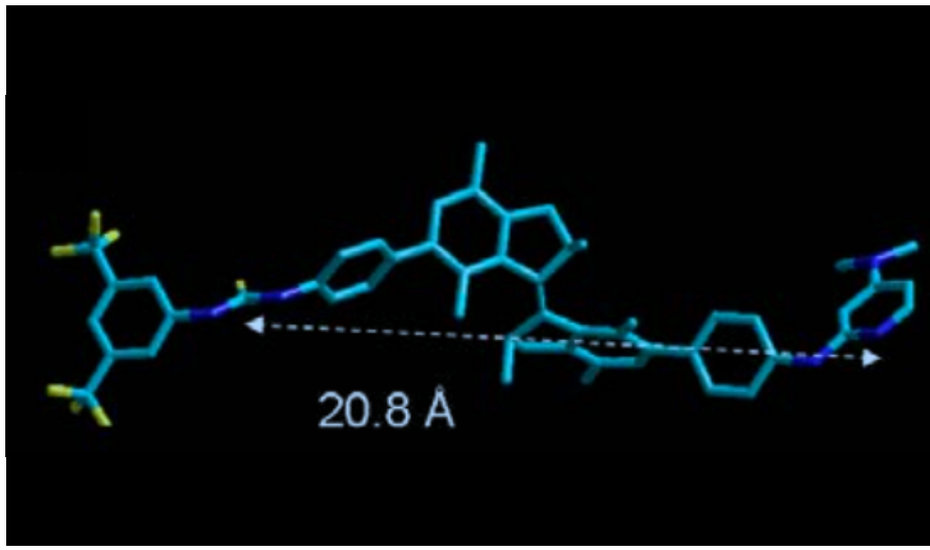
(2*R*,2'*R*)-(*P*,*P*)-*cis* catalyst

- ***stimuli responsive 3-stage rotary cycle***
- ***cooperative catalysis***
- ***rotor controls chirality of system***
- ***distinct enantioselectivity at each stage***

Wang, J.; Feringa, B. L. *Science* **2011**, *331*, 1429.

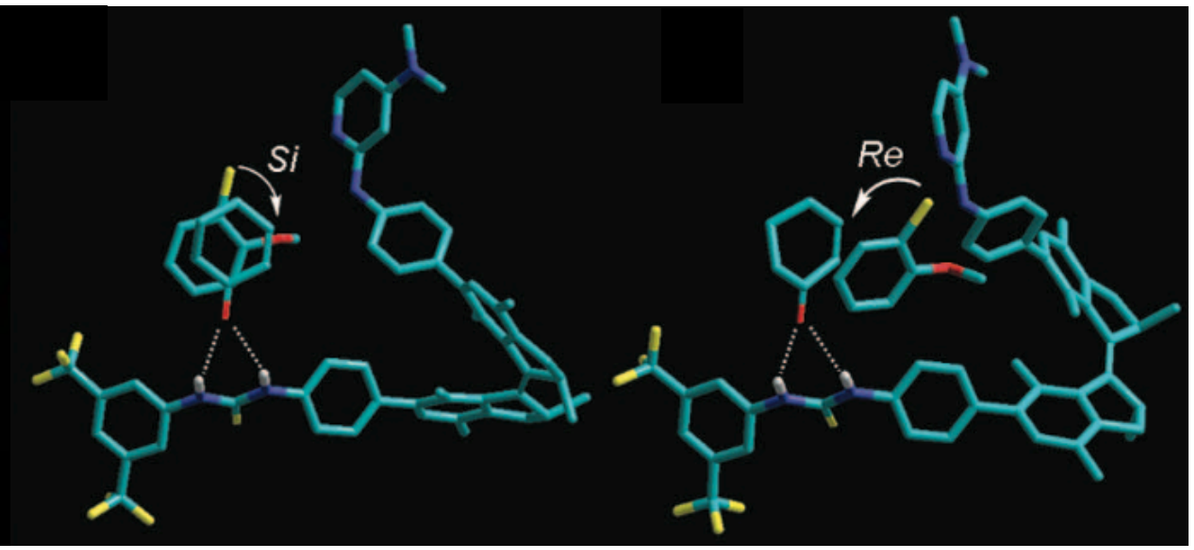
Chiral Catalysis Using Molecular Machines

