The Yang Research Group
Precise Synthesis Lab at Tongji University

同济大学
TONGJI UNIVERSITY

Topic

环丙烷化与骨架编辑新策略
Suero

汇 报 人： 赵珂

时　间　：2026. 09. 25

01 Author Introduction



Marcos García Suero

Professional experience

2014年10月-至今，加泰罗尼亚化学研究所（ICIQ），教授；

2010年5月-2014年10月，剑桥大学，博士后，导师：**Matthew Gaunt**；

2005年夏，哈佛大学，博士期间访问，导师： Andrew Myers；

2003年9月-2009年2月，Enrique Moles 有机金属化学研究所， 博士；导师： José Barluenga、Josefa Flórez；

1999年9月-2003年6月，西班牙奥维耶多大学，学士；

Research

有机合成化学；卡宾化学；自由基化学；光氧化还原催化；立体收敛性合成

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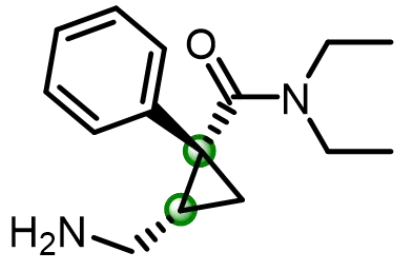
02 骨架编辑

03 Proposal

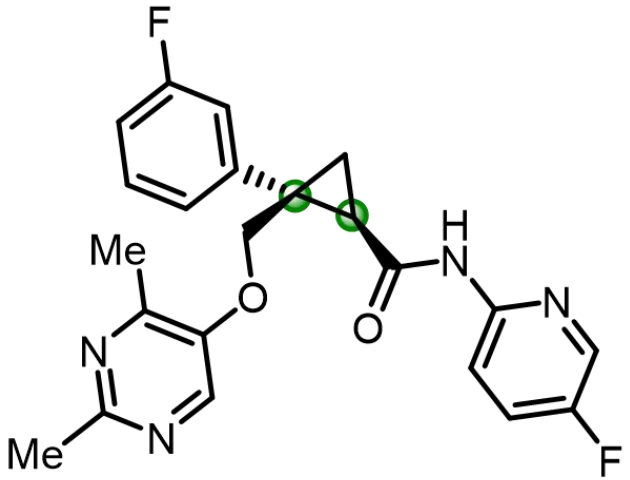
01 研究背景

环丙烷是最小的环状结构，具有较大的结构张力和刚性三维构型，广泛存在于生物活性分子。

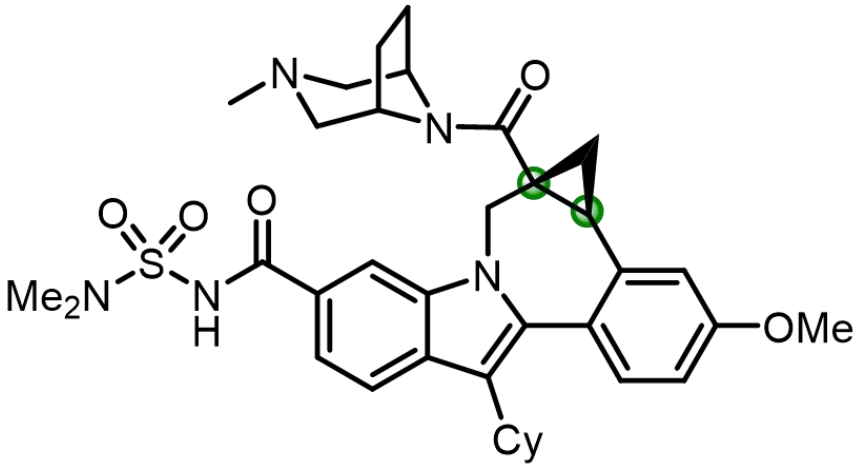
截至 2016 年，已有至少 46 种 FDA 已上市药物含环丙烷结构，其数量级已接近经典含氟药物。



米那普仑（治疗抑郁症）



莱博雷生（治疗失眠）

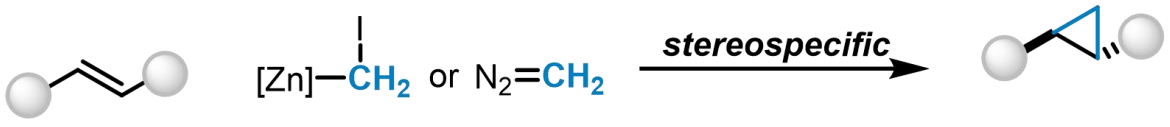


BMS-791325（治疗肝炎）

因此，开发高效、高选择性的环丙烷合成方法，一直是有机合成化学家关注的焦点。

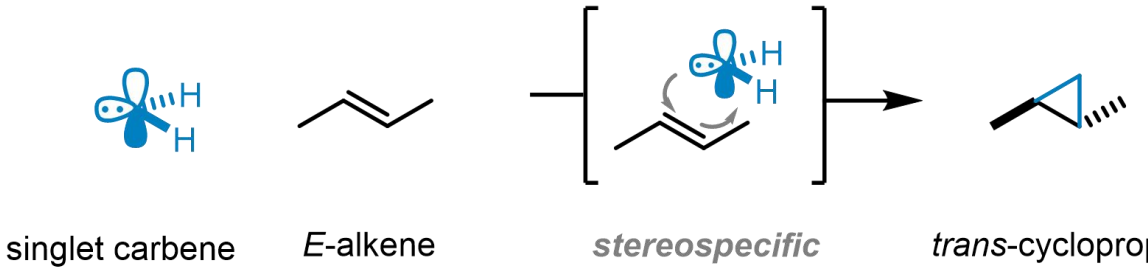
01 研究背景

(1) Traditional strategy for cyclopropane

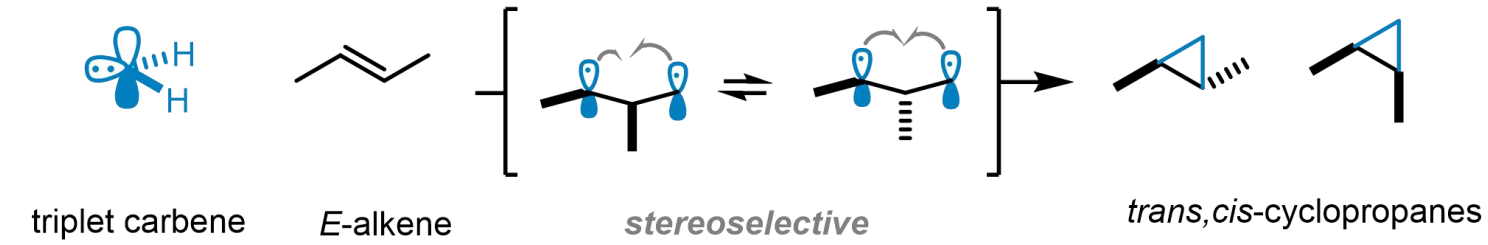


E-alkene　not commercially available　prevalent core in drug molecules

(2) Fundamental reactivity of carbene species



singlet carbene　*E*-alkene　*stereospecific*　*trans*-cyclopropane



triplet carbene　*E*-alkene　*stereoselective*　*trans,cis*-cyclopropanes

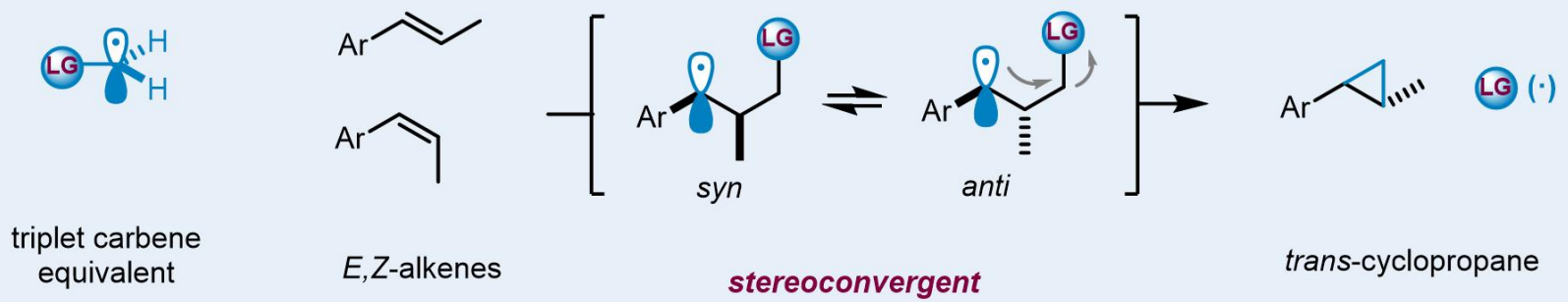
（1）E-烯烃在商业上往往难以获得，且价格昂贵。

（2）三重态卡宾由于立体选择性，无法实现单一构型的精准构建

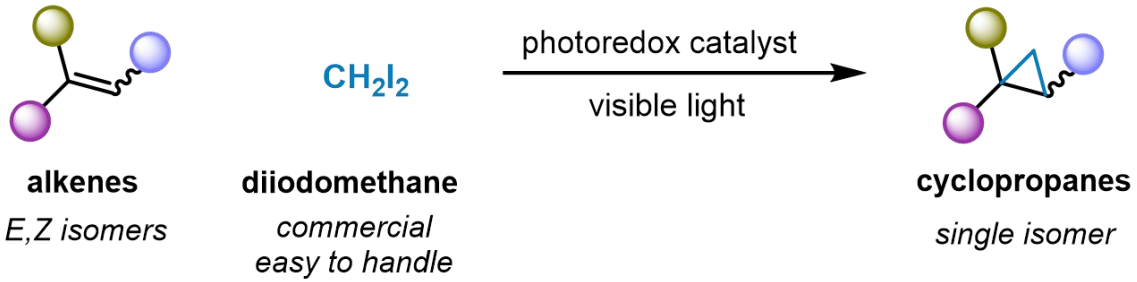
（3）传统方法还需要使用易爆、剧毒的重氮试剂或对水敏感的有机金属试剂，官能团耐受性差，难以用于复杂分子的后期修饰。

01 研究背景

(3) Novel reactivity cncept: radical carbenoid cyclopropanatin

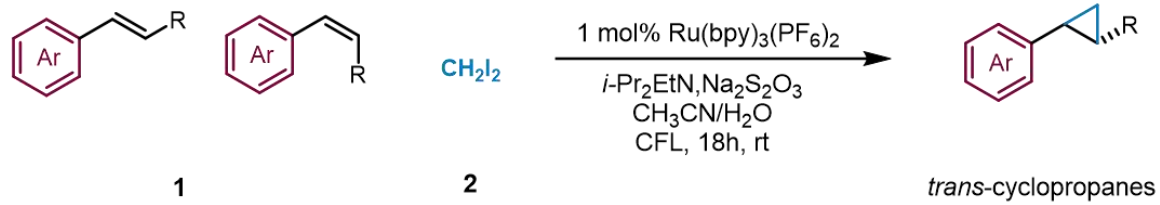


(4)Stereoconvergent cyclopropanatin by means of photoredox catalysis

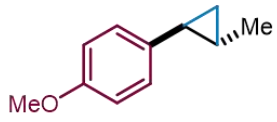


利用一种带有离去基团的三重态卡宾等价物与E/Z-烯烃混合物反应时，会经历一个立体收敛的过程。无论底物是顺式还是反式，最终都能通过C-C键旋转，转化为热力学更稳定的反式环丙烷。

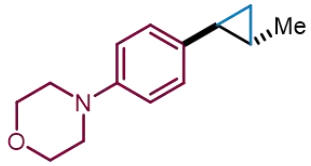
01 环丙烷化反应



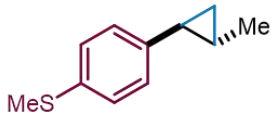
1 **2** *trans*-cyclopropanes **3**



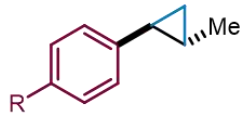
3a 65% [1a 1:2]



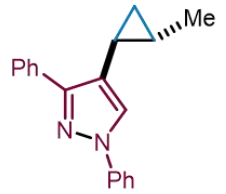
3b 84% [1b 1:3]



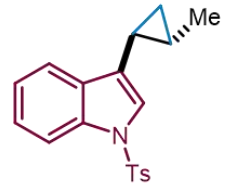
3c 84% [1c 1:1]



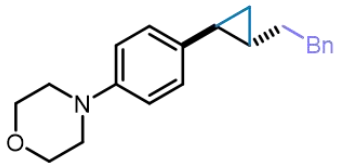
R=CF_3 3h 0% [1h 1:2]
R=CN 3i 22%[1i 1:2]
R=CO_2Me 3j 30% [1j 1:3]



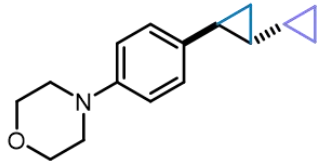
3k 75% [1k 1:3]



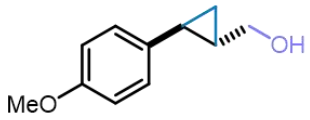
3l 48% [1l 3:4]



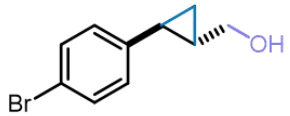
3m 59% [1m 1:9]



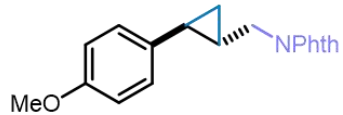
3n 80% [1n 1:1]



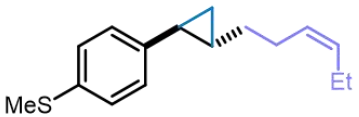
3q 94% [b]



3r 88% [b]



3t 75% [b]

