化学能驱动的旋转分子马达

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2023-11-24

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2. 联芳基型旋转分子马达

3. 索烃型旋转分子马达

4. 总结与展望

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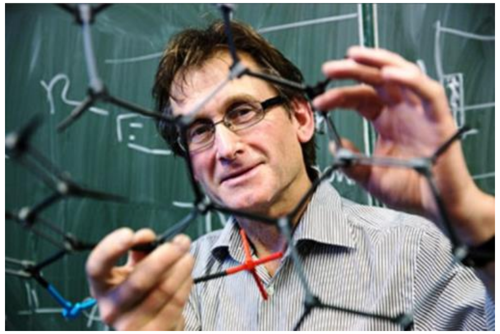
1. 背景介绍

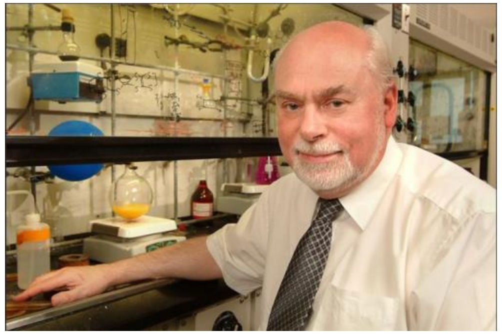
分子机器：是一种分子水平上的机器，它是一类通过外部刺激，如化学能、电能、光照等，将能量转化为可控运动的分子器件。

The 2016 Nobel Prize in Chemistry

"for the design and synthesis of molecular machines"



伯纳德 L 费林加
(Bernard L. Feringa)



弗雷泽 斯托达特
(J. Fraser Stoddart)

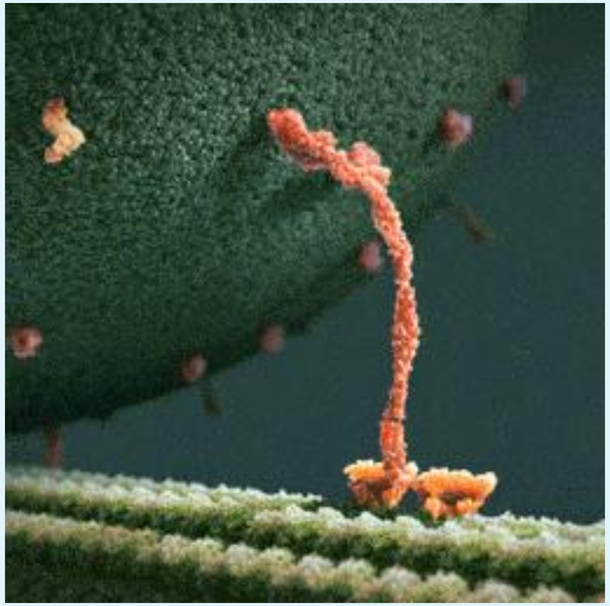
让-皮埃尔-索维奇
(Jean-Pierre Sauvage)

Alina L. Nussbaumer, et al. *Chem. Rev.* **2015,** *115*, 10081.

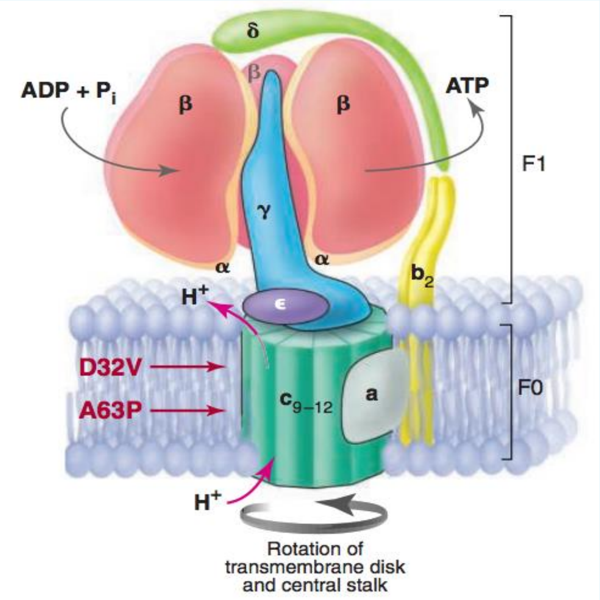
1. 背景介绍

复旦大学 Fudan University

马达蛋白无时无刻不在运输营养物质，使其发挥作用，并将废物和有害物质排出细胞。

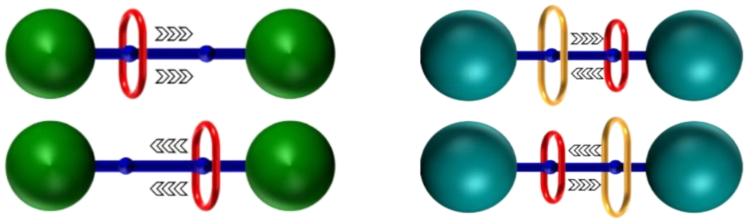


ATP合成酶是天然的分子转动马达，利用质子梯度的能量将ADP和磷酸转化成ATP。

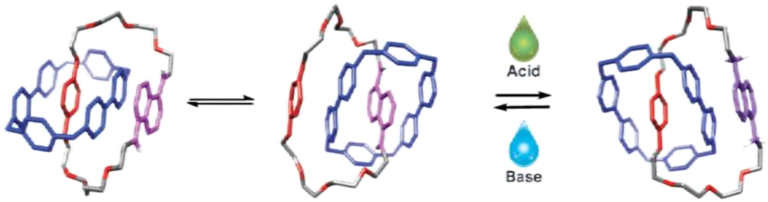


人造分子机器

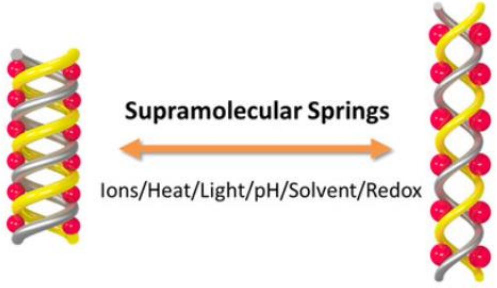
1. 背景介绍



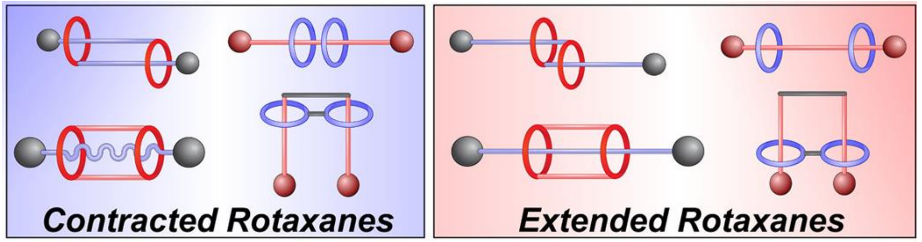
轮烷型分子梭
Nat. Chem. **2018**, *10*, 625.



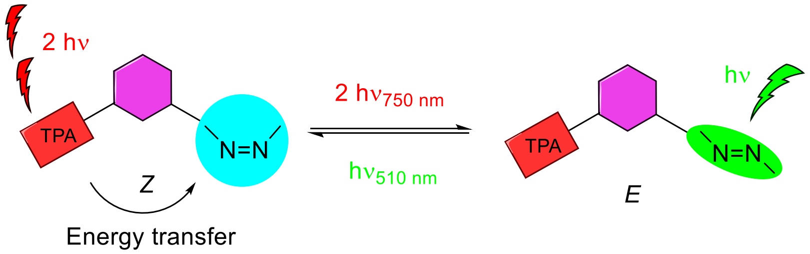
索烃型分子梭
J. Am. Chem. Soc. **2013**, 135, 17691.



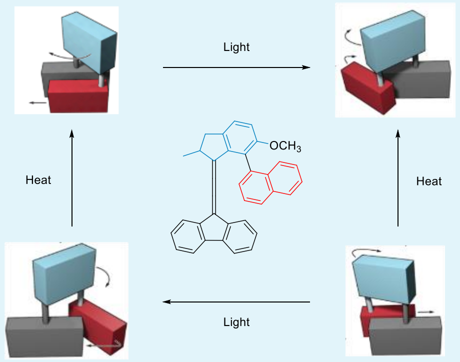
分子弹簧
Angew. Chem. Int. Ed. **2020**, *59*, 7319.



分子肌肉
Acc. Chem. Res. **2014**, *47*, 2186.



分子开关
Angew. Chem. Int. Ed. **2016**, *55*, 1544.



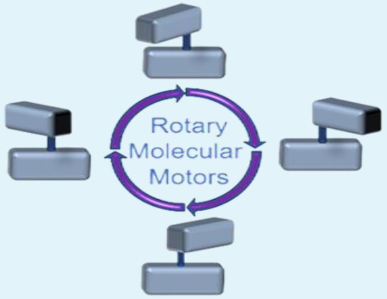
旋转分子马达
Science **2017**, *356*, 906.

1. 背景介绍

布朗运动

- 热力学第二定律
- 微观可逆性原理

产生机械能

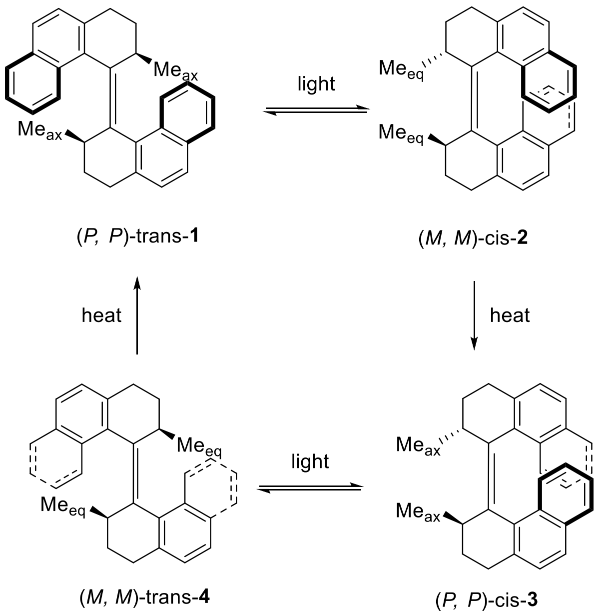


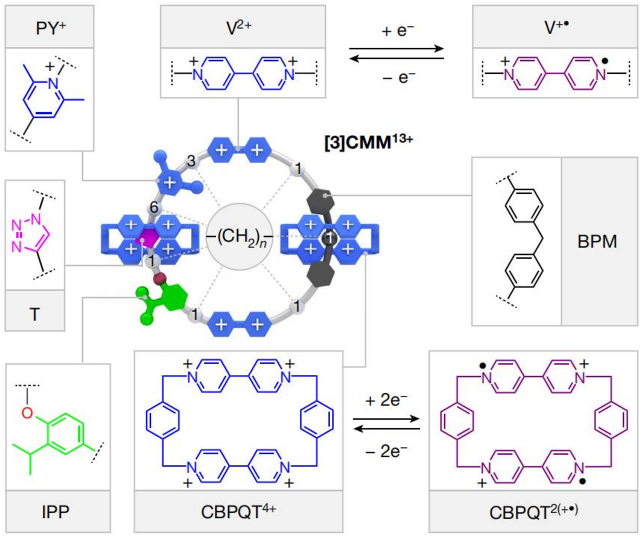
- 光能
- 电能

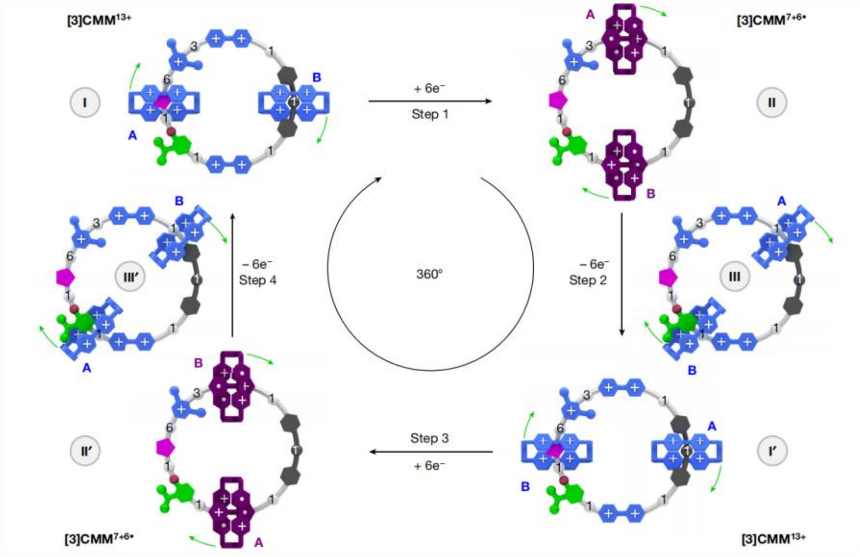
发展成熟

- 化学能

发展缓慢







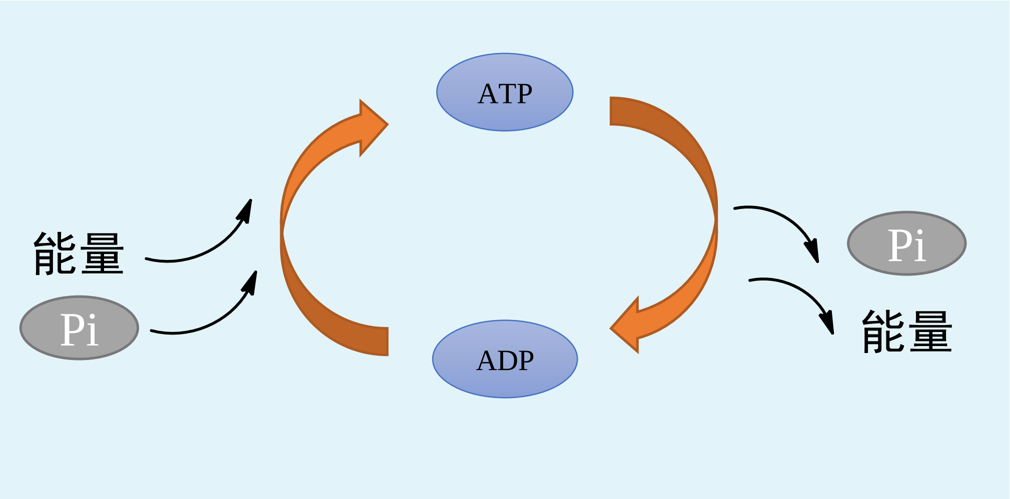
JACS Au **2023**, *3*, 1301.

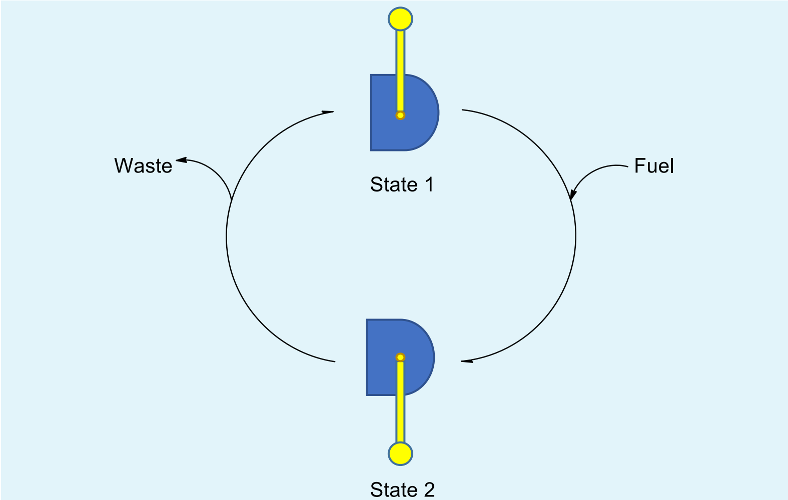
Nature **2023**, *613*, 280.

1. 背景介绍

化学能驱动的旋转分子马达存在的问题与挑战性

1. 化学反应有很多，但真正可以与旋转分子马达结合的反应很少。





2. 旋转的单向性、自主性，重复性，以及高效性。

Alberto Credi, et al. *Chem.Rev.* **2020**, *120*, 200.

