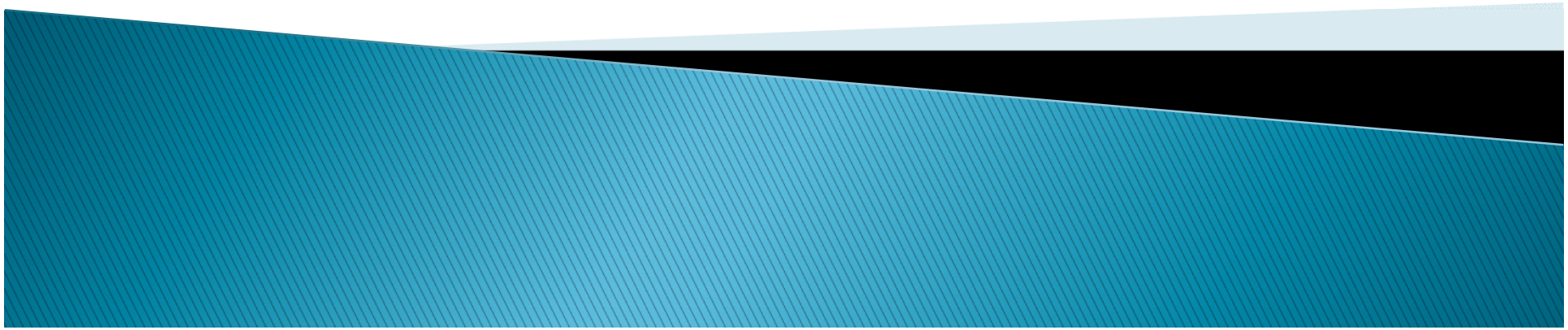
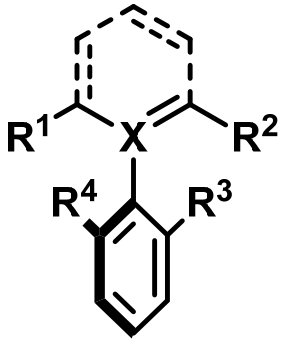
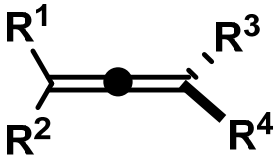
Helicenes, more than a century of interest

Fabien PEREZ – STeRéO – November 17th, 2015

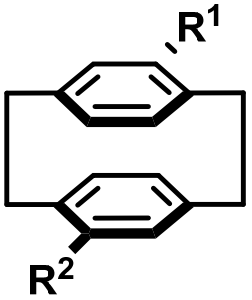


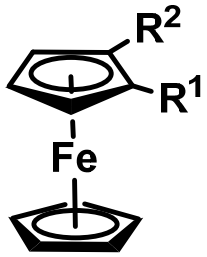
Chirality modes





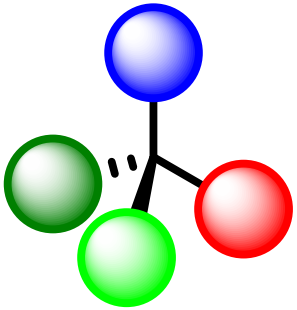
Axial chirality



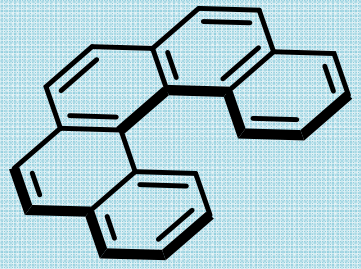


paracyclophane

Planar chirality

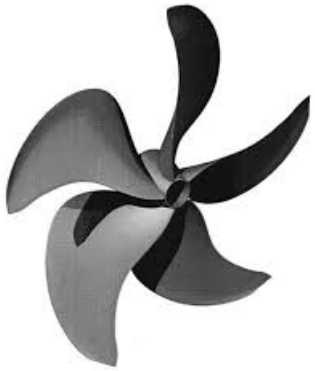


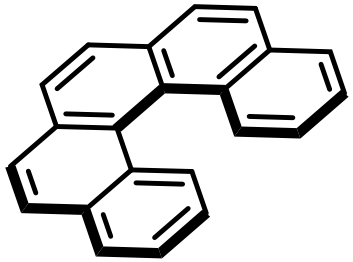
Stereogenic center

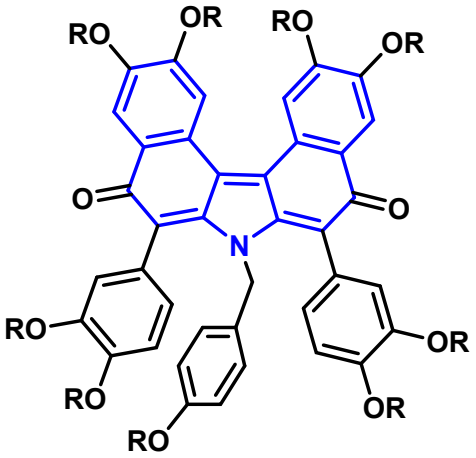


Helical chirality

Helix in our world





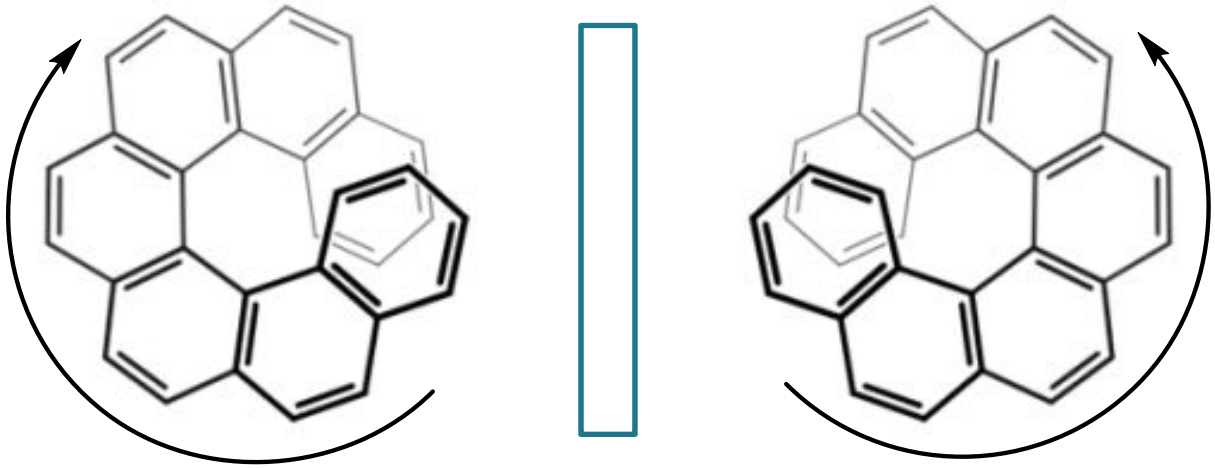


Outline

- Introduction on helicenes
- Racemic synthesis
- To enantiopure helicene
- Applications

Introduction on helicenes

- [n]helicene with n = number of *ortho*fused aromatic rings

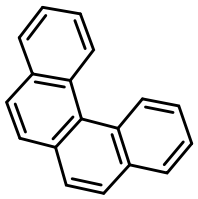


P-(+)
Clockwise helicity
Dextrorotatory rotation

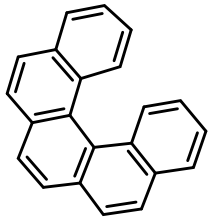
M-(-)
Anticlockwise helicity
Levorotatory rotation

Helicene timeline

1913
[4]helicene R. Weitzenböck



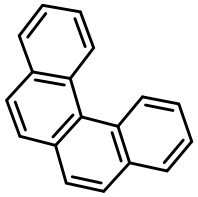
Helicene timeline



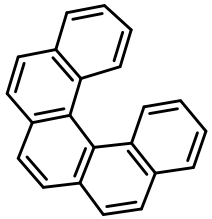
1918
[5]helicene

T. Oppenheimer

1913
[4]helicene



Helicene timeline



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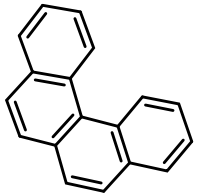
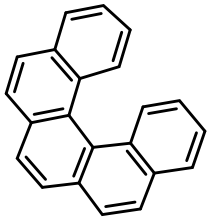
[5]helicene