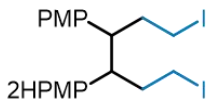


3w 55% [1w 1:1]

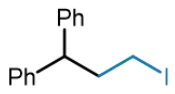


3x 5%

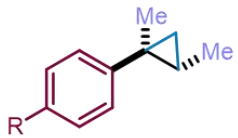
\+



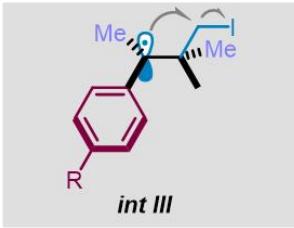
9 35%(1:1)



10 40%



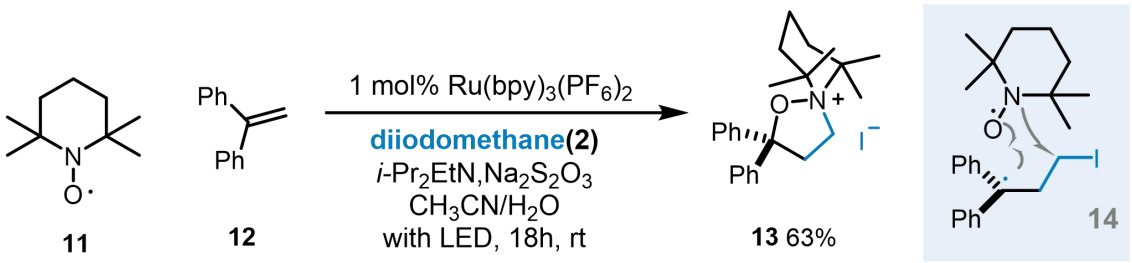
3y 73% [1y 1.5:1]



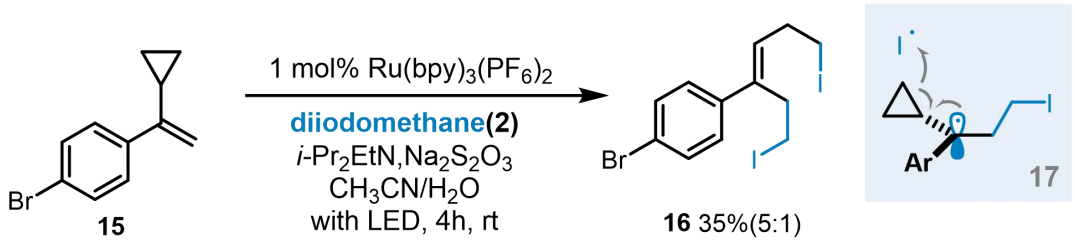
int III

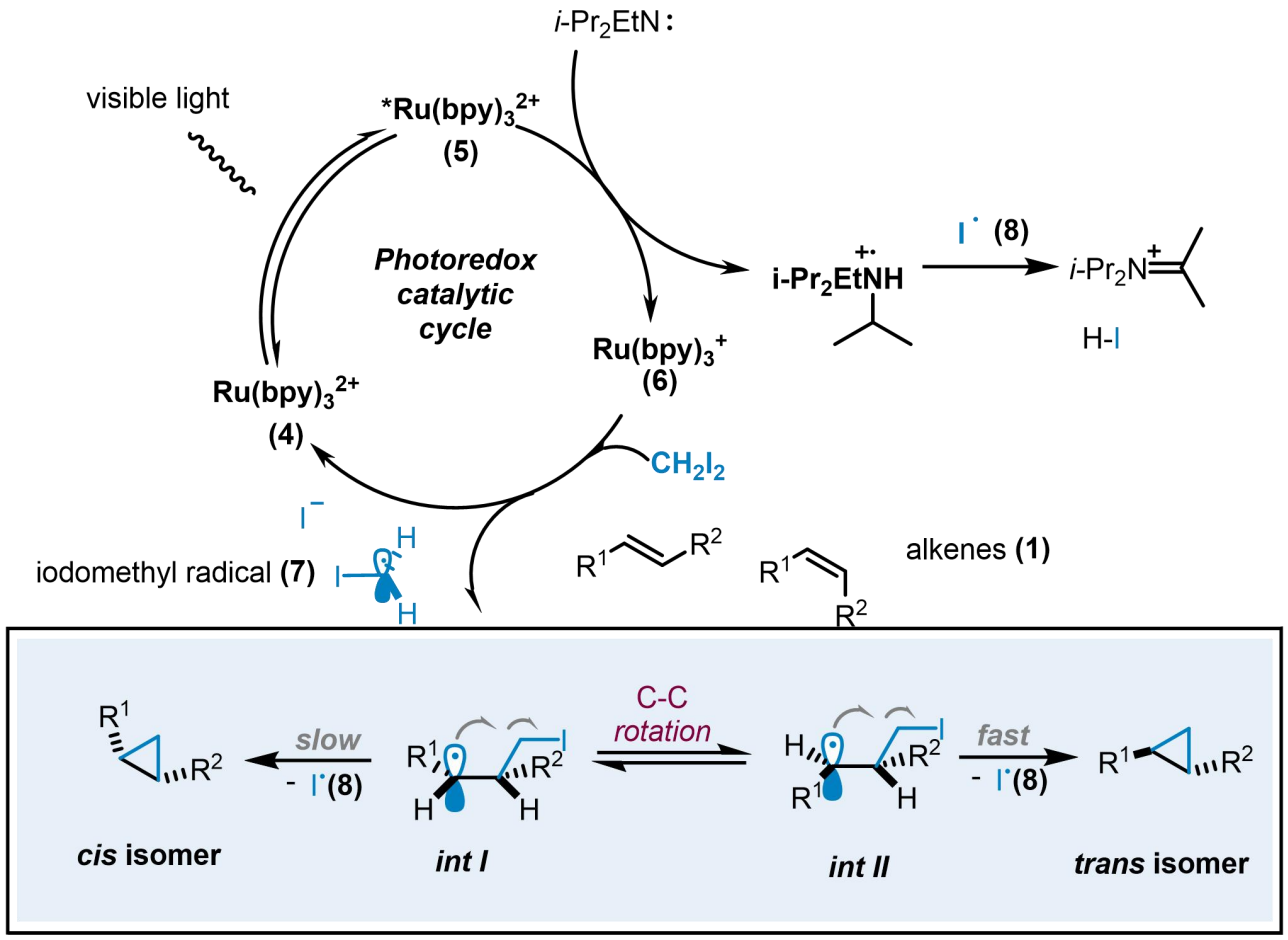
Angew. Chem. Int. Ed. **2017**, *56*, 1610

(1)TEMPO捕获实验：



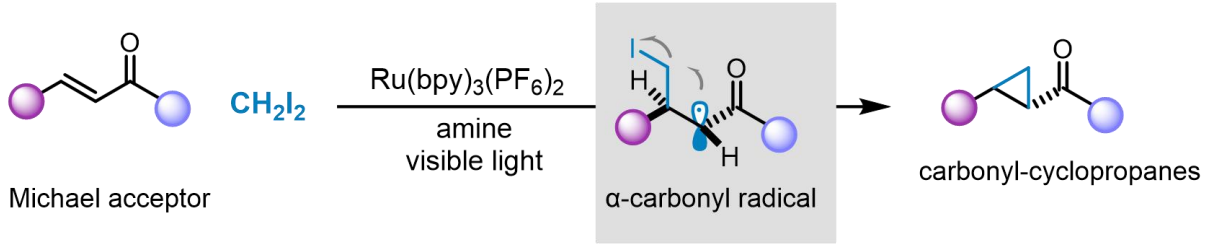
(2)环丙基自由基探针：

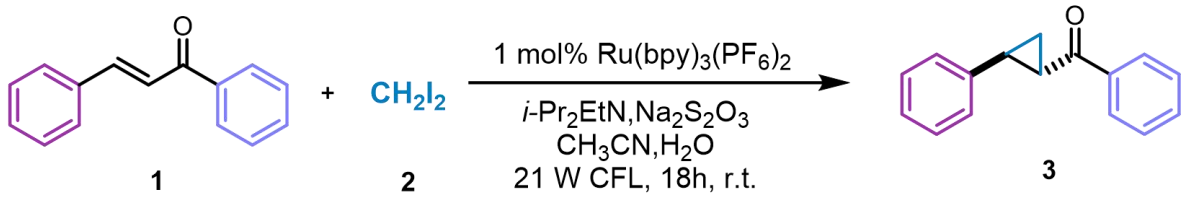


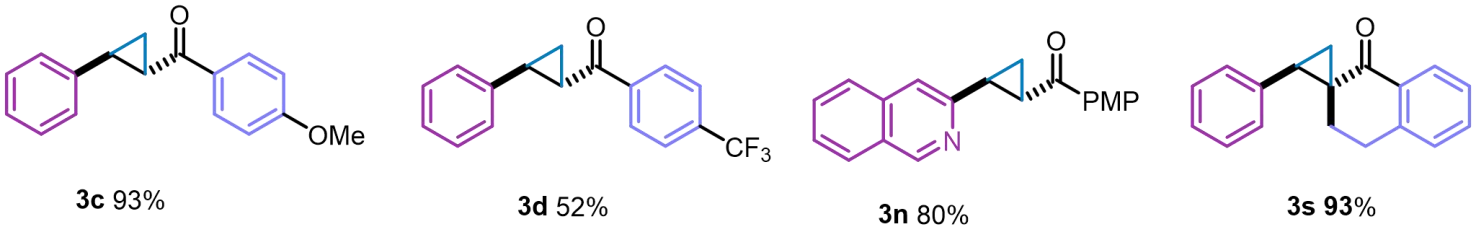


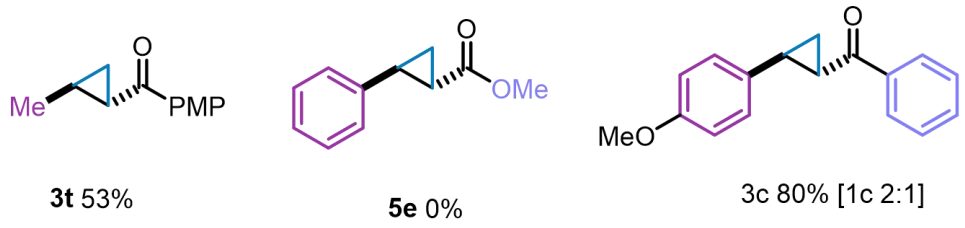
01 环丙烷化反应

Michael受体







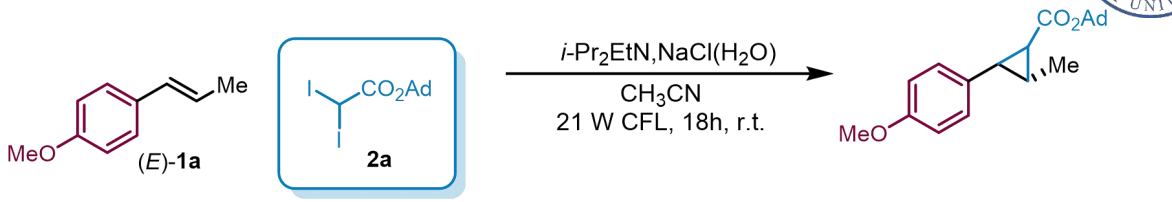


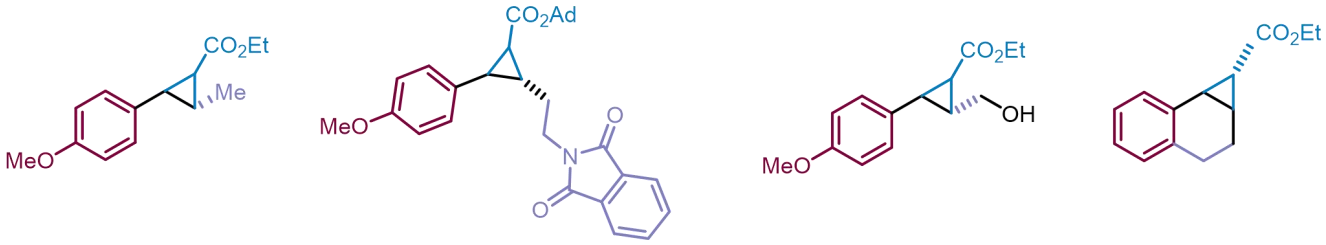
局限：需要贵金属光催化剂，且需要过量二碘甲烷。

Eur. J. Org. Chem. **2017**, *2122.*

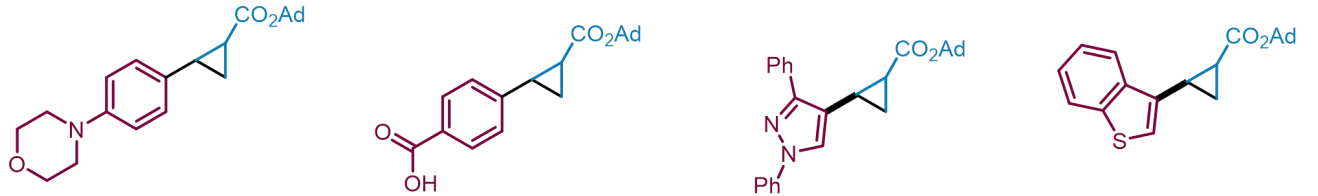
01 环丙烷化反应

gem-二碘甲基羰基试剂

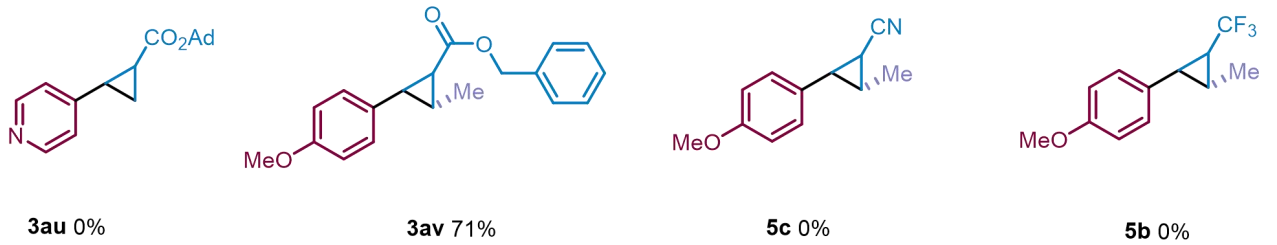




3b 88%　　**3e** 61%[c]　　**3f** 93%　　**3l** 48%



3u 88%　　**3ak** 38%　　**3ao** 73%[c](1:2)　　**3as** 38%[c](1:2)



