八面体手性金属配合物及其在不对称光催化反应中的应用

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导　师：朱灿 青年研究员

2022-10-21

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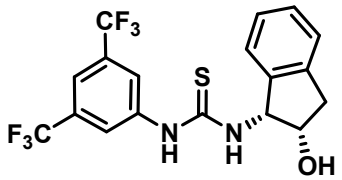
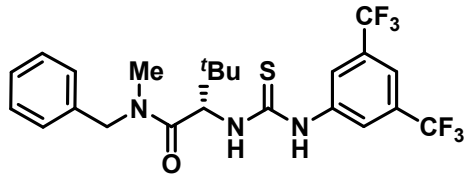
八面体手性金属配合物的发展

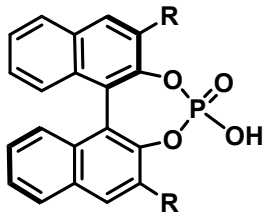
stereogenic carbon centers

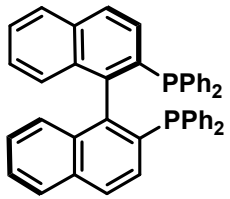


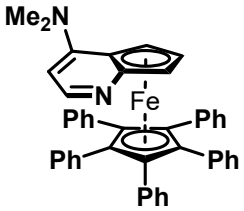
chiral axis

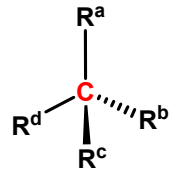


chiral plane

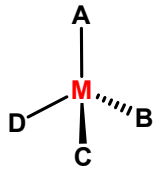




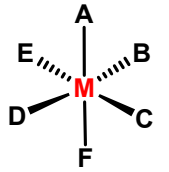




carbon-center

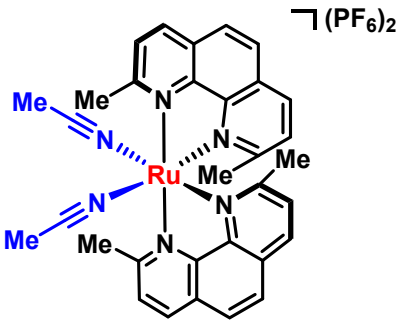


tetrahedral
metal center

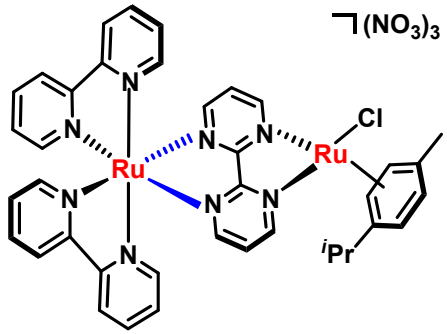


octahedral
metal center

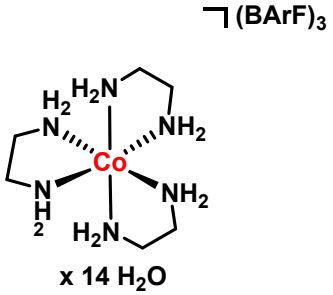
- **Fontecave (2003)**
- **Fontecave (2007)**
- **Gladysz (2008)**
- **Meggers (2013)**



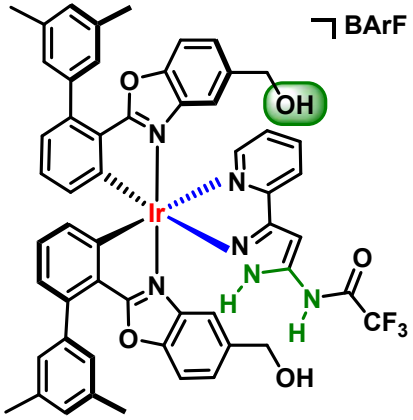
Oxidation of sulfides
2 mol% cat. 18% ee



