金属-氮宾插入烯烃下的不对称氮杂环丙烷化反应

Enantioselective Azirdination By Addition of Metal–Nitrenes to Olefins

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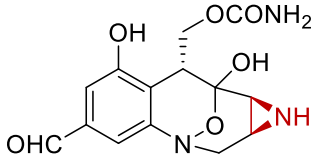
2025 年 09 月 26 日

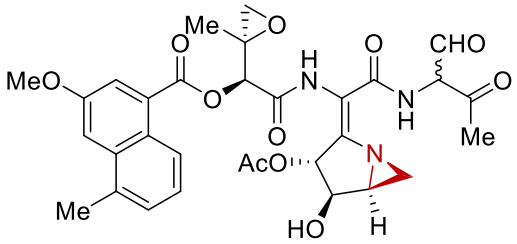
Content

Content

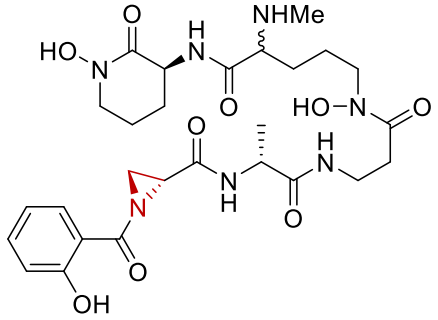
1 Background



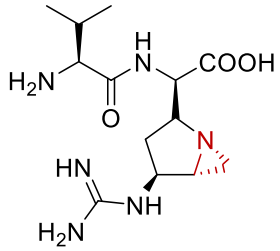
FR-9000482
潜在抗肿瘤活性



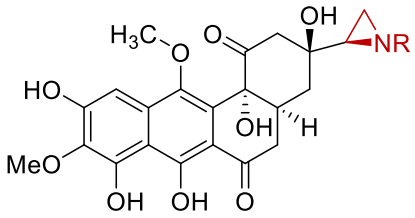
Azinomycin B
潜在抗肿瘤活性



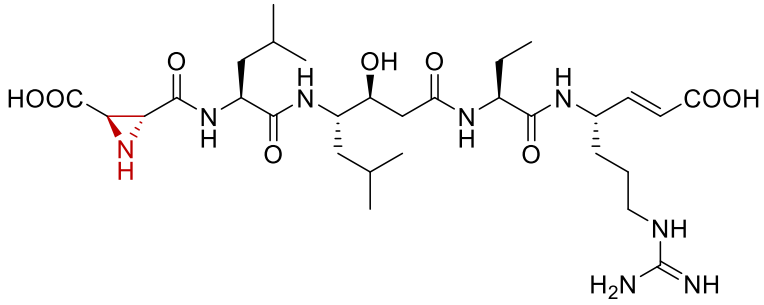
Madurastatin A1
抗菌活性



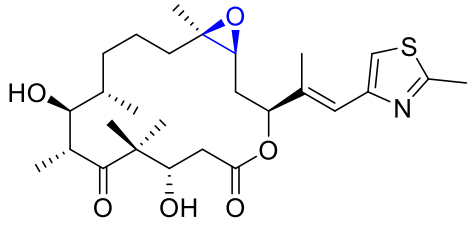
Ficellomycin
抗革兰氏阳性菌活性



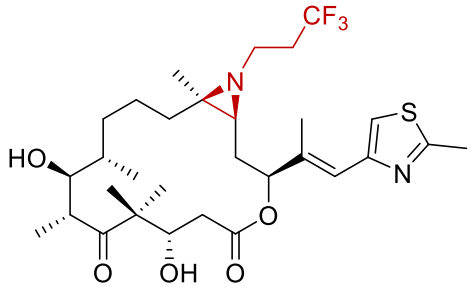
Azicemicin A: R = H;
Azicemicin B: R = Me
抗革兰氏阳性菌活性



Miraziridine
Cathepsin B抑制剂



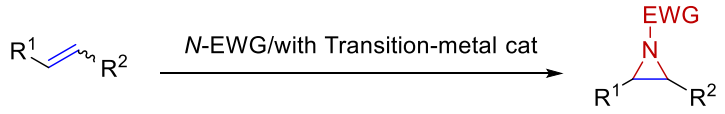
Epothilone B
IC_{50} = 1.27 nM (SKOV3)



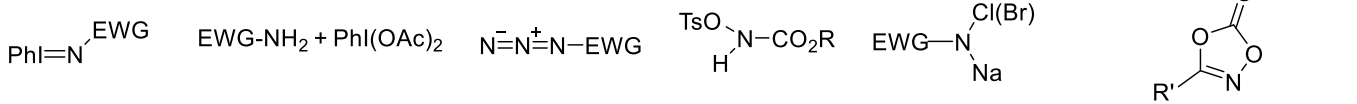
IC_{50} = 0.01 nM (SKOV3)

Komaki, H. et al. *J. Antibiot.* **2004**, *57*, 125−135. Furmeier, S. et al. *Eur. J. Org. Chem*. **2003**, *2003*, 649−659.
Takeuchi, T. et al. *J. Antibiot*. **1995**, *48*, 1148−1152. Takeuchi, T. et al. *J. Antibiot*. **1995**, *48*, 217−221.
Genisson, Y. et al. *Tetrahedron.* **2011**, *67*, 2570−2578. Dembitsky, V. M. et al. *Eur. J. Med. Chem*. **2009**, *44*, 3373−3387.
Nicolaou, K. C. et al. *J. Org. Chem*. **2020**, *85*, 2865−2917.

1 Background



Metal-nitrenoid sources



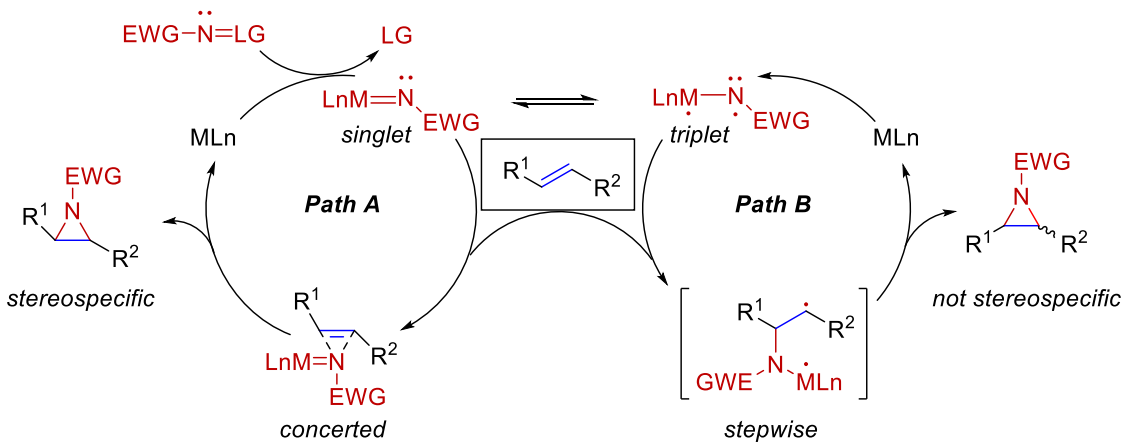
iminoiodinanes | Amine + oxidant | Organo azide | *N*-tosylate | Haloamine-T | 3-R'-1,4,2-dioxazol-5-one

Metal-nitrenoid species

M = Cu, Co, Ru, Rh, Mn, Fe, etc.
Ln = porphyrin, oxazoline, acac, imine, etc.

singlet *triplet*

Mechanism

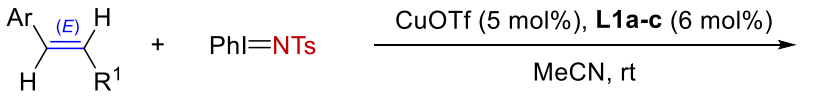


Luisi, R. et al. *Chem. Rev.* **2014**, *16,* 7881−7929. Wang, S.-G. et al. *ChemCatChem* **2024**, *16*, e202400791.

Content

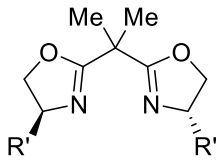
2.1 Metal–Nitrenes from Iminoiodinanes

a. Evans (1993)

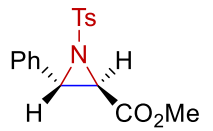


R^1 = H, Me, CO_2Ph, CO_2Me, $CO_2{}^tBu$

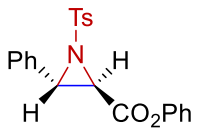
only 7 examples
up to 89% yield
97% ee



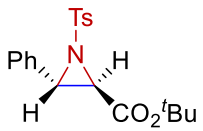
L1a, R' = Ph
L1b, R' = ^{t}Bu
L1c, R' = CMe_2Ph



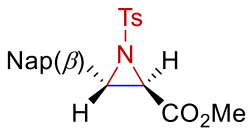
63%, 94% ee (1*R*, 2*S*)



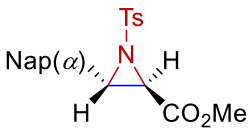
64%, 97% ee (1*R*, 2*S*)



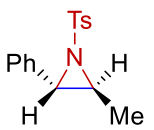
60%, 96% ee (1*R*, 2*S*)



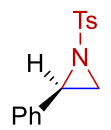
73%, 96% ee (1*R*, 2*S*)



76%, 95% ee (1*R*, 2*S*)

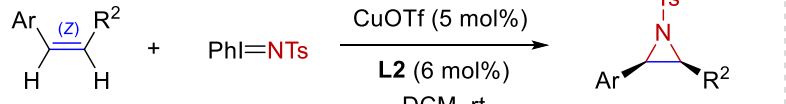


62%, 70% ee (1*S*, 2*R*)



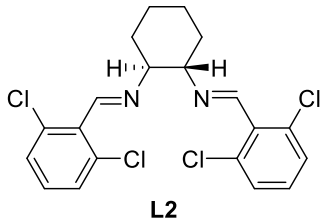
89%, 63% ee (*R*)

b. Jacobsen (1993)



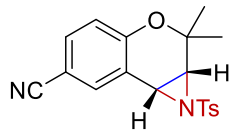
R^2 = H, alkyl

only 5 examples
up to 79% yield
>98% ee

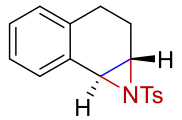


L2

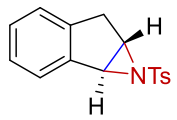
首次实现氮杂环丙烷骨架的不对称构建



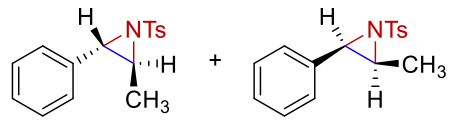
75%, >98% ee (3*R*, 4*R*)



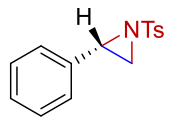
70%, 87% ee (1*R*, 2*S*)



50%, 58% ee (1*R*, 2*S*)



79%, (*cis*:*trans* = 3:1)
cis: 67% ee (1*R*, 2*S*), *trans*: 81% ee (1*S*, 2*S*)

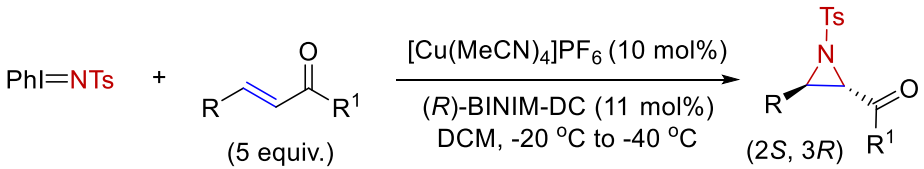


79%, 66% ee (*R*)

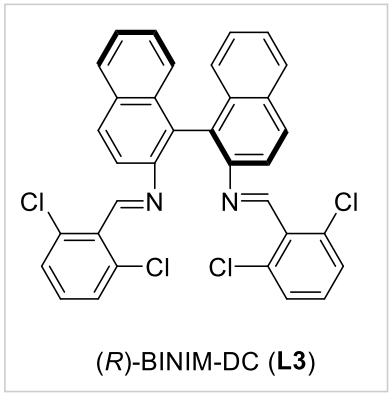
Evans, D.D. et al. *J. Am. Chem. Soc.* **1993**, *115*, 5328−5329. Jacobsen, E.N. et al. *J. Am. Chem. Soc*. **1993**, *115*, 5326−5327.

2.1 Metal–Nitrenes from Iminoiodinanes

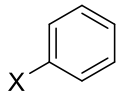
Suga (2003)



R = ***Aryl***, 52-87% yield, er > 83:17

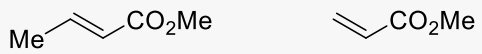


(*R*)-BINIM-DC (**L3**)

R = 

X = H, Cl. CN, Me

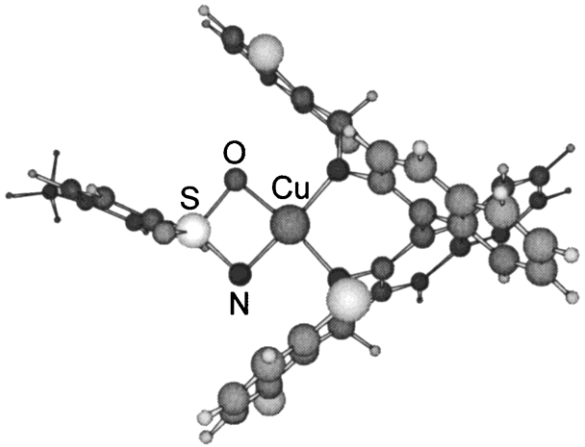
R^1 = O^{t}Bu, OMe, OPh, Me, Ph



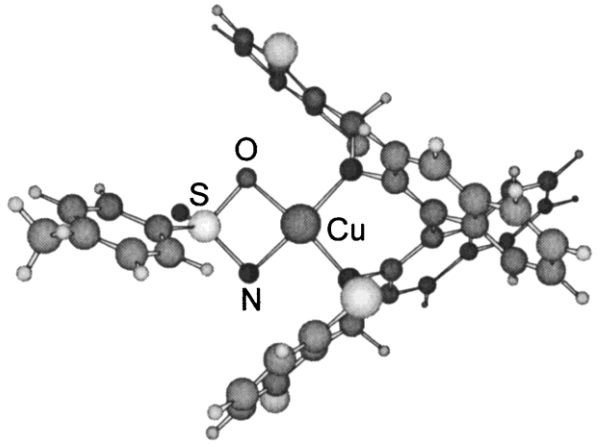
13% yield, er: 68:32

30% yield, er: 71:29

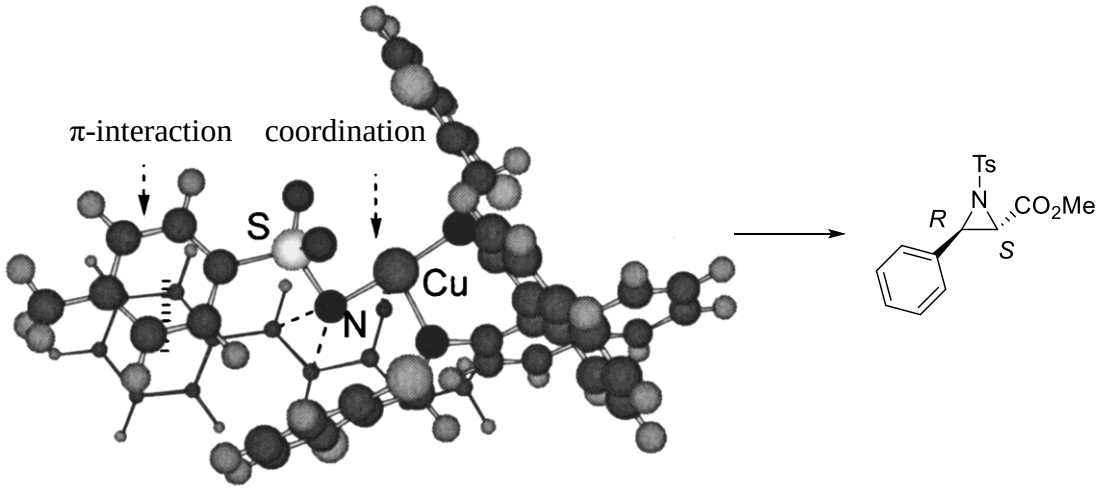
low enantioselectivity



Intermediate A



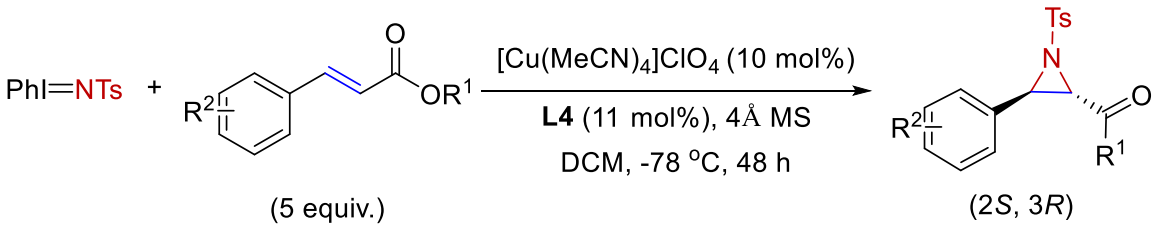
Intermediate B



Suga, H. et al. *Bull. Chem. Soc. Jpn.* **2003**, *76,* 189−199.

2.1 Metal–Nitrenes from Iminoiodinanes

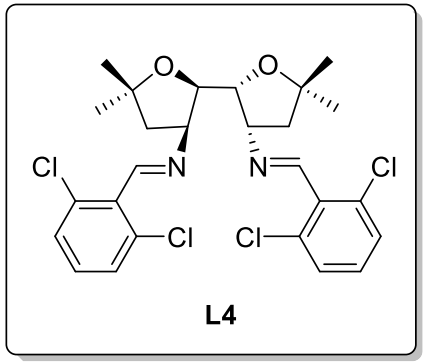
Ding (2006)



(5 equiv.)

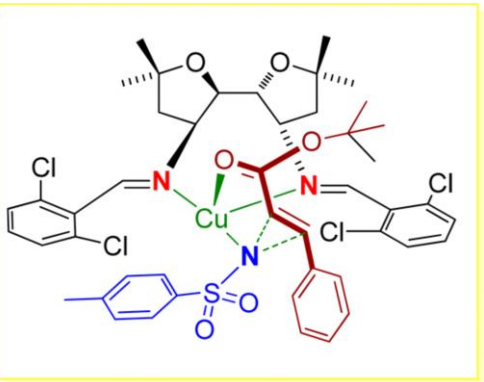
(2*S*, 3*R*)

R^2 = ***Aryl***, 67-99% yield, er > 90:10



L4

Entry	R^1	R^2	Yield (%)	ee (%)	Config.
1	Me	H	97	87.6	2*S*, 3*R* (-)
2	Ph	H	96	87.1	2*S*, 3*R* (-)
3	^{t}Bu	H	99	> 99	2*S*, 3*R* (-)
4	^{t}Bu	4-F	99	97.8	(-)
5	^{t}Bu	4-Cl	97	98.1	(-)
6	^{t}Bu	4-Br	97	98.3	2*S*, 3*R* (-)
7	^{t}Bu	4-Me	86	94.4	(-)
8	^{t}Bu	4-MeO	95	80.1	(+)
9	^{t}Bu	2-NO_2	63	98.6	(+)
10	^{t}Bu	2,3-$(MeO)_2$	67	97.0	(+)



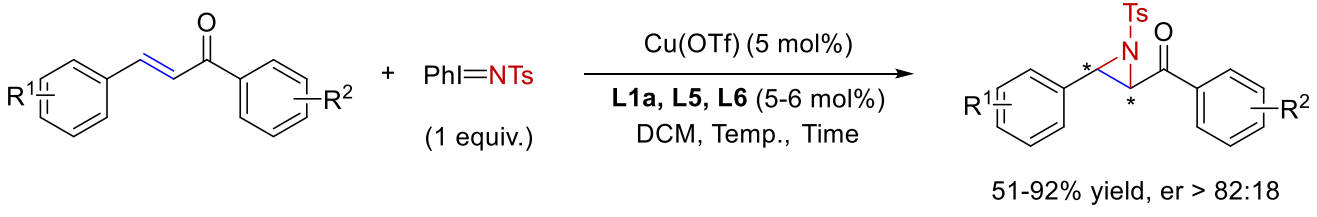
top view

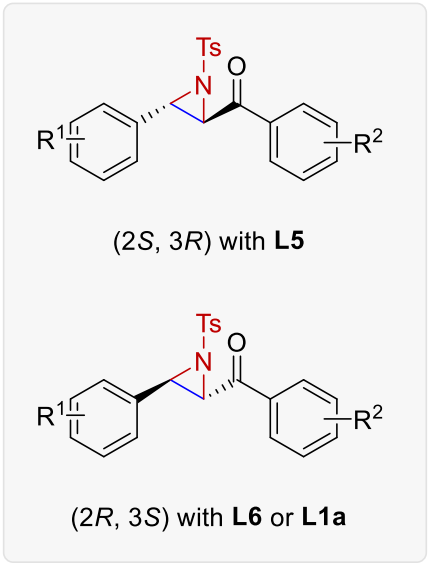
Entries 1-3 通过对照文献旋光度确定绝对构型；Entry 6 通过单晶确定绝对构型，表格中其他产物均为未知产物，未明确给出绝对构型，仅测定旋光

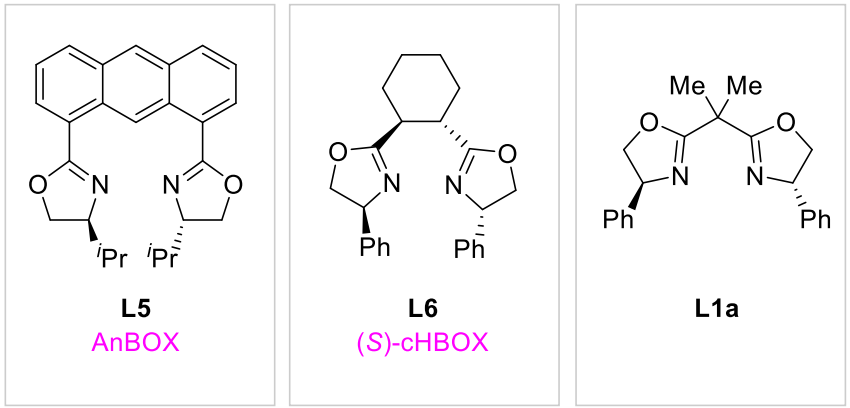
Ding, K. et al. *Chem. Eur. J.* **2006**, *12*, 4568–4575.

