未活化芳烃去芳构化反应的研究进展

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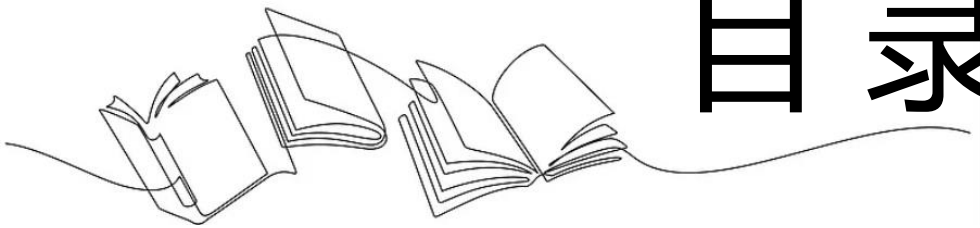
指导老师：　朱灿 青年研究员
日期：　　2026.3.13

目录



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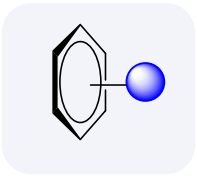
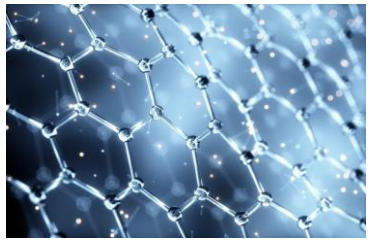


- 物质科学中最基础、最重要的**有机结构单元**之一。
- 苯环是连接基础有机化学与应用世界（医药、材料、生命科学）最核心、最成功的**桥梁**。

稳定性

有机化学  **应用世界**

医药领域

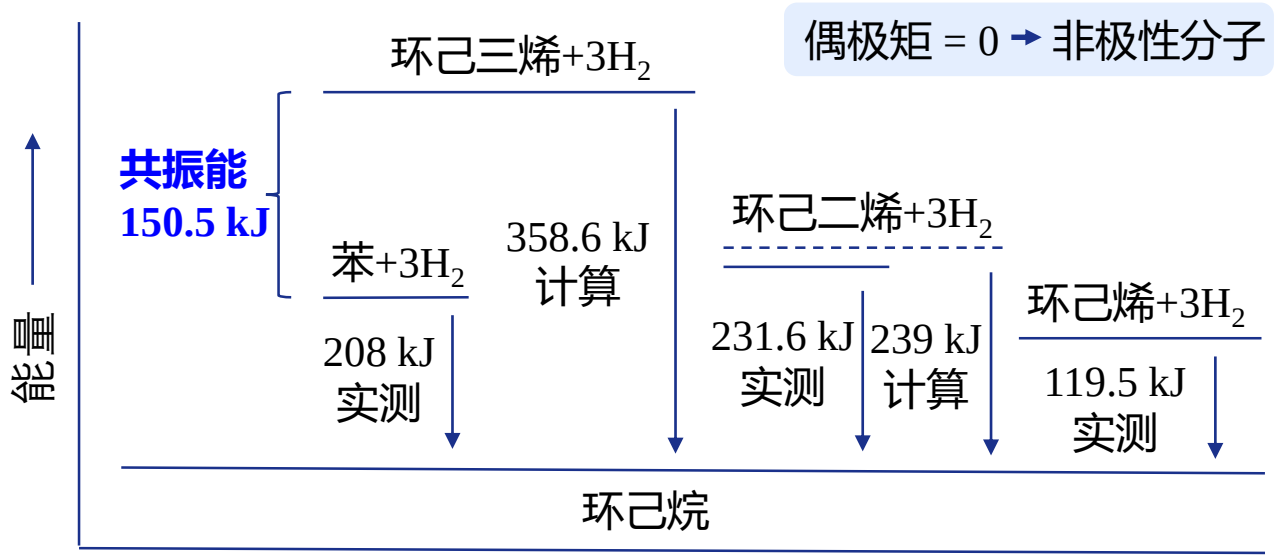


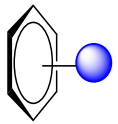
材料领域

能源领域

生命科学领域

苯环大π键：高度离域、能量极低、芳香性极强的共轭体系

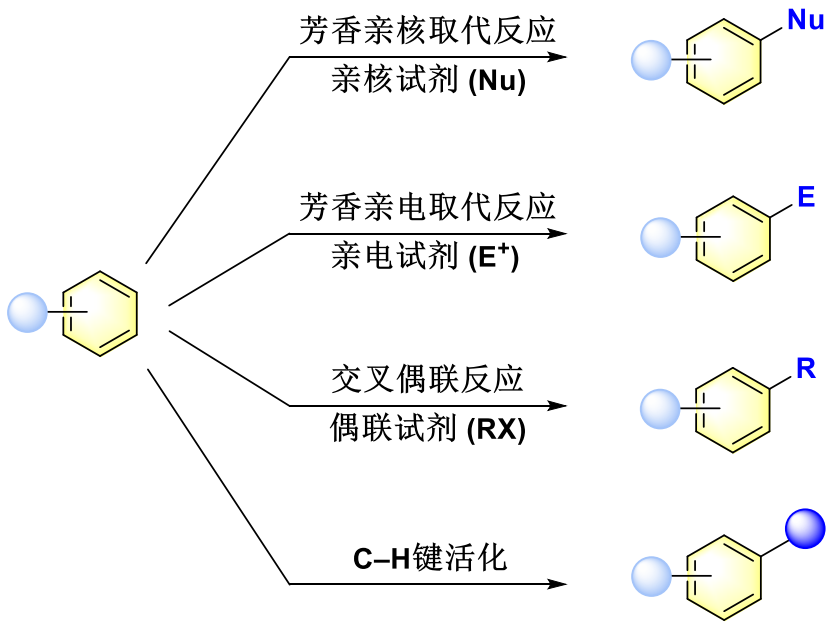




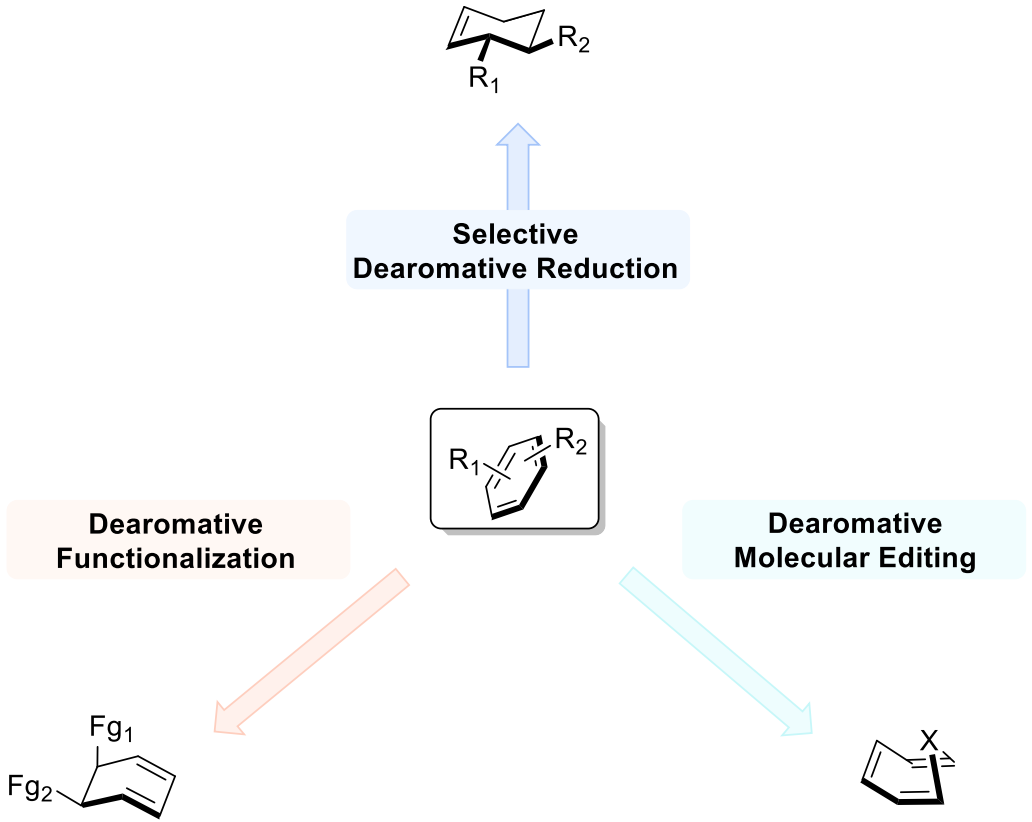
- 平面
- 稳定（共振能约150.5 kJ）
- 难以被极化

苯环的环内结构的编辑转化：极具挑战性

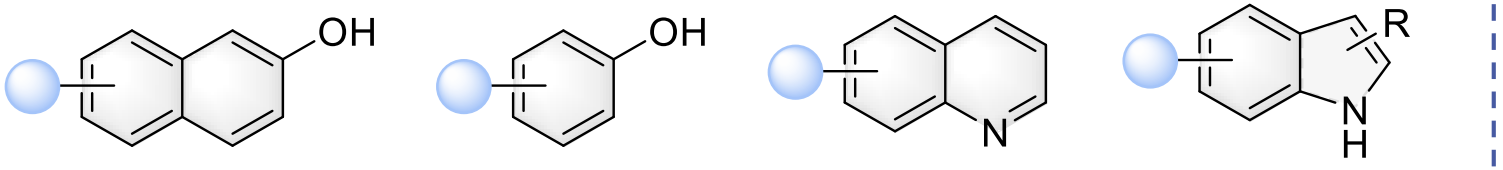
外围官能团化：发展较为成熟



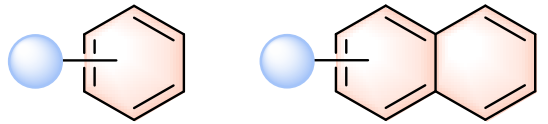
- 药物化学“逃离平面”概念 (2009年)
- **Dearomatization**
- 降低药物毒性、优化其药代动力学特性



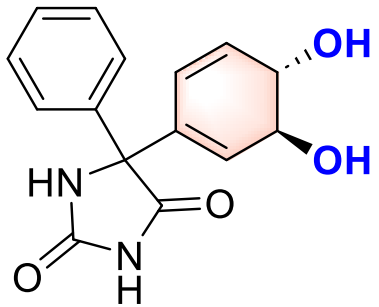
活化芳烃



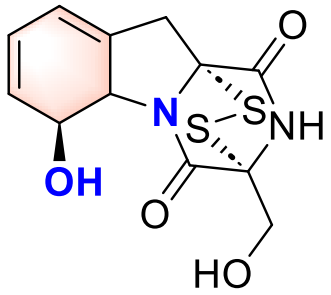
未活化芳烃



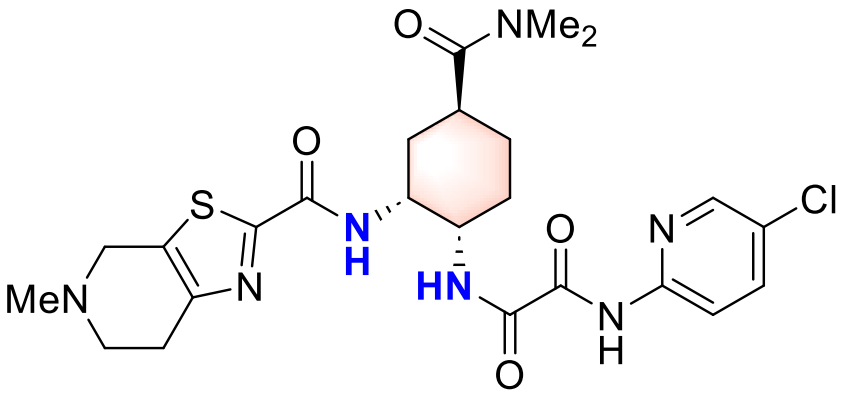
未活化芳烃的去芳构化策略在药物分子全合成中的应用



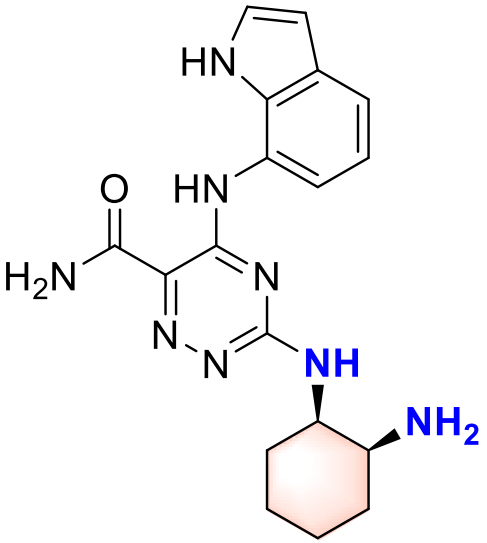
苯妥英衍生物
(抗癫痫药)



胶霉毒素
(抗菌、抗病毒)

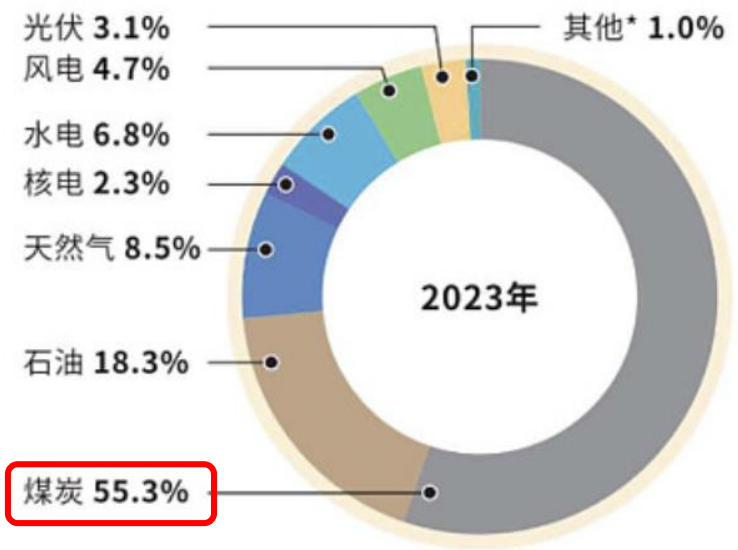


依度沙班
(抗凝药)



Syk-抑制剂
(抑制吞噬作用和减少抗体产生)

中国能源安全现状：富煤、贫油、少气

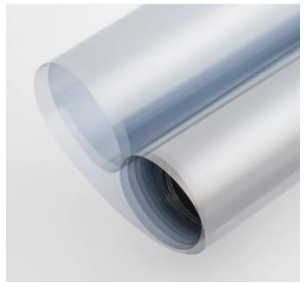


煤化工

干馏产物		主要成分
出炉煤气	焦炉气	H_2、CH_4、CO、乙烯
	粗氨水	NH_3、铵盐
	粗苯	**苯、甲苯、二甲苯**
煤焦油		**苯、甲苯、二甲苯**、**萘**、酚类
焦炭		沥青、碳

未活化苯环的工业处理方法 → **加氢** / **氧化** / ……

结构复杂、高附加值产品



大宗化学品
低价出售

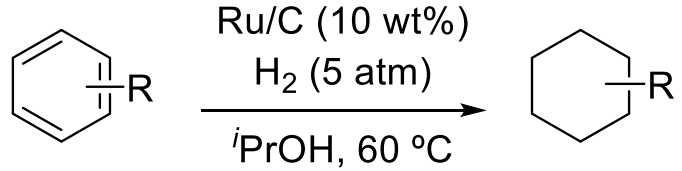
燃料

目录

➢ 还原策略（氢化）

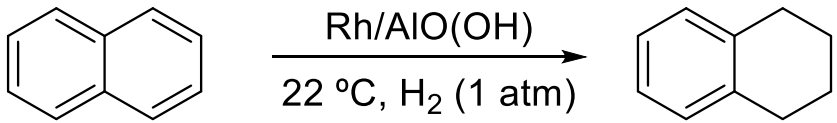
- 1901年，Sabatier和Senderens做出在细金属粉存在下苯加氢反应的第一份报告
- IFP法（200–225 °C, 50 atm）DSM法（400 °C, 30 atm）……

