Synthetic Organic Molecular Machines: Academic Curiosities or Potentially Useful Technology?

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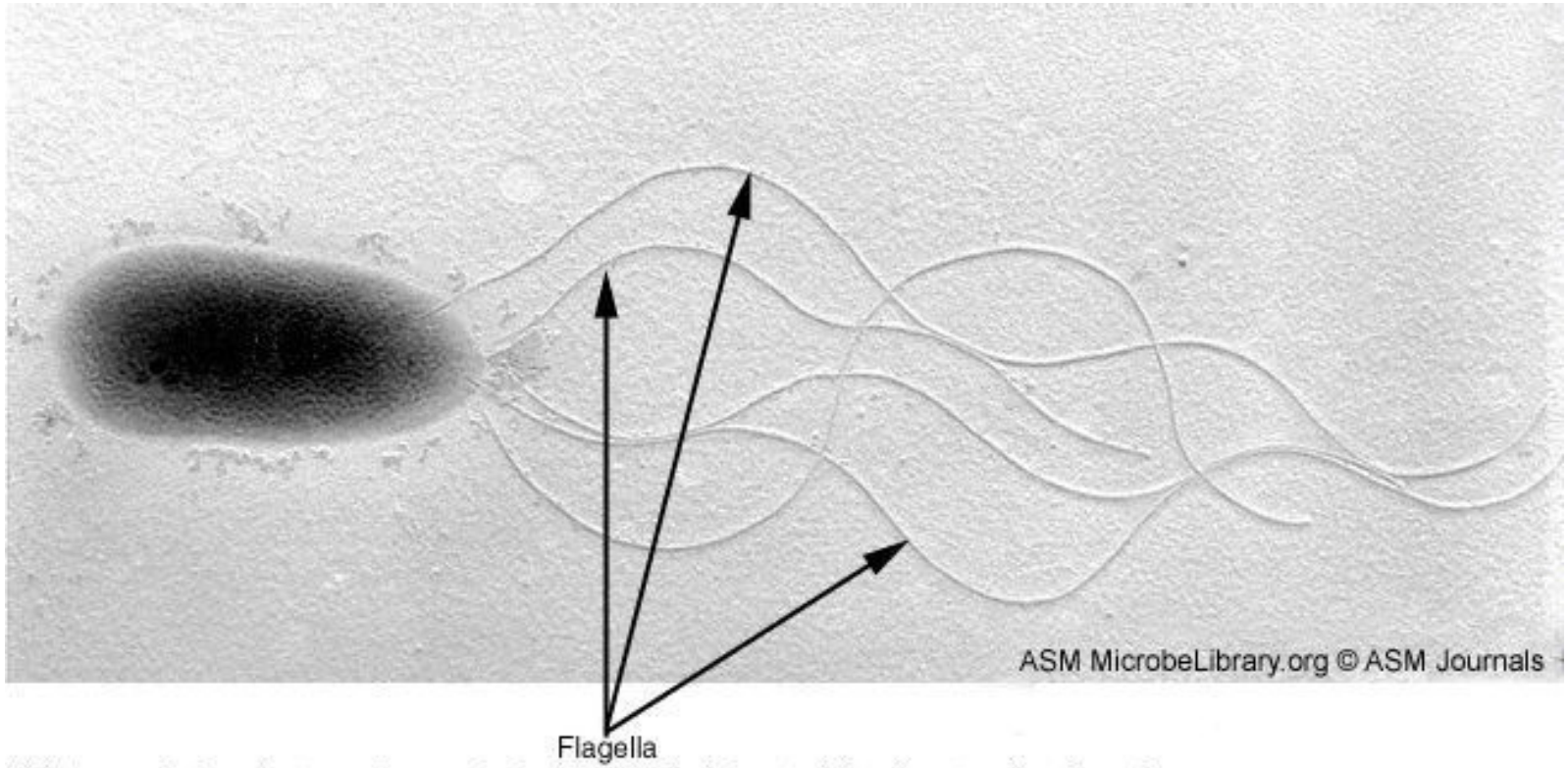
Department of Chemistry
Materials Science Institute
University of Oregon
July 29, 2004

The Inspiration: Biological Molecular Motors

Flagellar Motors of Bacteria: Energy-Driven Rotation About An Axis



This transmission electron micrograph shows six polarly located flagella extending from the bacterium, *Pseudomonas putida*. In this case, the cell is 2 µm in length, and each flagellum is ~5 to 7 µm long.

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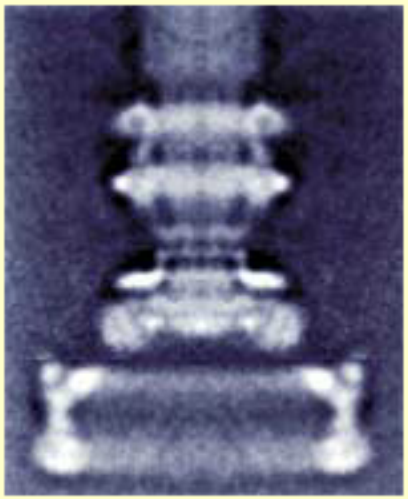
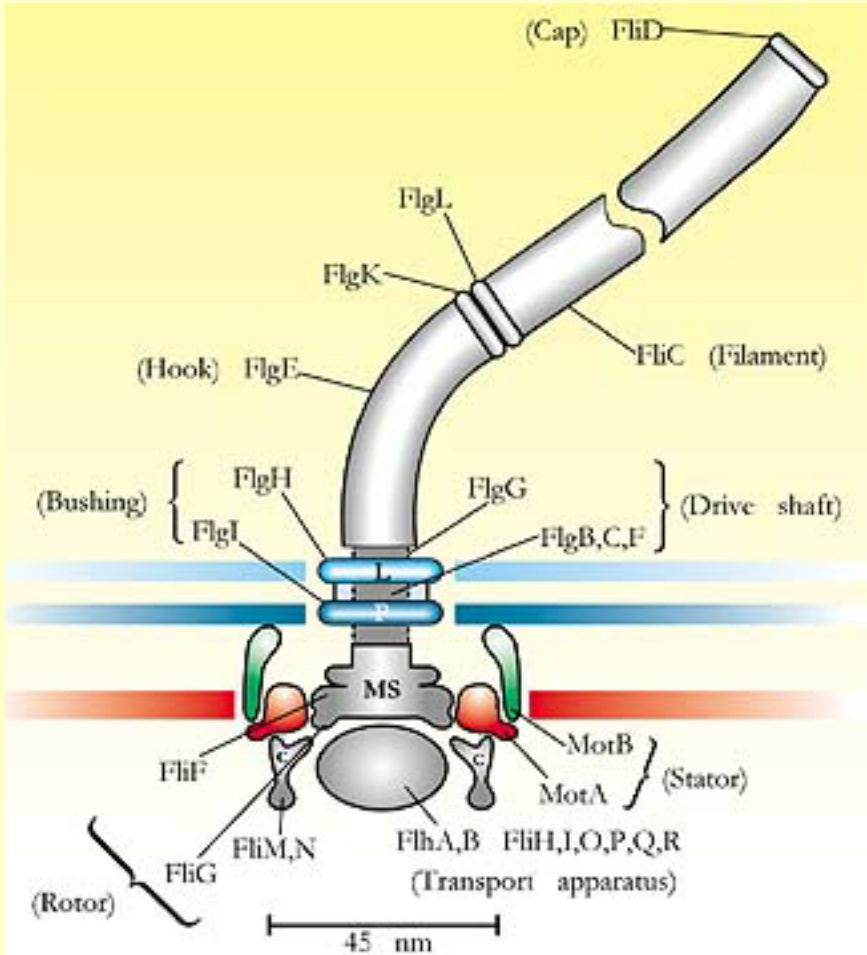
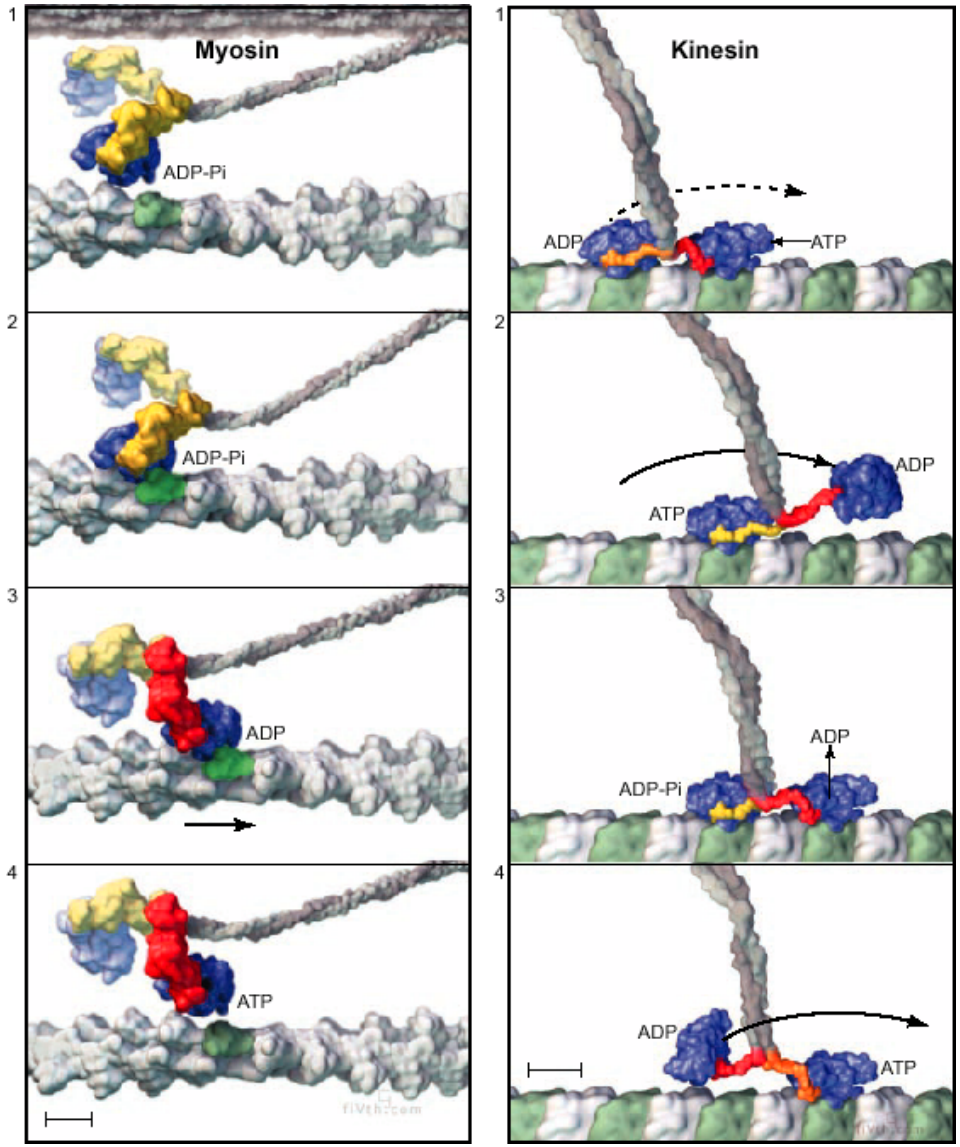


Figure 2. Bacterial motor and drive train.