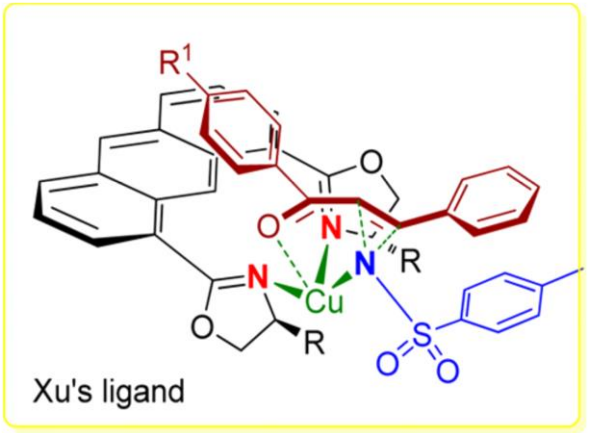
2.1 Metal–Nitrenes from Iminoiodinanes

Xu (2005 and 2007)

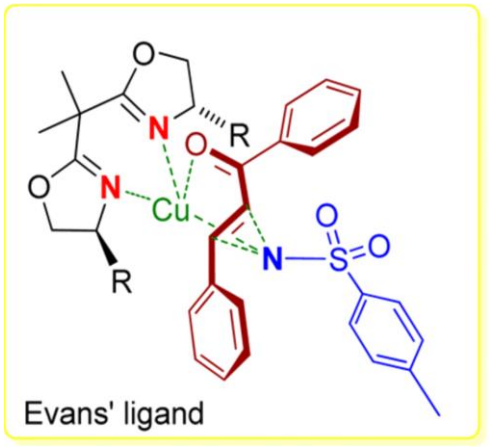








底物苯环和配体骨架
存在相互作用
底物苯环靠近配体

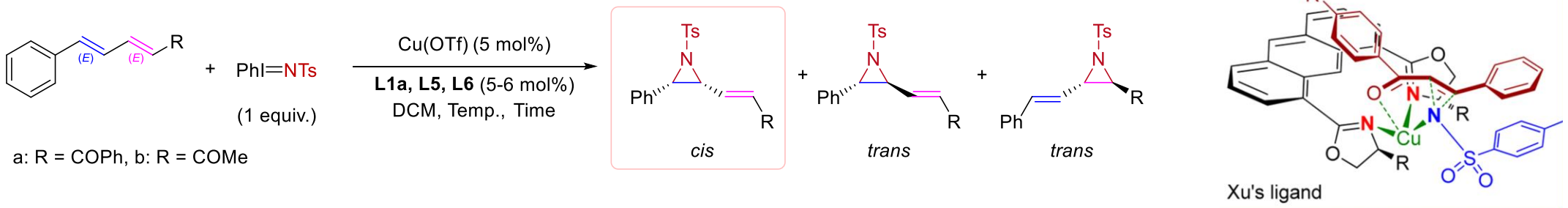


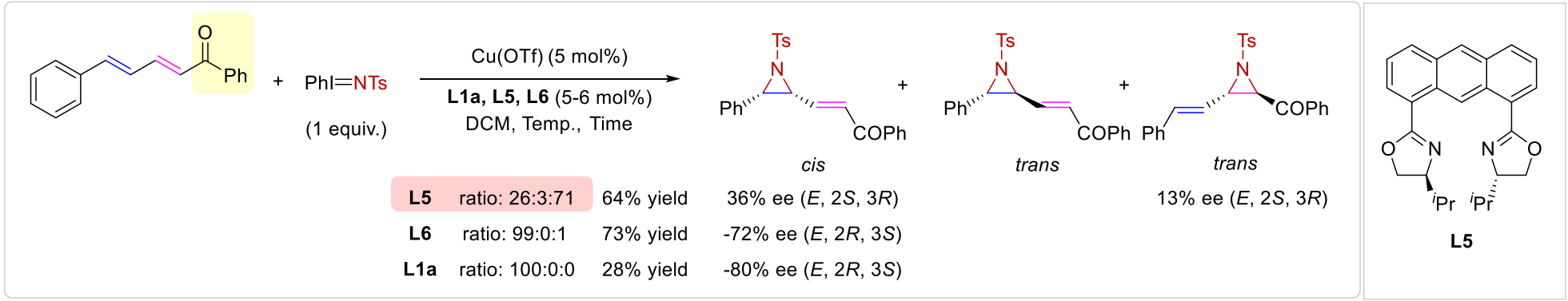
受到位阻影响
底物苯环远离配体

Xu, J. et al. *J. Org. Chem*. **2005**, *70*, 10155−10158. Xu, J. et al. *Tetrahedron: Asymmetry* **2007**, *18*, 878−884.

2.1 Metal–Nitrenes from Iminoiodinanes

Xu (2006)

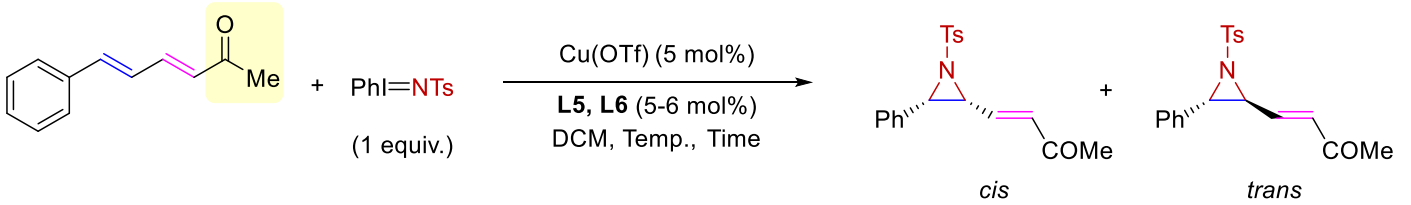




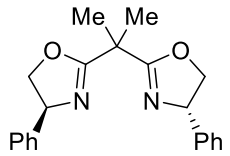
L5	ratio: 26:3:71	64% yield	36% ee (*E*, 2*S*, 3*R*)
L6	ratio: 99:0:1	73% yield	-72% ee (*E*, 2*R*, 3*S*)
L1a	ratio: 100:0:0	28% yield	-80% ee (*E*, 2*R*, 3*S*)

13% ee (*E*, 2*S*, 3*R*)

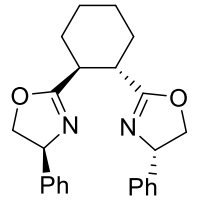
L5



L5	ratio: 100:0	51% yield	-6% ee (*E*, 2*R*, 3*S*)
L6	ratio: 100:0	25% yield	-19% ee (*E*, 2*R*, 3*S*)



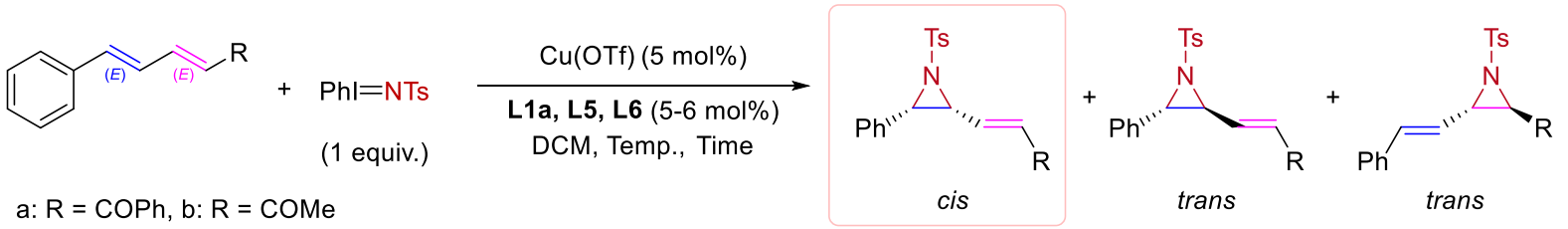
L1a

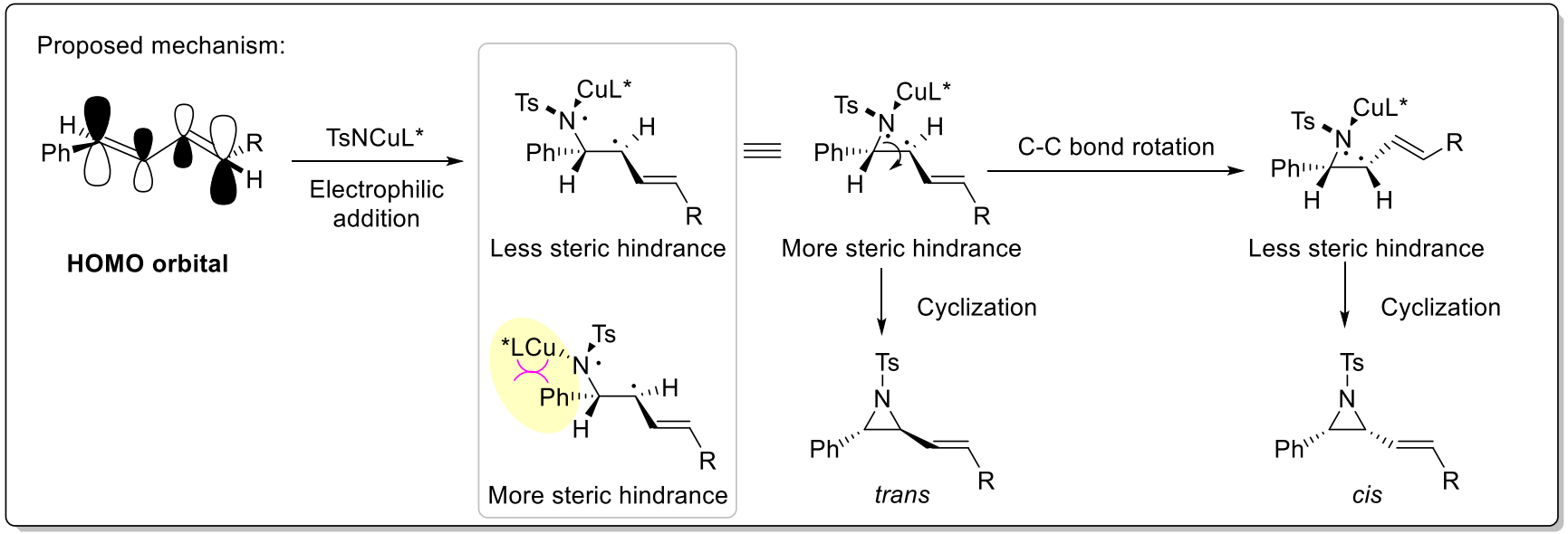


L6

Xu, J. et al. *Chirality* **2006**, *18*, 575–580.

2.1 Metal–Nitrenes from Iminoiodinanes

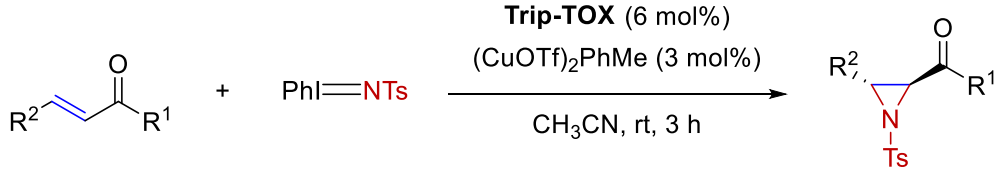




Xu, J. et al. *Chirality* **2006**, *18*, 575–580.

2.1 Metal–Nitrenes from Iminoiodinanes

Gelman (2021)

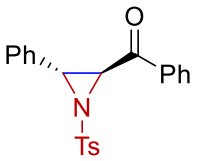


R^1 = Aryl, Furyl, Thienyl, Naphthyl, R^2 = Aryl

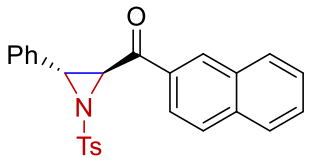
up to 93% yield, 99% ee

C_3对称性进一步

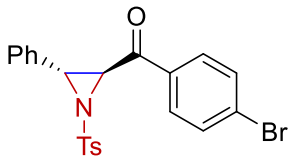
降低底物与催化剂空间自由度



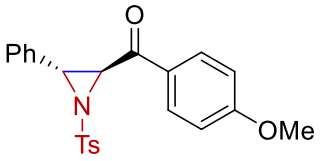
Trip-TOX 93% yield, 76% ee
AnBOX 80% yield, 96% ee



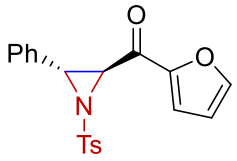
70% yield, 70% ee



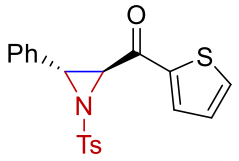
Trip-TOX 80% yield, 77% ee
AnBOX 64% yield, 50% ee



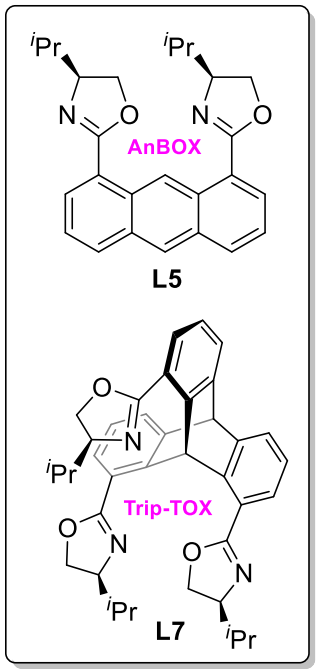
Trip-TOX 63% yield, 77% ee
AnBOX 74% yield, 62% ee

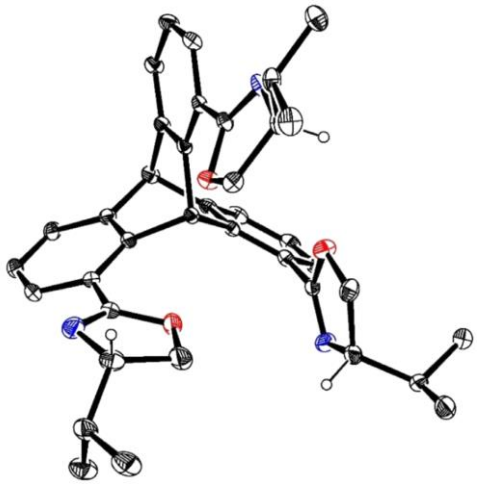


64% yield, 62% ee



62% yield, 71% ee

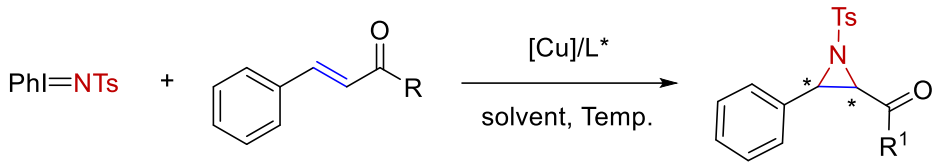




Gelman, D. et al. *J. Organomet. Chem*. **2021**, *941*, 121804–121811.

2.1 Metal–Nitrenes from Iminoiodinanes

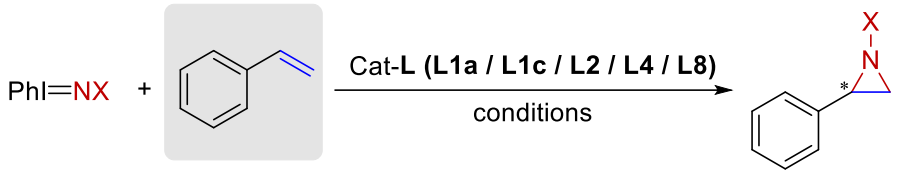
查尔酮类底物



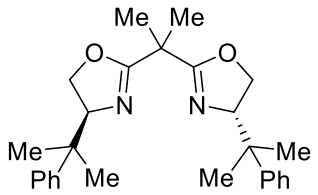
up to 99% yield, 99% ee

活性高、通过底物配位、
手性配体修饰控制立体选择性

更具挑战性的苯乙烯底物



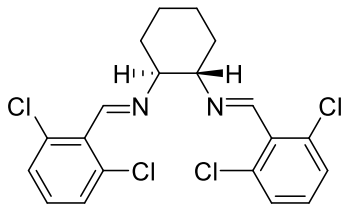
Evans (1993)



L1c

Cat: CuOTf (5 mol%), **L1c** (6 mol%)
styrene, 0 °C, 2.5 h
X = Ts, 89%, er: 81.5:18.5
(*R*) configuration

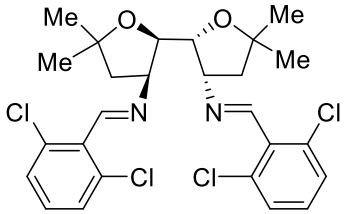
Jacobsen (1993)



L2

Cat: CuOTf (10 mol%), **L2** (11 mol%)
DCM, -78 °C
X = Ts, 79%, er: 83:17
(*R*) configuration

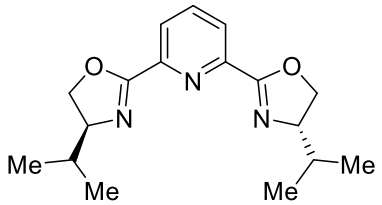
Ding (2006)



L4

Cat: $[Cu(MeCN)_4]ClO_4$ (10 mol%), **L4** (5 mol%)
4Å MS, DCM, -78 °C, 48 h
X = Ts, 99%, er: 64:36
(*S*) configuration

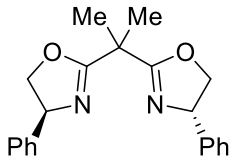
Bolm (2008)



L8

Cat: $Fe(OTf)_2$ (5 mol%), **L5** (30 mol%)
4Å MS, MeCN, rt, 1 h
X = Ts, 72%, er: 70:30
(*R*) configuration

Hutchings (2003)



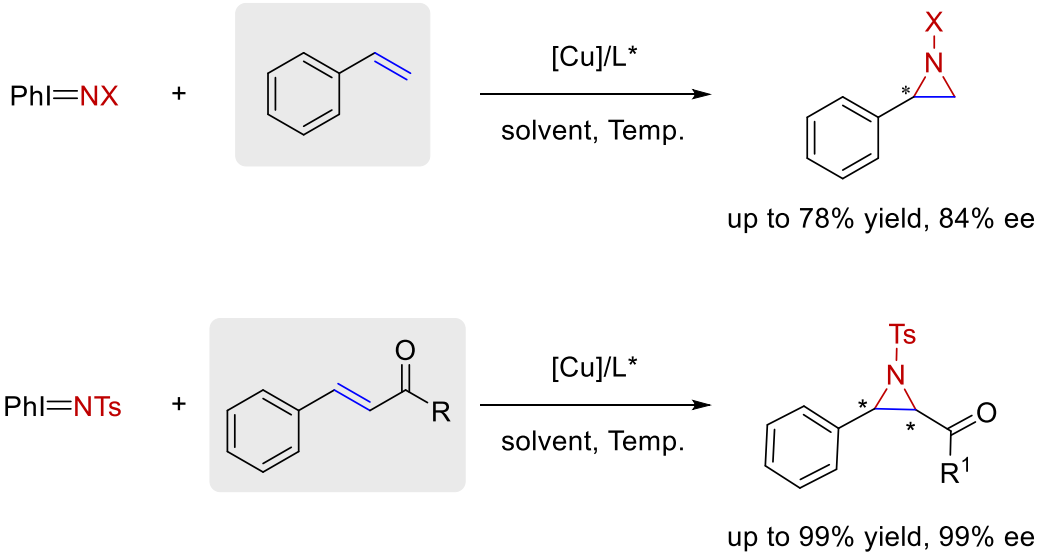
L1a

Cat: Zeolite CuHY, **L1a** (7 mol%)
4Å MS, MeCN, rt, 1 h
X = Ts, 78%, er: 88:12
X = Ns, 78%, er: 92:8

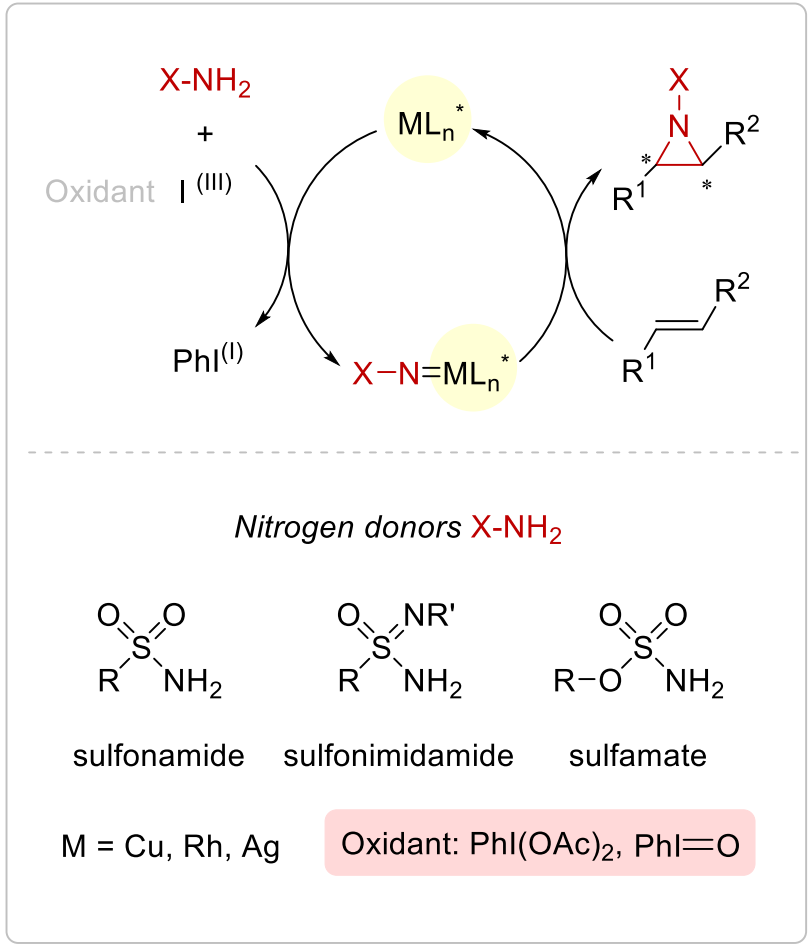
Evans, D.D. et al. *J. Am. Chem. Soc.* **1993**, *115*, 5328−5329. Jacobsen, E.N. et al. *J. Am. Chem. Soc*. **1993**, *115*, 5326−5327.
Ding, K. et al. *Chem. Eur. J.* **2006**, *12*, 4568−4575. Bolm, C. et al. *Adv. Synth. Catal*. **2008**, *350*, 1835−1840.
Hutchings, G. J. et al. *Chem.Commun*. **2003**, 2808−2809. Hutchings, G. J. et al. *Top. Catal.* **2003**, *25*, 81−88.