开发更温和的加氢条件



Sajiki, H. et al. *Chem. Eur. J.* **2009**, *15*, 6953−6963

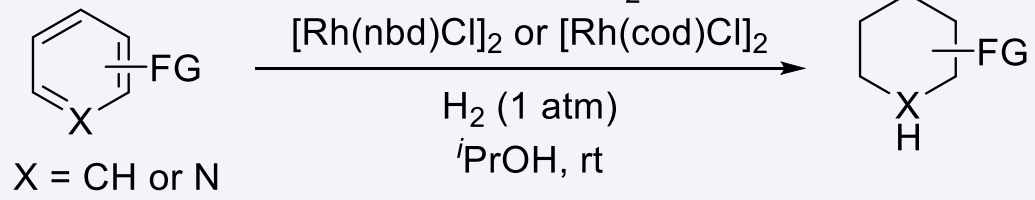
利用纳米级过渡金属催化剂



Park, J. et al. *Chem. Commun.* **2005**, *45*, 5667−5669

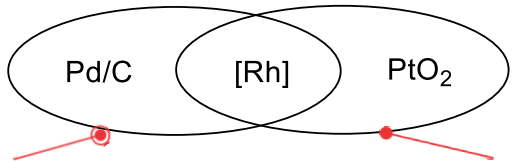
➢ 还原策略（氢化）

更温和的条件



Yu, Z.-X. et al. *Org. Lett.* **2024**, *26*, 34583462

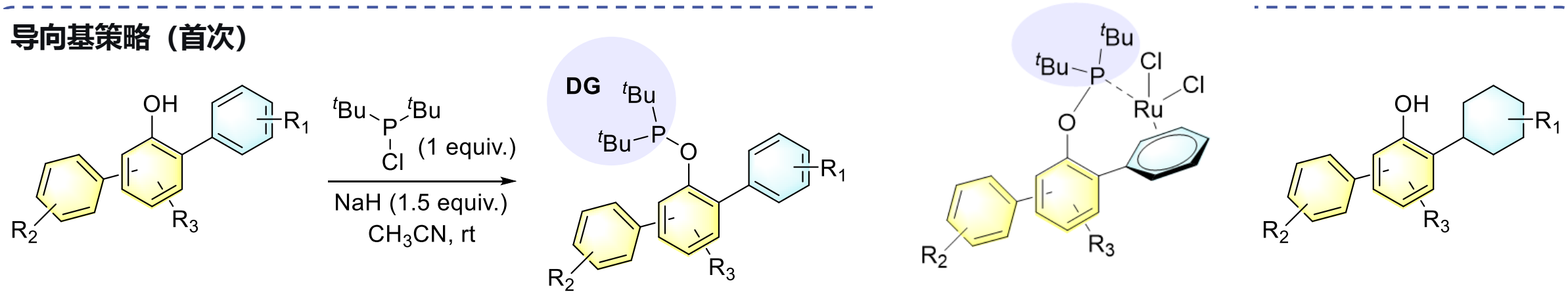
双金属协同催化机制



高活性
尤其适合含氧芳环（如酚醚）

全空气稳定
操作简便

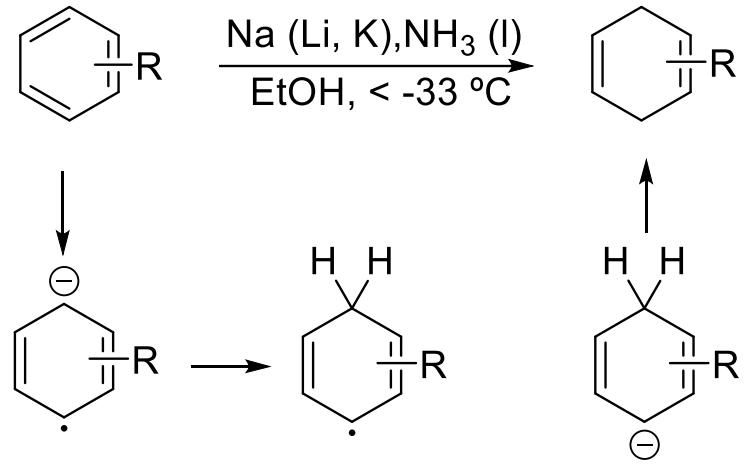
导向基策略（首次）



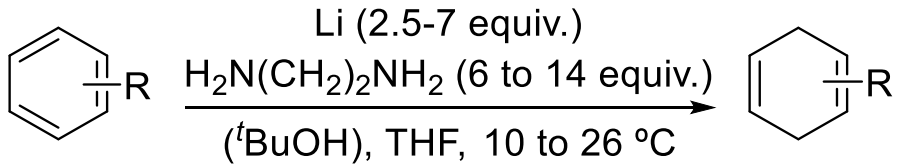
Dong, G. B. et al. *Nat. Catal.* **2025**, *8*, 931−938

➢ 还原策略（Birch还原）

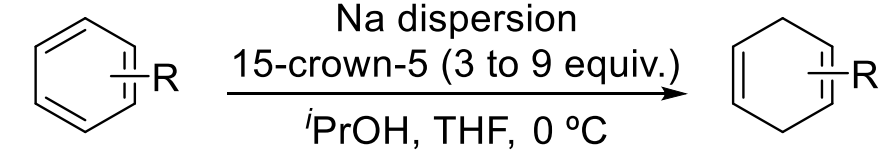
经典



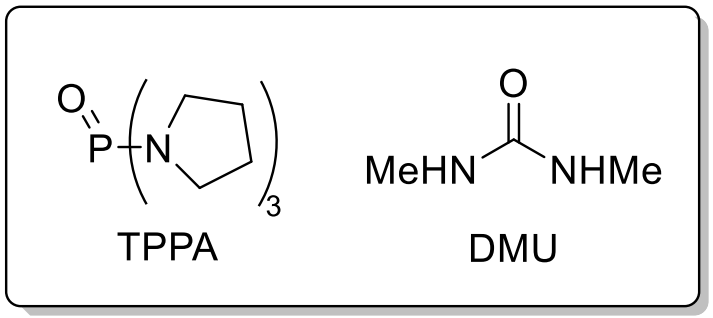
Birch, A. J. *J. Chem. Soc*. **1944**, 430−436



Koide, J. et al. *Science*. **2021**, *374*, 741−746



An, J. et al. *Org. Lett*. **2018**, *20*, 3439−3442

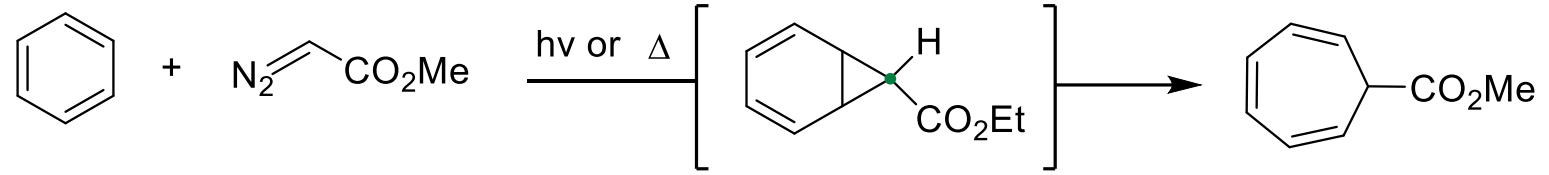


100 g scale

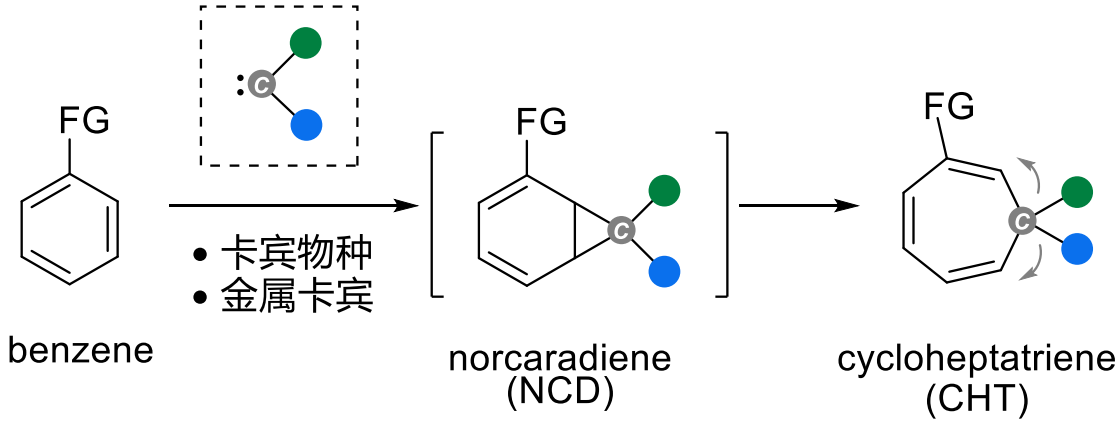
Baran, P. S. et al. *Science*. **2019**, *363*, 838−845

➢ 周环反应策略（Büchner 扩环反应）

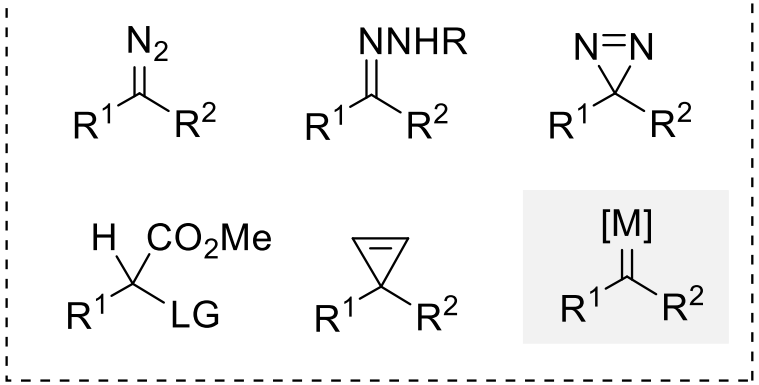
经典



Büchner, E. et al. *Ber.* **1885**, *18*, 2377−2379

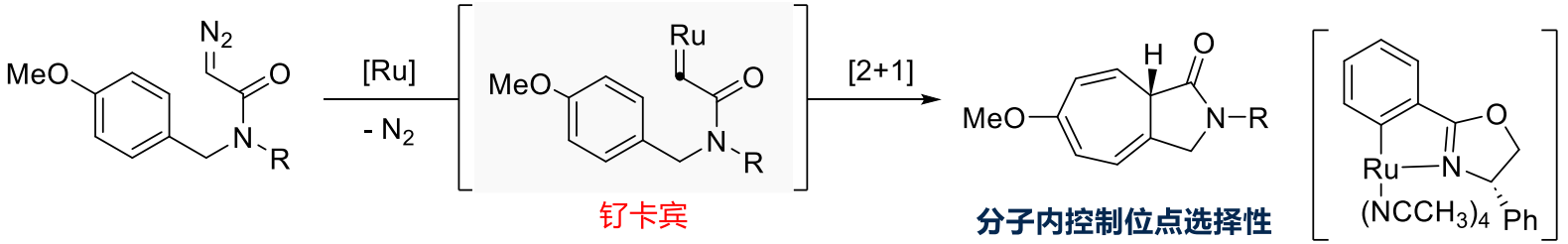


卡宾前体



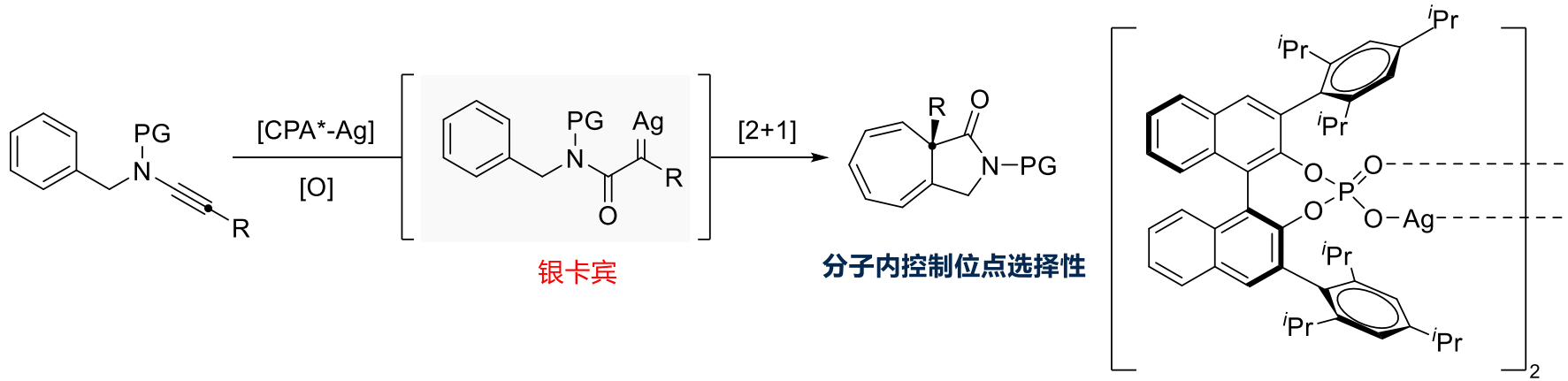
关键瓶颈： 依赖高活性卡宾物种、位点选择性控制难、未实现大规模的低成本精准转化

重氮作为卡宾前体，Pd催化的原位苯环SCAI-RE反应



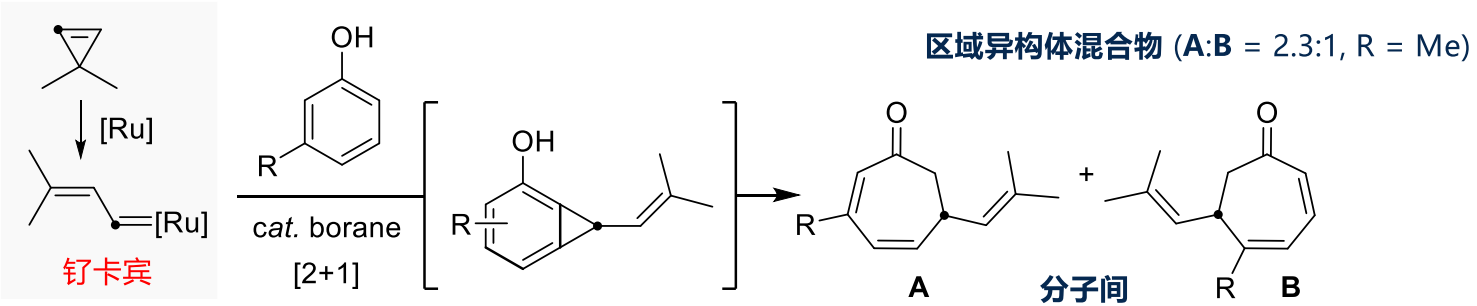
Iwasa, S. et al. *Chem. Commun.* **2019**, *55*, 13398−13401

金属Ag卡宾中间体促进的苯环SCAI-RE反应



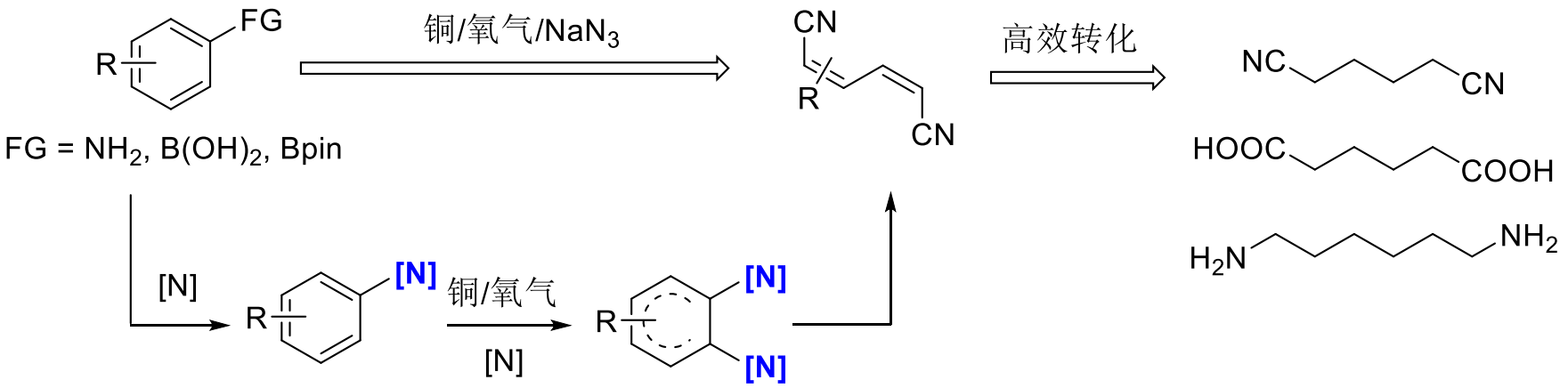
Nemoto, T. et al. *J. Am. Chem. Soc.* **2021**, *143*, 604−611