Above: Rotationally averaged reconstruction of electron micrographs of purified hook-basal bodies. The rings seen in the image and labeled in the schematic diagram (right) are the L ring, P ring, MS ring, and C ring. (*Digital print courtesy of David DeRosier, Brandeis University .*)





Ronald D. Vale, R. D.; Milligan, R. A. The Way Things Move: Looking Under the Hood of Molecular Motor Proteins, *Science*, **2000**, *288*, 88-95.

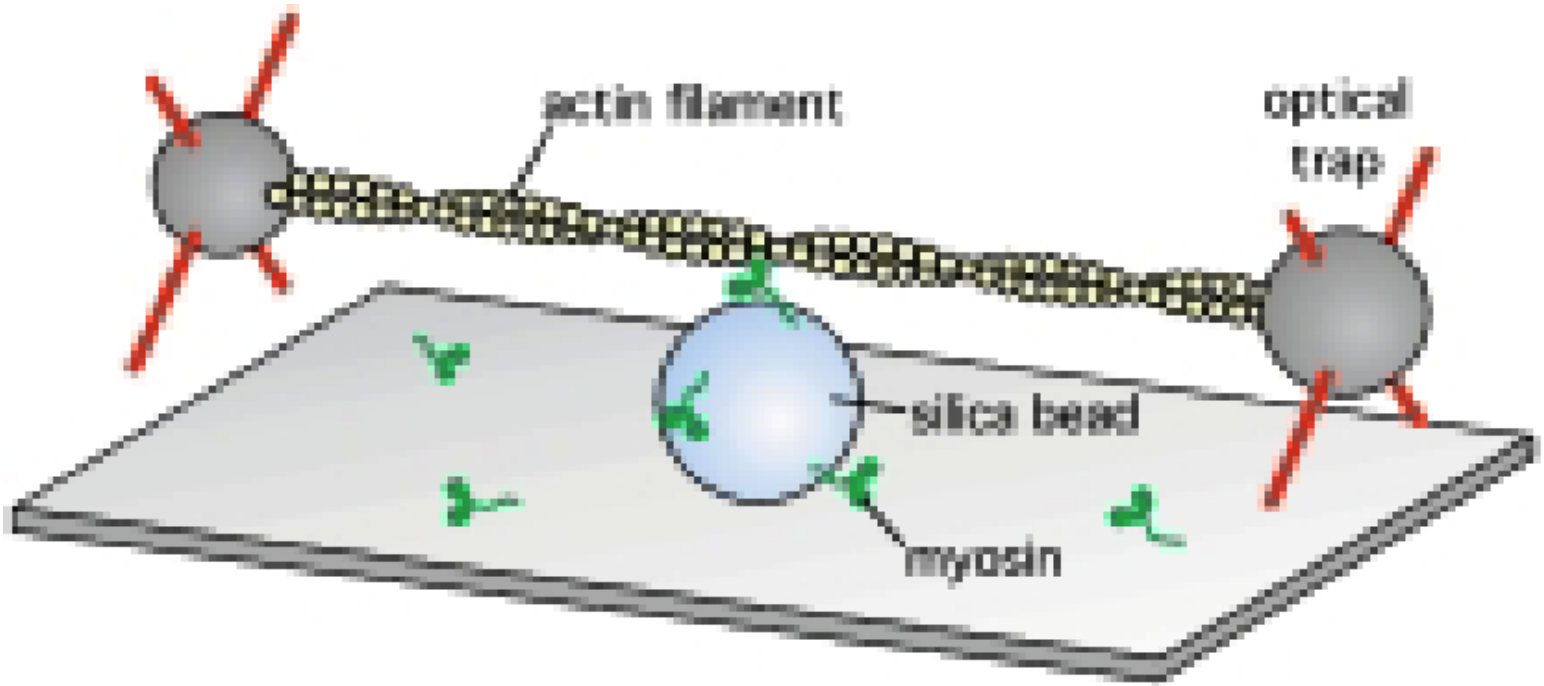
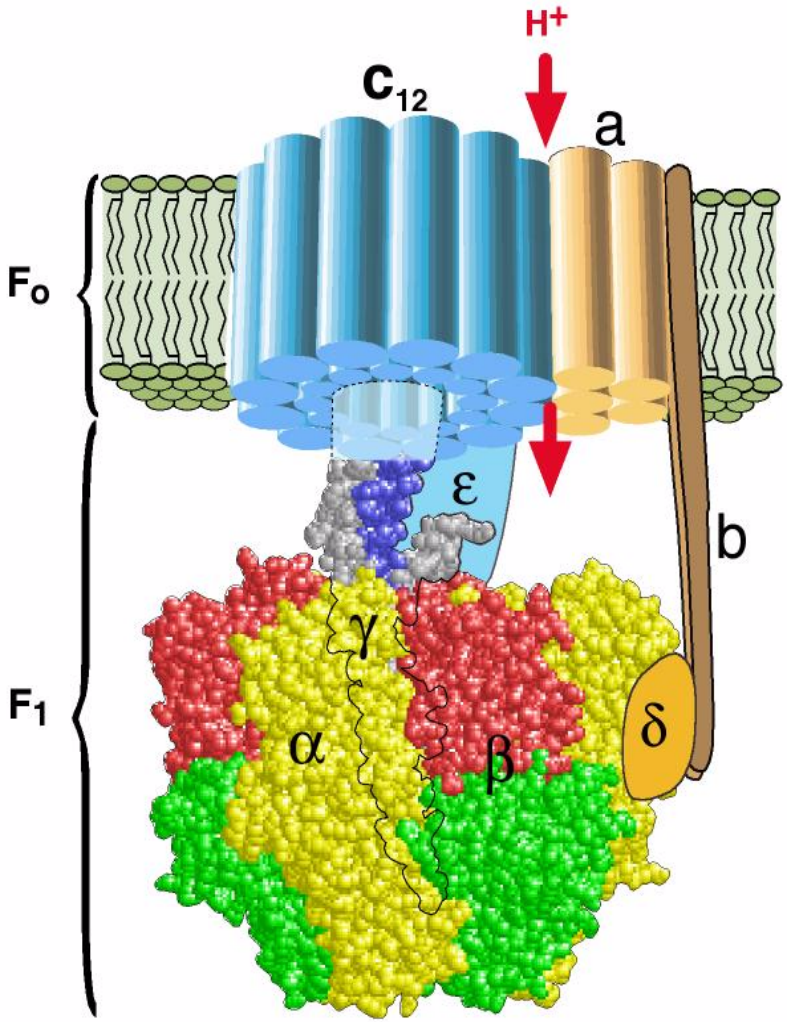


Figure 2. Experimental geometry used[19] to observe single myosin molecules binding and pulling an actin filament. The filament was attached at either end to a trapped bead. These beads were used to stretch the filament taut and move it near surface-bound silica beads that were decorated sparsely with myosin molecules. Adapted with permission from ref. [19] (Copyright© Macmillan Magazines Ltd 1994).

The Inspiration: Biological Molecular Motors

F_1F_0 ATP Synthase: Energy-Driven Rotation About An Axis



H. Wang and G. Oster (1998). Nature 396:279-282.

Adaptation Of A Biological Motor To A ÑProof-of-PrincipleÓ Nanotechnological Application