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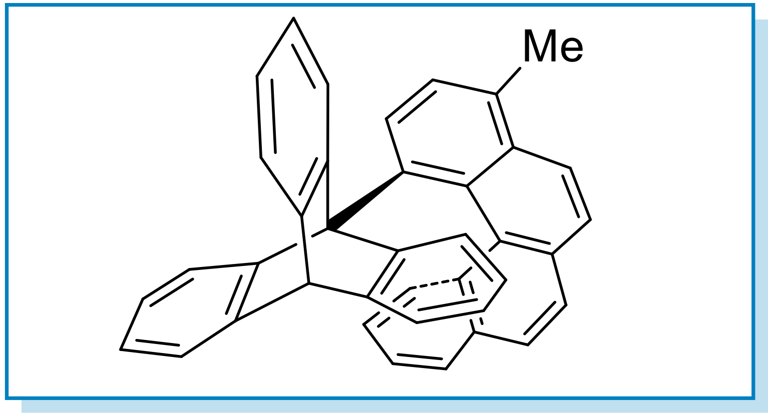
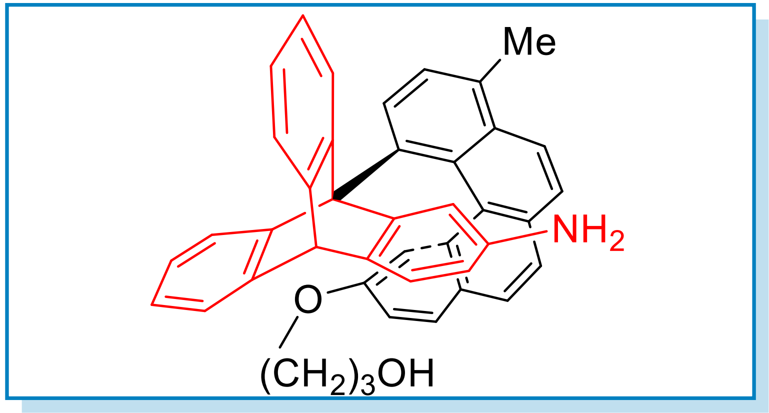
2. 联芳基型旋转分子马达

首次实现了化学驱动的分子马达的单向120 °旋转





$\Delta G^{\ddagger}$ = 25 kcal mol^{-1} ($t_{1/2}$ = 63.2 h, 298.15 K)

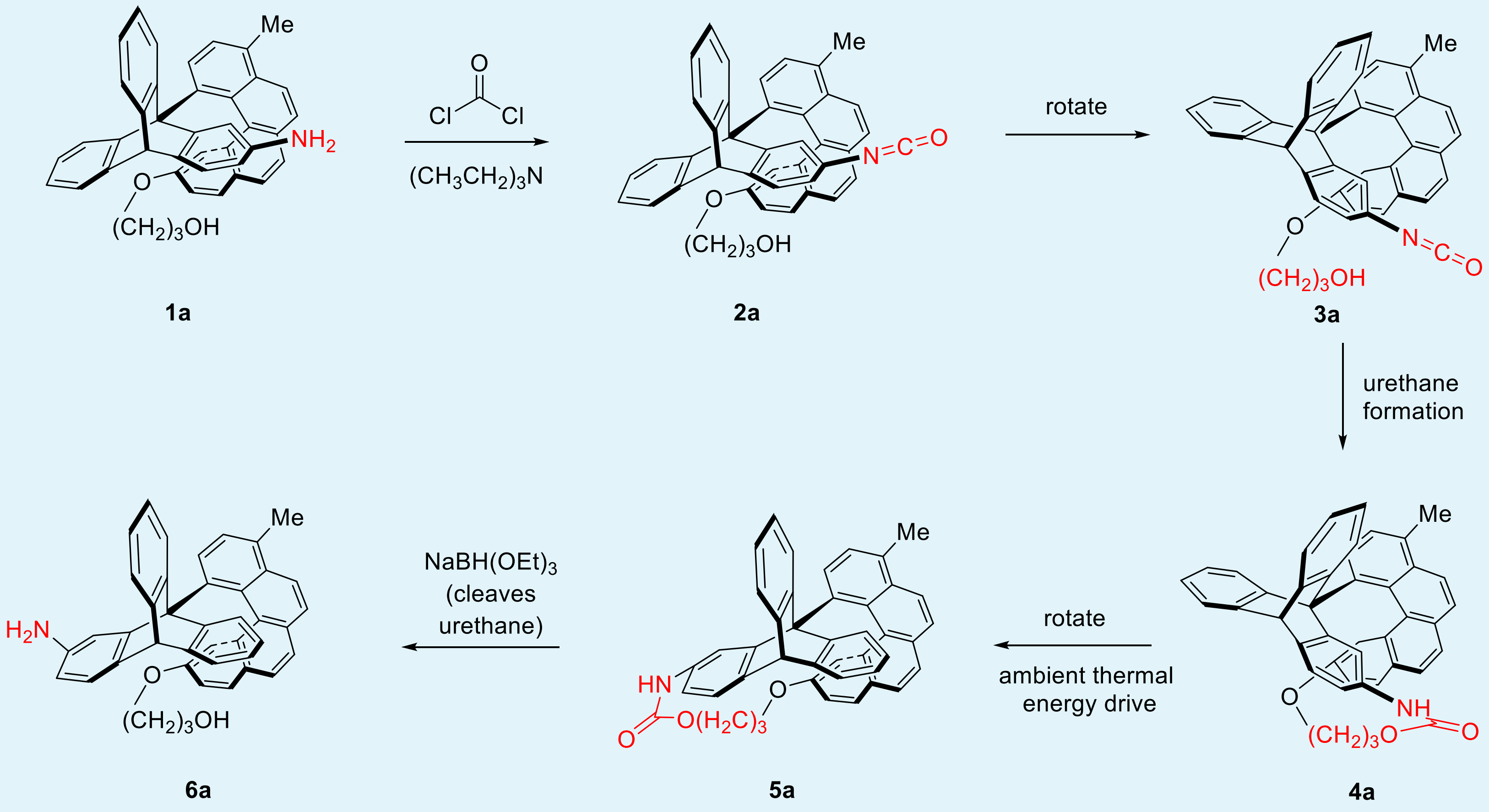
VS

$\Delta G^{\ddagger}$ = 3-5 kcal mol^{-1} (一般碳碳单键)

T. Ross Kelly, et al. *Nature* **1999**, *401*, 150.

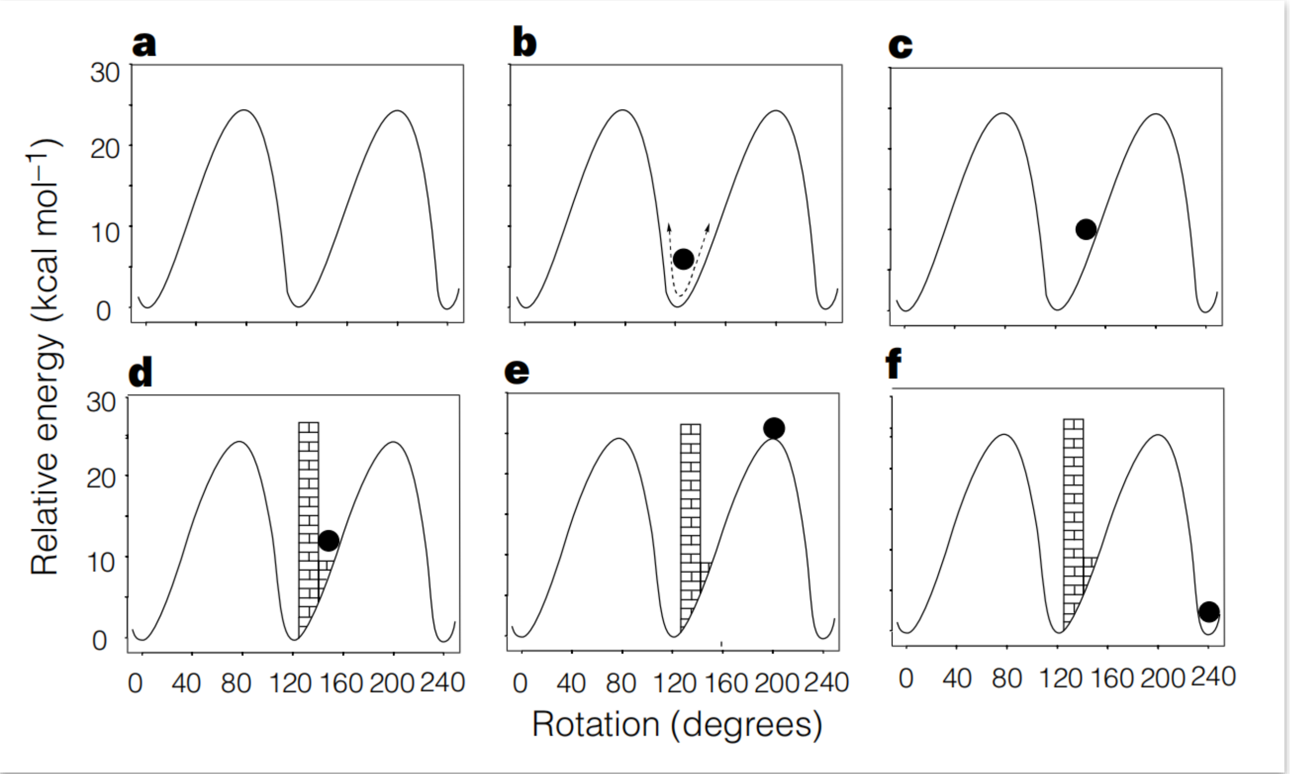
2. 联芳基型旋转分子马达

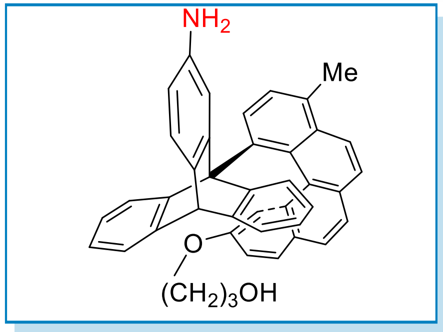
分子马达旋转的分步操作步骤



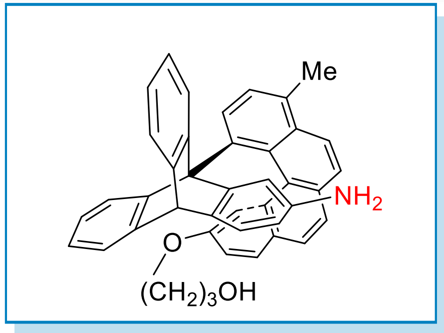
2. 联芳基型旋转分子马达

旋转的相对能量图

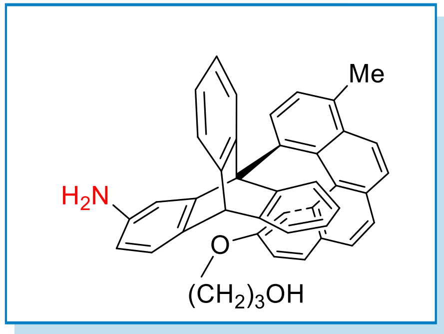




7a



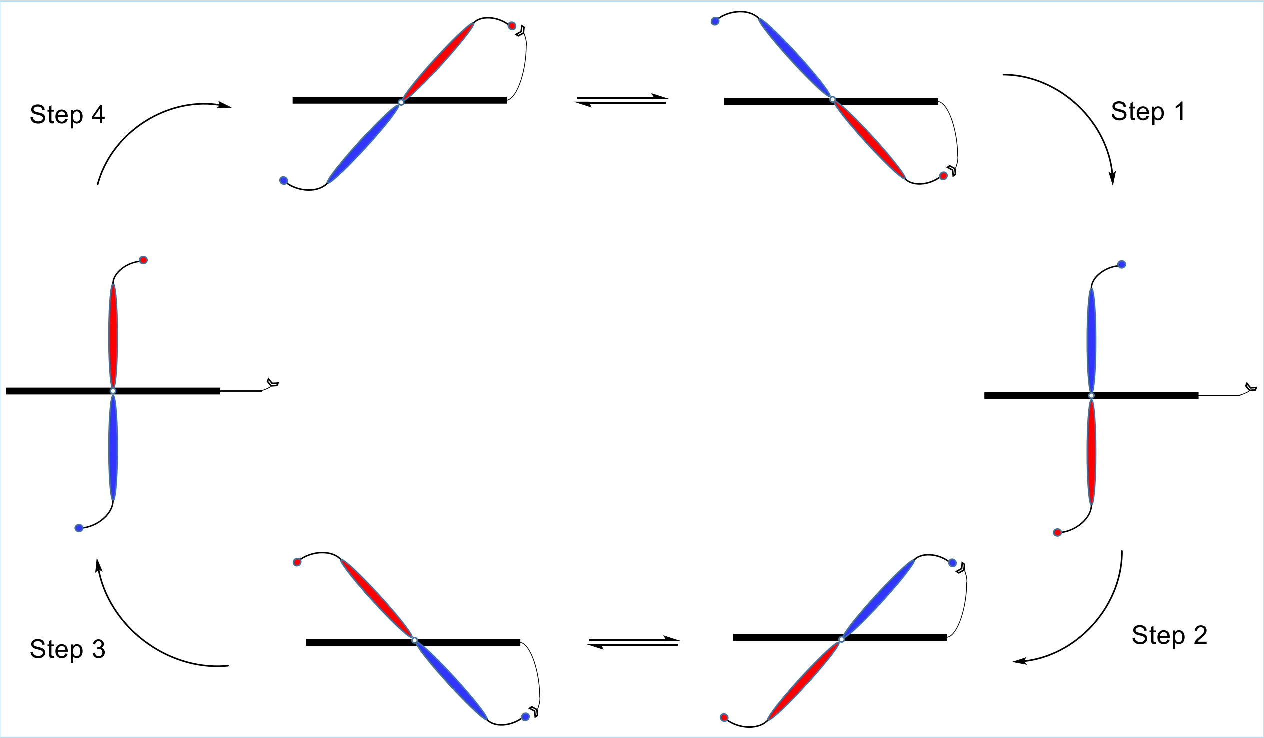
1a

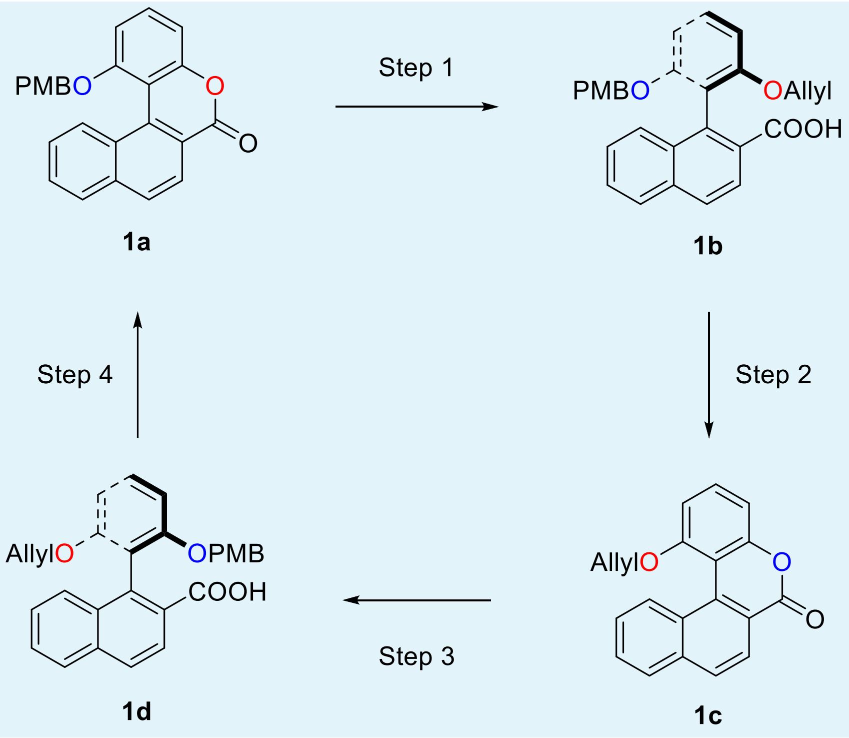


6a

2. 联芳基型旋转分子马达

基于受阻联芳基化合物，实现了分子马达360 °的单向旋转

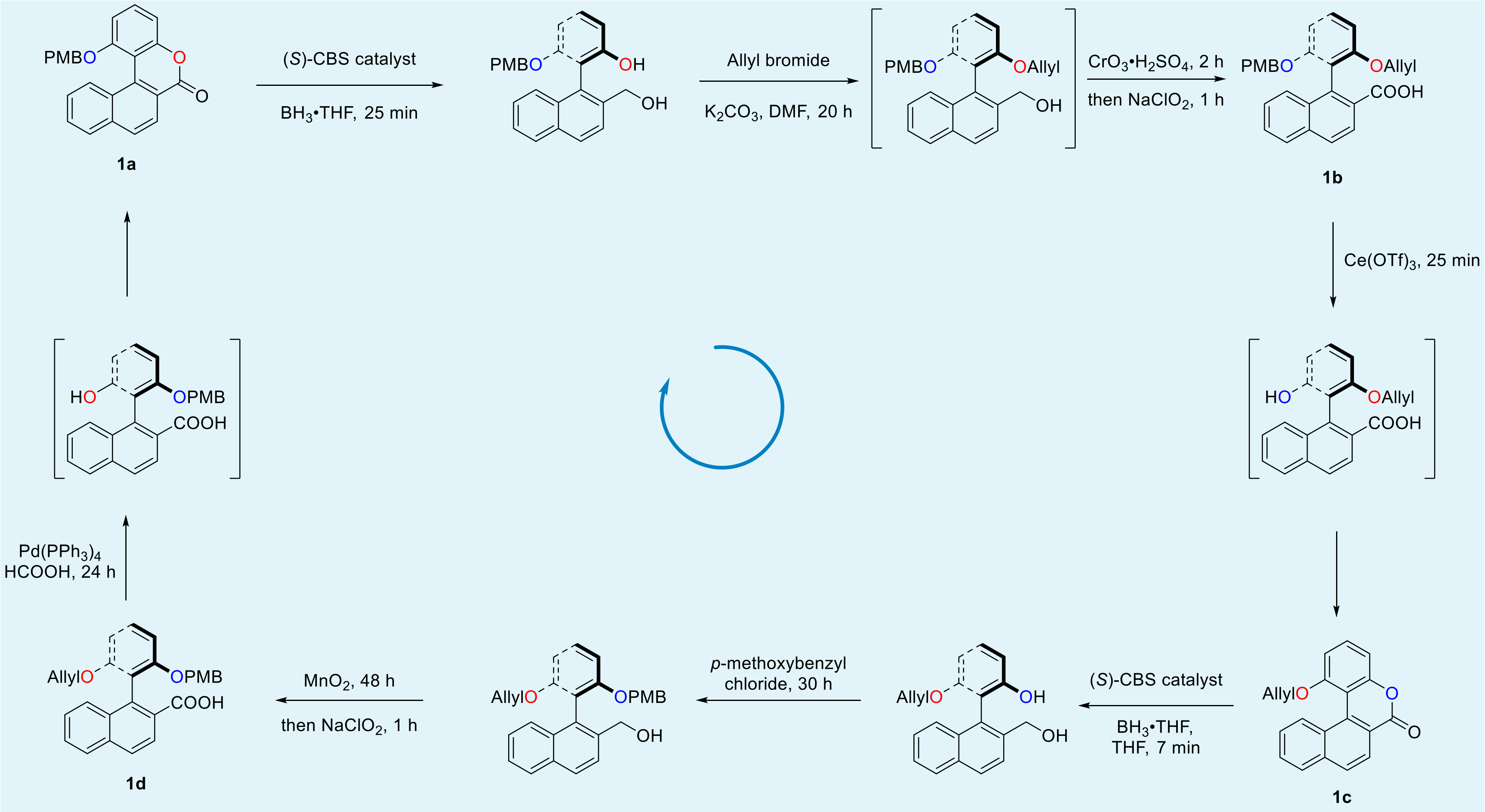




Ben L. Feringa, et al. *Science*, **2005**, *310*, 80.