金属Ru卡宾中间体促进的苯环SCAI-RE反应

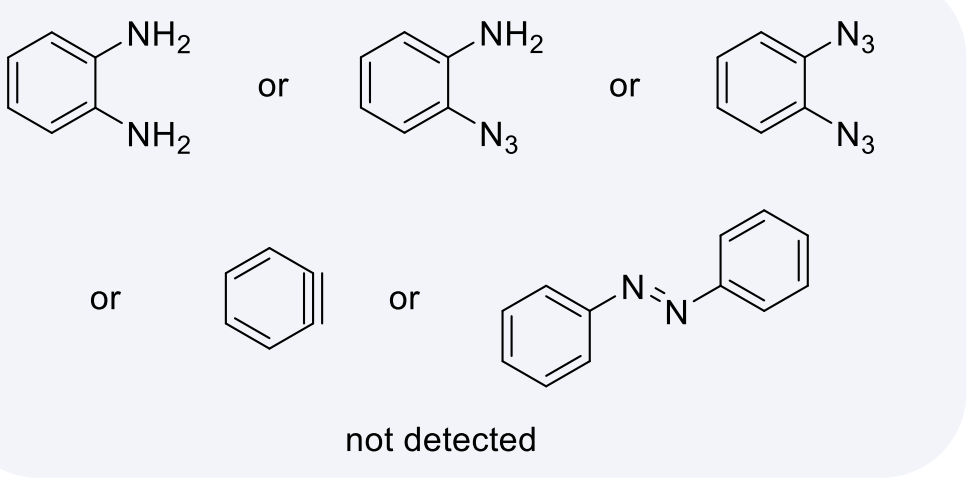


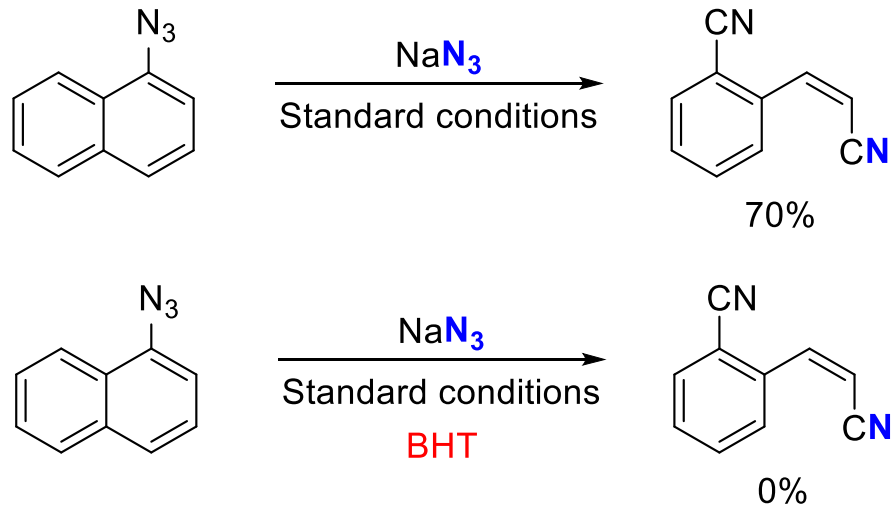
Jiang, Y. J. et al. *Angew. Chem. Int. Ed.* **2024**, *63*, e202416468

➢ 周环反应策略（开环裂解策略）



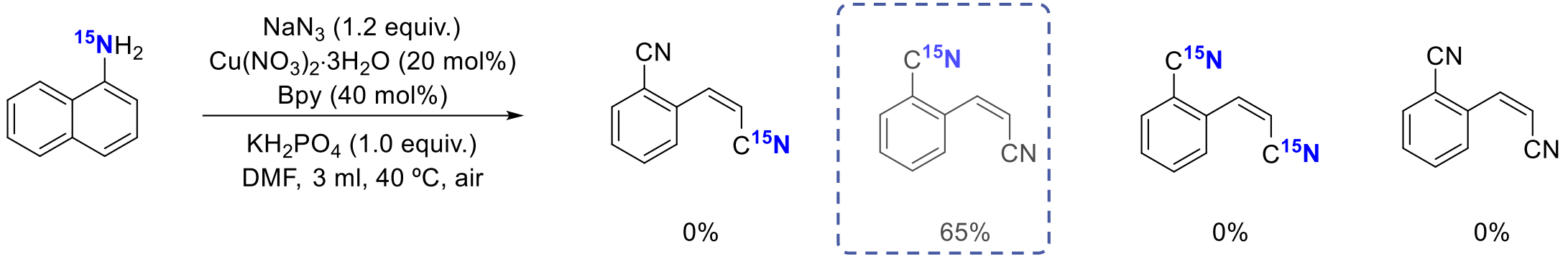
进一步探究反应机理

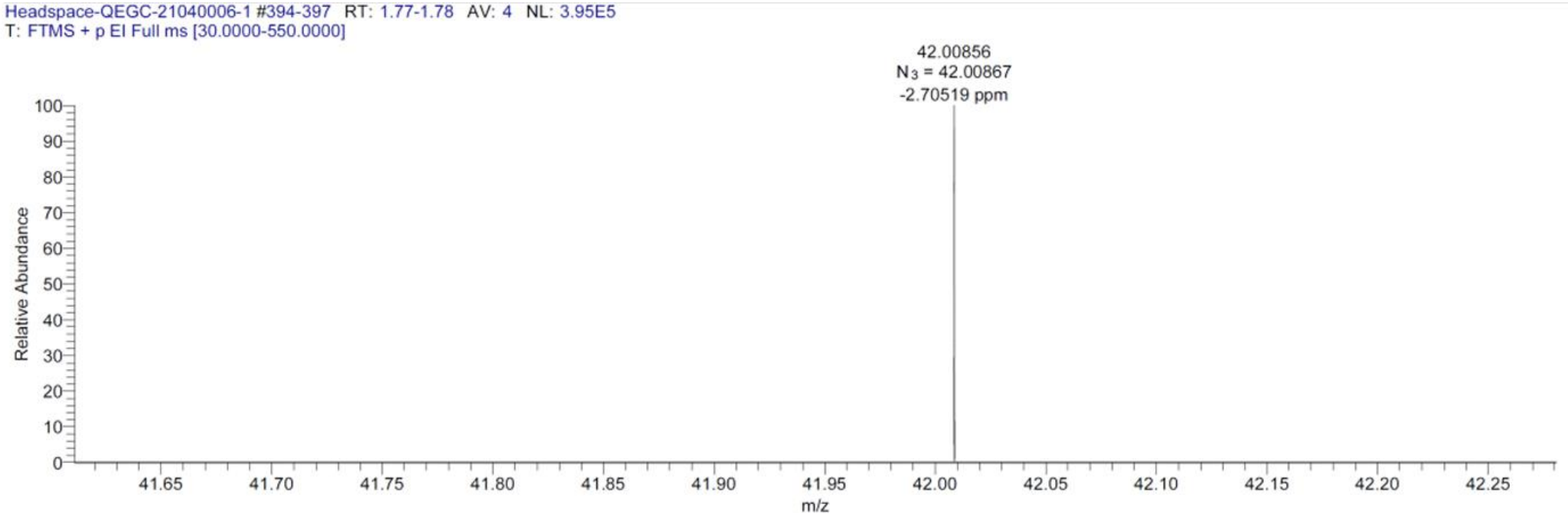




Jiao, N. et al. *Nature*. **2021**, *597*, 64–69

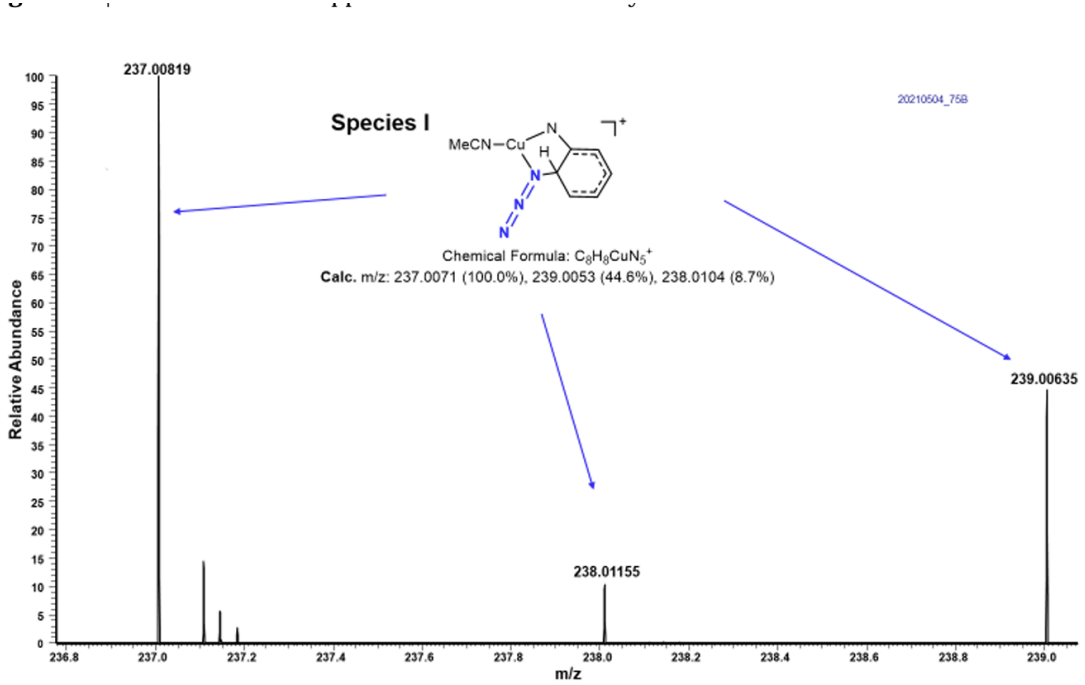
➢ 周环反应策略（开环裂解策略）

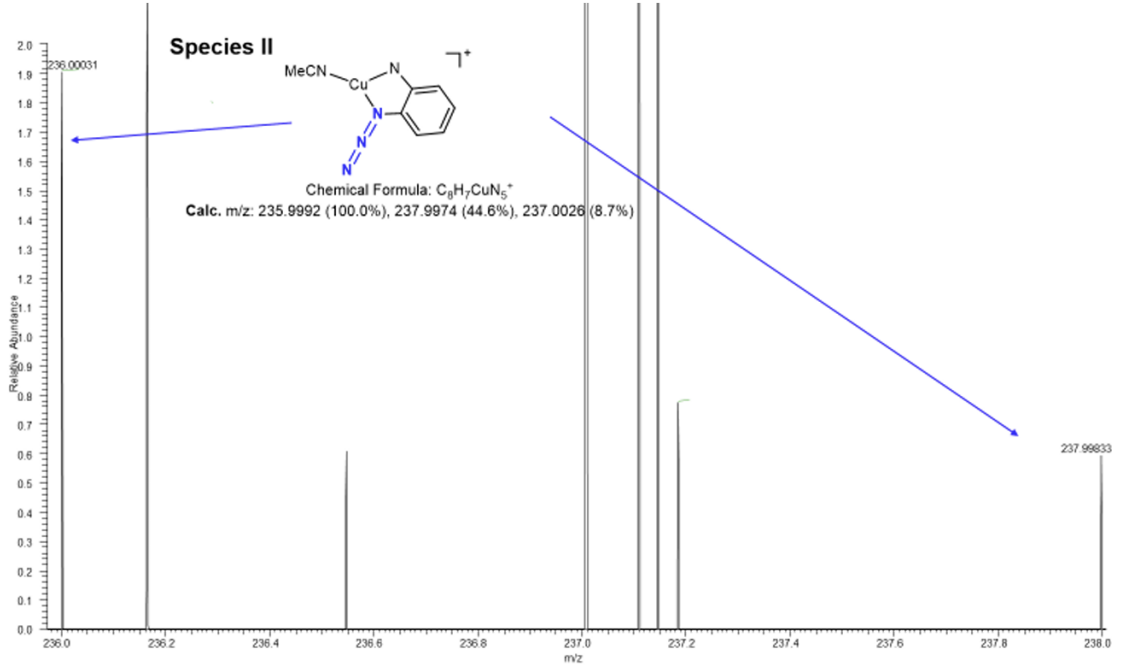




Jiao, N. et al. *Nature*. **2021**, *597*, 64−69

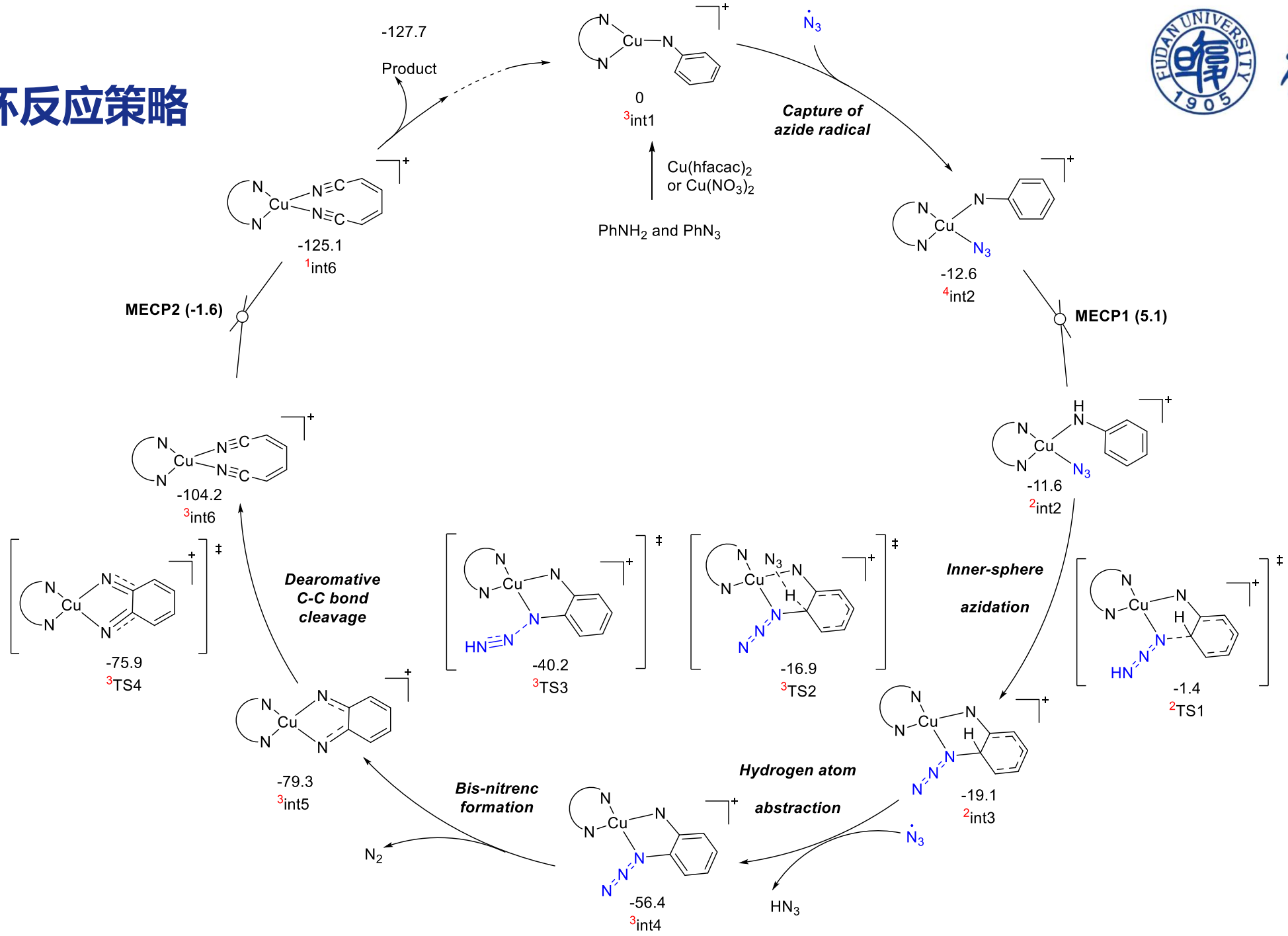
➢ 周环反应策略（开环裂解策略）



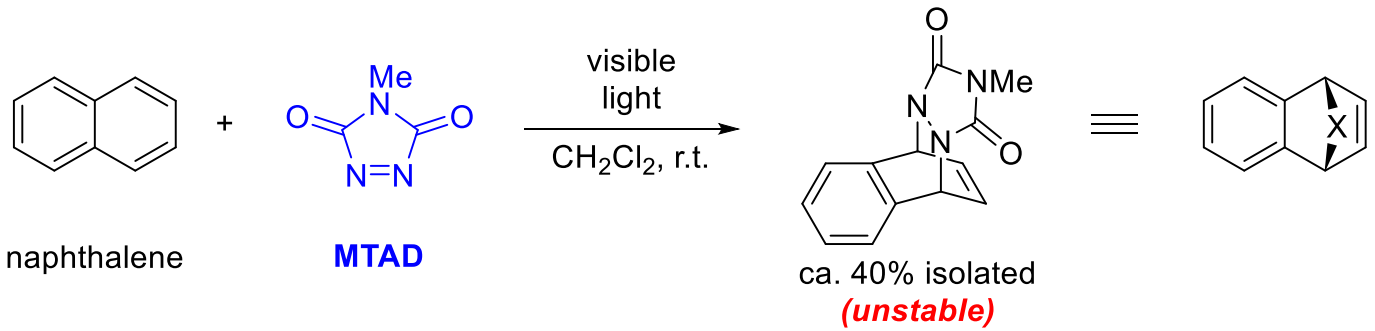


Jiao, N. et al. *Nature*. **2021**, *597*, 64−69

➢ 周环反应策略

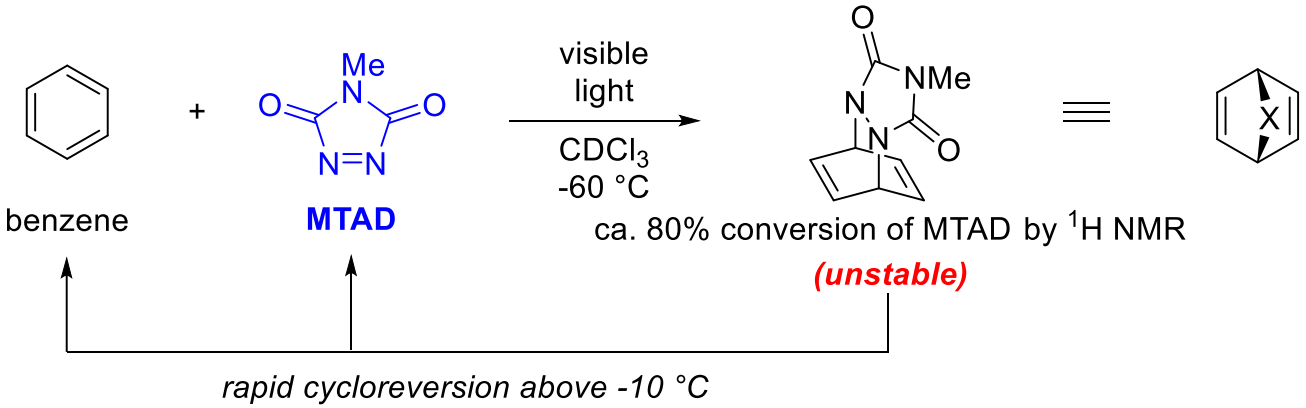

-127.7
Product
0
3int1
Cu(hfacac)2
or Cu(NO3)2
PhNH2 and PhN3
N3
Capture of
azide radical
-12.6
4int2
MECP1 (5.1)
-11.6
2int2
Inner-sphere
azidation
-1.4
2TS1
-19.1
2int3
Hydrogen atom
abstraction
-16.9
3TS2
-40.2
3TS3
-56.4
3int4
HN3
N2
Bis-nitrenc
formation
-79.3
3int5
Dearomative
C-C bond
cleavage
-75.9
3TS4
-104.2
3int6
MECP2 (-1.6)
-125.1
1int6