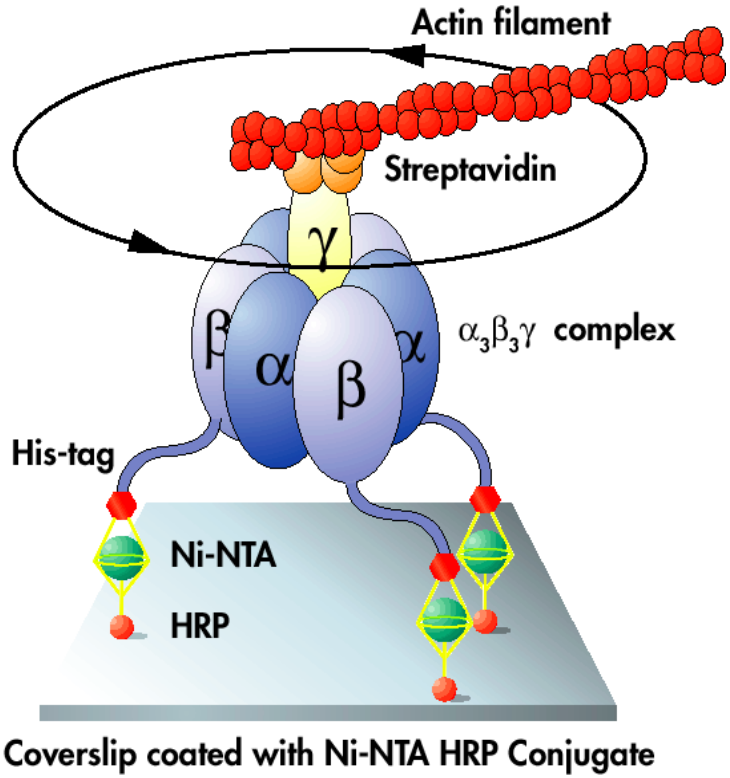
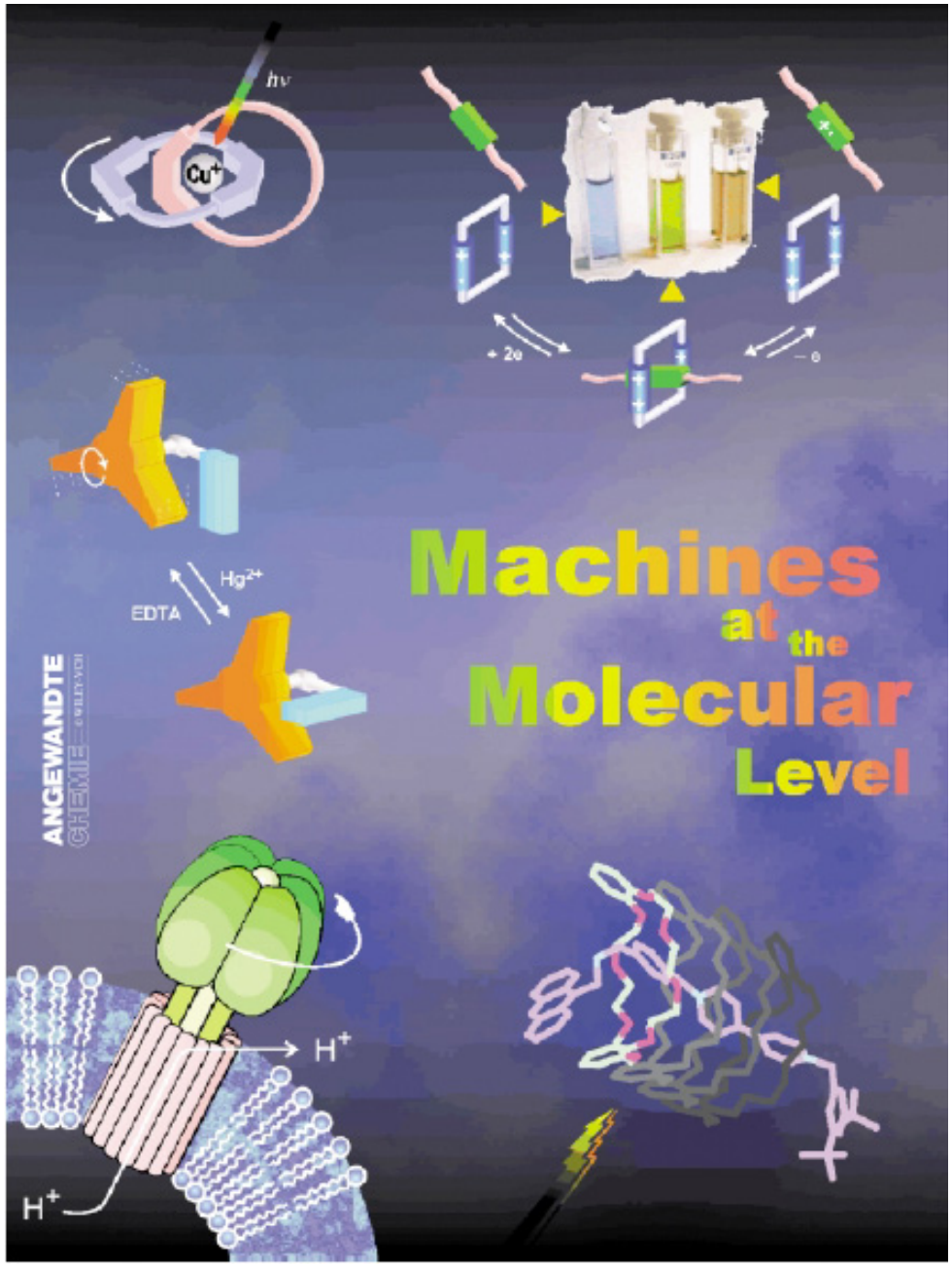


Figure 1 *The system used for observation of the rotation of the γ-subunit in the F1-ATPase $\alpha_3\beta_3\gamma$ subcomplex.*

Noji, H.; Yasuda, R.; Yoshida, M.; Kinosita, Jr., K. Direct Observation of the Rotation of F1-ATPase, *Nature*, **1997**, *386*, 299-302.



Angew. Chem. Int. Ed. Engl. **2000**, *39*, 3348-3391

Molecular-Scale Machines

What would be the utility of such machines? Who knows? I cannot see exactly what would happen, but I can hardly doubt that when we have some control of the arrangement of things on a molecular scale we will get an enormously greater range of possible properties that substances can have, and of the different things we can do.

Richard P. Feynman[1] (1959)

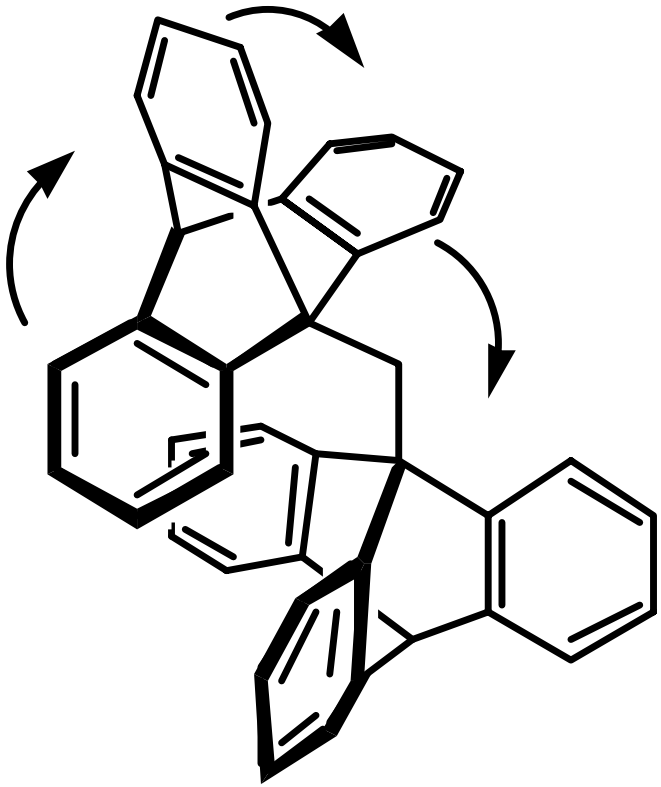
[1]There's Plenty of Room at the Bottom
An Invitation to Enter a New Field of Physics

This classic talk was given by Richard Feynman on December 29th 1959 at the annual meeting of the American Physical Society at the California Institute of Technology (Caltech) and was first published in the February 1960 issue of Caltech's Engineering and Science, which owns the copyright.

Molecular Machines

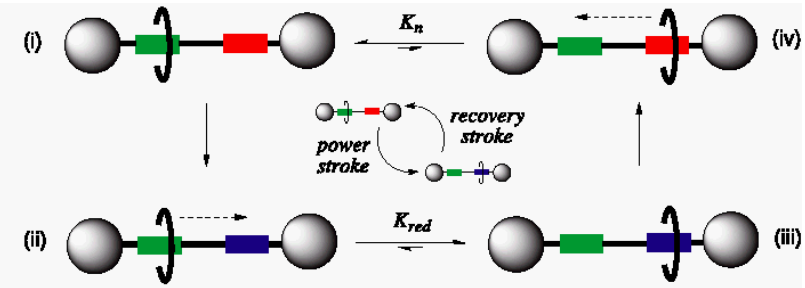
- Gears
- Axles
- Switches
- Ratchets

Tritycene Molecular Gears

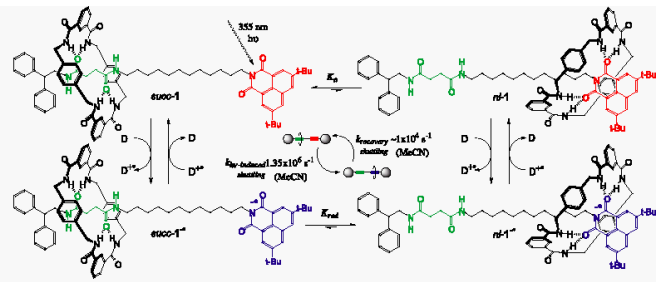


Mislow, K., "Molecular machinery in organic chemistry."
Chemtracts: Organic Chemistry **1989**, *2*, 151.

A Fast "Molecular Piston"*



Scheme 1. Translational submolecular motion in a stimuli-responsive molecular shuttle: (i) The macrocycle initially resides at the preferred (green) station; (ii) a reaction occurs (red → blue) changing the relative binding potentials of the two stations such that (iii) the macrocycle "shuttles" to the now-preferred (blue) station. In the special case that the reverse reaction (blue → red) now occurs (iv), the components return to their original positions. Such cyclable, externally driven, mechanical motions with a "power stroke" and a "recovery stroke" are reminiscent of the workings of a simple piston (inset).

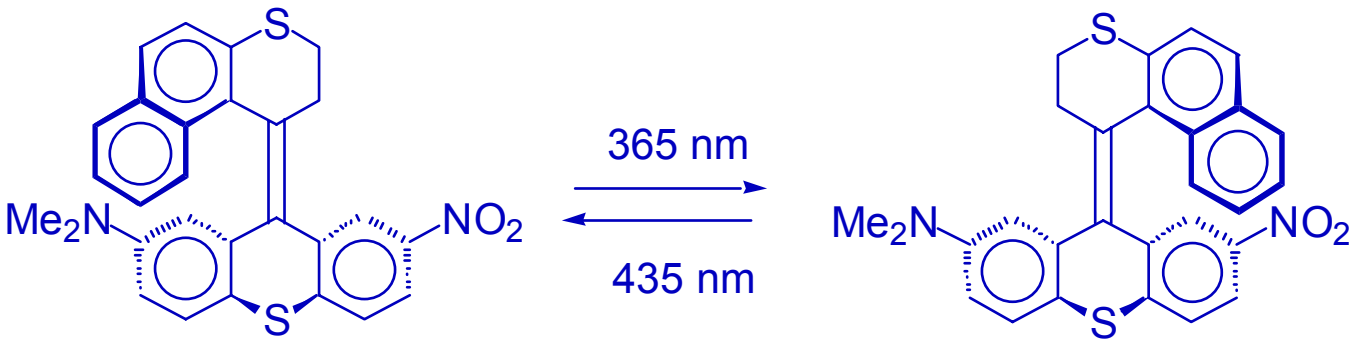


Scheme 2. A photoresponsive, H-bond–assembled, molecular shuttle **1**. Before the 355-nm laser pulse, the translational conformer *succ*-**1** is predominant because the *ni* station is a poor H-bond acceptor (K_n < 0.01). After photoreduction by an external donor (D; DABCO, TMPD, or biphenyl), the equilibrium between *succ*-**1**$^{\bullet-}$ and *ni*-**1**$^{\bullet-}$ changes (K_{red} >1500) because *ni*$^{\bullet-}$ is a powerful H-bond acceptor and back-electron transfer is slow (spin forbidden). Because the absorption maximum (λ_{max}) of *ni*-**1**$^{\bullet-}$ is located at shorter wavelength than that of *succ*-**1**$^{\bullet-}$, the sum of the absorptions shifts to the blue. The rate at which the absorption shifts (k_{shift}) is related to the rate of change in the relative populations of *succ*-**1**$^{\bullet-}$ and *ni*-**1**$^{\bullet-}$, i.e., the time taken for light-induced shuttling of the macrocycle (~1 μs, MeCN). After charge recombination (~100 μs, MeCN), the macrocycle shuttles back to its original position. Cycling of this process at 10^4 times per second generates ~10^{-15} W of mechanical power for each shuttle.

