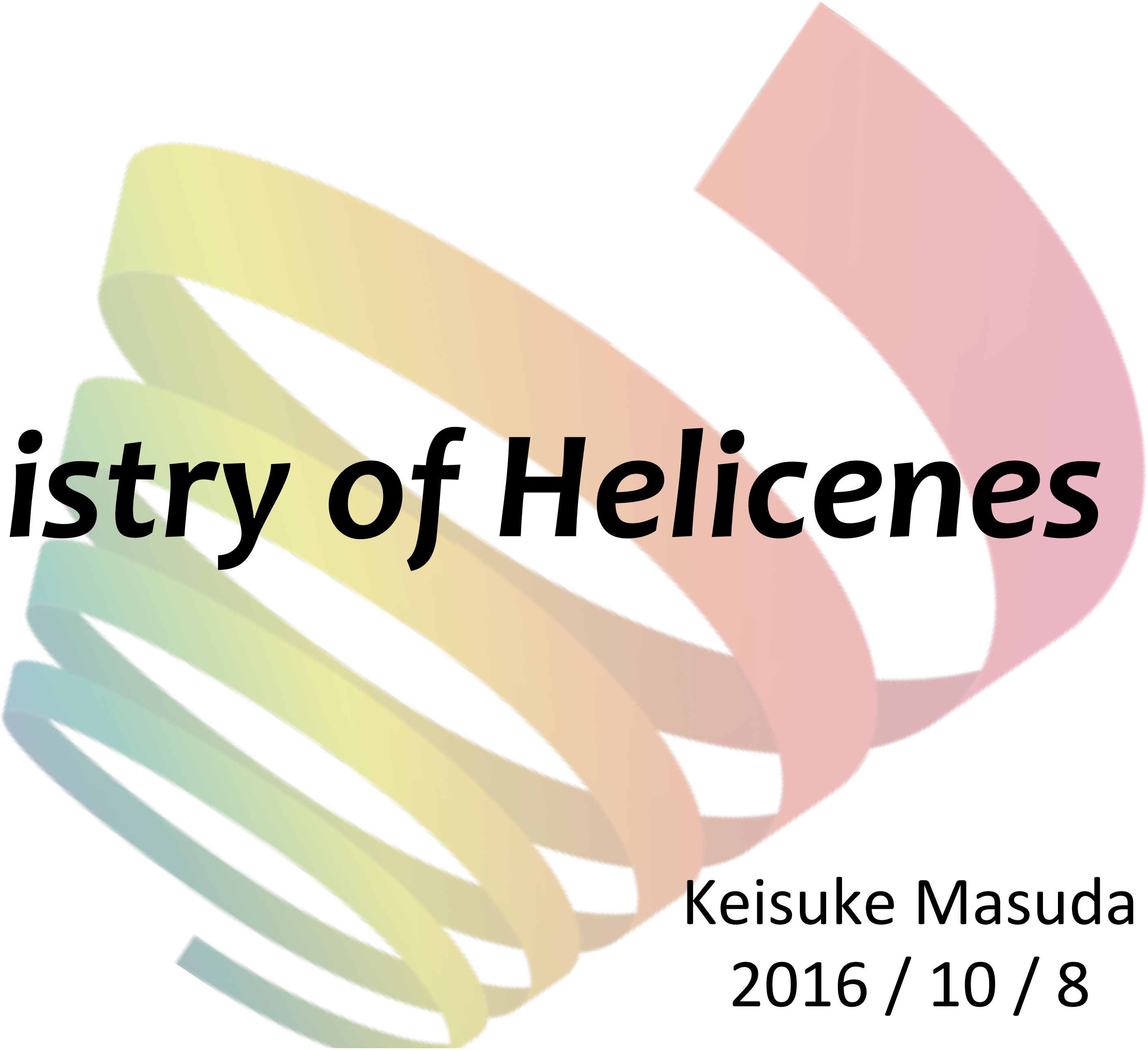
Chemistry of Helicenes



Keisuke Masuda
2016 / 10 / 8

Background: Helicenes

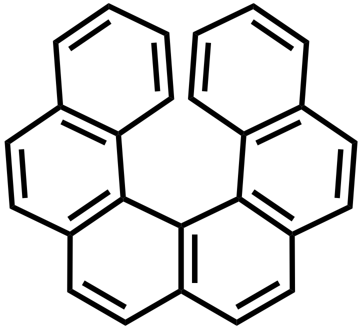
Class of polyaromatic molecule
- **Charactorized by several (4 or more) ortho-fused aromatic rings**
- **Very large specific rotation**
  ± 1670 ° (for [5]helicene), ± 9620 ° (for [13]helicene)

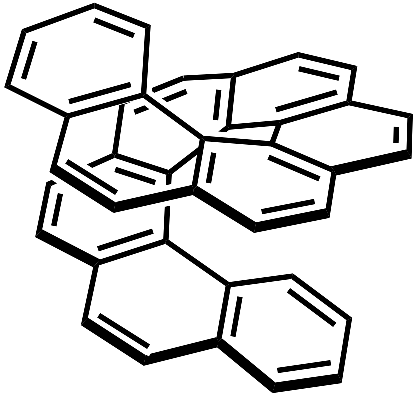
Nomencleture

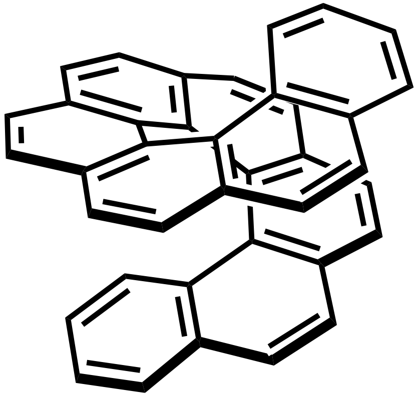
Continuously chiral
- **Use [n] helicene for unsubtstituted systems**
  n = number of ortho-fused rings

Directionary
- **Right-handed helicenes are denated *P* (Plus)**
- **Left-handed helicenes are denated *M* (Minus)**

Axial chirality
- **No stereogenic centers**
- **Difined by a 3-dimensional space curve**


[6]helicene

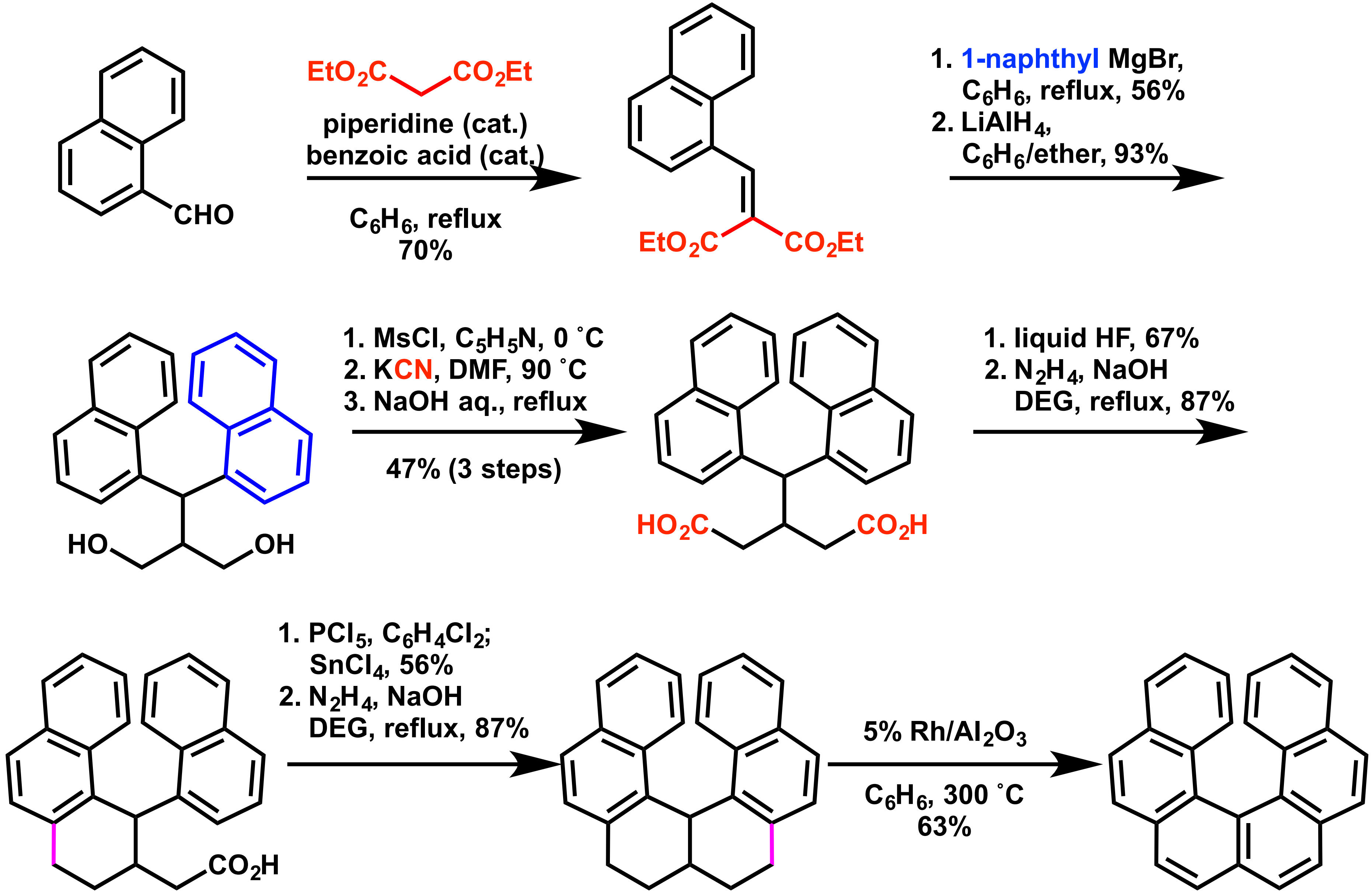

(*P*)-[6]helicene
(*P*)-hexahelicene


(*M*)-[6]helicene
(*M*)-hexahelicene

Narcis, M.; Takenaka, N. *Eur. J. Org. Chem.* **2014**, 21.

Contents

First Synthesis of Hexahelicene

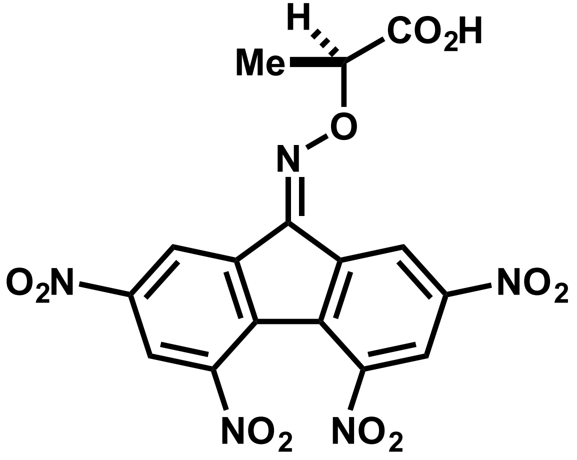


Newman, M. S.; Lednicer, D. *J. Am. Chem. Soc.* **1956**, *78*, 4756.

Resolution of Hexahelicene

Resolution of TAPA

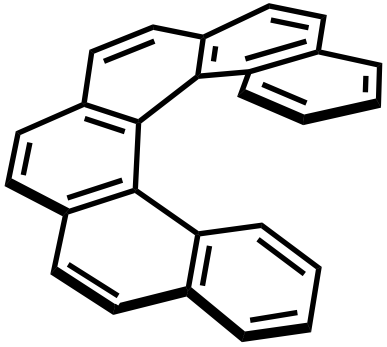
- **2-(2,4,5,7-tetranitoro-9-fluorenylideneaminooxy)-propionic acid**
- **Novel technique for optical resolution of racemic compound**
- **Formation of diastereomeric charge-transfer complex**



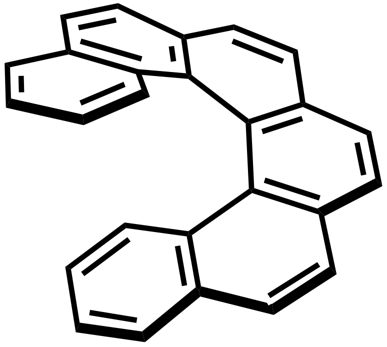
(*S*)-(-)-TAPA

Specific Rotation

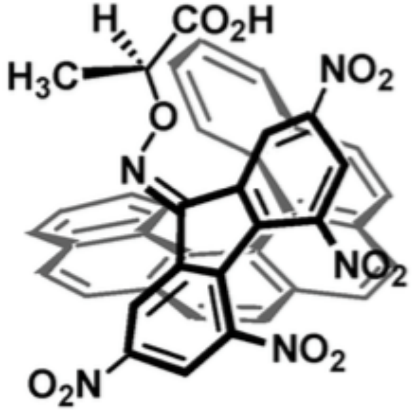
- **(*M*)-[6]helicene: $[\alpha]^{D}_{24}$= -3640°**
- **(*P*)-[6]helicene: $[\alpha]^{D}_{25}$= +3707°**



(*M*)-[6]helicene



(*P*)-[6]helicene

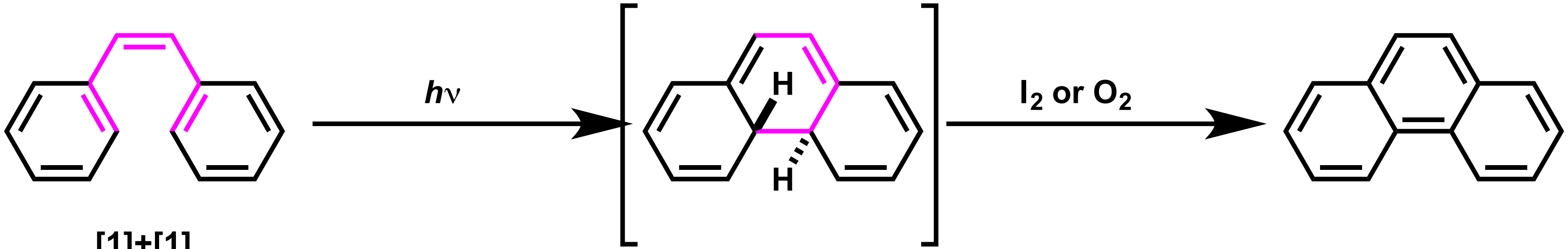


CT complex

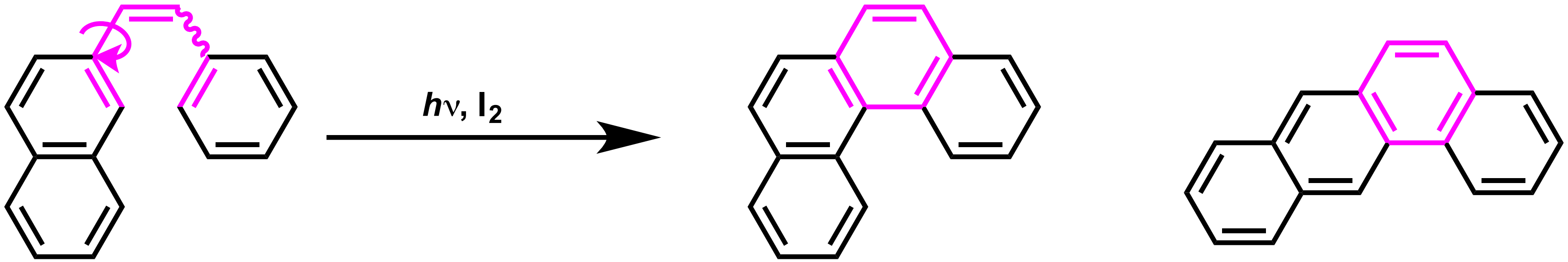
Newman, M. S.; Lednicer, D. *J. Am. Chem. Soc.* **1956**, *78*, 4756.
Newman, M. S.; Lutz, W. B. *J. Am. Chem. Soc.* **1956**, *78*, 2469.