Proof of concept: stimuli-responsive chiral catalysis using molecular machines



(2*R*,2'*R*)-(*P*,*P*)-*trans*

S/R = 49/51

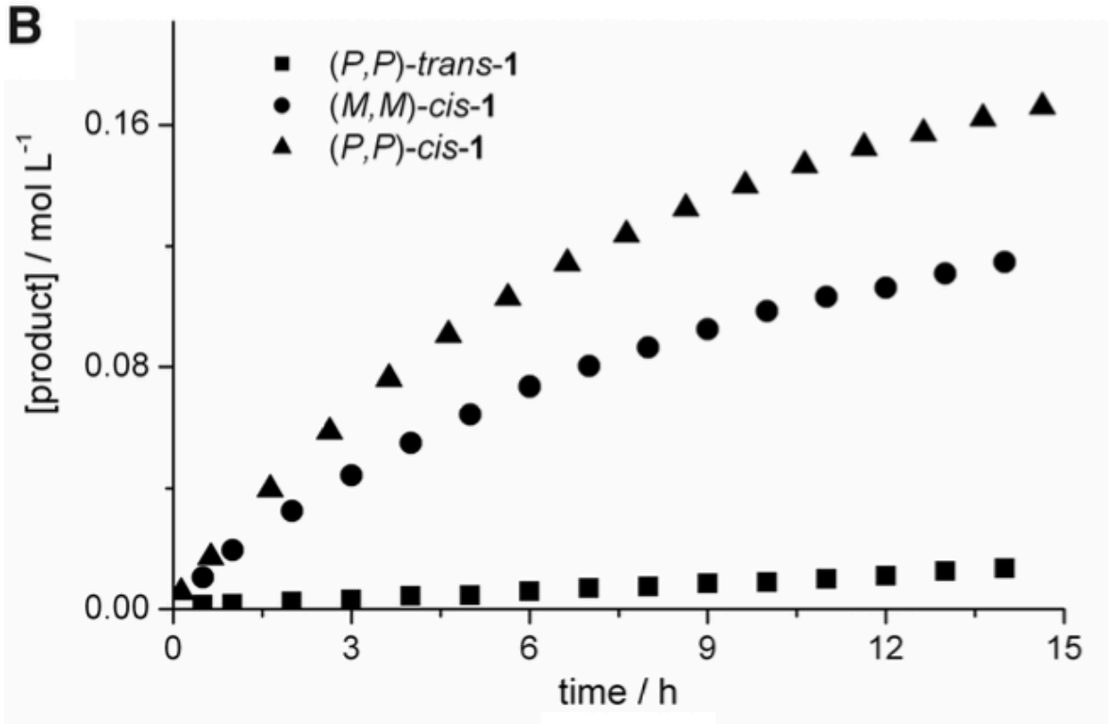


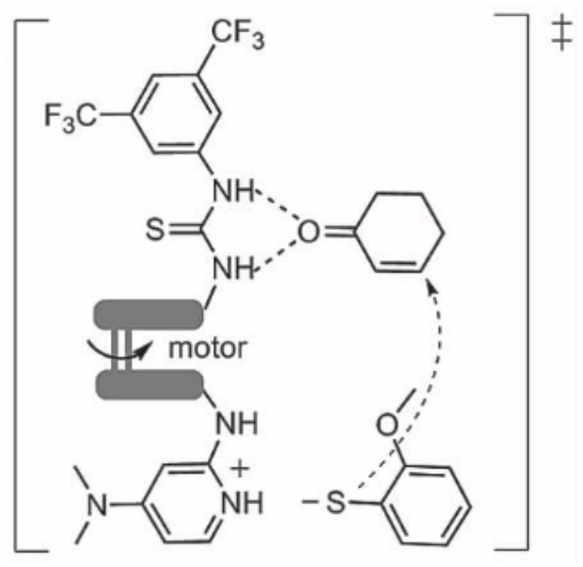
(2*R*,2'*R*)-(*M*,*M*)-*cis*

S/R = 75/25

(2*R*,2'*R*)-(*P*,*P*)-*cis*

S/R = 23/77

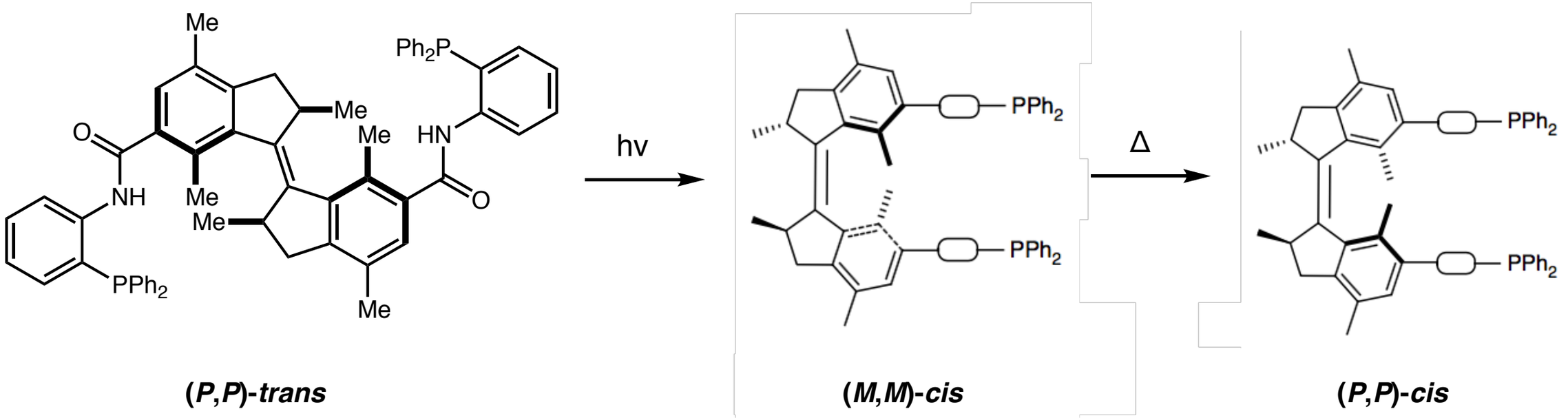


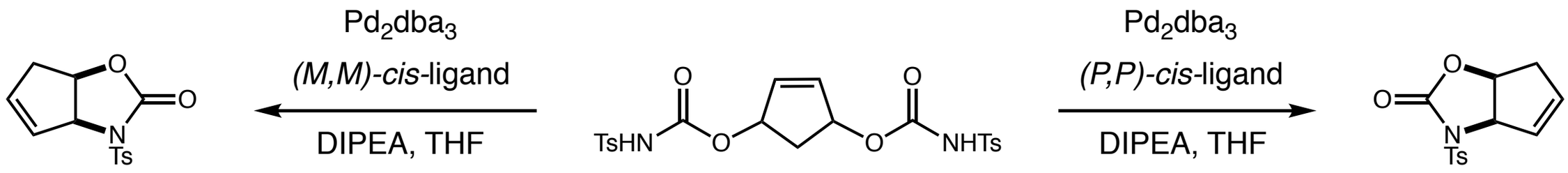


cooperative catalysis is key for reactivity and stereoselectivity

Chiral Catalysis Using Molecular Machines

Proof of concept: stimuli-responsive chiral catalysis using molecular machines

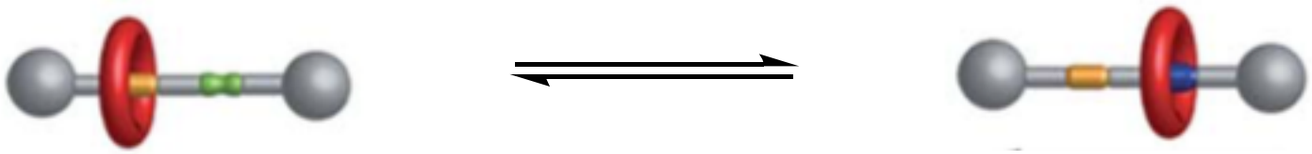


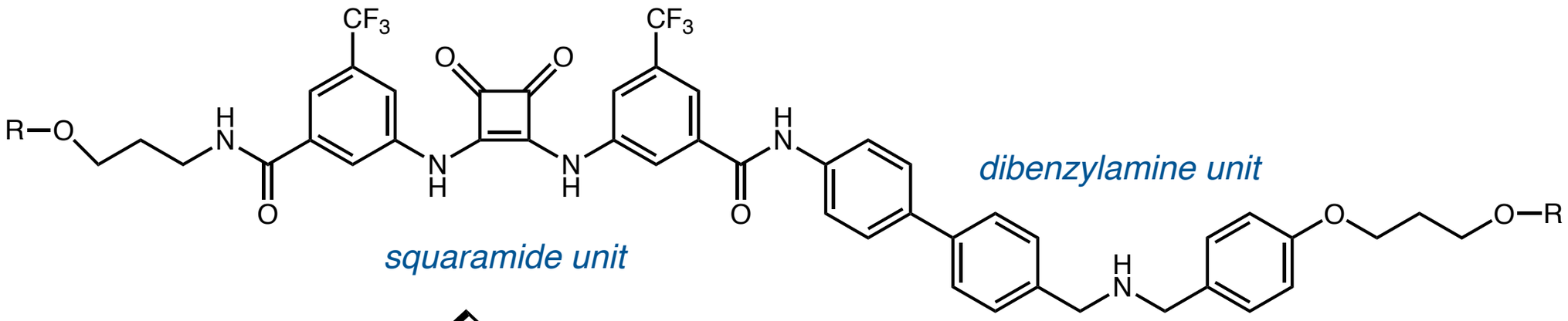


stimuli-responsive ligands can be designed for asymmetric transition metal catalysis

Zhao, D.; Neubauer, T. M.; Feringa, B. L. *Nat. Commun.* **2015**, *6*, 1–7.