1913
[4]helicene



Helicene timeline



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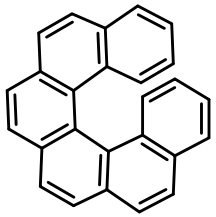
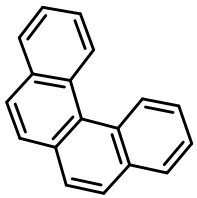
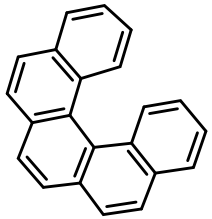


1955
[6]helicene

1913
[4]helicene



Helicene timeline



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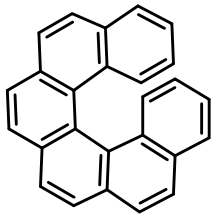

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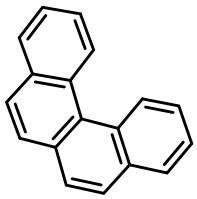
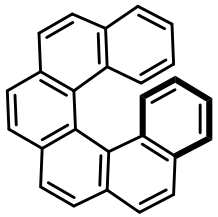
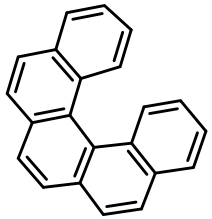
1913
[4]helicene



1956
Resolution of
[6]helicene



Helicene timeline



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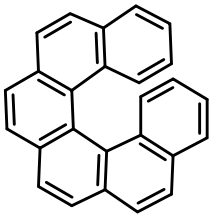

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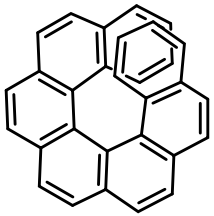
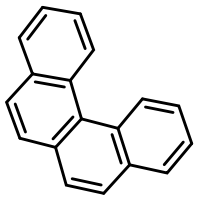
[6]helicene



1967
[7]helicene

1913
[4]helicene



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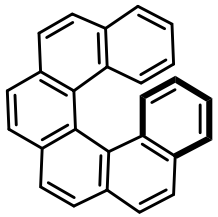
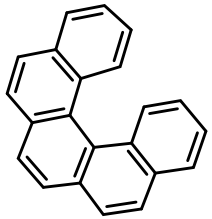
Resolution of
[6]helicene



Helicene timeline



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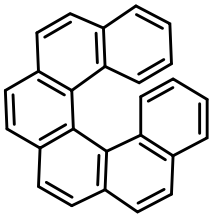

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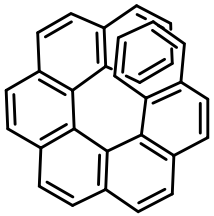

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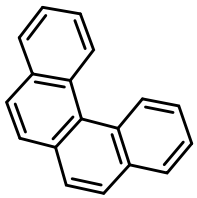

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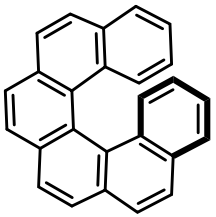
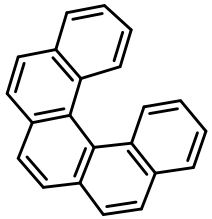
Resolution of
[6]helicene



1971
Asymmetric synthesis
Induced
by polarized light

H. Kagan

Helicene timeline



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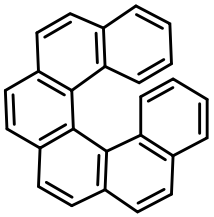

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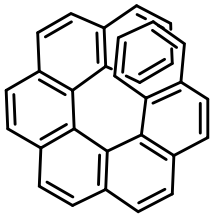
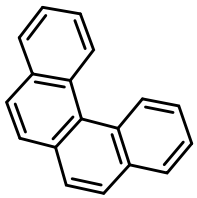


1967
[7]helicene

1990
First non photochemical Synthesis of helicene

T. J. Katz

1913
[4]helicene



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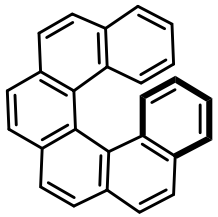
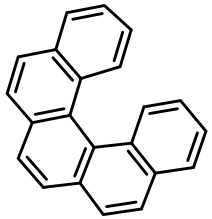
Resolution of [6]helicene



1971
Asymmetric synthesis Induced by polarized light

Helicene timeline



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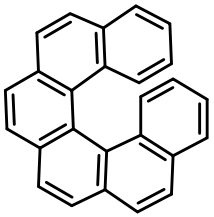

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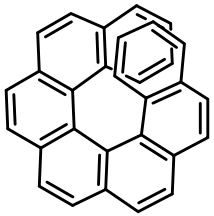

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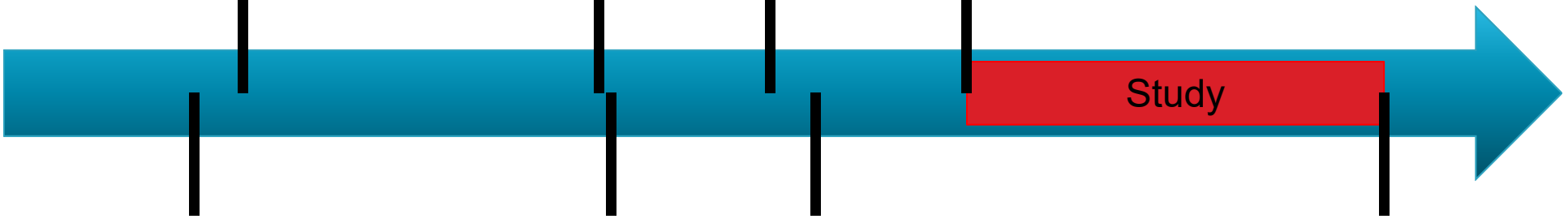
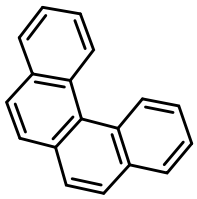
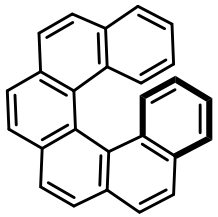


1913
[4]helicene



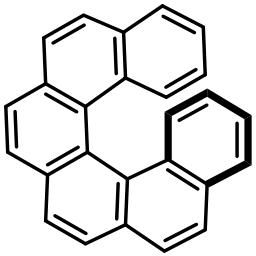
1956
Resolution of [6]helicene



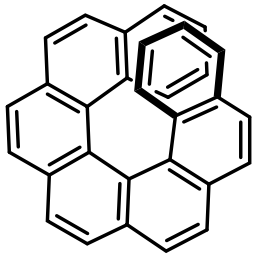
1971
Asymmetric synthesis Induced by polarized light

2015
Remains of interest

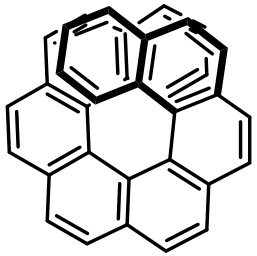
General properties



[6]helicene
$t_{1/2}$ = 13 min
at 221,4 °C
$E_{a(27\ °C)}$ = 35,6 kcal/mol



[7]helicene
$t_{1/2}$ = 26 min
at 286,2 °C
$E_{a(27\ °C)}$ = 41,1 kcal/mol



[8]helicene
$t_{1/2}$ = 54 min
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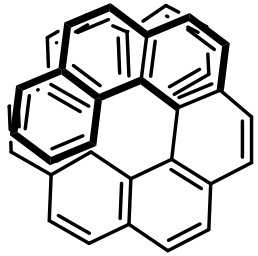
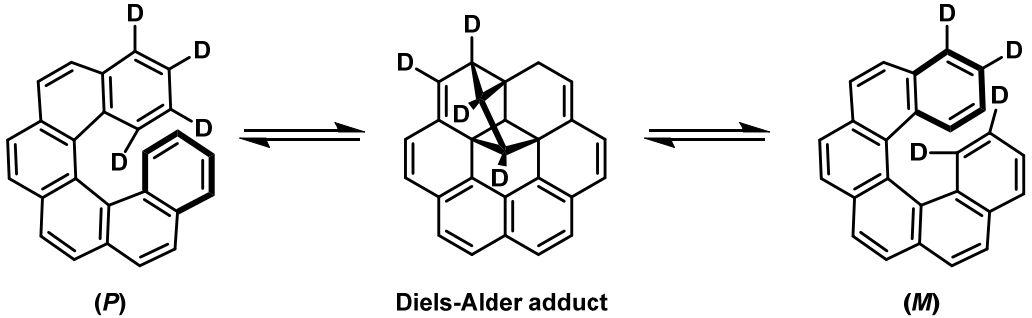
$E_{a(27\ °C)}$ = 41,6 kcal/mol