Content

2.2 Metal–Nitrenes from Amides Derivatives



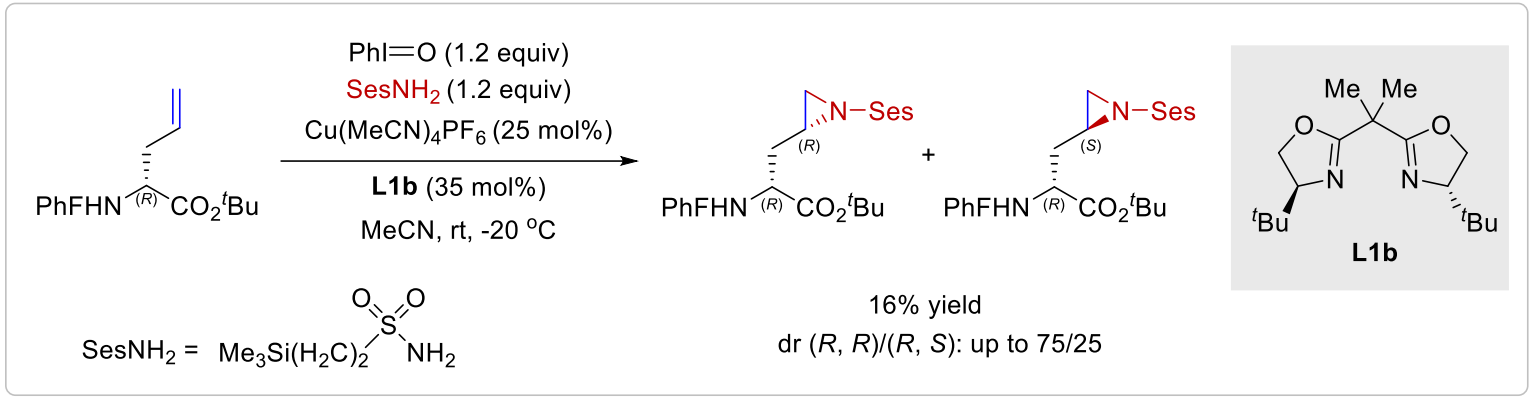
底物类型相对单一、亚胺类前体不稳定



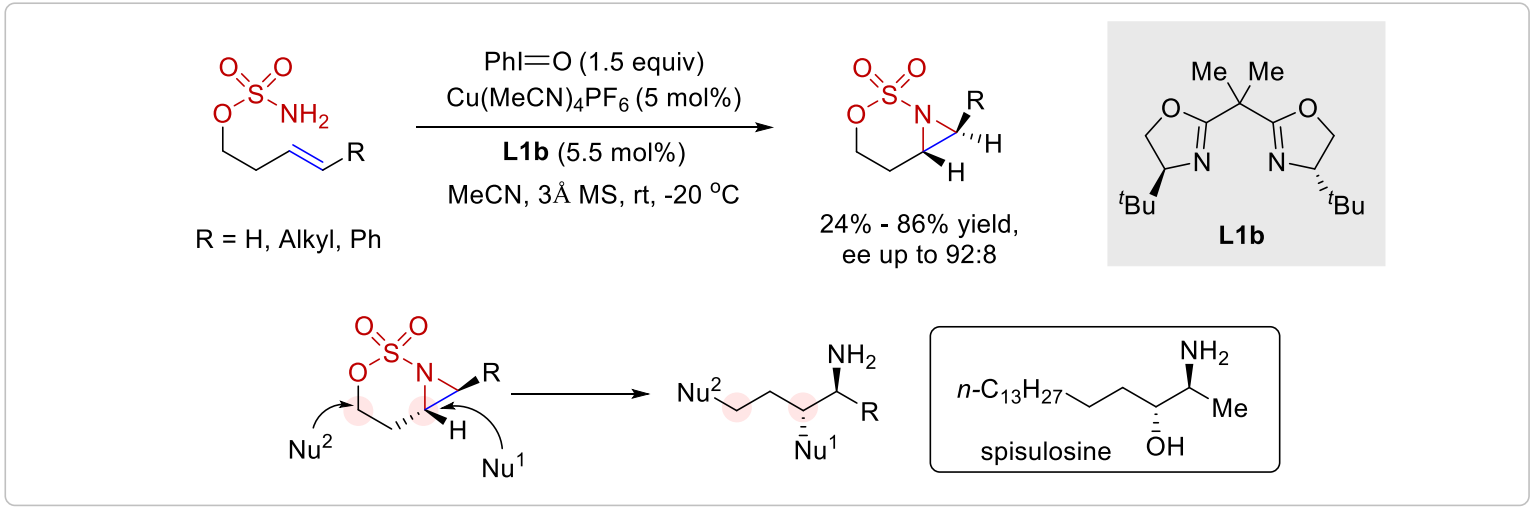
Luisi, R. et al. *Chem. Rev.* **2014**, *16,* 7881−7929. Wang, S.-G. et al. *ChemCatChem* **2024**, *16*, e202400791.

2.2 Metal–Nitrenes from Amides Derivatives

Dodd and Dauban (2004)



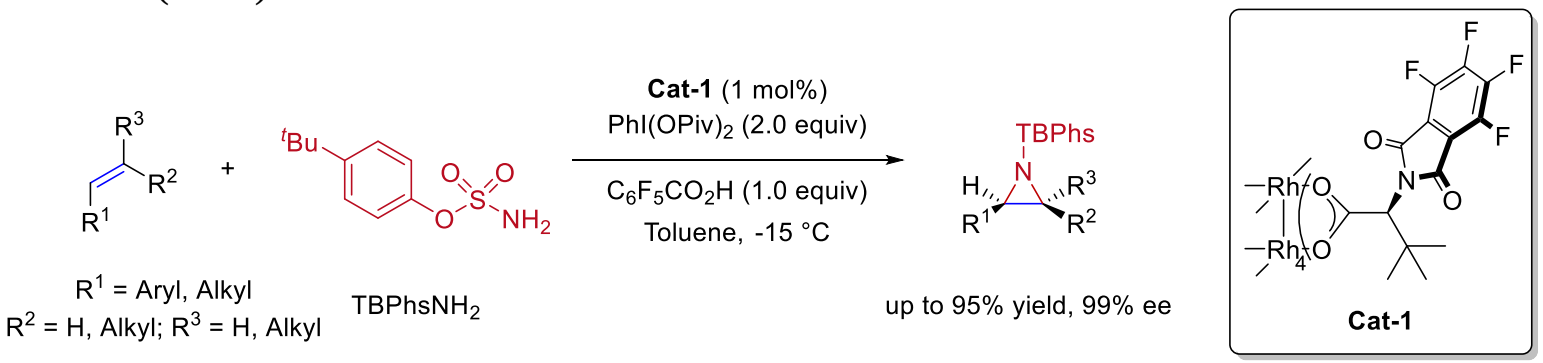
Dodd and Dauban (2007)



Dauban, P., Dodd, R. H. et al. *Tetrahedron* **2004**, *60*, 5889−5897. Dauban, P., Dodd, R. H. et al. *Synthesis* **2007**, *8*, 1251−1260.

2.2 Metal–Nitrenes from Amides Derivatives

Dauban (2022)

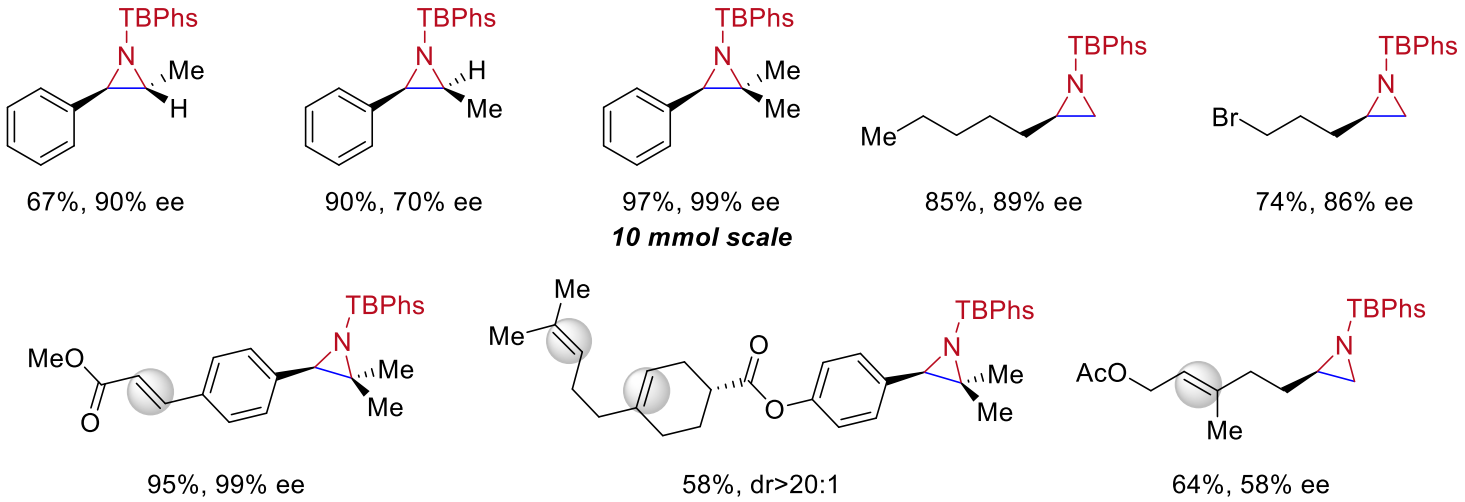


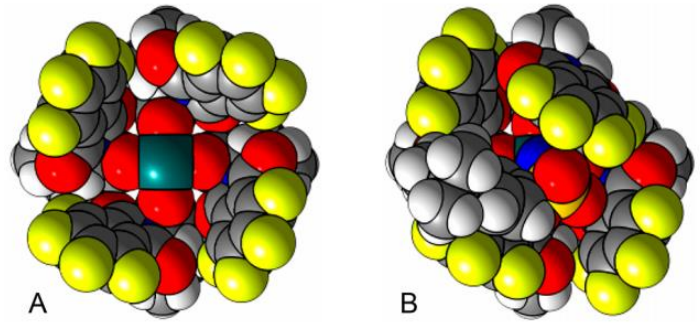
R^1 = Aryl, Alkyl
R^2 = H, Alkyl; R^3 = H, Alkyl

$TBPhsNH_2$

up to 95% yield, 99% ee

Selected examples

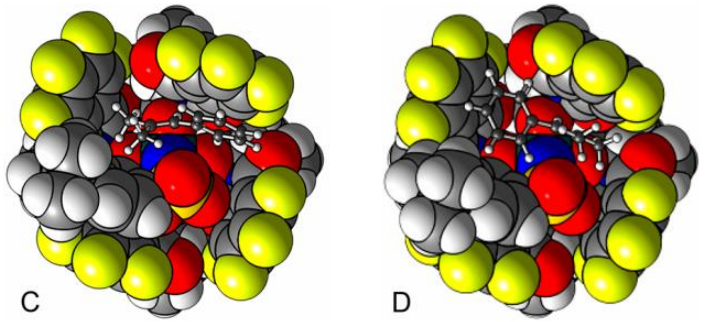




$^3Rh_2$

$^3Rh_2N$

2



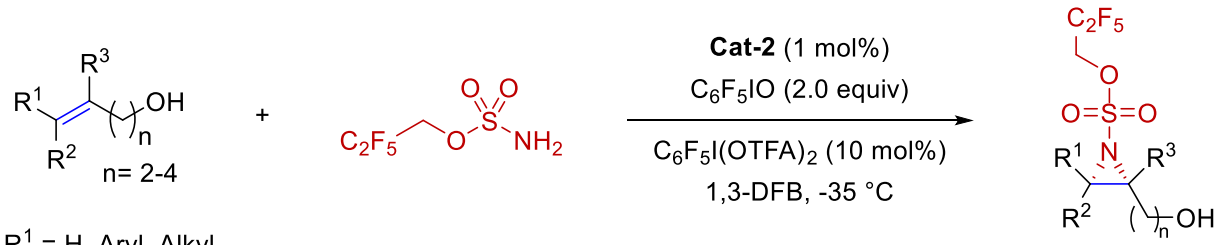
$^3RhN{:}Styr_{Si}$

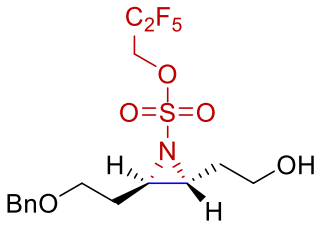
$^3RhN{:}Styr_{Re}$

Dauban, P. et al. *J. Am. Chem. Soc.* **2022**, *144*, 17156−17164.

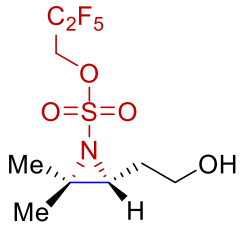
2.2 Metal–Nitrenes from Amides Derivatives

Phipps (2023)

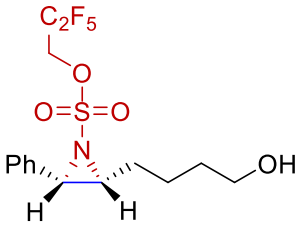




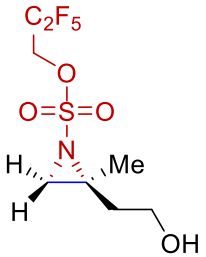
from *Trans*-substrate
53%, 91% ee



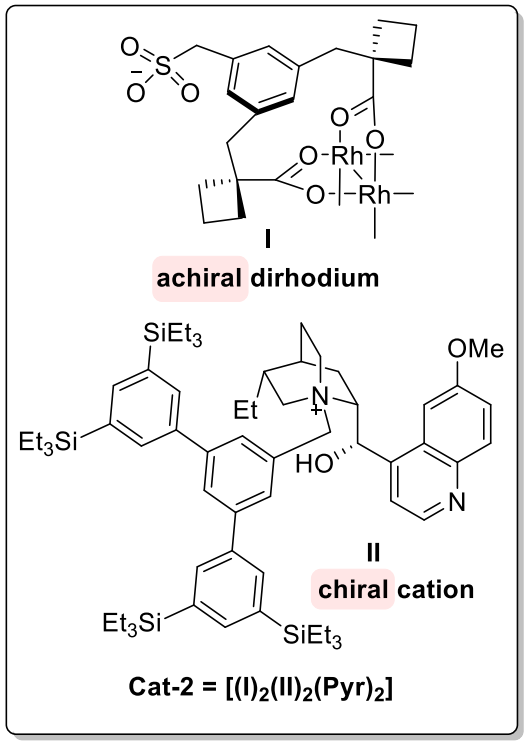
73%, 86% ee

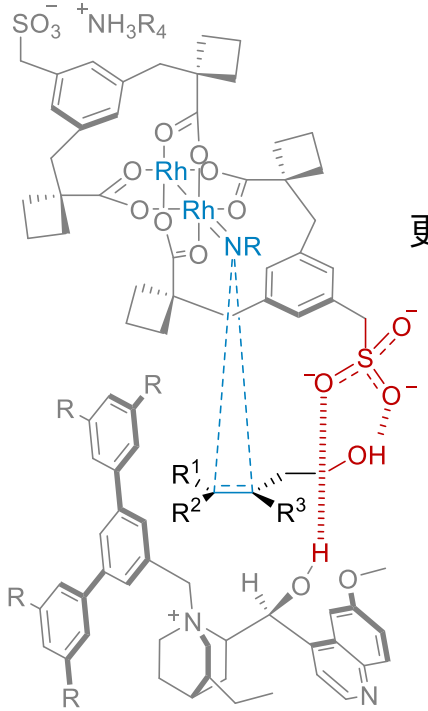


from *Cis*-substrate
72%, 96% ee



72%, 96% ee





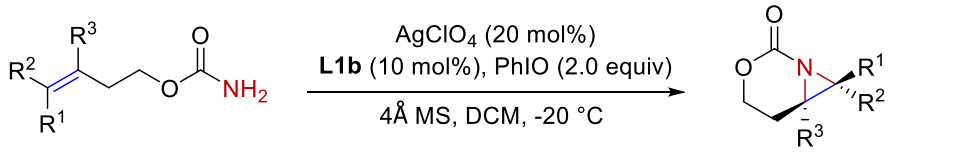
离子对作用构造出
更加牢固的手性空腔

Phipps, R. J. et al. *J. Am. Chem. Soc.* **2023**, *145*, 7516−7527.

2.2 Metal–Nitrenes from Amides Derivatives

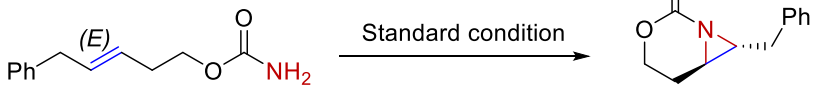
Schomaker (2017)

首次实现Ag催化体系下的不对称氮杂环丙烷化反应



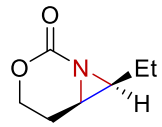
up to 87% yield, 92% ee

Selected examples

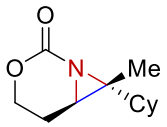


80% yield, 91% ee

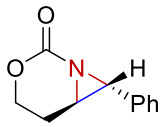
55% yield, 88% ee



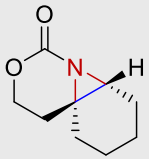
83% yield, 91% ee



84% yield, 90% ee

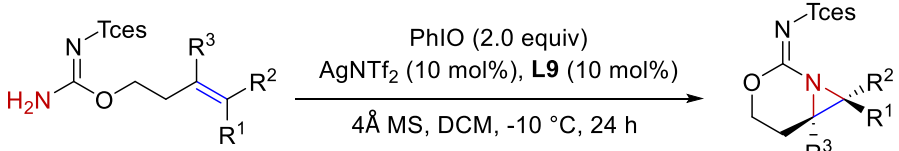


52% yield, 70% ee



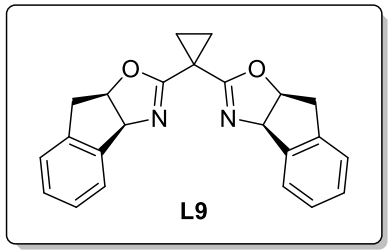
89% yield, 22% ee

Schomaker (2024)

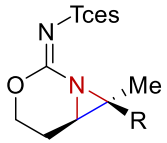


up to 92% yield
99% ee

Tces =

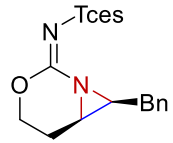


Selected examples



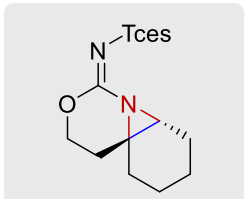
R = Bn, 80% yield, 96% ee

R = Et, 62% yield, 94% ee

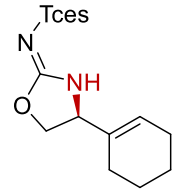


L9: 92% yield, 97% ee

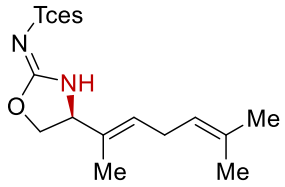
L1b: 75% yield, 35% ee



83% yield, 42% ee



37% yield, 67% ee



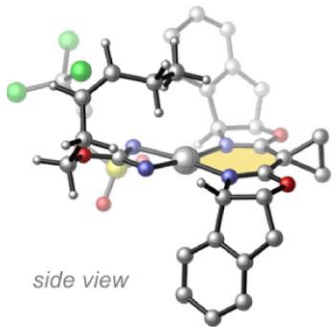
21% yield, 49% ee

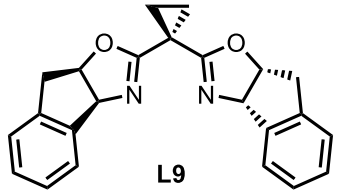
烯丙位胺化副产物

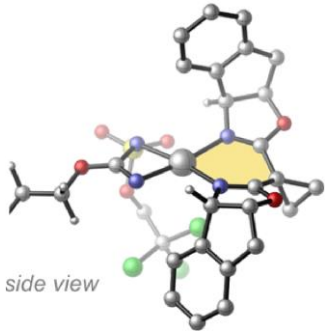
Schomaker, J. M. et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 9944−9948. Schomaker, J. M. et al. *Chem. Commun.* **2024**, *60*, 224−227.

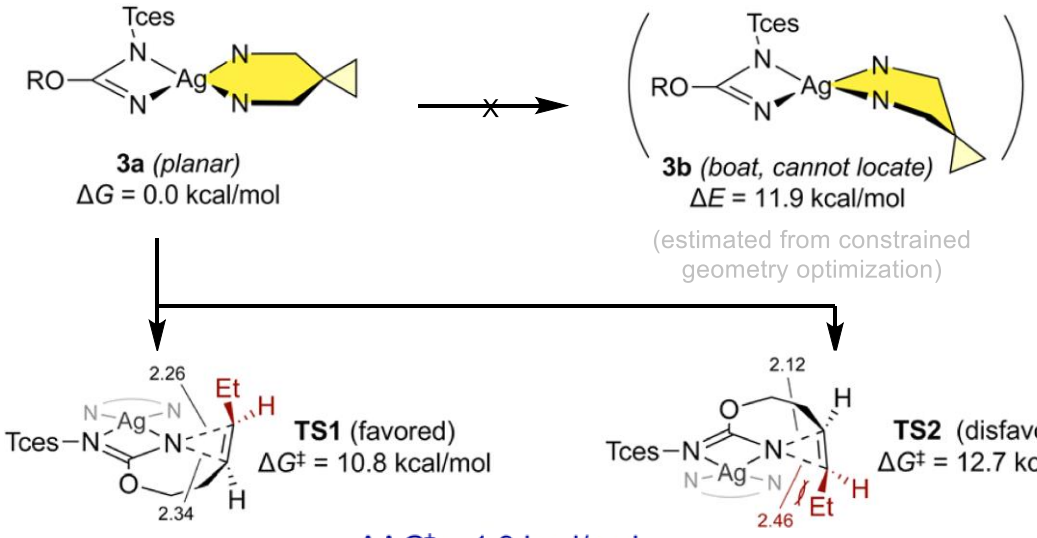
2.2 Metal–Nitrenes from Amides Derivatives

Enantiondution with rigid ligand **L9**

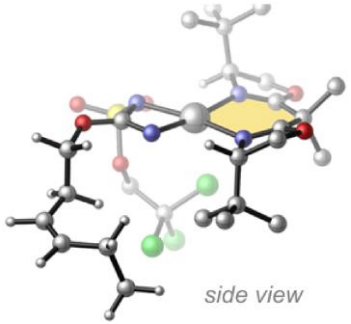


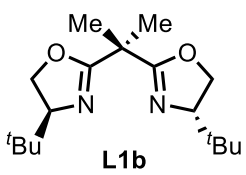


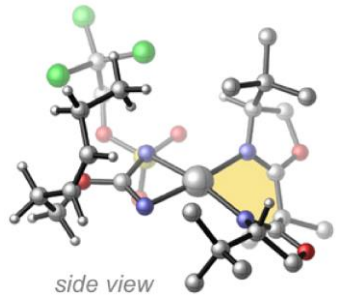


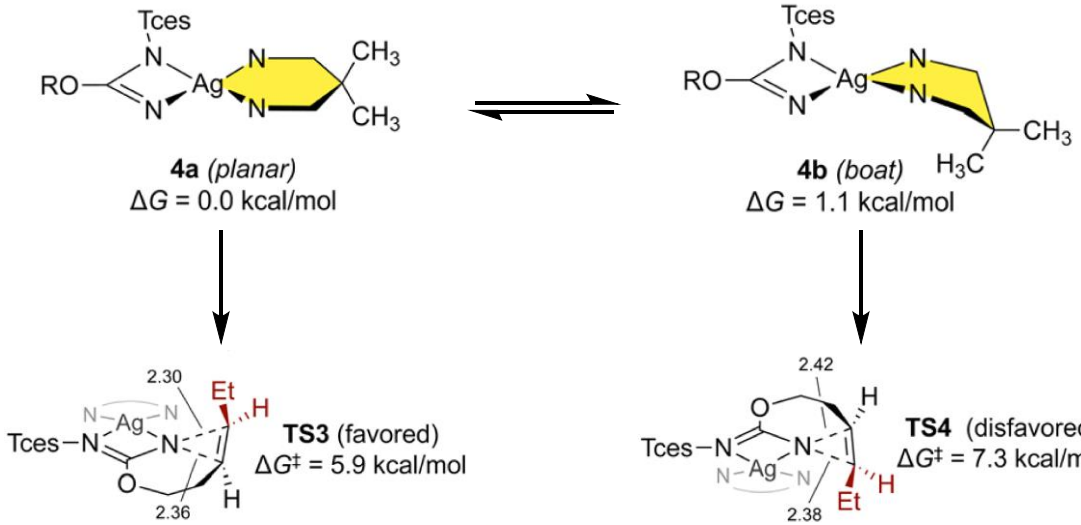


Enantiondution with flexible ligand **L1b**







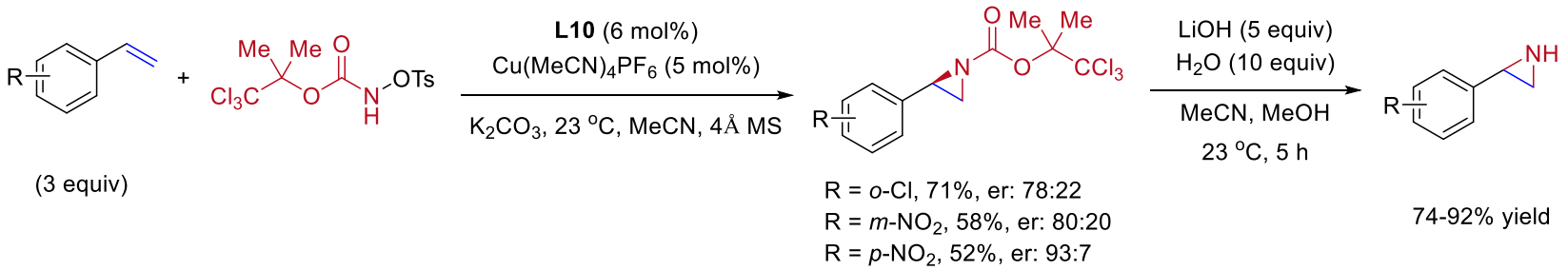


Schomaker, J. M. et al. *Chem. Commun.* **2024**, *60*, 224−227.