Transfer hydrogenation
0.5 mol% cat. 26% ee



Michael addition
9 mol% cat. 33% ee

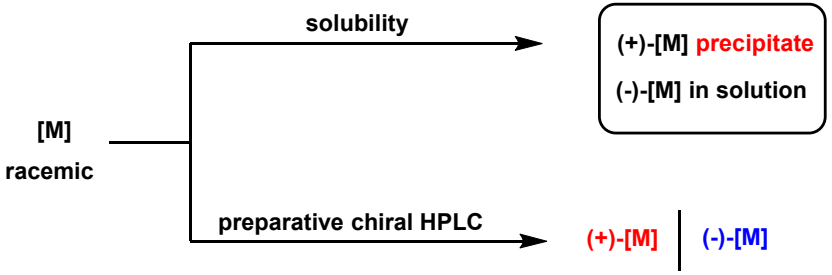


Transfer hydrogenation
0.1 mol% cat. 94% ee

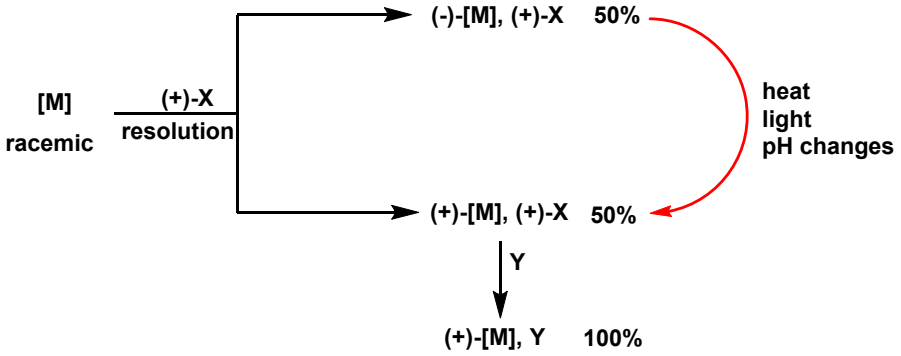
Acc. Chem. Res. **2017**, *50*, 320-330
Angew. Chem. Int. Ed. **2013**, *52*, 14021-14025