Use of Rotaxanes as On/Off Switches for Catalysis

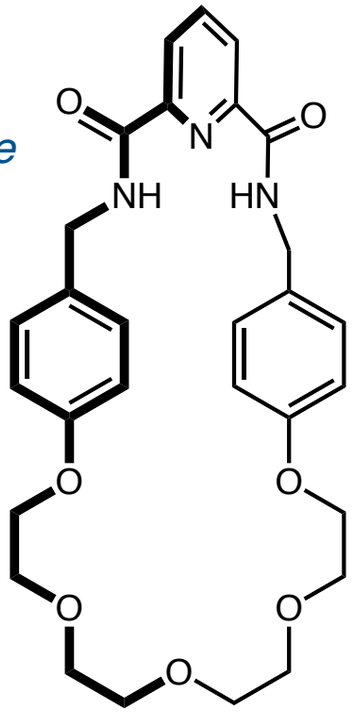




rotaxane thread

pyridyl-2,6-dicarboxyamide

crown ether



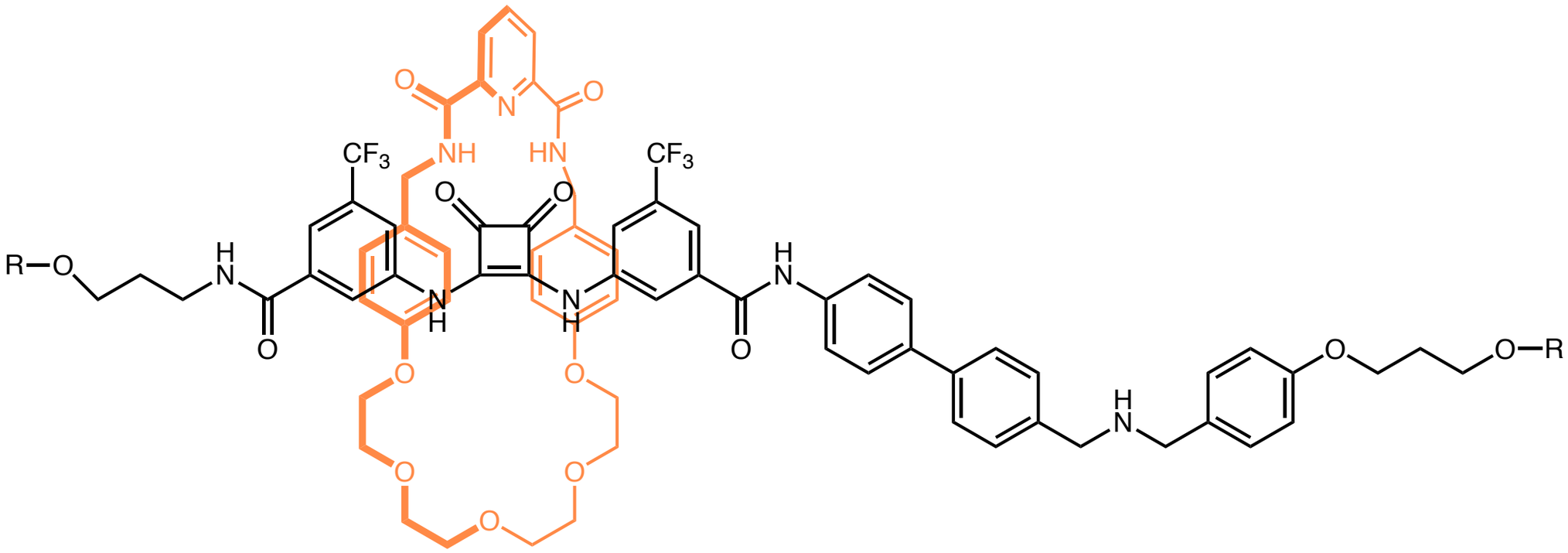
rotaxane macrocycle

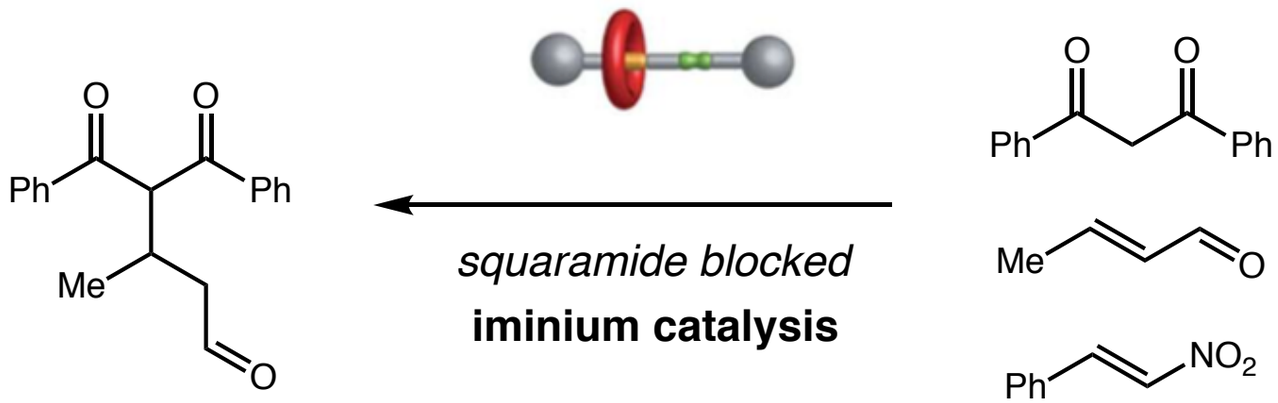
squaramide of thread binds to pyridyl-2,6-dicarboxyamide unit of macrocycle

dibenzylamine of thread binds to crown ether region of macrocycle, but only when protonated

Beswick, J.; Blanco, V.; De Bo, G.; Leigh, D. A.; Lewandowska, U.; Lewandowski, B.; Mishiro, K. *Chem. Sci.* **2015**, *6*, 140–143.

Use of Rotaxanes as On/Off Switches for Catalysis





40% yield
trace impurity

Beswick, J.; Blanco, V.; De Bo, G.; Leigh, D. A.; Lewandowska, U.; Lewandowski, B.; Mishiro, K. *Chem. Sci.* **2015**, *6*, 140–143.