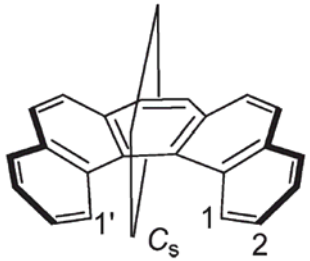


[9]helicene
$t_{1/2}$ = 123 min
at 293,5 °C
$E_{a(27\ °C)}$ = 42,3 kcal/mol

R. H. Martin. *Tetrahedron. Lett*. **1972,** *35*, 3707

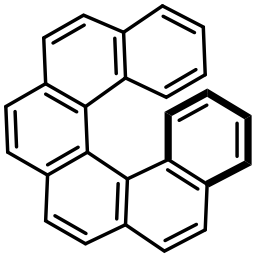


R. H. Martin. *Tetrahedron.* **1974,** *30*, 347



M. Patzschke. *Chem. Eur. J.* **2009,** *30*, 347

General properties



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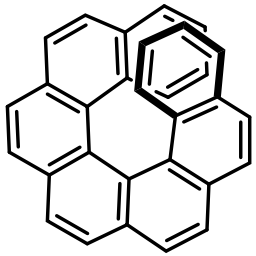

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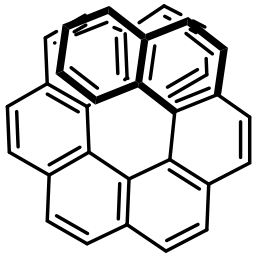

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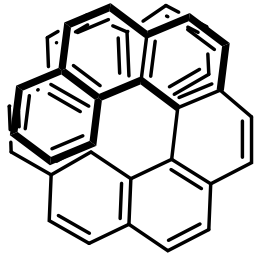

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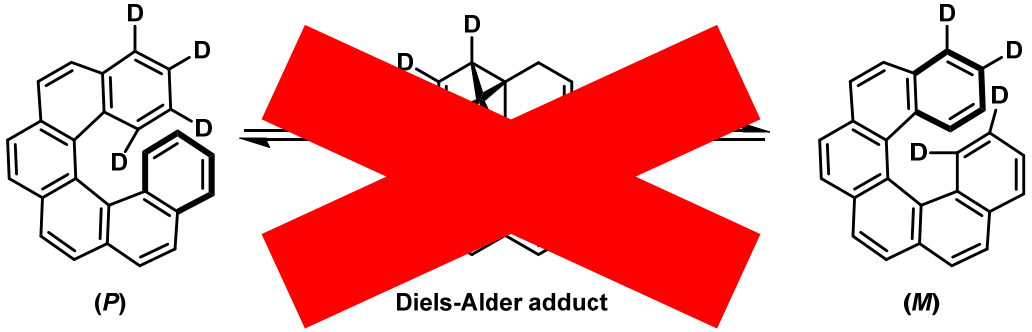
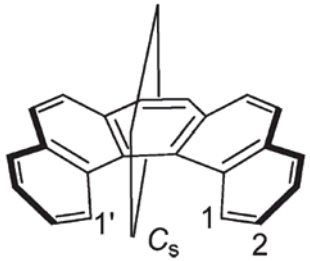
$E_{a(27\ °C)}$ = 42,3 kcal/mol

R. H. Martin. *Tetrahedron. Lett*. **1972,** *35*, 3707



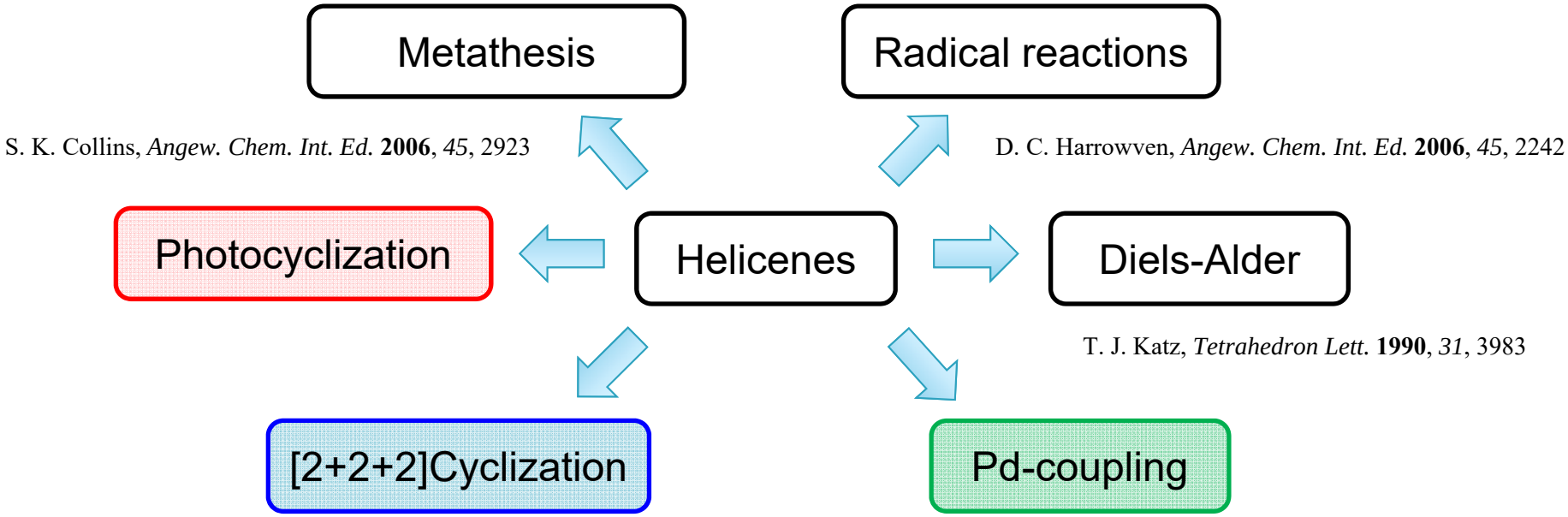
R. H. Martin. *Tetrahedron.* **1974,** *30*, 347