Oxidative Photocyclization

- Oxidative photocyclization of stilbene-like molecules
- The intermediate trans-dihydrophenanthrene is trapped with I_2 or O_2



[1]+[1]



[2]+[1]

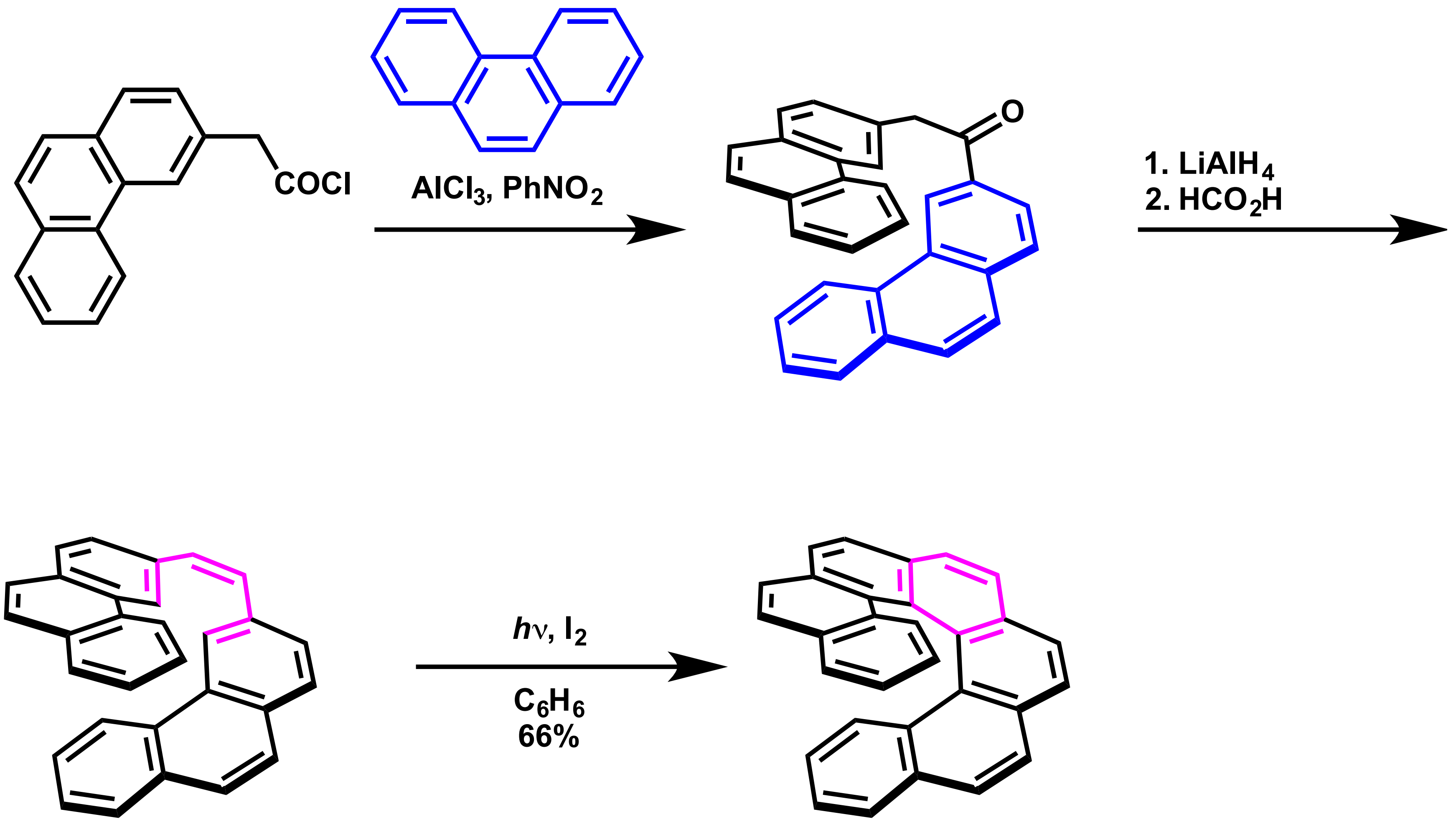
[4]helicene
74%

benzanthracene
<1%

Only the cis-isomer is reactive, but the trans-isomer can still be used since cis-trans isomerization of stilbene derivatives occurs readily under the conditions.

Mallory, F. B.; Mallory, C. W. *Organic Reactions.* xx.

Synthesis of [7] Helicene

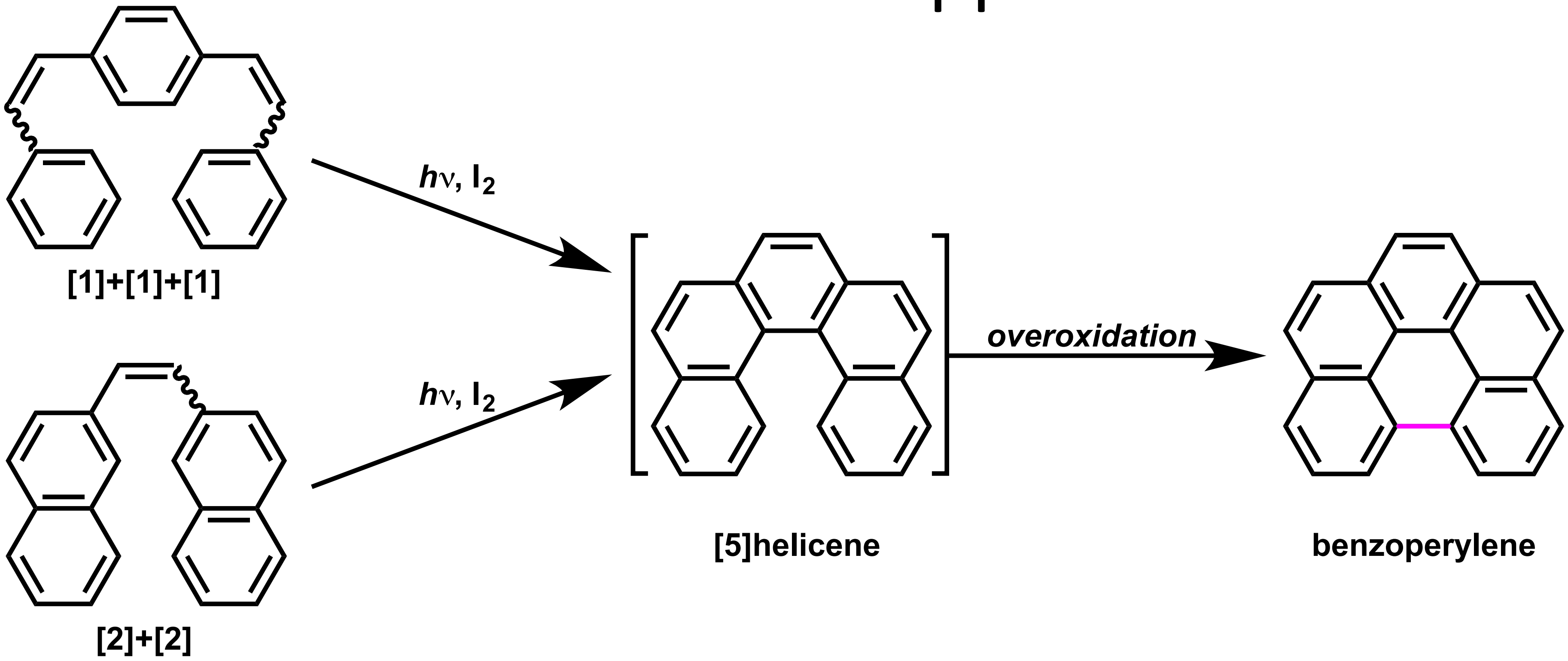


[3]+[3]

[7]helicene

Flammang-barbieux, M.; Nasielski, J.; Martin, R. H. *Teterahedron, Lett.* **1967**, *8*, 743.

Photochemical Approach

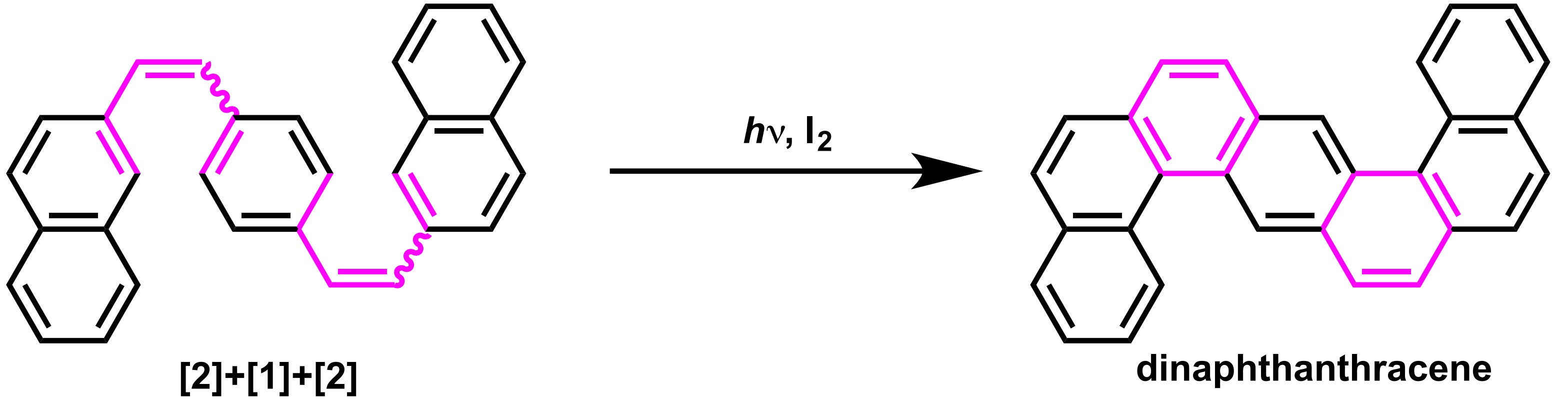


[1]+[1]+[1]

[2]+[2]

[5]helicene

benzoperylene

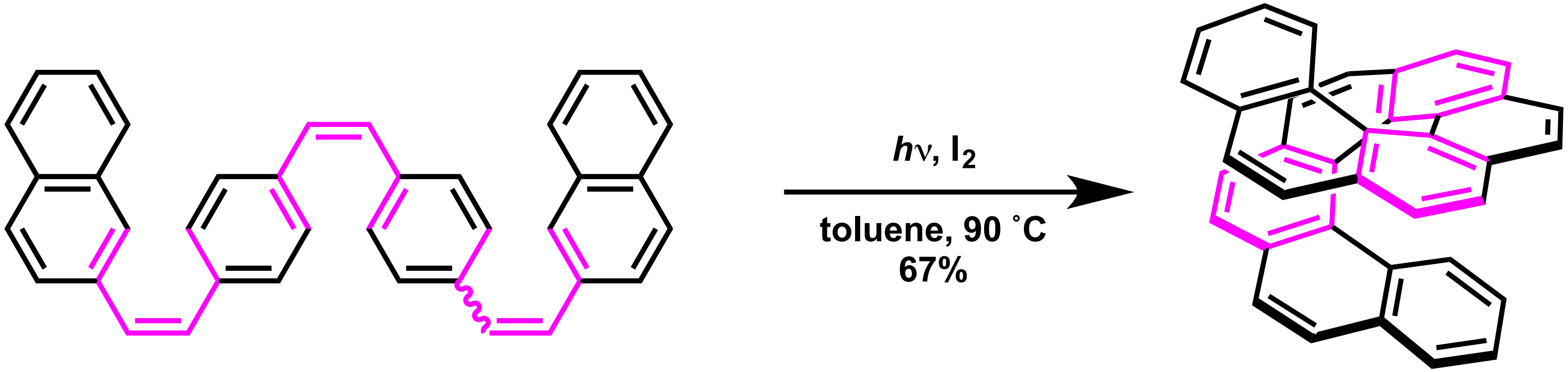


[2]+[1]+[2]

dinaphthanthracene

Newman, M. S.; Lednicer, D. *J. Am. Chem. Soc.* **1956**, *78*, 4756.
Newman, M. S.; Lutz, W. B. *J. Am. Chem. Soc.* **1956**, *78*, 2469.

Synthesis of [9] Helicene



hν, I_2

toluene, 90 ˚C
67%

[2]+[1]+[1]+[2]

[9]helicene

interplanar angle

A–G: 21.7°
B–H: 8.7°
C–I: 18.3°

pitch of inner helix (Å)

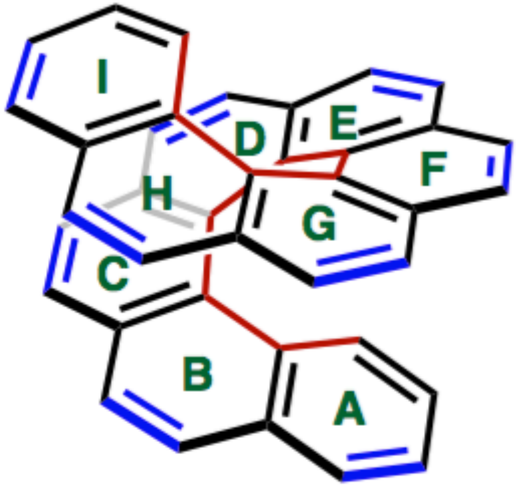
A–G: 3.22
B–H: 3.26
C–I: 3.20

Average: 3.22

pitch of outer helix (Å)

A–G: 4.11
B–H: 3.64
C–I: 3.95

Average: 3.90



C–C bonds at inner helix (Å)

A: 1.42
B: 1.46
C: 1.46
D: 1.43
E: 1.45
F: 1.44
G: 1.45
H: 1.46
I: 1.41

Average: 1.44

C–C bonds at outer helix (Å)