3au 0%　　**3av** 71%　　**5c** 0%　　**5b** 0%

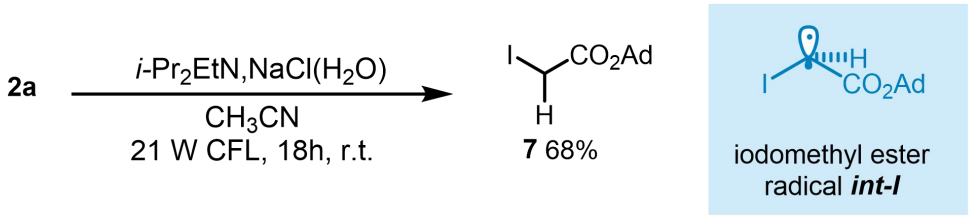
(1) 无过渡金属,无重氮试剂
(2) 可见光驱动
(3) 操作简单、可放大
(4) 官能团容忍性好

Chem. Sci., **2019**, 10, *9374.*

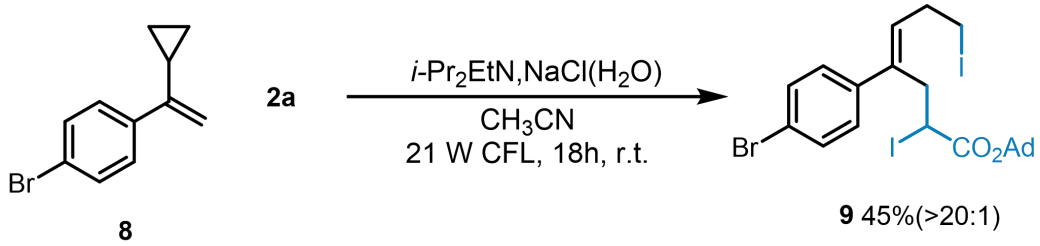
01 环丙烷化反应

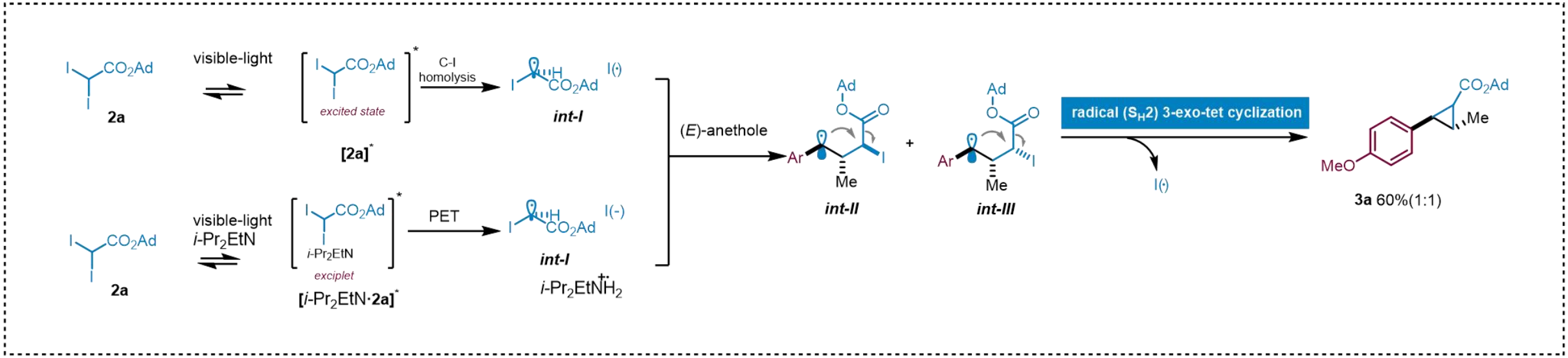
同济大学 TONGJI UNIVERSITY

(1)自由基的生成与捕获：
证明碘甲基酯自由基生成



(2)环丙烷自由基探针：
证明 int-I 能对烯烃进行自由基加成





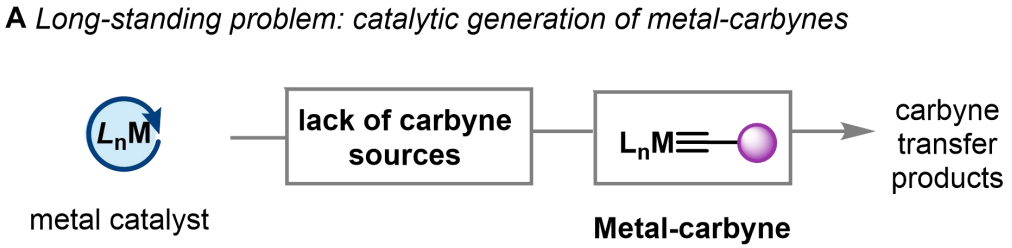
CONTENT

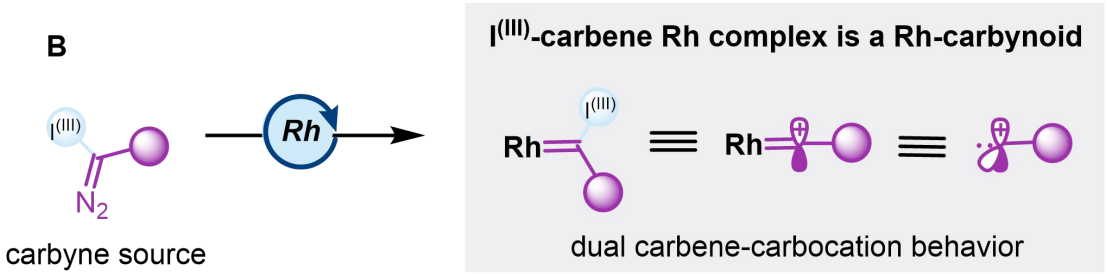
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02 骨架编辑

03 Proposal



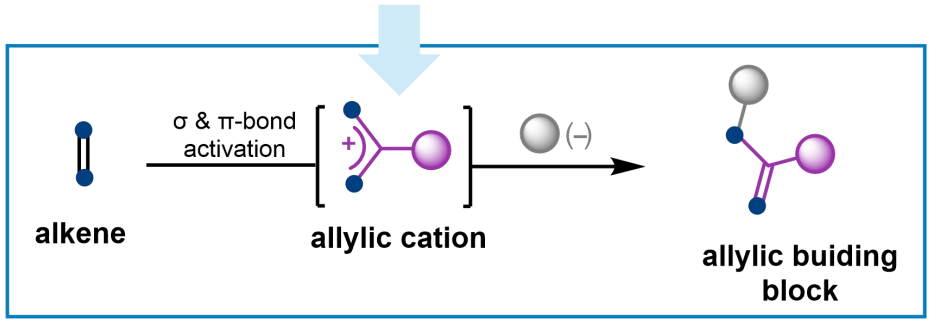


双重卡宾–碳正离子行为

既有卡宾的亲电性；

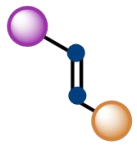
又有碳正离子的亲电性；

还有自由基的反应性。

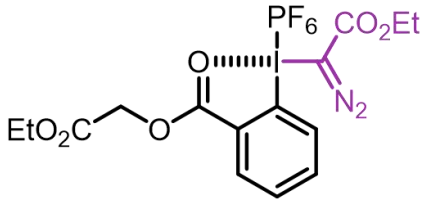


金属卡拜来源匮乏 → 用 Rh-carbynoid 替代 → 实现烯烃的 σ/π 键活化 → 构建烯丙基砌块。

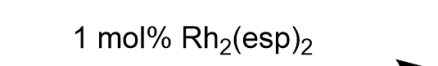
J. Am. Chem. Soc. **2019**, 141, *15509.*

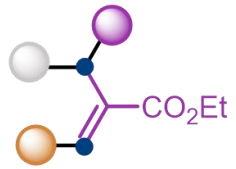


chemical feedstock

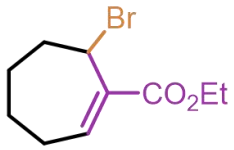


carbyne source 2e

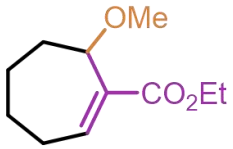




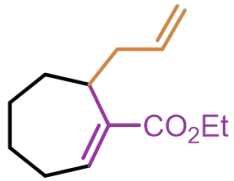
allylic building block



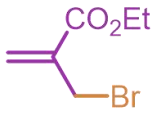
6a 76%(13%)
with Bu_4NBr



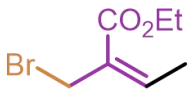
6c 72%(5%)
with MeOH



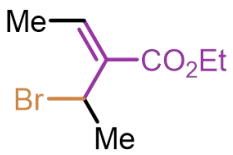
6p 94%
with allyl-$SnBu_3$



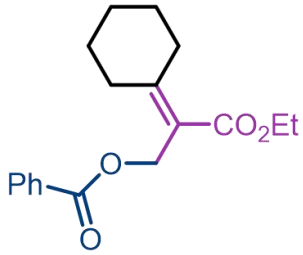
6s 75%
with Bu_4NBr



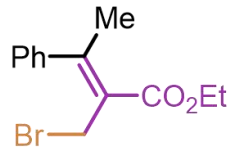
6t 89%((*l*:*b*=14:1),*l* = 3:1(Z:E)
with Bu_4NBr



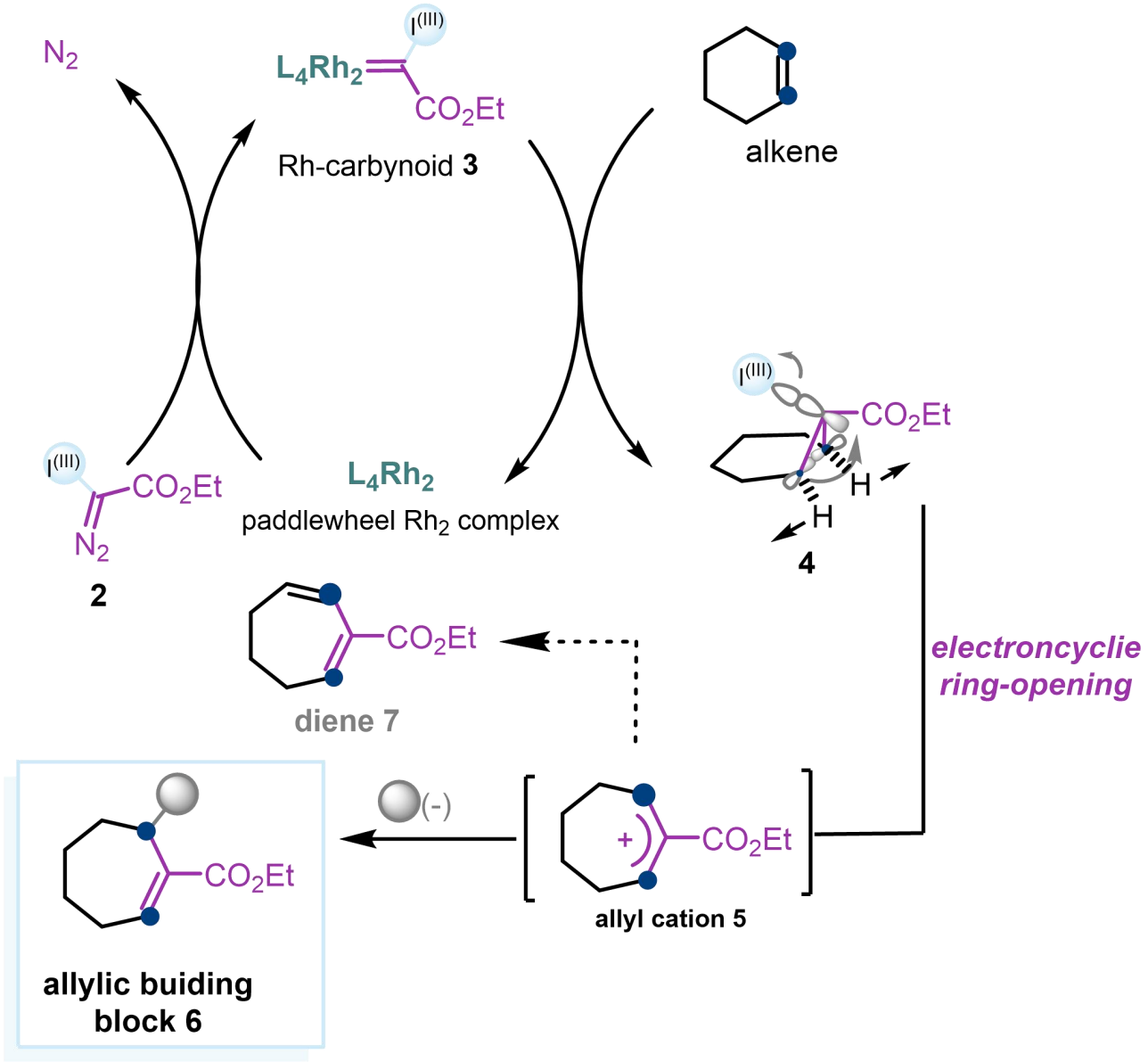
6x 70% 10:1(Z:E)