手性金属配合物的合成方法

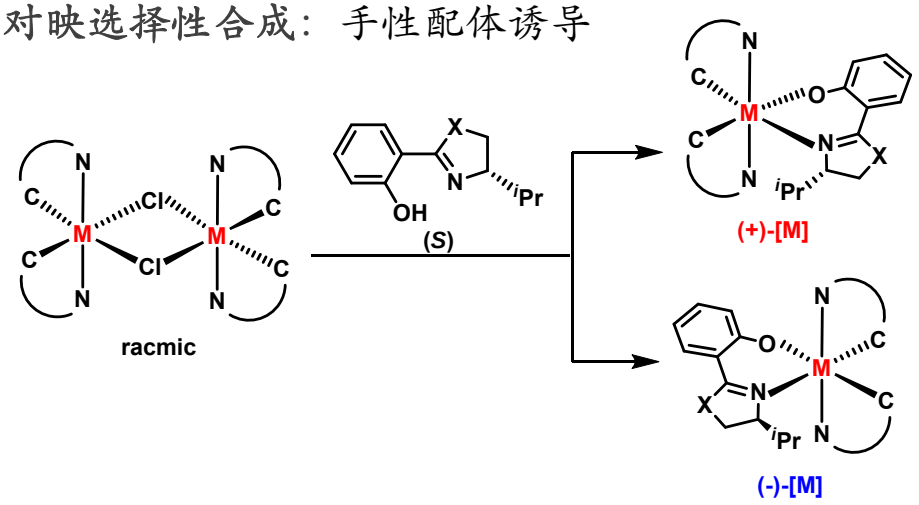
(1)手性拆分：根据对映异构体理化性质差异



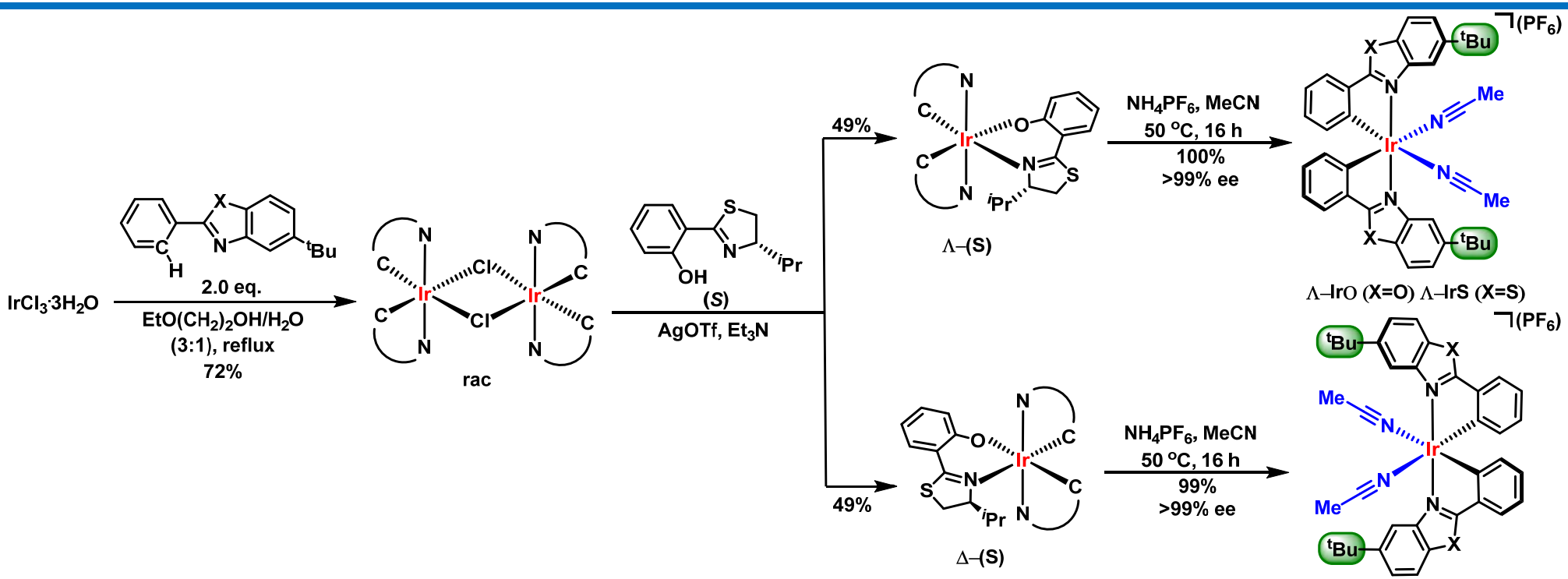
(2)不对称转化：促使其中一个异构体发生差向异构化

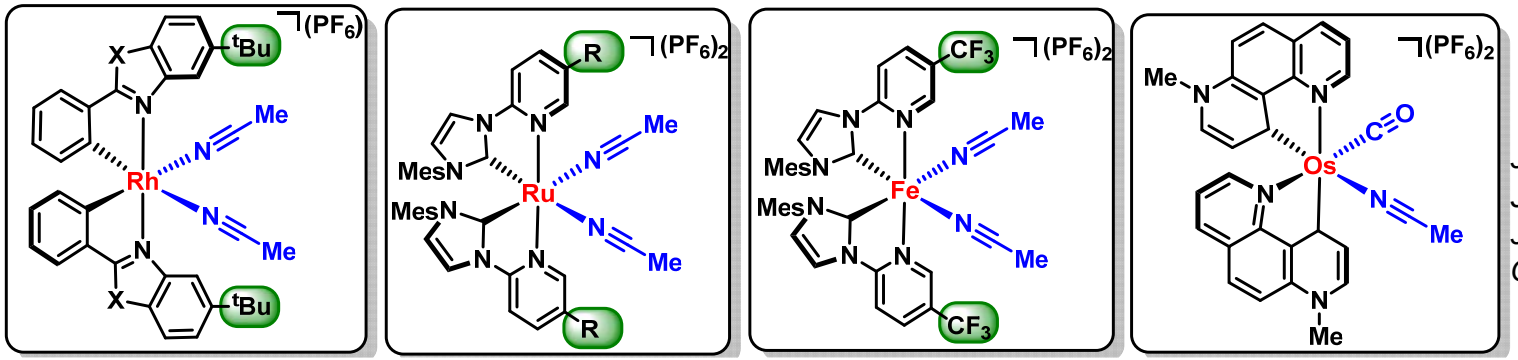


(3)非对映选择性合成：手性配体诱导



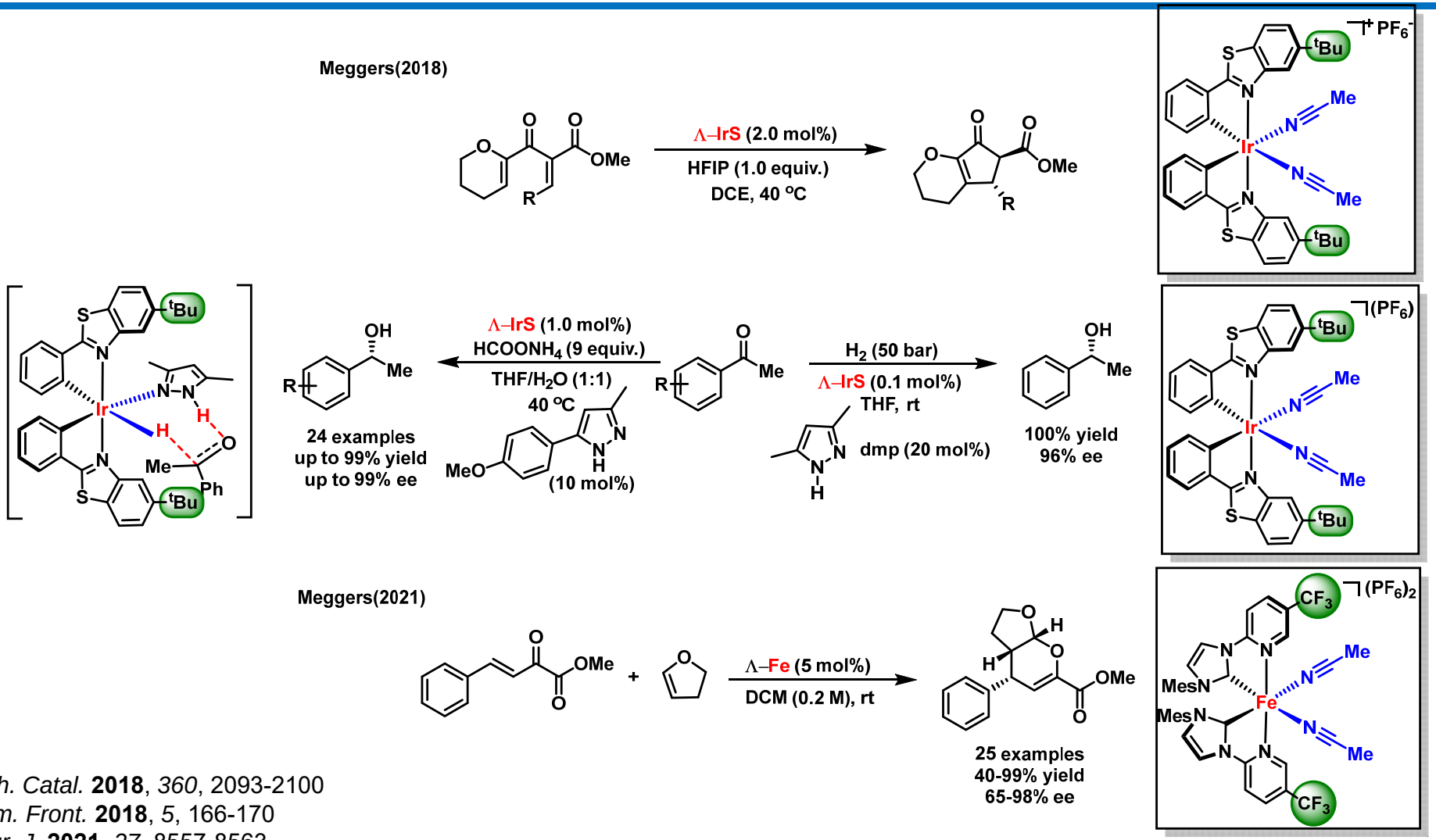