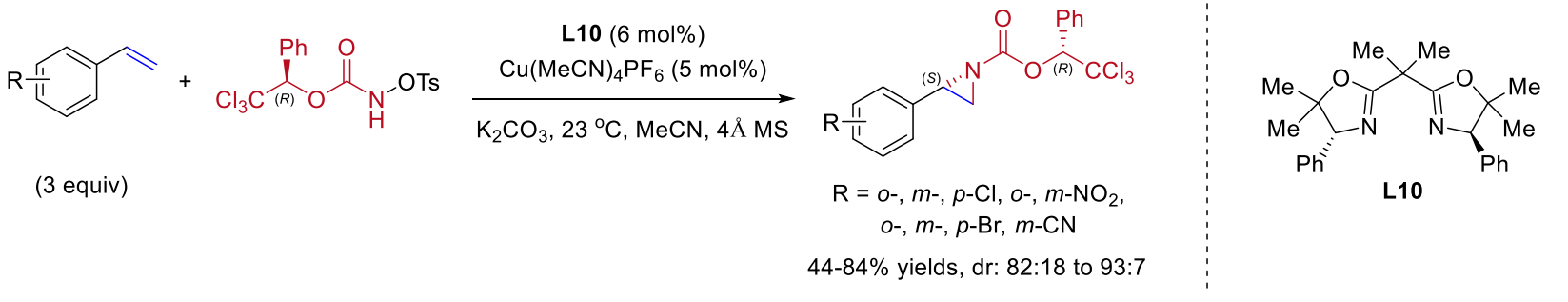
Content

2.3 Metal–Nitrenes from Hydroxylamine Derivatives

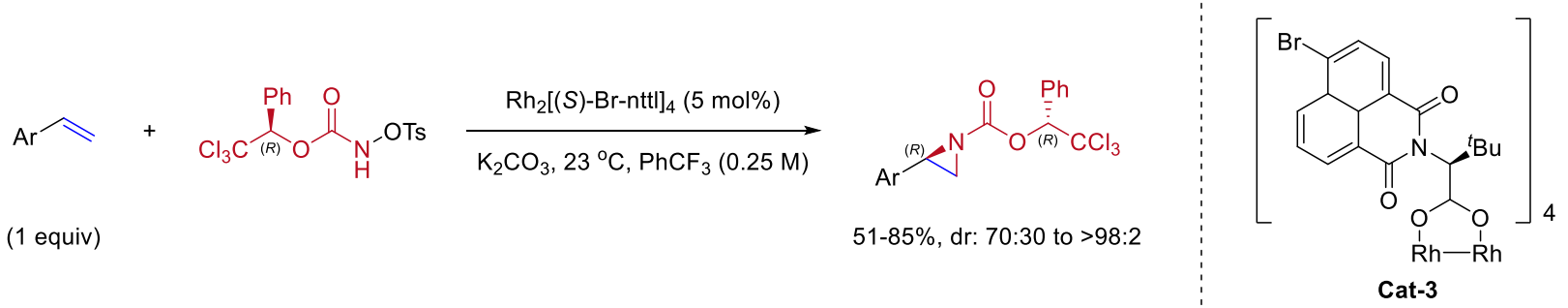
Lebel (2010)



Lebel (2012)



Lebel (2011)

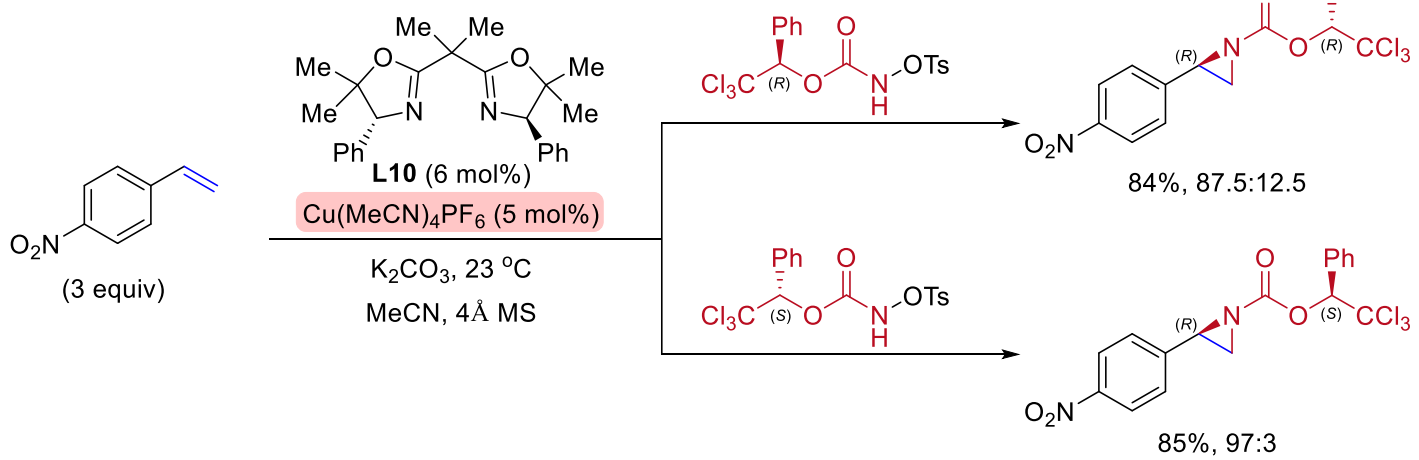


首次实现Rh催化体系下的不对称氮杂环丙烷化反应

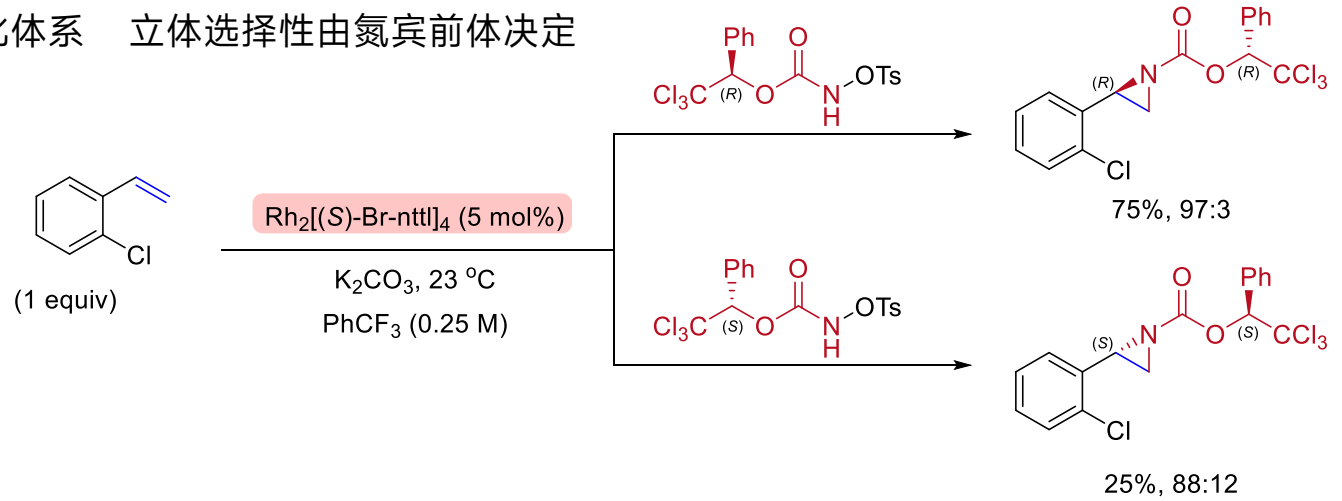
Lebel, H. et al. *Pure Appl. Chem*. **2010**, *82*, 1827−1833. Lebel, H. et al. *Tetrahedron* **2012**, *68*, 3396−3409. Lebel, H. et al. *Org. Lett*. **2011**, *13*, 5460−5463.

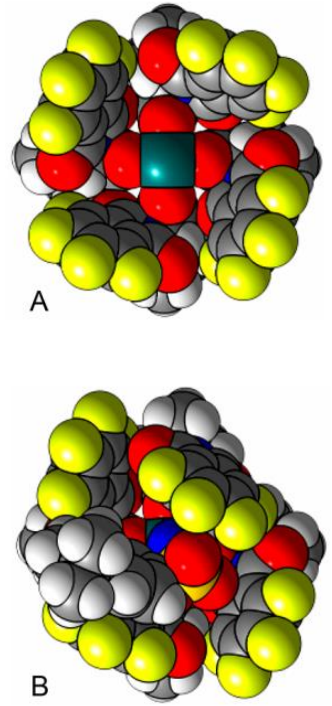
2.3 Metal–Nitrenes from Hydroxylamine Derivatives

Cu催化体系　立体选择性由手性配体决定



Rh催化体系　立体选择性由氮宾前体决定



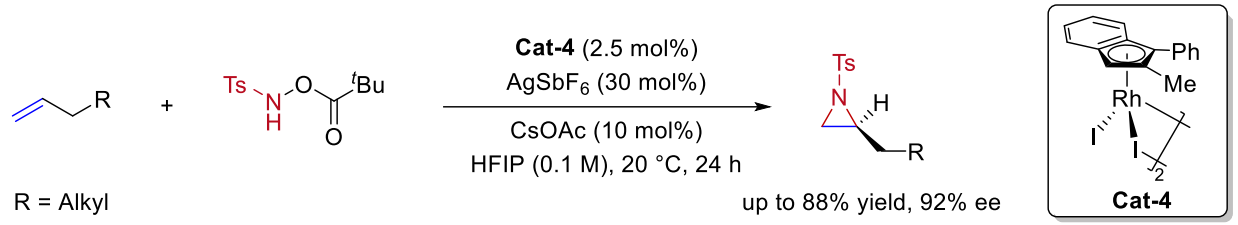


手性Rh催化剂具有手性口袋，
其在和氮宾前体配位后结构相互靠近，
压缩手性口袋的立体空间，
进而影响后续烯烃插入方向

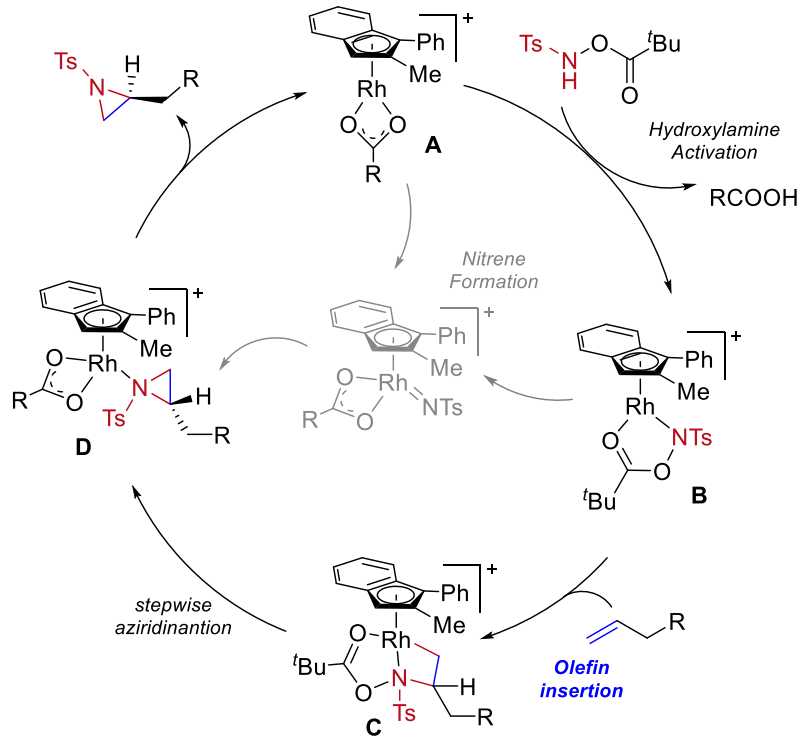
Lebel, H. et al. *Tetrahedron* **2012**, *68*, 3396−3409. Lebel, H. et al. *Org. Lett*. **2011**, *13*, 5460−5463.

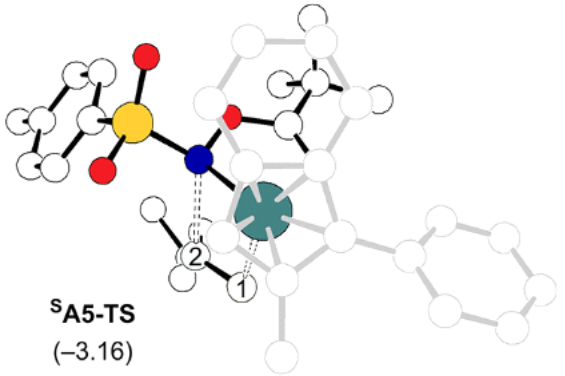
2.3 Metal–Nitrenes from Hydroxylamine Derivatives

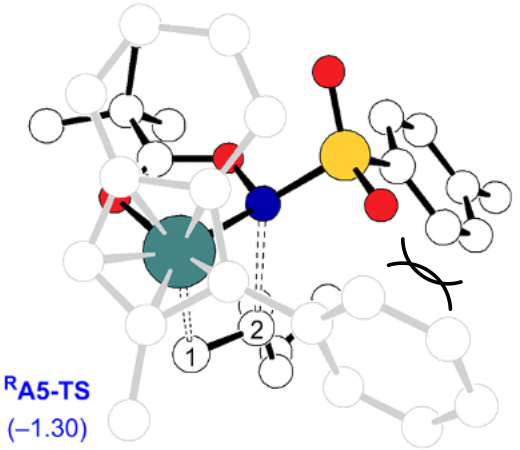
Blakey (2024)

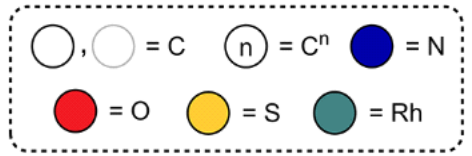


Mechanistic Proposal





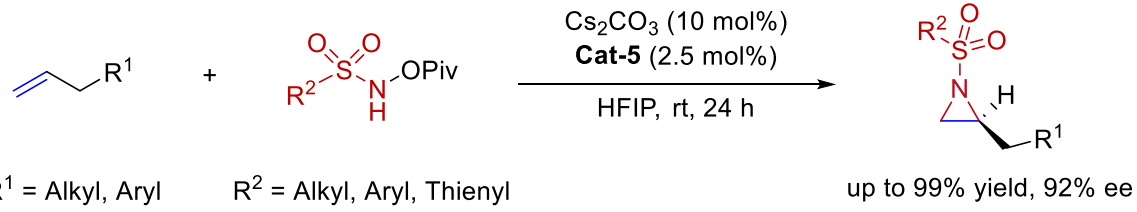




Blakey, S. B. et al. *J. Am. Chem. Soc.* **2024**, *146*, 1447−1454.

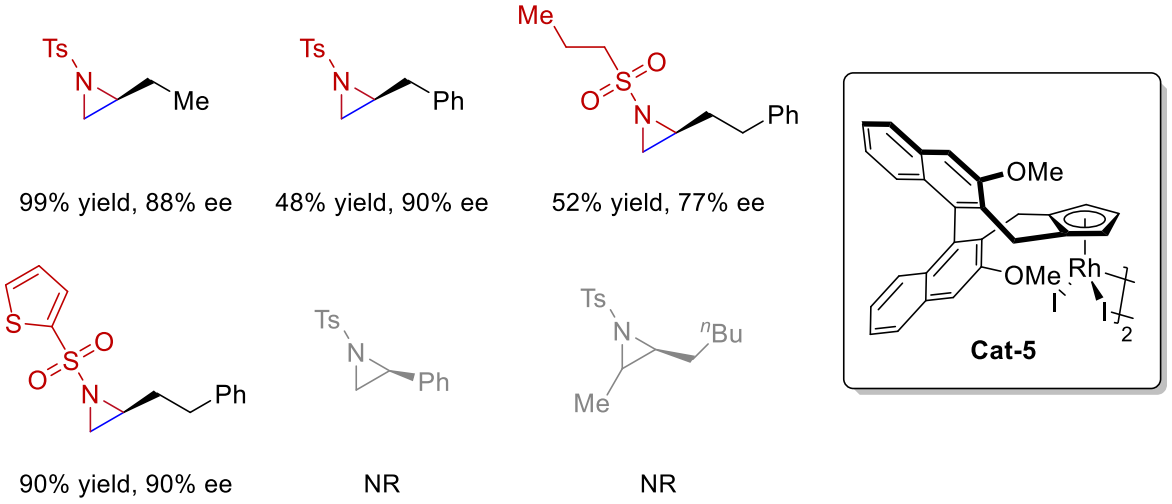
2.3 Metal–Nitrenes from Hydroxylamine Derivatives

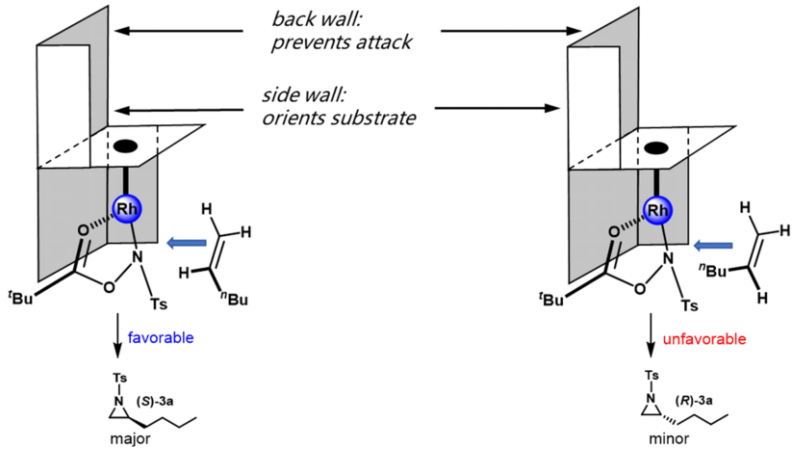
Wang (2024)



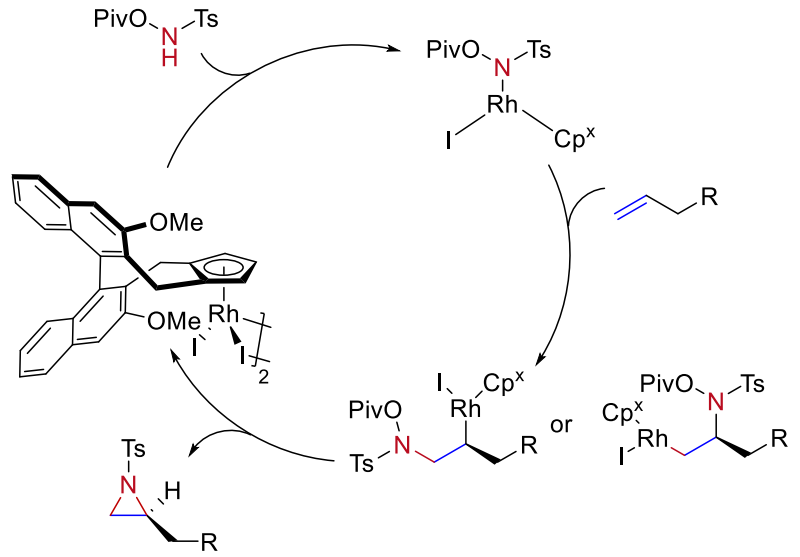
R^1 = Alkyl, Aryl R^2 = Alkyl, Aryl, Thienyl up to 99% yield, 92% ee

Selected examples





Mechanistic Proposal

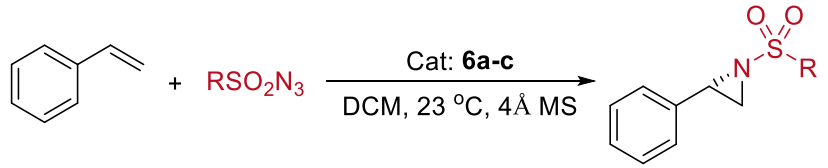


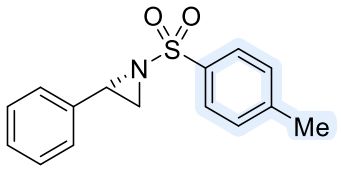
Wang, S. et al. *Angew. Chem. Int. Ed.* **2024**, *63*, e202400502.