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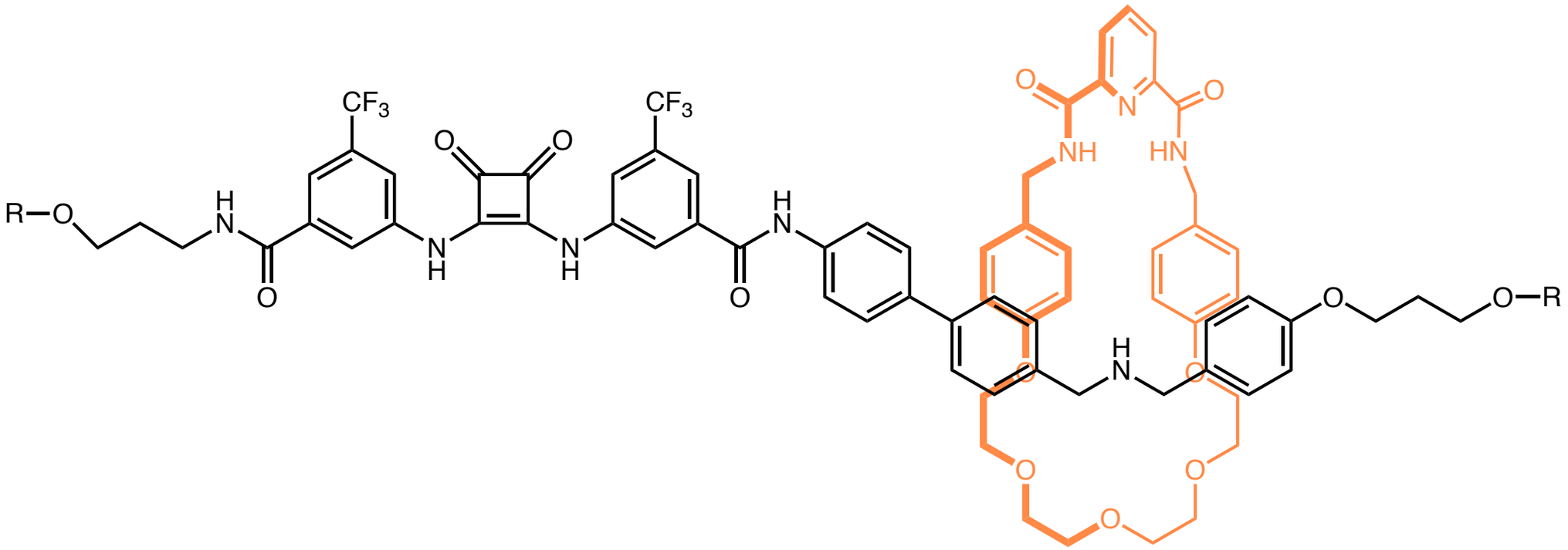
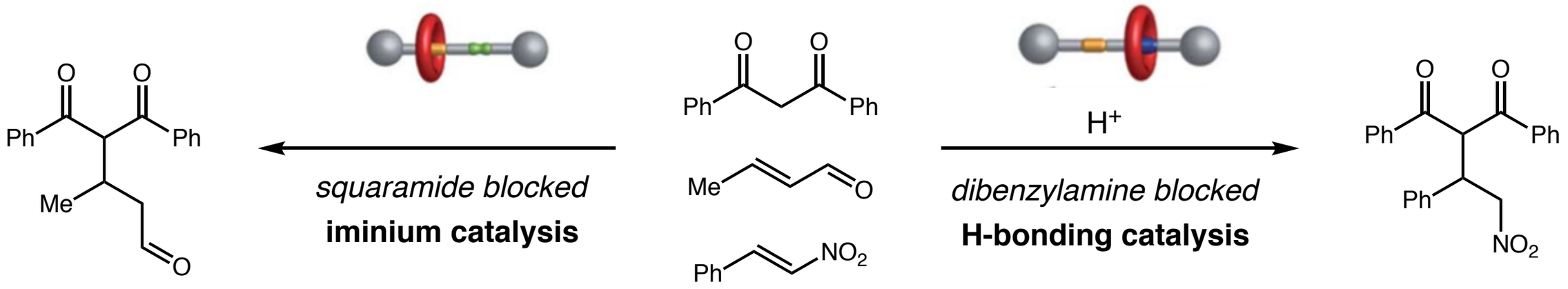


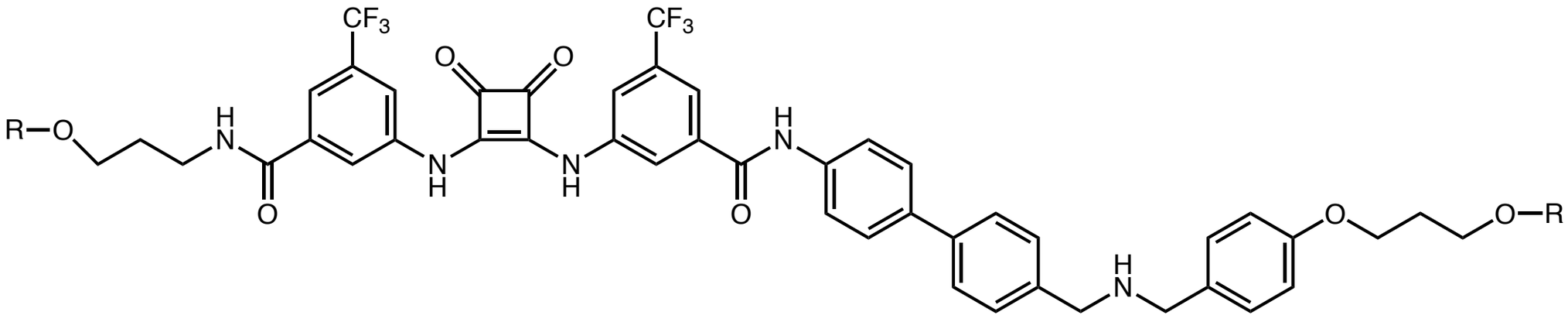


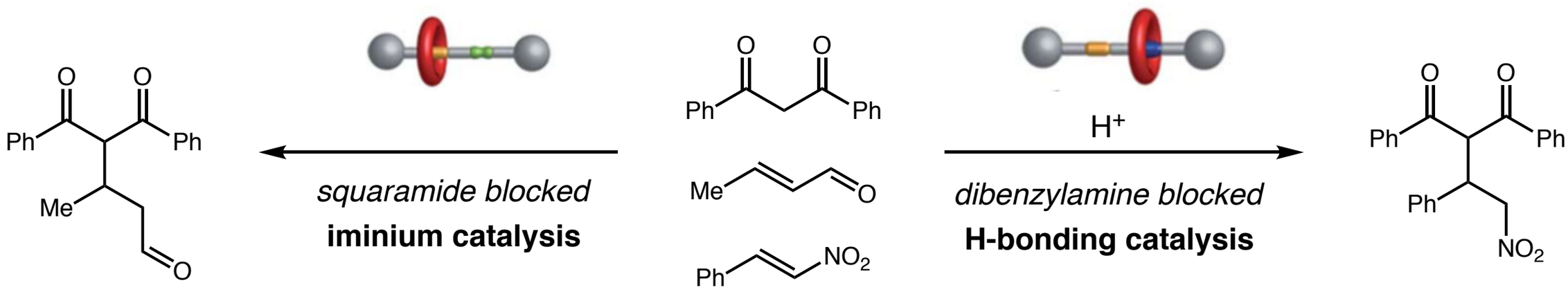
40% yield
trace impurity

75% yield
trace impurity

Beswick, J.; Blanco, V.; De Bo, G.; Leigh, D. A.; Lewandowska, U.; Lewandowski, B.; Mishiro, K. *Chem. Sci.* **2015**, *6*, 140–143.

Use of Rotaxanes as On/Off Switches for Catalysis





1:1 ratio of products observed when free catalyst is used

Beswick, J.; Blanco, V.; De Bo, G.; Leigh, D. A.; Lewandowska, U.; Lewandowski, B.; Mishiro, K. *Chem. Sci.* **2015**, *6*, 140–143.