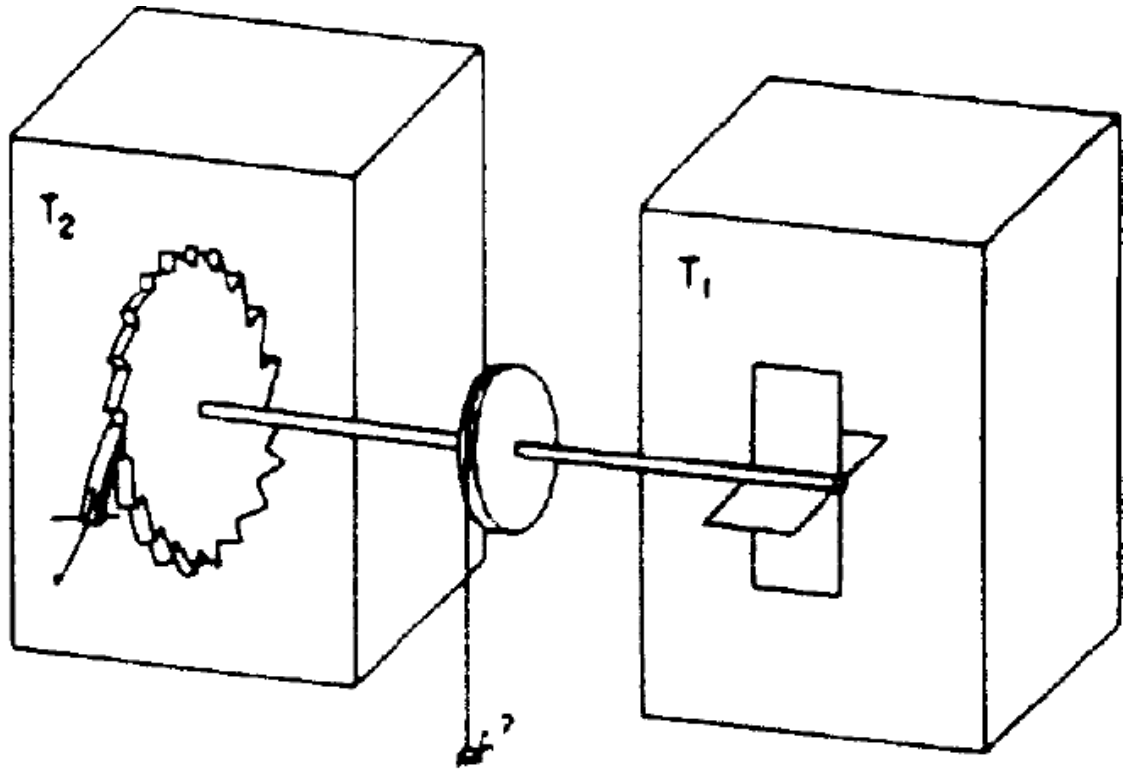
Brouwer, A. M., et al., "Photoinduction of Fast, Reversible Translational Motion in a Hydrogen-Bonded Molecular Shuttle", *Science.* **2001**, *291,* 2124-2128.

*Inspired by J. Fraser Stoddart and others

On-Off Two State Reversible Switches



Feringa, B. L., et al., "Chiroptical Molecular Switches", *Chem. Rev.* **2000**, *100*, 1789-1816



The ratchet and pawl machine

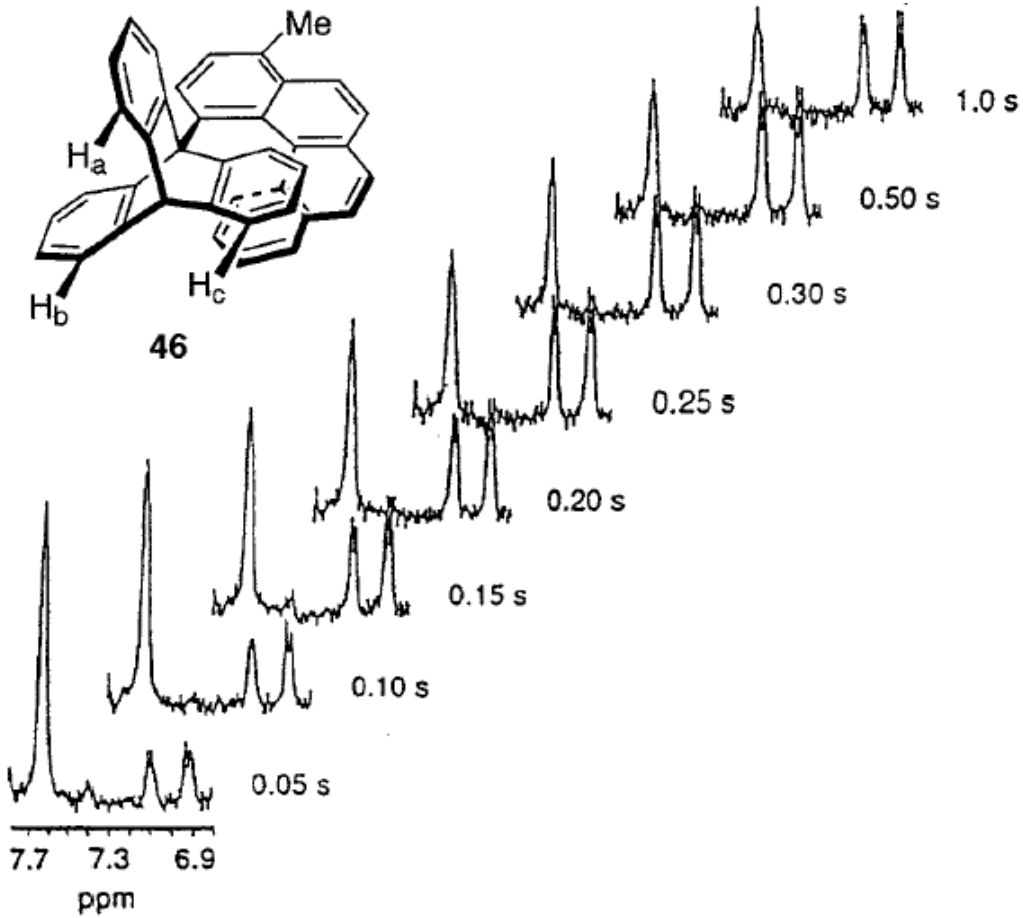


Fig. 17. Results of spin polarization transfer experiment at 160 °C (calibrated temperature). The resonances for H_a, H_b and H_c (see **46**) appear at δ 7.6, 7.1 and 6.9 ppm (not necessarily respectively). The spin of the proton resonating at δ 7.6 was polarized, and transfer of that polarization was monitored over time

Kelly, T. R.; Sestelo, J. P. "Rotary motion in single-molecule machines," *Structure and Bonding (Berlin, Germany)* **2001**, *99*, 19-53.
Kelly, T. R. "Progress toward a Rationally Designed Molecular Motor," *Acc. Chem. Res.* **2001**, *34*, 514-522.

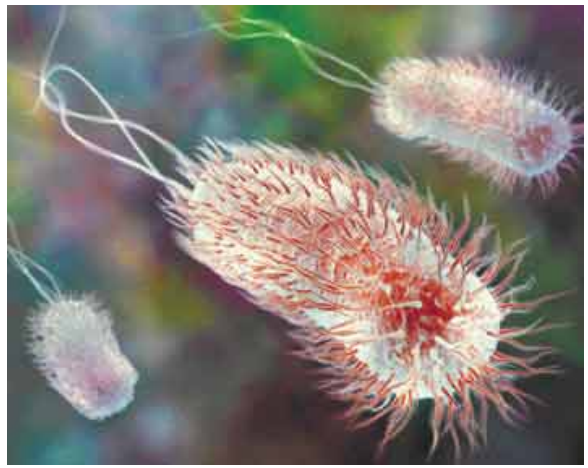
Designing Molecular Motors: What Do We Need To Do?

Two Fundamental Principles Of All Motors

1) ***Asymmetry*** of Motor ***Produces*** ***Directionality*** of Motion

2) Put ***Energy In***,
Get ***Directed Molecular Motion***
And ***Useful Work Out***

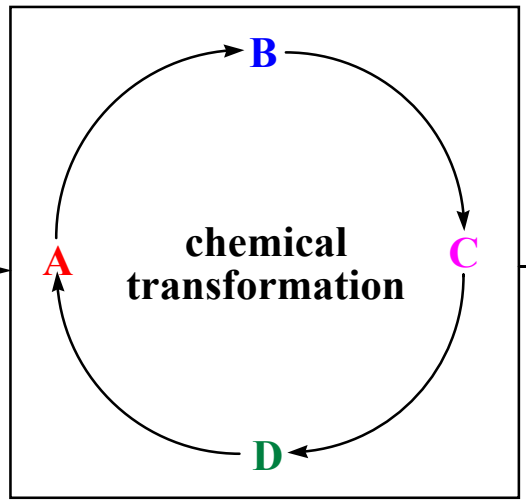
Biological Rotary Motors: Principles Exemplified