Content

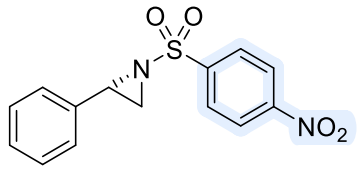
2.4 Metal–Nitrenes from Azides

Katsuki (2004 and 2007)



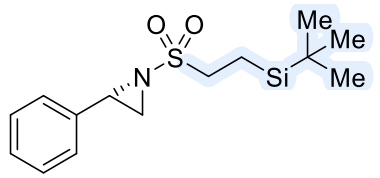


Cat 6a (2 mol%), 71%, er: 94:6 (TON = 36)



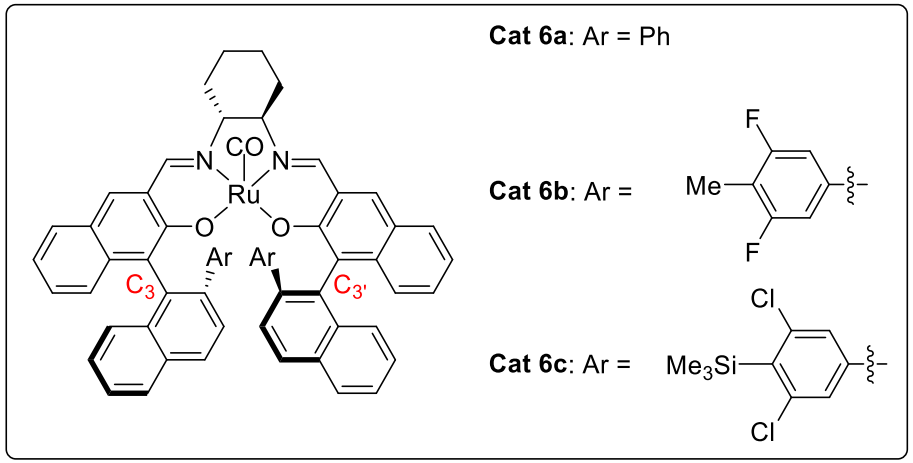
Cat 6b (0.09 mol%), 78%, er: 92:8 (TON = 867)

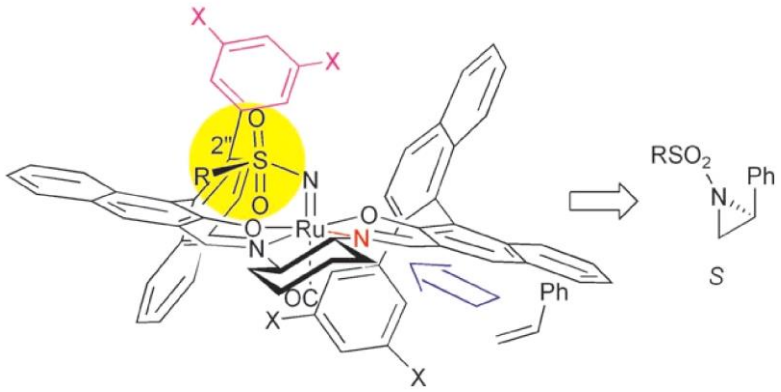
Cat 6b (1 mol%), 34%, er: 92:8 (TON = 34)



Cat 6c (1 mol%), 99%, er: 96:4 (TON = 99)

Cat 6c (0.1 mol%), 93%, er: 93:7 (TON = 982)

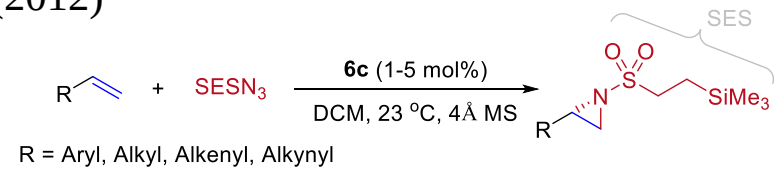


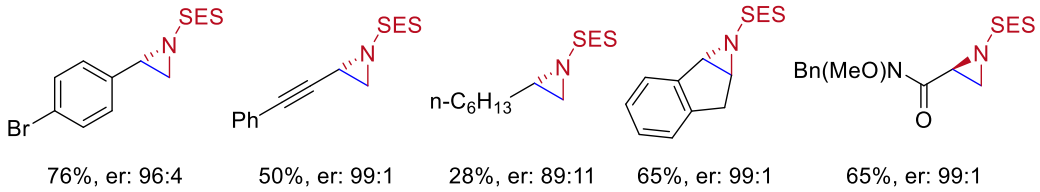


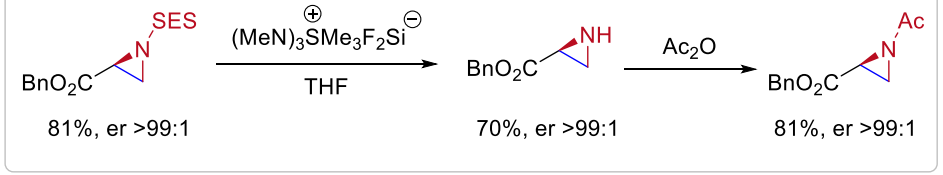
Katsuki, T. et al. *Chem. Commun*. **2004**, 2060−2061. Katsuki, T. et al. *Chem. Asian. J*. **2007**, *2*, 248−256.

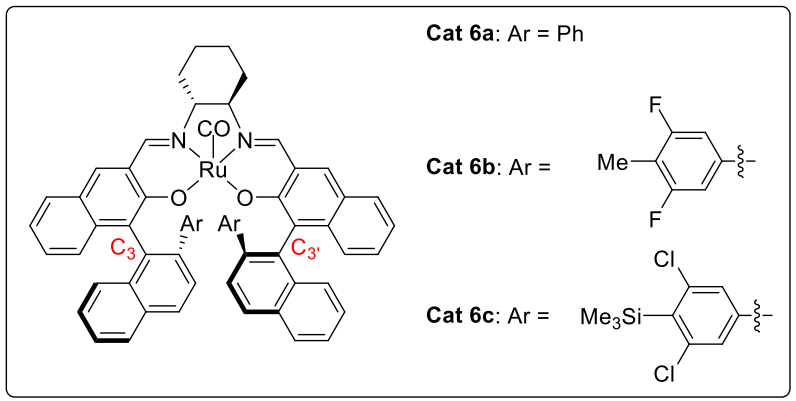
2.4 Metal–Nitrenes from Azides

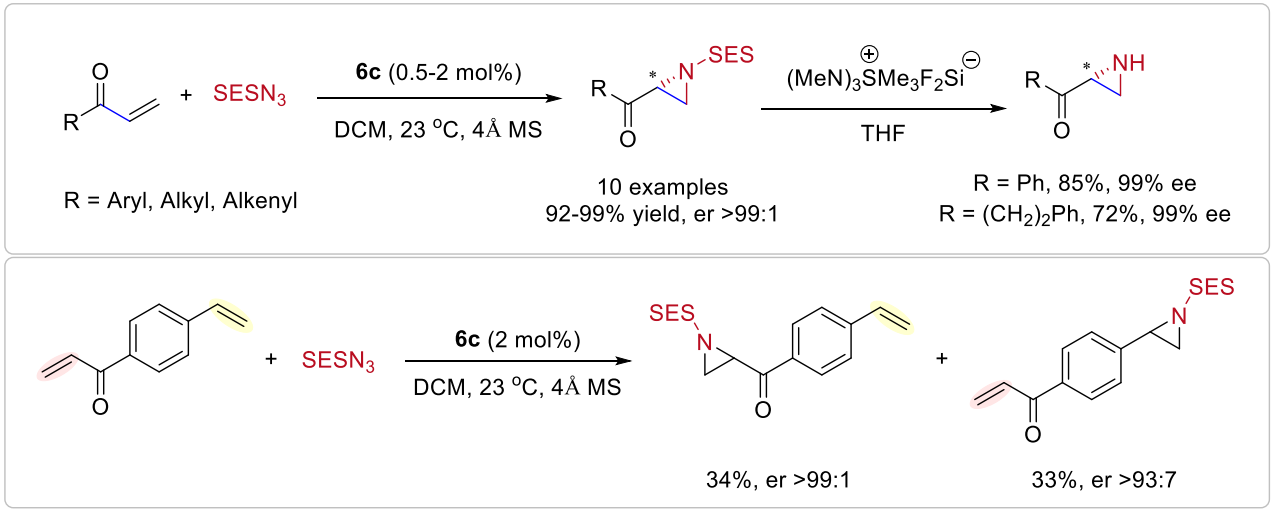
Katsuki (2012)

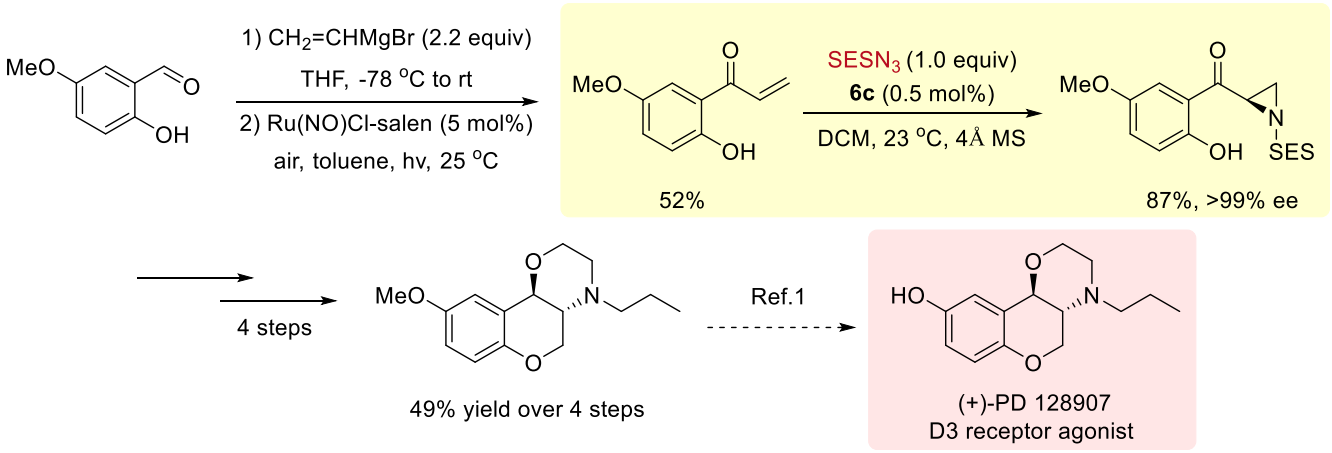






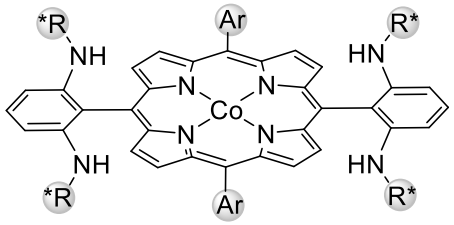




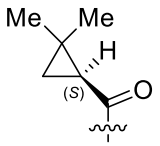
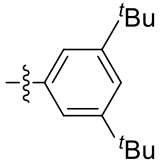


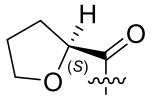
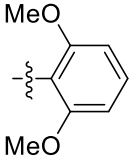
Katsuki, T. et al. *Org. Lett.* **2012**, *14*, 4658−4661. Katsuki, T. et al. *Chem. Commun*. **2012**, *48*, 7188−7190.

2.4 Metal–Nitrenes from Azides

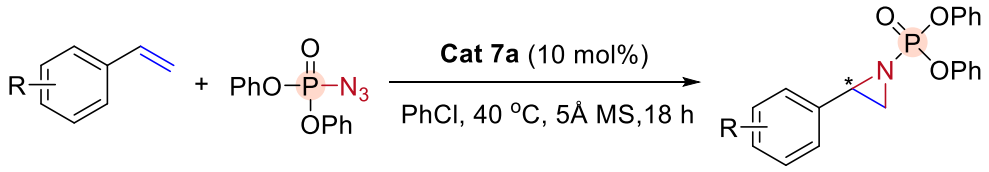


[Co(D$_2$-Por*)]

Cat 7a: R =  Ar = 

Cat 7b: R =  Ar = 

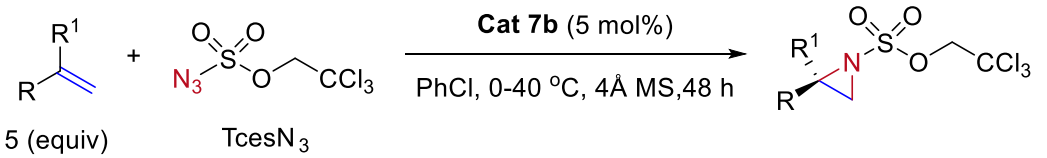
Peter Zhang (2008)



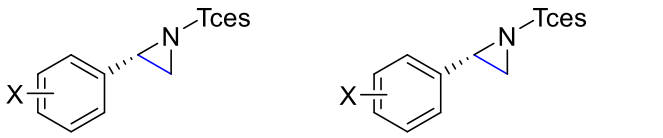
R = *o*-, *m*-, *p*-Me, *o*-, *m*-,*p*-Br
p-^{t}Bu, *p*-Cl, *p*-F, *p*-CF_3, *m*-NO_2

52-88% yields
er: 55:45 to 78:22

Peter Zhang (2009)

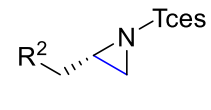


5 (equiv) $TcesN_3$

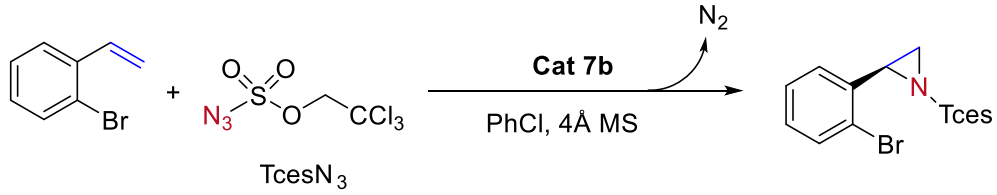


85-92%, er: 90:10 to 97:3
X = H, EDG, EWG

X = H, 48%, er: 90:10
X = *p*-Cl, 43%, er: 90:10



R^2 = Ph, 26%, er: 97:3
R^2 = *n*-Pr, 42%, er: 96:4



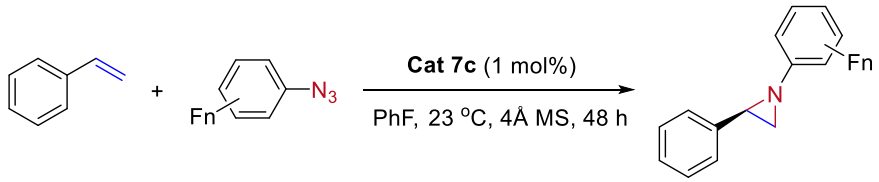
$TcesN_3$

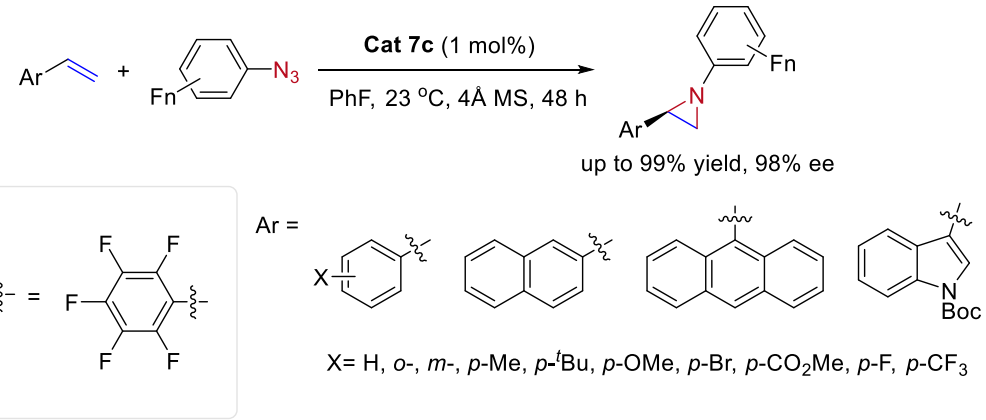
Entry	Cycle	Temp/°C	Yield (%)	ee (%)
1	First	rt	95	96
2	Second	rt	89	94
3	Third	rt	81	94

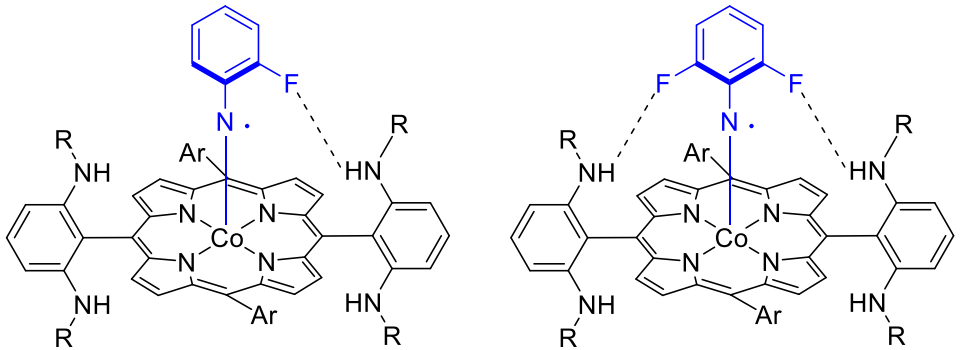
Zhang, X. P. et al. *J. Org. Chem*. **2008**, *73*, 7260−7265. Zhang, X. P. et al. *Chem. Commun*. **2009**, 4266−4268.

2.4 Metal–Nitrenes from Azides

Peter Zhang (2013)

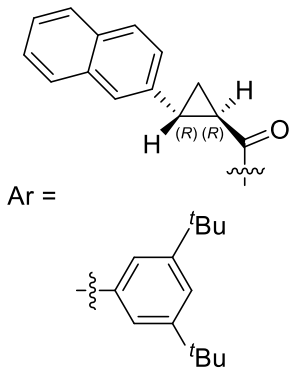






[Co(D_2-Por*)] Cat 7c

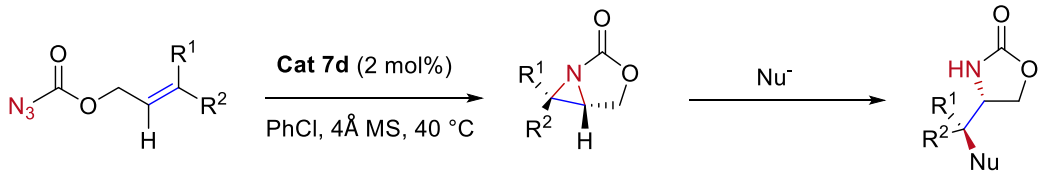
Cat 7c: R =



Zhang, X. P. et al. *Angew. Chem. Int. Ed*. **2013**, *52*, 5309−5313.

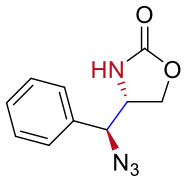
2.4 Metal–Nitrenes from Azides

Peter Zhang (2017)