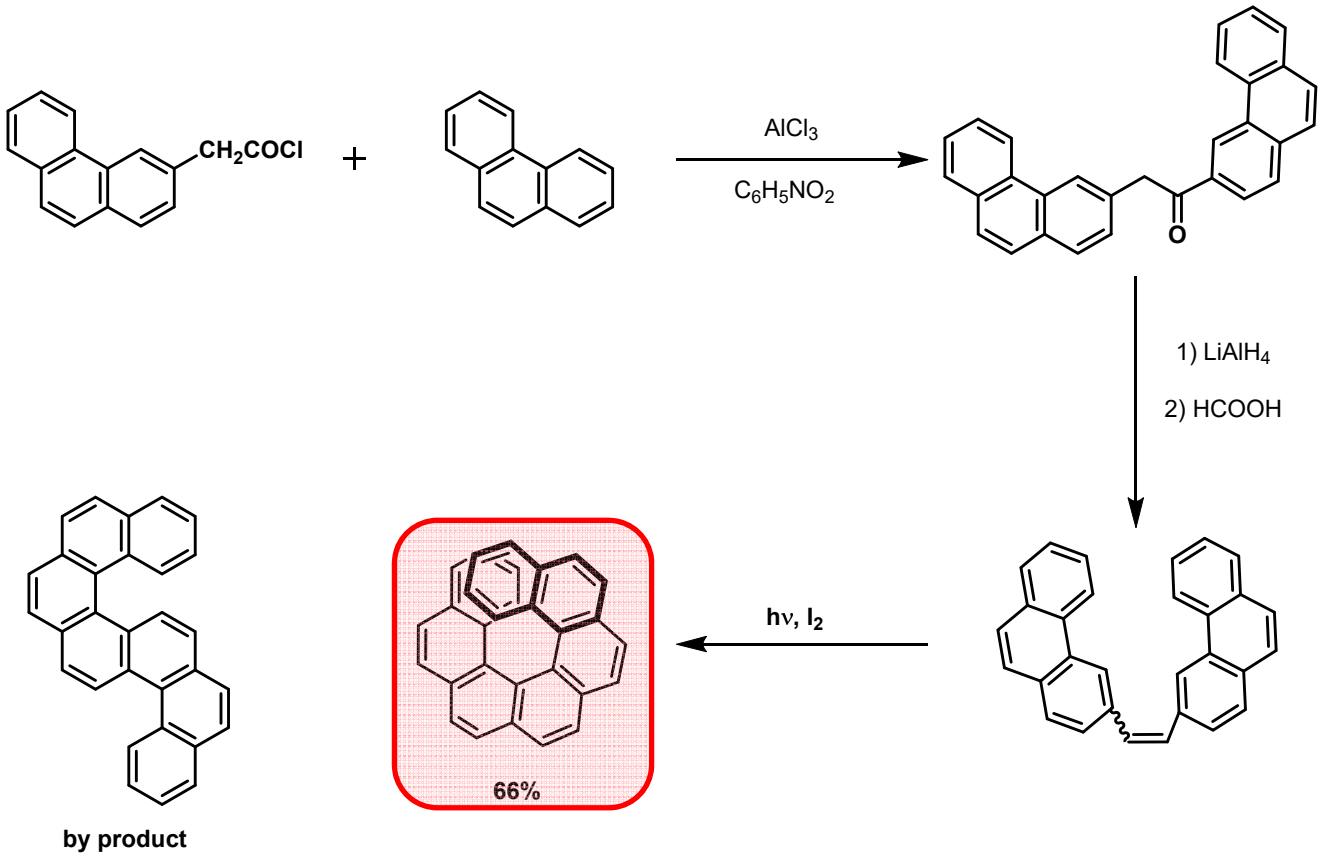
M. Patzschke. *Chem. Eur. J.* **2009,** *30*, 347

Synthesis of helicenes, racemic series

Racemic synthesis overview

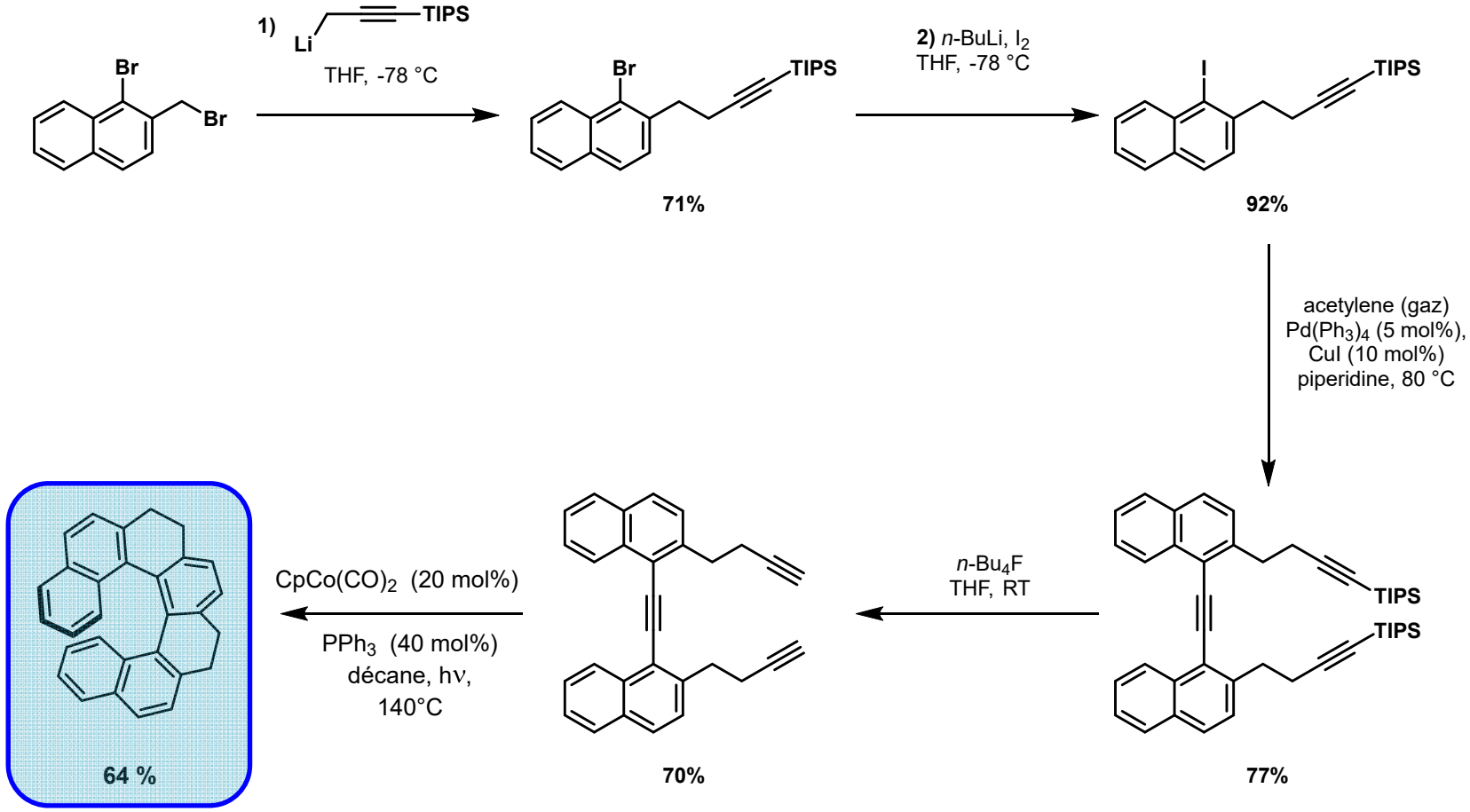


Photocyclisation



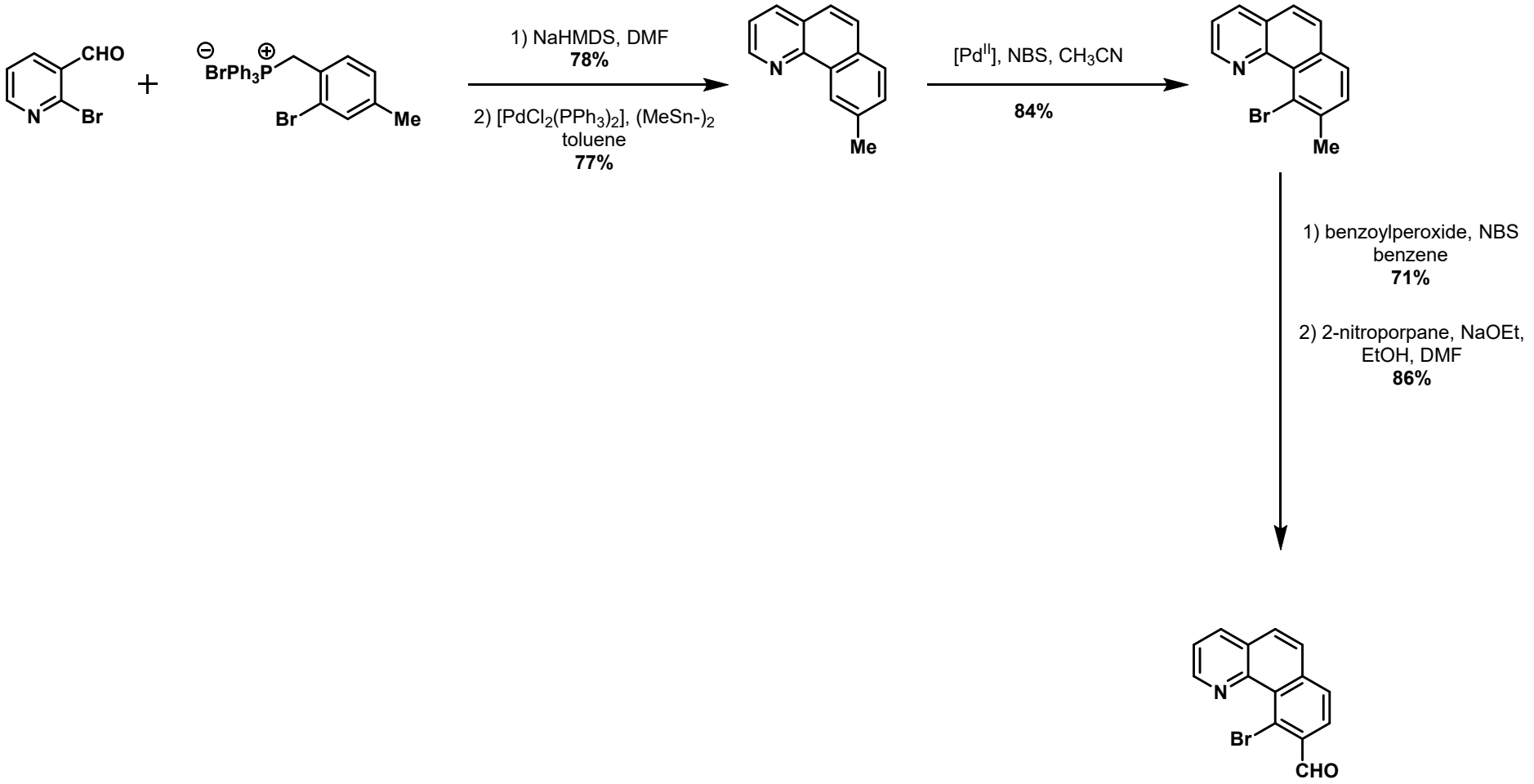
R. H. Martin *Tetrahedron. Lett*. **1967,** *8*, 743