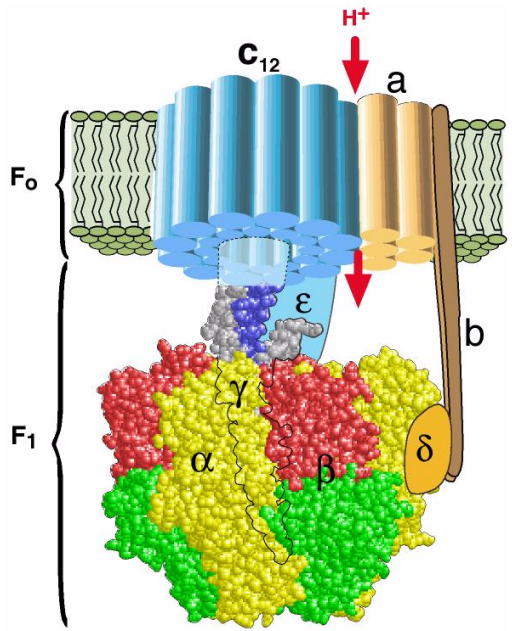
ASYMMETRY IN MOTOR OR POWER SOURCE

ENERGY*

*Chemical, Light, Electrochemical

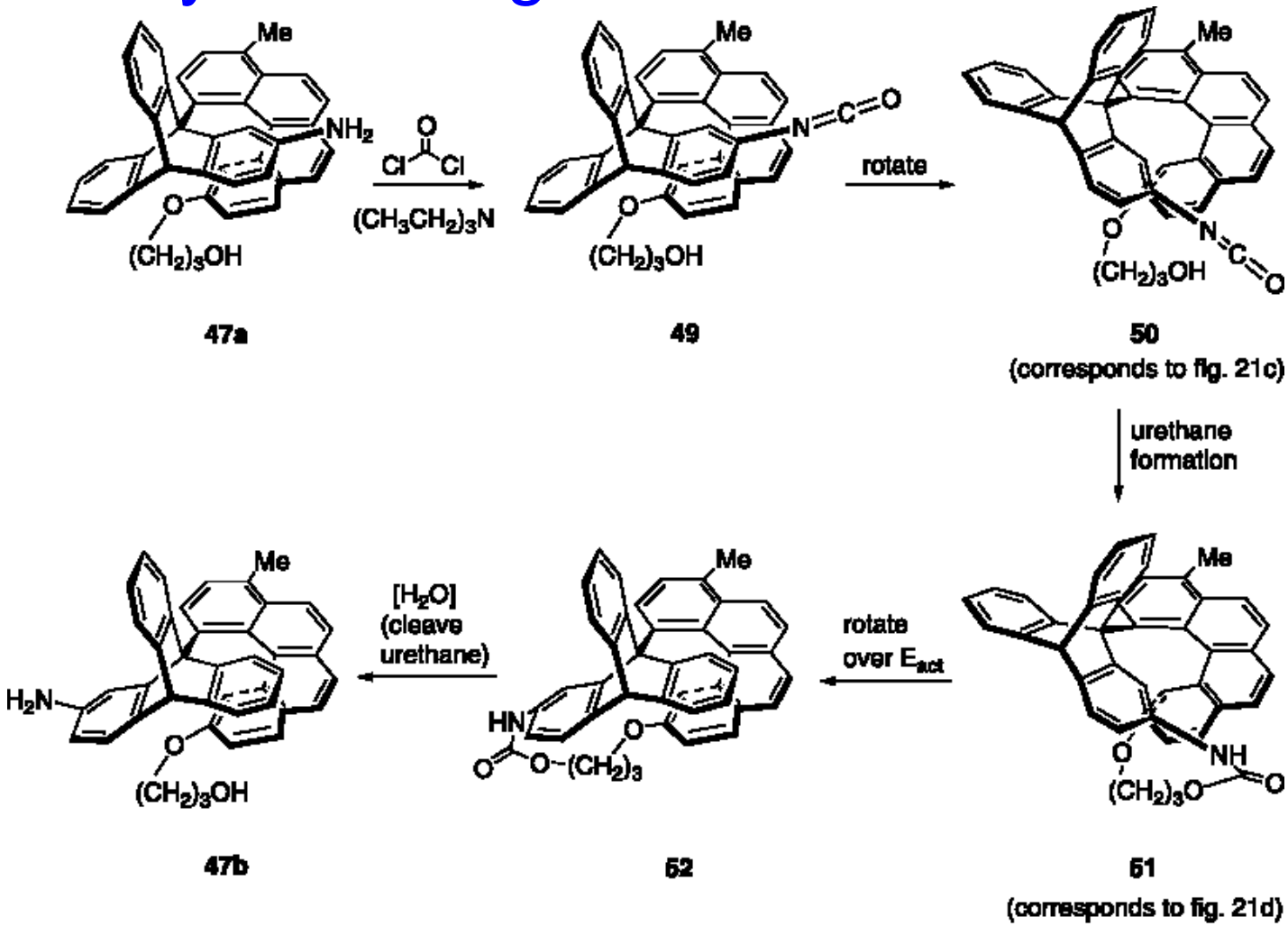


WORK



H. Wang and G. Oster (1998). Nature 396:279-282.

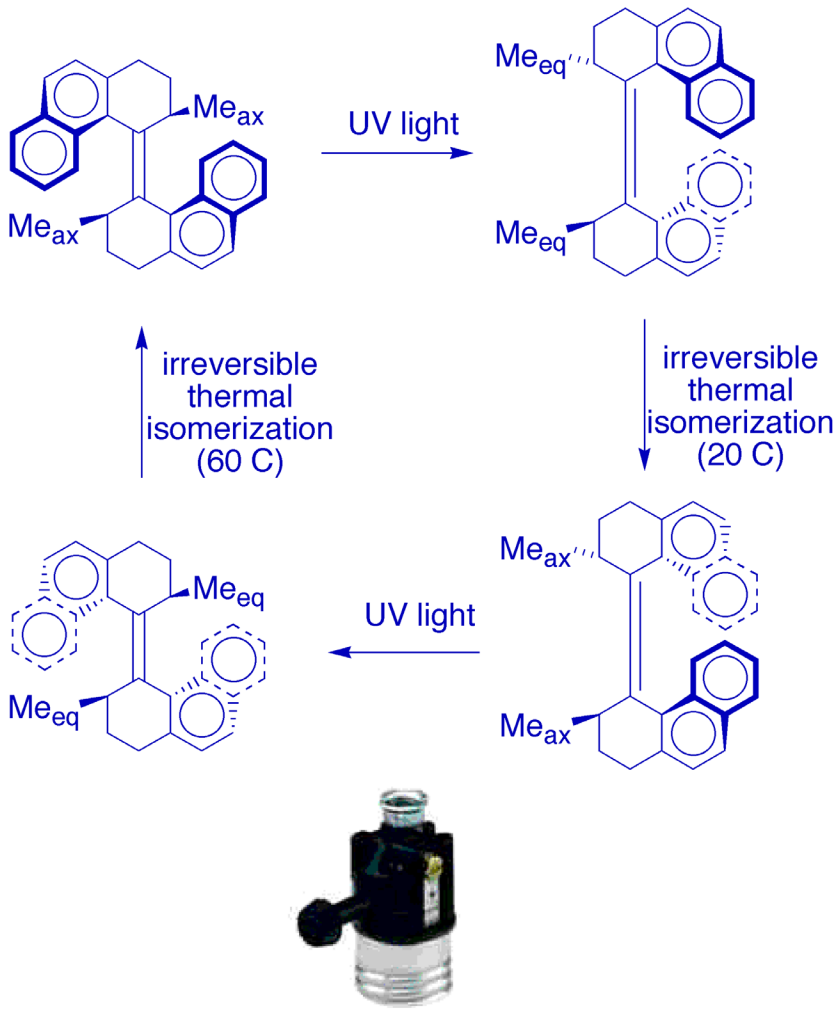
Ross Kelly: 120 Degree Directed Bond Rotation



Scheme 9. Proposed sequence of events in the chemically powered rotation of 47a to 47b

Kelly, T. R.; Sestelo, J. P. "Rotary motion in single-molecule machines," *Structure and Bonding (Berlin, Germany)* **2001**, *99*, 19-53.
Kelly, T. R. "Progress toward a Rationally Designed Molecular Motor," *Acc. Chem. Res.* **2001**, *34*, 514-522.

Ben Feringa
Rotary Switches
Undirectional Rotation In A Chiral Molecular Switch
The First Light-Driven Molecular Motor



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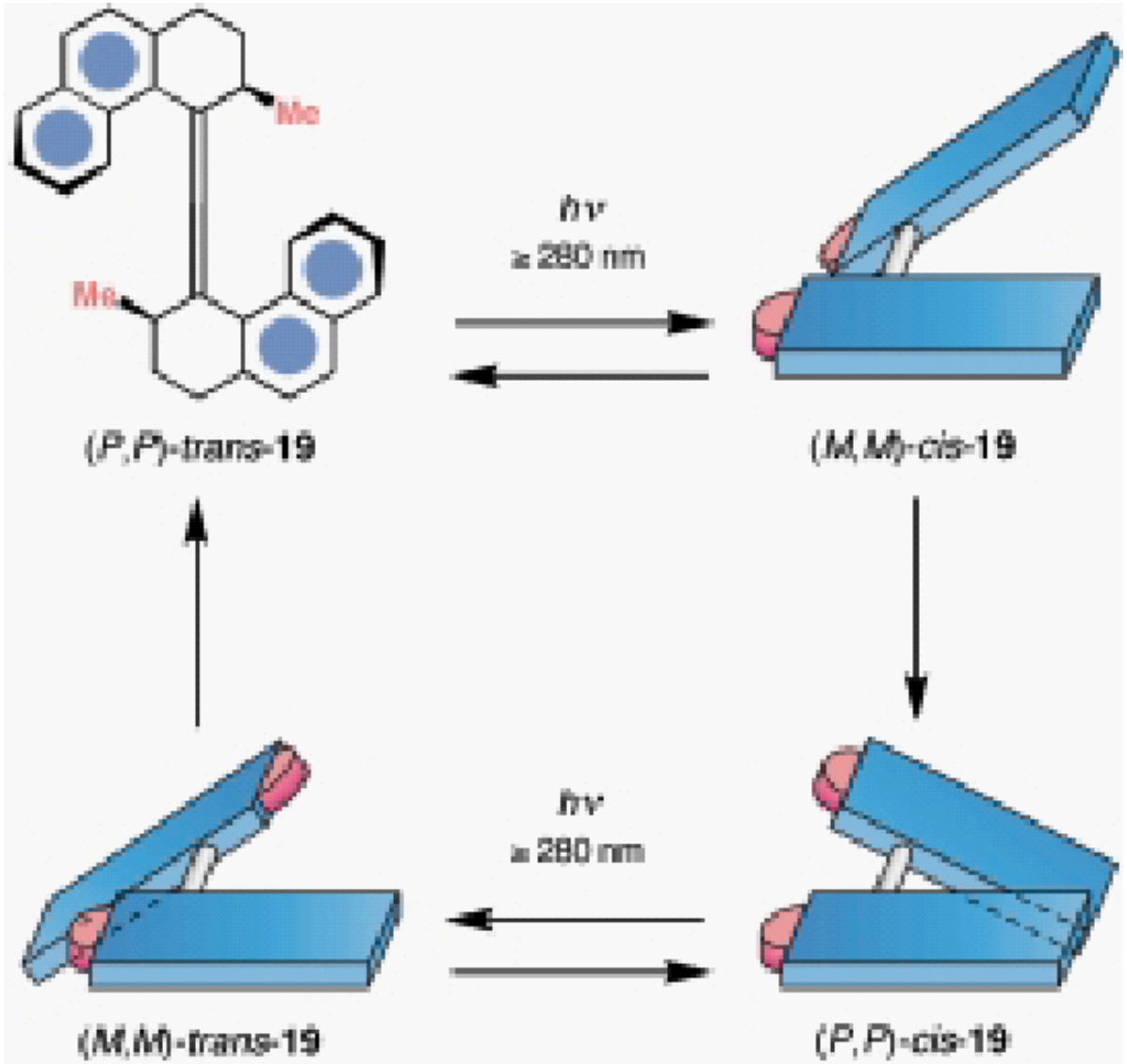
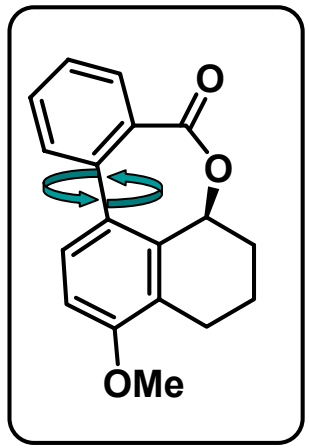
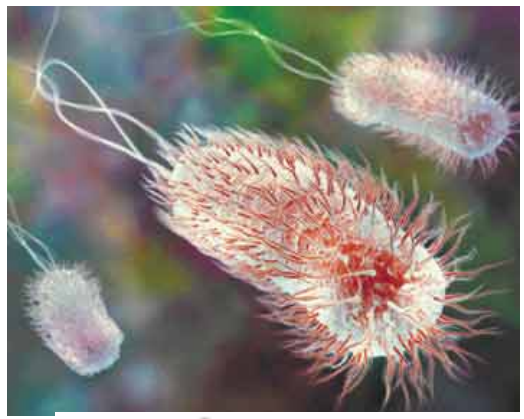