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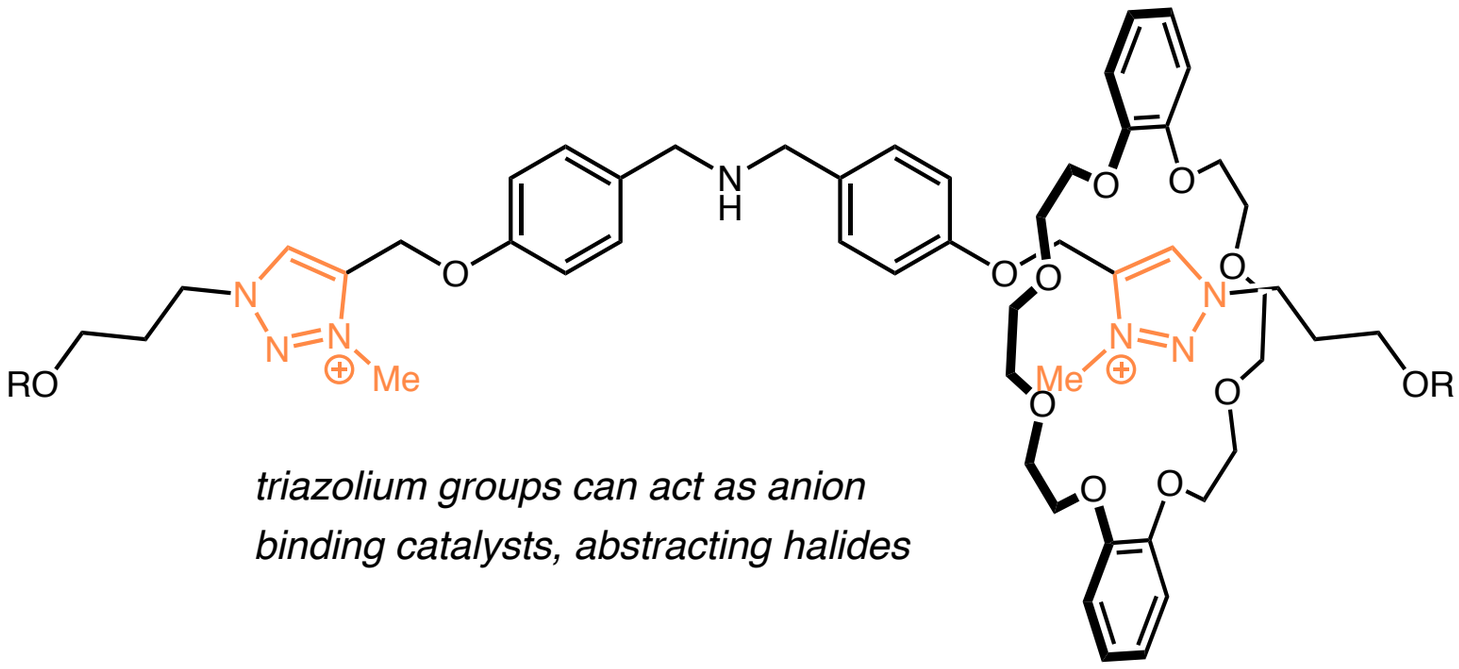
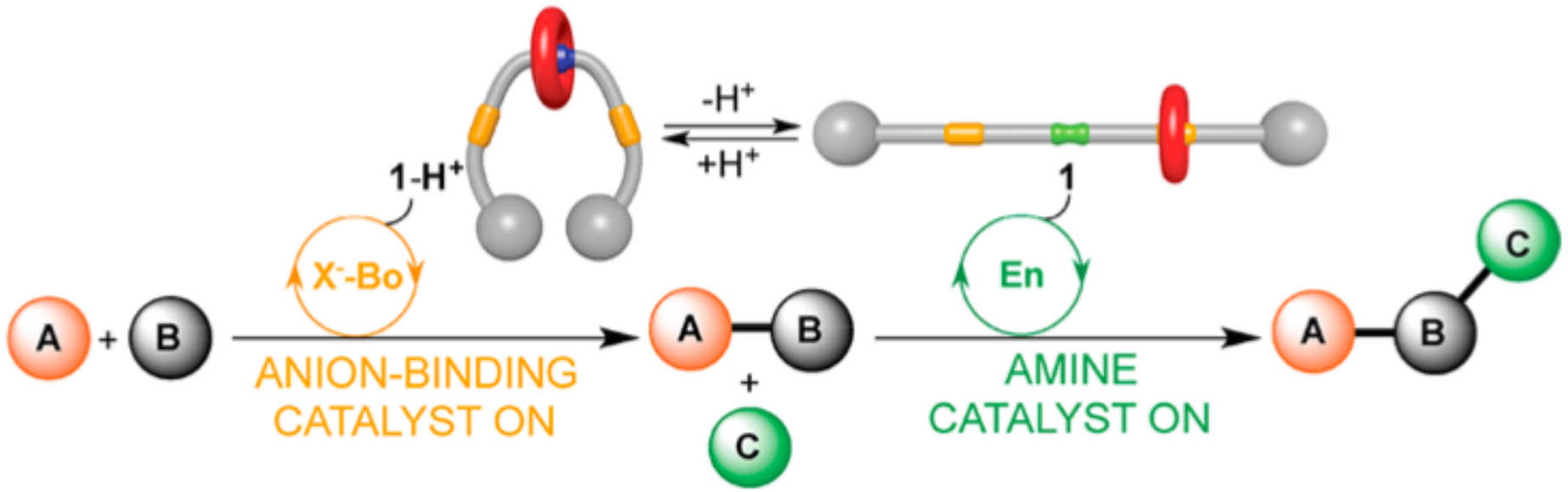