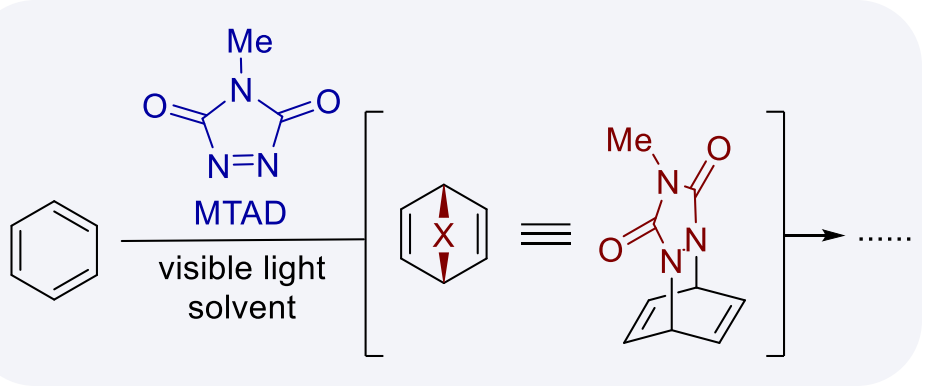
➢ 周环反应策略（光介导的环加成）



Sheridan, R. S. et al. *J. Am. Chem. Soc.* **1984**, *106*, 5368−5370

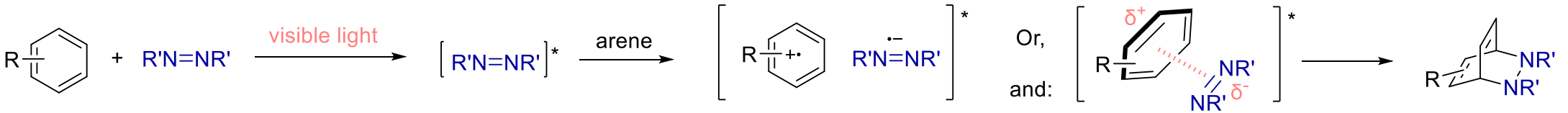
David Sarlah

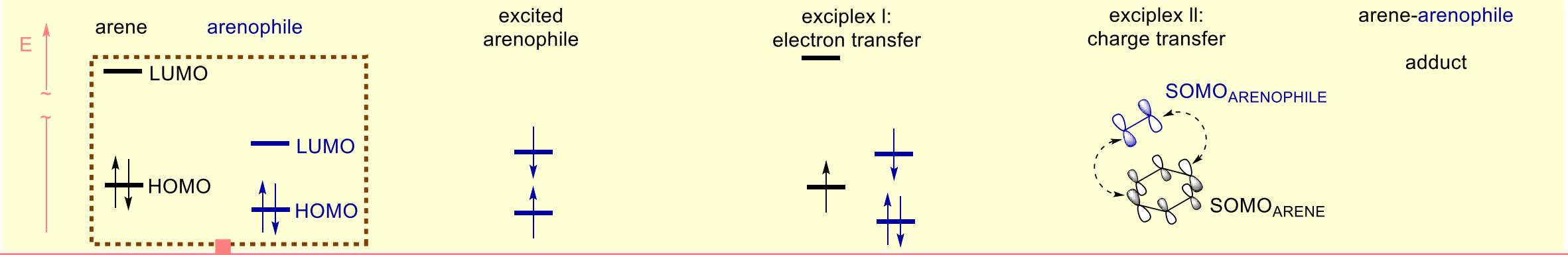




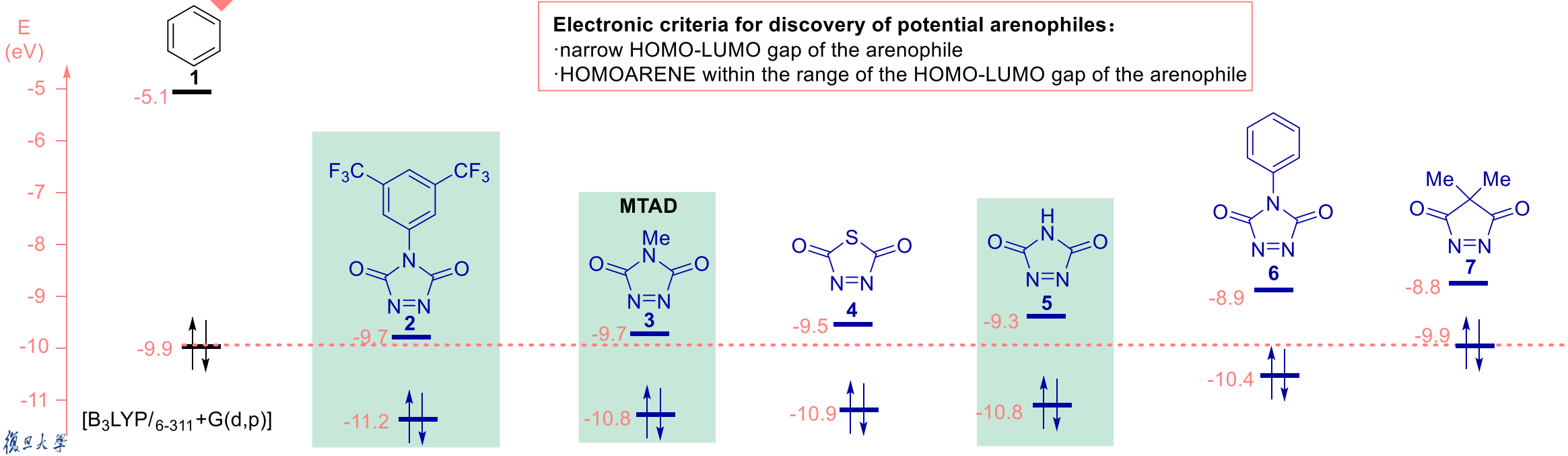
Sheridan, R. S. et al. *J. Am. Chem. Soc.* **1989**, *111*, 9247−9249

研究内容：未活化芳烃去芳构化的研究进展



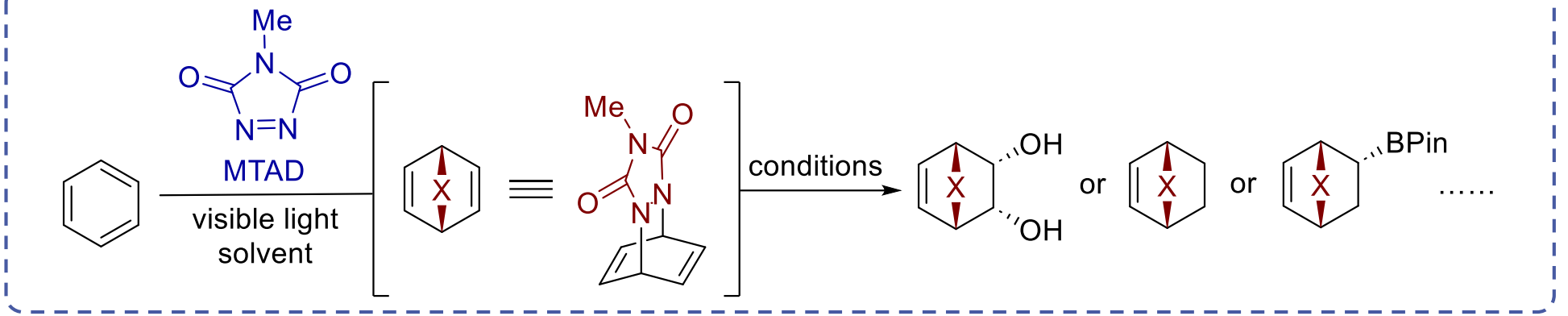


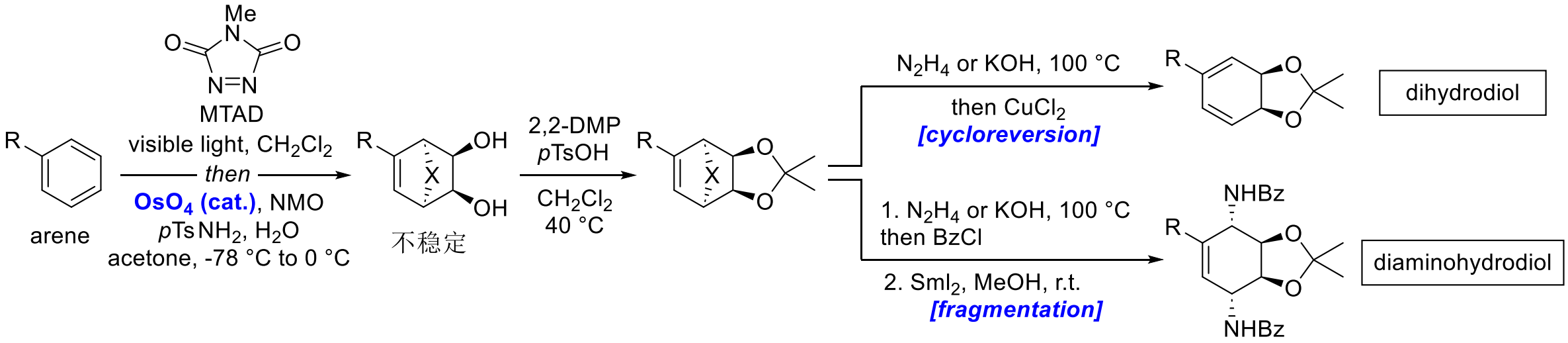
Electronic criteria for discovery of potential arenophiles：
·narrow HOMO-LUMO gap of the arenophile
·HOMOARENE within the range of the HOMO-LUMO gap of the arenophile



➢ 周环反应策略（光介导的环加成）

策略一：基于环加成物碳碳双键单元的官能团化反应

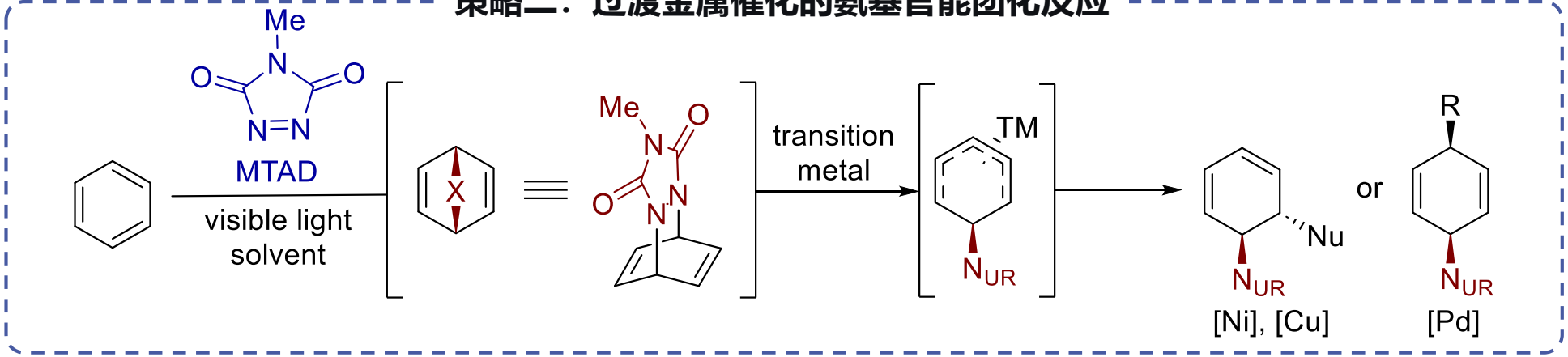


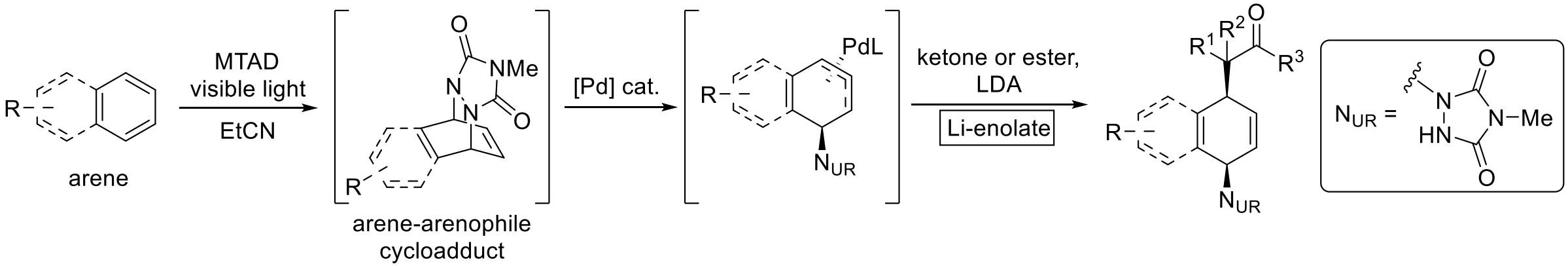


Sarlah, D. et al. *Nat. Chem.* **2016**, *8*, 922–928

➢ 周环反应策略（光介导的环加成）

策略二：过渡金属催化的氨基官能团化反应

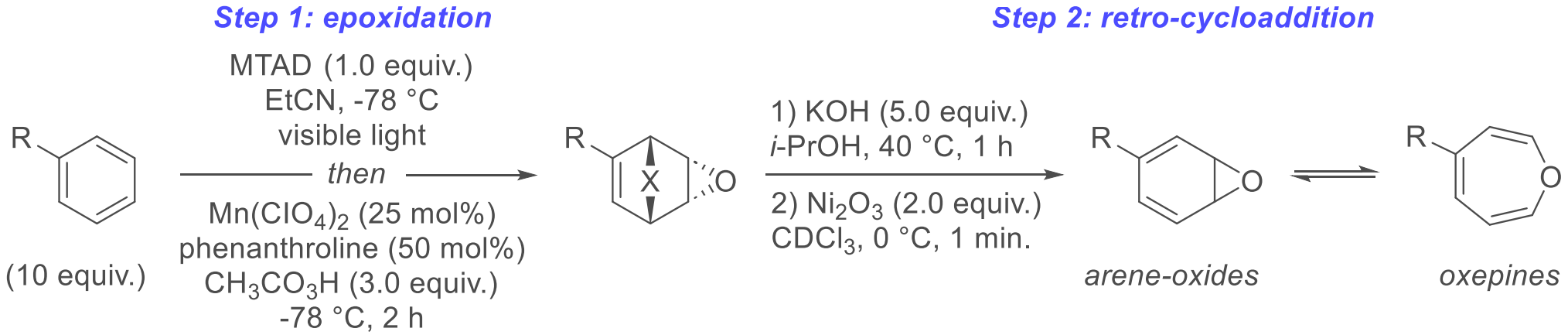




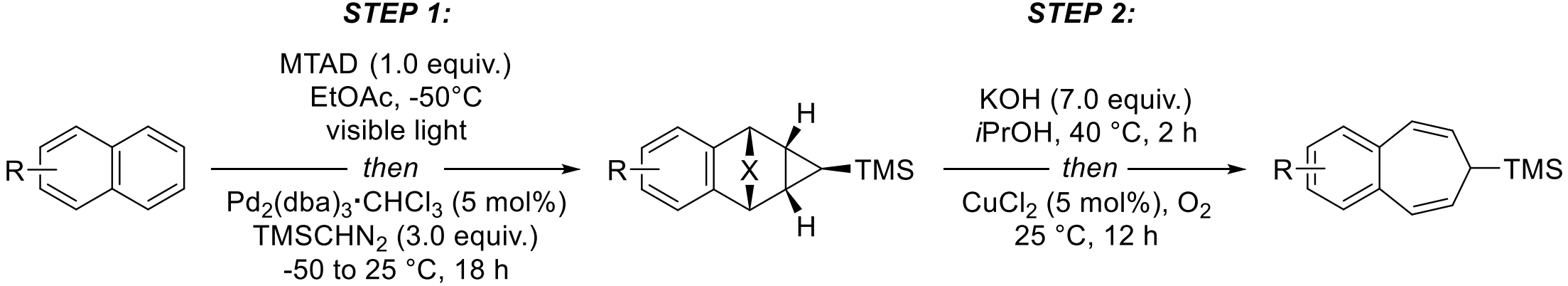
Sarlah, D. et al. *J. Am. Chem. Soc.* **2017**, *139*, 17787−17790