[2+2+2] cyclization



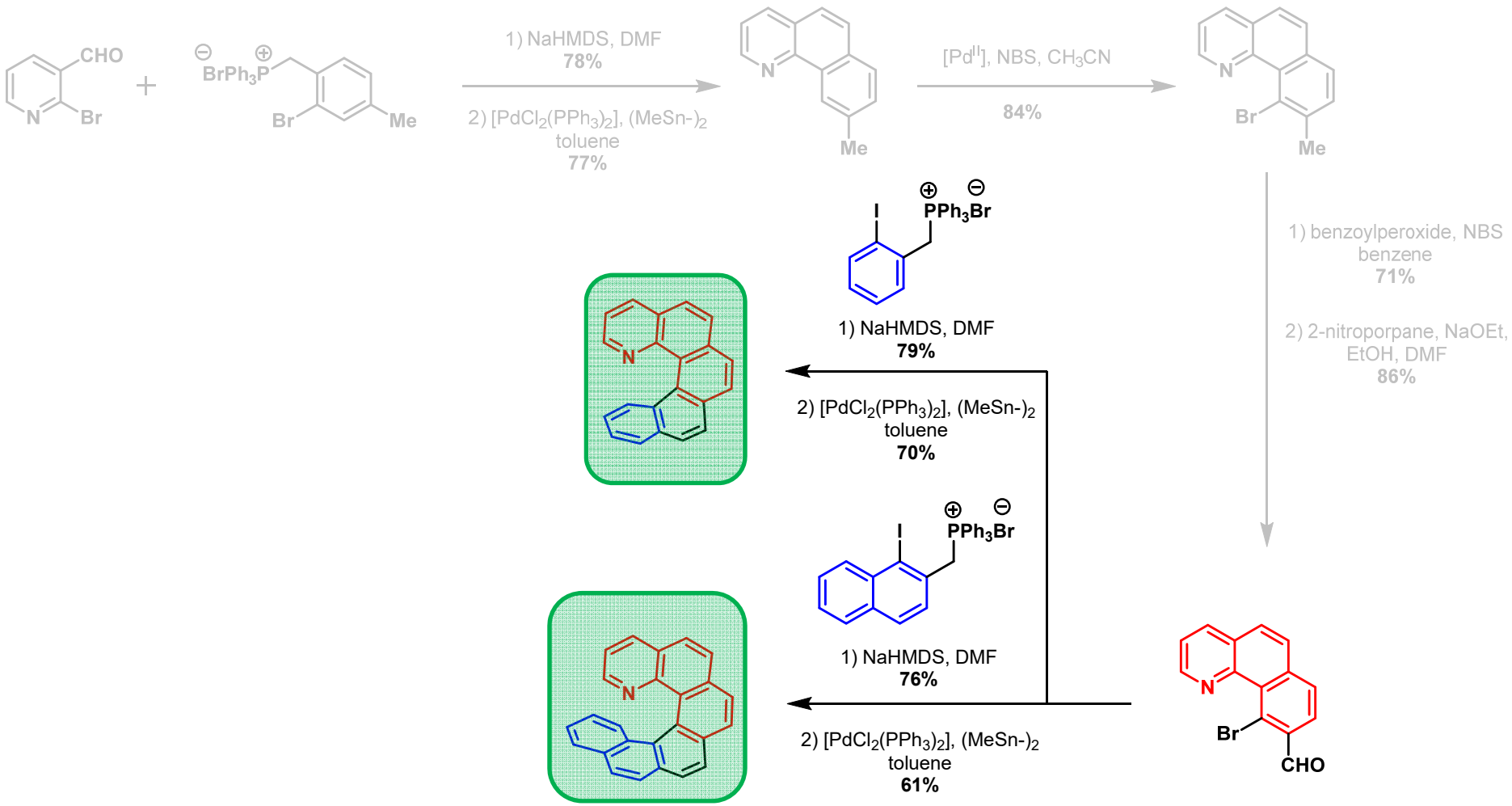
I. G. Stará, I. Starý *Tetrahedron. Lett.* **1999,** *40*, 1993

azahelicene



N. Takenaka, *Angew. Chem. Int. Ed.* **2008**, 9708

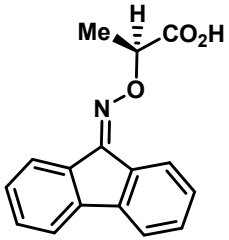
azahelicene



N. Takenaka, *Angew. Chem. Int. Ed.* **2008**, 9708

En route for enantiopure helicenes

Optical resolution



(-)-TAPA

Cristal picking

chiral HPLC

M. S. Newmann, *J. Am. Chem. Soc.* **1956**, *78*, 4765

E. Gilav, *J. Chem. Soc. Chem. Commun.* **1976**, 99

Enzymatic resolution

enantiopure helicene

Asymmetric rearrangement

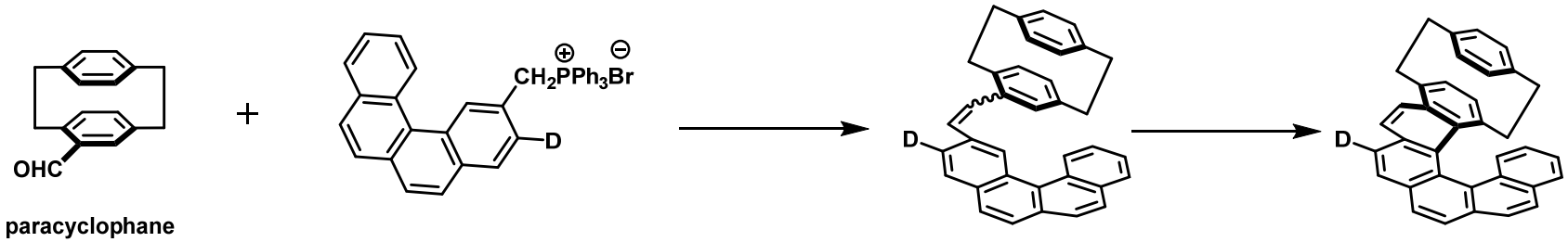
T. J. Katz, Tetrahedron Lett. **1990**, *31*, 3983