八面体手性金属配合物合成





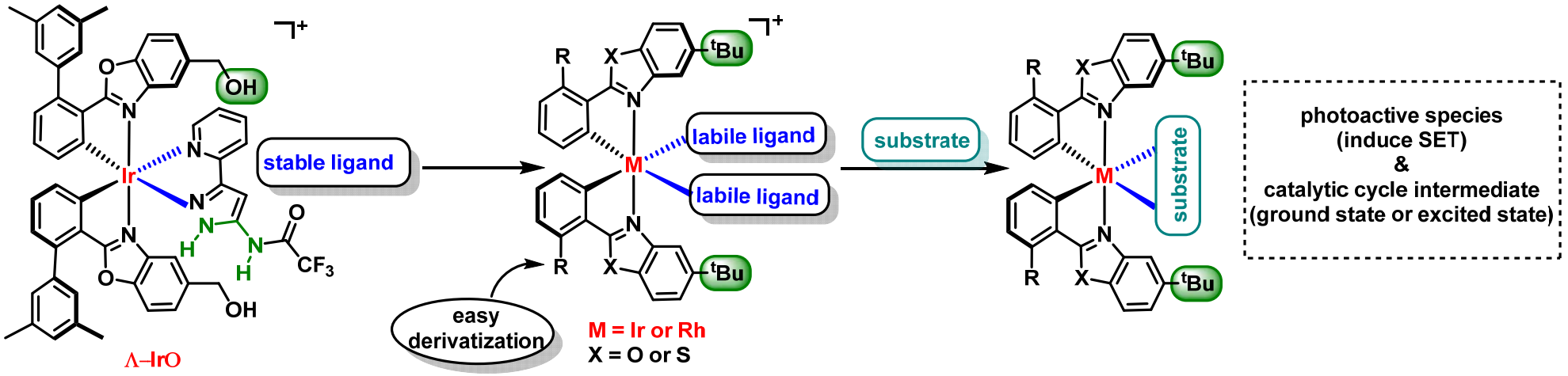
J. Am. Chem. Soc. **2014**, *136*, 2990-2993
J. Am. Chem. Soc. **2017**, *139*, 4322−4325
J. Am. Chem. Soc. **2019**, *141*, 4569-4572
Chem. Commun. **2020**, *56*, 7714-7717