triazolium groups can act as anion binding catalysts, abstracting halides

Proposal: Leverage On/Off Switch on Rotaxanes For Tandem Catalysis

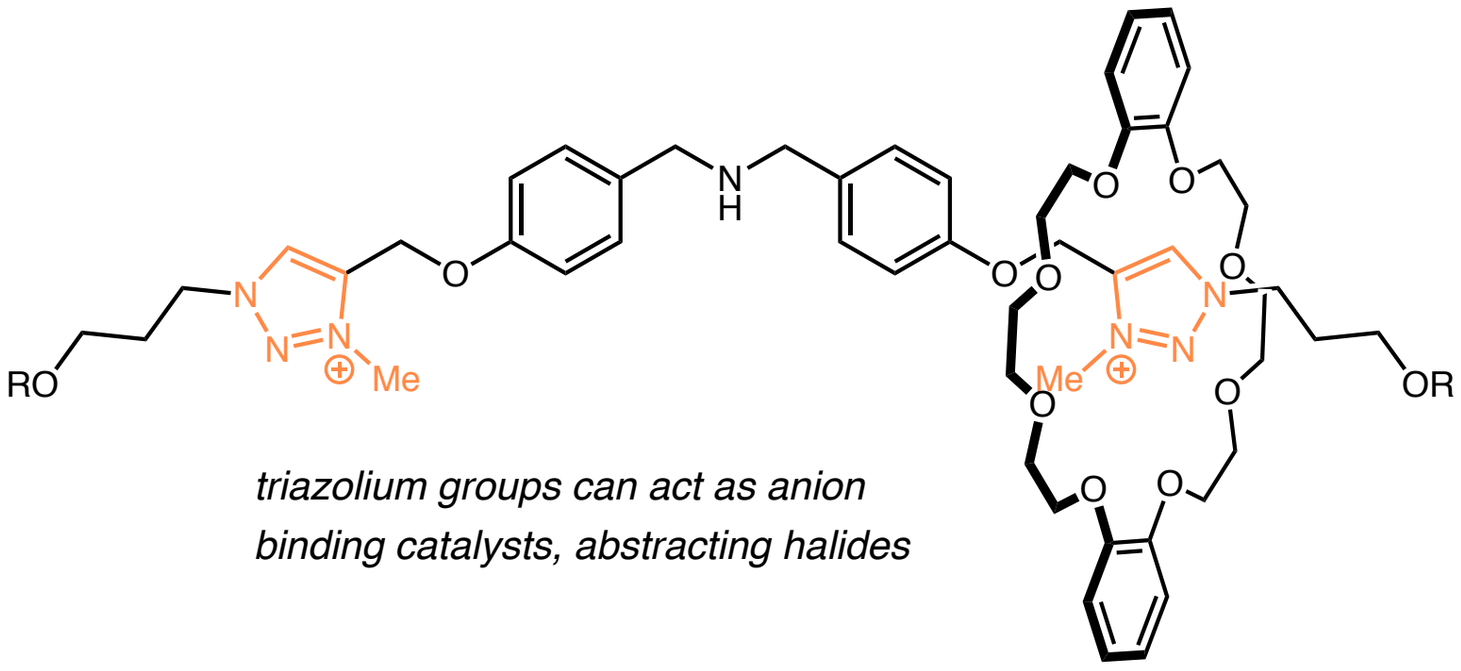


halide abstraction;
radical addition to olefin

enamine catalysis;
nucleophilic addition to olefin

Eichstaedt, K.; Jaramillo-Garcia, J.; Leigh, D. A.; Marcos, V.; Pisano, S.; Singleton, T. A. *J. Am. Chem. Soc.* **2017**, *139*, 9376–9381.

Use of Rotaxanes as On/Off Switches for Catalysis



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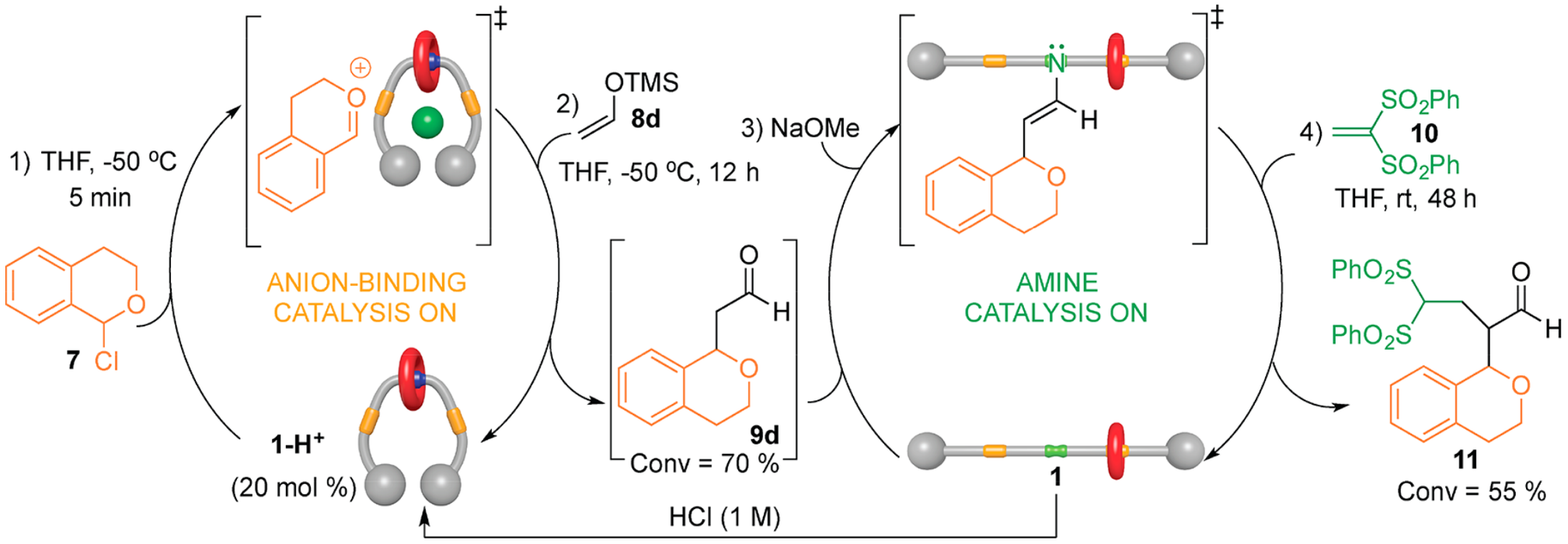
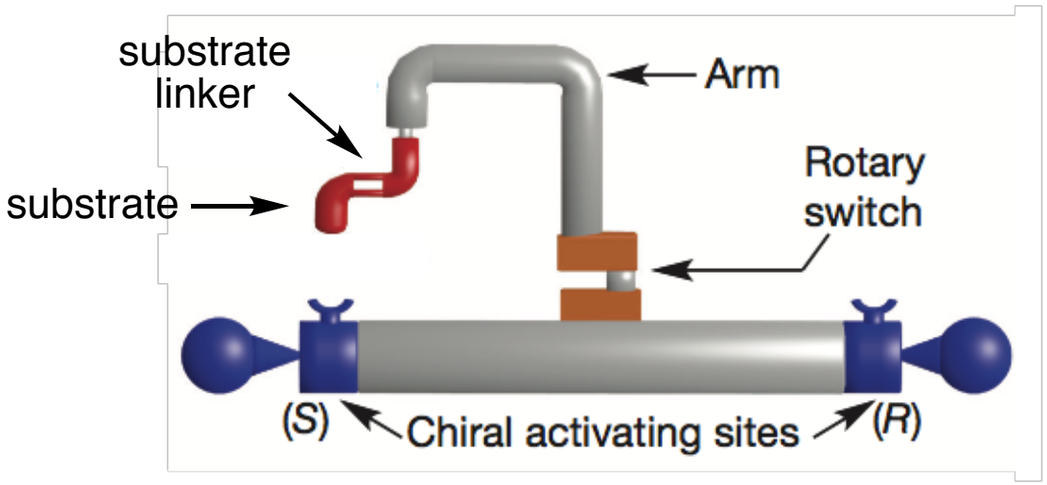
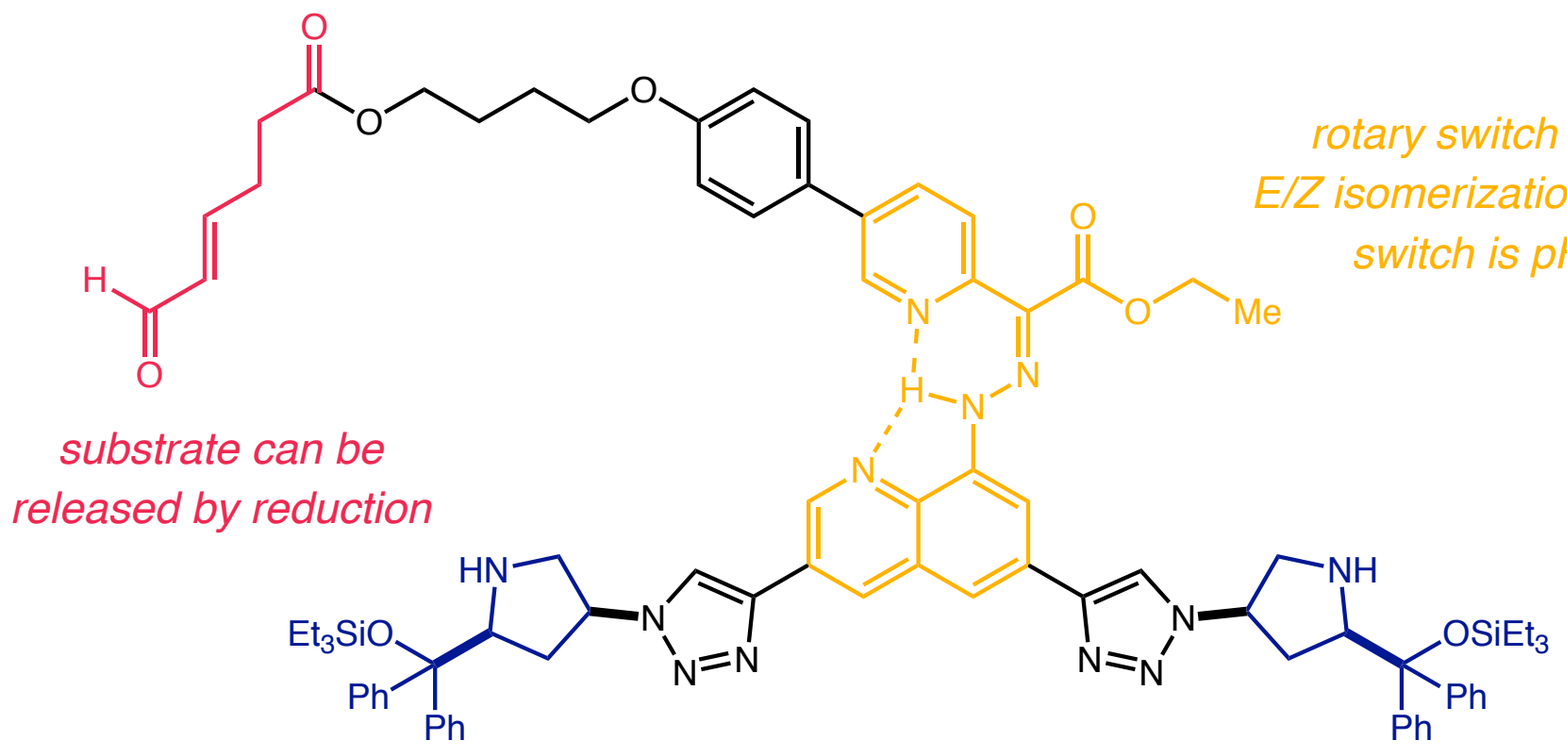