T. J. Katz, Tetrahedron Lett. **1990**, *31*, 3983

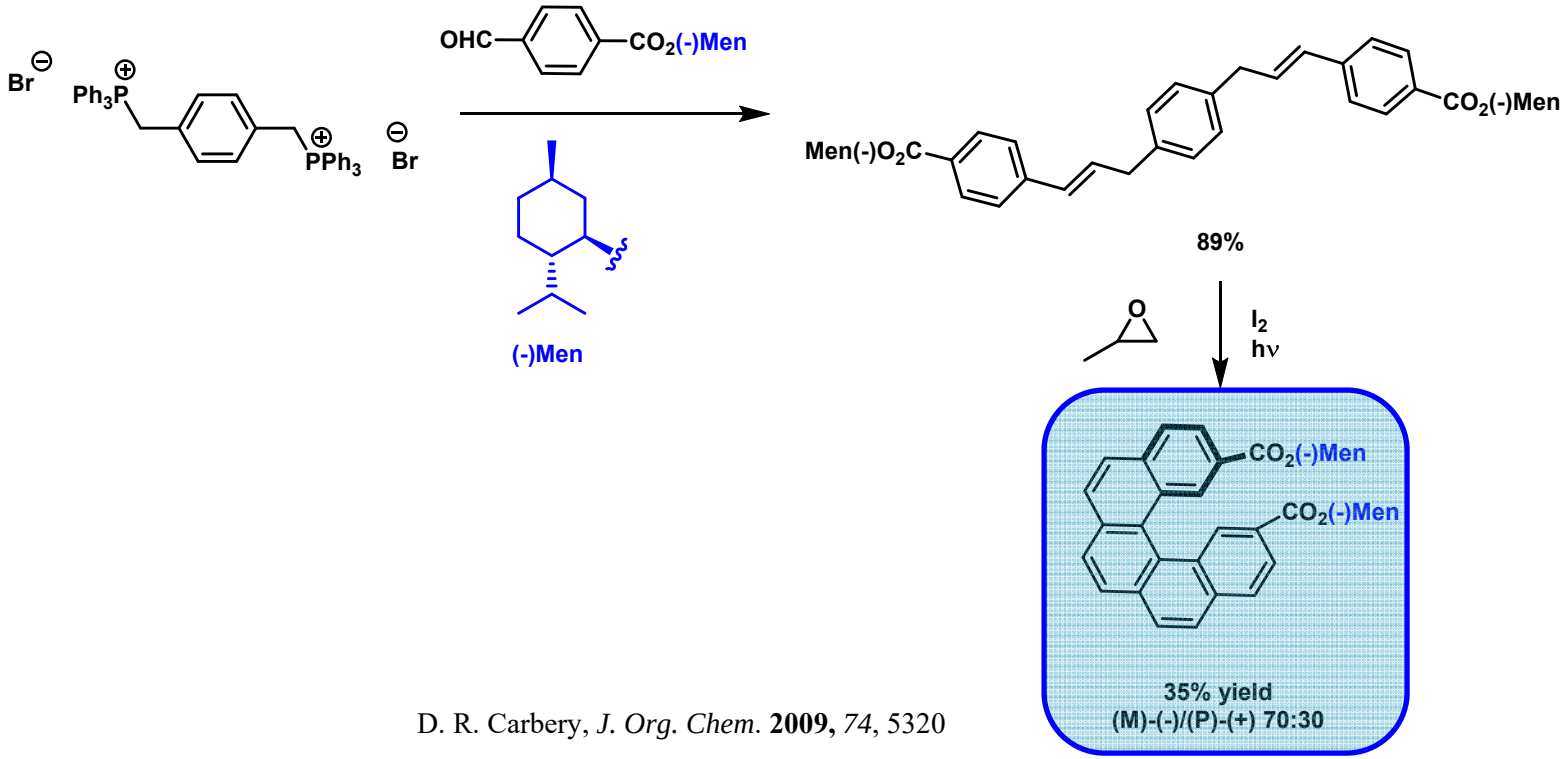
Enantioselective synthesis

Chiral auxiliary

Use of chiral auxiliary

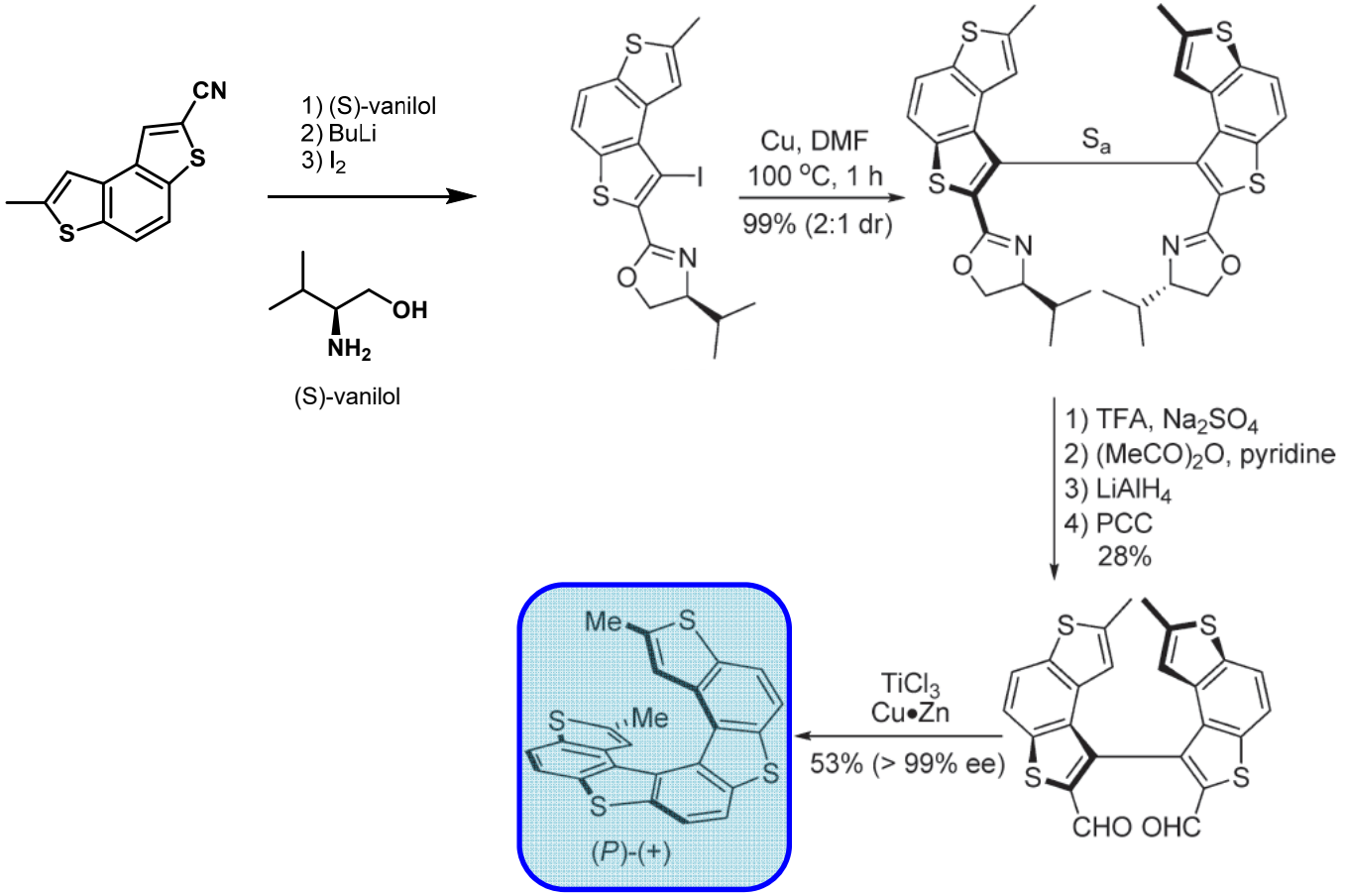


R. H. Martin, *Tetrahedron Lett*. **1972,** *28*, 2842



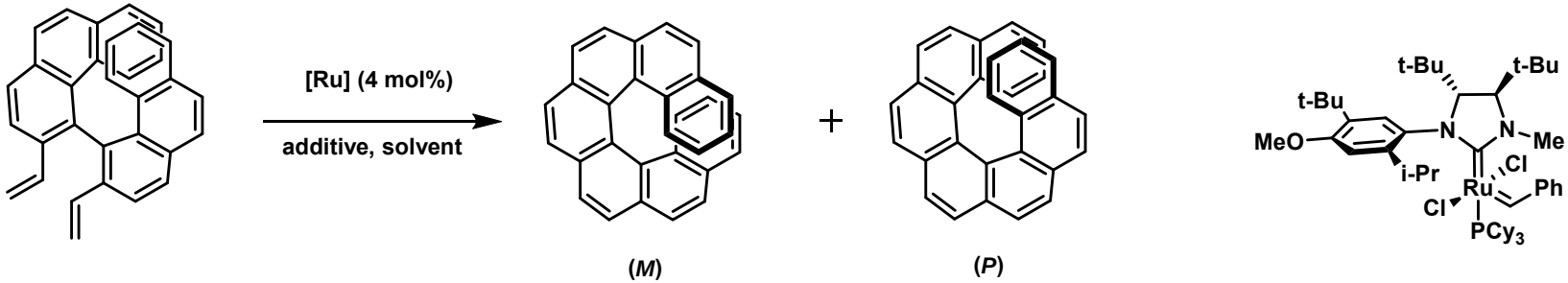
D. R. Carbery, *J. Org. Chem*. **2009,** *74*, 5320