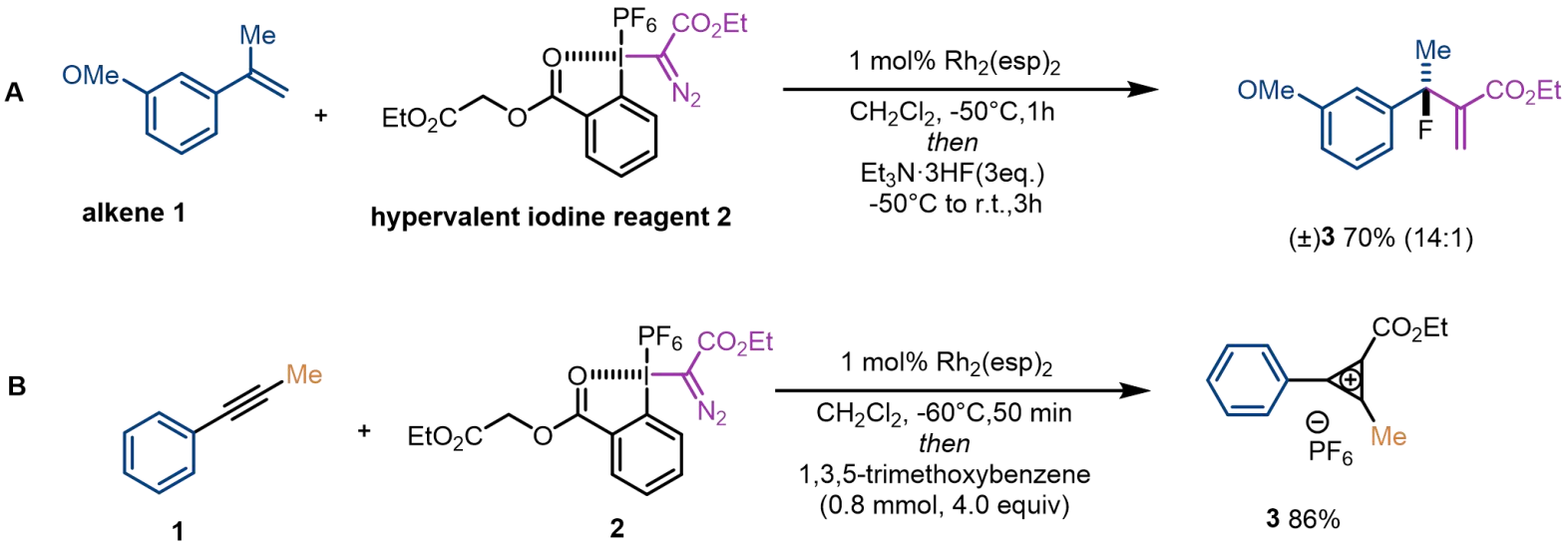


6ac 62% (*l*:*b*=4:1)(15%)



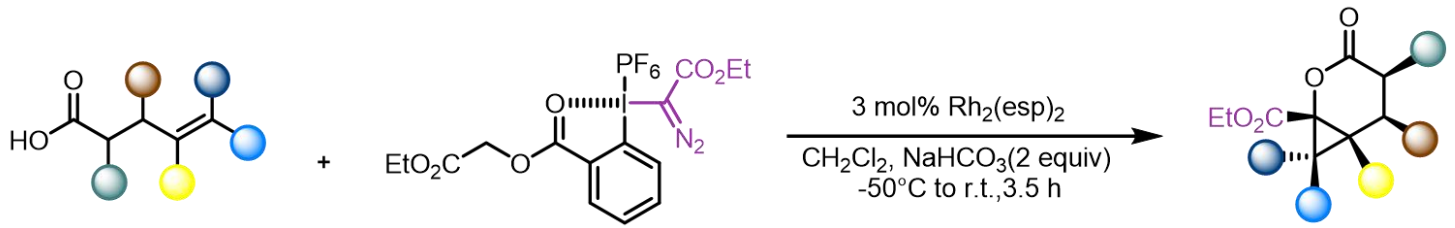
6ab 72% (*l*:*b*=>20:1)14:1(*Z*:*E*)


N2
L4Rh2
CO2Et
Rh-carbynoid 3
alkene
CO2Et
N2
2
L4Rh2
paddlewheel Rh2 complex
CO2Et
H
H
4
electroncyclie
ring-opening
CO2Et
diene 7
(-)
+
CO2Et
allyl cation 5
CO2Et
allylic buiding
block 6

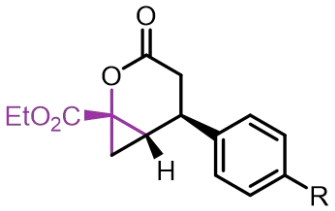


Chem. Sci., **2022**, *13*, 4327.
J. Am. Chem. Soc. **2022**, *144*, 16737.

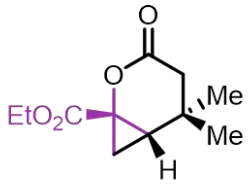
Rh-carbynoid 与羧酸反应生成 Fischer 型酰氧基 Rh(II)-卡宾



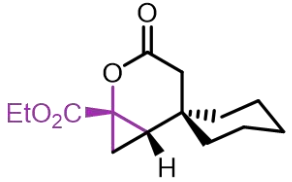
1 + 2 → 3



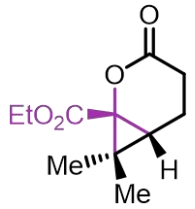
3a R=H,72%(>20:1)
3c R=OMe,50%(>20:1)
3f R=CF_3,45%(>20:1)



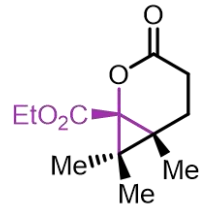
3j 81%(>20:1)



3k 85%(>20:1)

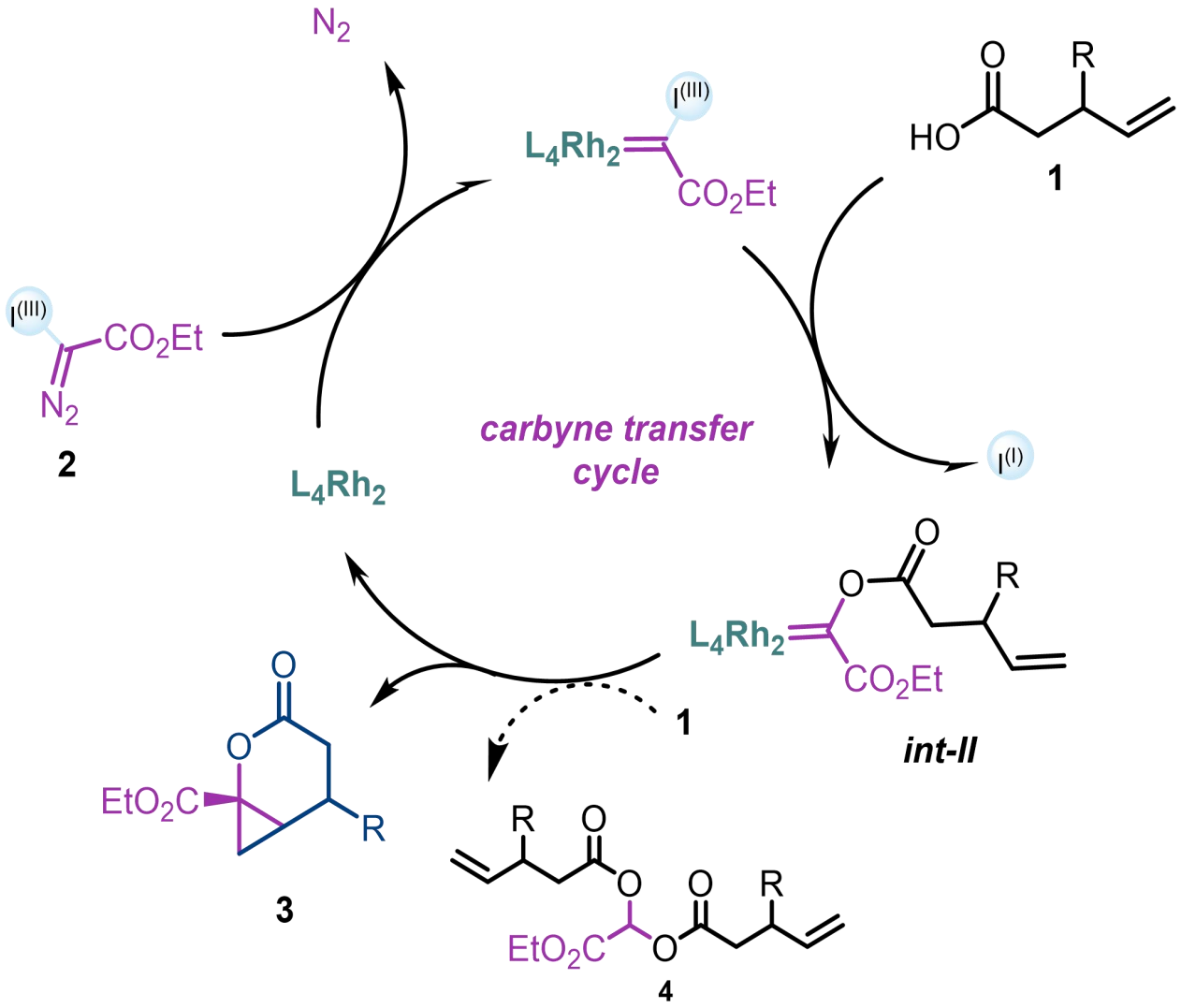


3r 61%(>20:1)



3s 30%(>20:1)

J. Am. Chem. Soc. **2023**, *145*, 4975.


N2
L4Rh2
CO2Et
HO
O
R
1
I(III)
CO2Et
N2
2
carbyne transfer cycle
L4Rh2
I(I)
L4Rh2
CO2Et
int-II
1
EtO2C
R
3
EtO2C
4

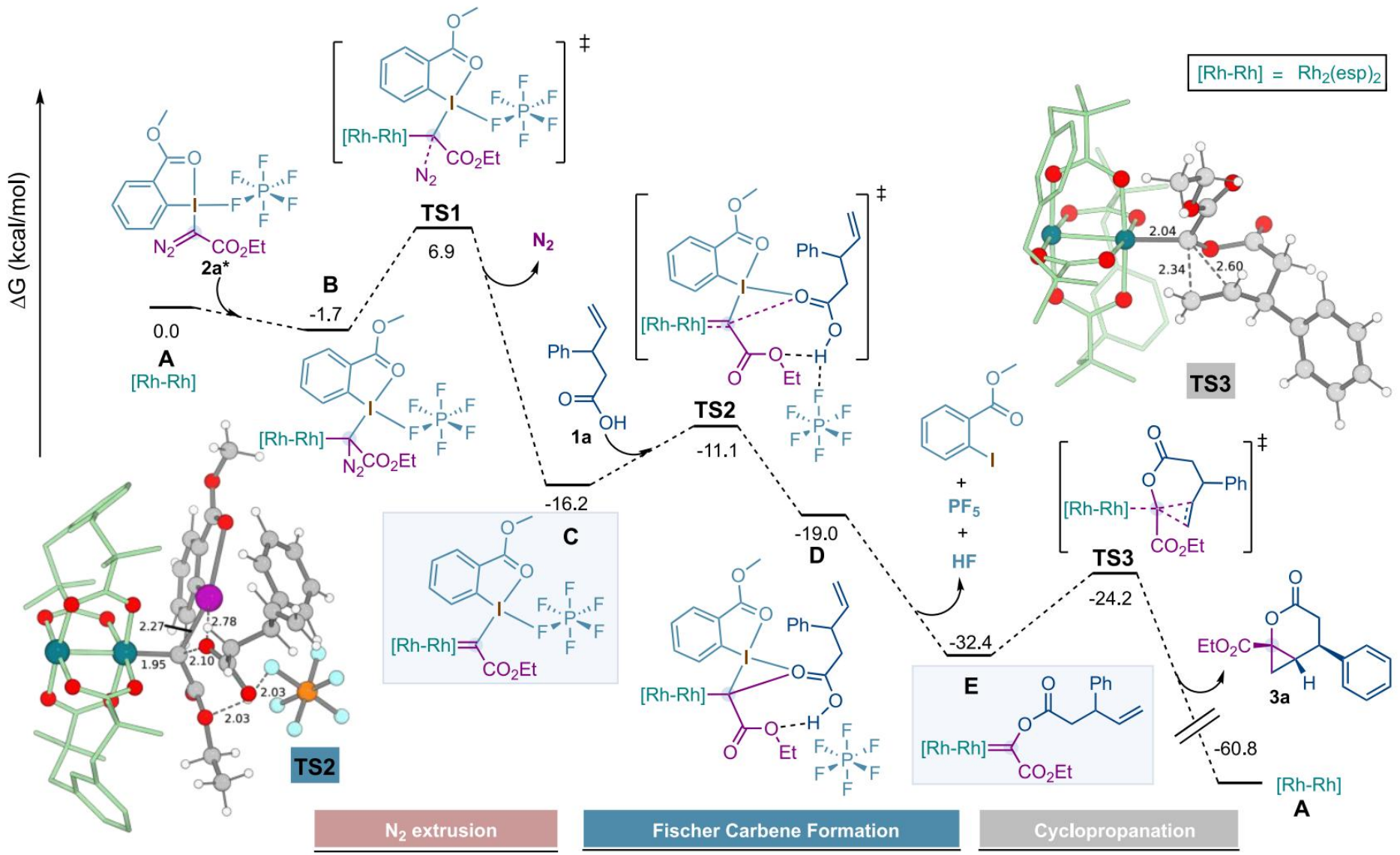
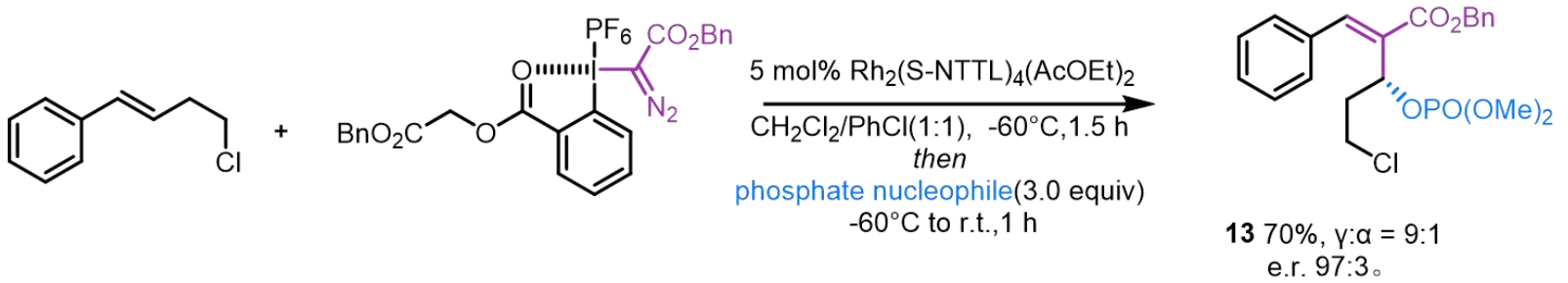