Scheme 17. The light-fueled rotary motor **19** undergoes[74] unidirectional rotation in *n*-hexane at 333 K upon irradiation at appropriate wavelengths.

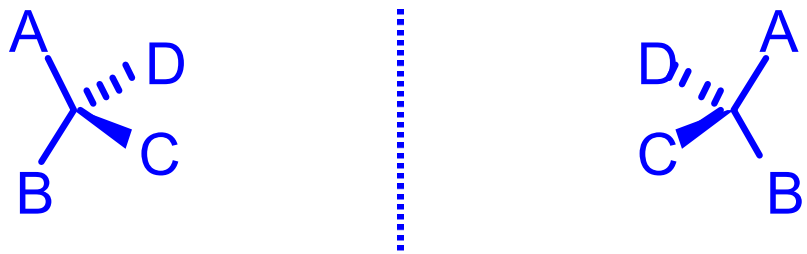
Synthetic Molecular Motor Research Goals



- Understand and control motion on a molecular scale
- Design and synthesize molecular systems capable of controlled unidirectional motion
- Understand and mimic efficiency only found in biological motors
- Incorporation of synthetic motors into materials and devices

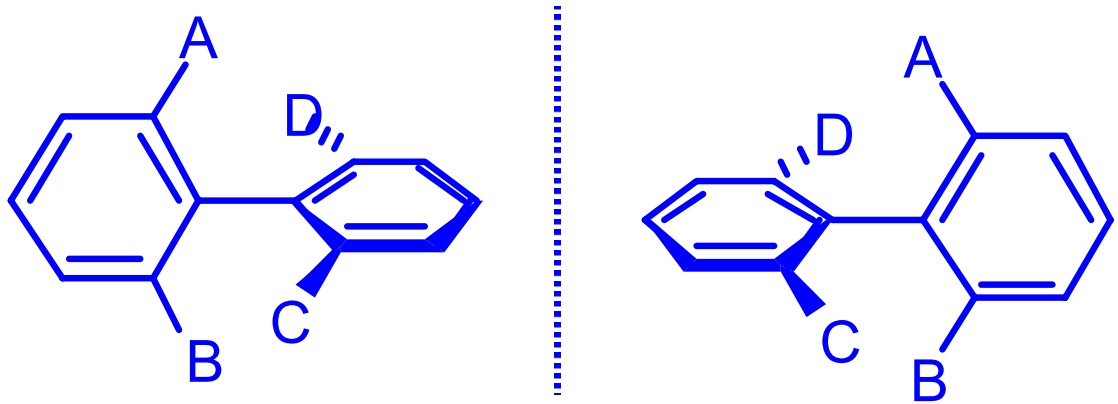


"standard" chirality at sp^3 carbon



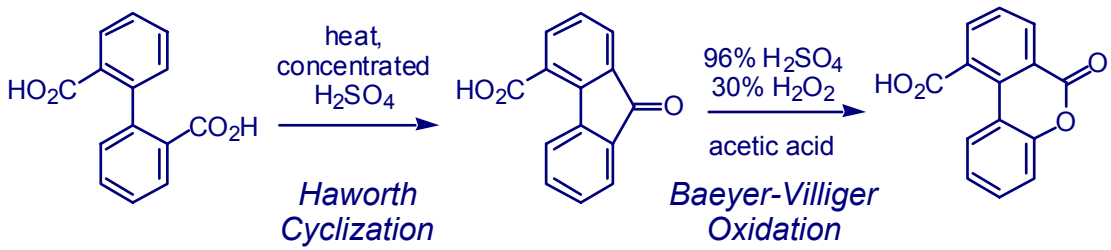
enantiomers

chirality without a stereogenic atom: biaryl atropisomerism

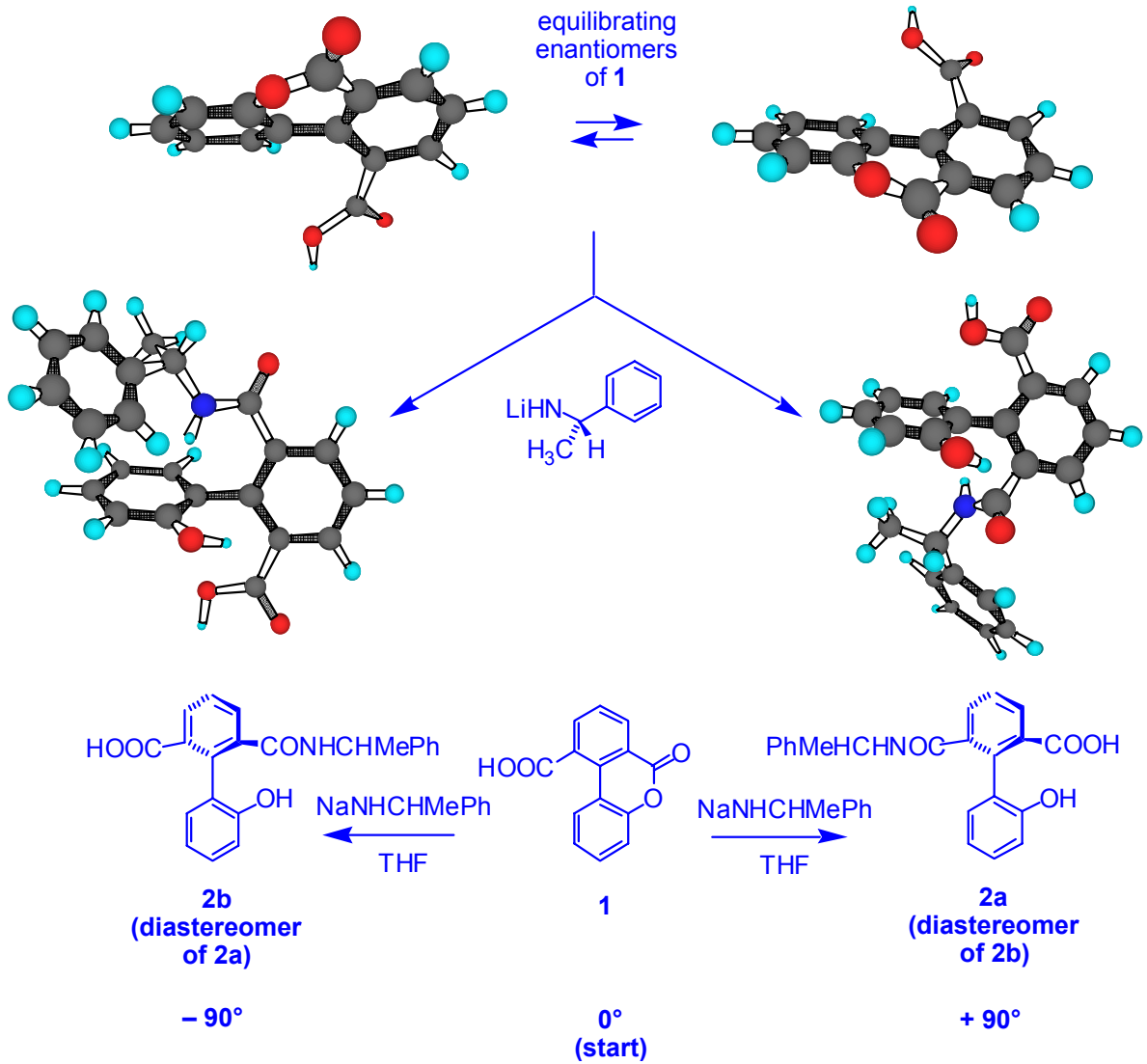


enantiomers

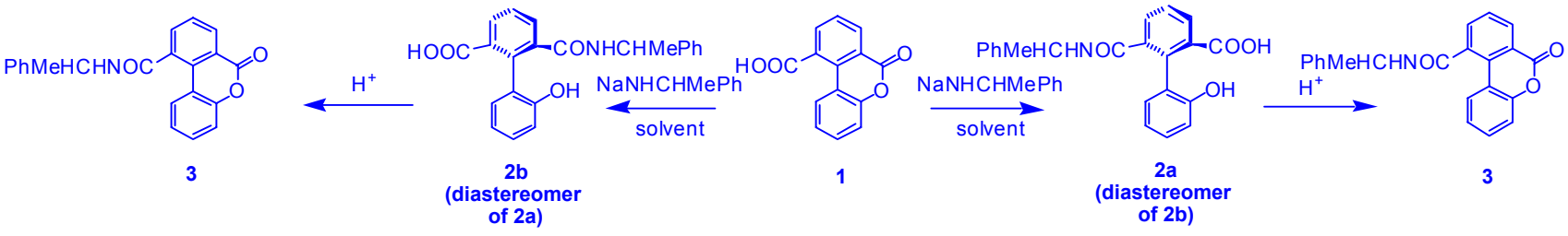
Simple Synthesis of A Molecular Motor Core



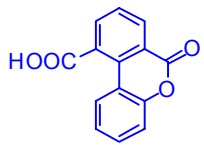
Directed Bond Rotation:
90 Degree ~3:1 Diastereoselective Ring Opening of the Motor Core