A: 1.39
B: 1.33
C: 1.41
D: 1.36
E: 1.37
F: 1.34
G: 1.35
H: 1.35
I: 1.38

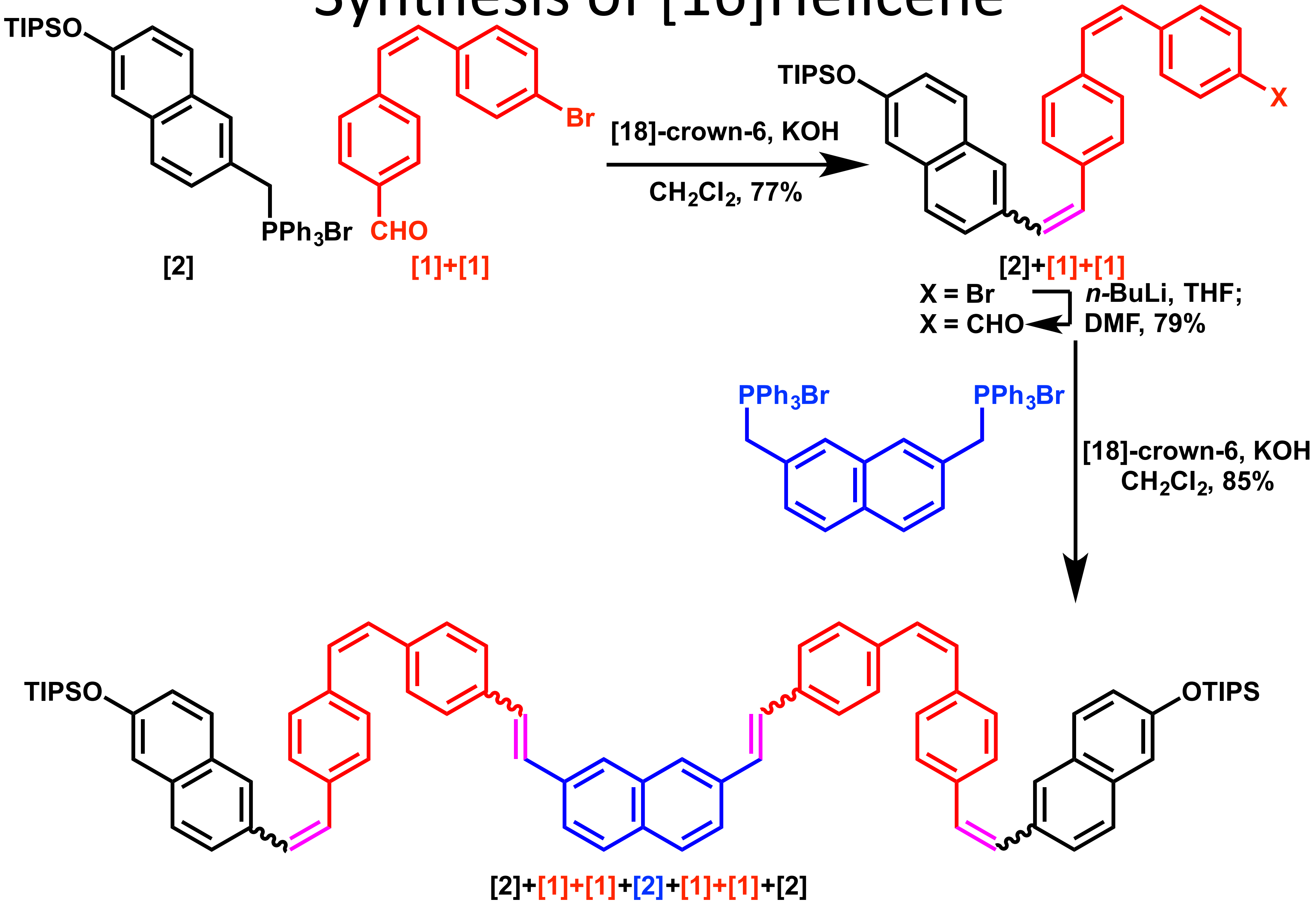
Average: 1.36

cf.

1.40 Å

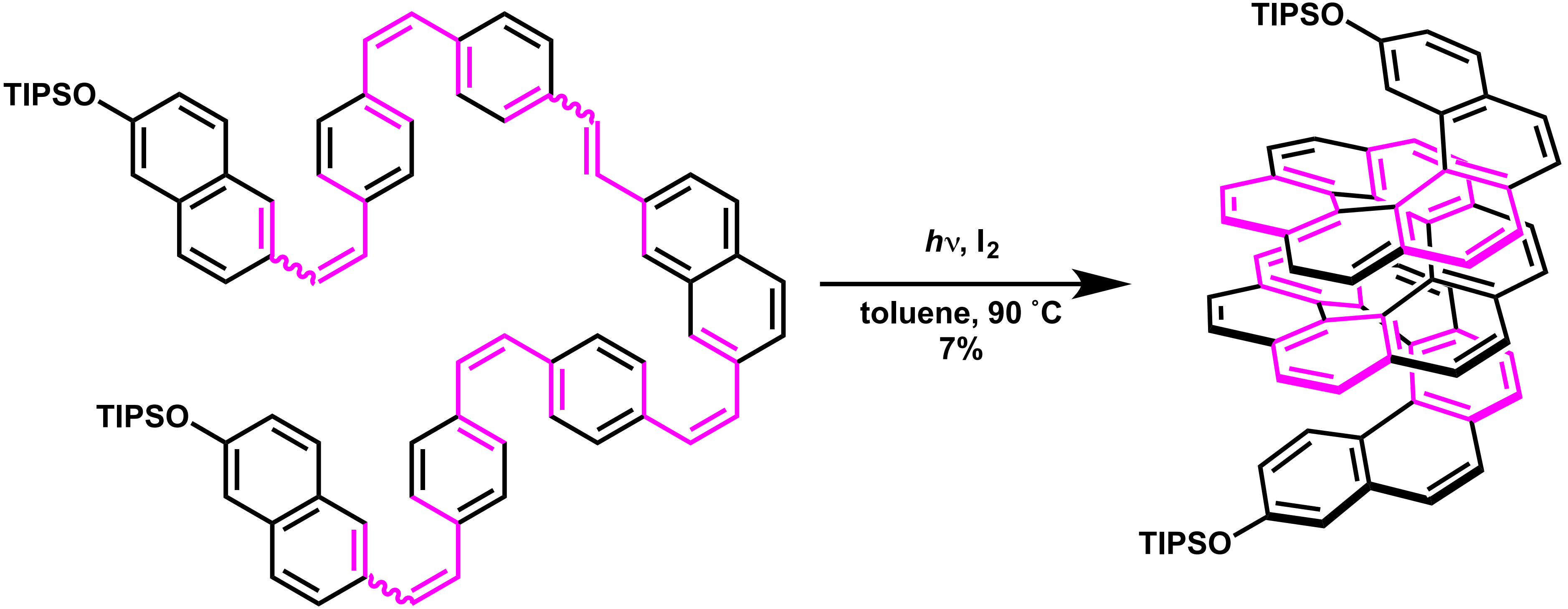
Mori, K.; Murase, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 6847.

Synthesis of [16]Helicene



Mori, K.; Murase, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 6847.

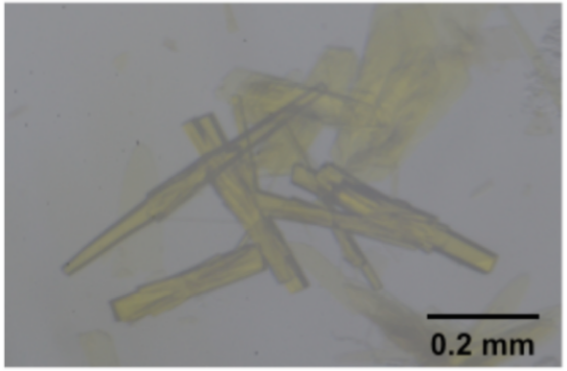
Synthesis of [16]Helicene

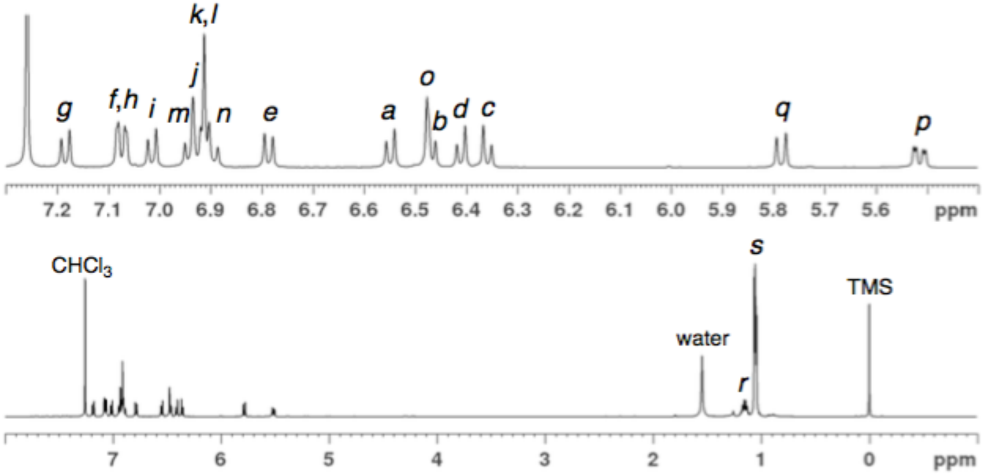


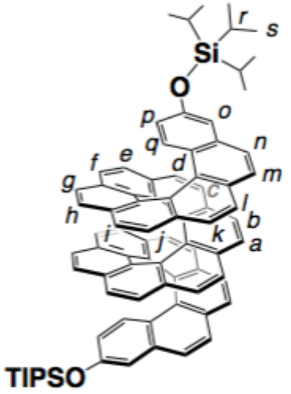
$h\nu$, I_2

toluene, 90 °C

7%

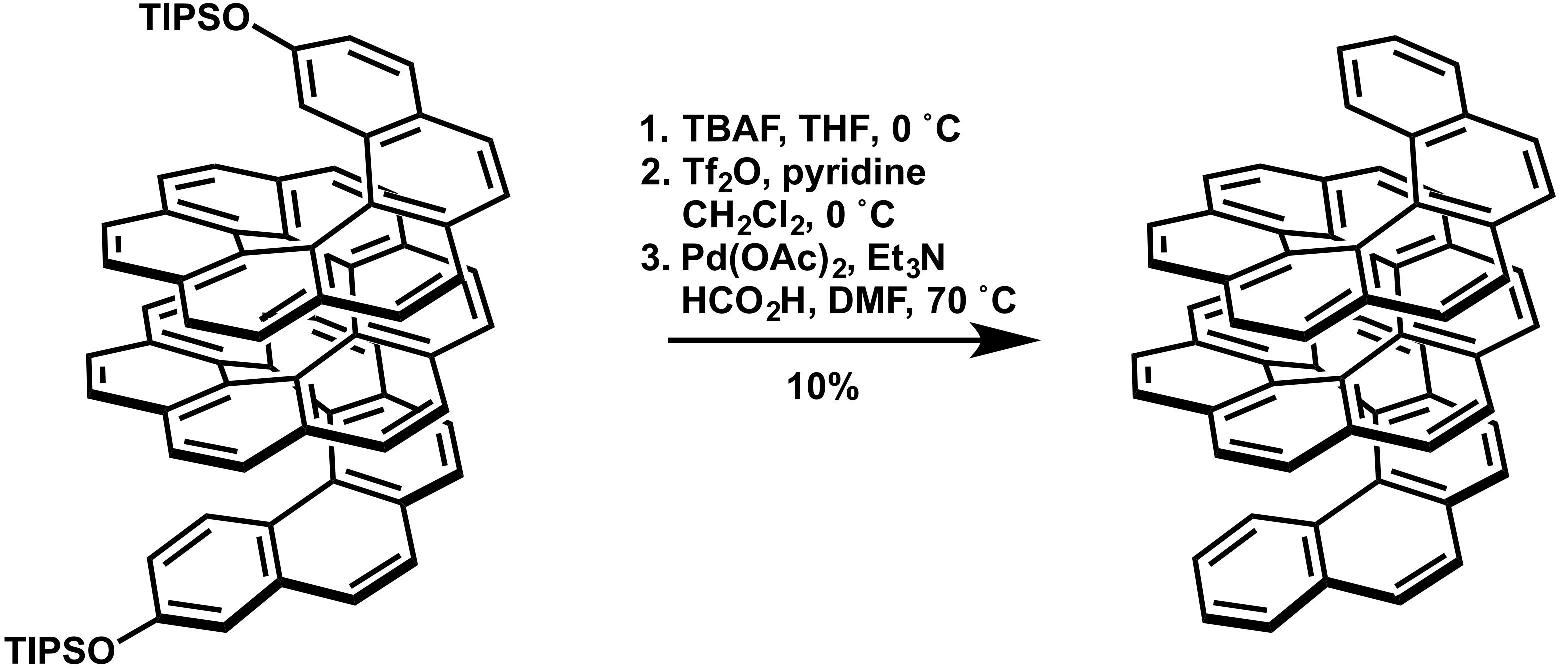






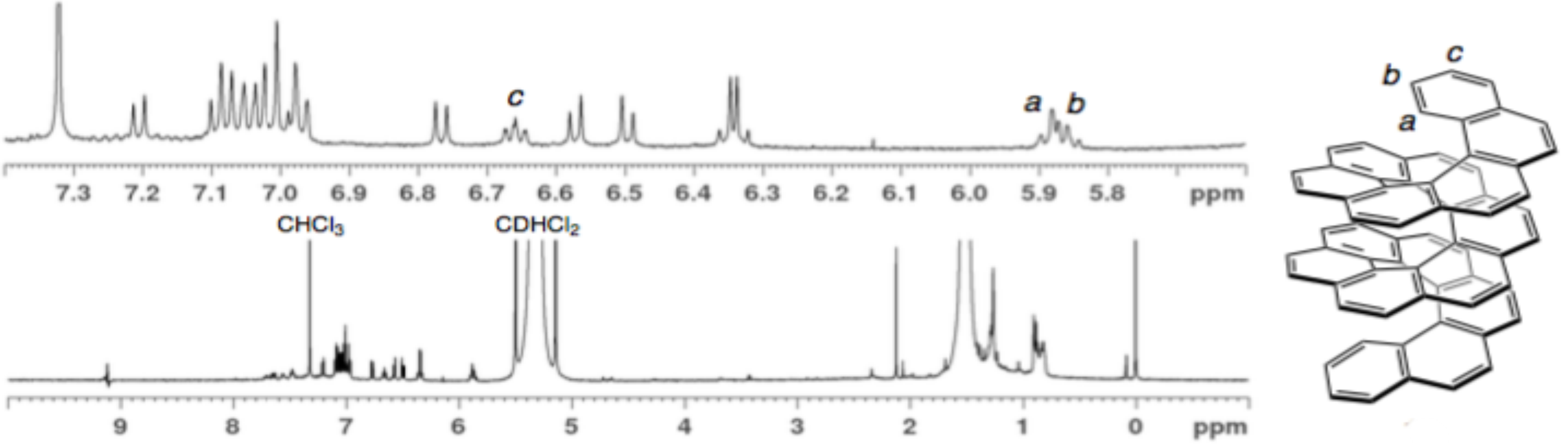
Mori, K.; Murase, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 6847.

Synthesis of [16]Helicene



1. TBAF, THF, 0 ˚C
2. Tf_2O, pyridine
   CH_2Cl_2, 0 ˚C
3. $Pd(OAc)_2$, Et_3N
   HCO_2H, DMF, 70 ˚C

10%



Mori, K.; Murase, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 6847.