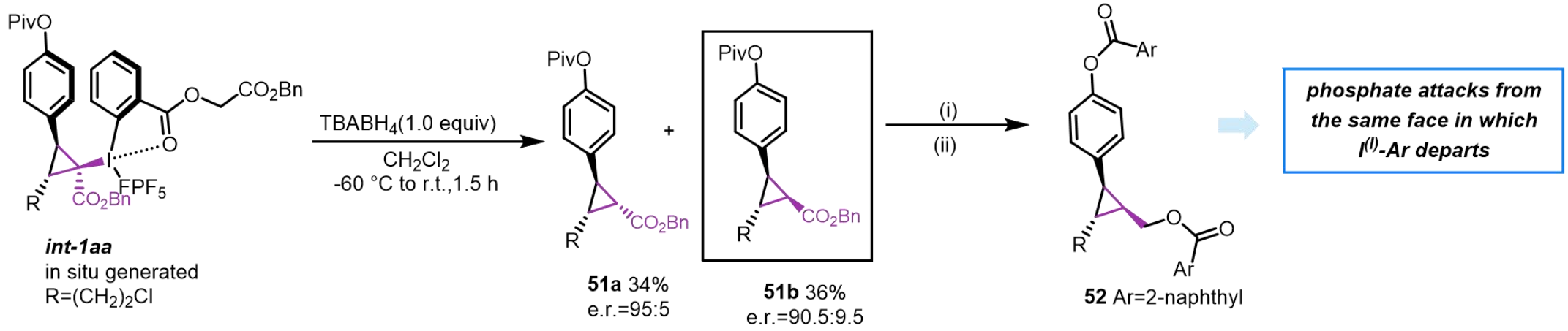
Figure 3. Free energy profile for the catalyzed reaction between **1a** and **2a*** with $Rh_2(esp)_2$.

利用手性 Rh-carbynoid 和磷酸酯亲核试剂，在烯烃的 C(sp²)–C(sp²) 键中插入单价碳，生成对映富集的烯丙基磷酸酯



13 70%, γ:α = 9:1
e.r. 97:3。

a



int-1aa
in situ generated
R=$(CH_2)_2Cl$

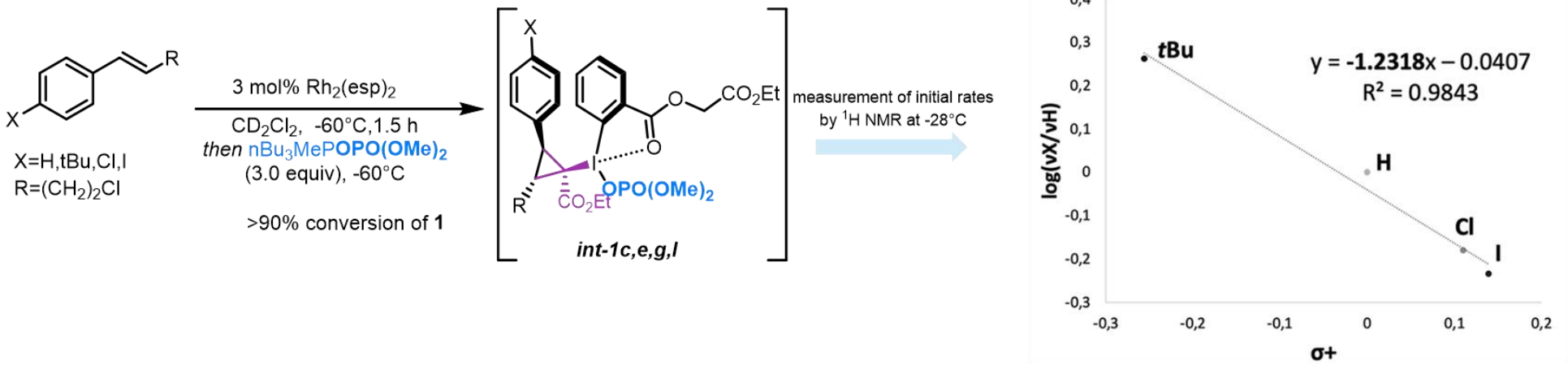
51a 34%
e.r.=95:5

51b 36%
e.r.=90.5:9.5

52 Ar=2-naphthyl

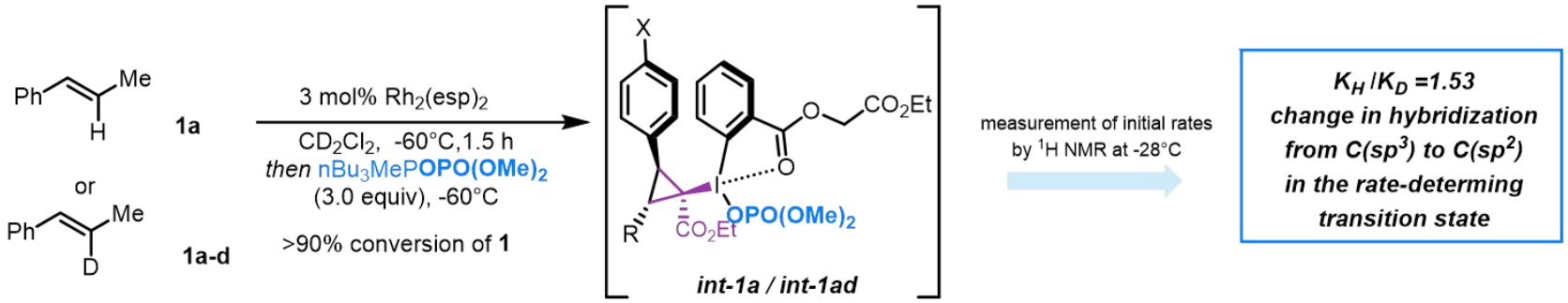
J. Am. Chem. Soc. **2024,** 146, *21837.*

(1)Hammett 图: 反应常数为负值，表明在过渡态中有正电荷积累。

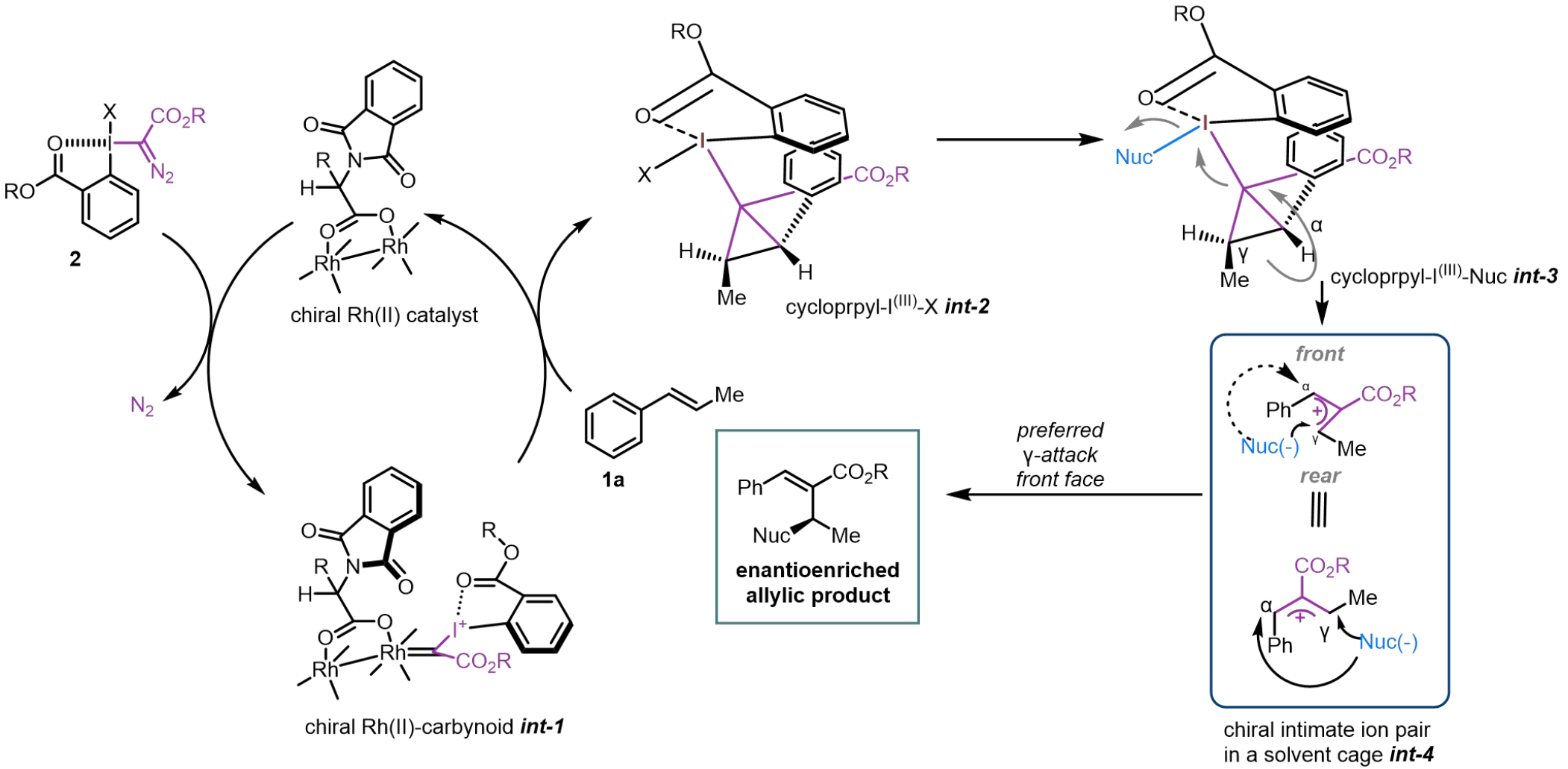


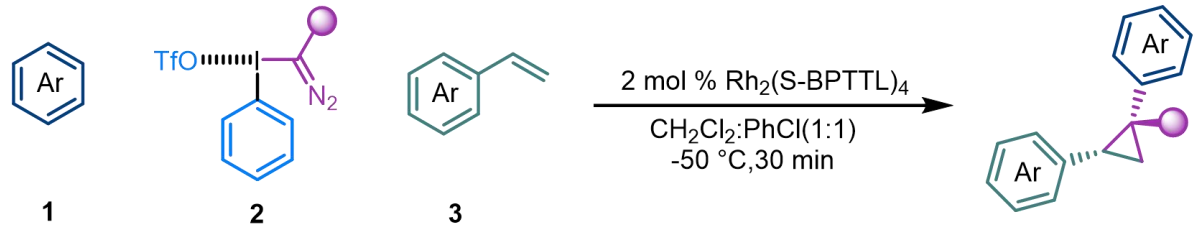
ρ^+= -1.2
positive charge accumulation in the rate-determining transition state

(2)动力学同位素效应 (KIE): 推断决速步是电环化开环，而非 C–H 键活化

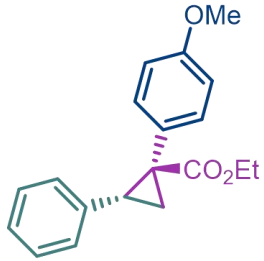


K_H/K_D =1.53
change in hybridization from C(sp^3) to C(sp^2) in the rate-determing transition state

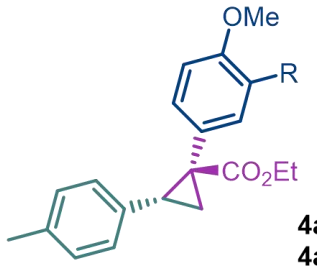

2
chiral Rh(II) catalyst
cycloprpyl-I(III)-X int-2
cycloprpyl-I(III)-Nuc int-3
1a
enantioenriched allylic product
preferred γ-attack front face
front
rear
chiral intimate ion pair in a solvent cage int-4
chiral Rh(II)-carbynoid int-1



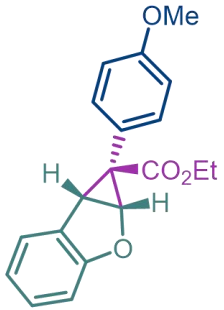
1 2 3



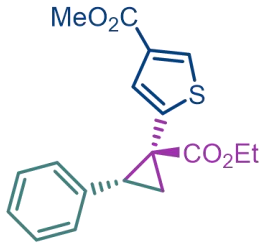
4a 87%(99:1)