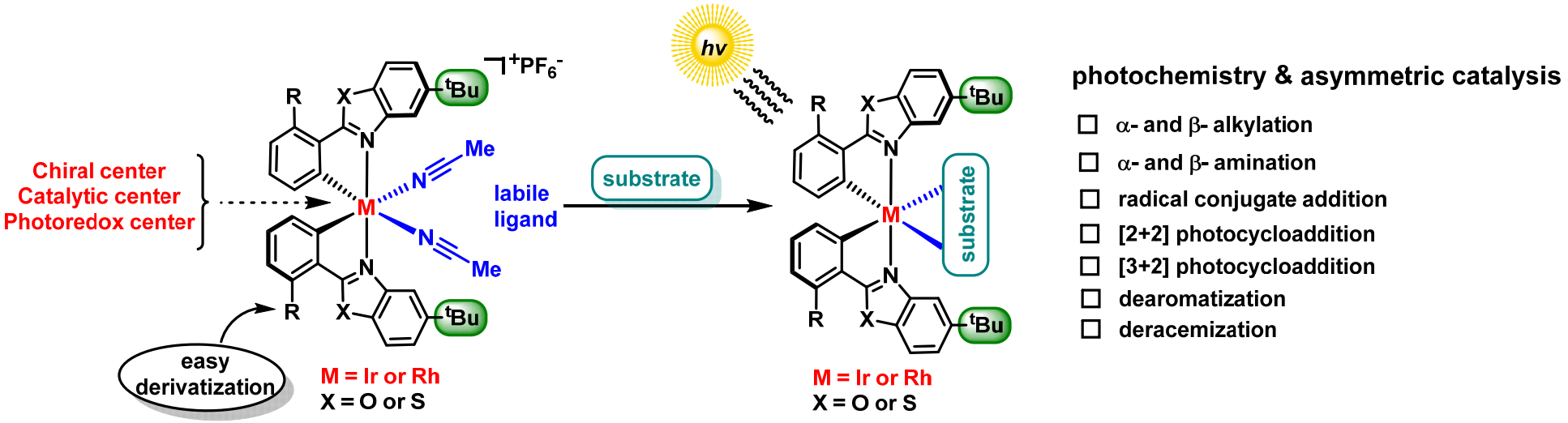
八面体手性金属配合物应用



Adv. Synth. Catal. **2018**, *360*, 2093-2100
Org. Chem. Front. **2018**, *5*, 166-170
Chem. Eur. J. **2021**, *27*, 8557-8563

八面体手性金属配合物设计





photochemistry & asymmetric catalysis

- ☐ α- and β- alkylation
- ☐ α- and β- amination
- ☐ radical conjugate addition
- ☐ [2+2] photocycloaddition
- ☐ [3+2] photocycloaddition
- ☐ dearomatization
- ☐ deracemization