2. 联芳基型旋转分子马达

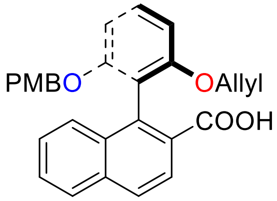
分子马达旋转的分步操作步骤



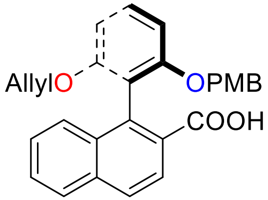
经过多步官能团操作，完成分子马达360 °旋转，总产率21%

2. 联芳基型旋转分子马达

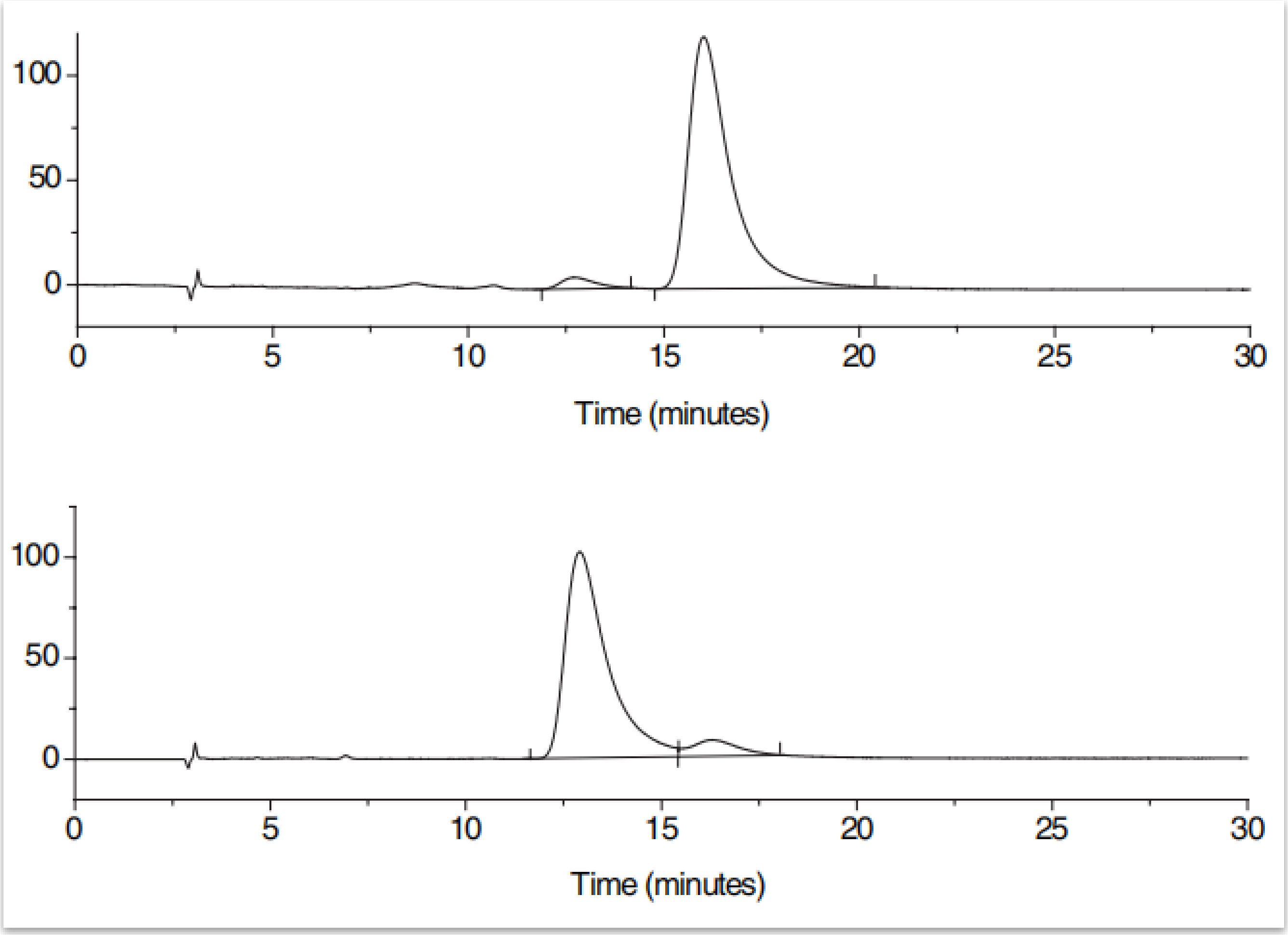
HPLC谱图



1b

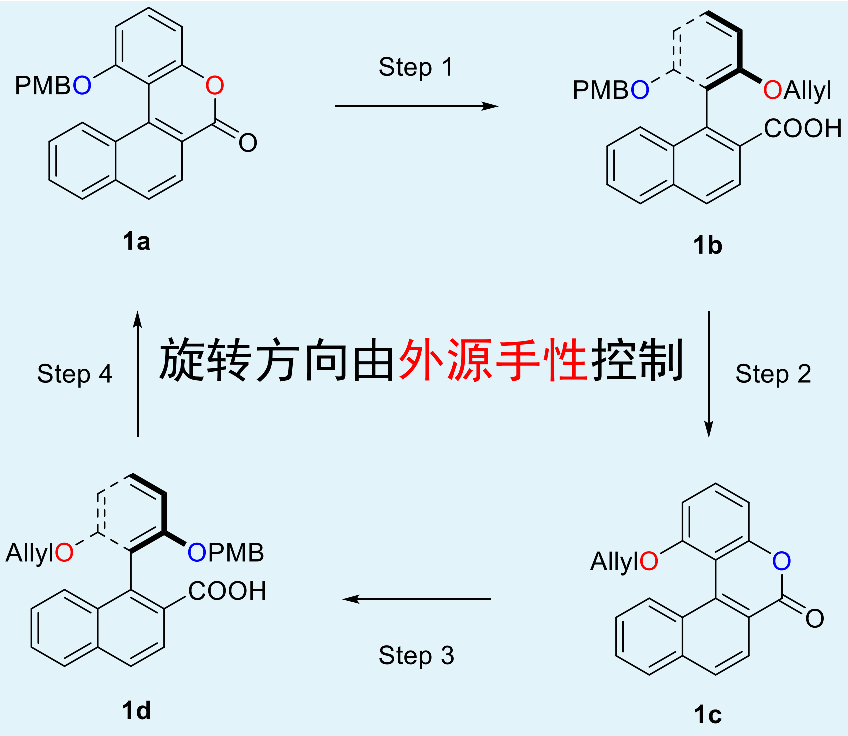


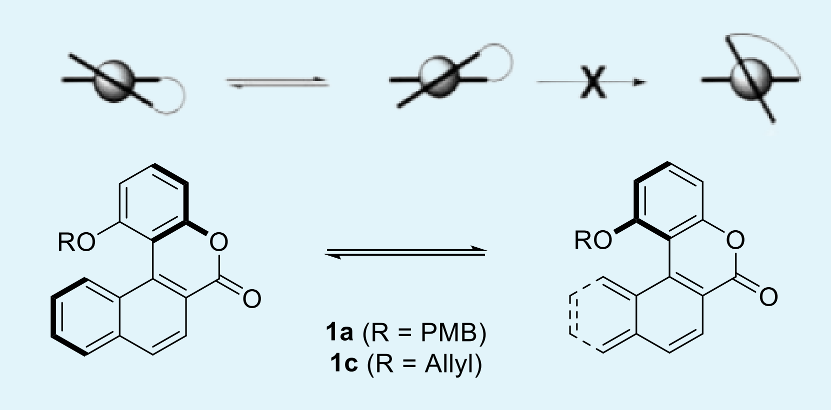
1d



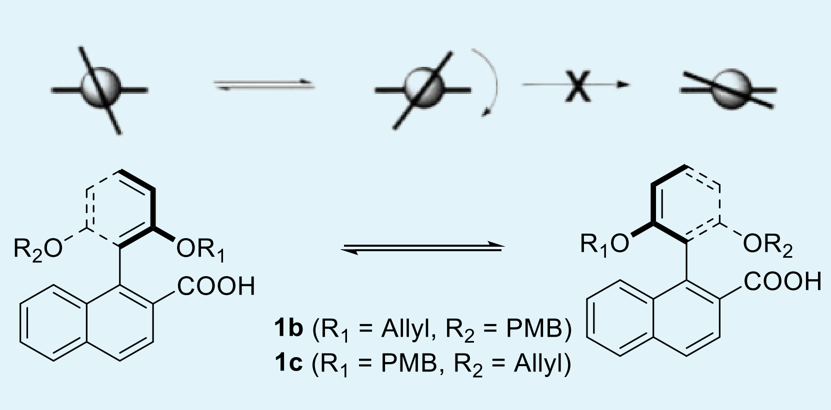
单向旋转的分子马达占比90%

2. 联芳基型旋转分子马达





类似的结构，旋转的半衰期是毫秒到分钟量级(室温)，容易消旋。



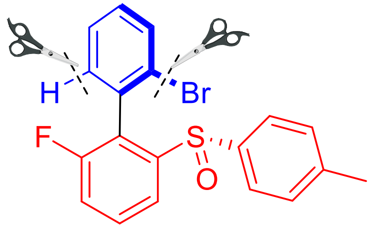
实验： **1b**和**1d**在100 °C加热2 h，构型没有变化，难消旋。

G. Bringmann, et al. *J. Organomet. Chem.* **2002**, *661*, 31.

2. 联芳基型旋转分子马达

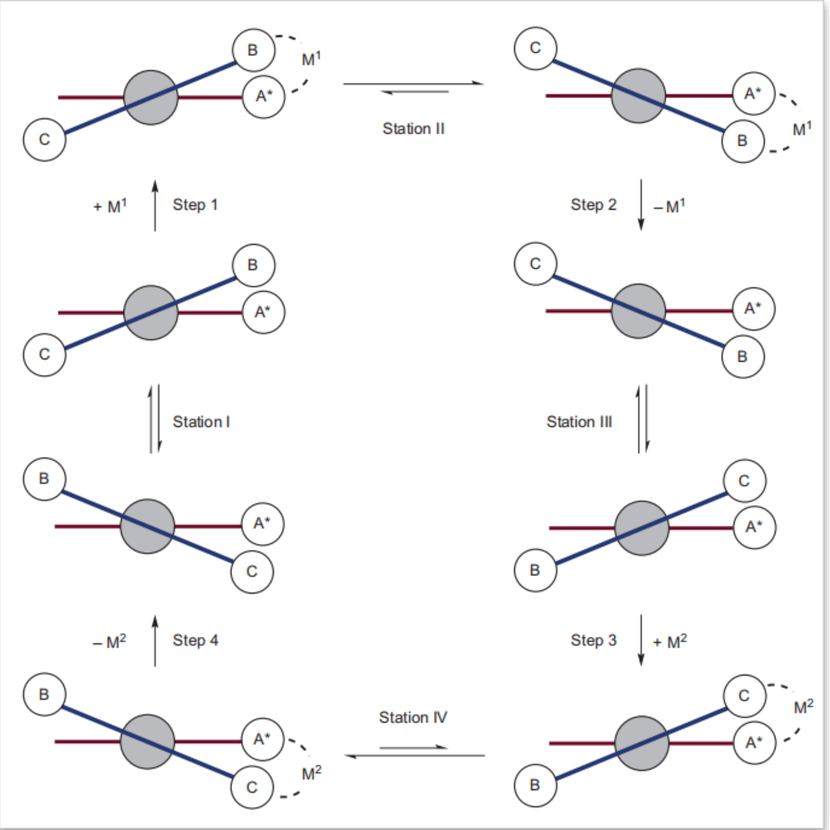
与钯的氧化还原循环相结合，实现分子马达360 º单向旋转

旋转方向由内源手性控制，无需额外手性试剂



(*S*, *M*)-**1**

$\Delta G^{\ddagger}$ = 37 kcal mol^{-1} (298.15 K)



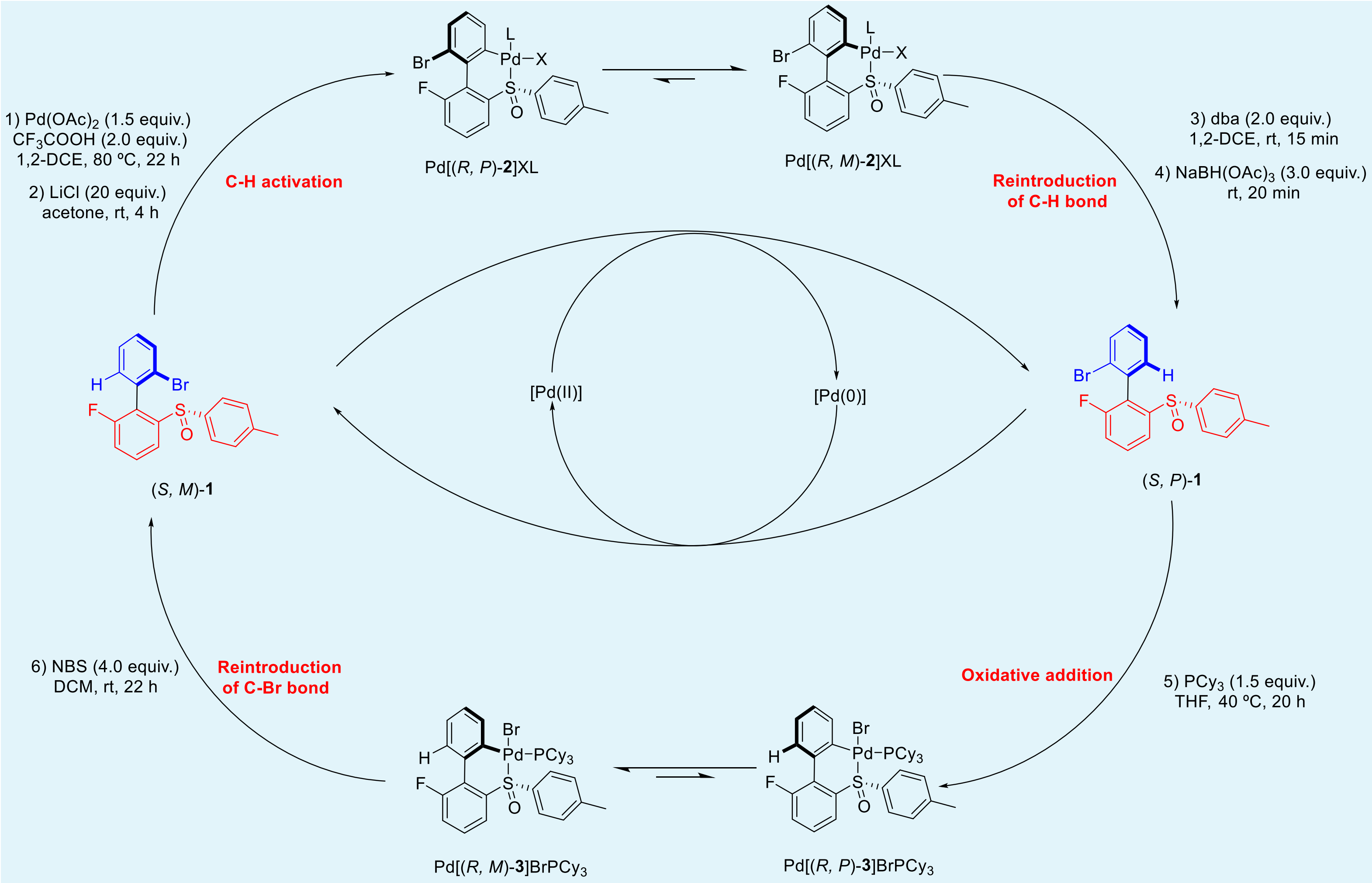
Ben L. Feringa, et al. *Nature Chem.* **2016**, *8*, 860.

2. 联芳基型旋转分子马达

复旦大学 Fudan University

分子马达旋转的分步操作步骤

ΔG‡ = 23.7 kcal mol-1 (298.15 K)



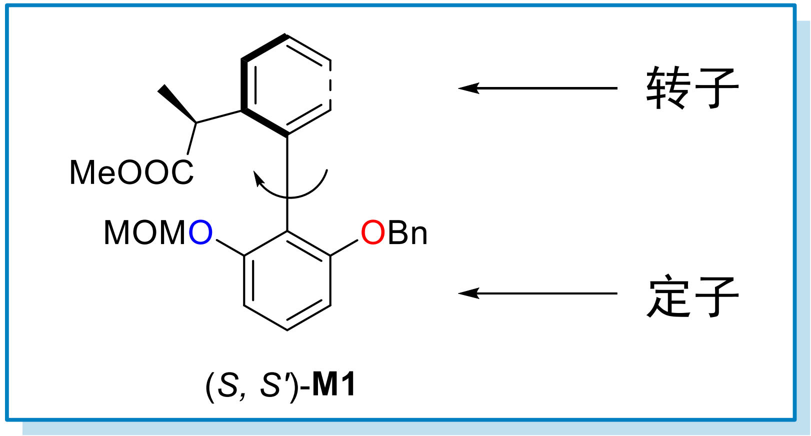
ΔG‡ = 19.8 kcal mol-1 (298.15 K)

从(*S*, *M*)-**1** : (*S*, *P*)-**1** =50 : 1开始，完成一次旋转，得到 (*S*, *M*)-**1** : (*S*, *P*)-**1** =1.0 : 1.3 ， 总产率19%

2. 联芳基型旋转分子马达

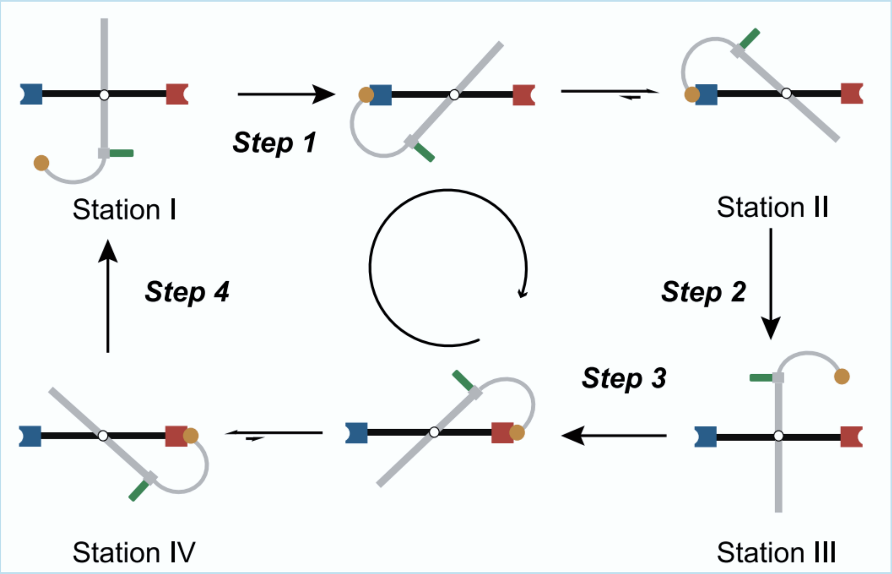
基于受阻联芳基化合物，实现了分子马达360 °的单向旋转

旋转方向由内源手性控制



(*S*, *S*')-**M1**

$\Delta G^{\ddagger}$ = 32.6 kcal mol^{-1} (433.15 K)