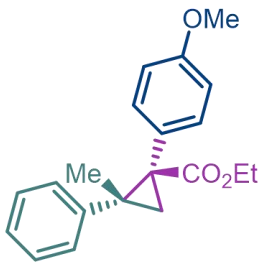
4ac R=F,47%(96:4)
4ae R=I, 38%(96:4)
4ag R=Et,67%(98:2)



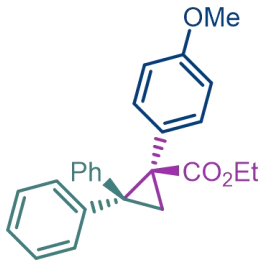
4v 50%(97:3)



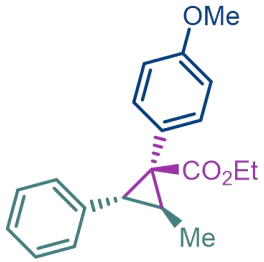
4as 35%(95:5)



4r 32%(85:15)

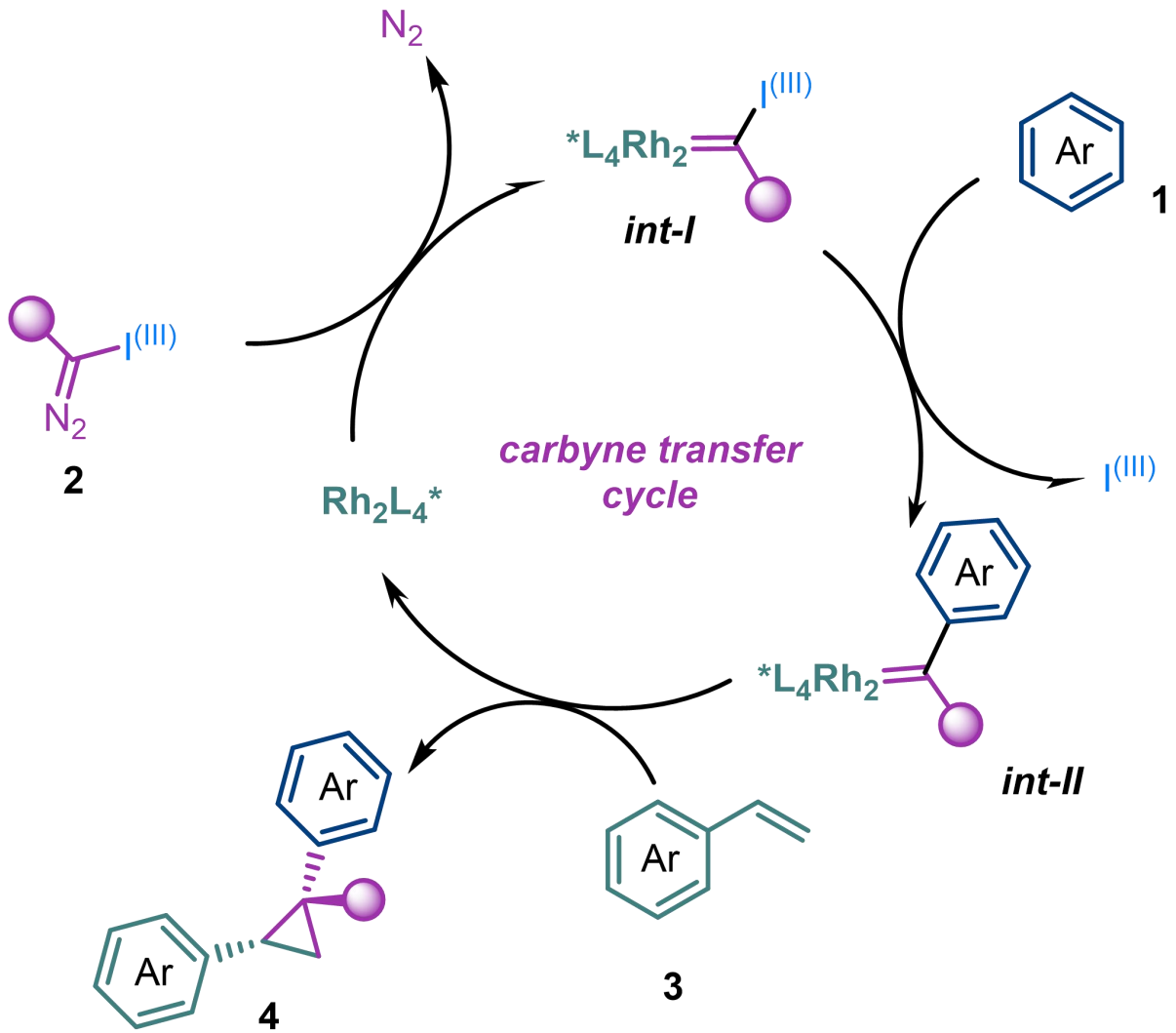


4s 62%(96:4)



4t n.d.

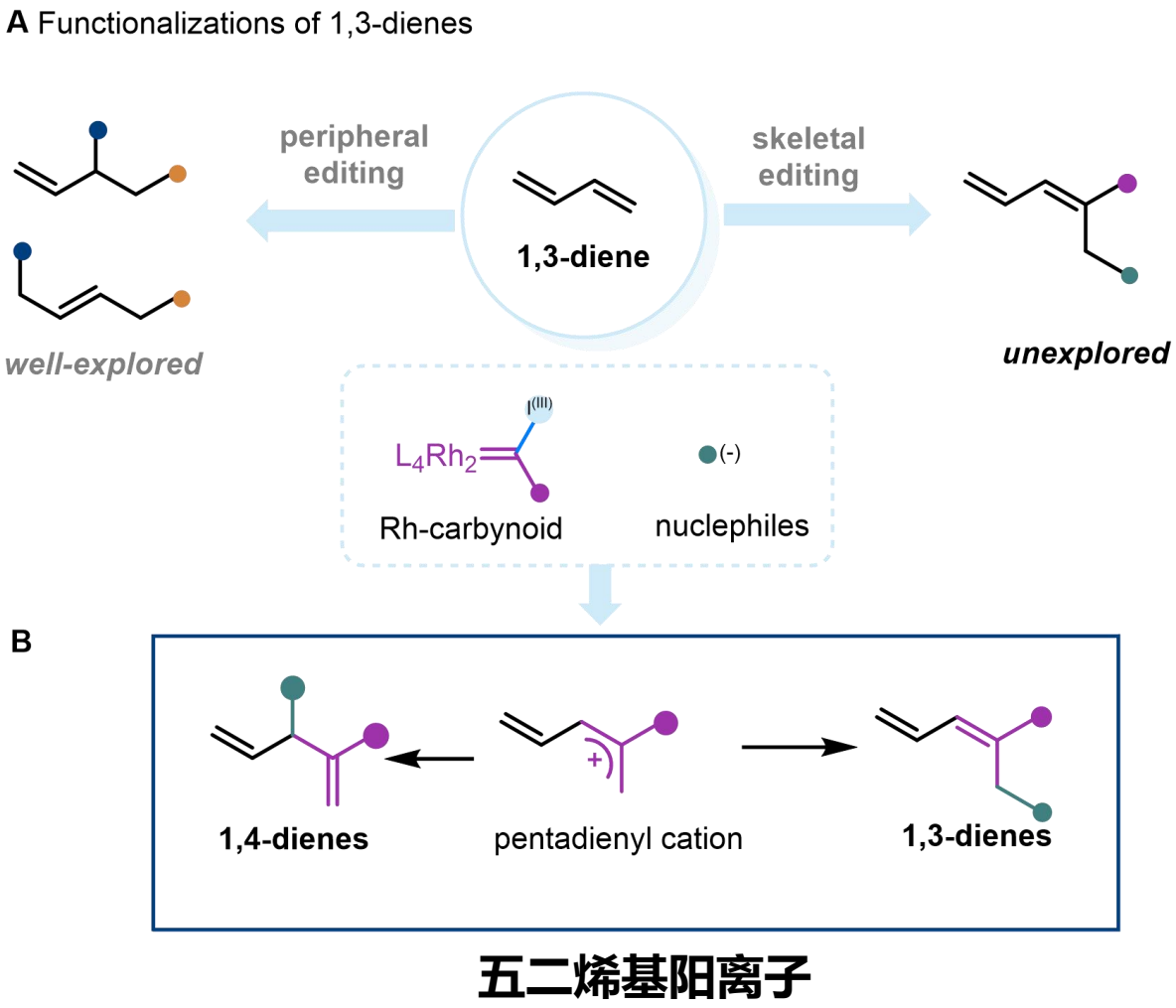
J. Am. Chem. Soc. **2025**, *147*, 13120



关键: 手性 Rh-carbynoid 对富电子芳烃的 C–H 键进行**区域选择性官能化**，生成手性 Rh(II)-卡宾，再与烯烃发生**立体专一性环丙烷化。**

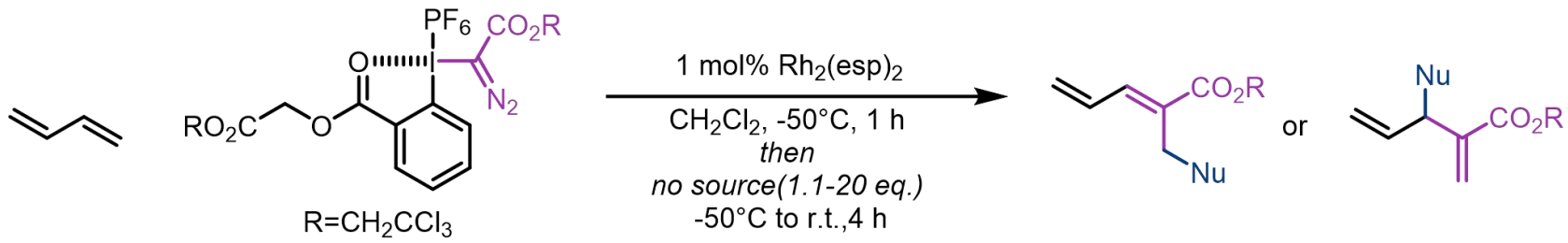
02 骨架编辑

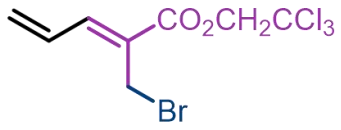
自 Diels-Alder 反应发现以来，1,3-二烯已成为复杂天然产物、药物分子和聚合物合成中最重要的砌块之一。