Completion of a 180 Degree Rotation by Lactonization



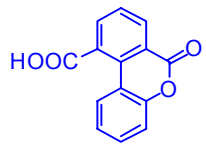
Remove amide (or ester)



1 (– 180°)

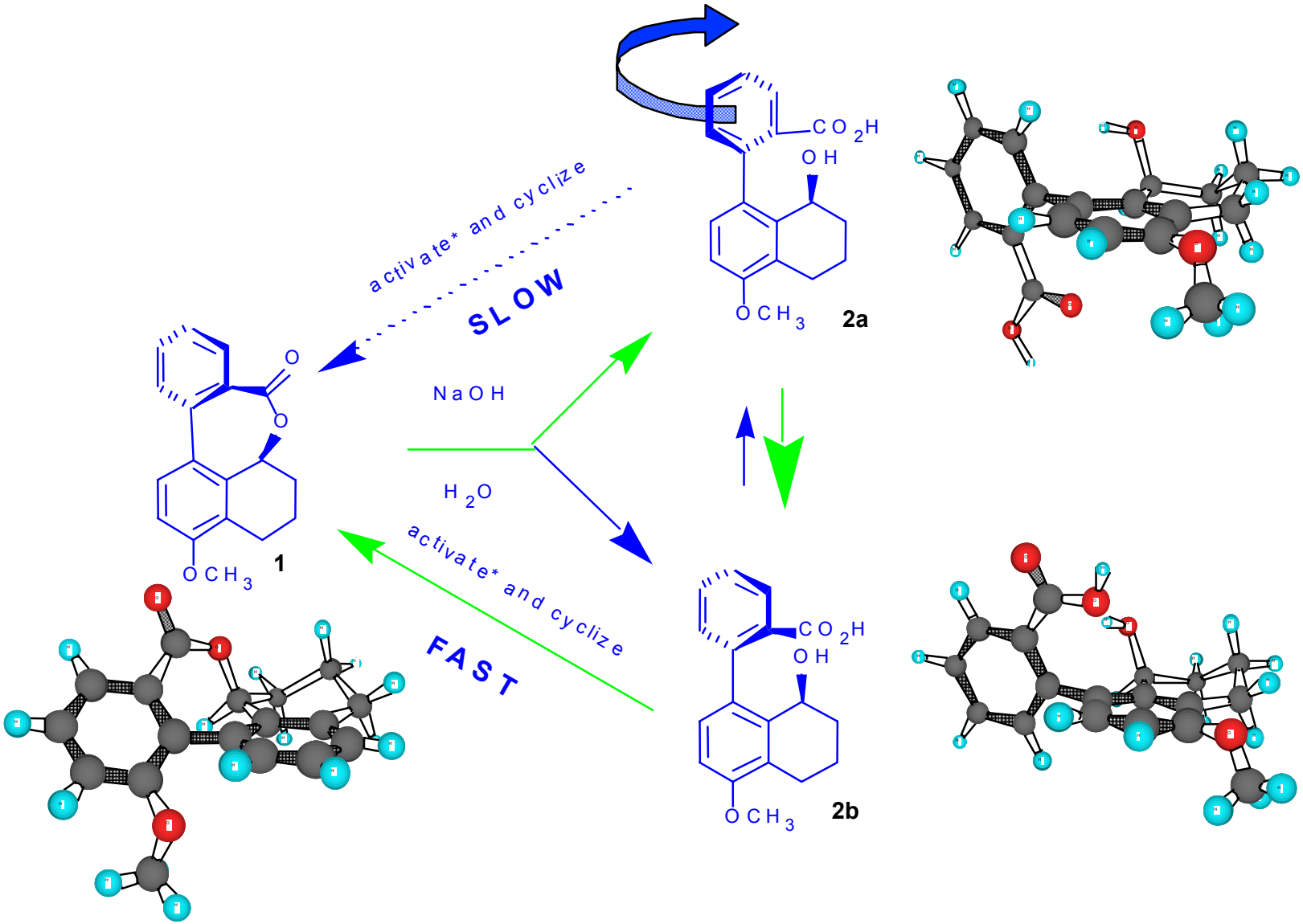
Problem: Amide Is Not Easy To Cleave To Start Another 180 Degree Rotation Cycle

Remove amide (or ester)



1 (+ 180°)

Proposed Motor: Chemically Driven



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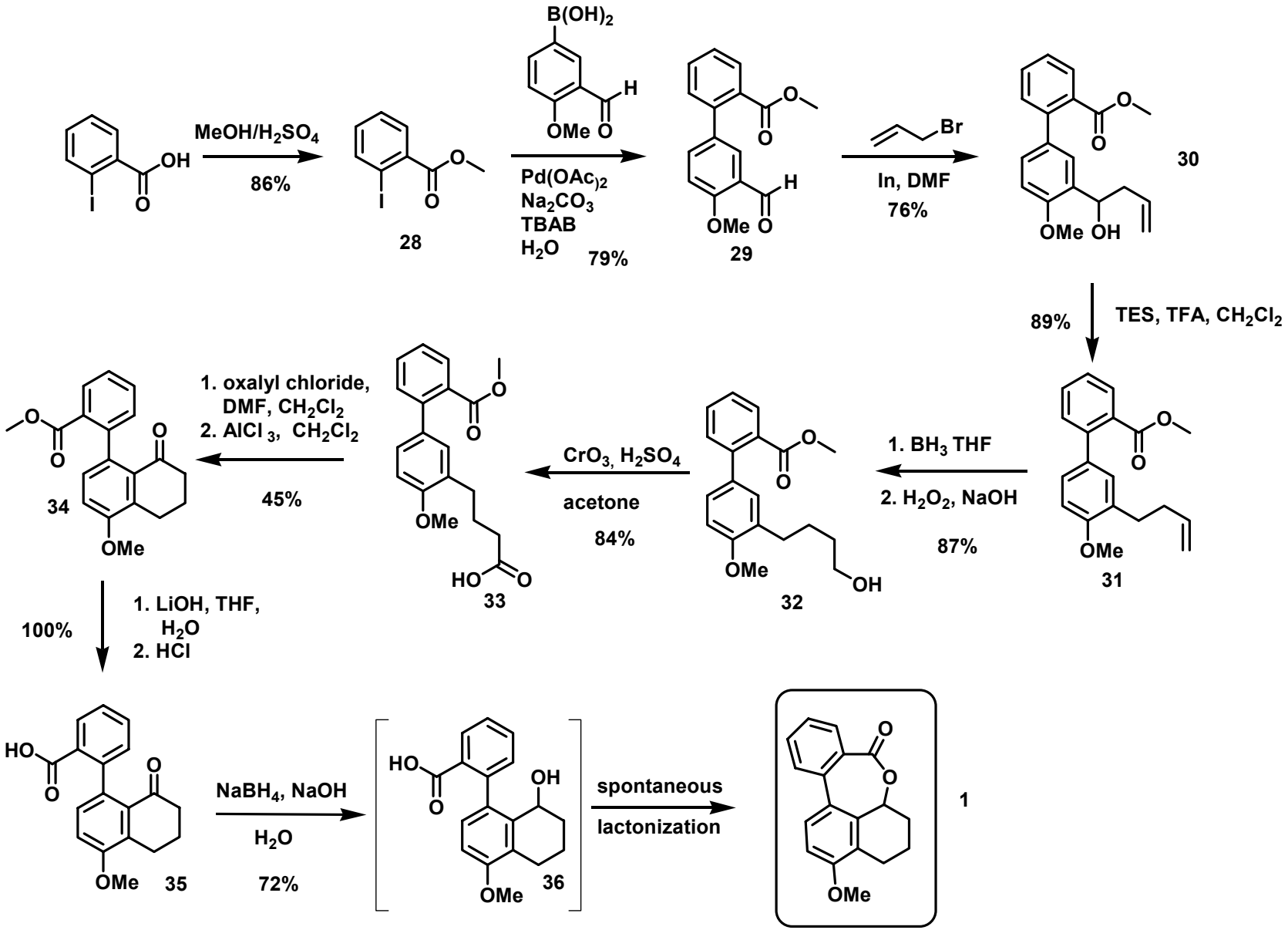
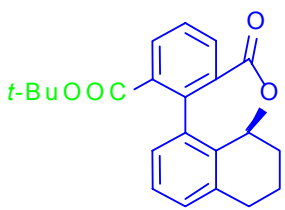

MeOH/H2SO4
86%
28
B(OH)2
OMe O
H
Pd(OAc)2
Na2CO3
TBAB
H2O
79%
29
Br
In, DMF
76%
30
89%
TES, TFA, CH2Cl2
31
1. BH3 THF
2. H2O2, NaOH
87%
32
CrO3, H2SO4
acetone
84%
33
1. oxalyl chloride,
DMF, CH2Cl2
2. AlCl3, CH2Cl2
45%
34
100%
1. LiOH, THF,
H2O
2. HCl
35
NaBH4, NaOH
H2O
72%
36
spontaneous
lactonization
1

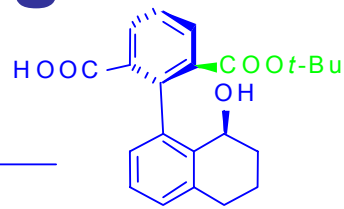
Proposed Motor: Chemically Driven Stepping Motor



35 $_{\text{backward}}$

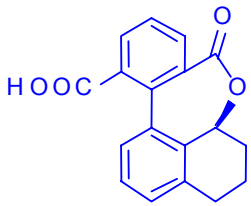
180 degrees backward
from **33 (-90)**

activate acid, cyclize



34a

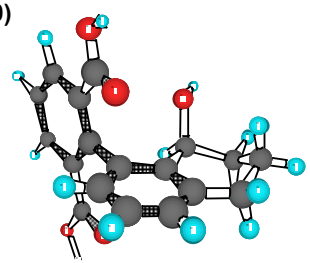
90 degrees backward
from **33 (-90)**

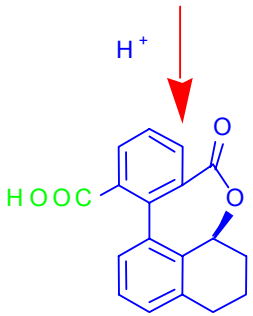


33 (0)