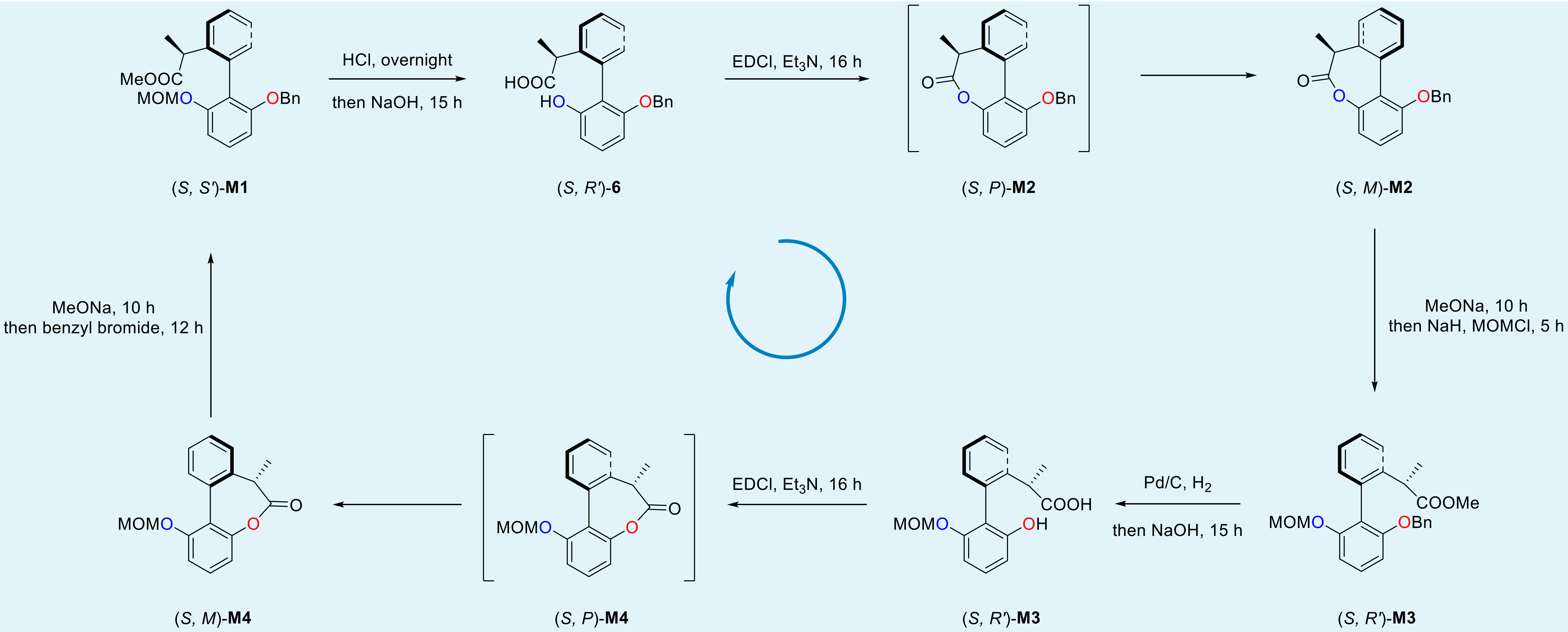


Depeng Zhao, et al. *Chem.* **2020**, *6*, 2420.

2. 联芳基型旋转分子马达

分子马达旋转的分步操作步骤

$\Delta G^{\ddagger}$ = 22.6 kcal mol^{-1} (298.15 K)

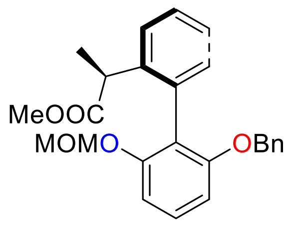


$\Delta G^{\ddagger}$ = 21.9 kcal mol^{-1} (298.15 K)

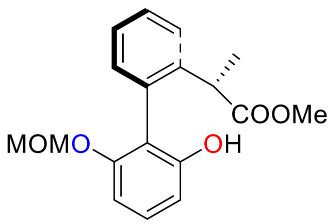
经过多步官能团操作，完成分子马达360 °旋转，总产率57%

2. 联芳基型旋转分子马达

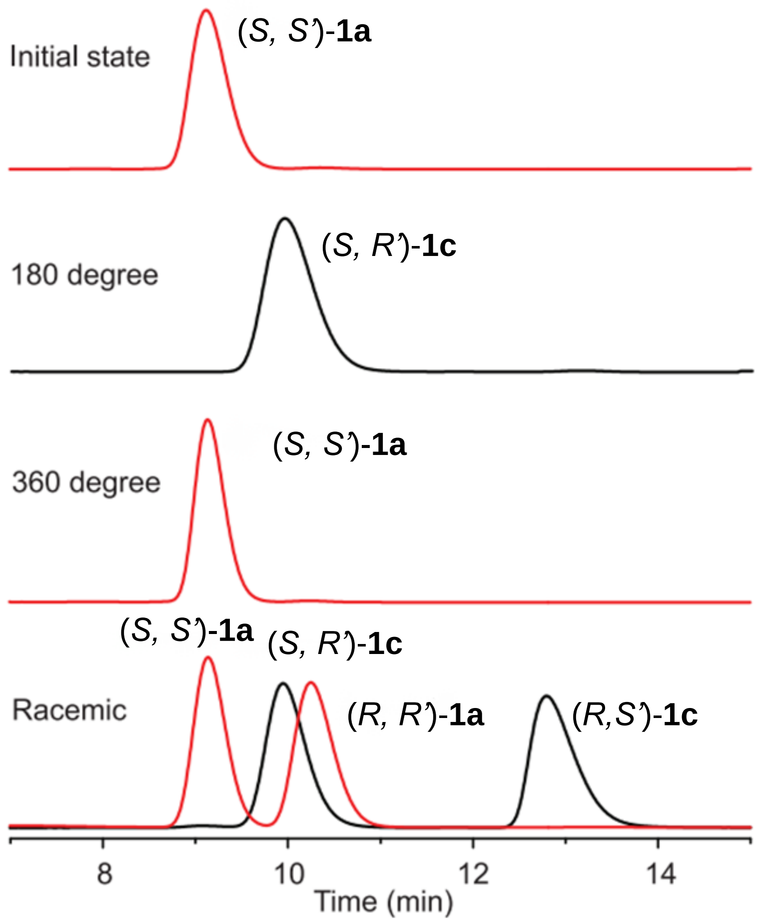
HPLC谱图



(*S*, *S*')-**1a**



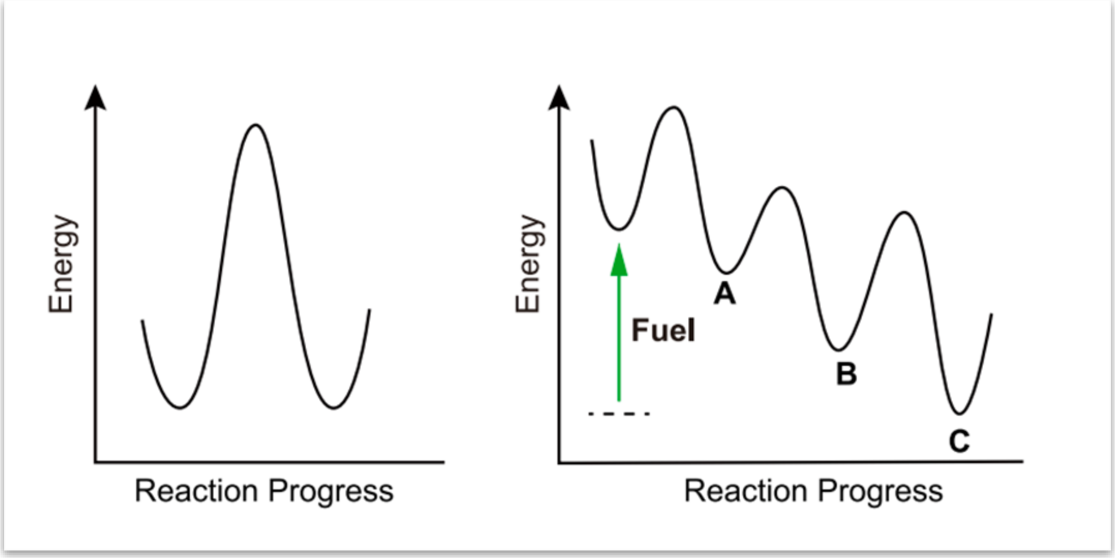
(*S*, *R*')-**1c**

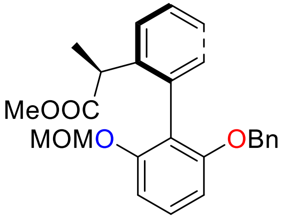


单向旋转的分子马达占比>99%

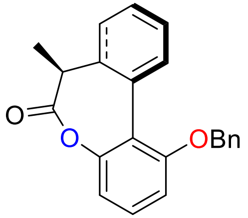
2. 联芳基型旋转分子马达

旋转的能量简图

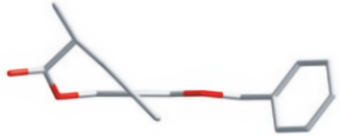


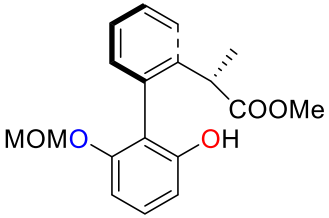


(*S*, *S'*)-**1a**

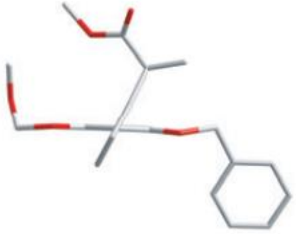


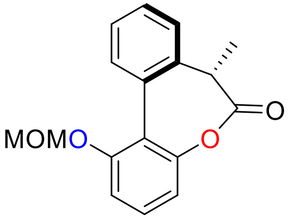
(*S*, *M*)-**1b**





(*S*, *R'*)-**1c**

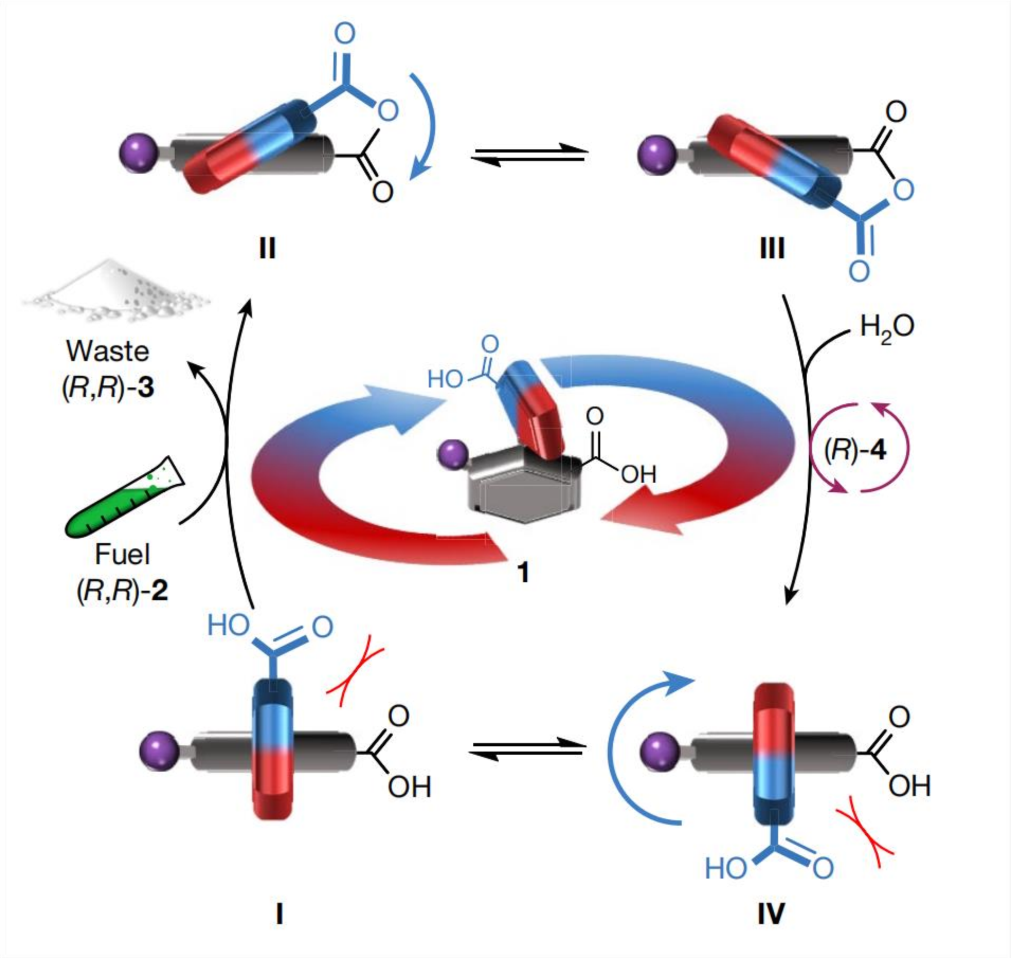




(*S*, *M*)-**1d**

2. 联芳基型旋转分子马达

首次实现了基于受阻联芳基化合物的分子马达360 °自主旋转，无需分步操作



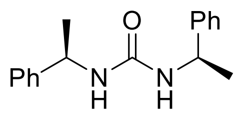
背景反应：只有3%的(*R*, *R*)-**2**水解，脱水和水解过程可以兼容

David, A. Leigh, et al. *Nature* **2022**, *604*, 80.

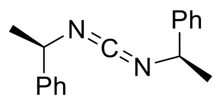
2. 联芳基型旋转分子马达

分子马达自主旋转的过程

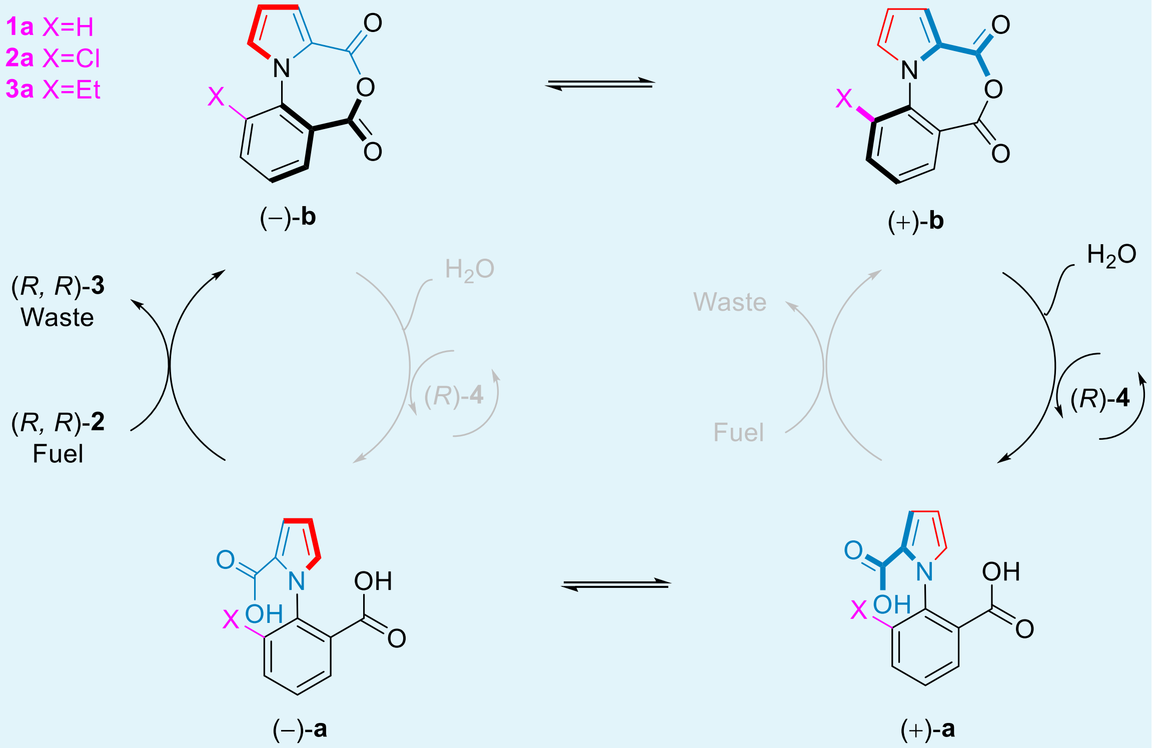
旋转方向由外源手性控制

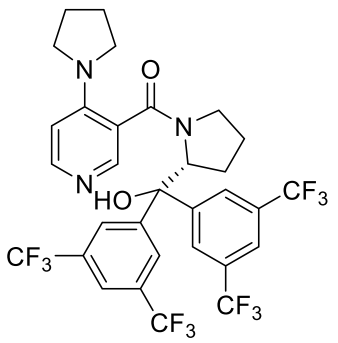


(*R*, *R*)-**3**



(*R*, *R*)-**2**

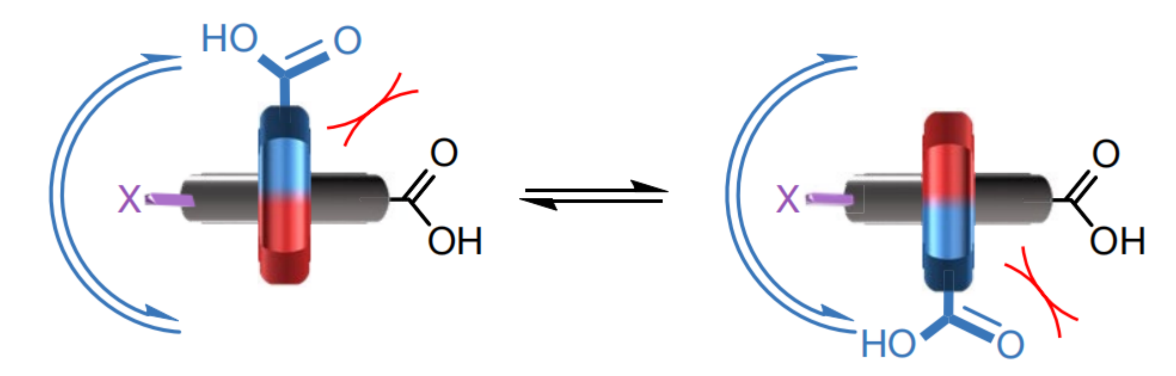




(*R*)-**4**

2. 联芳基型旋转分子马达

旋转能垒



-COOH越过-X旋转能垒

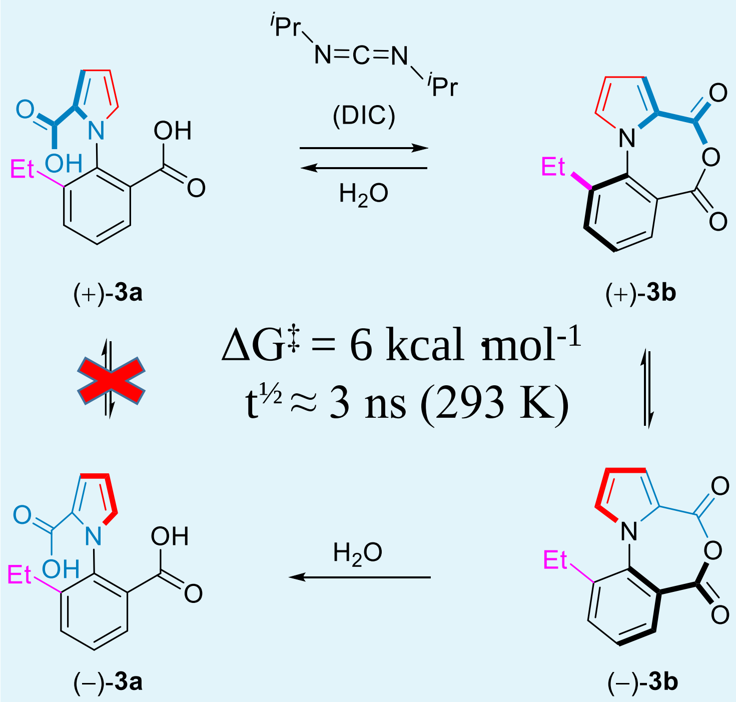
1a (X = H) $\Delta G^{\ddagger}$ = 16 kcal mol^{-1}, $t^{1/2} \approx$ 3 ns (293 K)