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0. Property of Helicenes

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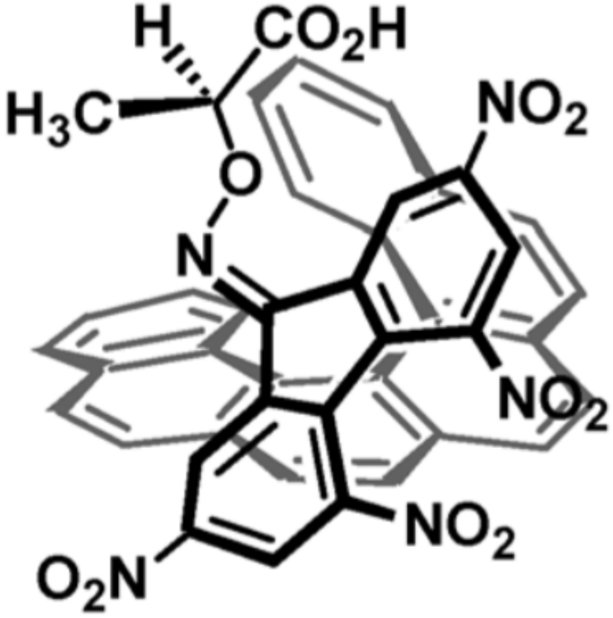
Asymmetric Catalysis

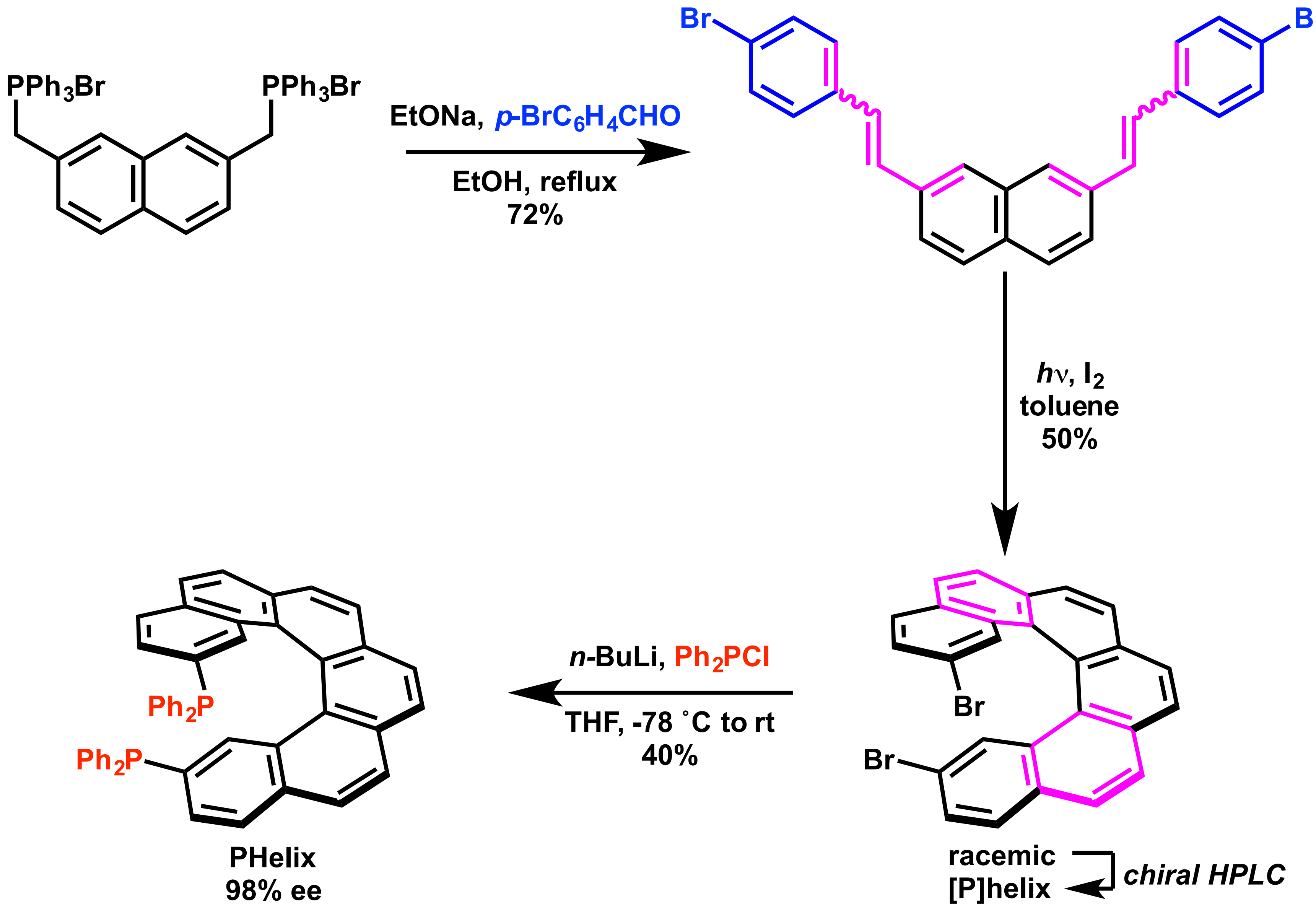
Why use helicens in asymmetric catalysis?

- **Rigidity / thermal stability**
- **Difine a large chiral pocket**
- **Highly amenable to charge-transfer complesation**



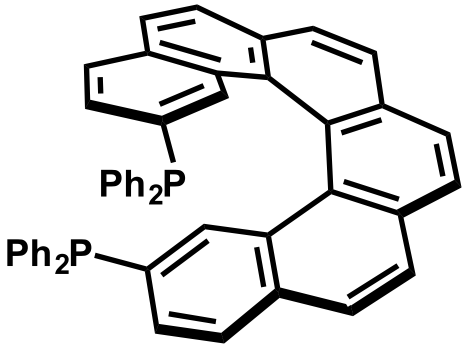
M. Gingras. *Chem. Soc. Rev*. **2013**, *42*, 1051

Synthesis of Helix Ligand

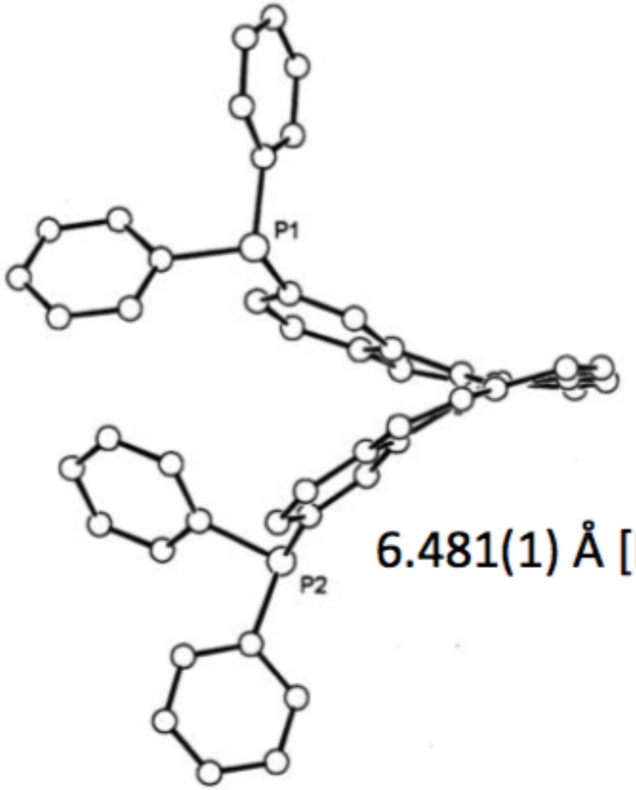


Reetz, M.; Beuttenmüller, E.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 3211.

Helitical Phosphines



PHelix



6.481(1) Å [P1–P2]

Although PHelix is formally a diphosphine, it is more likely behaving as a monodentate ligand

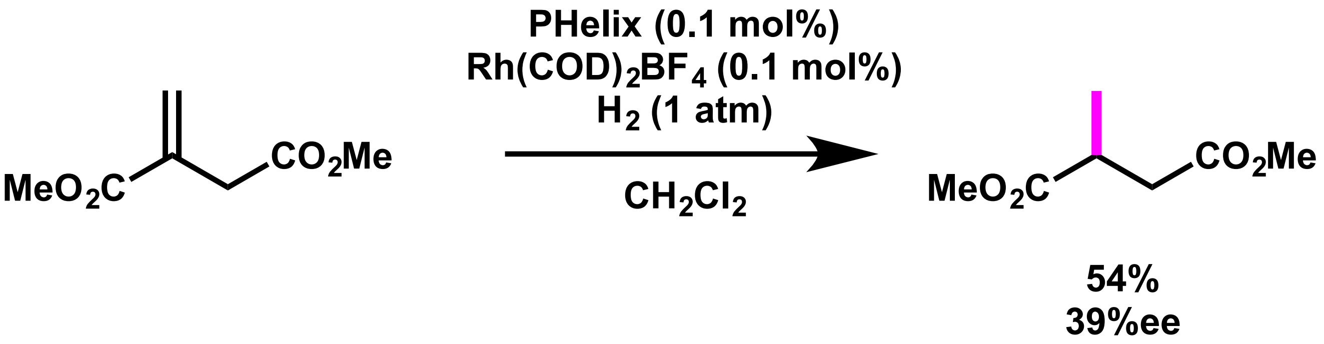
- **Multiple signals in 31P NMR**
- **η3-C3H5PdCl-PHelix complex**
- **Main peak at 33.6 ppm**
- **Smaller signals at 24.1, 27.2, 27.9, and 28.0 ppm**

Crystal structure

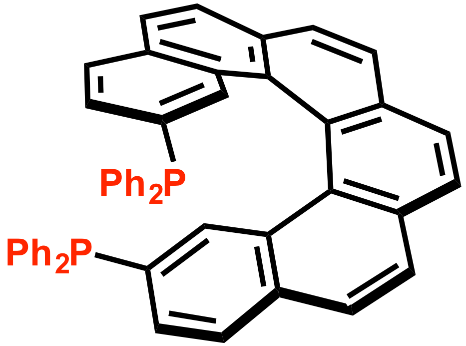
- **P1–P2 distance in PHelix is too large to chelate metalCrystal structure**

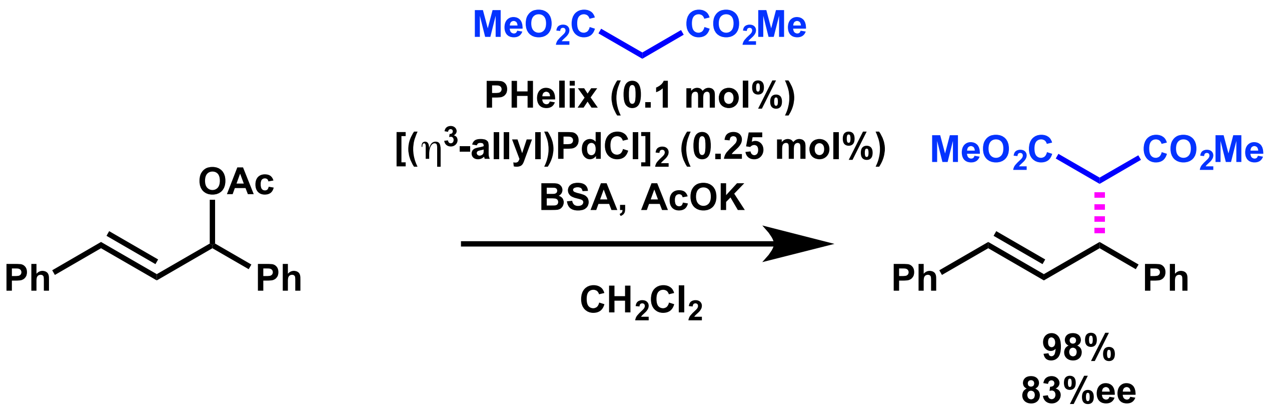
Reetz, M.; Sostmann, S. *J. Org. Chem.* **2000**, *603*, 105.

Helitical Phosphines

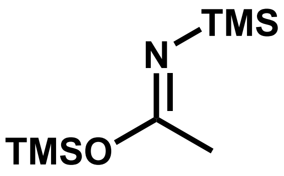

PHelix (0.1 mol%)
$Rh(COD)_2BF_4$ (0.1 mol%)
H_2 (1 atm)
CH_2Cl_2

54%
39%ee


PHelix


$MeO_2C\text{–}CH_2\text{–}CO_2Me$
PHelix (0.1 mol%)
$[(\eta^3\text{-allyl})PdCl]_2$ (0.25 mol%)
BSA, AcOK
CH_2Cl_2

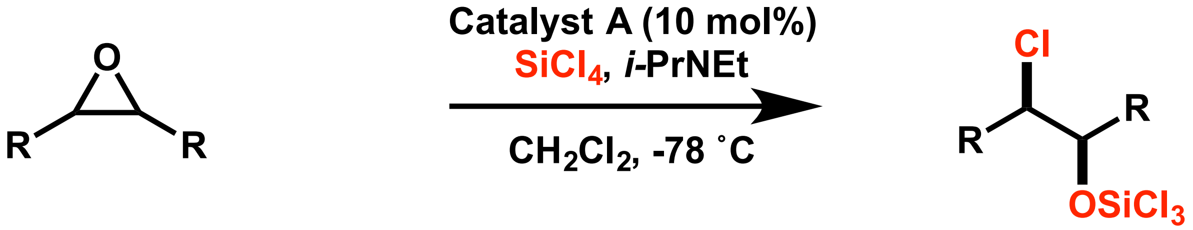
98%
83%ee


BSA

Reetz, M.; Beuttenmüller, E.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 3211.
Reetz, M.; Sostmann, S. *J. Org. Chem.* **2000**, *603*, 105.

Helicenes in Organocatalysis

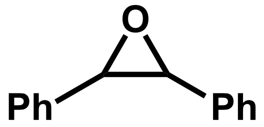
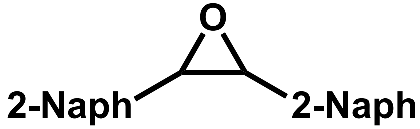
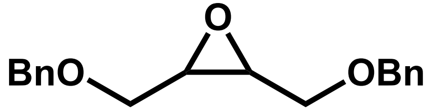
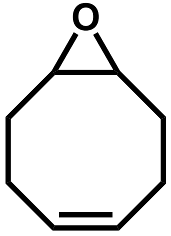
Desymmetrization of *meso* epoxides with chlorosilane

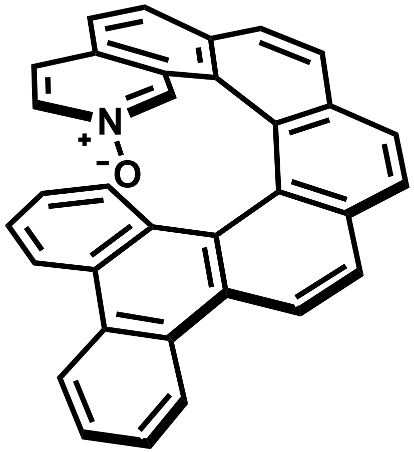


Catalyst A (10 mol%)

$SiCl_4$, *i*-PrNEt

CH_2Cl_2, -78 ˚C

entry		result
1		77%, 94%ee
2		76%, 92%ee
3		72%, 65%ee
4		74%, 33%ee

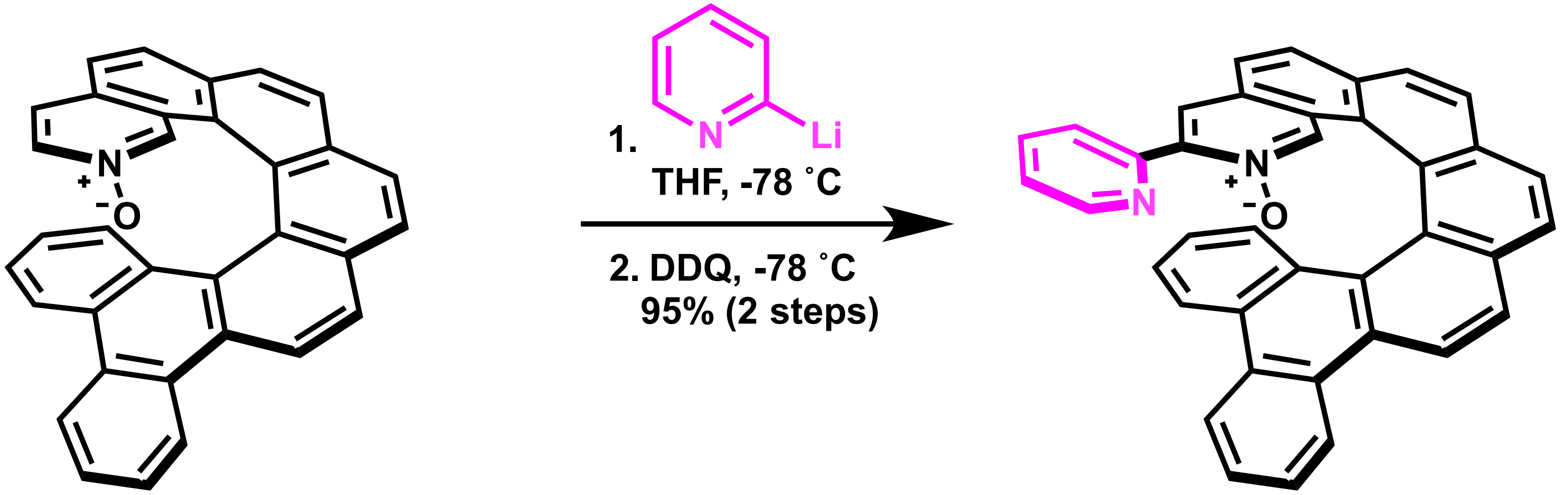


Catalyst A

Takenaka, N.; Sarangthem, R.; Captain, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 9708.