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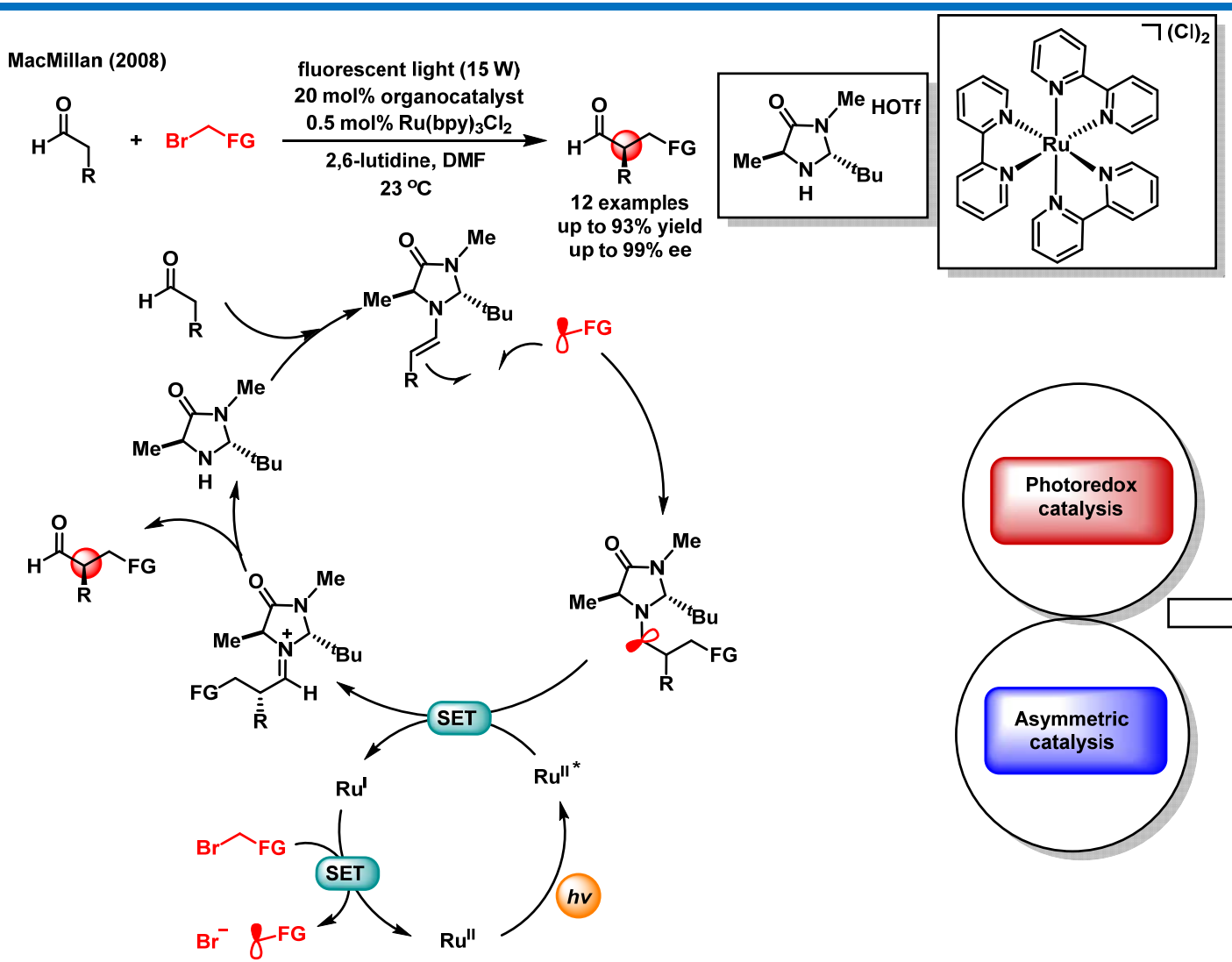
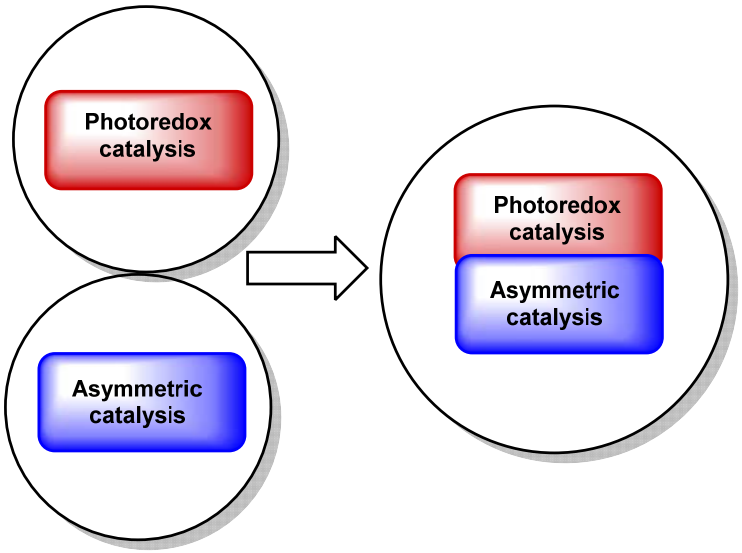
不对称光催化反应背景介绍

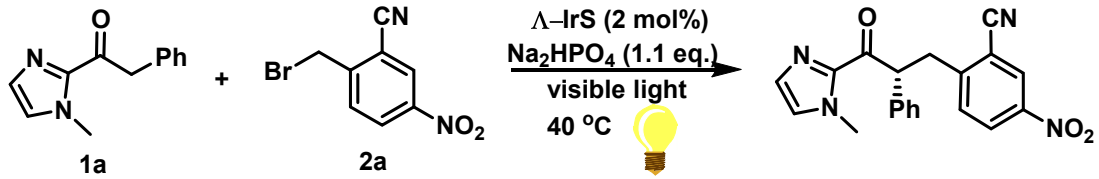


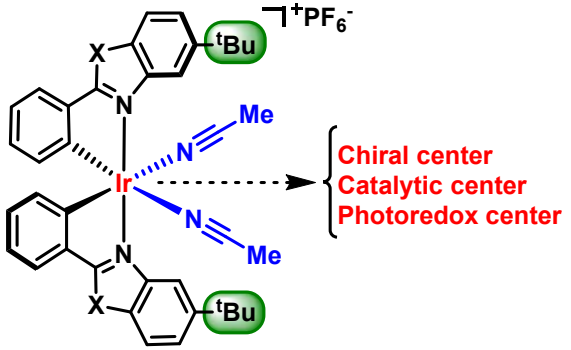


Science **2008**, *322*, 77−80

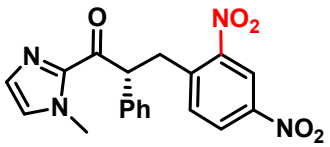
酰基咪唑α-烷基化反应

Meggers (2014)