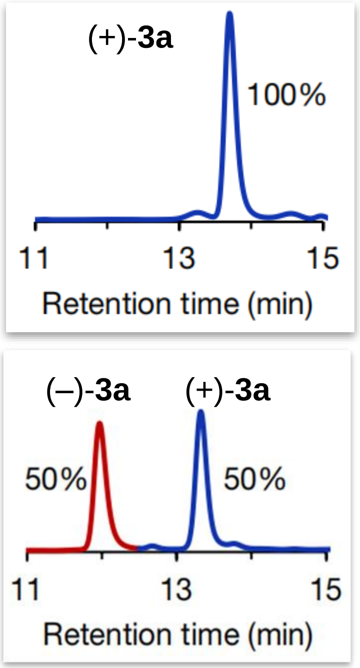
2a (X = Cl) $\Delta G^{\ddagger}$ = 27 kcal mol^{-1}, $t^{1/2} \approx$ 280 days (293 K)

3a (X = Et) $\Delta G^{\ddagger}$ = 33 kcal mol^{-1}, $t^{1/2} \approx$ 22000 years (293 K)

-COOH越过-COOH旋转能垒:

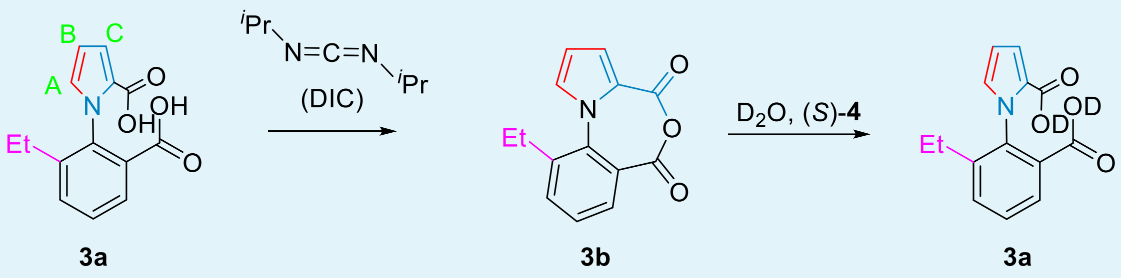
$\Delta G^{\ddagger}$ = 133 kcal mol^{-1}, $t^{1/2} \approx 10^{78}$ years (293 K)

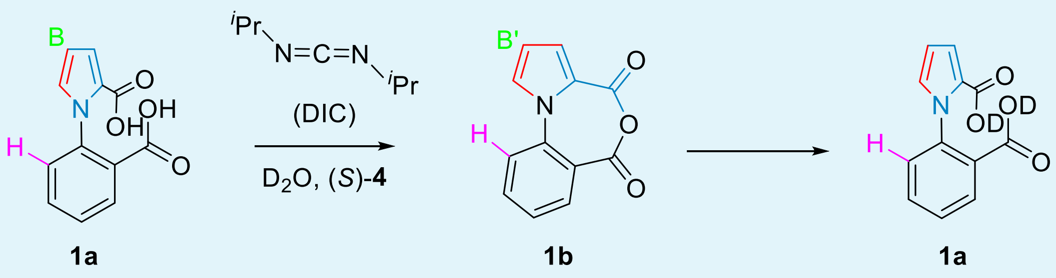


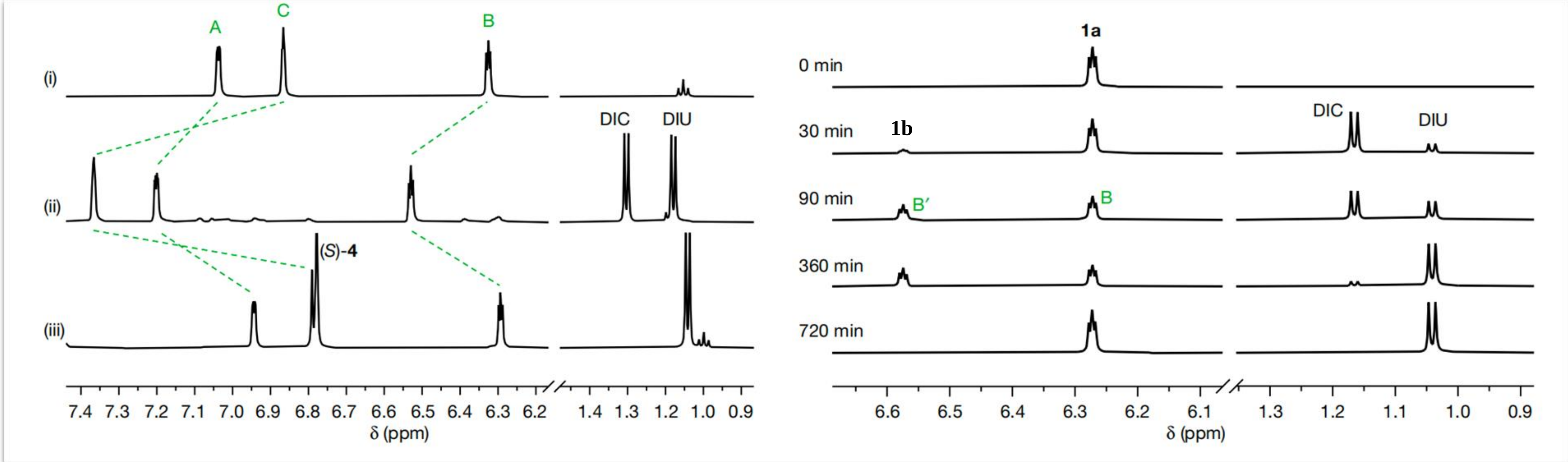


不添加DIC，原料(+)-**3a** 的*ee*值在18小时后没有变化

脱水与水解

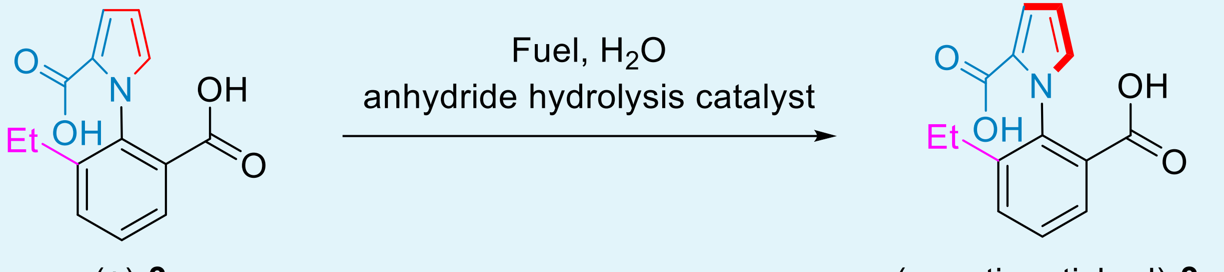

B
C
A
N
O
OH
OH
Et
O
^{i}Pr
N=C=N
^{i}Pr
(DIC)
3a
N
O
O
O
Et
3b
D$_2$O, (*S*)-**4**
N
O
OD
OD
Et
O
3a


B
N
O
OH
OH
H
O
1a
^{i}Pr
N=C=N
^{i}Pr
(DIC)
D$_2$O, (*S*)-**4**
B'
N
O
O
O
H
1b
N
O
OD
OD
H
O
1a

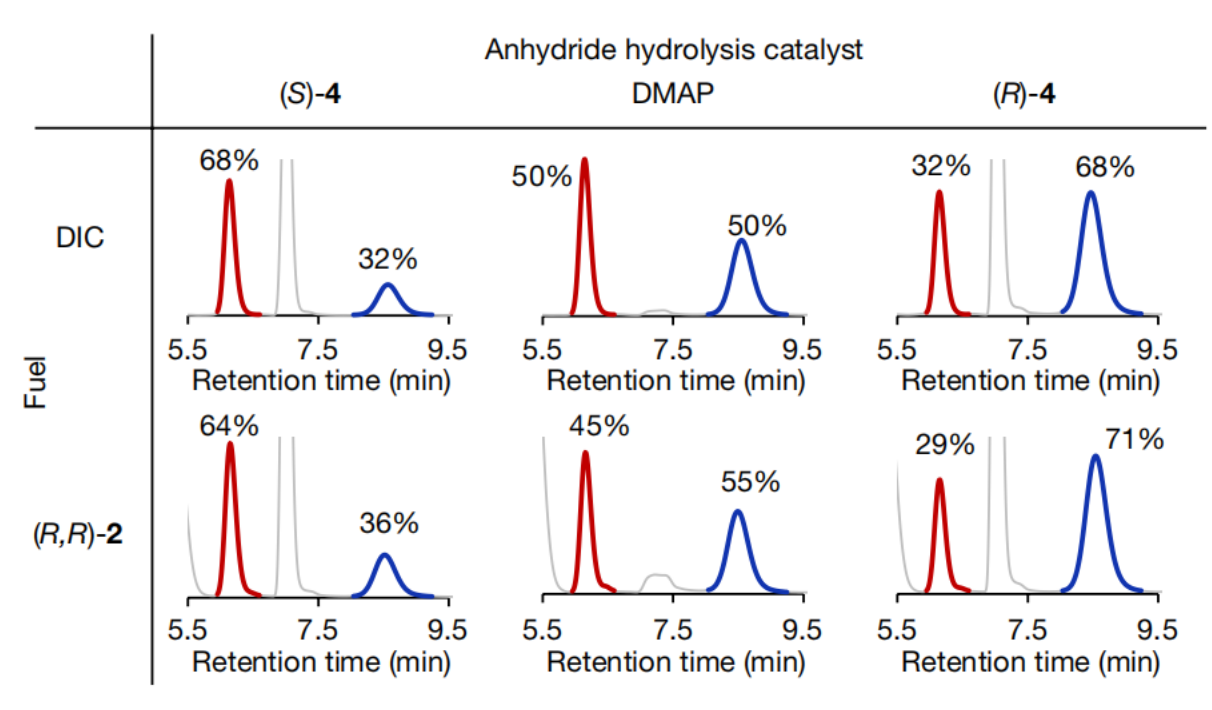

A
C
B
(i)
(ii)
(iii)
DIC
DIU
(*S*)-**4**
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2
1.4 1.3 1.2 1.0 0.9
δ (ppm)
1a
0 min
30 min
1b
90 min
B′
B
360 min
720 min
DIC
DIU
6.6 6.5 6.4 6.3 6.2 6.1
1.3 1.2 1.1 1.0 0.9
δ (ppm)

2. 联芳基型旋转分子马达

旋转的单向性



(±)-**3a** (enantioentiched)-**3a**



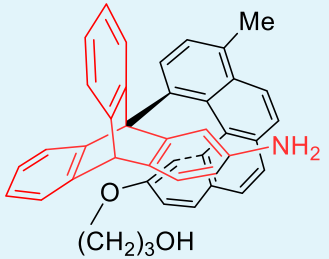
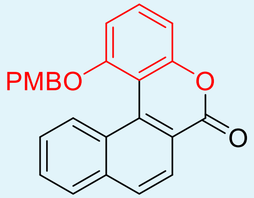
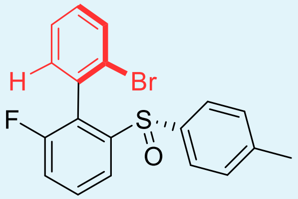
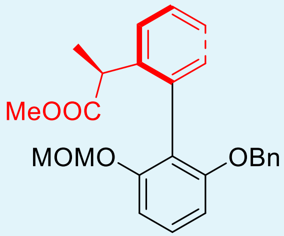
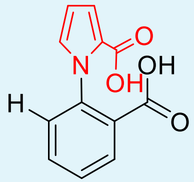
Fuel	Hydrolysis catalyst	Ratio (–)-**3a** : (+)-**3a**	***ee*** $_{(+)\text{-}\mathbf{3a}}$%
DIC	(*S*)-**4**	2.1 : 1.0	-36%
DIC	DMAP	1.0 : 1.0	0%
DIC	(*R*)-**4**	1.0 : 2.1	36%
(*R*, *R*)-**2**	(*S*)-**4**	1.8 : 1.0	-28%
(*R*, *R*)-**2**	DMAP	1.0 : 1.2	10%
(*R*, *R*)-**2**	(*R*)-**4**	1.0 : 2.4	42%

Racemic (±)-**3a** was fuelled ([**3a**] = 2.5 mM, [hydrolysis catalyst] = 2.5 mM, [fuel] = 12.5 mM in MES-buffered (100 mM, pH_{obs} = 5.10) dioxane: H_2O (7:3, v/v) at 10 °C. After 48 h the samples were analysed by chiral HPLC to determine enantio-enrichment.

外源手性试剂对分子马达的旋转方向控制较差

2. 联芳基型旋转分子马达

成环–开环策略

1999年 T. Ross Kelly课题组	2005年 Ben L. Feringa课题组	2016年 Ben L. Feringa课题组	2020年 Depeng Zhao课题组	2022年 David, A. Leigh课题组
				
120 º	360 º	360 º	360 º	360 º
里程碑意义	外源手性 控制方向 多步操作	内源手性 控制方向 多步操作	内源手性 控制方向 多步操作	外源手性 控制方向 一步操作

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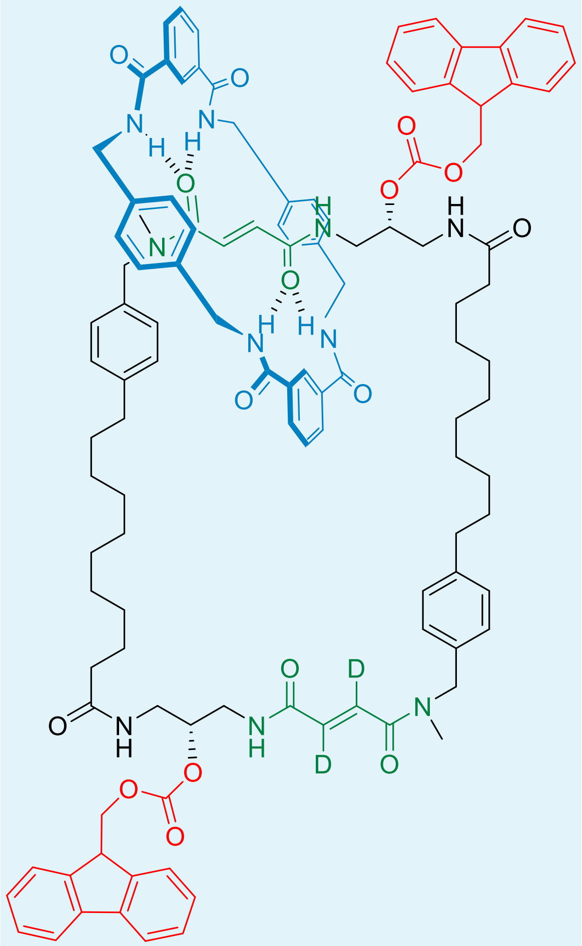
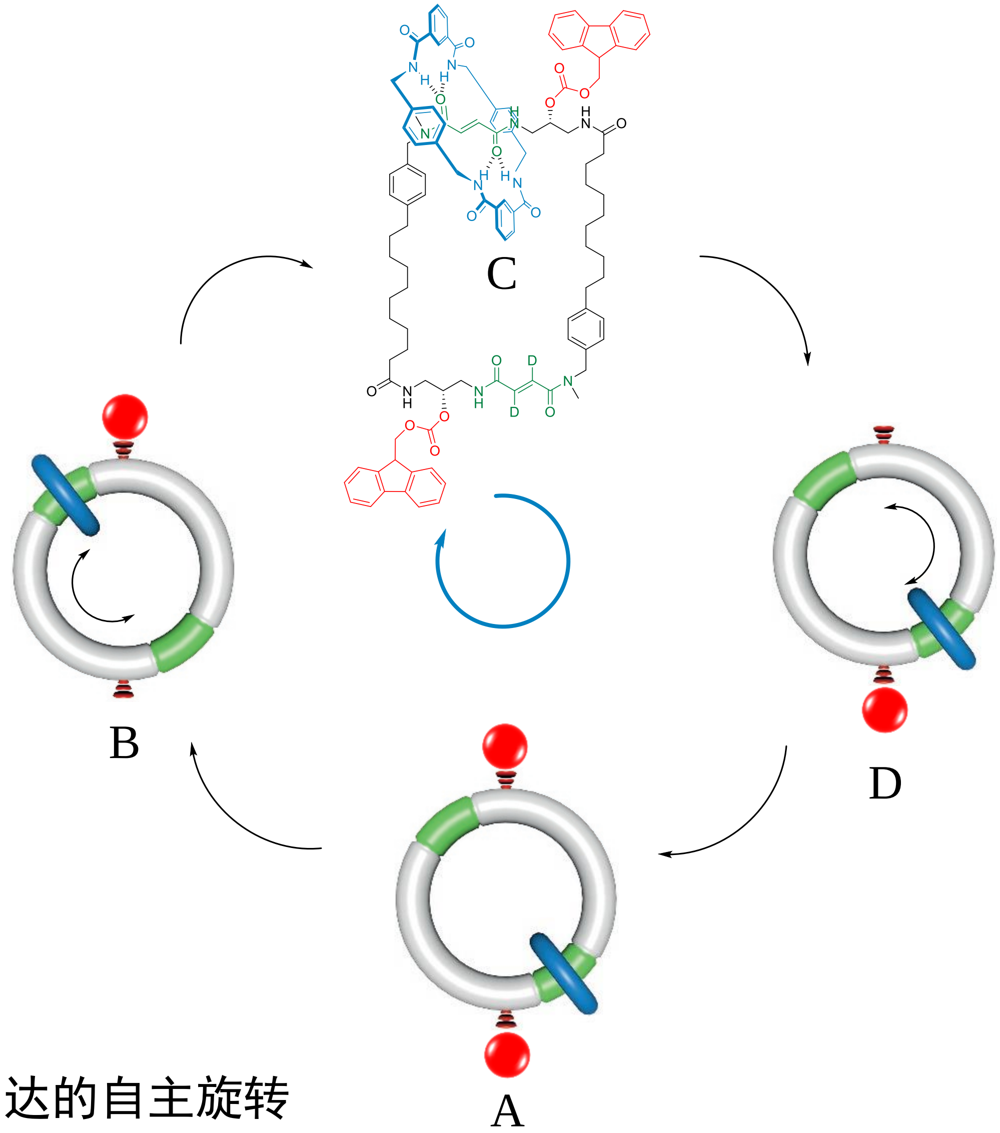
3. 索烃型旋转分子马达