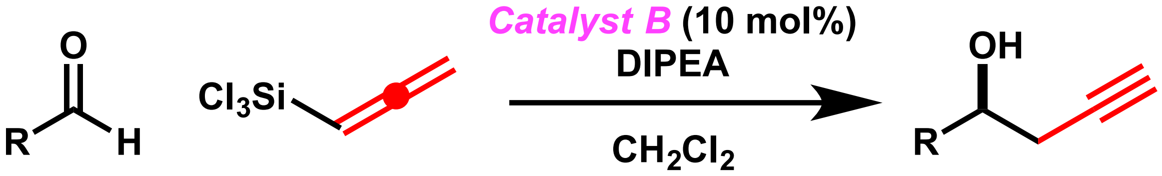
Lewis Base Catalyst

Synthesis of bidentate Lewis base catalyst



Catalyst A *Catalyst B*

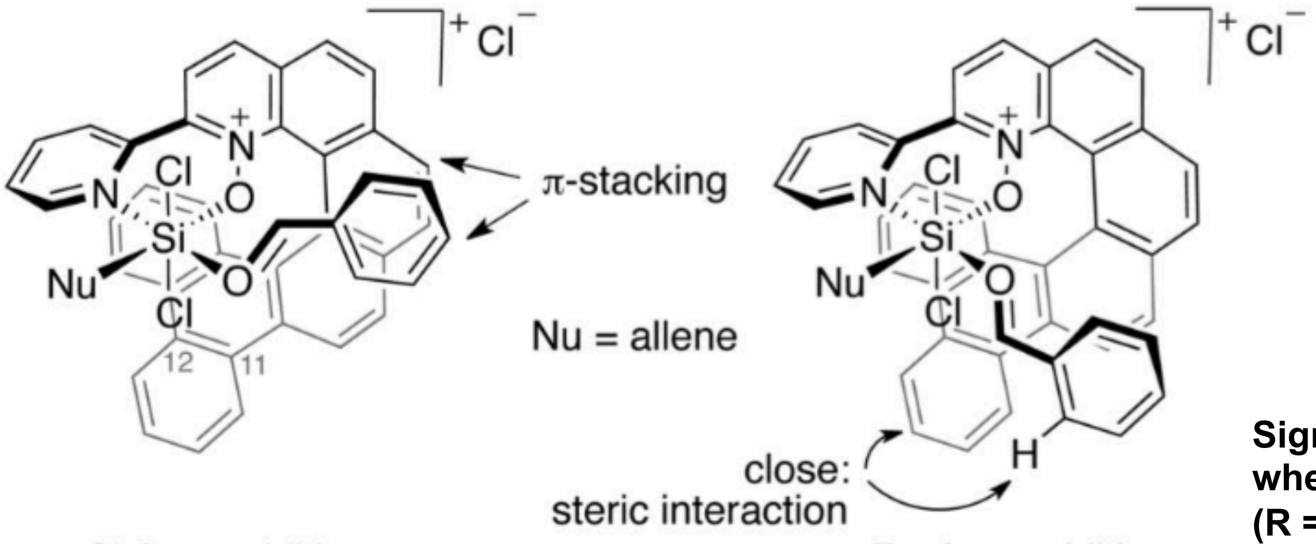
Activation of allenyltrichlorosilan



entry	substrates	result
1	R = Ph	87% 86%ee
2	R = 2-naph	86% 84%ee
3	R = Cy	80% 59%ee

Chen, J.; Captain, B. ; Takenaka, N. *Org. Lett.*. **2011**, *13*, 1654.

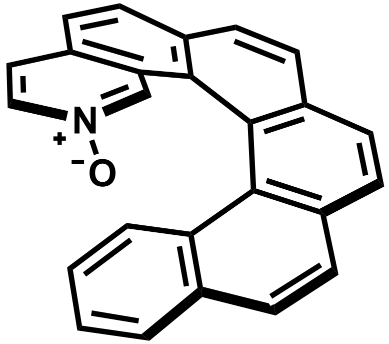
Lewis Base Catalyst



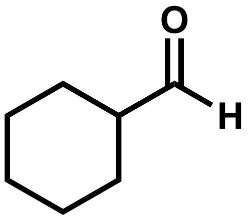
Si face addition
Favored

Re face addition
Disfavored

Significant drop in ee when this catalyst was used instead (33% ee)



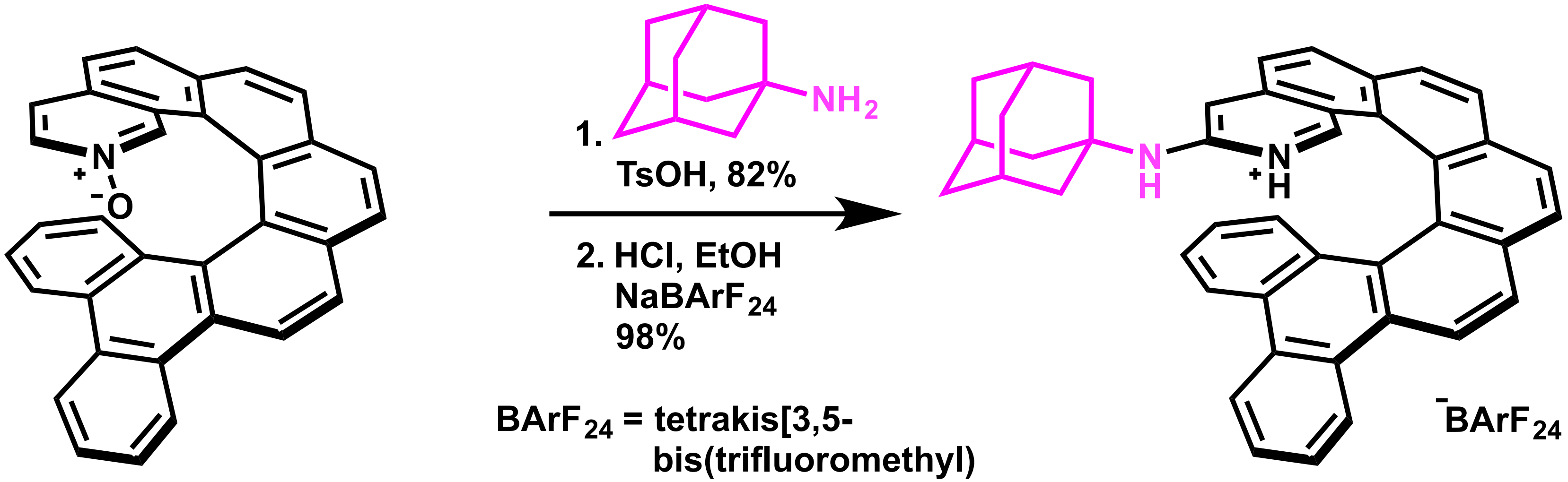
Significant drop in ee (59% ee) when this substrate was use (R = aryl for all other substrates)



Chen, J.; Captain, B. ; Takenaka, N. *Org. Lett.* **2011**, *13*, 1654.

H-bond Donor Catalysis

Synthesis of H-bond donor catalyst

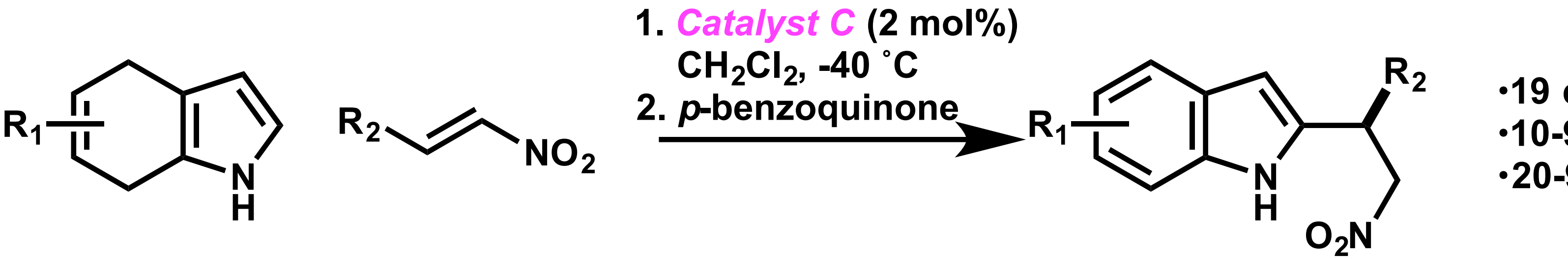


BArF$_{24}$ = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate

Catalyst A

Catalyst C

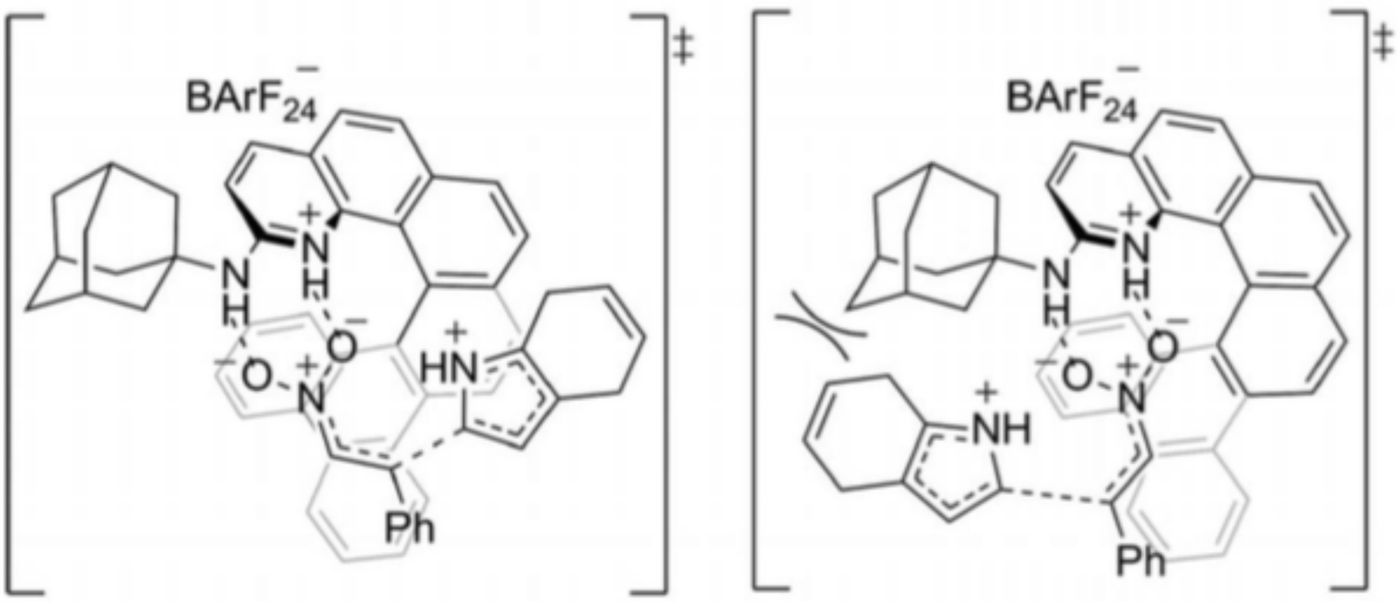
Addition of dihydroindoles to nitroalkenes



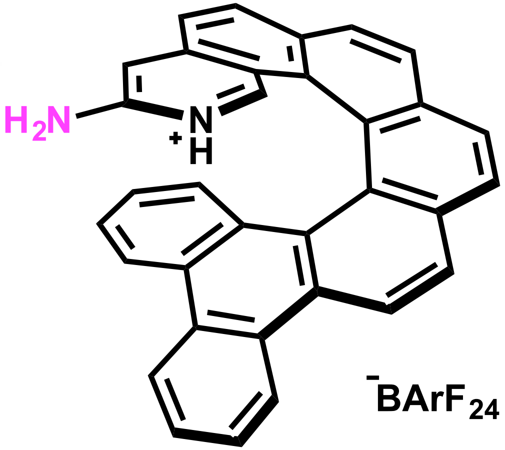
- 19 examples
- 10-90% yield
- 20-96%ee

Takenaka, N.; Captain, B.; Sarangthem, R.; Chandrakumar, A. *J. Am. Chem. Soc.* **2010**, *132*, 4536.

H-bond Donor Catalysis



Enantioselectivity drops off rapidly for this catalyst (adamantyl group removed):



Takenaka, N.; Captain, B.; Sarangthem, R.; Chandrakumar, A. *J. Am. Chem. Soc.* **2010**, *132*, 4536.