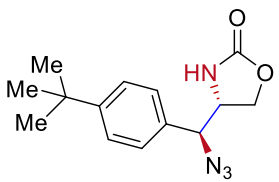


up to 99% yield, >99% ee, 99% de

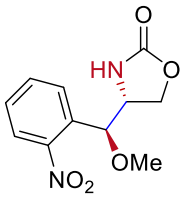
Selected examples



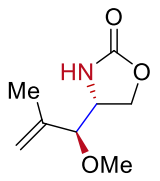
92%, >99% ee
99% de



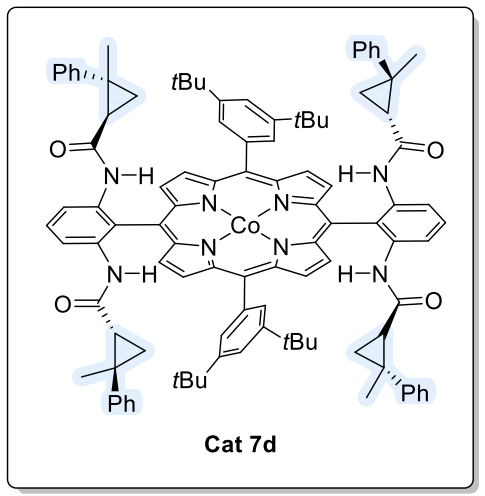
95%, 93% ee
99% de



99%, 94% ee
99% de

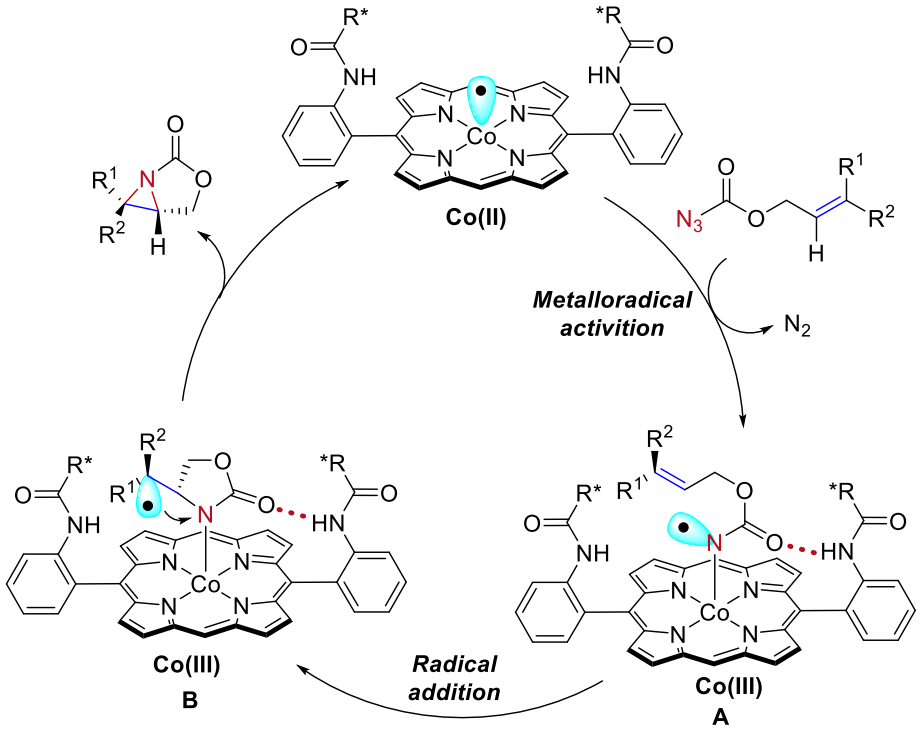


94%, 93% ee
99% de



Cat 7d

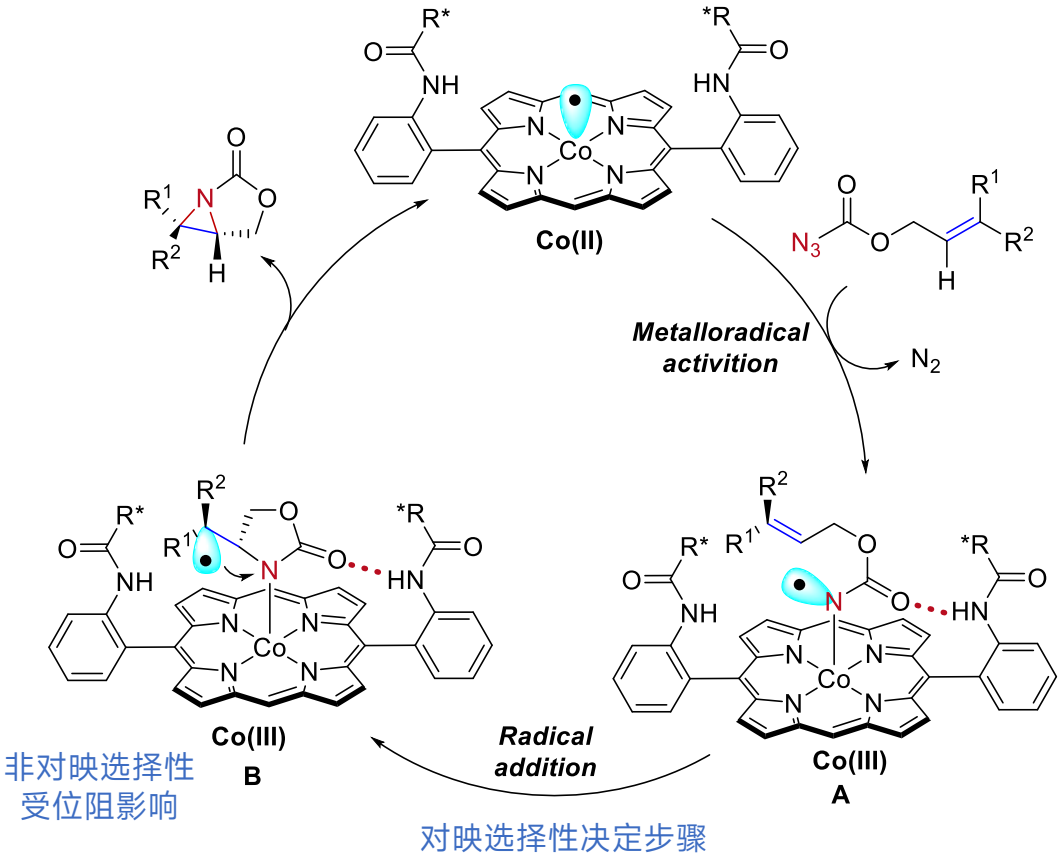
Mechanistic Proposal



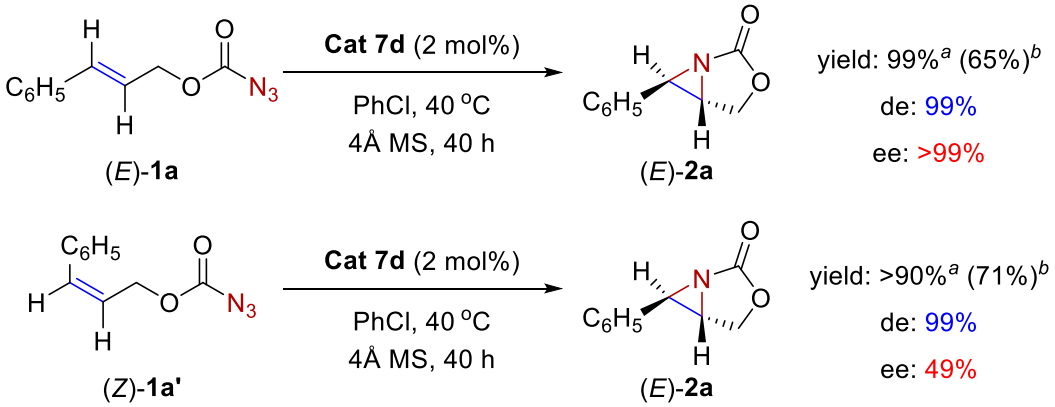
Zhang, X. P. et al. *J. Am. Chem. Soc.* **2017**, *139*, 9164−9167.

2.4 Metal–Nitrenes from Azides

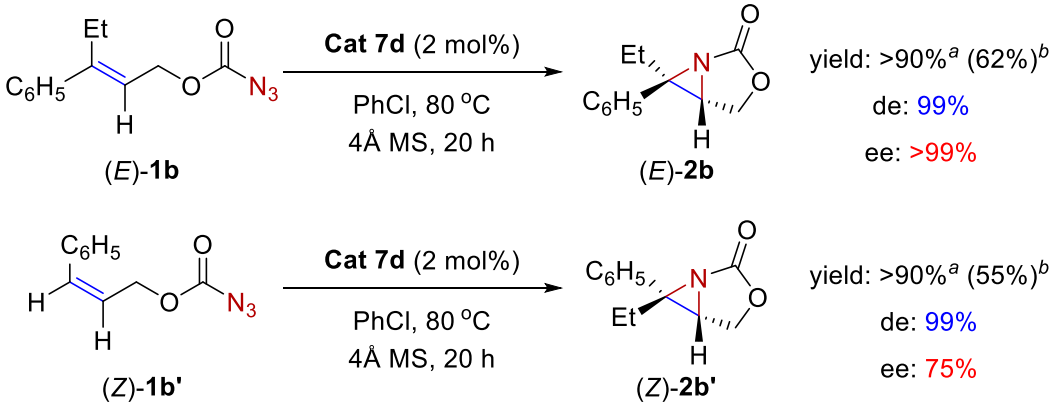
Mechanistic Proposal



A. Diastereoconvergent Asymmetric Radical Bicyclization of Azidoformates



B. Diastereospecific Asymmetric Radical Bicyclization of Azidoformates

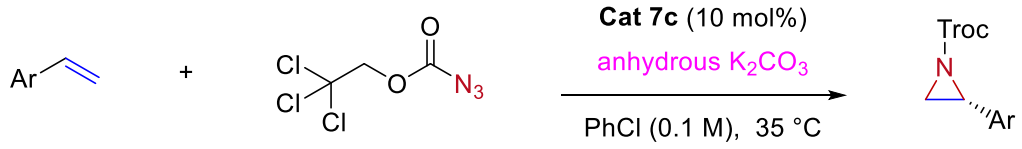


[a]NMR yields. [b]Isolated yields. Note: Aziridines were unstable toward workup.

Zhang, X. P. et al. *J. Am. Chem. Soc.* **2017**, *139*, 9164−9167.

2.4 Metal–Nitrenes from Azides

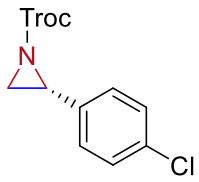
Peter Zhang (2021)



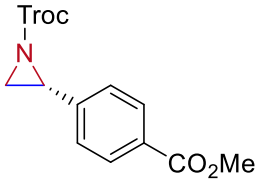
(TrocN$_3$)

up to 99% yield, 94% ee

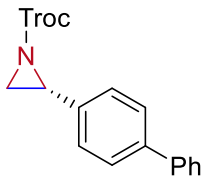
Selected examples



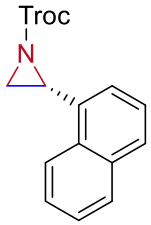
99%, 94% ee



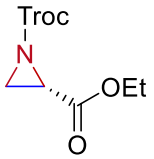
71%, 92% ee



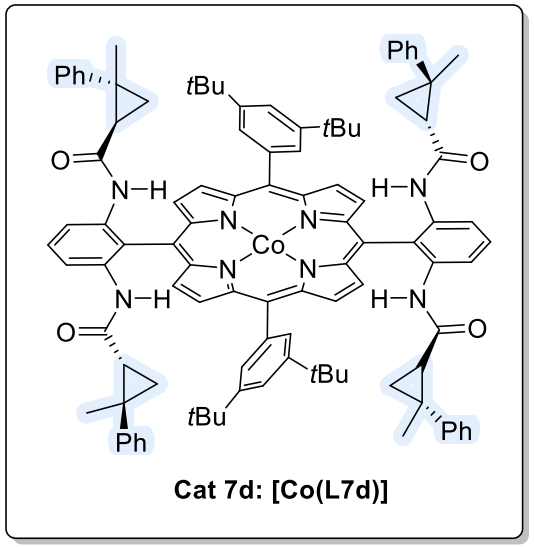
70%, 90% ee



93%, 94% ee



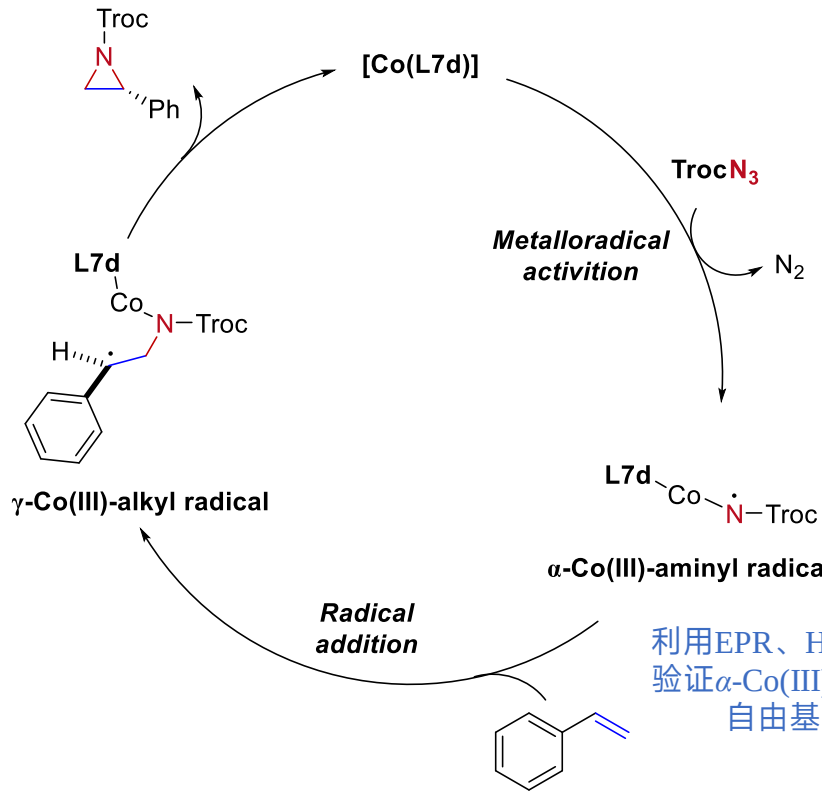
43%, 82% ee



Cat 7d: [Co(L7d)]

K_2CO_3: 除水、抑制Co(III)路易斯酸性

Mechanistic Proposal

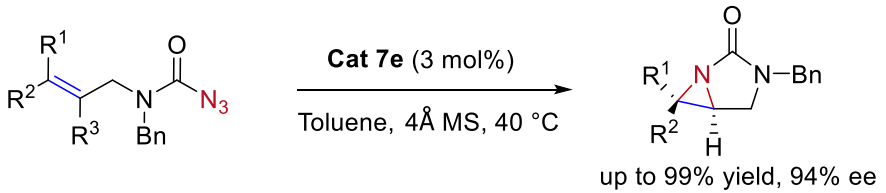


利用EPR、HMRS验证α-Co(III)氨基自由基

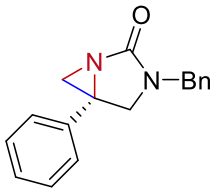
Zhang, X. P. et al. *Chem* **2021**, *7*, 1120−1134.

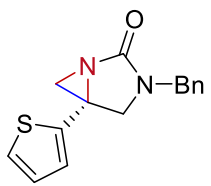
2.4 Metal–Nitrenes from Azides

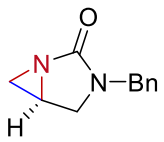
Peter Zhang (2024)

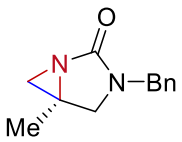


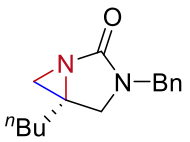
Selected examples

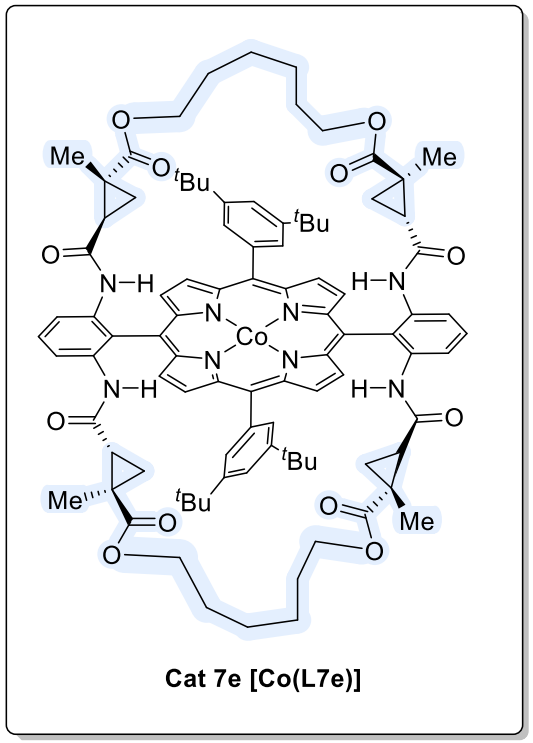

96%, 90% ee


96%, 86% ee

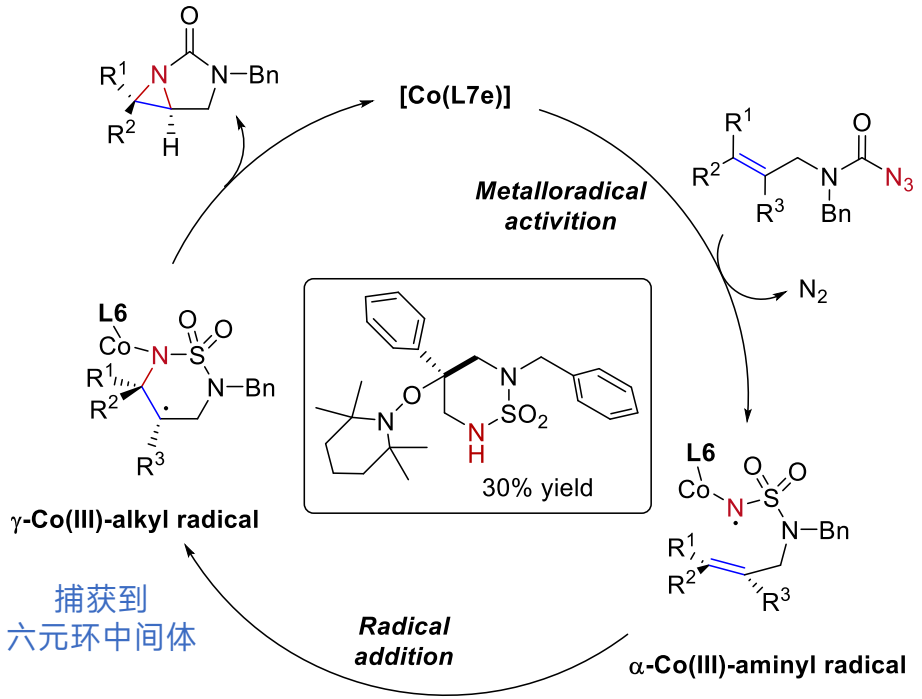

96%, 81% ee


50%, 65% ee


88%, 52% ee



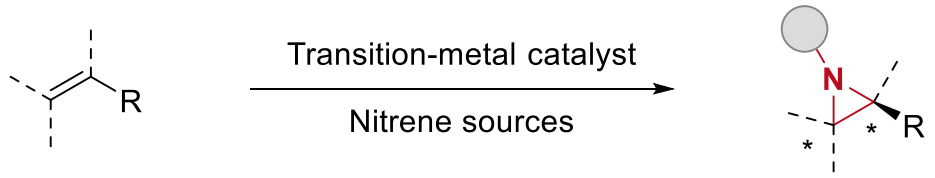
Mechanistic Proposal



Zhang, X. P. et al. *Chem* **2024**, *10*, 283−298.

Content

3 Summary and outlook



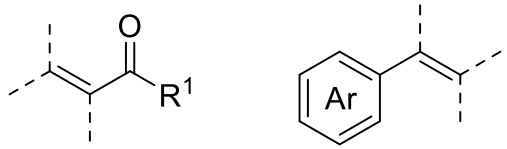
R = EWG, Ar, or Alkyl

Chiral aziridine

Transition-metal

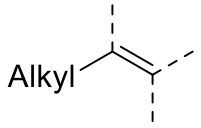
26 Fe $3d^6 4s^2$ 55.85	27 Co $3d^7 4s^2$ 58.93	29 Cu $3d^{10} 4s^2$ 63.55
44 Ru $4d^7 5s^1$ 101.1	45 Rh $4d^8 5s^1$ 102.9	47 Ag $4d^{10} 5s^1$ 107.9

Activated Alkenes



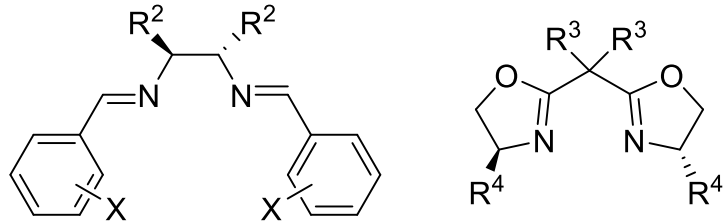
α, β-unsaturated styrene

Unactivated Alkenes



·Low Polarity
·Low Functionalization
·Minimal Steric Differentiation

Chiral Ligand

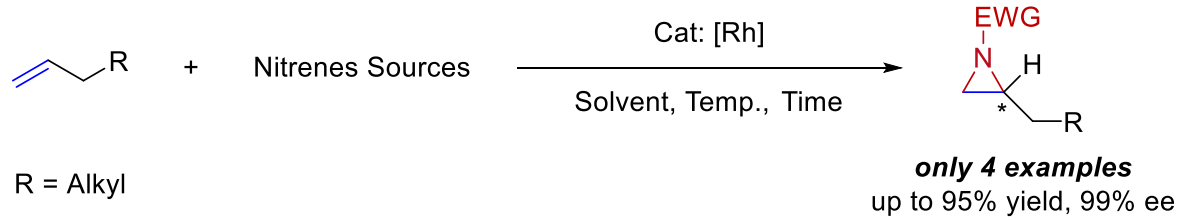


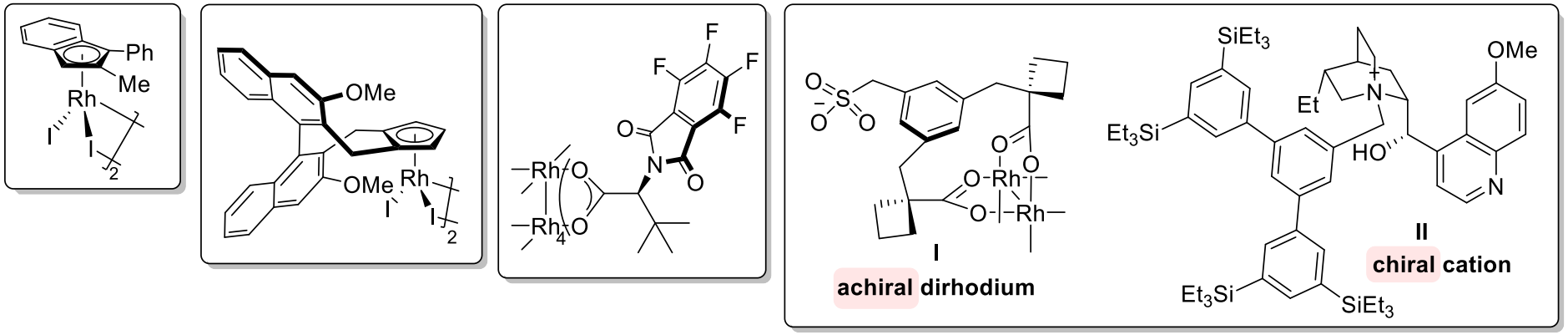
Chiral Metal Complex

Ru, Rh, Co

3 Summary and outlook

非活化烯烃分子间不对称氮杂环丙烷化反应





非活化烯烃分子间不对称氮杂环丙烷化研究较少，

现有工作集中在Rh催化体系，体系复杂，

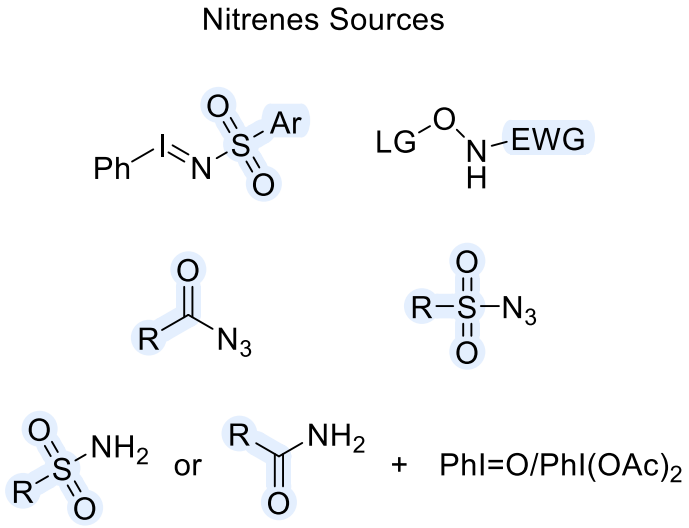
手性催化剂制备难度大

发展丰产金属Fe、Cu体系

合成活性匹配的配体骨架

3 Summary and outlook

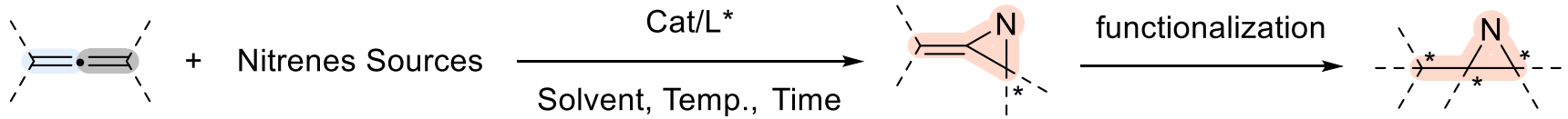
无保护基团的氮杂环丙烷不对称构建



氮宾前体均连有吸电子基，
只能够直接构建具有吸电子*N*-保护基的
氮杂环丙烷

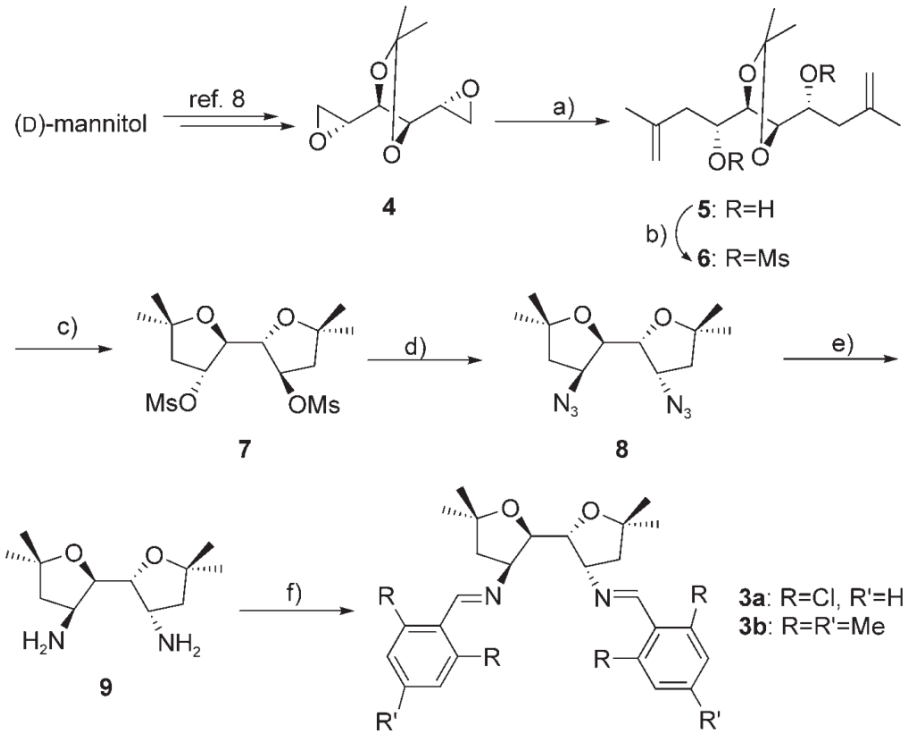
后续具有NH的氮宾前体
直接实现氮杂环丙烷的不对称构建

联烯的选择性氮宾插入



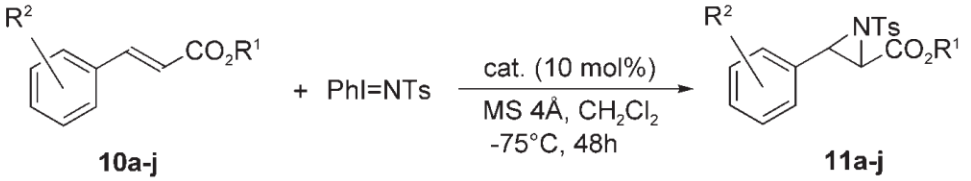
Thank you for your attention !