绕“轨道”旋转

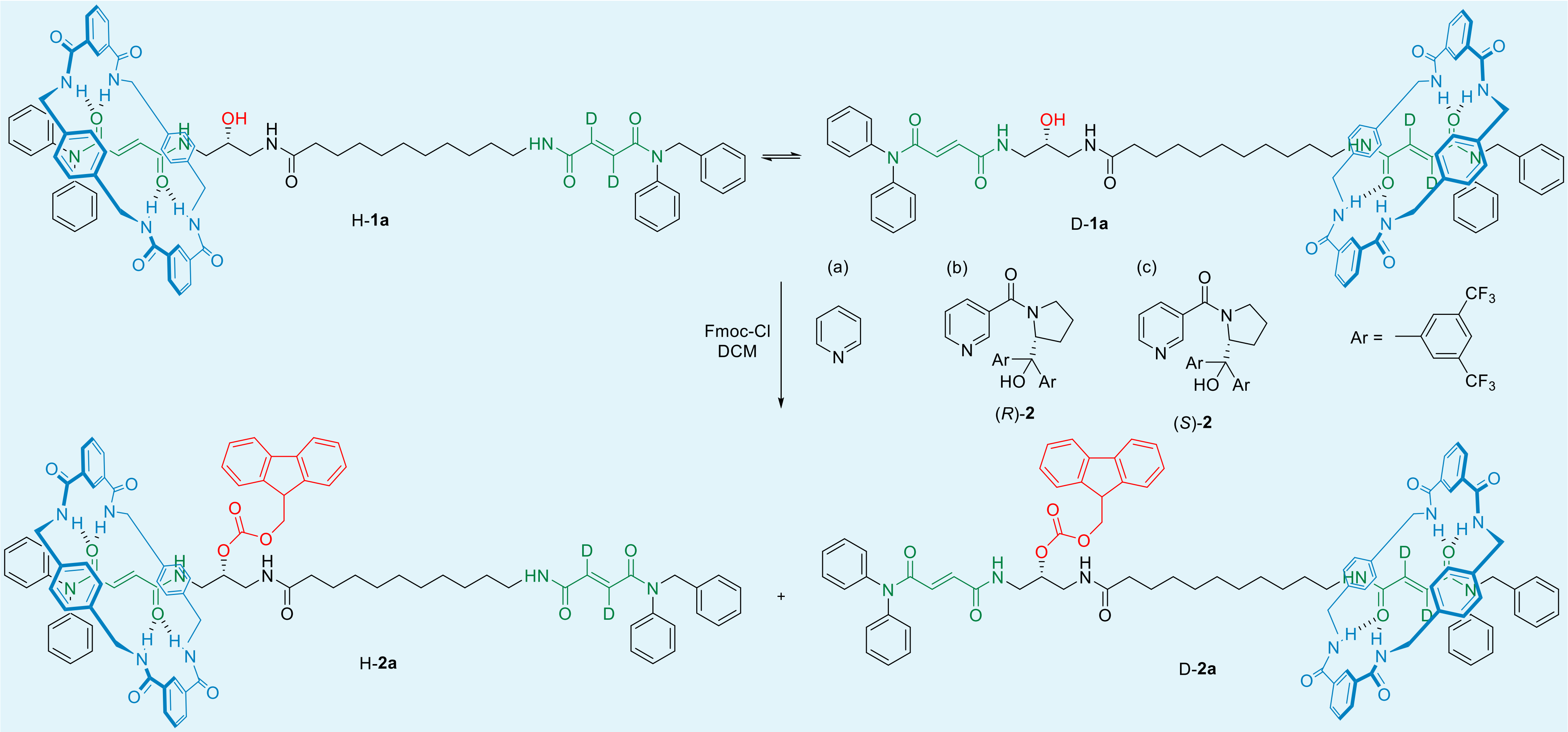




通过保护与脱保护策略，实现了化学驱动的索烃型分子马达的自主旋转

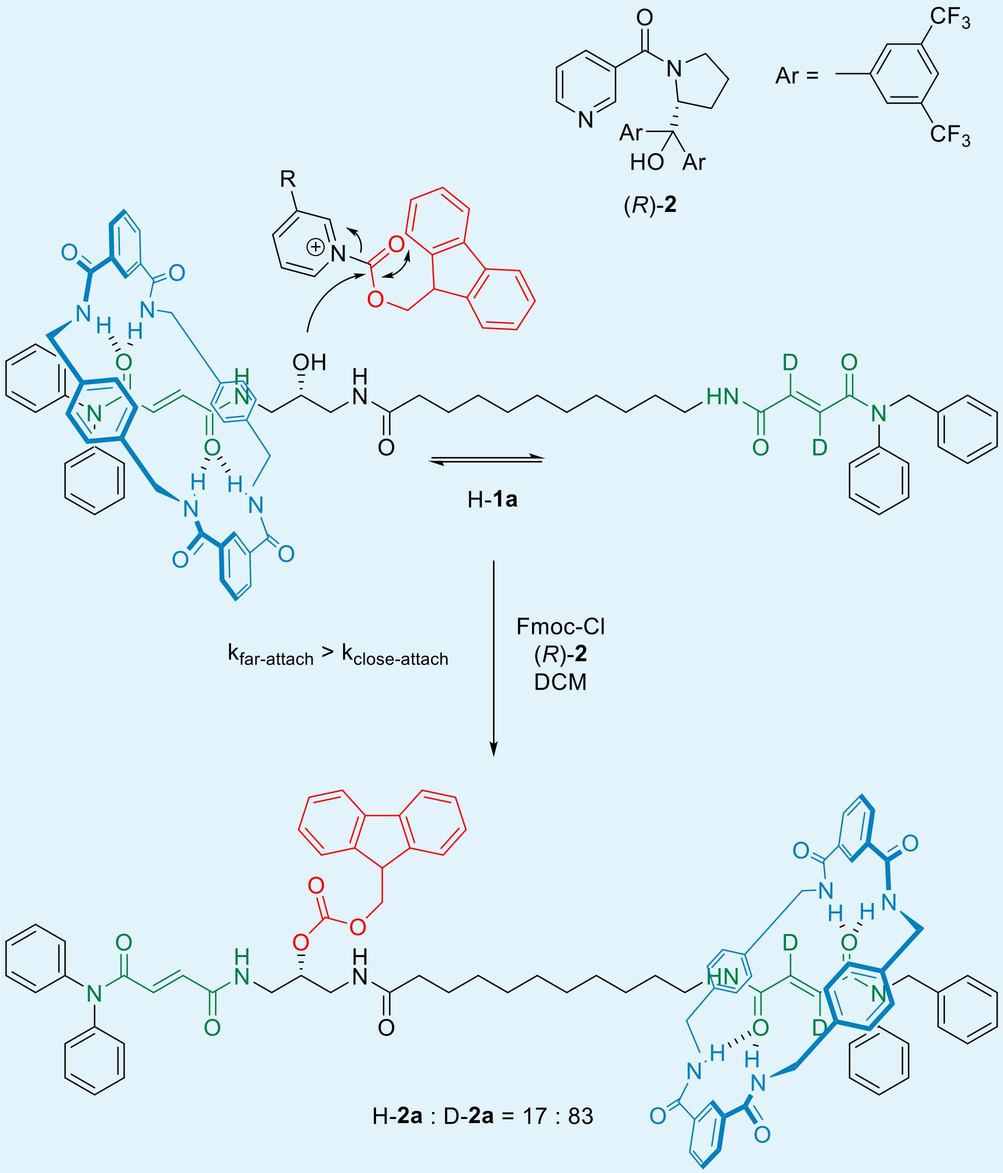
David, A. Leigh, et al. *Nature* **2016**, 534, 235.

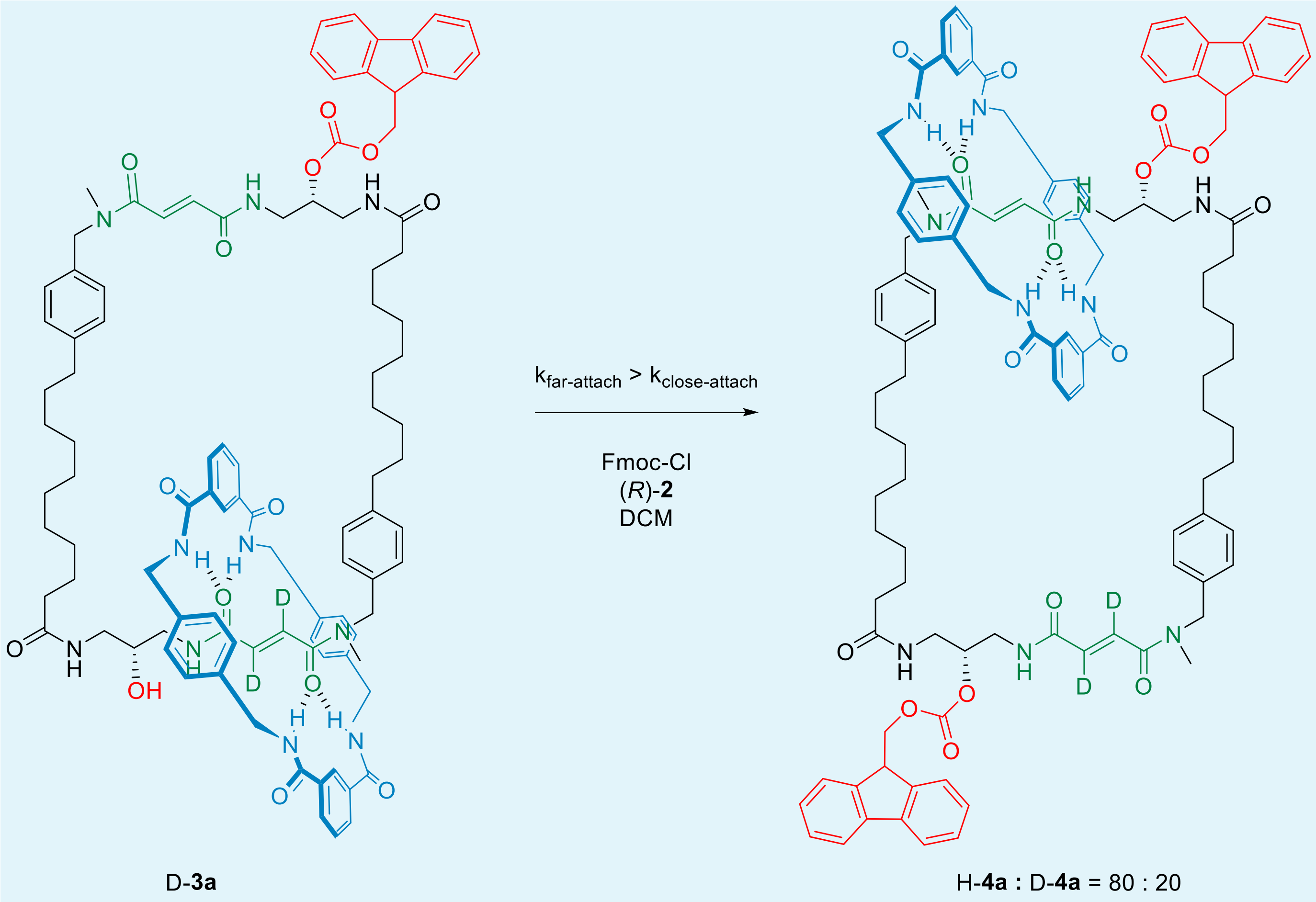
3. 索烃型旋转分子马达



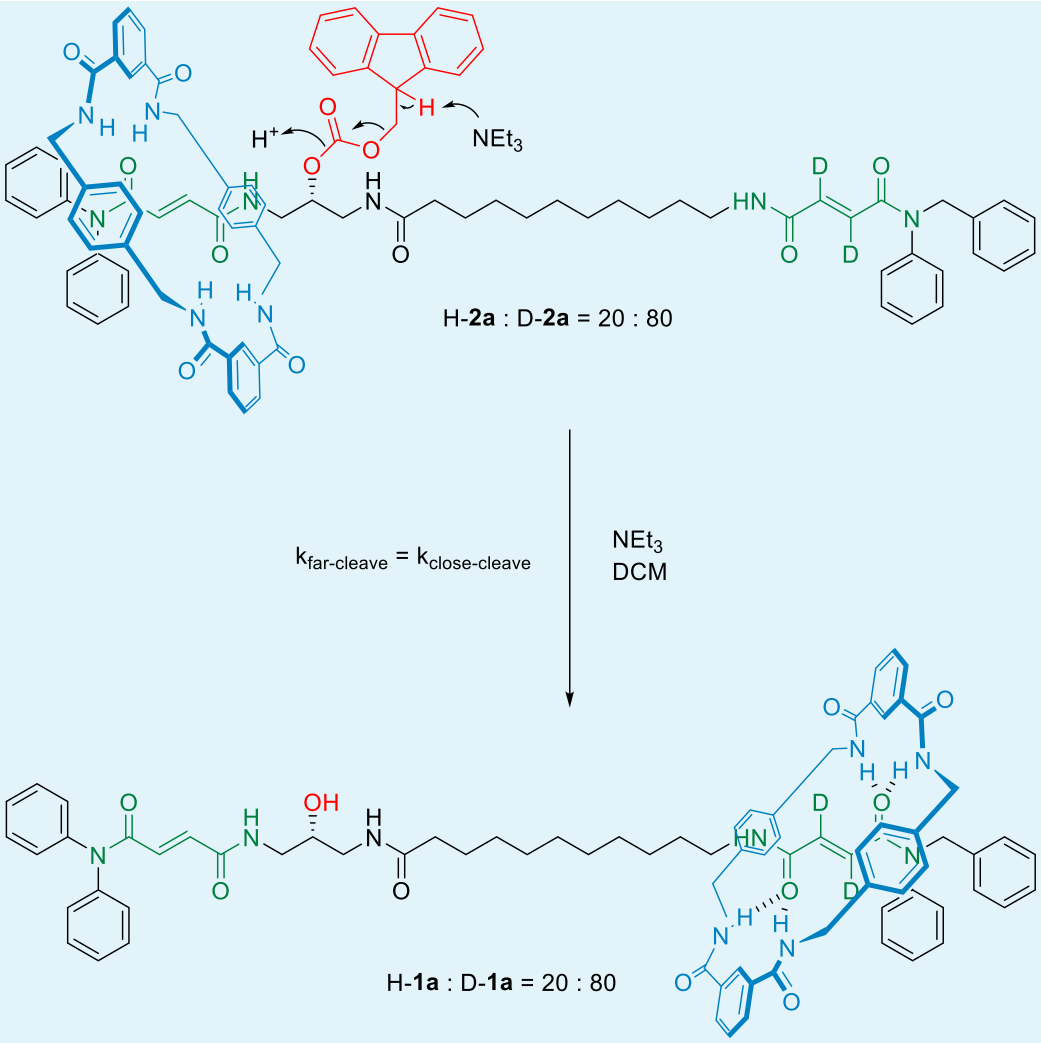
Conditions	Catalyst	Product Distribution
(a)	Pyridine	**H-2a : D-2a** = 39 : 61
(b)	(*R*)-**2**	**H-2a : D-2a** = 17 : 83
(c)	(*S*)-**2**	**H-2a : D-2a** = 19 : 81