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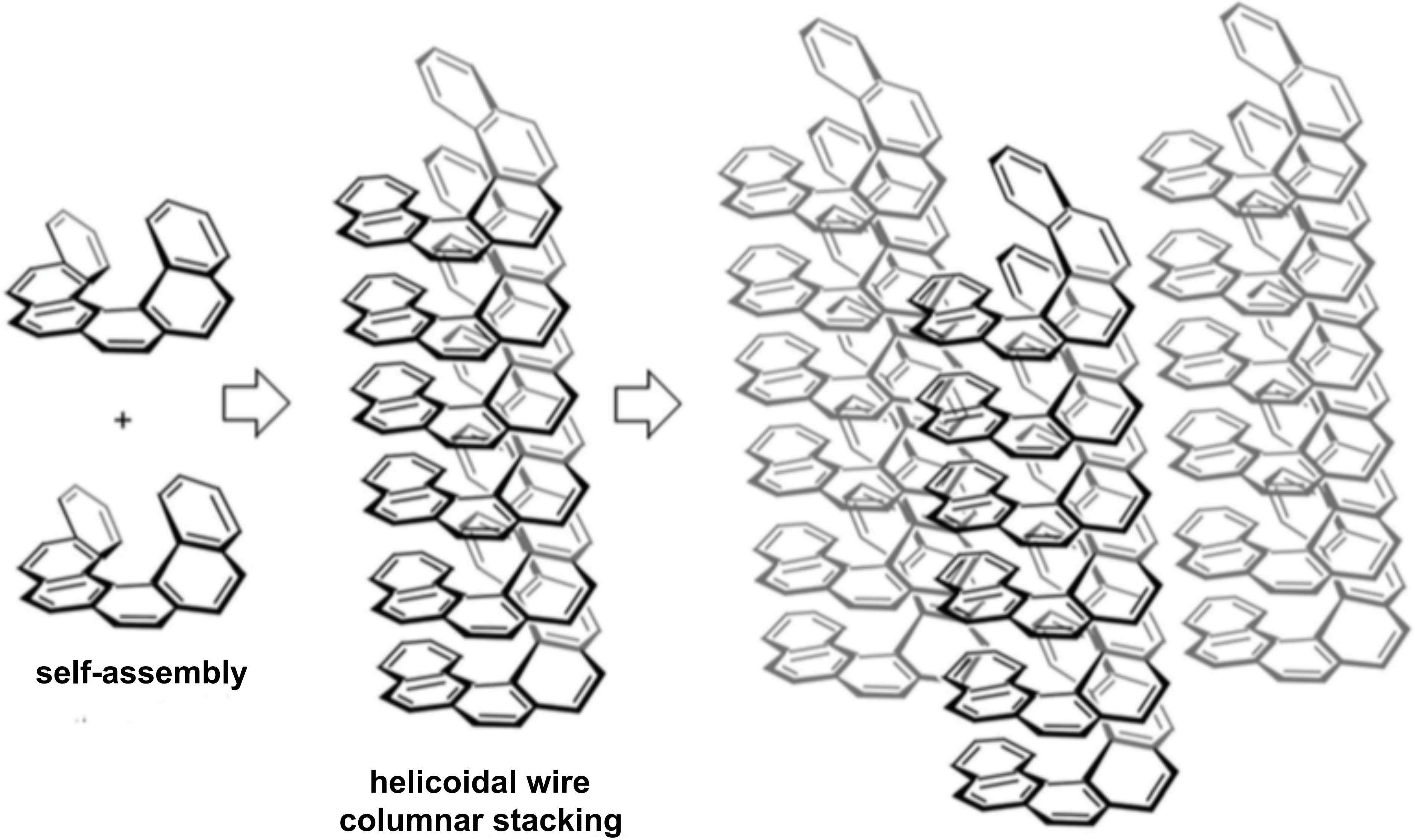
Self-Assembly



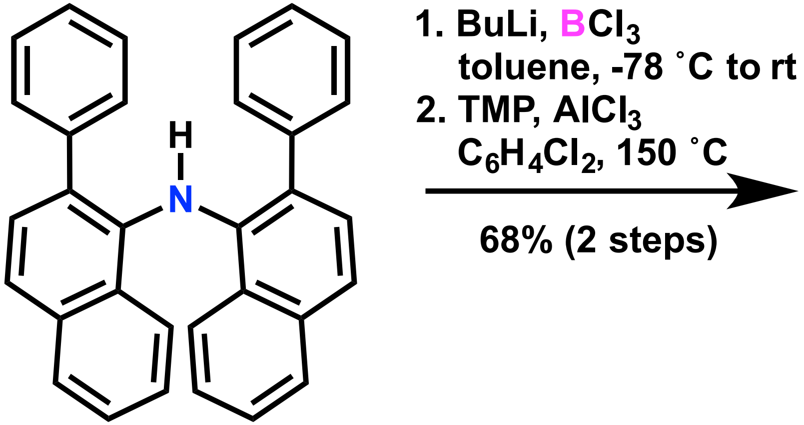
self-assembly

helicoidal wire
columnar stacking

twisted helicoidal fibers

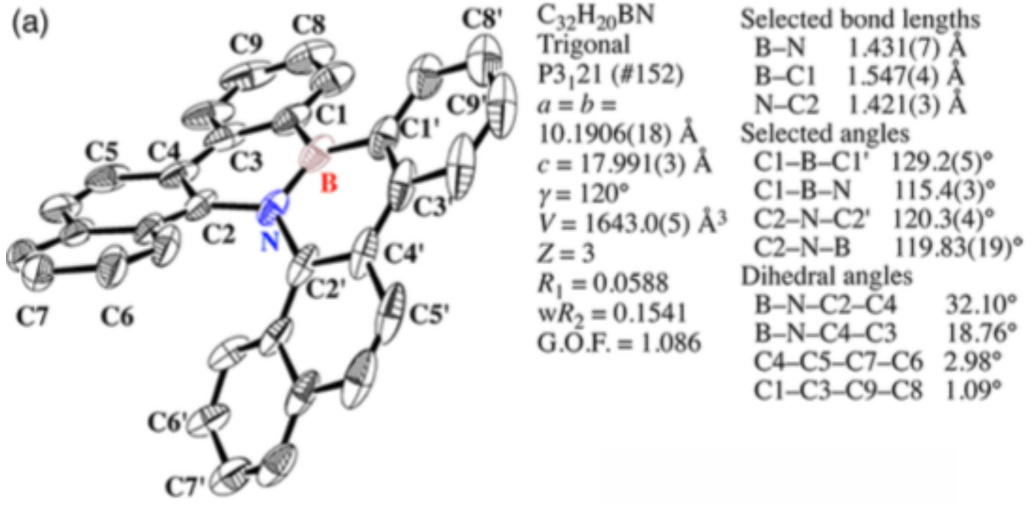
Verbiest, T.; Elshocht, S. Kauranen, M.; Hellemans, L.; Snauwaert, J.; Nuckolls, C.; Katz, T.; Persoons, A. *Sciene.* **1998**, *282,* 913.

Double Helicene



1. BuLi, BCl_3
toluene, -78 ˚C to rt
2. TMP, $AlCl_3$
$C_6H_4Cl_2$, 150 ˚C

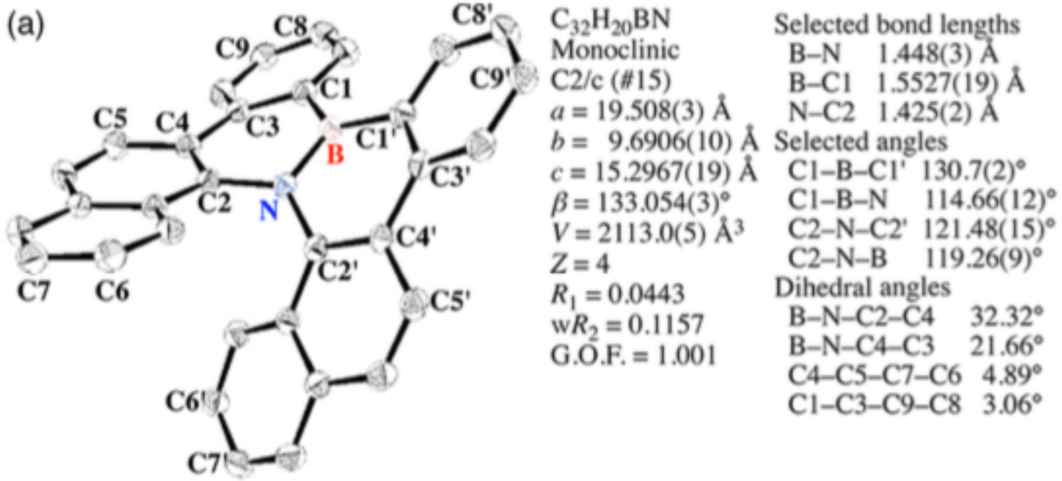
68% (2 steps)



$C_{32}H_{20}BN$
Trigonal
$P3_121$ (#152)
$a = b =$ 10.1906(18) Å
$c = 17.991(3)$ Å
$\gamma = 120°$
$V = 1643.0(5)$ Å^3
$Z = 3$
$R_1 = 0.0588$
$wR_2 = 0.1541$
G.O.F. = 1.086

Selected bond lengths	
B–N	1.431(7) Å
B–C1	1.547(4) Å
N–C2	1.421(3) Å
Selected angles	
C1–B–C1'	129.2(5)°
C1–B–N	115.4(3)°
C2–N–C2'	120.3(4)°
C2–N–B	119.83(19)°
Dihedral angles	
B–N–C2–C4	32.10°
B–N–C4–C3	18.76°
C4–C5–C7–C6	2.98°
C1–C3–C9–C8	1.09°

***rac*-NB[6]Helicene**



$C_{32}H_{20}BN$
Monoclinic
C2/c (#15)
$a = 19.508(3)$ Å
$b =$ 9.6906(10) Å
$c = 15.2967(19)$ Å
$\beta = 133.054(3)°$
$V = 2113.0(5)$ Å^3
$Z = 4$
$R_1 = 0.0443$
$wR_2 = 0.1157$
G.O.F. = 1.001

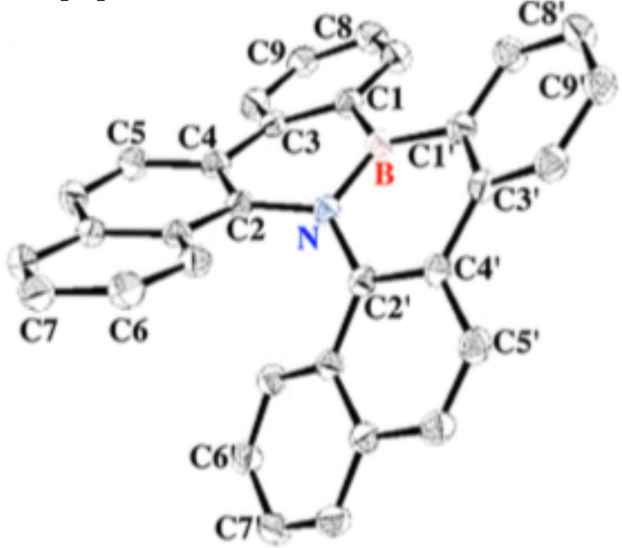
Selected bond lengths	
B–N	1.448(3) Å
B–C1	1.5527(19) Å
N–C2	1.425(2) Å
Selected angles	
C1–B–C1'	130.7(2)°
C1–B–N	114.66(12)°
C2–N–C2'	121.48(15)°
C2–N–B	119.26(9)°
Dihedral angles	
B–N–C2–C4	32.32°
B–N–C4–C3	21.66°
C4–C5–C7–C6	4.89°
C1–C3–C9–C8	3.06°

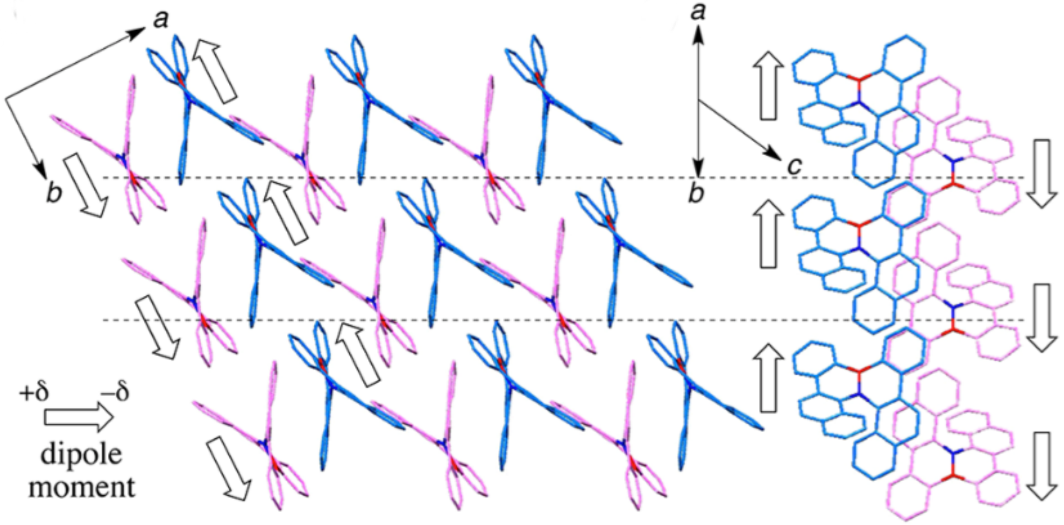
(*P*)-NB[6]Helicene

Hatakeyama, T.; Hashimoto, S.; Oba, T.; Nakamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 19600.

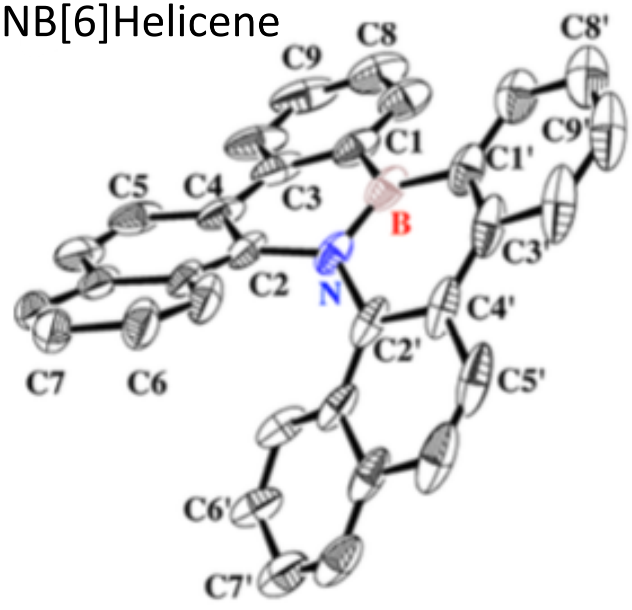
Double Helicene

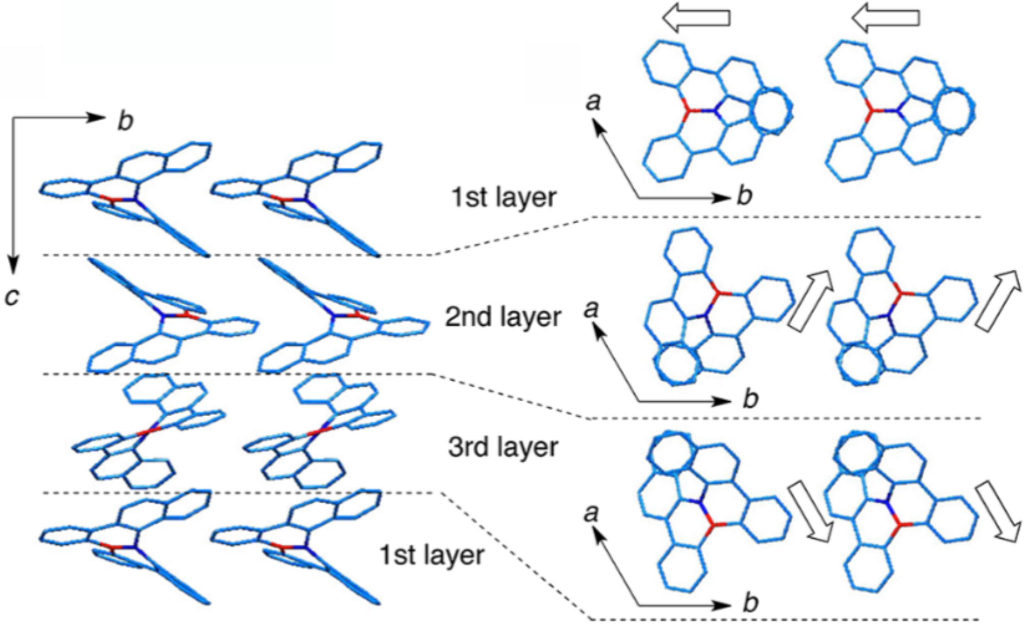
rac-NB[6]Helicene





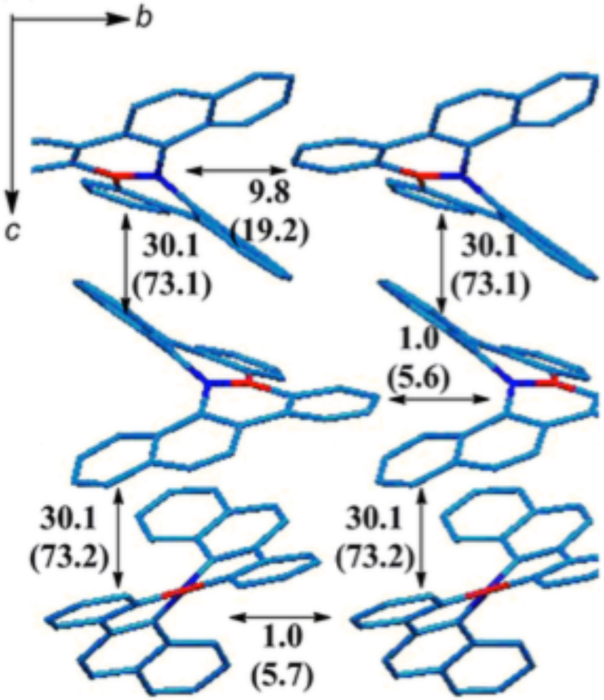
(*P*)-NB[6]Helicene

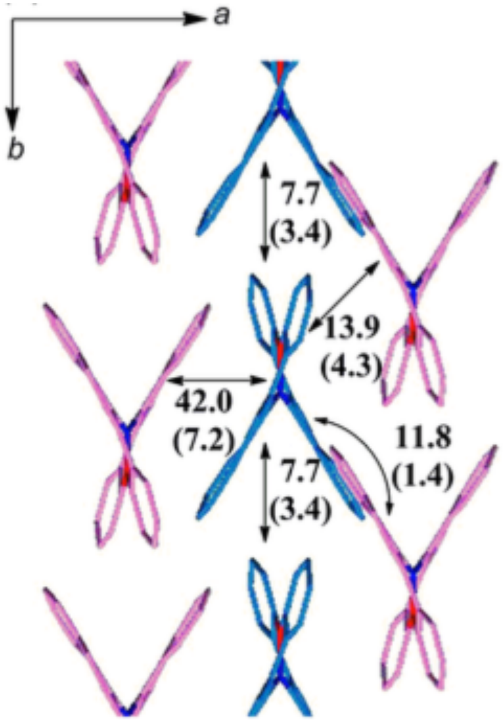




Hatakeyama, T.; Hashimoto, S.; Oba, T.; Nakamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 19600.