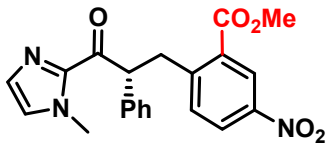




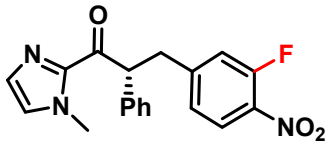
Λ–IrO (X=O) Λ–IrS (X=S)



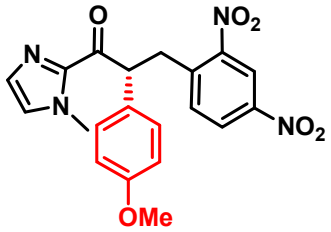
2 h, 97% yield, 99% ee



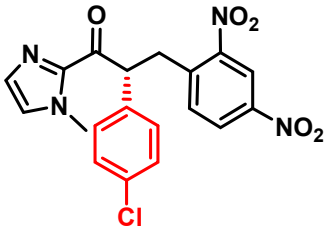
2 h, 98% yield, 99% ee



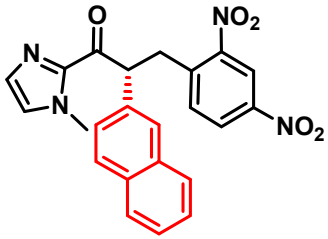
6 h, 97% yield, 94% ee



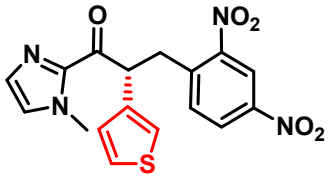
2 h, 97% yield, 97% ee



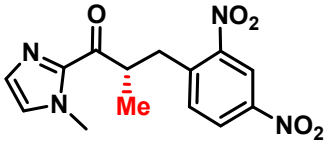
2 h, 98% yield, 96% ee



2 h, 99% yield, 98% ee



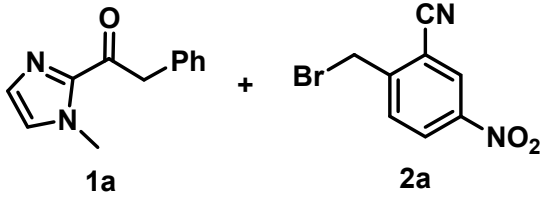
2 h, 99% yield, 97% ee



2 h, 87% yield, 97% ee

机理探究

(1)

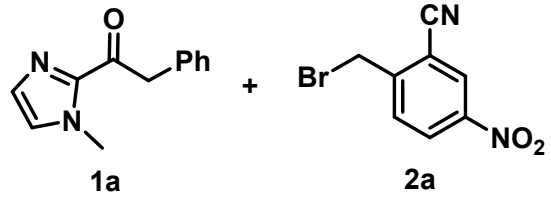


1a　　2a

Λ–IrS (2 mol%)
visible light
under air

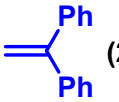
No product

(2)

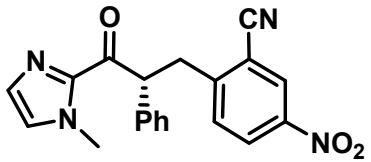


1a　　2a

Λ–IrS (2 mol%)
visible light

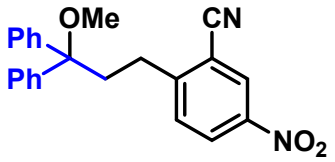


(2.5 eq.)



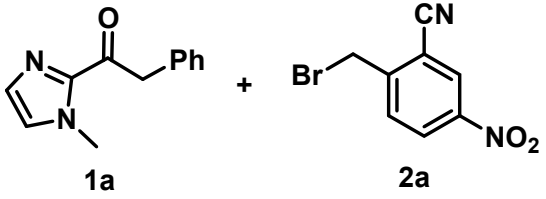
6% yield

+



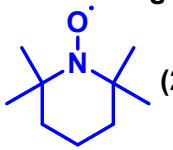
57% yield

(3)

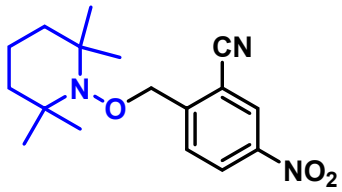


1a　　2a

Λ–IrS (2 mol%)
visible light

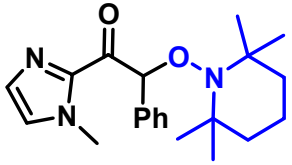


(2.5 eq.)