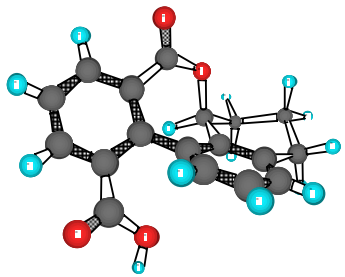
NaO*t*-Bu

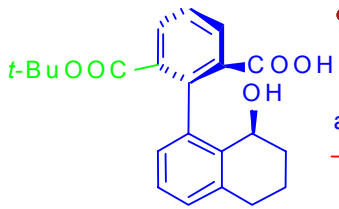
t-BuOH





33 (–180)

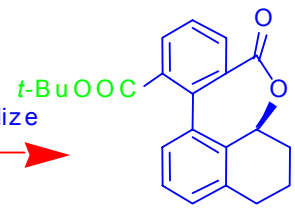




34b

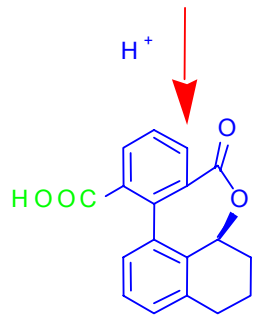
90 degrees forward
from **33 (+90)**

activate acid, cyclize



35 $_{\text{forward}}$

180 degrees forward
from **33 (+180)**



35 (+180)

Red = Pathway of a 180 degree bond rotation in the preferred "forward" direction

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Adaptation Of A Biological Motor To A ÑProof-of-PrincipleÓ Nanotechnological Application

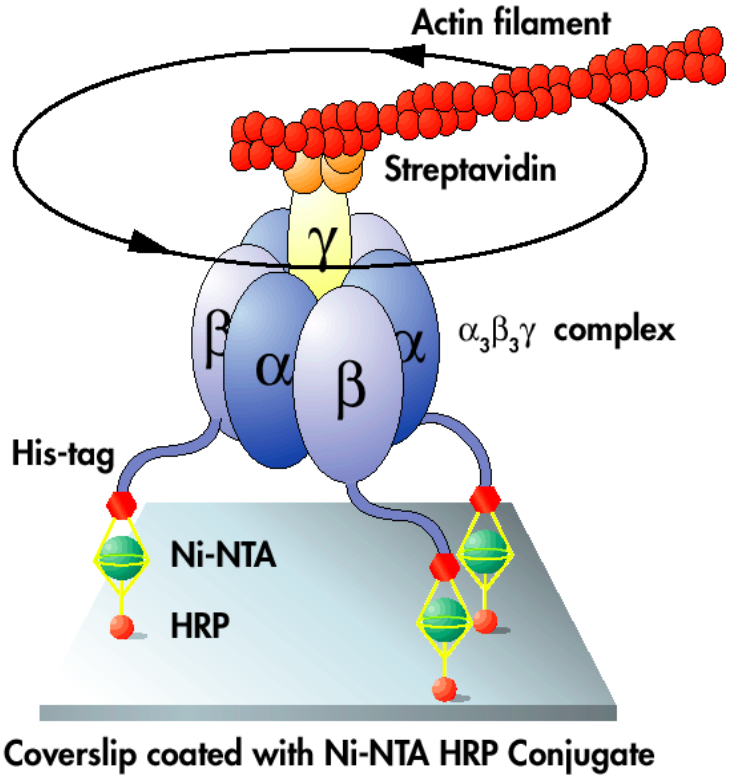
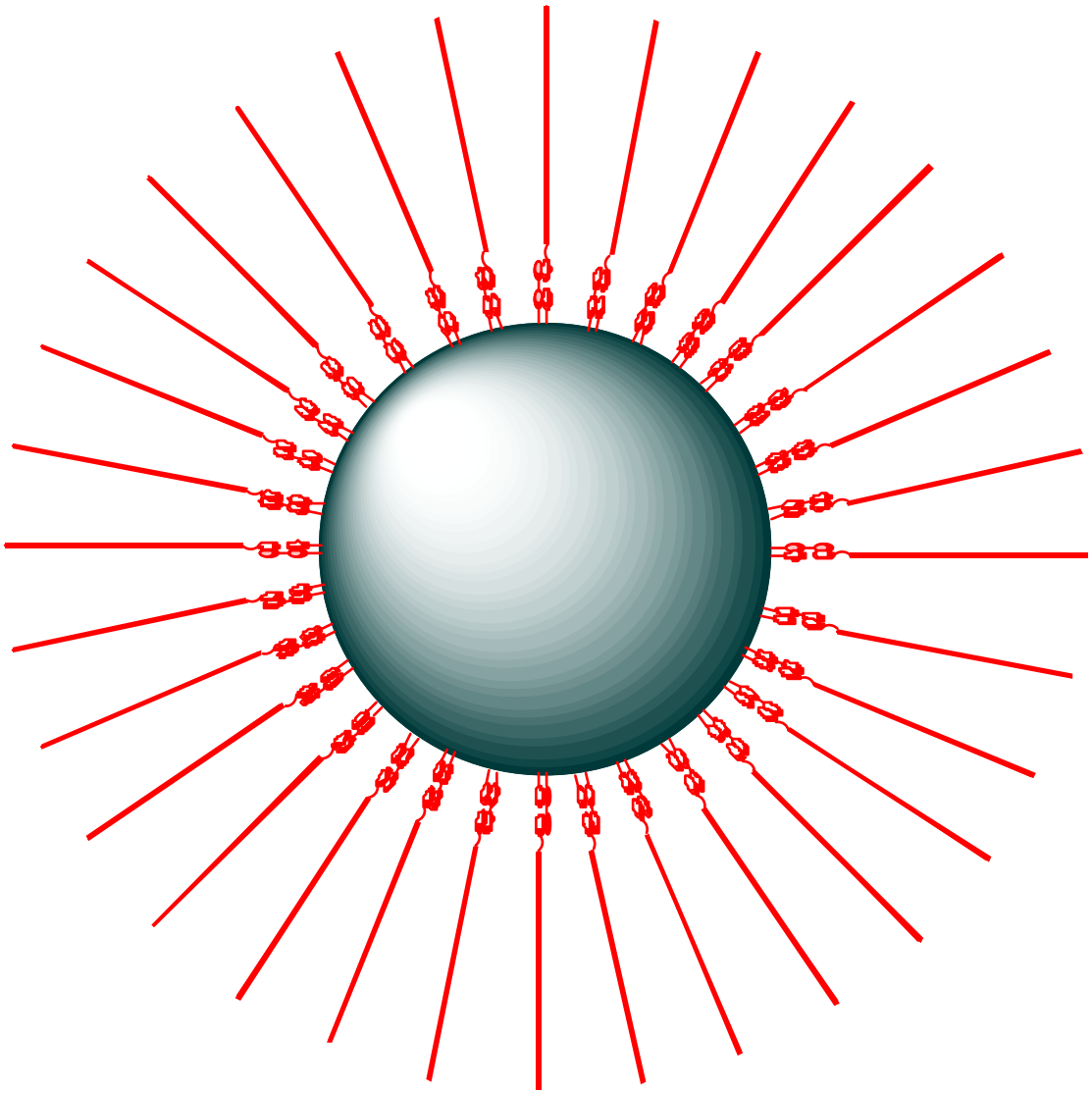


Figure 1 *The system used for observation of the rotation of the γ-subunit in the F1-ATPase $\alpha_3\beta_3\gamma$ subcomplex.*

Noji, H.; Yasuda, R.; Yoshida, M.; Kinosita, Jr., K. Direct Observation of the Rotation of F1-ATPase, *Nature*, **1997**, *386*, 299-302.

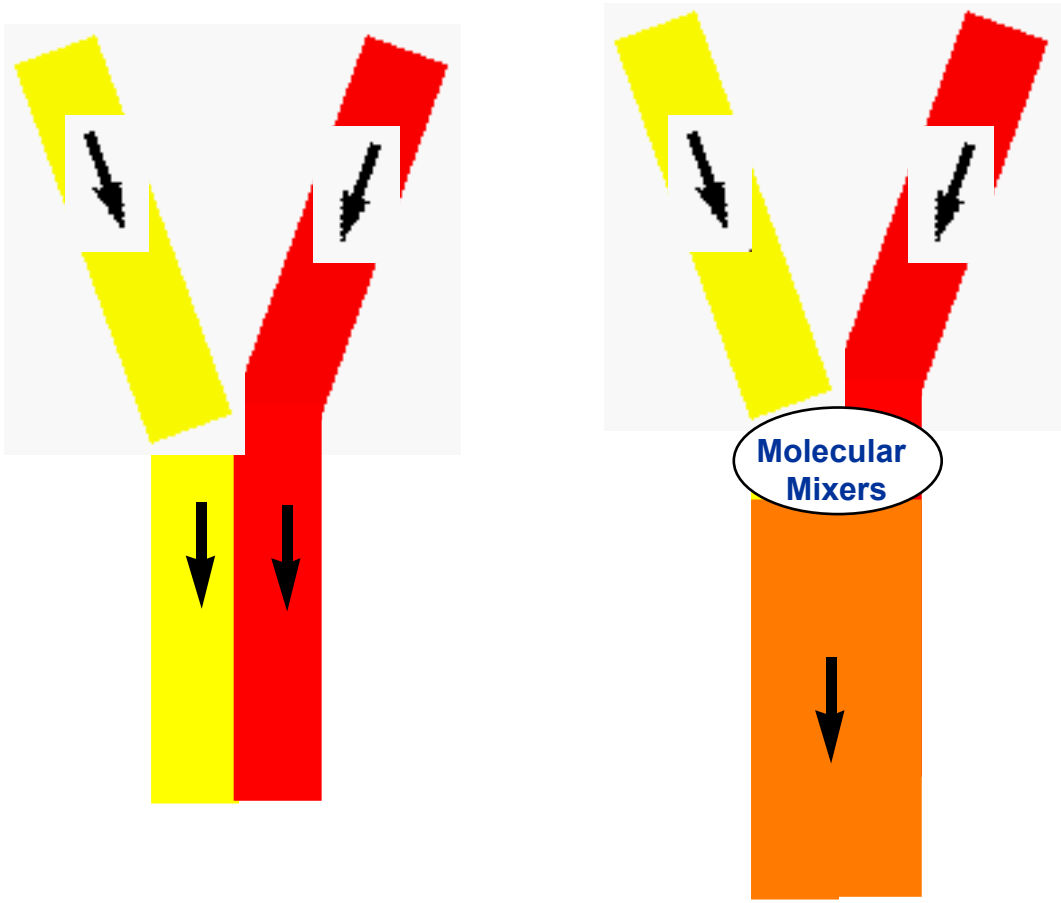
Photochemically-Driven Movement of a Particle?



hν

Particle "swims" towards or away from light

Application of Molecular Motor "Molecular Mixers" in Microfluidics?



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