Carrier Inversion Induced by Helical Homochirality



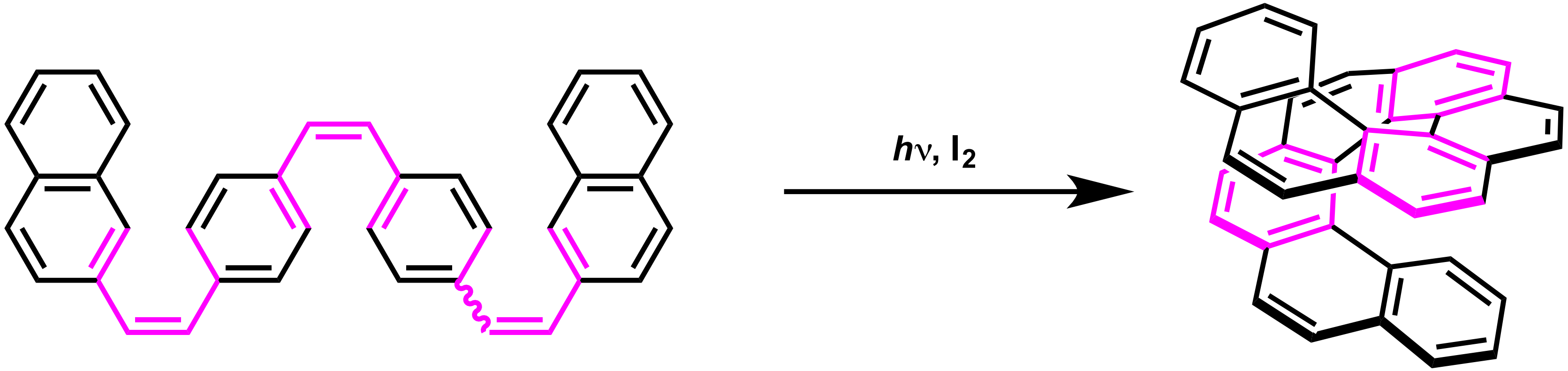


	μ_H [Hole mobility (cm^{2}N/sec)]	μ_E [Electron mobility (cm^{2}N/sec)]	
Silicon	450	1350	
rac-NB[6]Helicene	0.00079	4500	$\mu_H \ll \mu_E$ ➡ good n-type semiconductor
(*P*)-NB[6]Helicene	0.00046	-	$\mu_H \gg \mu_E$ ➡ good p-type semiconductor

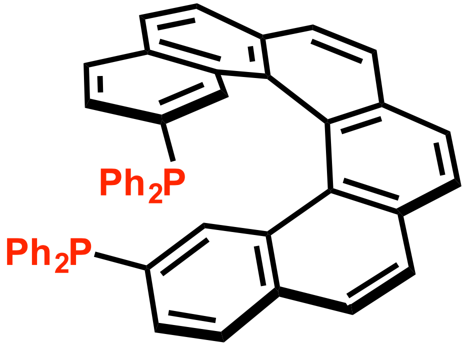
Hatakeyama, T.; Hashimoto, S.; Oba, T.; Nakamura, M. *J. Am. Chem. Soc.* **2012**, *134*, 19600.

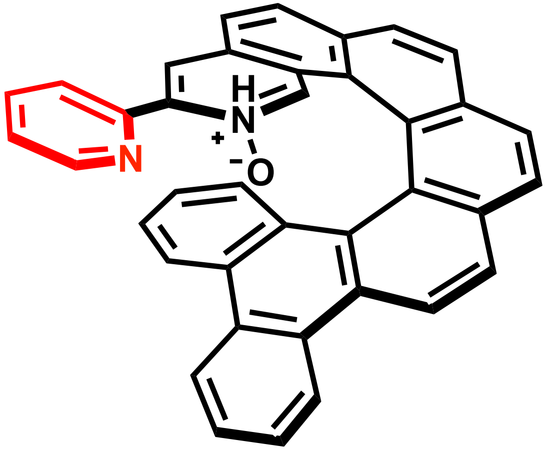
Summary

1. Synthesis of Helicene



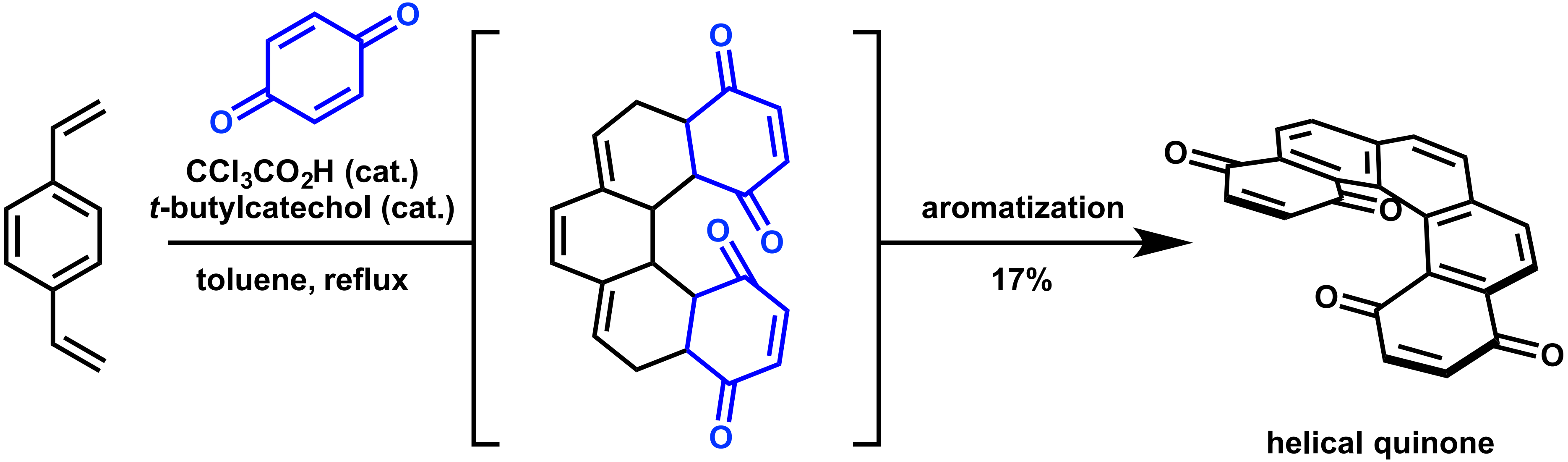
2. Application of Helicene





Appendix

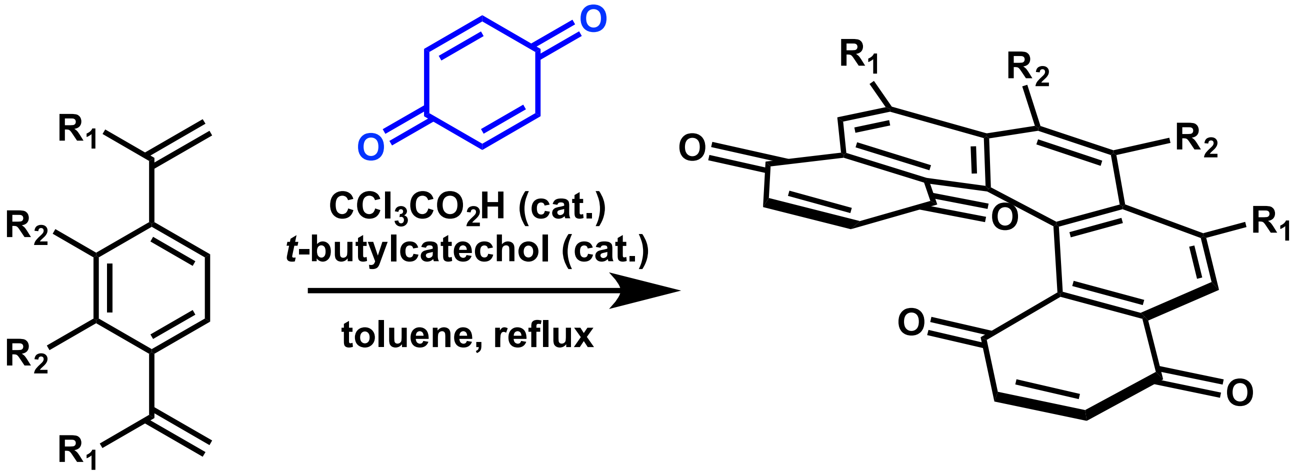
Diels-Alder Approach



CCl_3CO_2H (cat.)
t-butylcatechol (cat.)
toluene, reflux

aromatization
17%

helical quinone



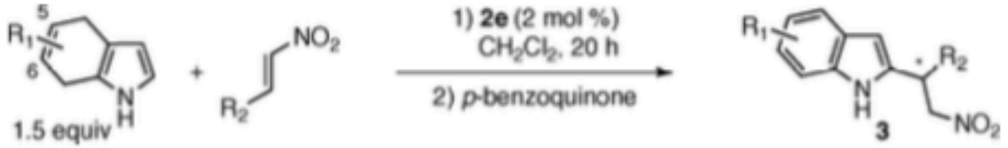
CCl_3CO_2H (cat.)
t-butylcatechol (cat.)
toluene, reflux

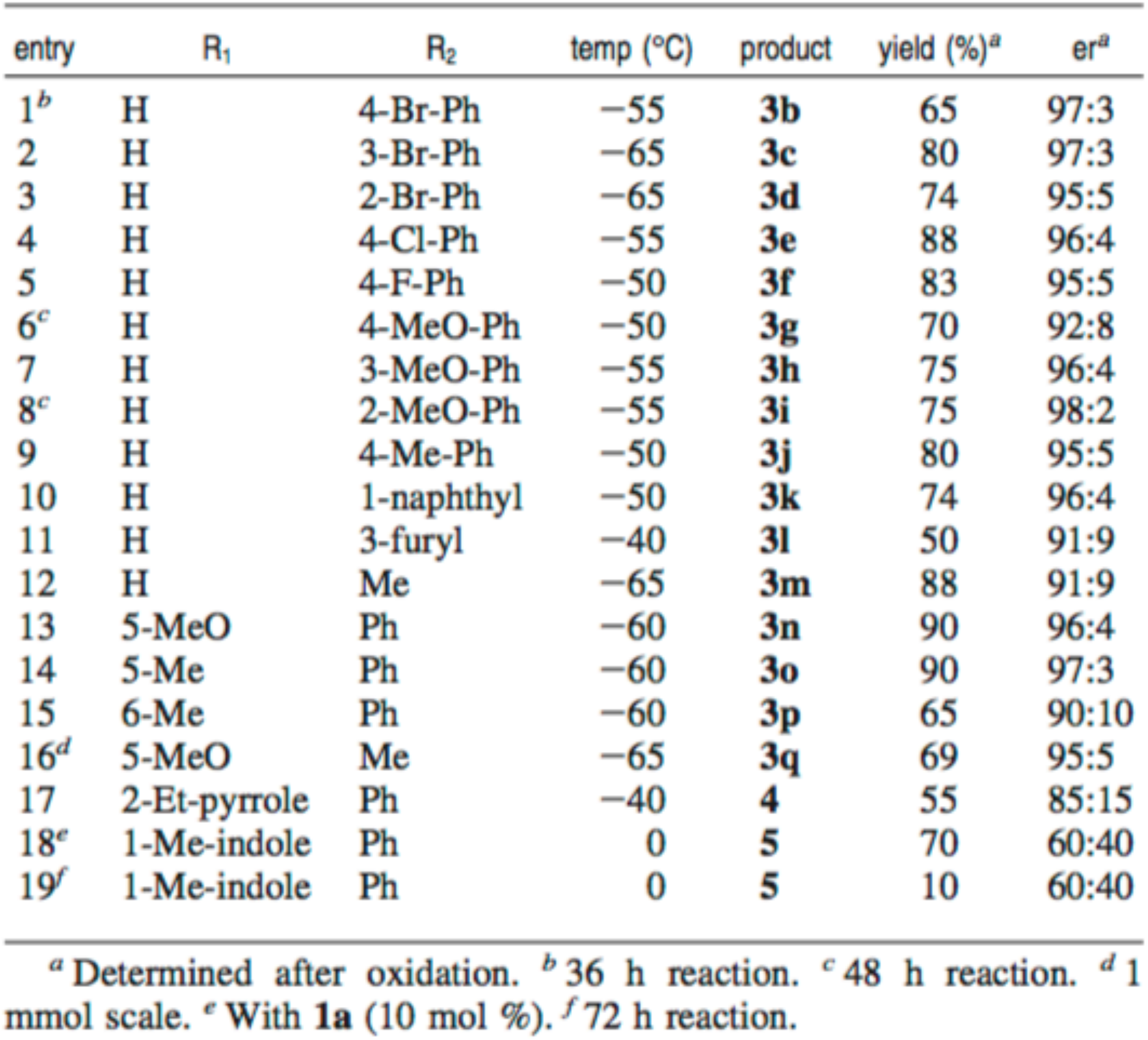
helical quinone

6%, R_1 = H, R_2 = H
13%, R_1 = H, R_2 = OMe
47%, R_1 = OMe, R_2 = H
42%, R_1 = OTBS, R_2 = H

Liu,L.; Katz, T. *Tetrahedron Lett.* **31**, *1990*, 3983.
Weidlich, H. A. *Ber*. **1998**, *71*, 1203