➢ 周环反应策略（光介导的环加成）

策略三：单原子插入介导的扩环反应

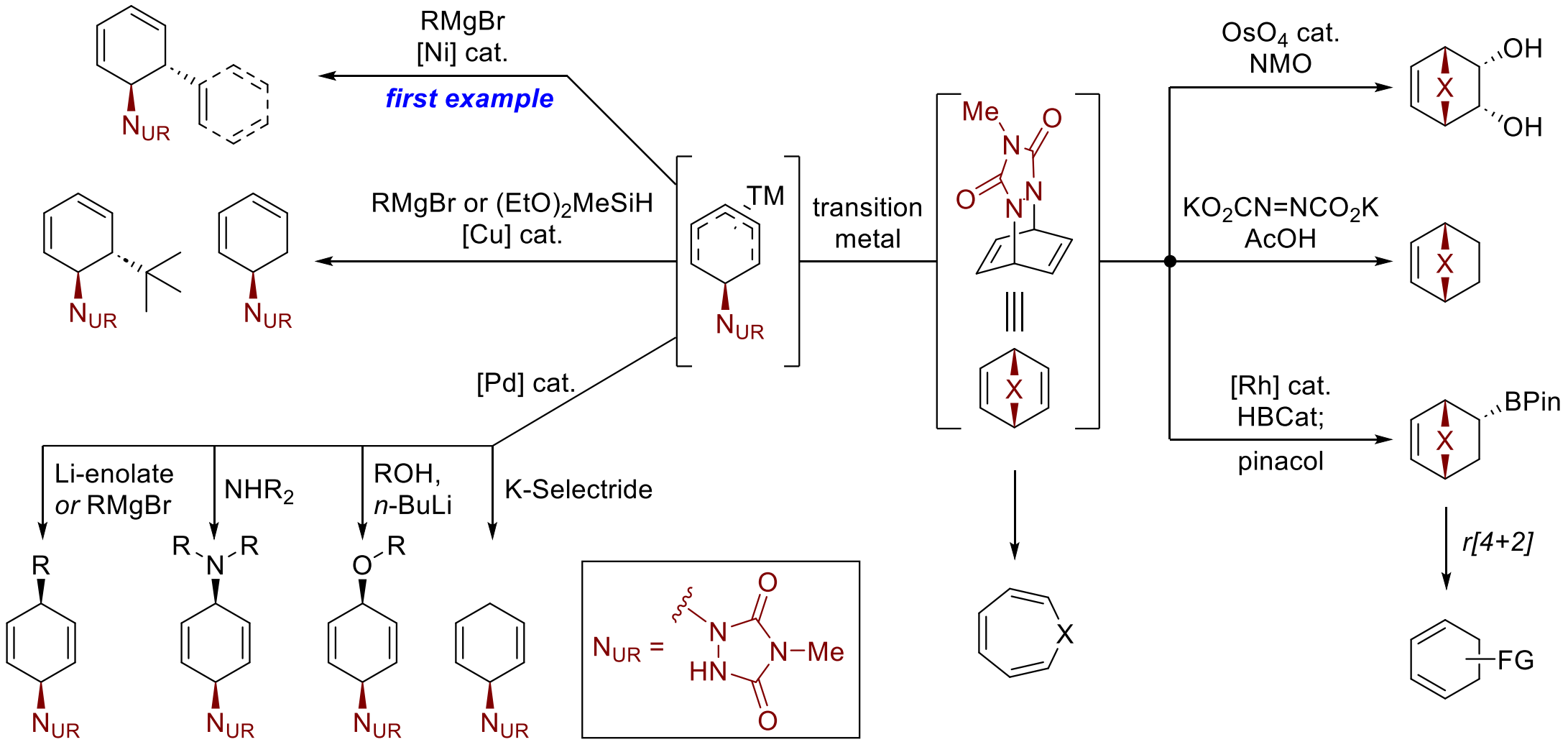


Sarlah, D. et al. *J. Am. Chem. Soc.* **2020**, *142*, 10125−10131



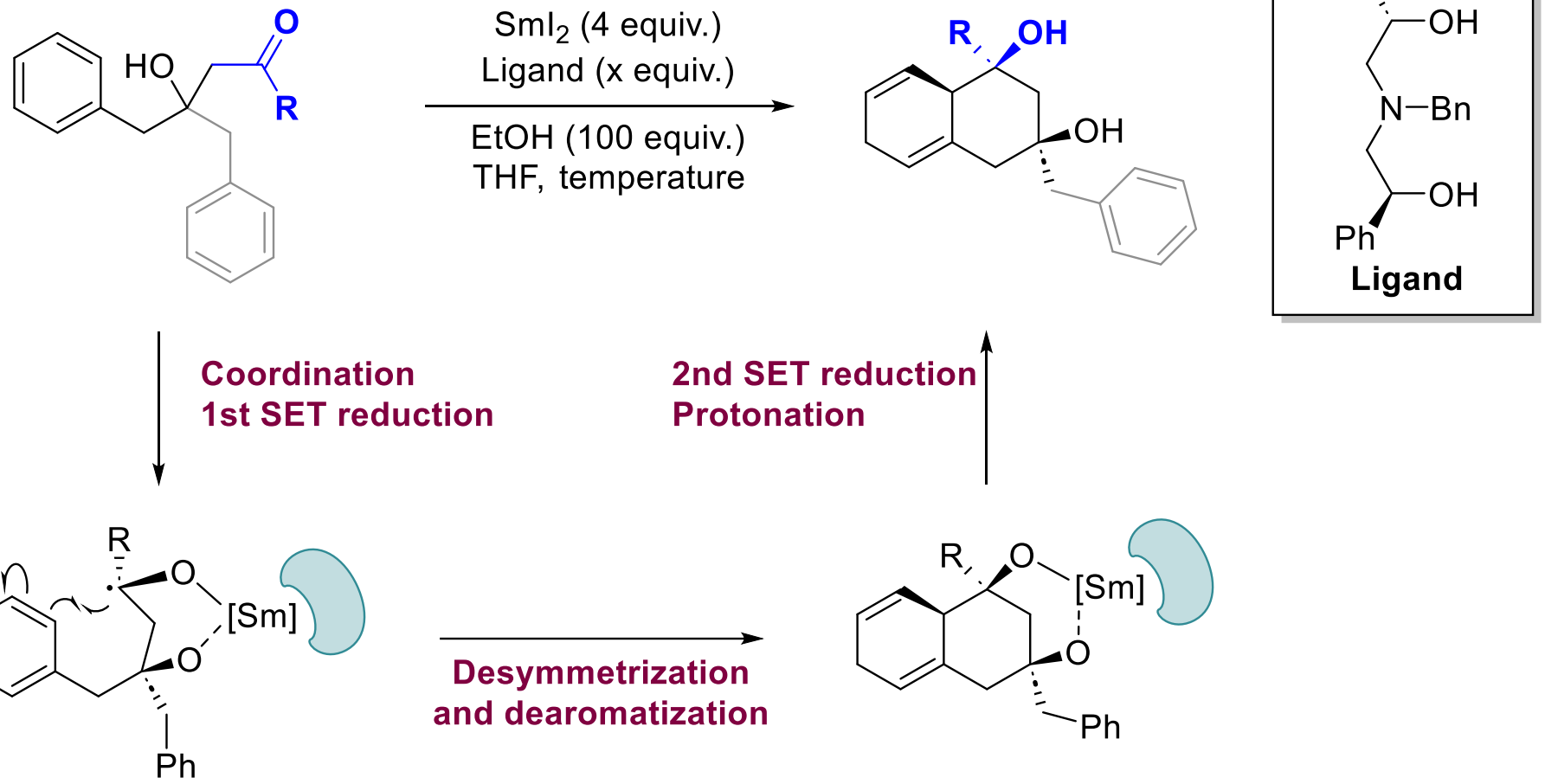
Sarlah, D. et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e20220801

➢ 周环反应策略（光介导的环加成）



➢ 自由基策略

- 单电子还原剂
- 三齿胺基二醇配体
- 含三个手性中心

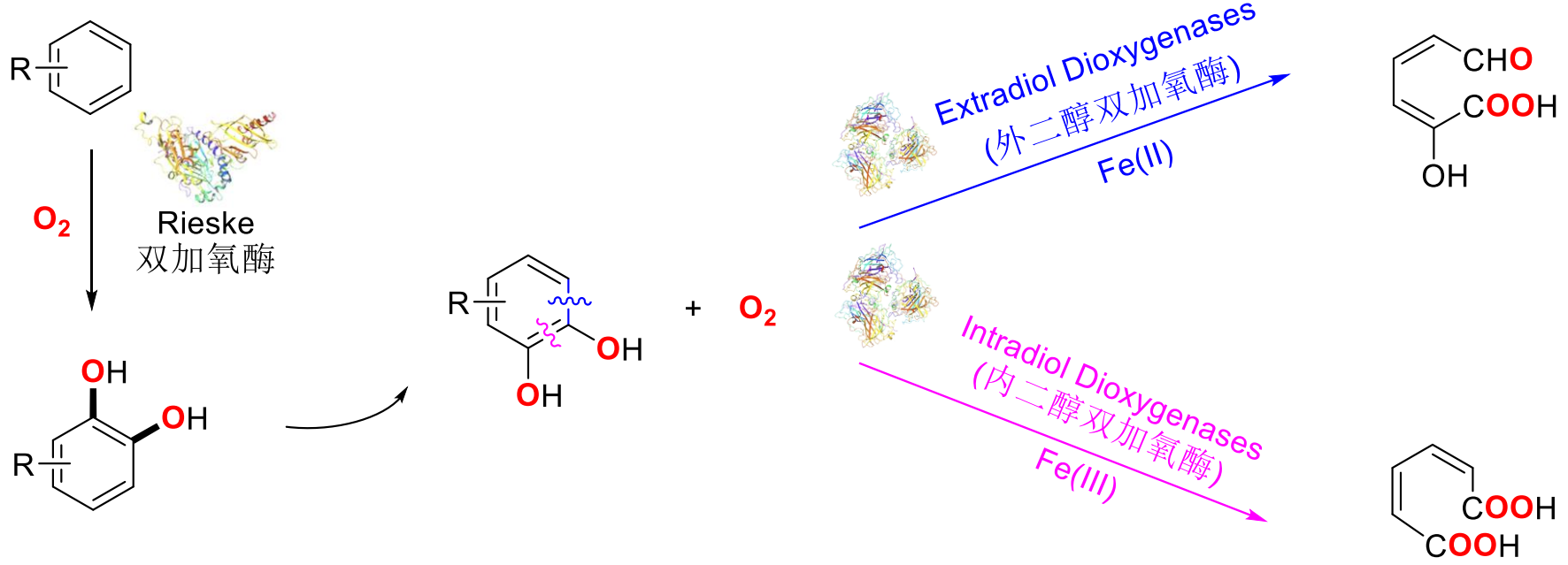


You, S. L. et al. *Nat. Synth.* **2022**, *1*, 401−406

➢ 自由基策略

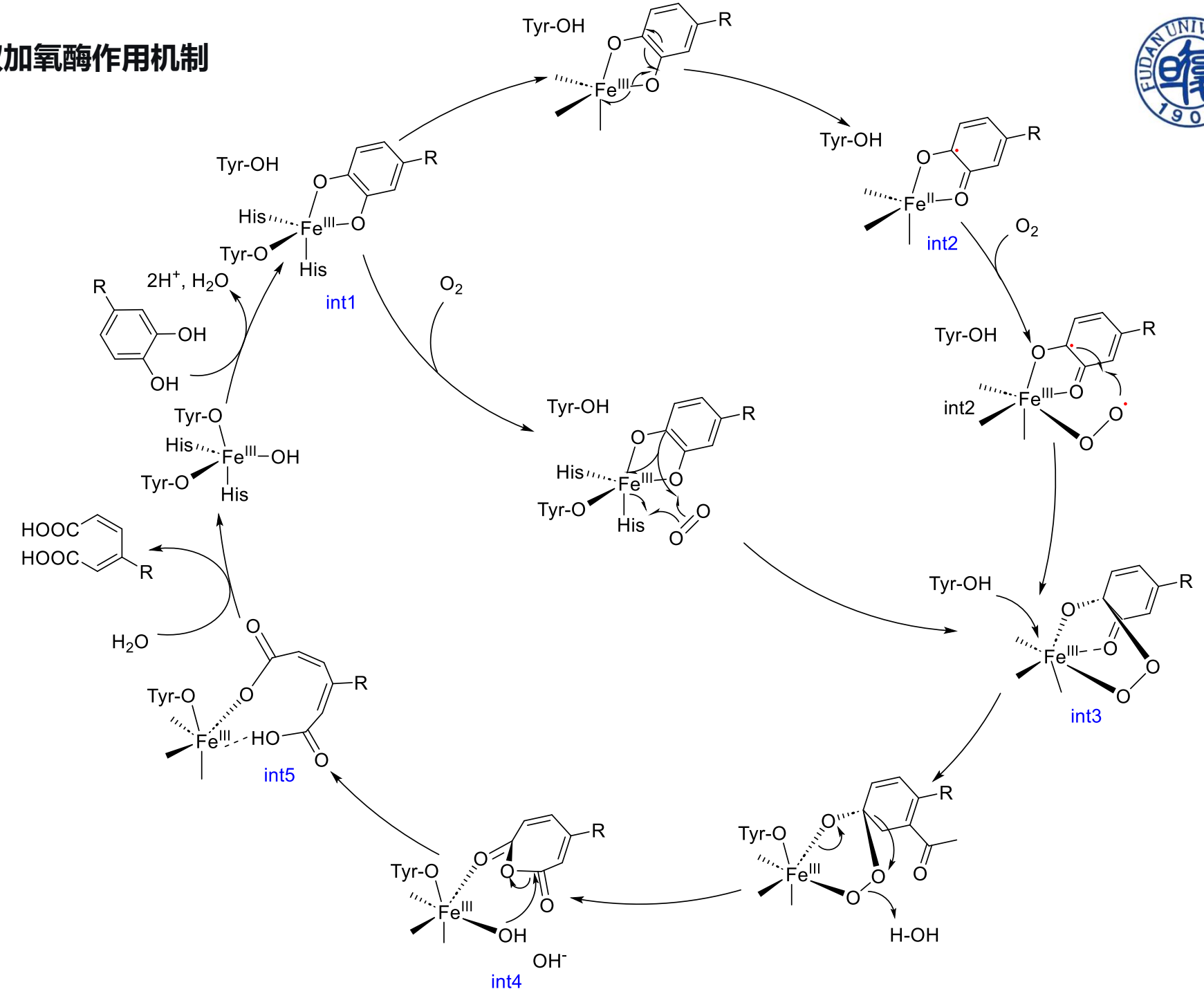
- ➢ O_2：稳定的三线态双自由基分子
- ➢ 大多数有机分子：单线态
- ➢ 直接反应**自旋禁阻**