Use of chiral auxiliary



K. Tanaka, *J. Org. Chem.* **1997,** *62*, 4465

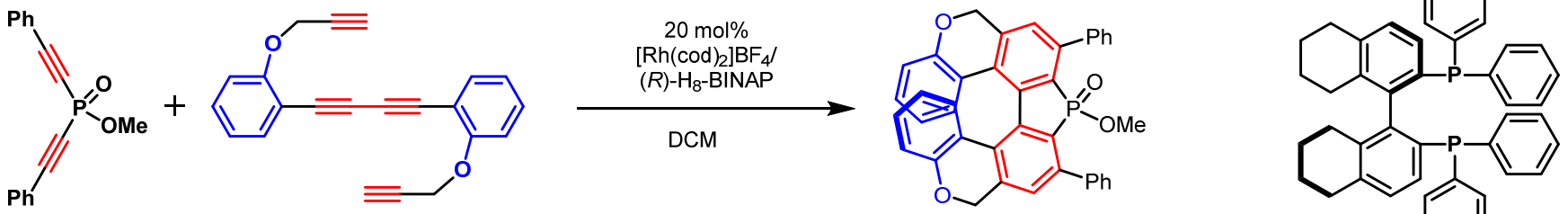
Enantioselective synthesis



Solvent	Additive	Conversion (%)	ee (%) (conf)
DCM	1-hexene	40	48 (*M*)
DCM	vinycyclohexane	43	53 (*M*)
Benzene	vinycyclohexane	32	65 (*M*)
C_6F_6	vinycyclohexane	38	80 (*M*)

S. K. Collins, *Chem Eur. J.* **2008,** *14*, 9323

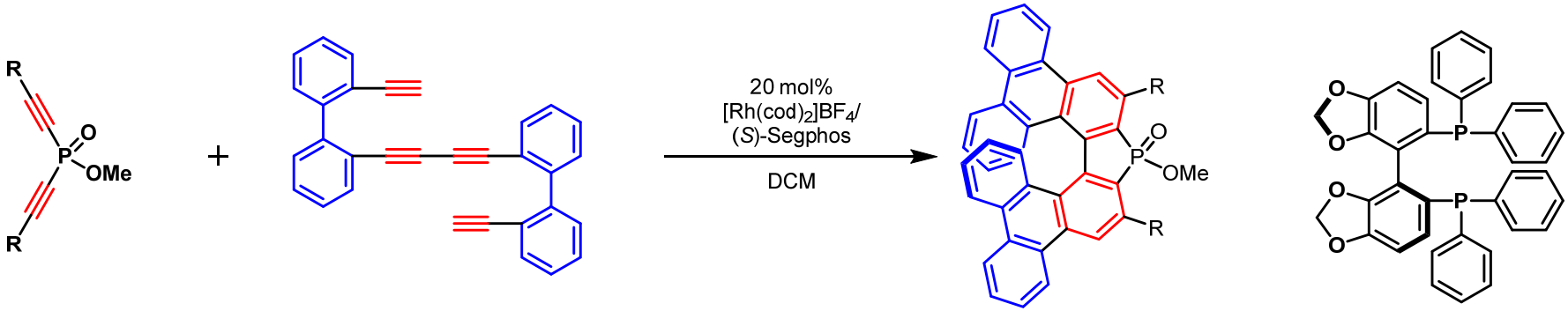
Enantioselective synthesis



40% yield
73% *ee*

(*R*)-H_8-BINAP

Tanaka, *Org. Lett.* **2010**, *12*, 1324



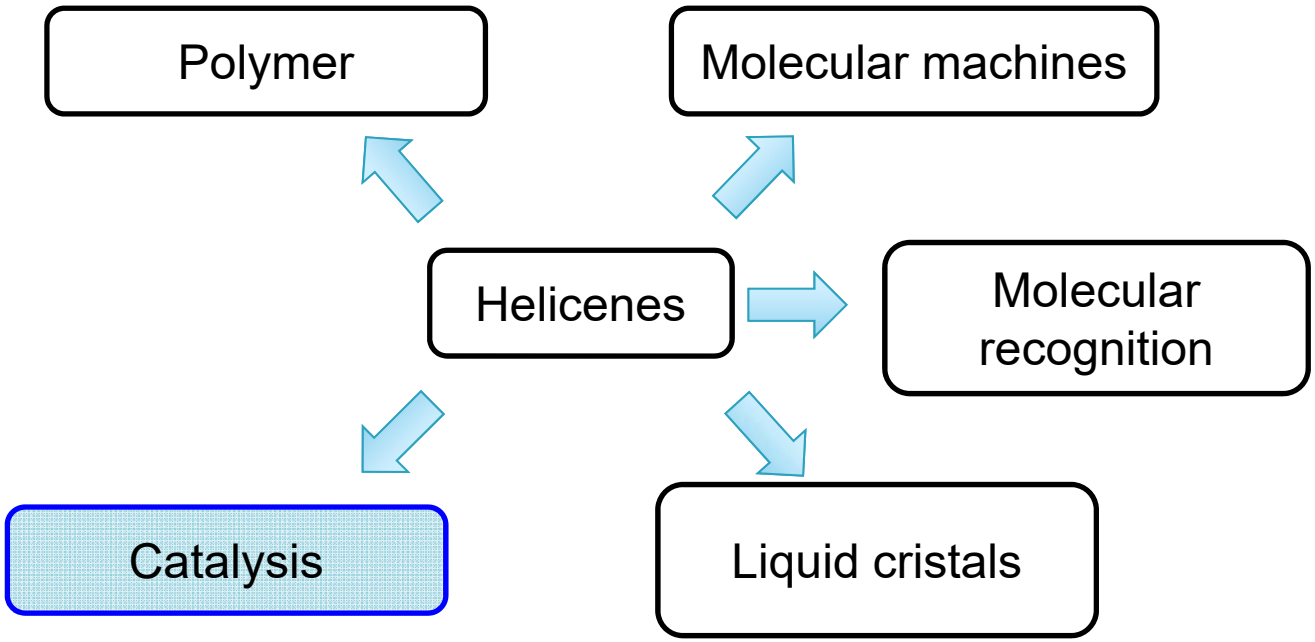
43-46% yield
75-68% *ee*

(*S*)-SEGPHOS

K. Tanaka, *J. Am. Chem. Soc.* **2012**, *134*, 4080

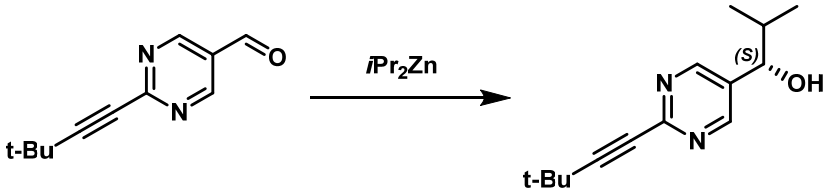
Applications

Applications



Helicene in catalysis

- Autocatalyzed reaction



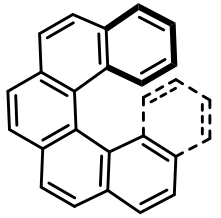
(P)-(+)-[5]helicene
(P)-(+)-[6]helicene

88-90% yield
95% *ee*

(*M*)-(-)-[5]helicene
(*M*)-(-)-[6]helicene

89-93% yield
93-94% *ee*

(*P*)-(+)-[5]helicene
(*P*)-(+)-[6]helicene



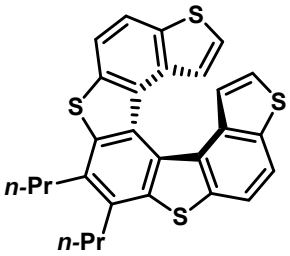
(*M*)-(-)-[5]helicene
(*M*)-(-)-[6]helicene