4 Supporting Information



Scheme 1. Synthesis of chiral 1,4-diamine **9** and its diimine derivatives (**3a–b**): a) C_3H_5MgBr, CuI (20%), THF, −30 °C, 93%; b) MsCl, Et_3N, 10 °C, >99%; c) CH_2Cl_2, $HClO_4$ (70% aq), 70%; d) NaN_3, DMF, 65%; e) 10% Pd/C, H_2 (1 atm), >99%; f) 2,6-dichlorobenzaldehyde or 2,4,6-trimethylbenzaldehyde, MeOH, reflux, 24 h, **3a**: 93%, **3b**: 75%.

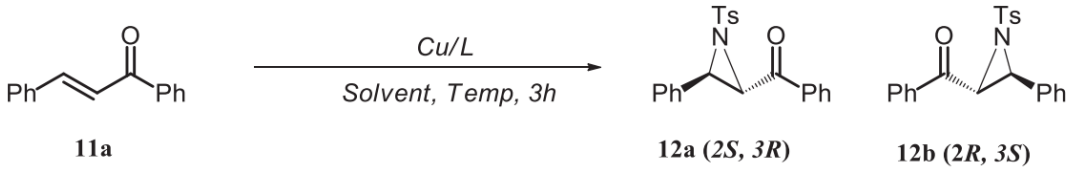
Table 2. Asymmetric aziridination of olefin derivatives.[a]



Entry	Substrate	R^1	R^2	Yield [%][b]	*ee* [%][c]	Config.[d]
1	**10a**	Me	H	97	87.6	2*S*,3*R* (−)
2	**10b**	Ph	H	96	87.1	2*S*,3*R* (−)
3	**10c**	*t*Bu	H	99	>99	2*S*,3*R* (−)
4	**10d**	*t*Bu	4-F	99	97.8	(−)
5	**10e**	*t*Bu	4-Cl	97	98.1	(−)
6	**10f**	*t*Bu	4-Br	97	98.3	2*S*,3*R* (−)
7	**10g**	*t*Bu	4-Me	86	94.4	(−)
8	**10h**	*t*Bu	4-MeO	95	80.1	(+)
9	**10i**	*t*Bu	2-NO_2	63	98.6	(+)
10	**10j**	*t*Bu	2,3-MeO	67	97.0	(+)

[a] The reactions were carried out with the ratio of **10**/PhI=NTs/**3a**/Cu 5:1:0.11:0.1 in a 0.125 mmol scale of PhI=NTs (0.042 M) in the presence of 100 mg of MS 4 Å. [b] The yield of isolated product. [c] The enantiomeric excess was determined by HPLC on Chiralcel columns. [d] The absolute configurations of **11a–c** and **11k–l** were determined by comparison of their optical rotations with those of literature data.[4b] The absolute configuration of (−)-**11f** was determined to be (2*S*,3*R*) by the Bijvoet method based on the anomalous dispersion of Br heavy atom.[10]

4 Supporting Information



11a **12a (2*S*, 3*R*)** **12b (2*R*, 3*S*)**

Entry	Ligand	[Cu]	[Cu] load	Solvent	Temp	Yield	%ee[a]
1	**9**	$(CuOTf)_2$·PhMe	5%	DCM	rt	91	51
2	**10**	$(CuOTf)_2$·PhMe	5%	DCM	rt	81	36
3	**9**	$(CuOTf)_2$·PhMe	3%	DCM	rt	82	59
4	**9**	$Cu(OTf)_2$	3%	DCM	rt	33	45
5	**9**	CuI	3%	DCM	rt	NR	-
6	**9**	CuCl	3%	DCM	rt	25	43
7	**9**	Cu(OAc)	3%	DCM	rt	NR	-
8	**9**	$(CuOTf)_2$·PhMe	3%	Chloroform	rt	NR	-
9	**9**	$(CuOTf)_2$·PhMe	3%	DCE	rt	70	48
10	**9**	$(CuOTf)_2$·PhMe	3%	THF	rt	NR	-
11	**9**	$(CuOTf)_2$·PhMe	3%	Toluene	rt	NR	-
12	**9**	$(CuOTf)_2$·PhMe	3%	Acetone	rt	80	67
13	**9**	$(CuOTf)_2$·PhMe	3%	Dioxane	rt	NR	-
14	**9**	$(CuOTf)_2$·PhMe	3%	DME	rt	69	69
15	**9**	$(CuOTf)_2$·PhMe	3%	CH_3CN	rt	93	76
16	**9**	$(CuOTf)_2$·PhMe	3%	CH_3CN	0°C	93	78

Reaction conditions: Chalcone (100mg, 0.48mmol), Ligand (5%eq), Cu precursor (the load is indicated), PhI=NTs (120mg, 0.32mmol), 3ml dry CH_3CN; a) Determined by HPLC with a chiral OD-H column using heptane/2-propanol (90:10, v/v) as the eluent.

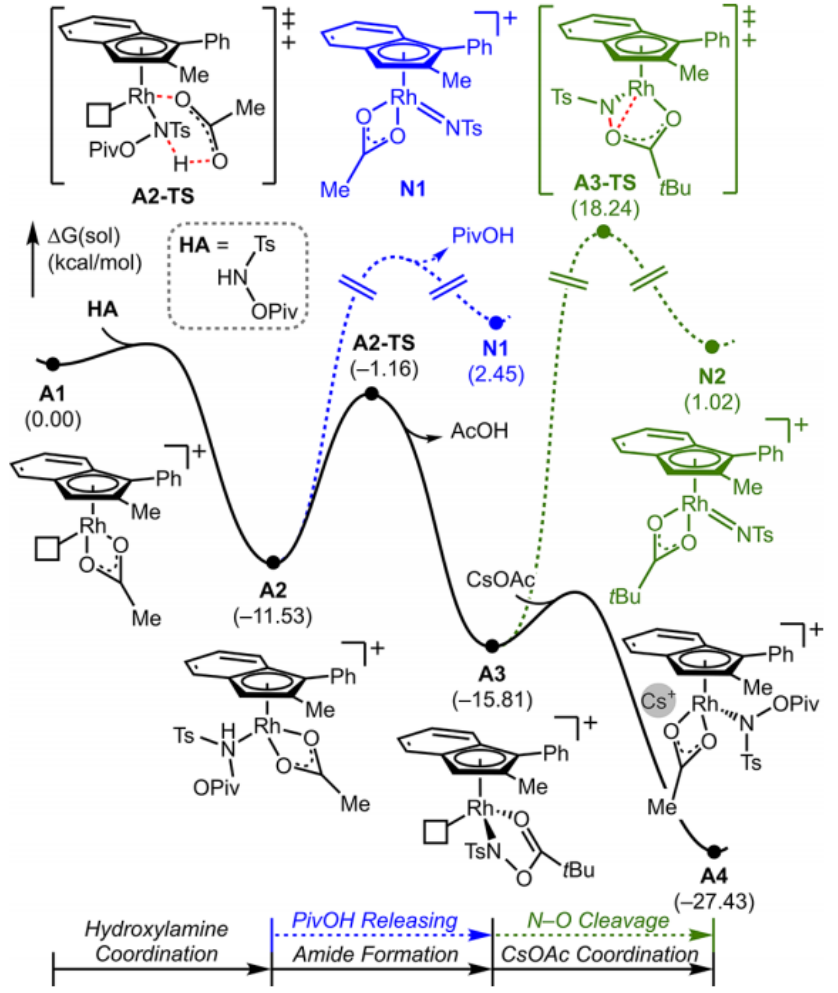
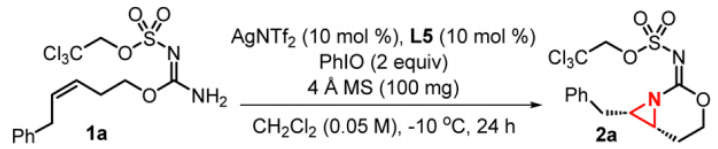


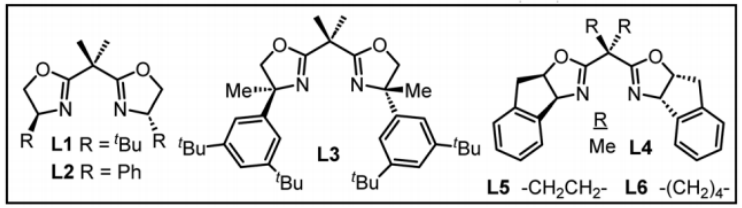
Figure 6. Free energy profile for the formation of **A4** from **A1**. Blue and green traces represent direct nitrene formation via N–O bond cleavage.

4 Supporting Information

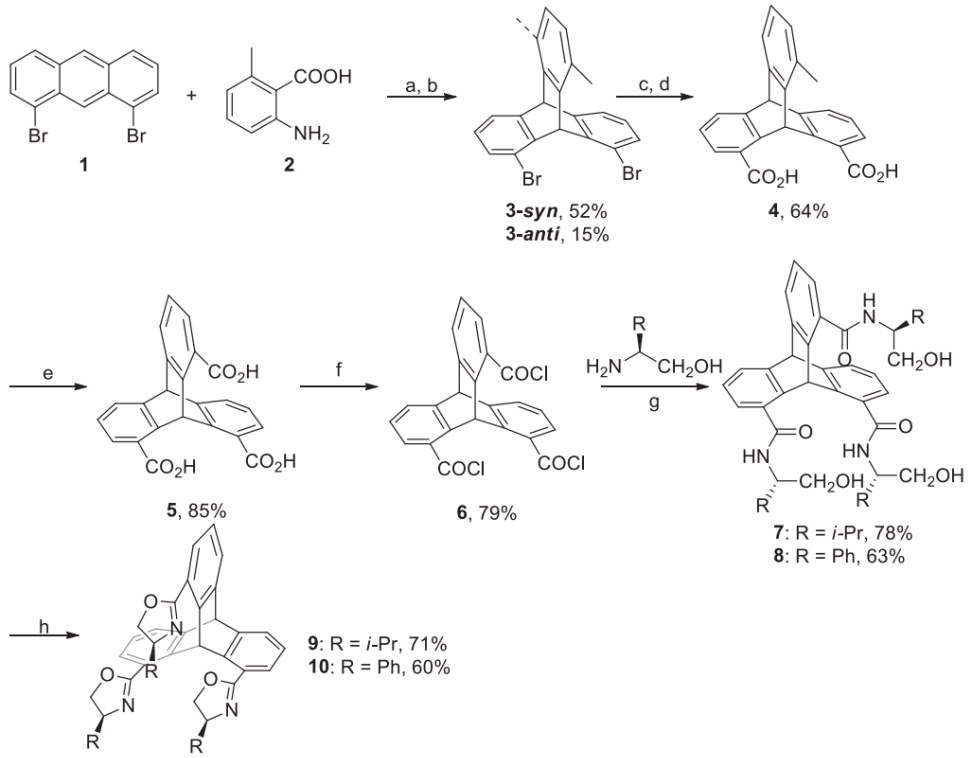
Table 1 Optimization of reaction conditions



Entry	Variation from standard conditions	Yield[a] (conversion, %)	ee[b] (%)
1	None	92 (98)	97
2	**L1** instead of **L5**	75 (89)	35
3	**L2** instead of **L5**	63 (77)	9
4	**L3** instead of **L5**	71 (85)	12
5	**L4** instead of **L5**	86 (96)	91
6	**L6** instead of **L5**	78 (89)	93
7	$AgClO_4$ instead of $AgNTf_2$	74 (92)	93
8	AgOTf instead of $AgNTf_2$	73 (90)	76
9	−20 °C, 24 h	26 (32)	96
10	$AgNTf_2$ (5 mol%), **L5** (5 mol%)	73 (92)	93
11	2.5 mmol scale	89[c] (>99)	95



[a] Reactions were carried out on a 0.1 mmol scale unless indicated otherwise. Yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b] The ee was determined by chiral HPLC after purification. [c] Isolated yield.



a) isopentylnitrite, DME, 80 °C; b) maleic anhydride, triglyme, reflux; c) BuLi, TMEDA, THF, -78 °C; d) CO_2, HCl; e) $NaOH_{aq}$ (2%), $KMnO_4$, reflux; f) $SOCl_2$, $CHCl_3$, reflux; g) TEA, DCM, RT; h) DDQ, PPh_3, DCM, reflux.

4 Supporting Information

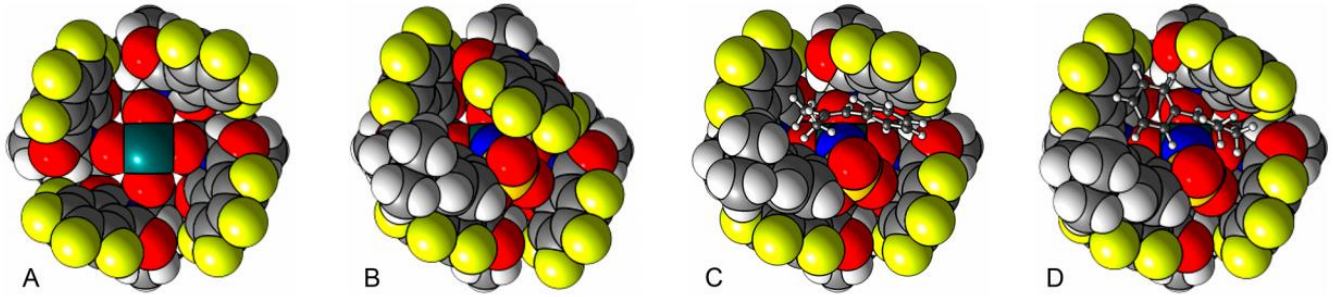


Figure 2. Views showing $^3Rh_2$ (A), $^3Rh_2N$ (B), $^3RhN{:}Styr_{Si}$ (C), and $^3RhN{:}Styr_{Re}$ (D). Different representations are used to provide evidence that the substrate (ball and sticks) fits in the catalytic pocket (van der Waals spheres). H, white; C, gray; N, blue; O, red; F, neon green; S, yellow.

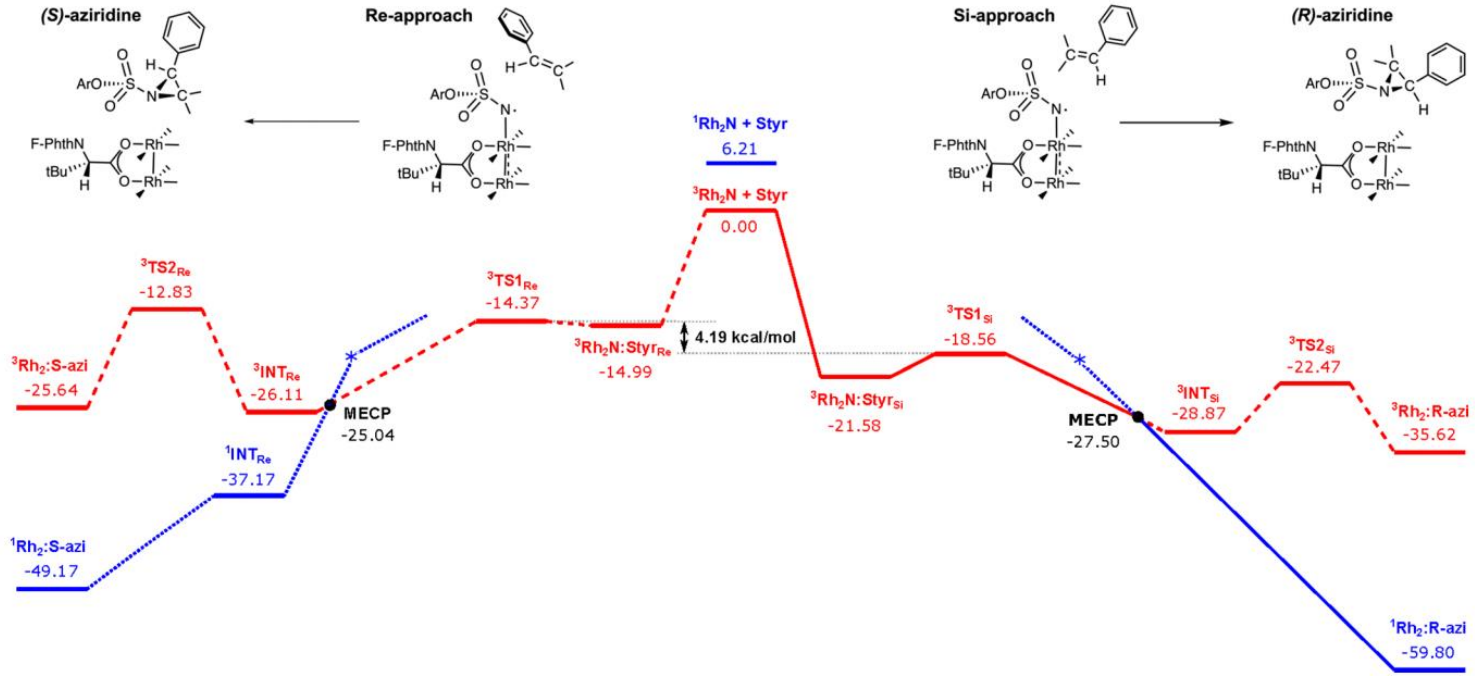
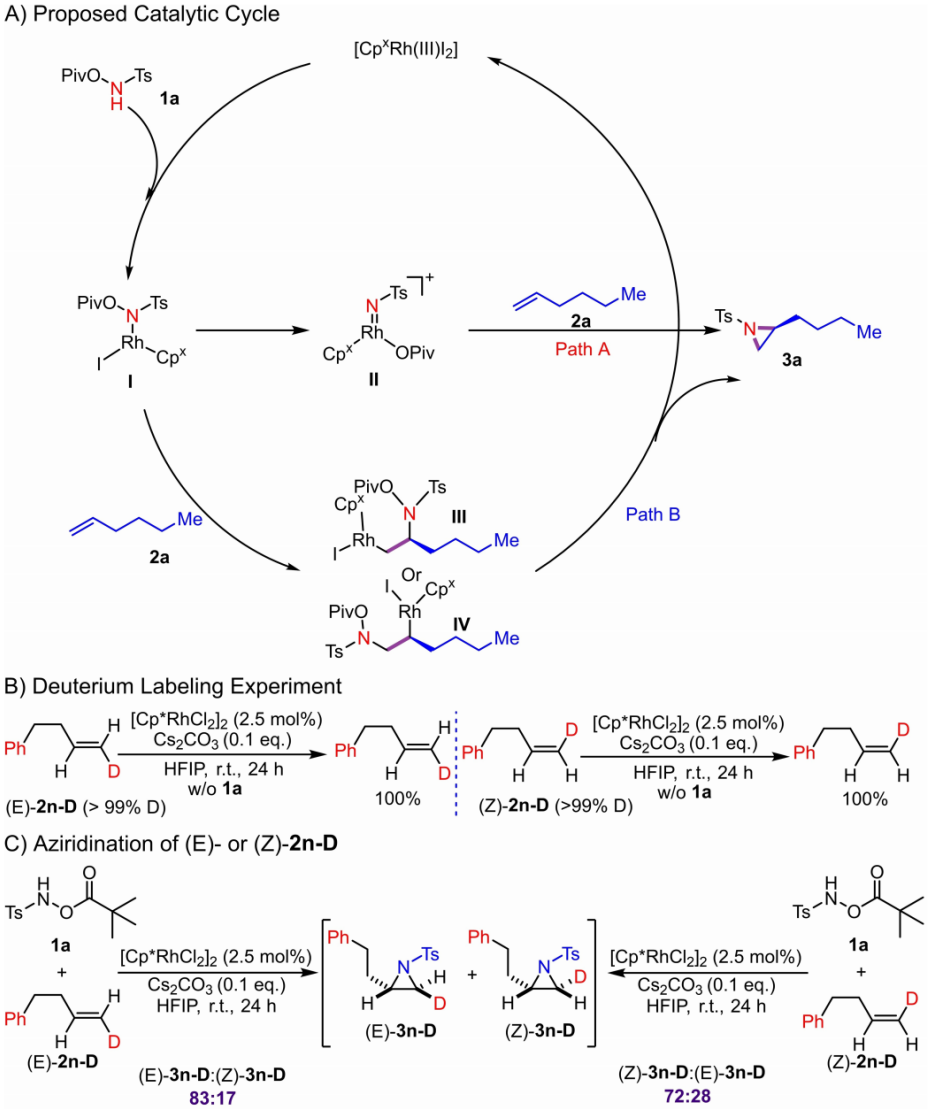
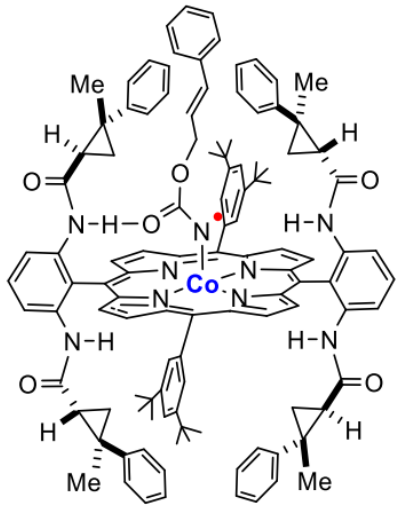


Figure 3. Extract of the computed two spin state mechanism (triplet in red, singlet in blue) showing the favored energy profile in plain line ($\Delta G_{258\ K}$ in kcal/mol); * indicates the position of pseudo-TS.