3. 索烃型旋转分子马达

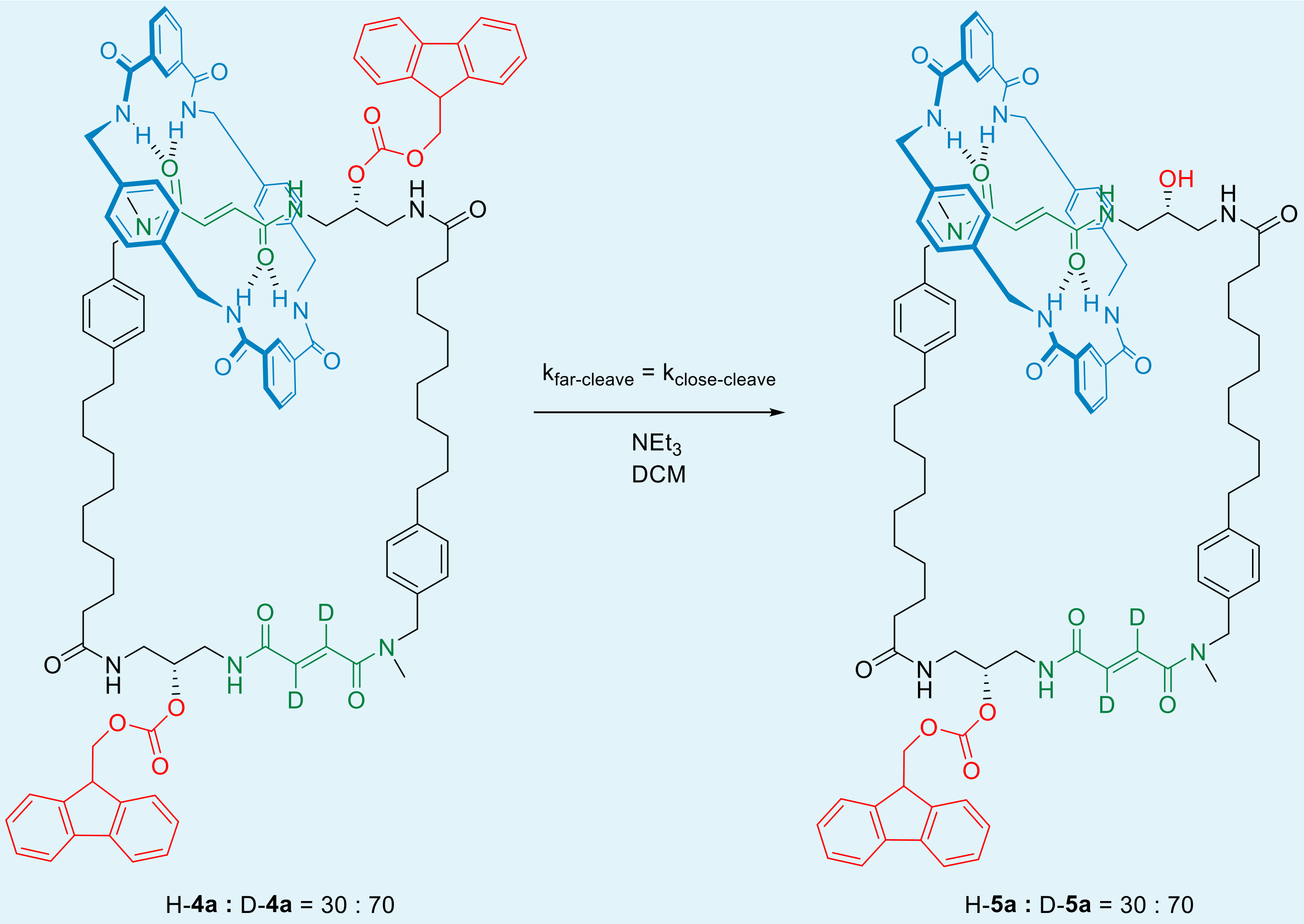

Ar =
CF_3
CF_3
(*R*)-**2**
H-**1a**
$k_{far\text{-}attach} > k_{close\text{-}attach}$
Fmoc-Cl
(*R*)-**2**
DCM
H-**2a** : D-**2a** = 17 : 83


D-**3a**
$k_{far\text{-}attach} > k_{close\text{-}attach}$
Fmoc-Cl
(*R*)-**2**
DCM
H-**4a** : D-**4a** = 80 : 20

3. 索烃型旋转分子马达

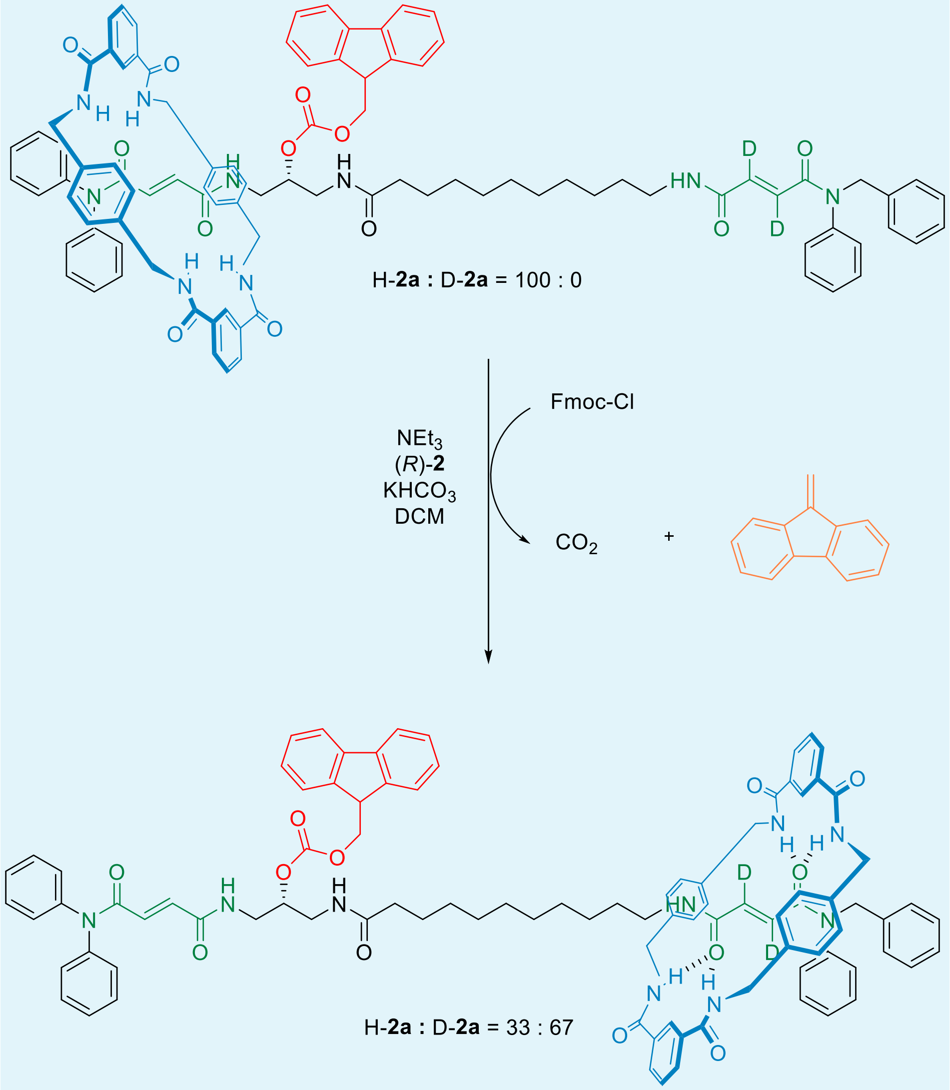


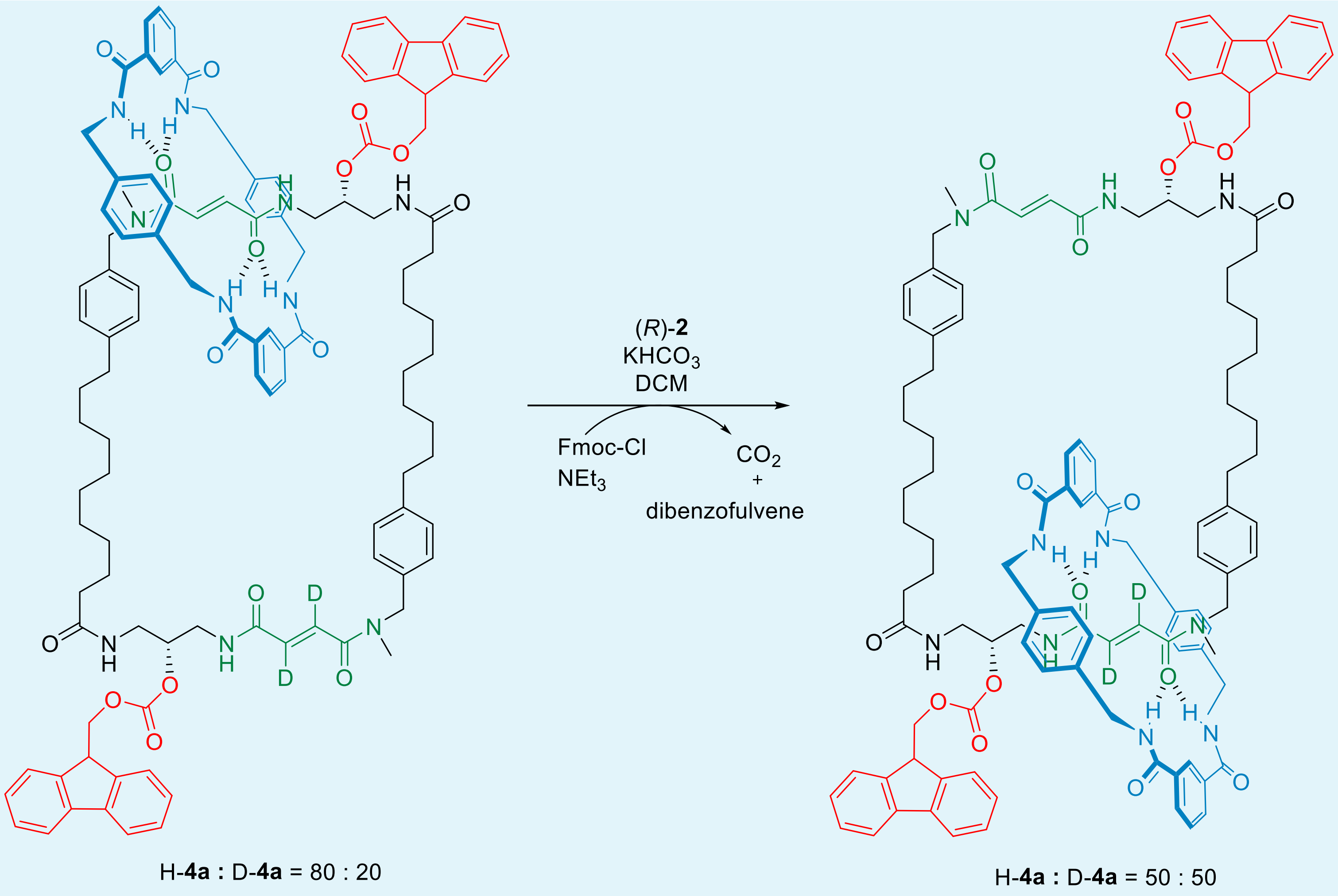
H⁺
NEt3
H-**2a** : D-**2a** = 20 : 80
k far-cleave = k close-cleave
NEt3
DCM
H-**1a** : D-**1a** = 20 : 80



k far-cleave = k close-cleave
NEt3
DCM
H-**4a** : D-**4a** = 30 : 70
H-**5a** : D-**5a** = 30 : 70

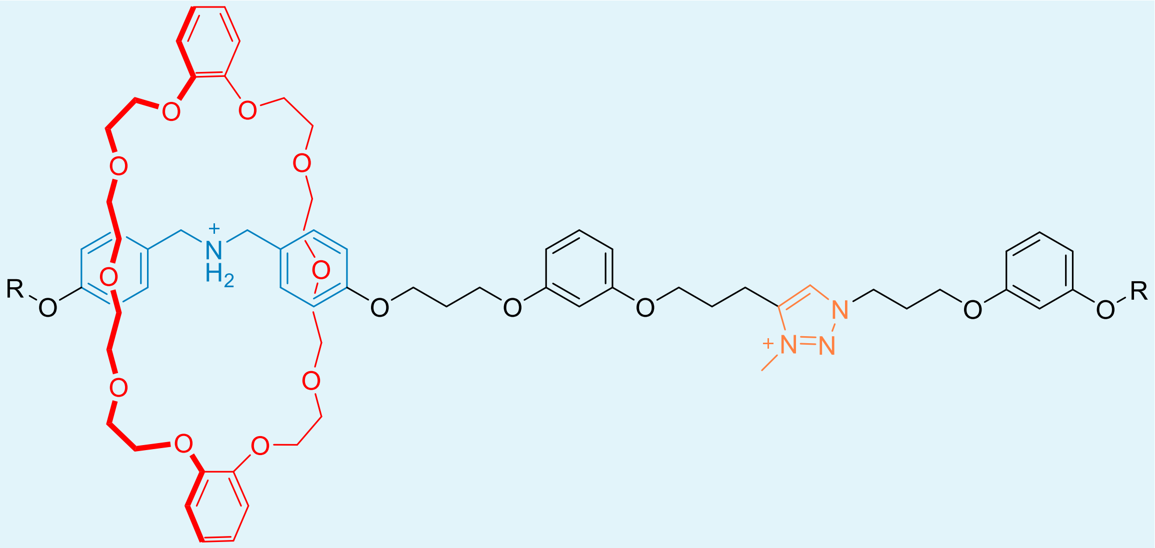
3. 索烃型旋转分子马达

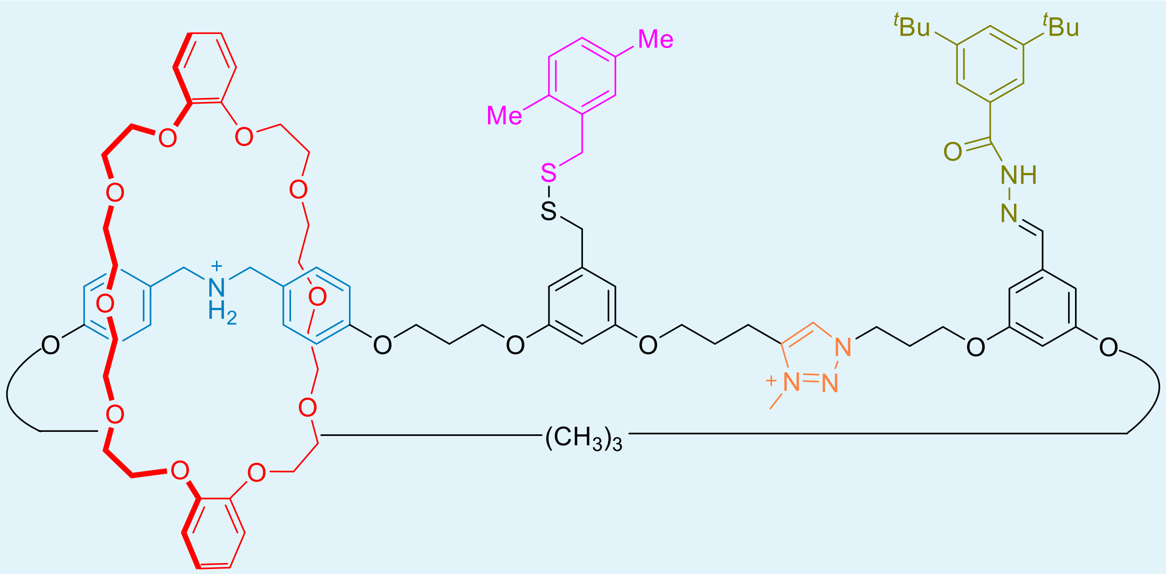

H-**2a** : D-**2a** = 100 : 0
Fmoc-Cl
NEt$_3$
(*R*)-**2**
KHCO$_3$
DCM
CO$_2$
+
H-**2a** : D-**2a** = 33 : 67


(*R*)-**2**
KHCO$_3$
DCM
Fmoc-Cl
NEt$_3$
CO$_2$
+
dibenzofulvene
H-**4a** : D-**4a** = 80 : 20
H-**4a** : D-**4a** = 50 : 50

3. 索烃型旋转分子马达

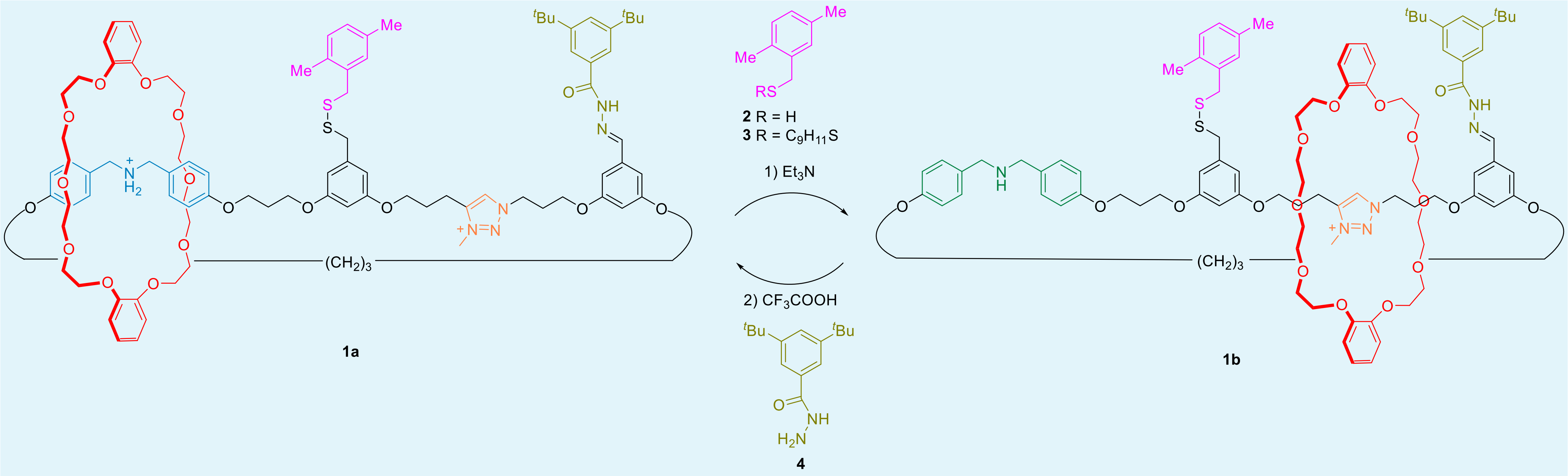
调节酸碱实现旋转





David, A. Leigh, et al. *Science* **2017**, *358*, 340.