(*P*)-(+)-tetrathia[7]helicene

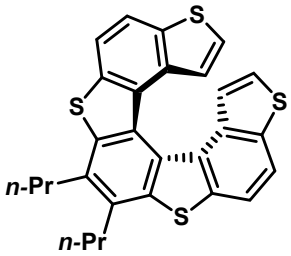
88% yield
99% *ee*

(*M*)-(-)-tetrathia[7]helicene

88% yield
95% *ee*



(*P*)-(+)-tetrathiahelicene



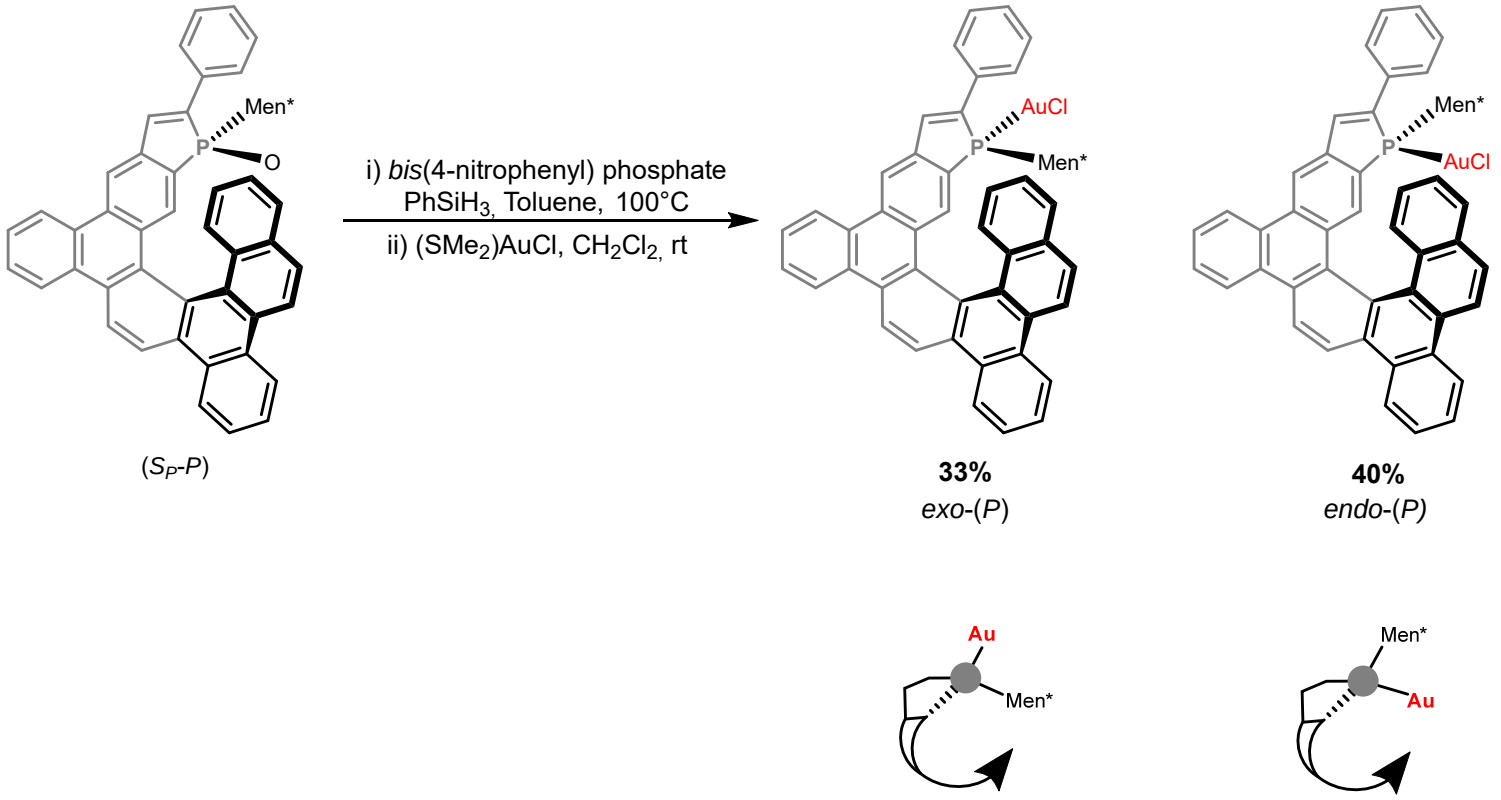
(*M*)-(-)-tetrathiahelicene

K. Soai, *Angew. Chem. Int. Ed.* **2001**, *40*, 1098

K. Soai, *Tetrahedron : Asymmetry*. **2006**, *17*, 2050

Helicene in catalysis

- Chiral ligand



(S_P-*P*)

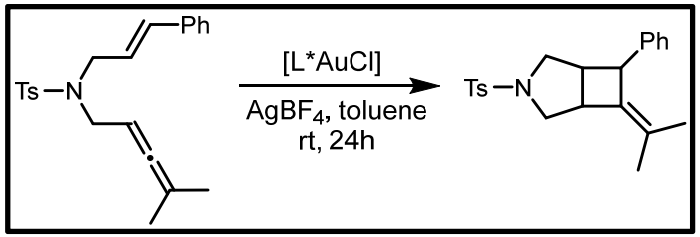
33%
exo-(*P*)

40%
endo-(*P*)

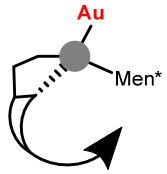
Marinetti, Angew. Chem. Int. Ed. **2014**, *53*, 861

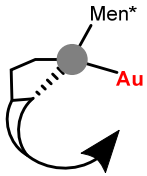
Helicene in catalysis

- Chiral ligand

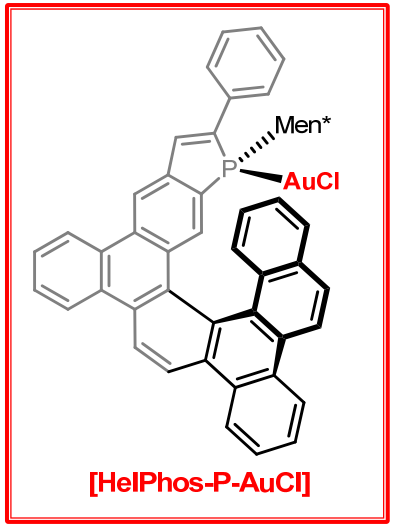


[L*AuCl] =





	Exo-(P)	Endo-(P)
Conv (%)	30	>95
ee (%)	41	**88**

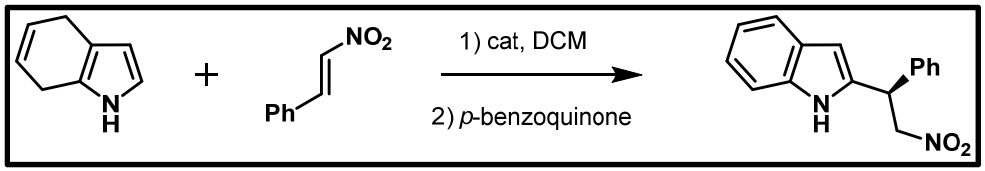


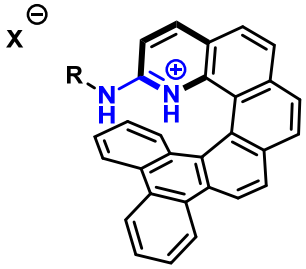
[HelPhos-P-AuCl]

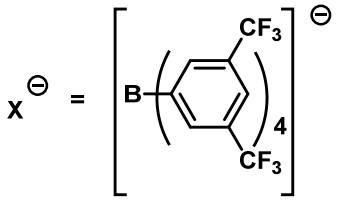
Marinetti, Angew. Chem. Int. Ed. **2014**, *53*, 861

Helicene in catalysis

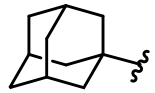
- Organocatalyst







ad =



R	mol%	Temp (°C)	time (h)	Yield (%)	*er*
H	10	-40	20	**85**	69:31
Bn	2	-40	20	**72**	69:31
t-Bu	2	-40	20	**79**	92:8
ad	2	-40	20	**88**	93:7
ad	0,5	-40	48	**80**	92:8

Takenaka, *J. Am. Chem. Soc.* **2010**, *132*, 4536

Conclusion

- Numerous ways to generate helicene
- Special properties
- Wide range of application
- Still studied after more a century

Thank you for you attention