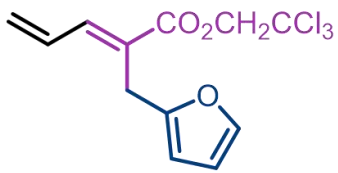
五二烯基阳离子

Chem. Sci., **2025**, *16*, 13042

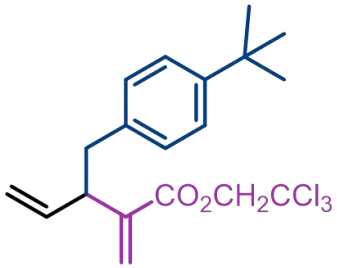




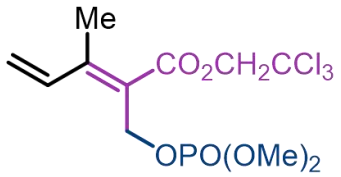
3a 82%
l:b >20:1
Z:E =7:1



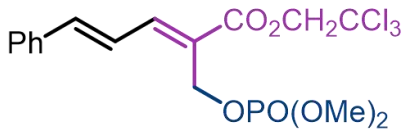
3i 57%
l:b >20:1
E:Z =2.8:1



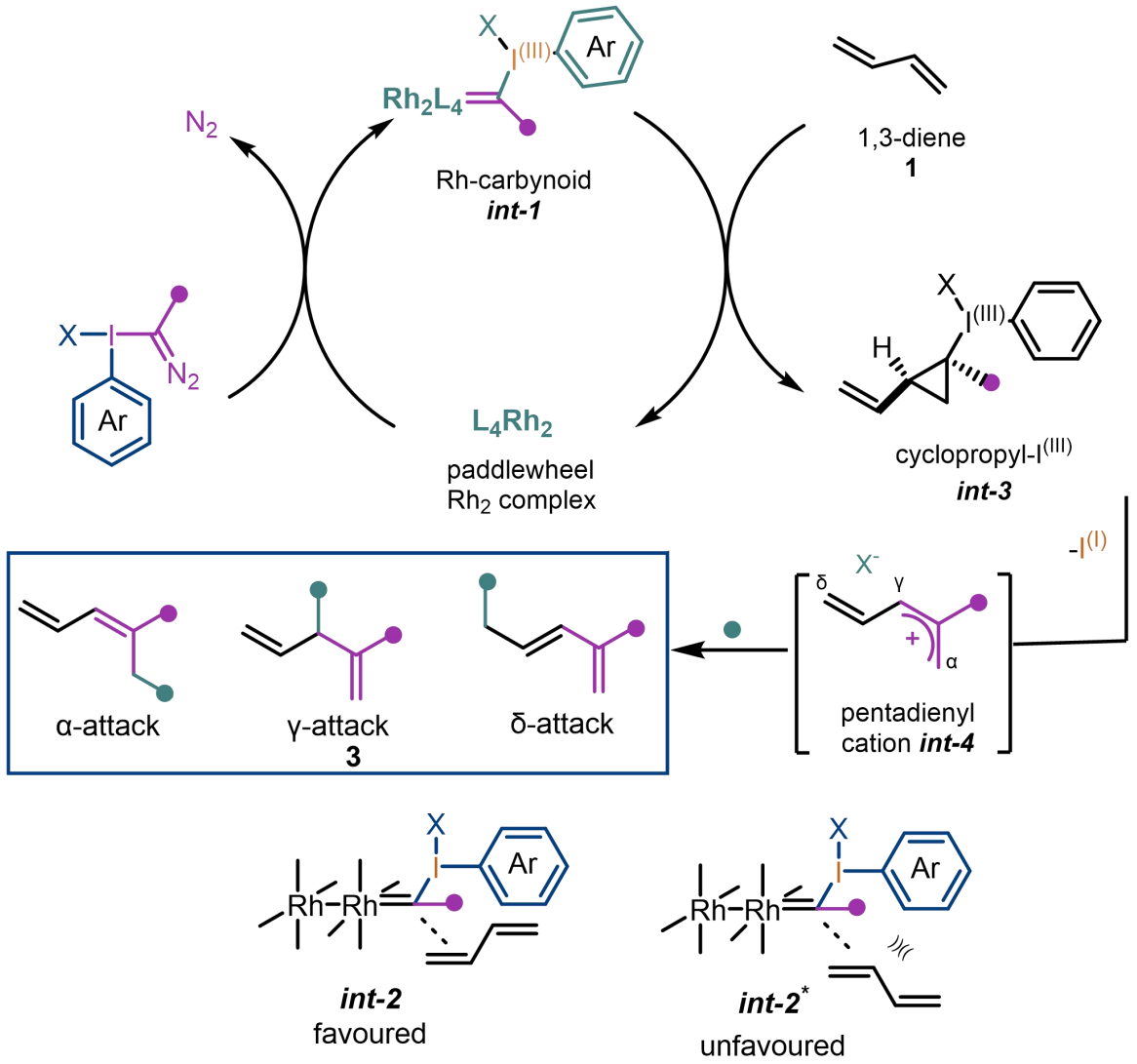
3w 41%
b:l >20:1



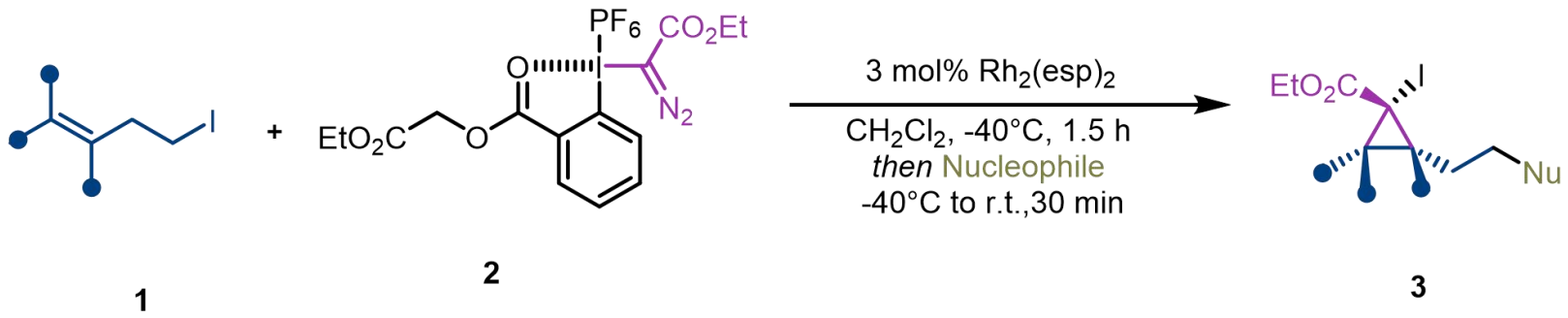
4a 50%
Z:E =1:1



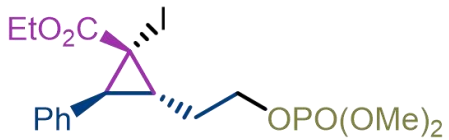
4b 40%
l:b >20:1,E:Z >20:1


Rh-carbynoid
int-1
1,3-diene
1
paddlewheel
Rh2 complex
cyclopropyl-I(III)
int-3
pentadienyl
cation int-4
α-attack
γ-attack
δ-attack
3
int-2
favoured
int-2*
unfavoured

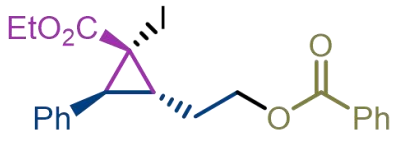
Rh-carbynoid 含有高价碘，发生氧化配体转移，催化生成alkyl-I(III) Rh-carbynoid



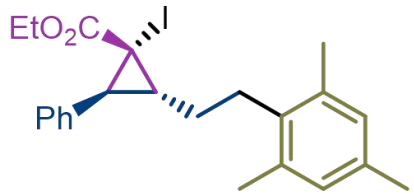
1 2 3



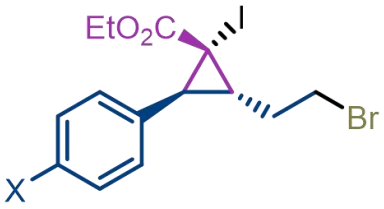
3a 72%



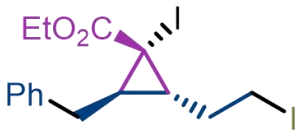
3m 75%



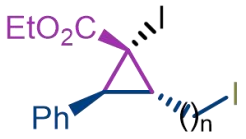
3y 93%



3aa X=CF_3, 72%
3ab X=Ph, 30%

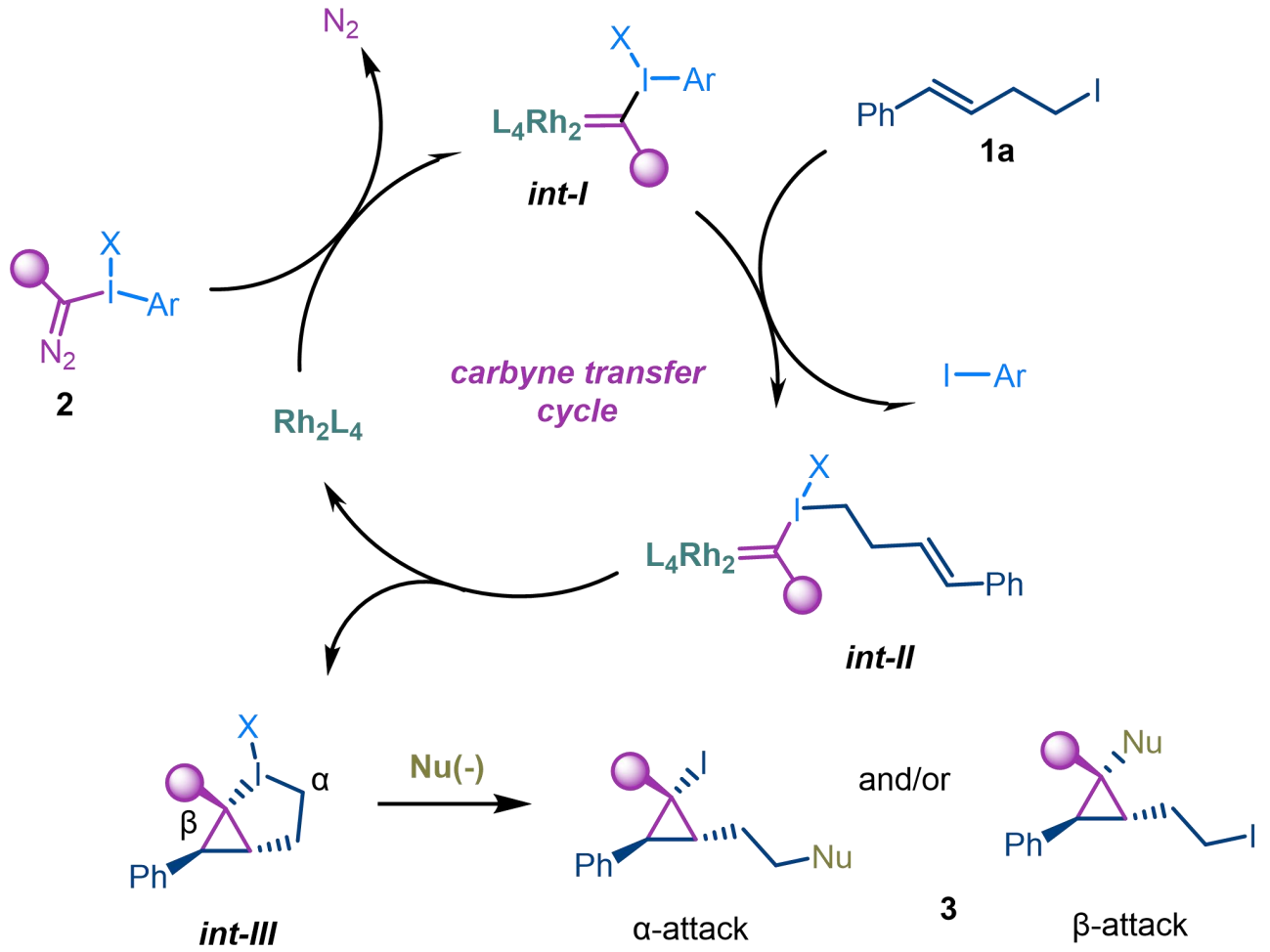


3aq 90%

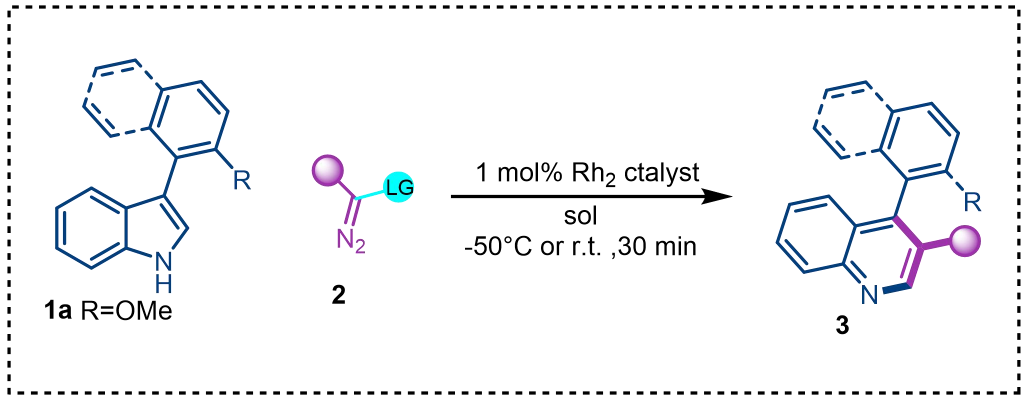


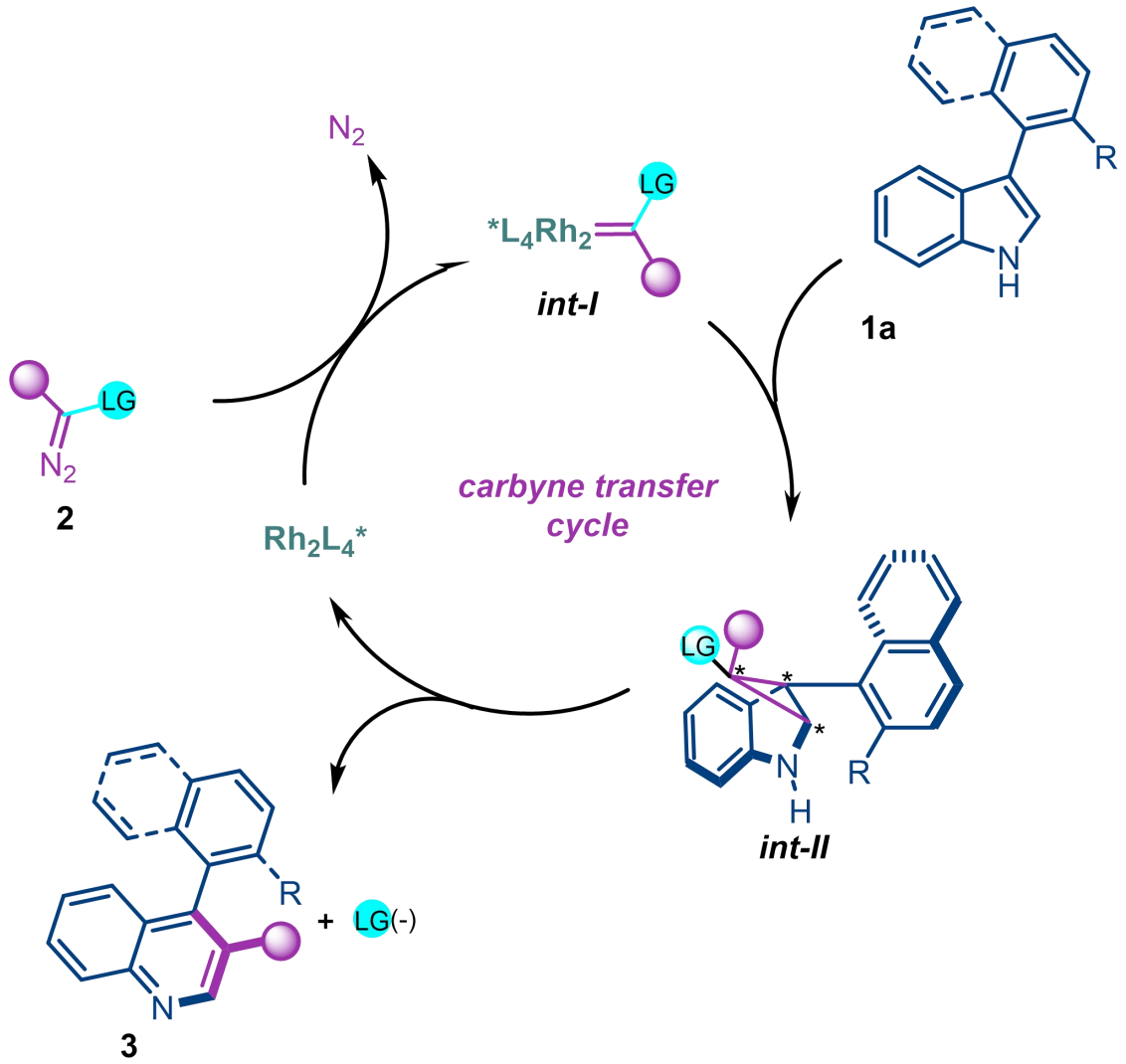
3aw n=0 0%
3ax n=2 0%
3ay n=3 50%
3az n=4 <5%