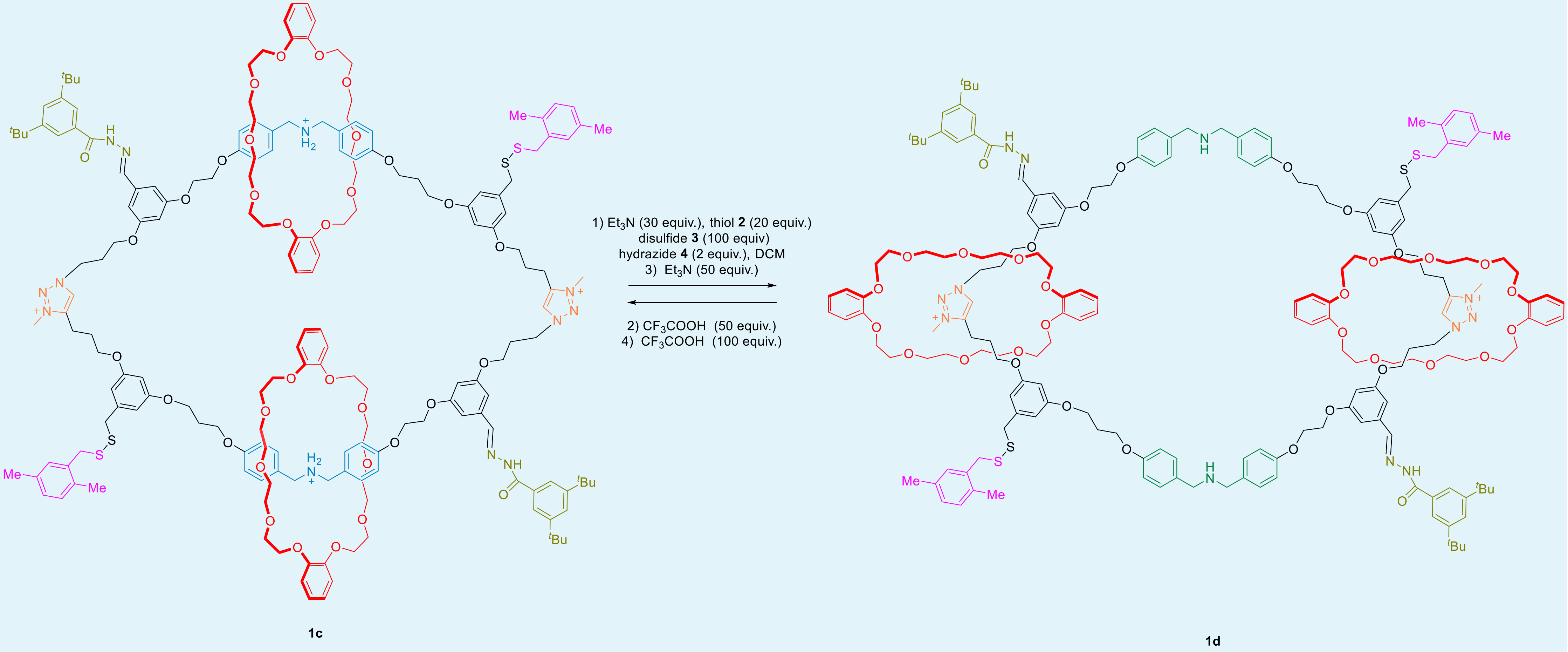
分步操作



一次酸碱循环后，大约有93%的冠醚完成了360°旋转

3. 索烃型旋转分子马达

分步操作

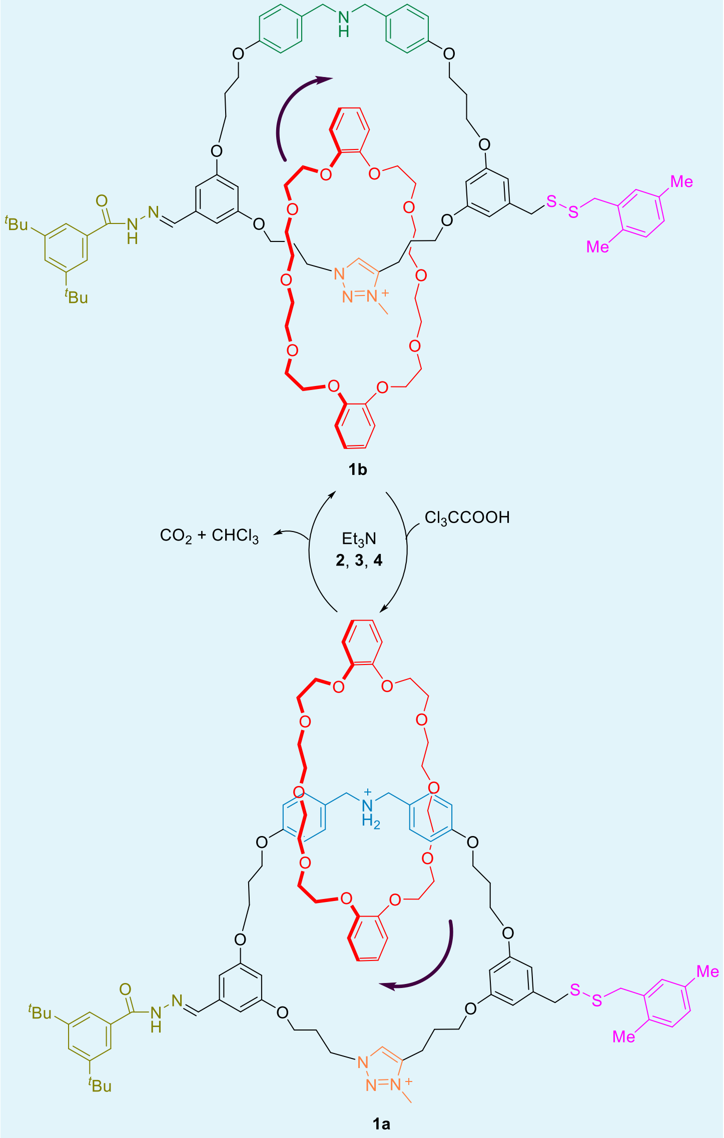


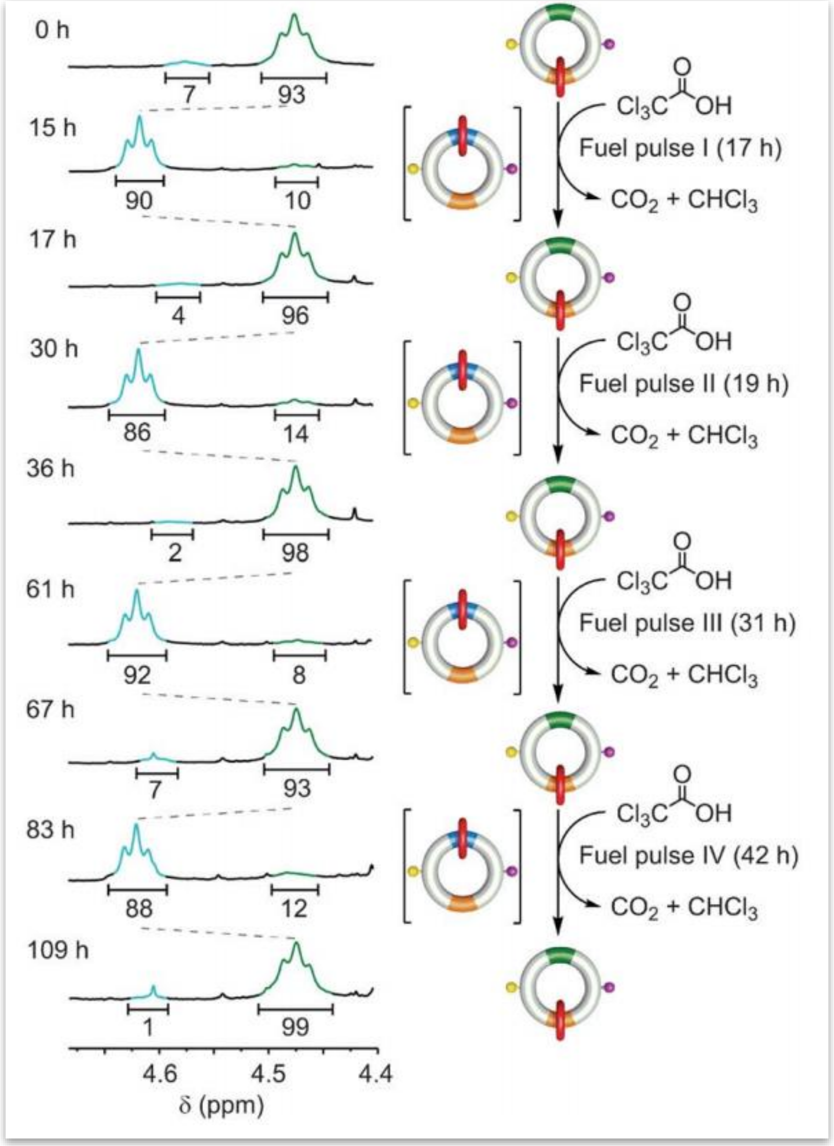
两次酸碱循环后，大约有65%的冠醚完成了360 °旋转

分步操作实现的旋转，需要加入过量的酸和碱，产生副产物盐，造成“化学燃料”的浪费。

3. 索烃型旋转分子马达

自主旋转





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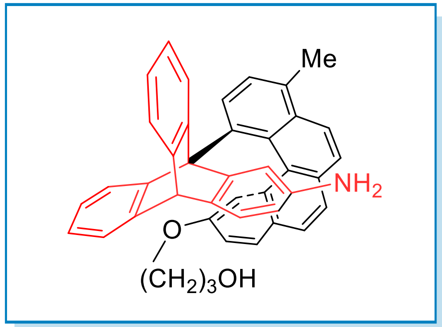
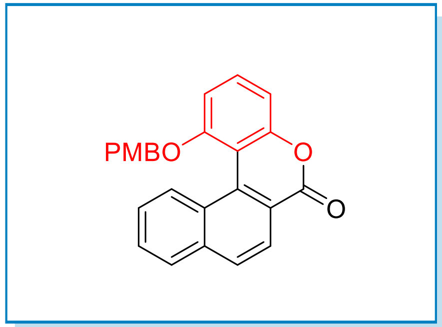
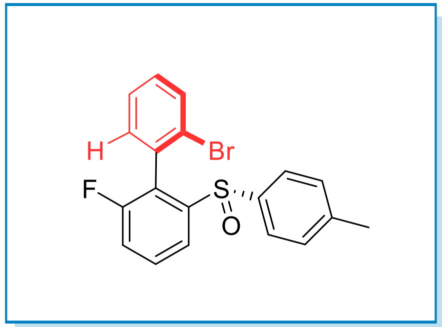
6. 总结与展望

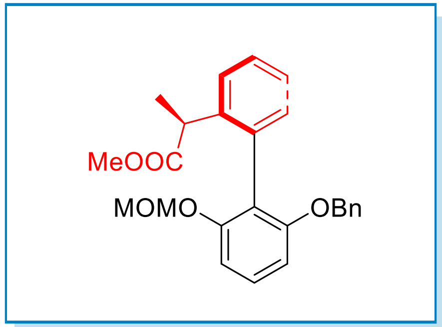
(1) 联芳基型分子马达——成环开环策略

1) 为了解决化学试剂兼容性问题，需要分步操作以实现分子马达的单向旋转

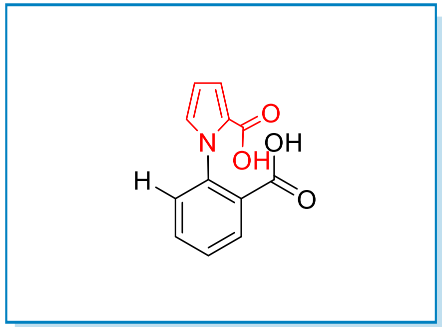








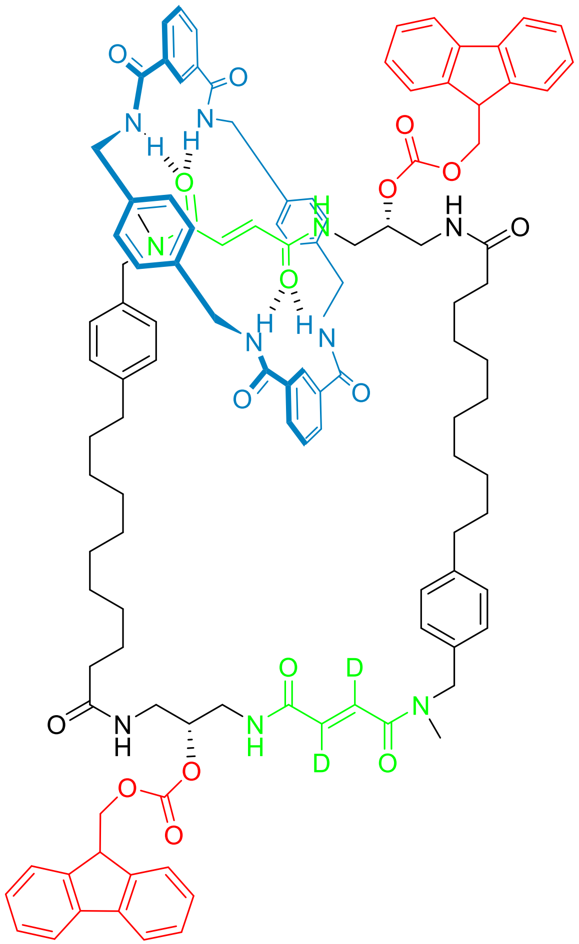
2) 一次性投料即可完成分子马达的旋转，实现了分子马达的自主单向旋转



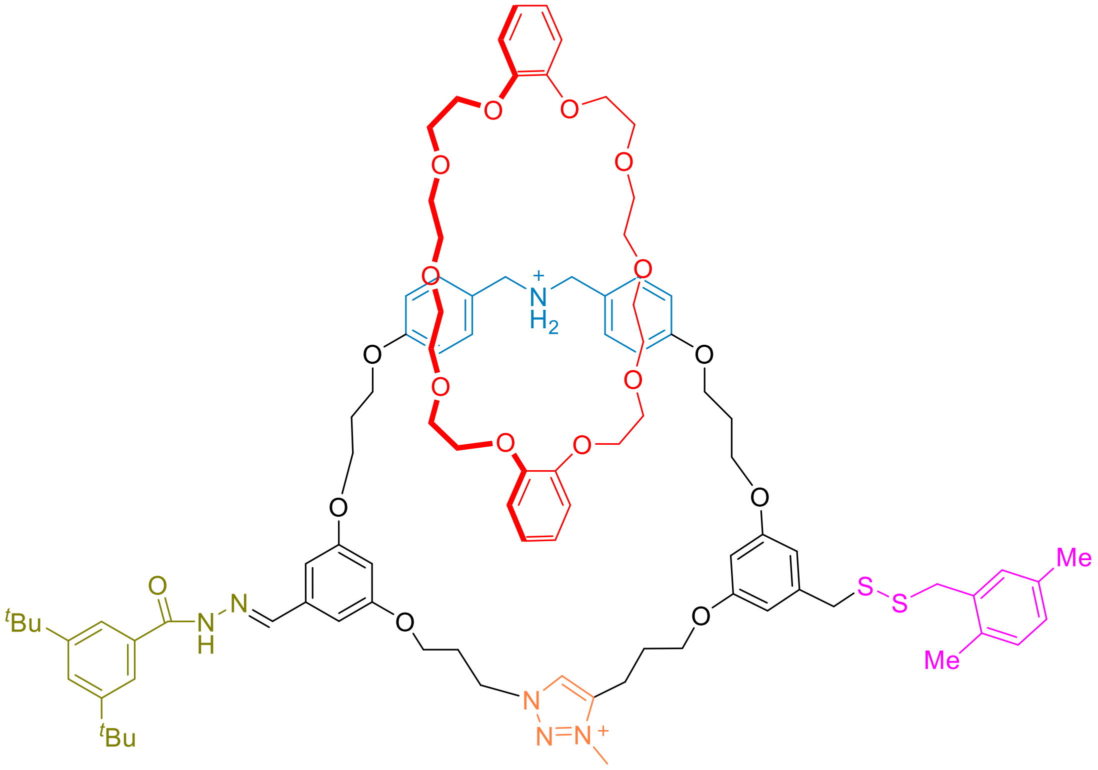
6. 总结与展望

(2) 索烃型旋转分子马达

1) Fmoc的保护与脱保护



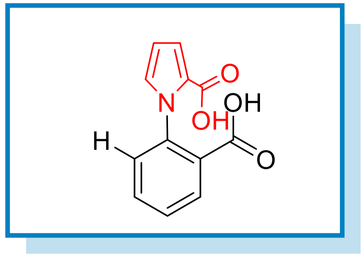
2) 调节酸碱



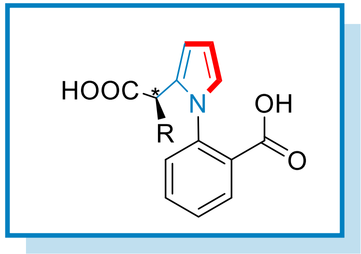
5. 总结与展望

展望

(1) 在分子马达中引入中心手性和轴手性

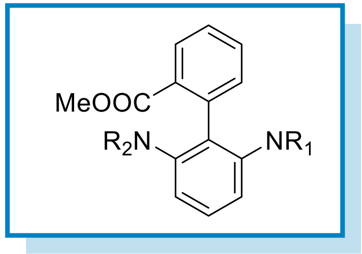


外源手性控制

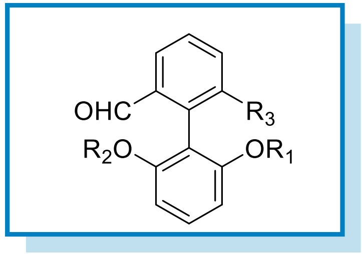


内源手性控制

(2) 设计新的分子马达骨架

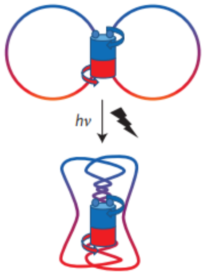


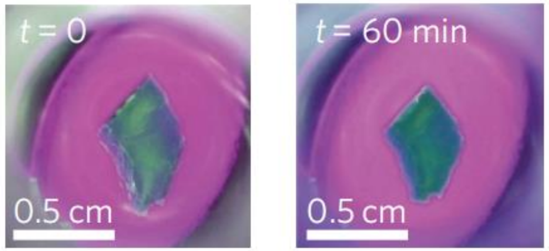
内酰胺



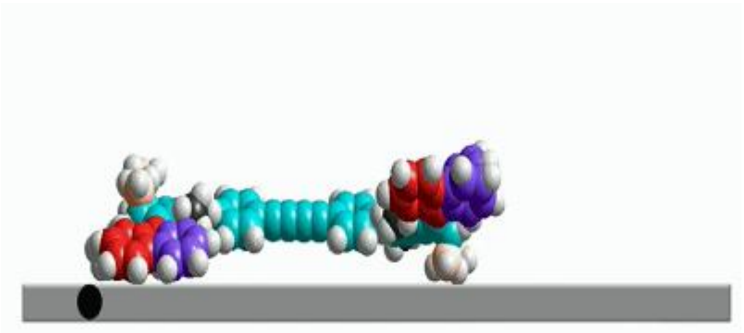
半缩醛

(3) 寻找化学能驱动的旋转分子马达的潜在应用





Nature Nanotech. **2015**, 10, 161.



Nature, **2011**, *479*, 208.

敬请各位老师和同学批评指导！

谢谢！