4 Supporting Information



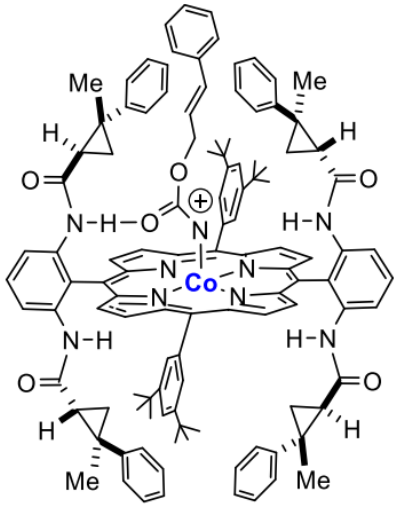


[M]•

α-Co(III)-aminyl radical **I**

-e^{-1}

ESI



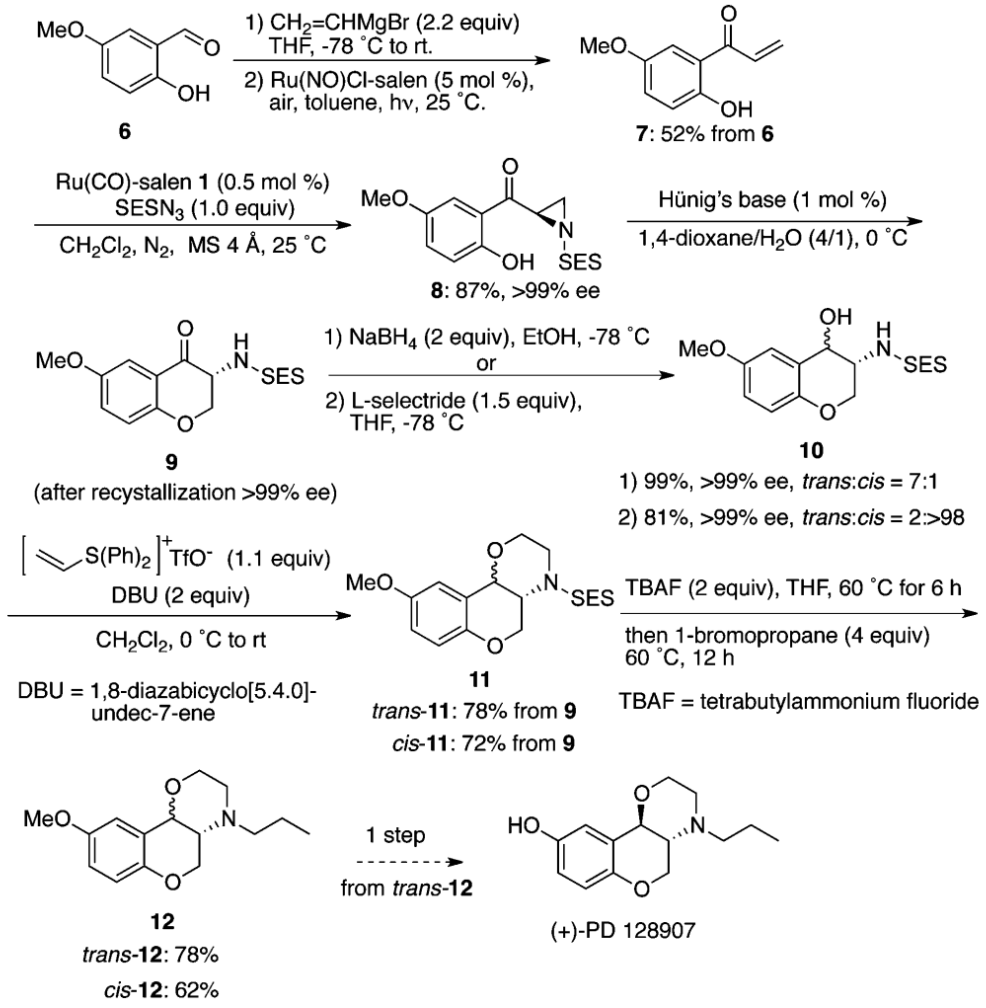
[M]$^+$

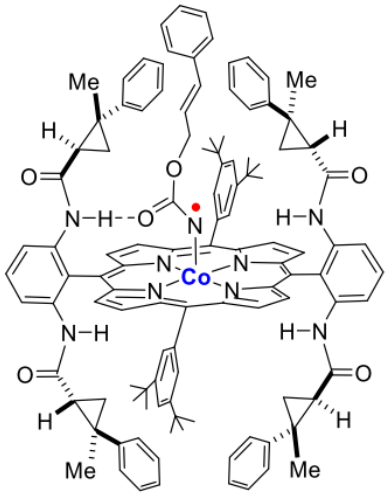
Chemical Formula: $C_{114}H_{113}CoN_9O_6^+$

Calculated Exact Mass: 1762.8140

4 Supporting Information

Scheme 3. Formal Asymmetric Synthesis of (+)-PD 128907





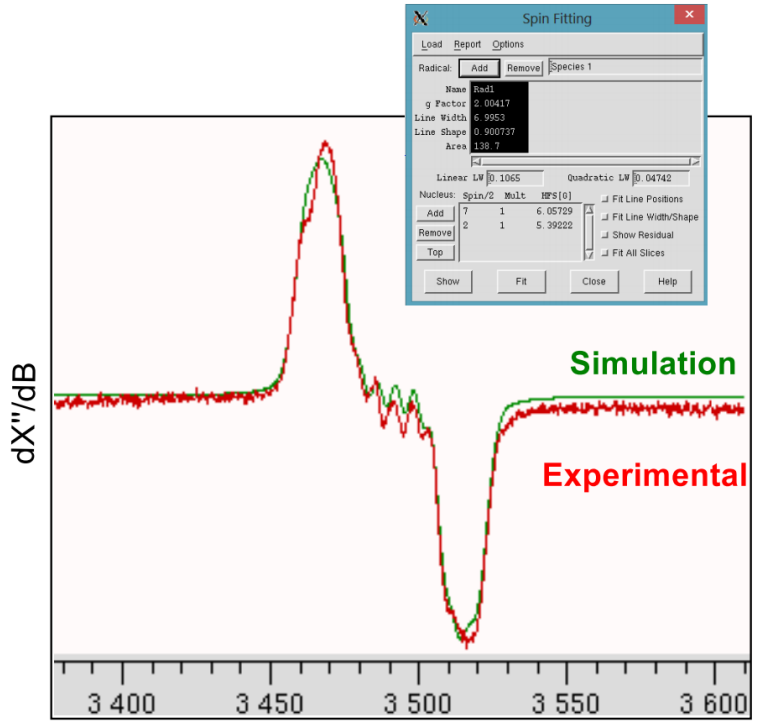
α-Co(III)-aminyl radical **I**

From simulation: g_{iso}: 2.00417;

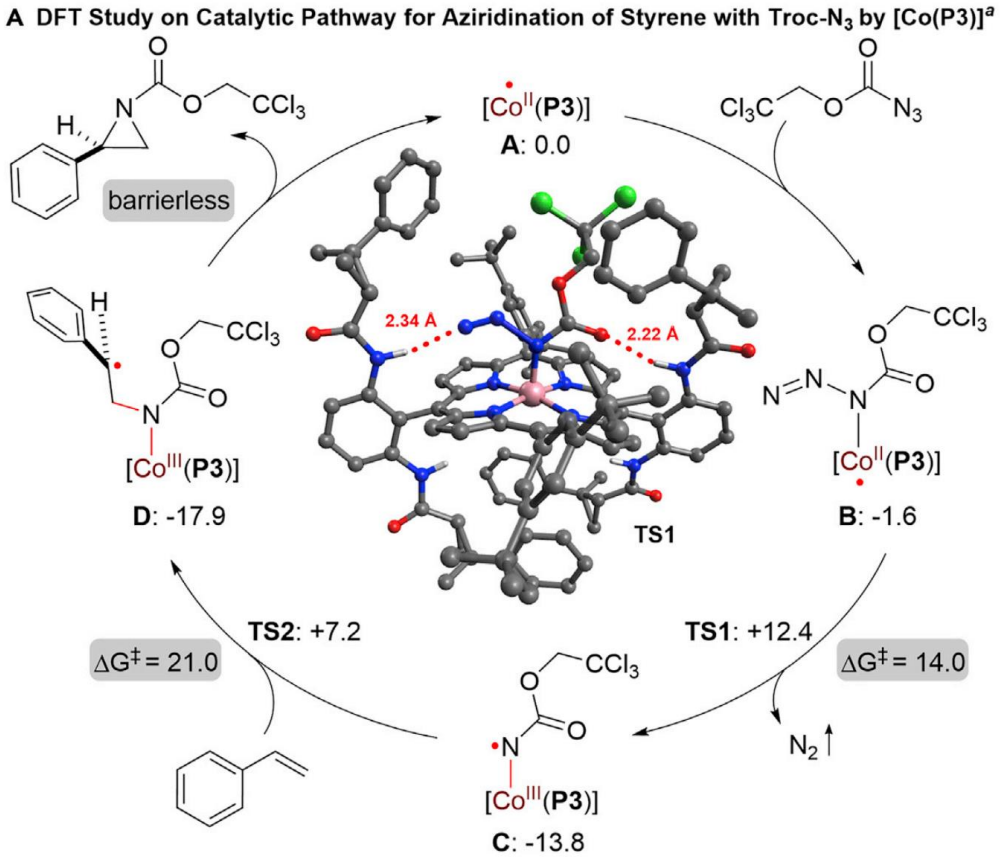
$A_{(Co)}$: 6.05729 x 2.00417 x 1.399611451 = 16.99 MHz

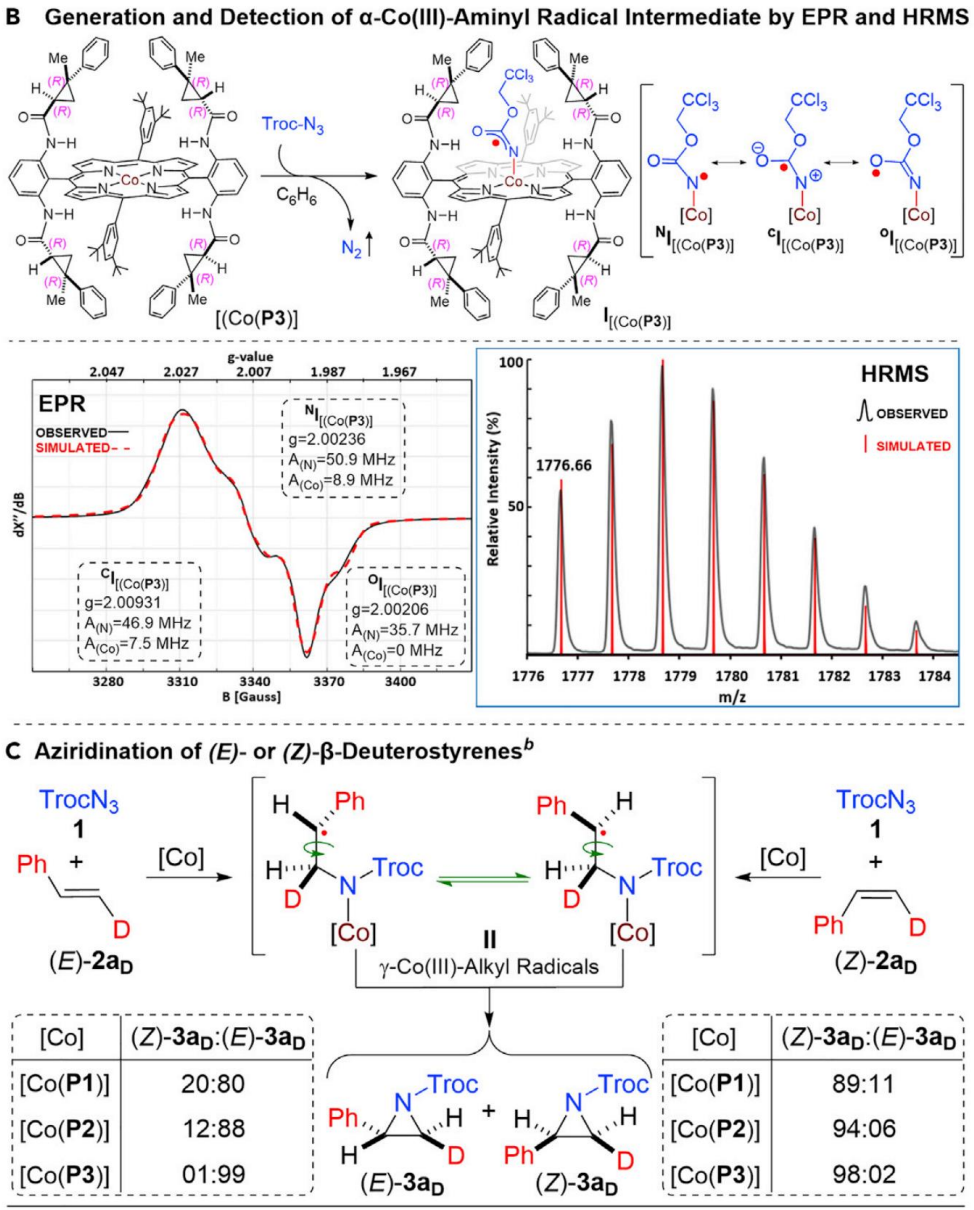
$A_{(N)}$: 5.39222 x 2.00417 x 1.399611451 = 15.1 MHz

From experimental: g_{iso}: 2.00406



4 Supporting Information

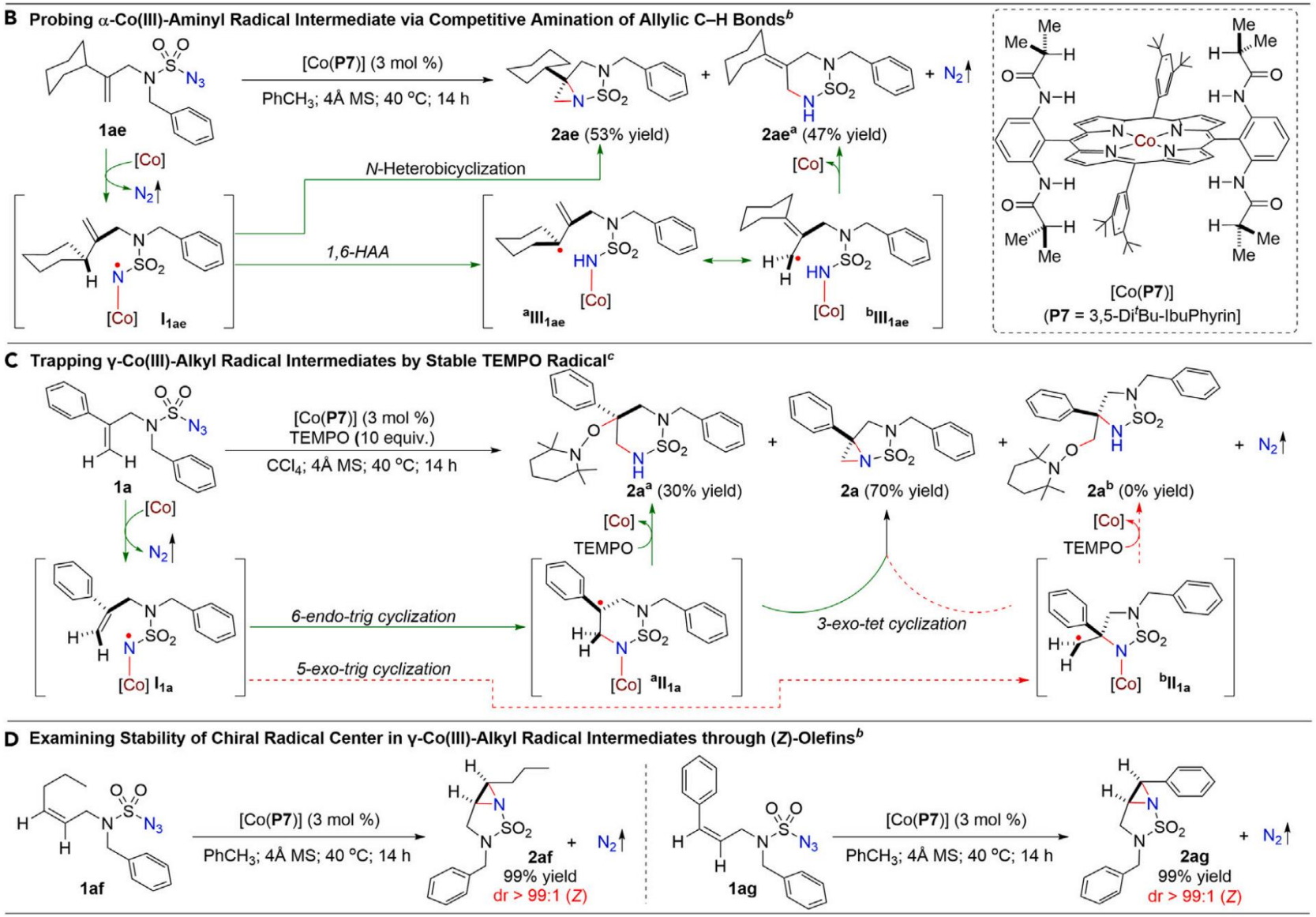




[Co]	(*Z*)-**3a**$_D$:(*E*)-**3a**$_D$
[Co(**P1**)]	20:80
[Co(**P2**)]	12:88
[Co(**P3**)]	01:99

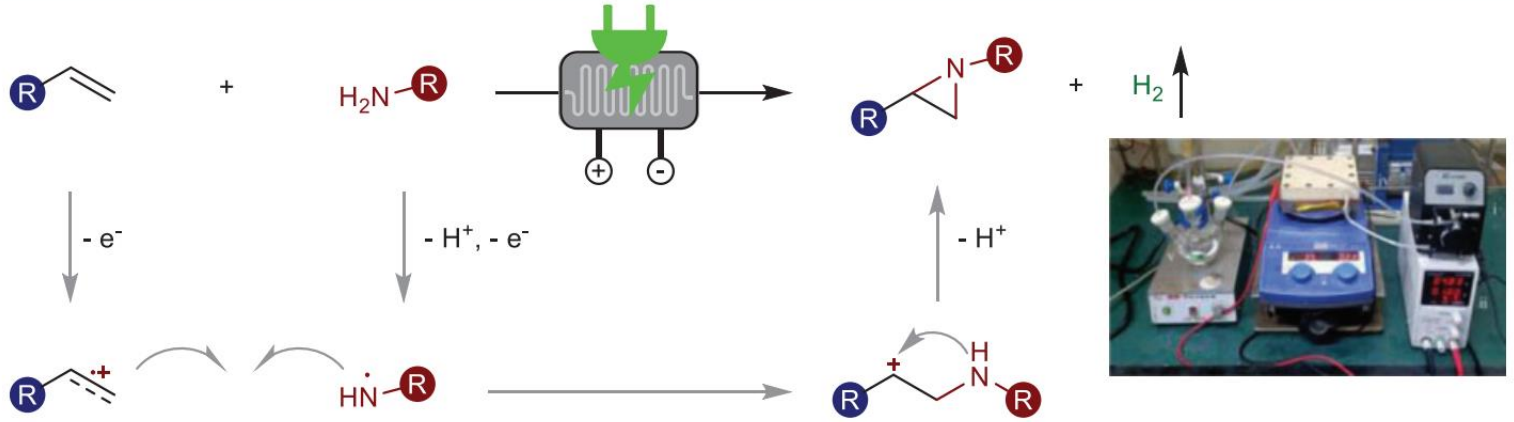
[Co]	(*Z*)-**3a**$_D$:(*E*)-**3a**$_D$
[Co(**P1**)]	89:11
[Co(**P2**)]	94:06
[Co(**P3**)]	98:02

4 Supporting Information



4 Supporting Information

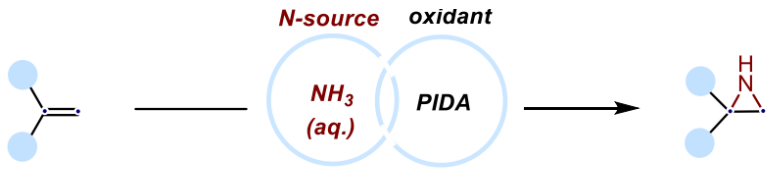
D This work: Electrochemical alkene aziridination via radical/radical cation cross-coupling to access aziridine



Highlights

- ✓ *Broad scope: mono-, di-, tri- and tetra-substituted unactivated alkenes*
- ✓ *> 15 Natural products & drug derivatives*
- ✓ *No metal-catalyst & No extra-oxidant*
- ✓ *Scalable preparation & Good tolerance*
- ✓ *Anticancer treatments in cell lines*

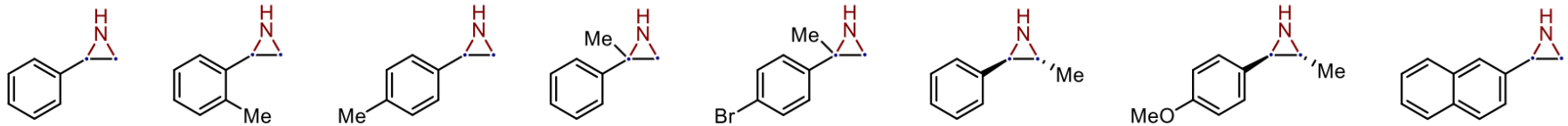
- *Short reaction time*
- *Practical protocol*
- *Commercial reagents*



TFE, 0 °C, 40 min

36 examples, up to 86%

Conditions A: PIDA (2 equiv), NH_3 (30 equiv)



- **2a**, 70%
- 55%
- 33%

2d, 68%

2e, 47%
nitrile, *21%*

2f, 90%

2g, 70%

2h, 45%
dr = 99:1
nitrile, *26%*

- **2i**, 25%
  dr = 95:5
  nitrile, *49%*
- traces

2j, 26%[a]
nitrile, *28%*