H-bond Donor Catalysis



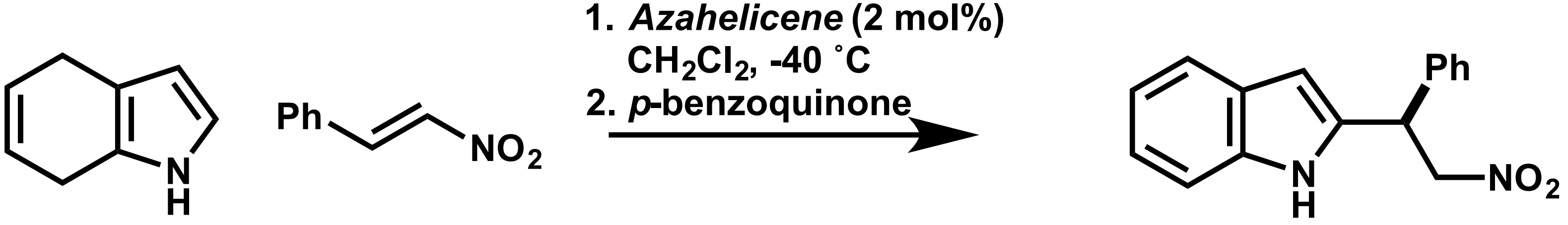


entry	R_1	R_2	temp (°C)	product	yield (%)[a]	er[a]
1[b]	H	4-Br-Ph	−55	**3b**	65	97:3
2	H	3-Br-Ph	−65	**3c**	80	97:3
3	H	2-Br-Ph	−65	**3d**	74	95:5
4	H	4-Cl-Ph	−55	**3e**	88	96:4
5	H	4-F-Ph	−50	**3f**	83	95:5
6[c]	H	4-MeO-Ph	−50	**3g**	70	92:8
7	H	3-MeO-Ph	−55	**3h**	75	96:4
8[c]	H	2-MeO-Ph	−55	**3i**	75	98:2
9	H	4-Me-Ph	−50	**3j**	80	95:5
10	H	1-naphthyl	−50	**3k**	74	96:4
11	H	3-furyl	−40	**3l**	50	91:9
12	H	Me	−65	**3m**	88	91:9
13	5-MeO	Ph	−60	**3n**	90	96:4
14	5-Me	Ph	−60	**3o**	90	97:3
15	6-Me	Ph	−60	**3p**	65	90:10
16[d]	5-MeO	Me	−65	**3q**	69	95:5
17	2-Et-pyrrole	Ph	−40	**4**	55	85:15
18[e]	1-Me-indole	Ph	0	**5**	70	60:40
19[f]	1-Me-indole	Ph	0	**5**	10	60:40

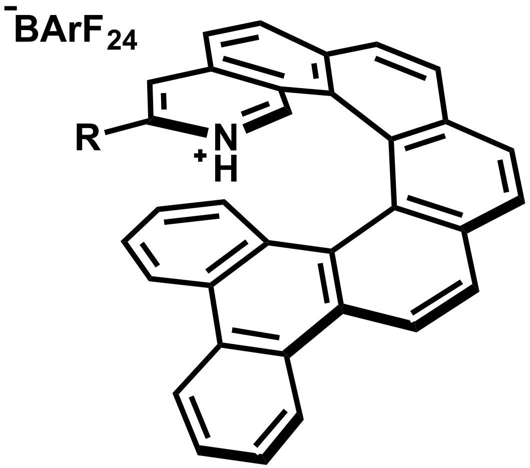
[a] Determined after oxidation. [b] 36 h reaction. [c] 48 h reaction. [d] 1 mmol scale. [e] With **1a** (10 mol %). [f] 72 h reaction.

Takenaka, N.; Captain, B.; Sarangthem, R.; Chandrakumar, A. *J. Am. Chem. Soc.* **2010**, *132*, 4536.

Helicenes in Organocatalysis



entry	*Azahelicene*	result
1	R = NH_2	71% 38%ee
2	R = NHBn	72% 38%ee
3	R = *t*Bu	79% 84%ee
4	R = NH1-ad	73% 66%ee
5	R = NH2-ad	88% 86%ee

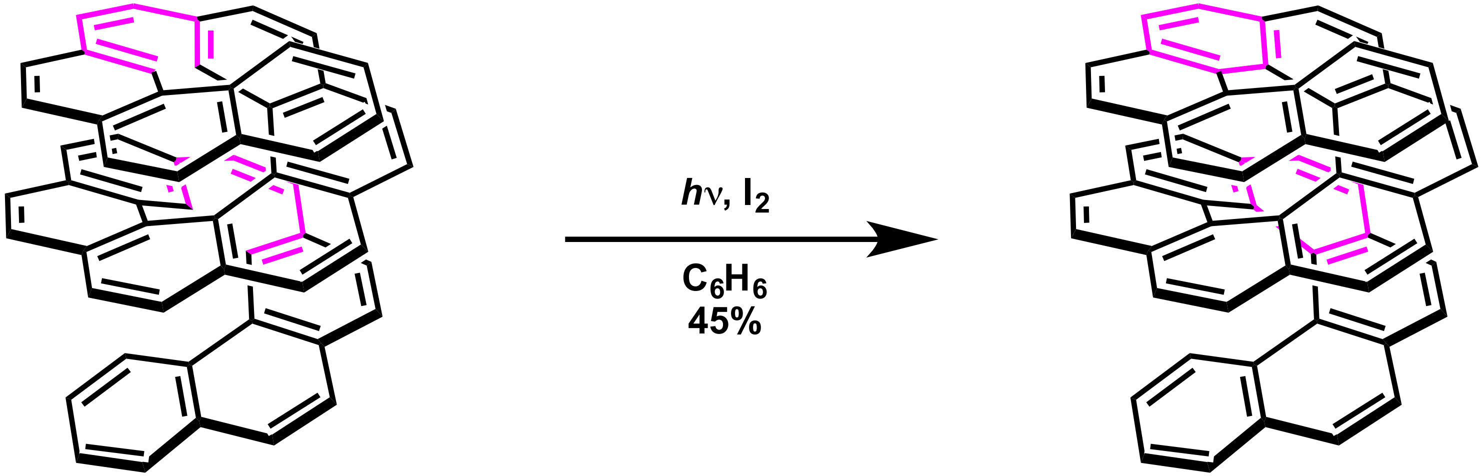


Azahelicene

$BArF_{24}$ = tetrakis[3,5-
bis(trifluoromethyl)
phenyl]borate

Newman, M. S.; Lednicer, D. *J. Am. Chem. Soc.* **1956**, *78*, 4756.
Newman, M. S.; Lutz, W. B. *J. Am. Chem. Soc.* **1956**, *78*, 2469.

Synthesis of [14] Helicene



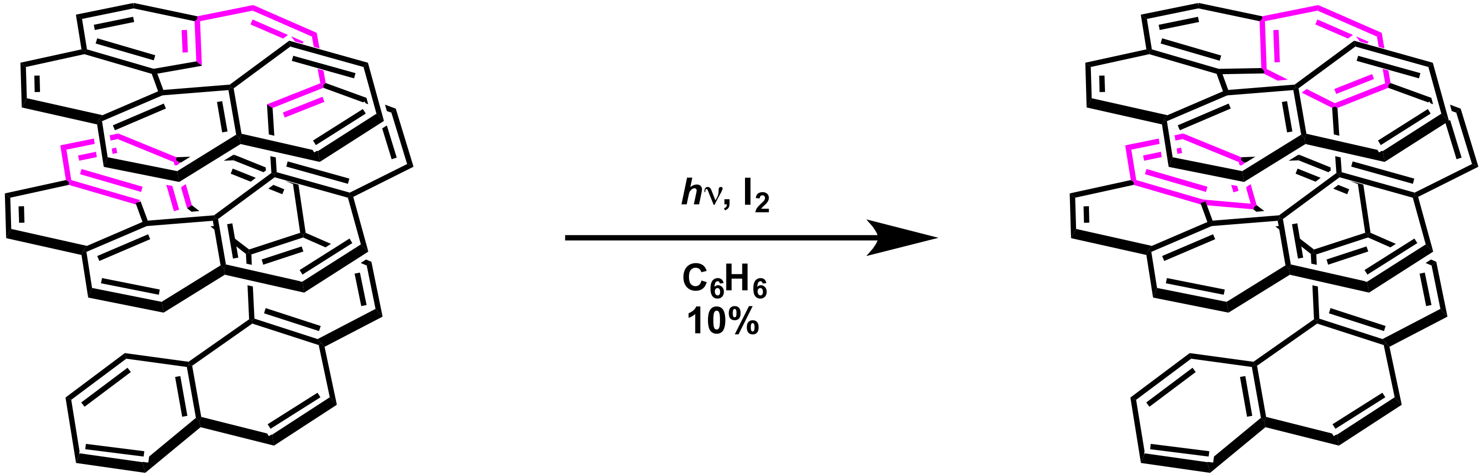
$h\nu$, I_2

C_6H_6

45%

[3]+[6]+[3]

[14]helicene



$h\nu$, I_2

C_6H_6

10%

[4]+[4]+[4]

[14]helicene

Flammang-barbieux, M.; Nasielski, J.; Martin, R. H. *Teterahedron, Lett.* **1967**, *8*, 743.

Possibility of Rewrite the Polymer

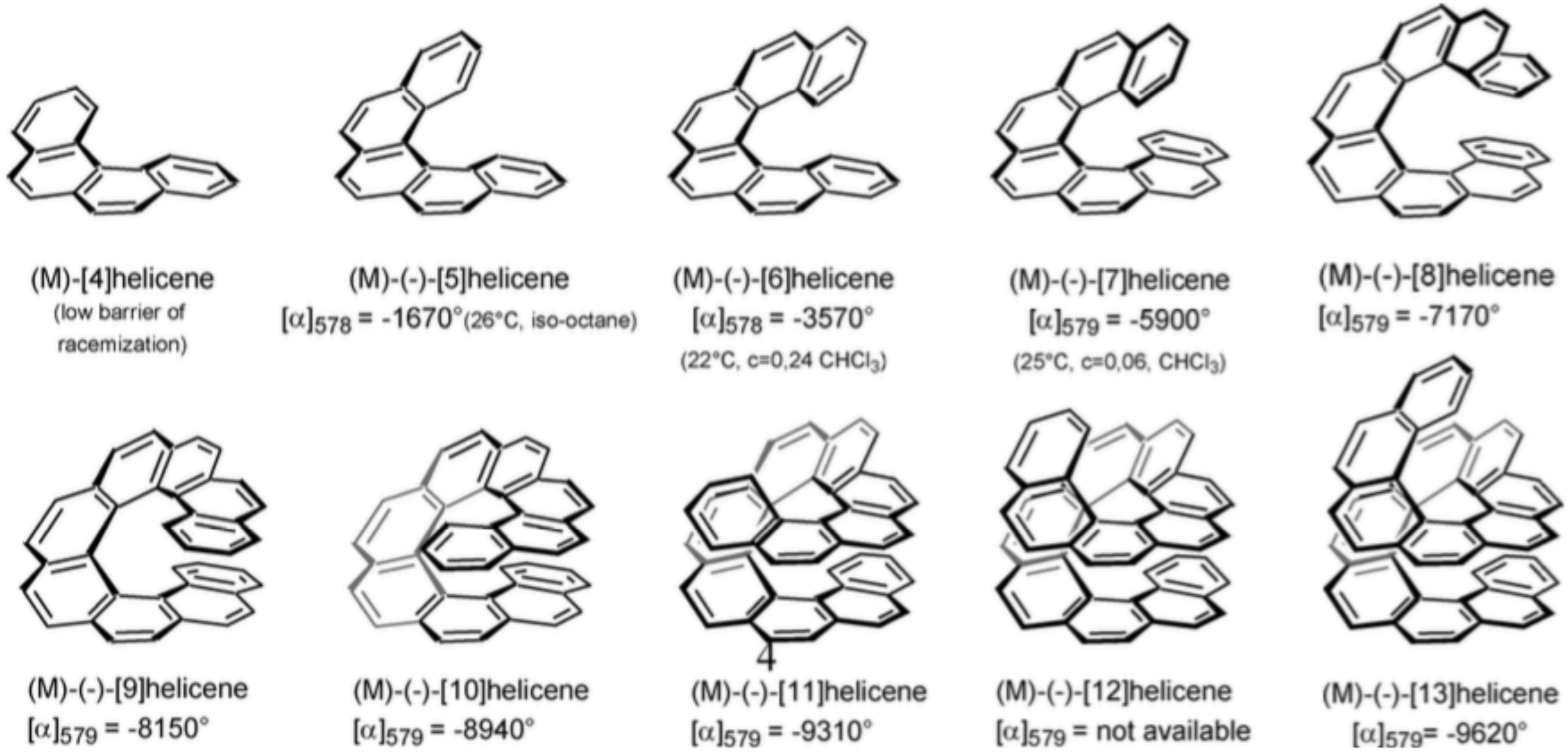
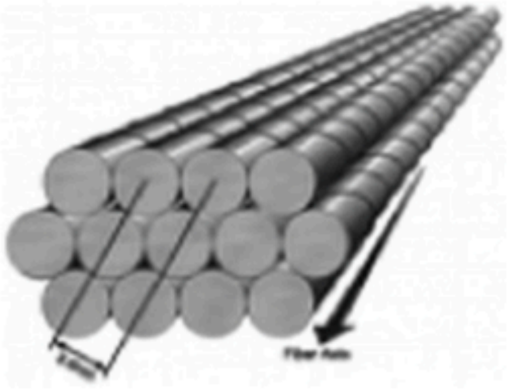
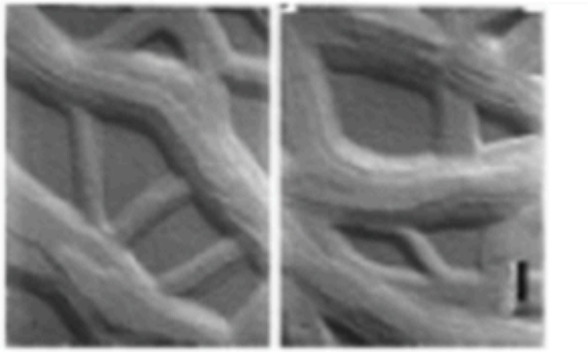


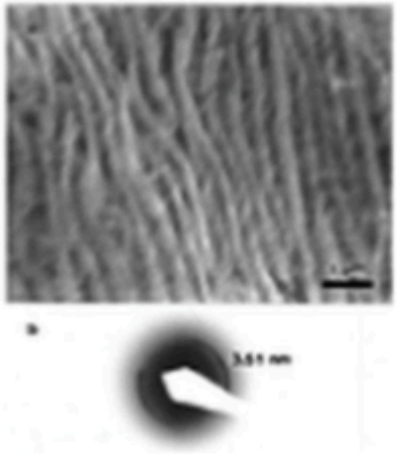
Fig. 2 List of carbohelicenes, their homochirality, absolute configuration and specific rotation at 25 °C in $CHCl_3$ ($c = 0.02$ g/100 mL) unless noted otherwise ($\lambda = 578$ or 579 nm). For (–)[5]helicene, see ref. 181; for (–)[6]helicene, see ref. 21; for (–)[7] to (–)[13]helicene: see ref. 10, 11, 85 and 86.

Lutz, J-F. *Nat. Commun.* **2015**, *6*.

Twisted Helicoidal Fibers







Lutz, J-F. *Nat. Commun.* **2015**, *6*.