Eichstaedt, K.; Jaramillo-Garcia, J.; Leigh, D. A.; Marcos, V.; Pisano, S.; Singleton, T. A. *J. Am. Chem. Soc.* **2017**, *139*, 9376–9381.

Stereodivergent Synthesis Using Molecular Machines



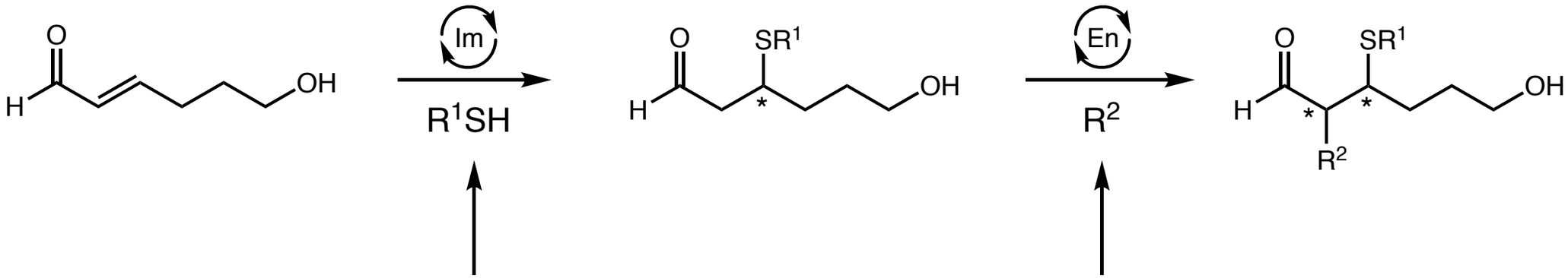
- ***mimics sequence-specific synthesis in biology***
- ***allows substrate to be moved between catalytic sites***
- ***enables stereospecific sequential synthesis***



chiral amine catalysts can faciliate iminium or enamine activation modes; sequential reactions

Kassem, S.; Lee, A. T. L.; Leigh, D. A.; Marcos, V.; Palmer, L. I.; Pisano, S. *Nature* **2017**, *549*, 374–378.