- ➢ 自然界中的酶利用**过渡金属或黄素辅因子**活化氧气
- ➢ 单核非血红素铁依赖的**双加氧酶**可以活化分子氧，参与**芳香族化合物**降解过程

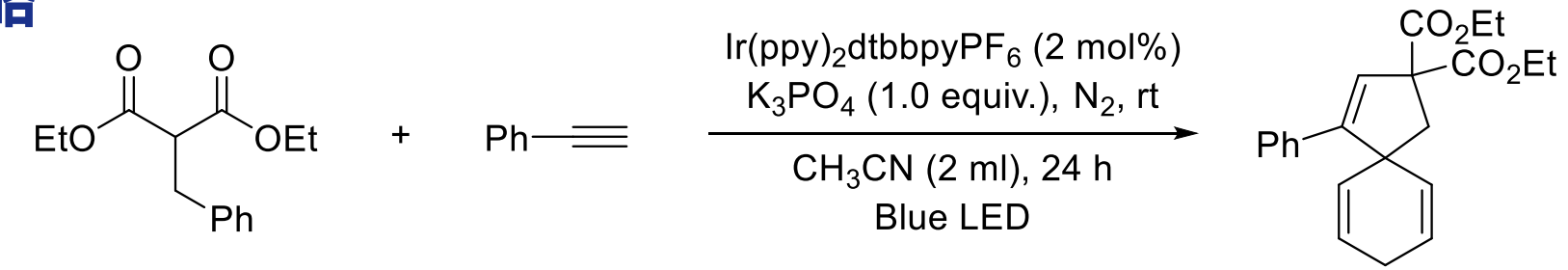


Liu, A. M. et al. *J. Biol. Inorg. Chem.* **2017**, *22*, 395−405

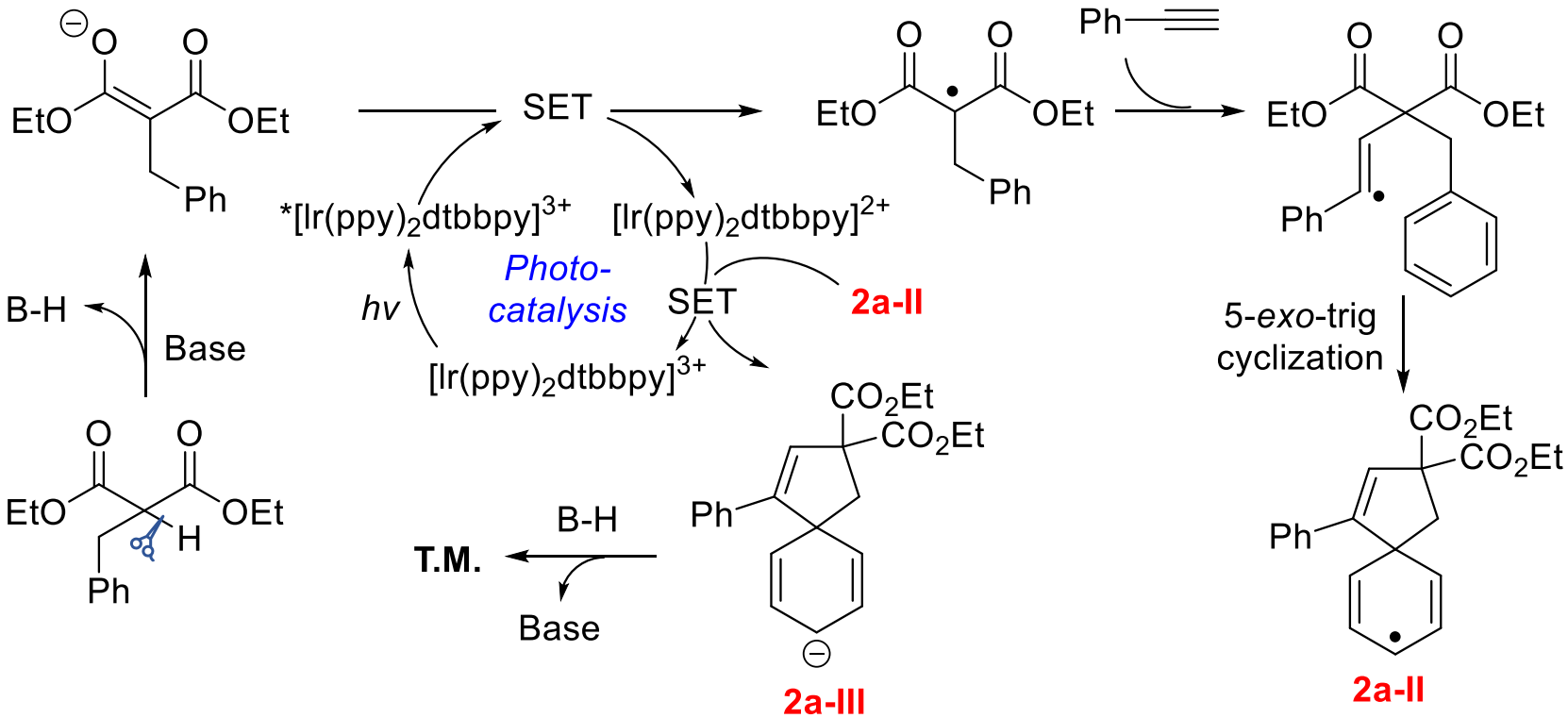
➢ 内二醇双加氧酶作用机制



➢ 自由基策略

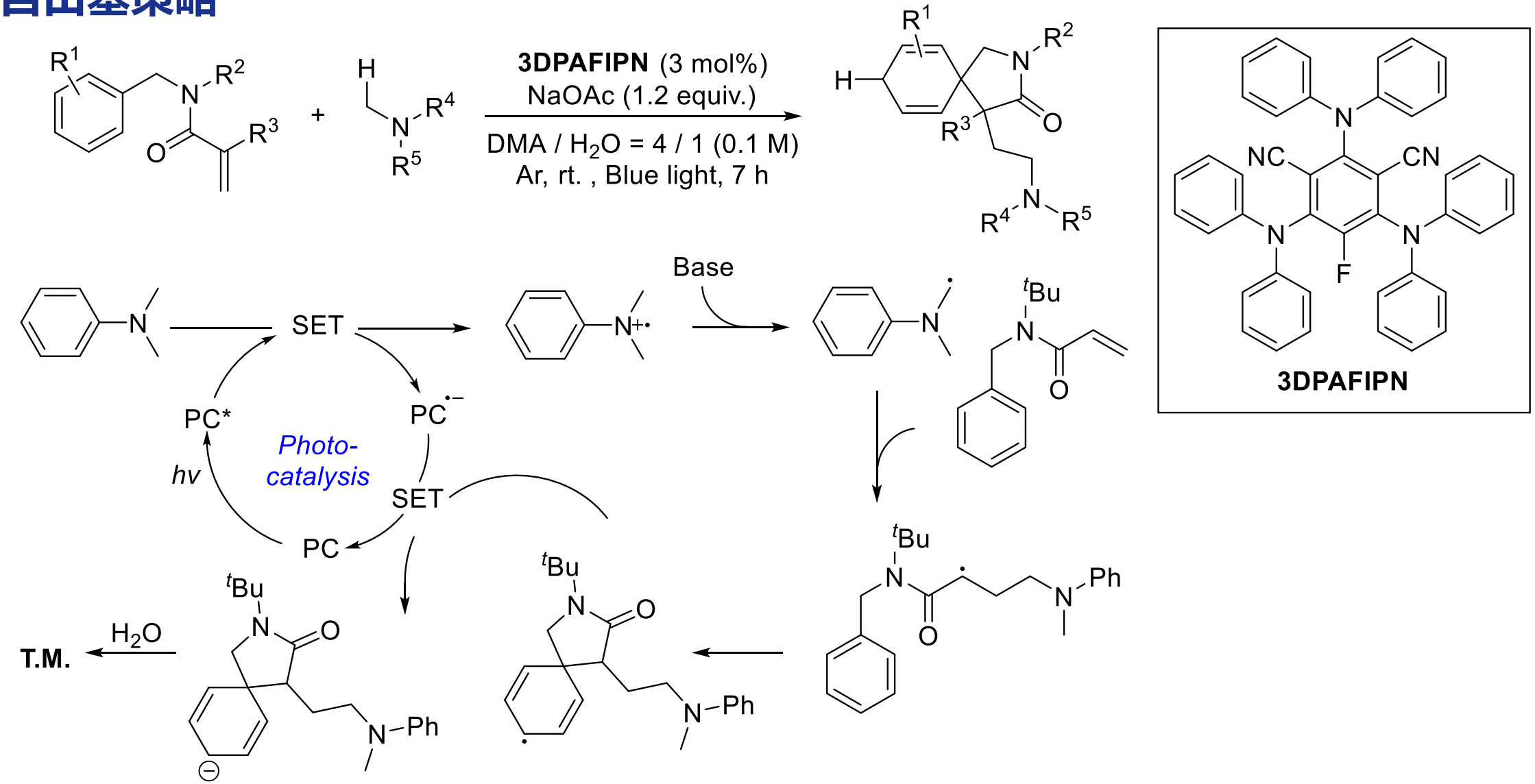


Possible mechanism：



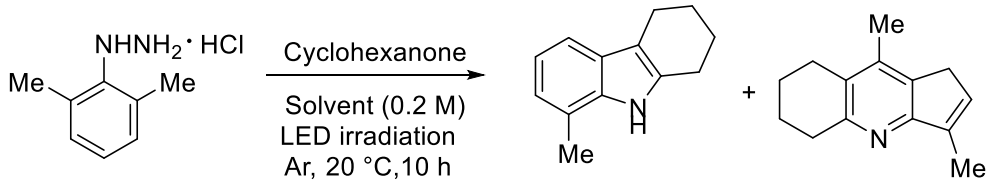
Reiser, O. et al. *Green Chem*. **2022**, *24*, 2772−2776

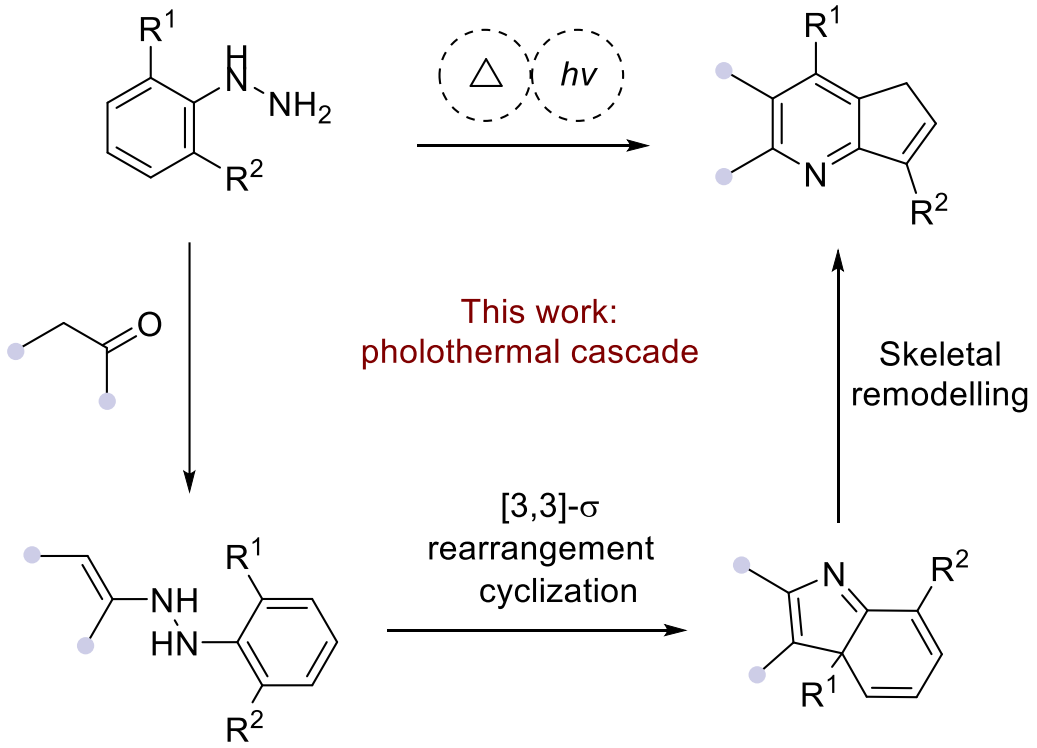
➢ 自由基策略



Yin, B. L. et al. *Org. Chem. Front.* **2024**, *11*, 3165−3172

➢ 自由基策略（光热串联活化）

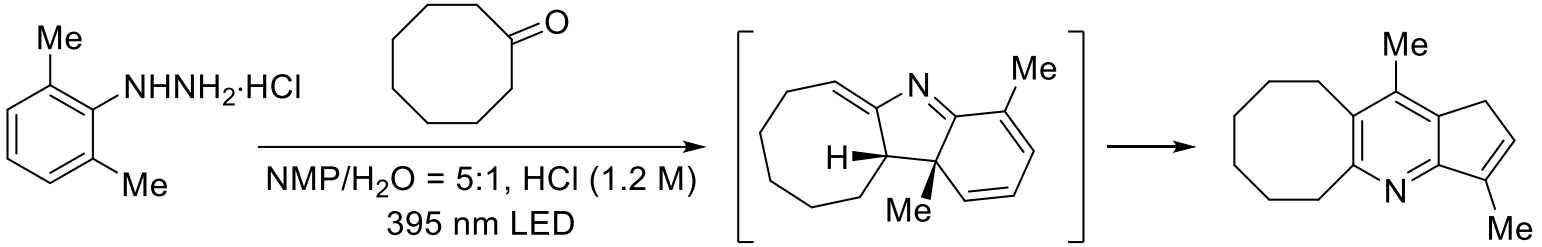




Entry	LED irradiation	Solvent	Yield of **2**(%)	Yield of **3a**(%)
1	395	MeOH	35	24
2	395	DMSO	15	35
3	395	DMF	16	39
4	395	MeCN	40	15
5	395	THF	17	31
6	395	TBME	26	41
7	395	NMP	10	73
8	395	PhCl	21	30
9[a]	395	NMP	7	82
10[b]	395	NMP	0	98
11[b]	370	NMP	16	60
12[b]	455	NMP	33	7
13[c]	395	NMP	45	0
14[d]	395	NMP	5	0