J. Am. Chem. Soc. **2025,** *147,* 31444.


N2
X
I—Ar
L4Rh2
int-I
Ph
I
1a
X
I—Ar
N2
2
Rh2L4
carbyne transfer cycle
I—Ar
X
L4Rh2
Ph
int-II
X
I
α
β
Ph
int-III
Nu(-)
I
Ph
Nu
α-attack
and/or
3
Nu
Ph
I
β-attack

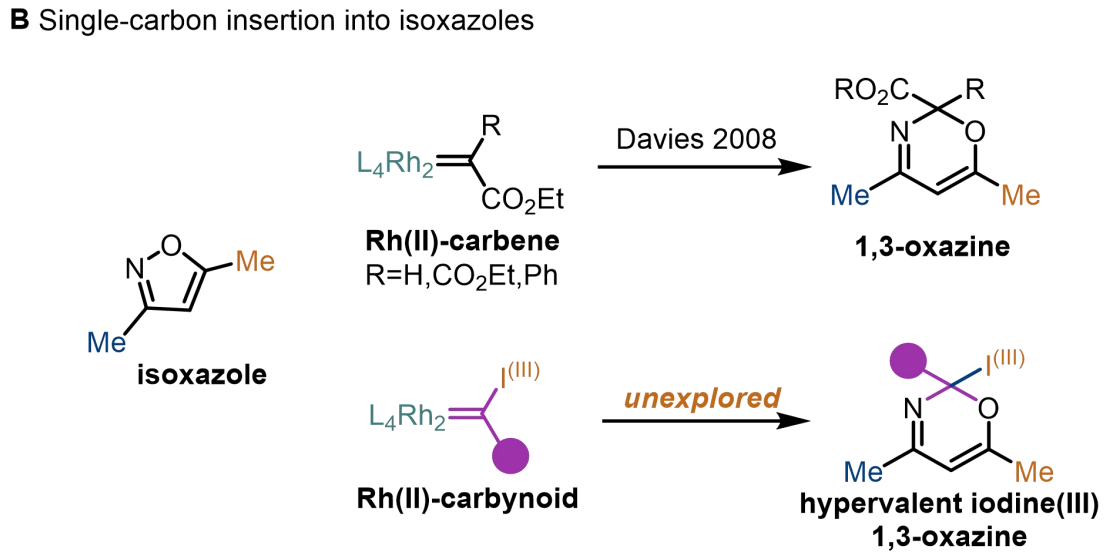
单碳插入构建轴手性喹啉

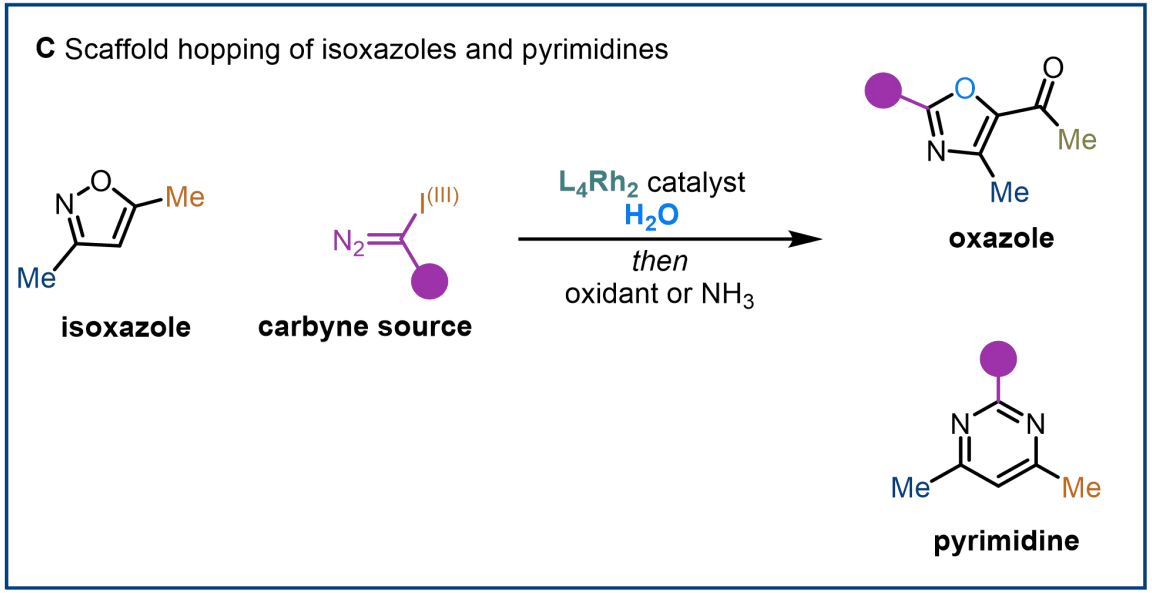




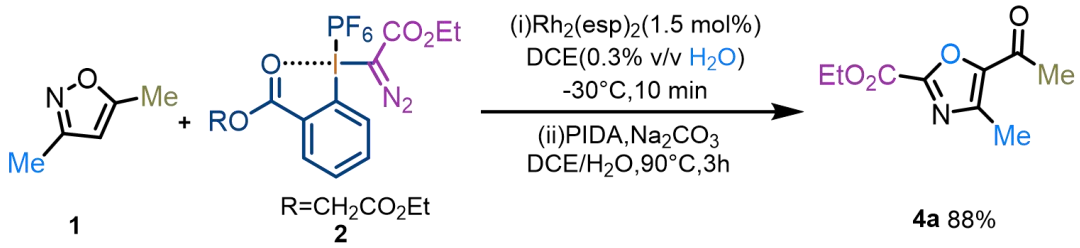
J. Am. Chem. Soc. **2025,** *147, 24206.*

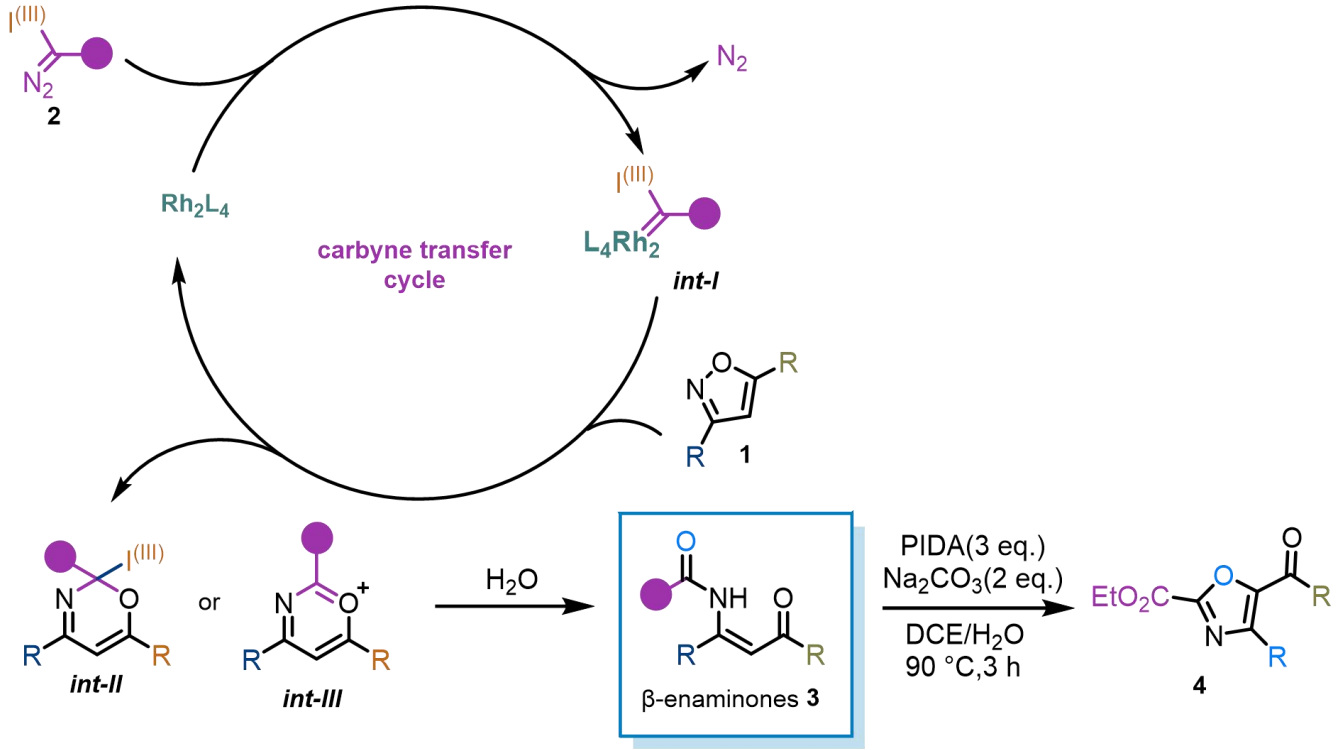
单碳插入扩展到杂环 N–O 键，实现了异噁唑的骨架跃迁





ACS Catal. **2026**, *16*, 13597.





β-烯胺酮3是一个多功能中间体，可以通过 PIDA 氧化环化转化为噁唑，或者与乙酸铵缩合转化为嘧啶。

CONTENT

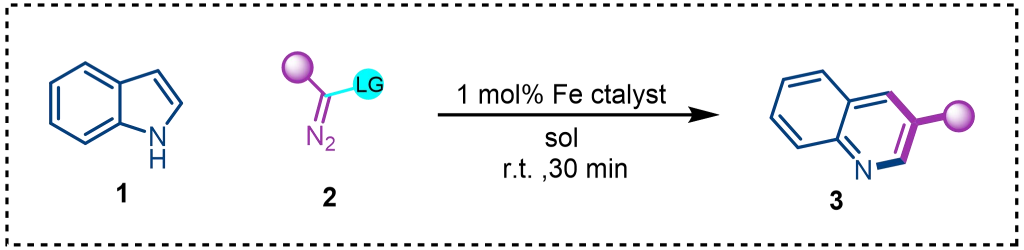
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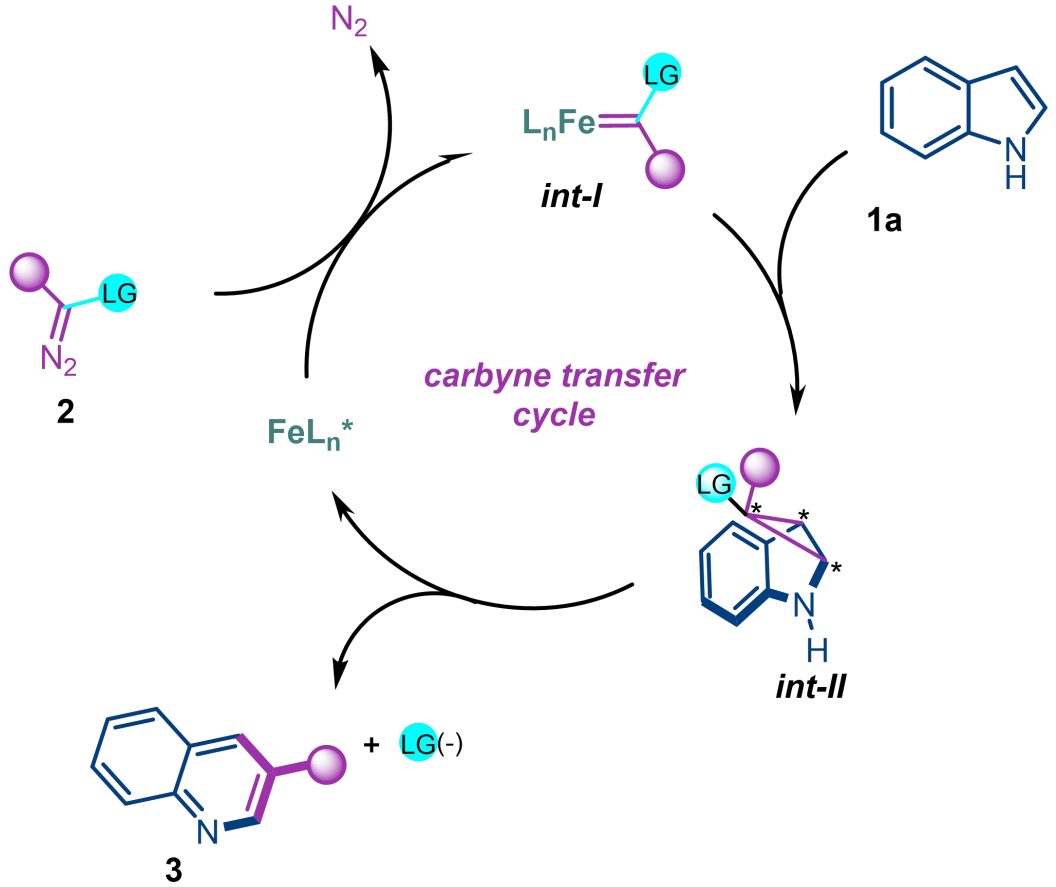
01 环丙烷化反应

02 骨架编辑

03 Proposal

03 Proposal


1 mol% Fe ctalyst
sol
r.t. ,30 min
1
2
3


N2
LG
LnFe
int-I
1a
2
FeLn*
carbyne transfer
cycle
int-II
+ LG(-)
3

敬请老师批评指正！

汇报人：赵珂

导　师：杨泽鹏　教授

时　间：2026. 09. 25