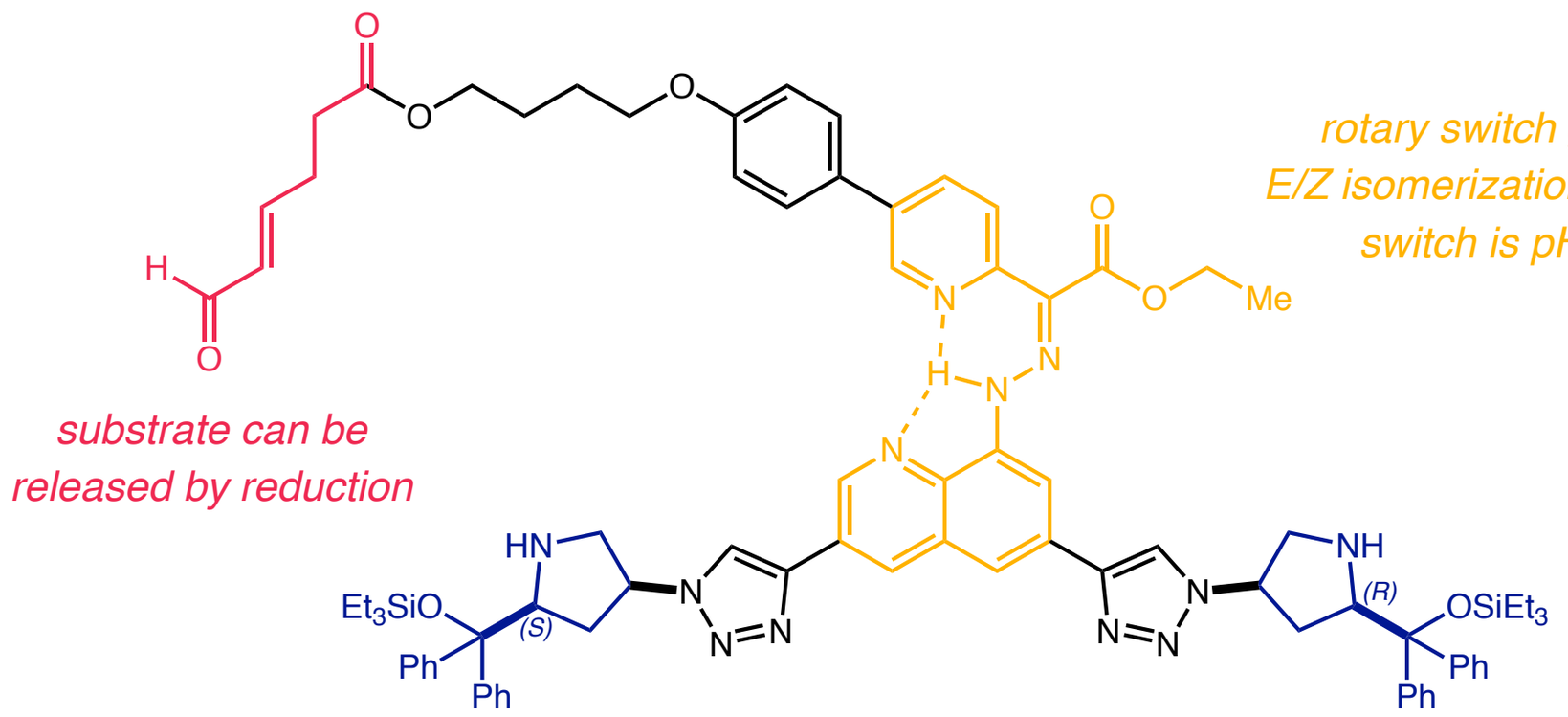
Stereodivergent Synthesis Using Molecular Machines



point of stereocontrol

point of stereocontrol

stereochemistry of products can be programmed; dependent on decision to engage rotary switch



substrate can be released by reduction

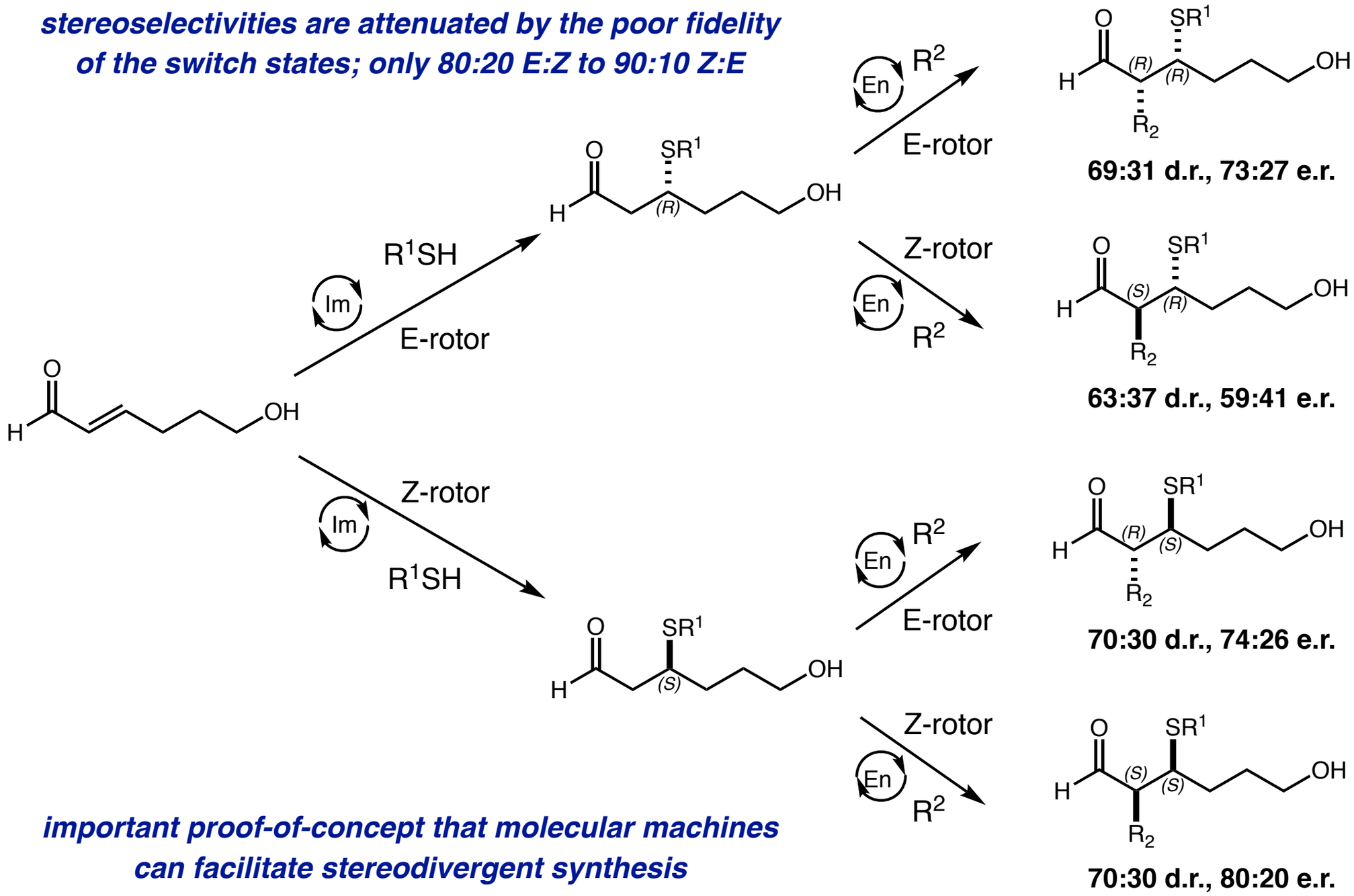
rotary switch governed by E/Z isomerization of hydrazone; switch is pH sensitive

chiral amine catalysts can faciliate iminium or enamine activation modes; sequential reactions

Kassem, S.; Lee, A. T. L.; Leigh, D. A.; Marcos, V.; Palmer, L. I.; Pisano, S. *Nature* **2017**, *549*, 374–378.

Stereodivergent Synthesis Using Molecular Machines

stereoselectivities are attenuated by the poor fidelity of the switch states; only 80:20 E:Z to 90:10 Z:E



important proof-of-concept that molecular machines can facilitate stereodivergent synthesis

Kassem, S.; Lee, A. T. L.; Leigh, D. A.; Marcos, V.; Palmer, L. I.; Pisano, S. *Nature* **2017**, *549*, 374–378.

Outline

Light Responsive Systems

Chemo Responsive Systems

Electrically Responsive Systems

Applications of molecular motors to organic synthesis