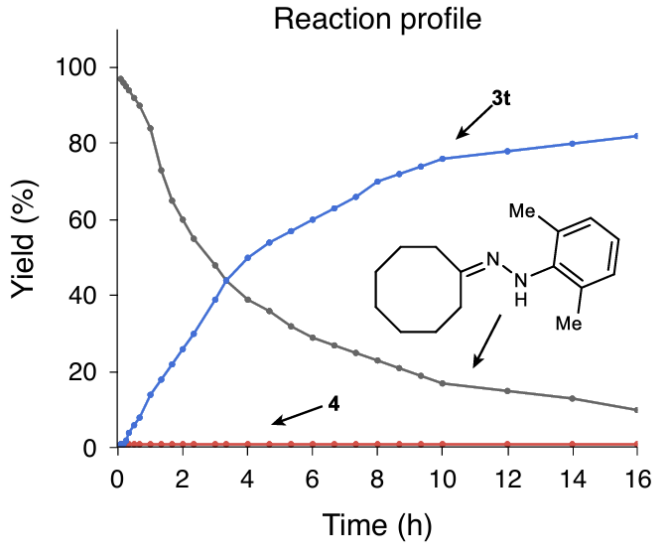
➢ 自由基策略（光热串联活化）

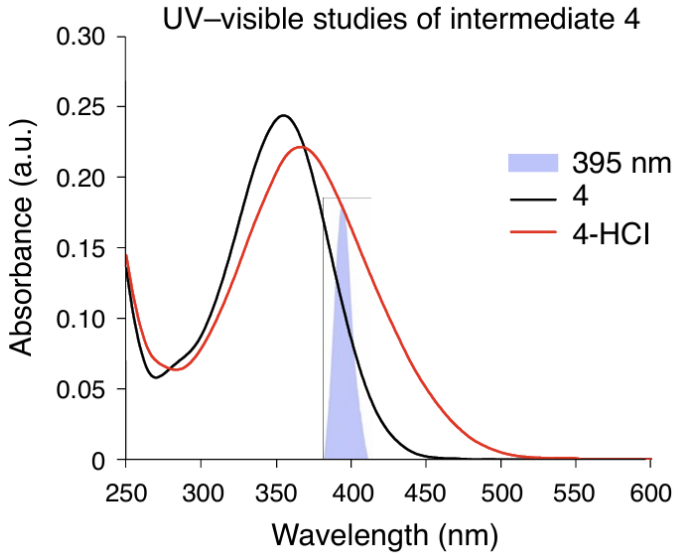
瞬态光吸收中间体的捕获与光谱表征

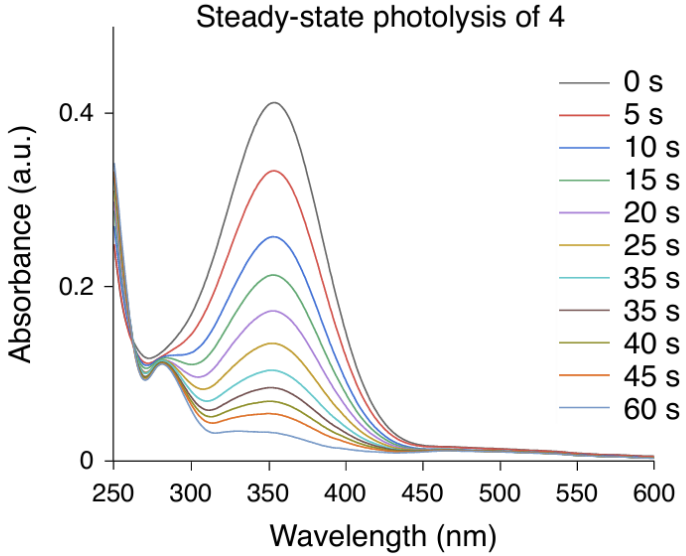


4

稳态光解实验

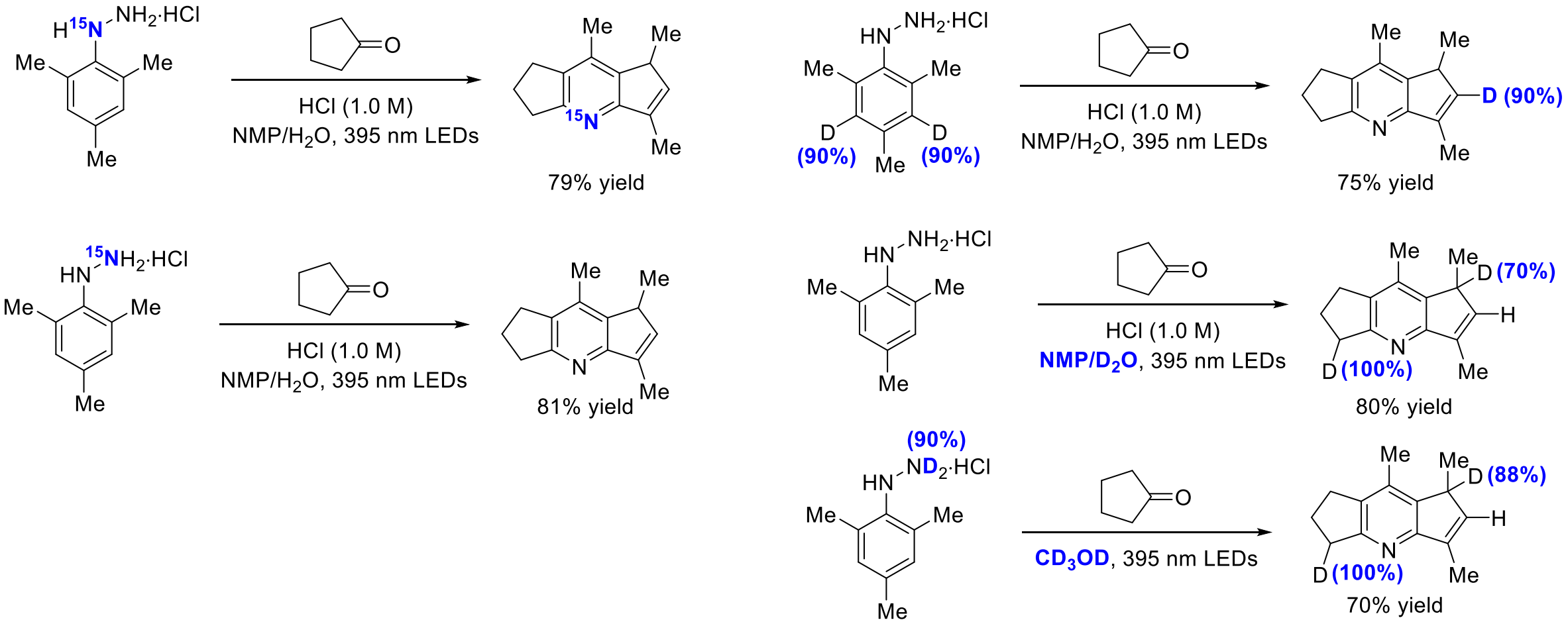




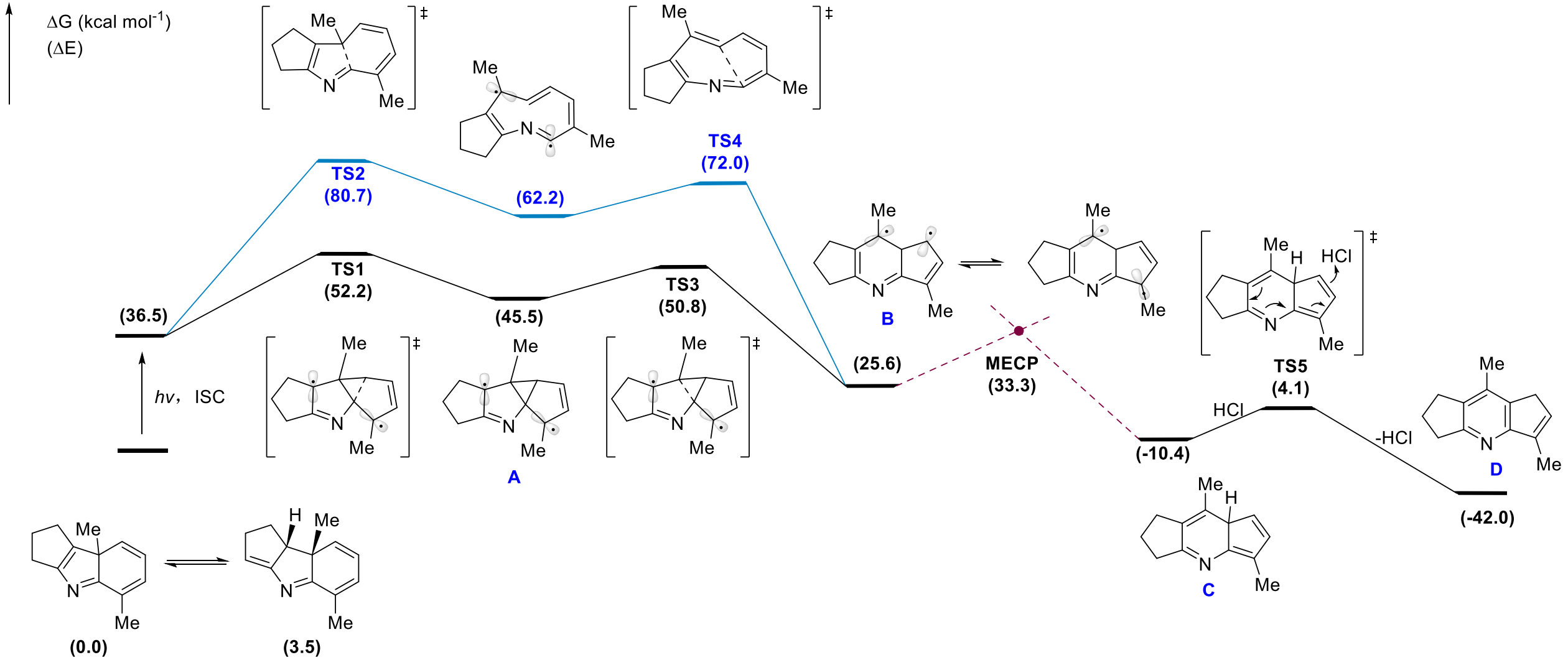


➢ 自由基策略（光热串联活化）

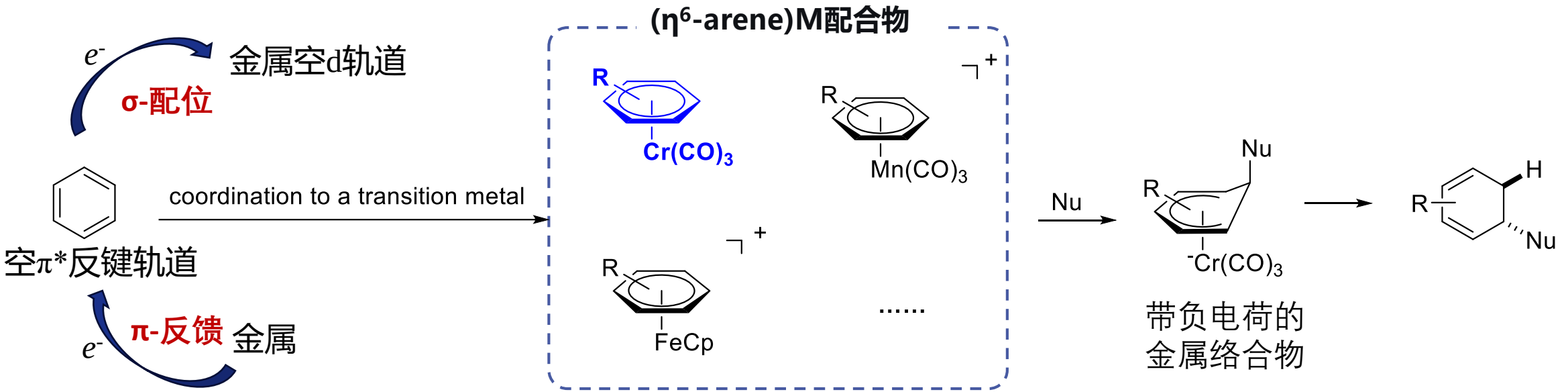
同位素标记实验追踪原子来源



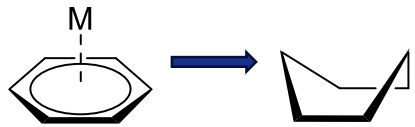
➢ 自由基策略（光热串联活化）



➢ 亲电活化策略



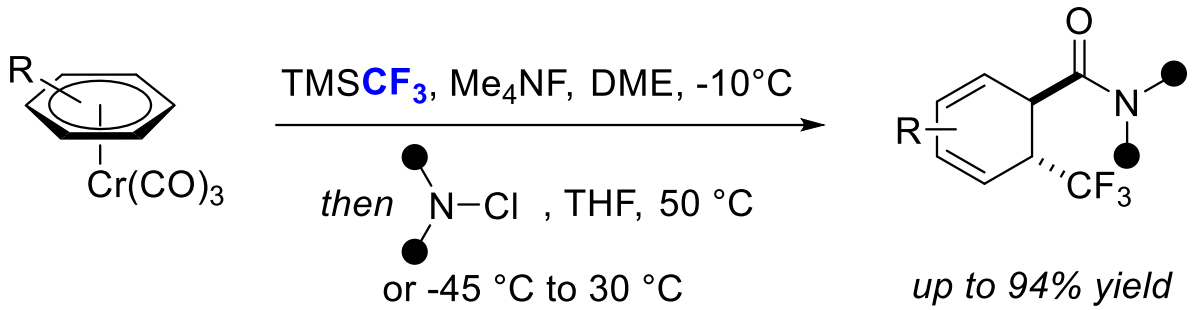
电子效应　　结构效应



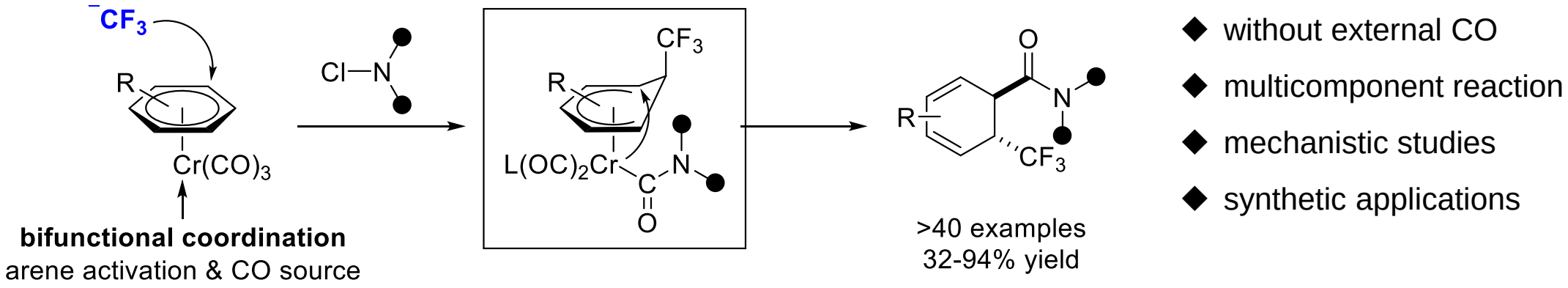
η6-配位策略活化苯环

➢ 亲电活化策略： 芳烃的亲核-亲电加成去芳构羰基化反应

李伟



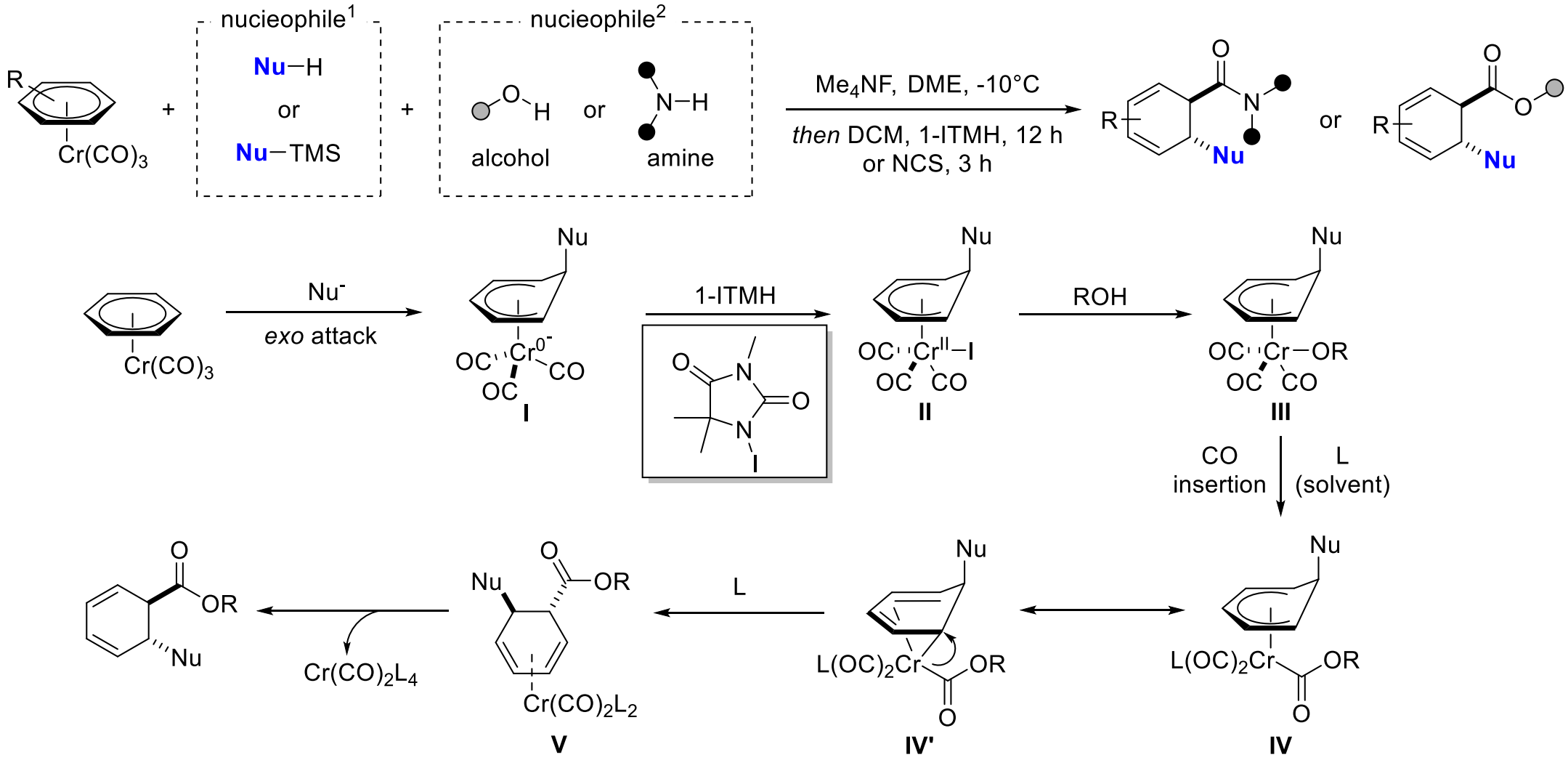
possible mechanism



- without external CO
- multicomponent reaction
- mechanistic studies
- synthetic applications

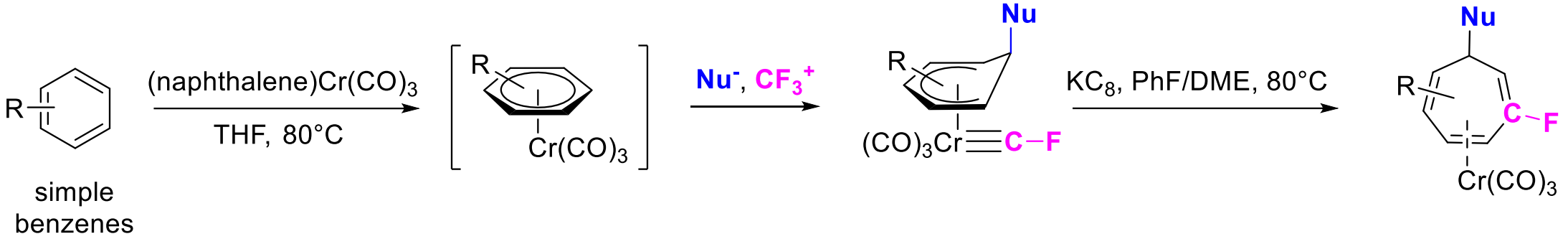
Li, W. et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202210312

➢ 亲电活化策略： 芳烃的亲核-亲核加成去芳构羰基化反应

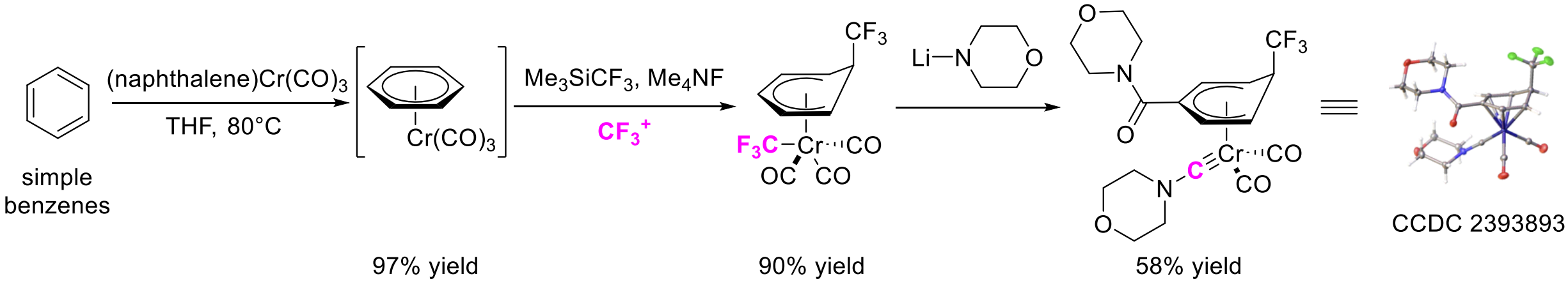


Li, W. et al. *Angew. Chem. Int. Ed.* **2024**, *63*, e202403917

➢ 亲电活化策略： 芳烃的亲核-卡拜碳原子插入的去芳构扩环反应

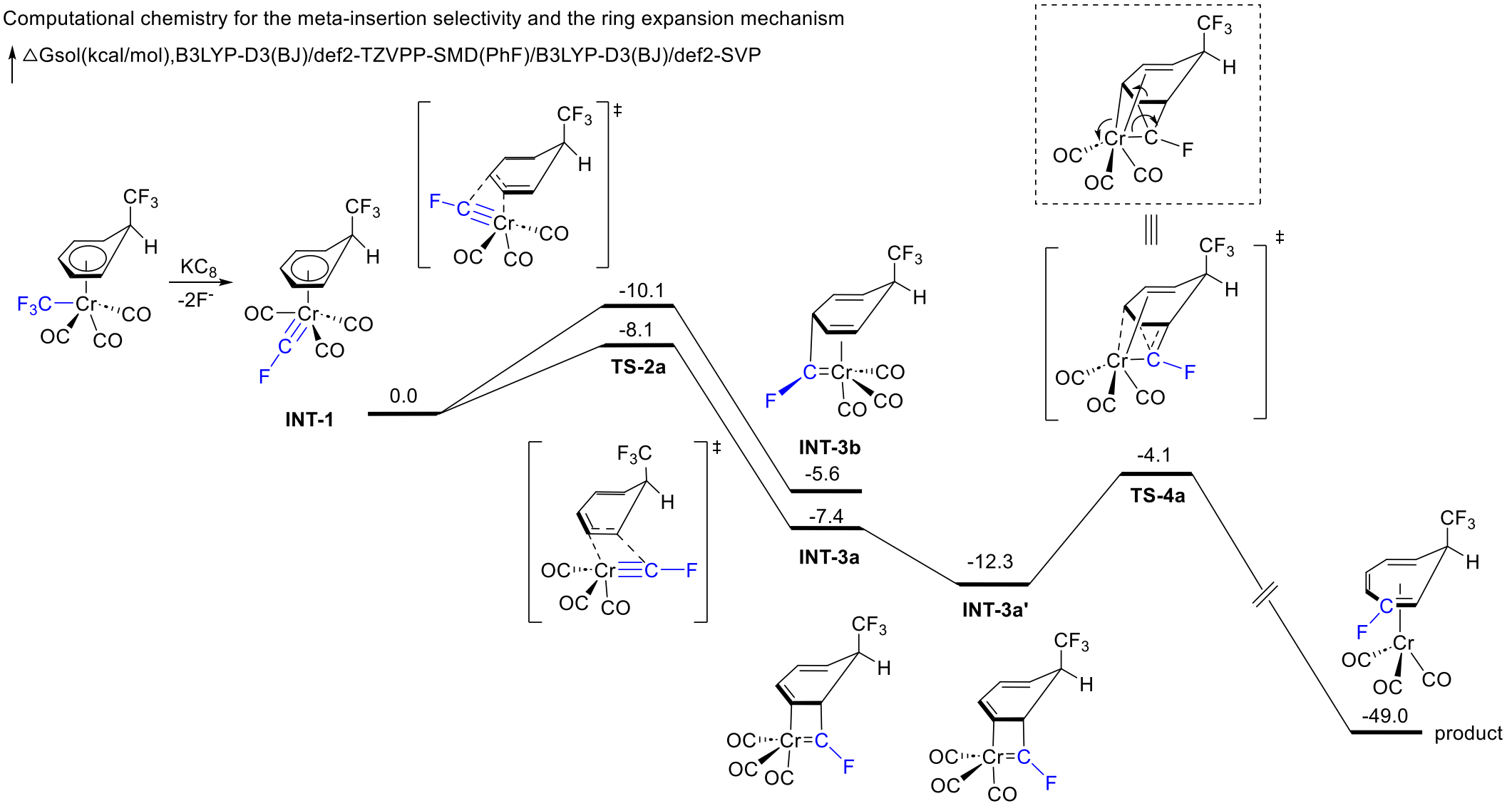


Li, W. et al. *J. Am. Chem. Soc.* **2025**, *147*, 44699−44707



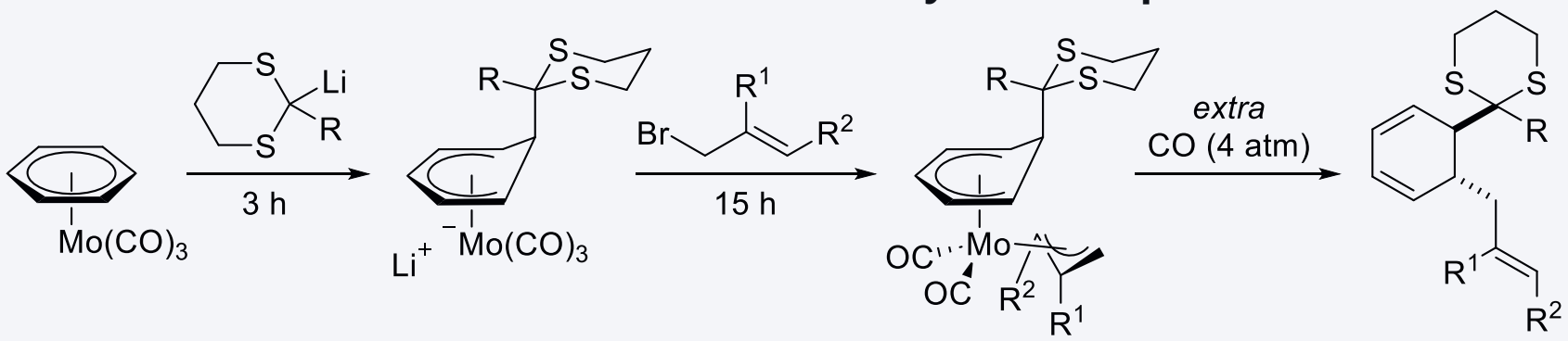
Computational chemistry for the meta-insertion selectivity and the ring expansion mechanism

↑ △Gsol(kcal/mol),B3LYP-D3(BJ)/def2-TZVPP-SMD(PhF)/B3LYP-D3(BJ)/def2-SVP

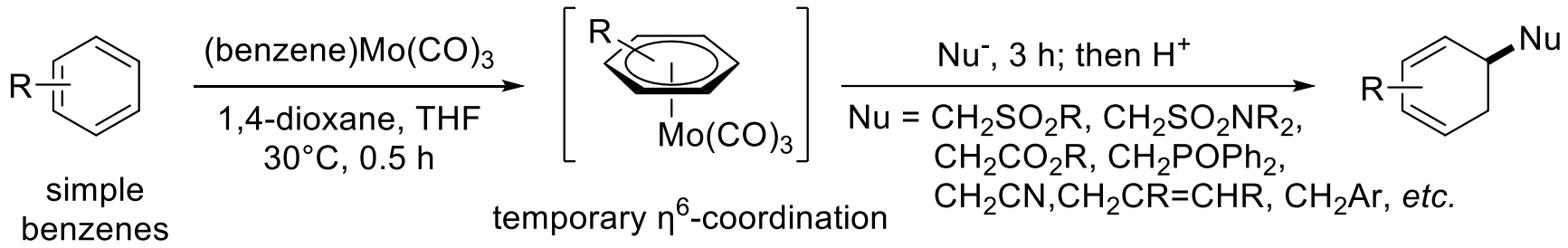


➢ 亲电活化策略

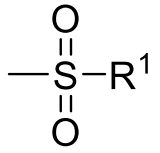
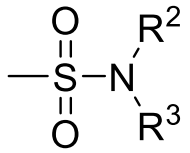
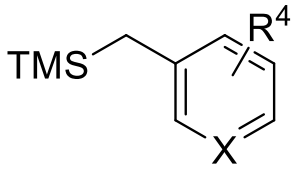
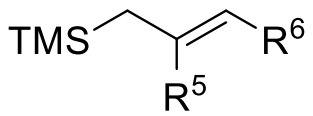
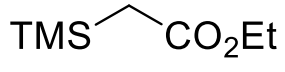
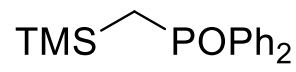
dearomative 1,2-difunctionalization via molybdenum η⁶-coordination



Kündig, E. P. et al. *Angew. Chem. Int. Ed.* **2002**, *41*, 4577–4579



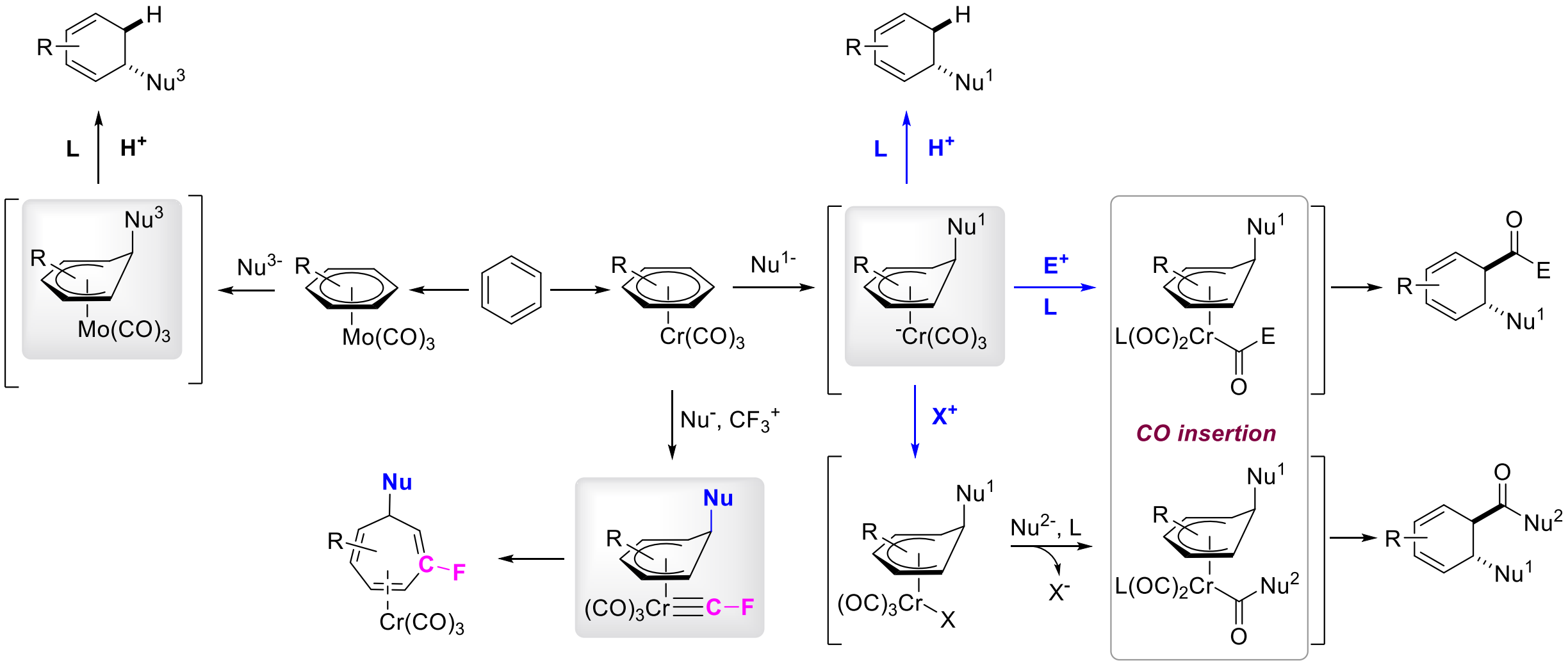
亲核试剂

Sulfone	***Sulfonamide***	***Benzyl***	***Allyl***	***Ester***	***Phosphinyl***
					

R1 = Allyl, benzyl

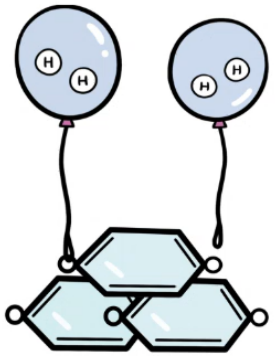
Li, W. et al. *J. Am. Chem. Soc.* **2025**, *147*, 39052–39059

➢ 亲电活化策略

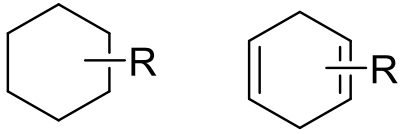

R
H
Nu3
L
H+
Nu3
Mo(CO)3
Nu3-
Mo(CO)3
Cr(CO)3
Nu1-
Nu1
-Cr(CO)3
E+
L
L(OC)2Cr
E
O
CO insertion
Nu-, CF3+
Nu
C–F
(CO)3Cr≡C–F
X+
(OC)3Cr
X
Nu2-, L
X-
Nu2

目录

总结



还原策略



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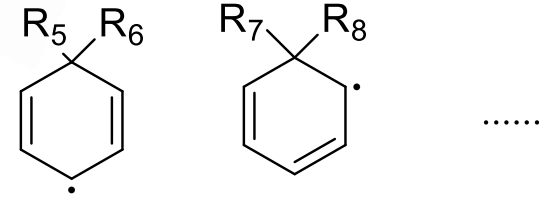
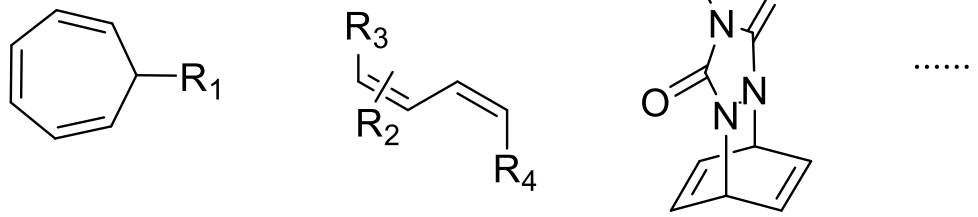
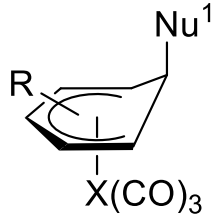
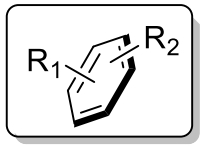


周环反应策略



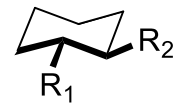
亲电活化策略





20th and 21st centuries

2020



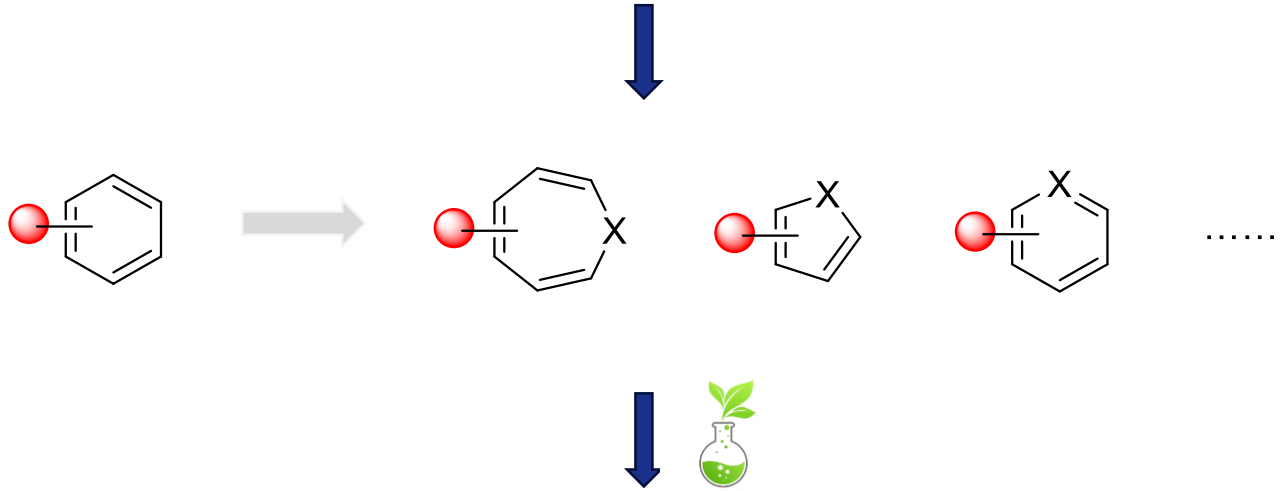
展望

区域选择性 ← 精准选择性控制 → 对映选择性

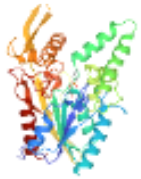
底物设计、配体调控或新型活化模式？

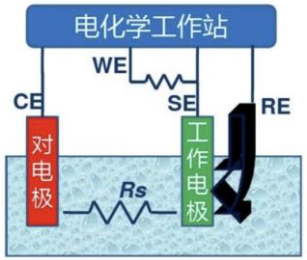
开发更普适、高效的催化体系？

未活化芳烃的去芳构化反应 →



Green Chemistry





欢迎各位老师同学批评指正！

谢谢大家！