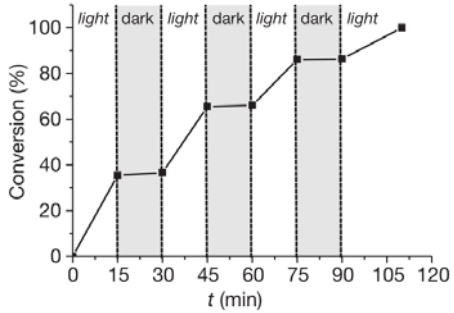
87% yield

+



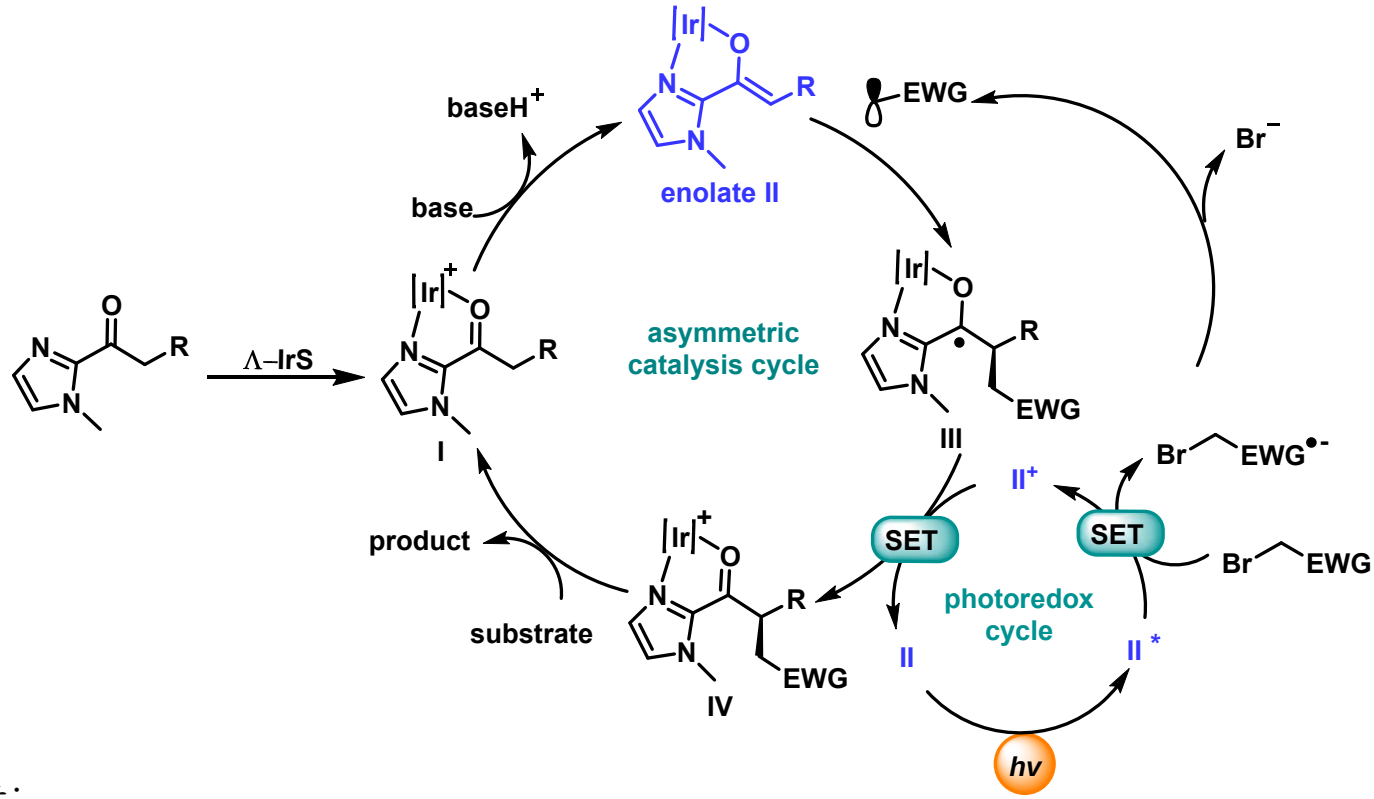
92% yield

(4)



Nature **2014**, *515*,100-103

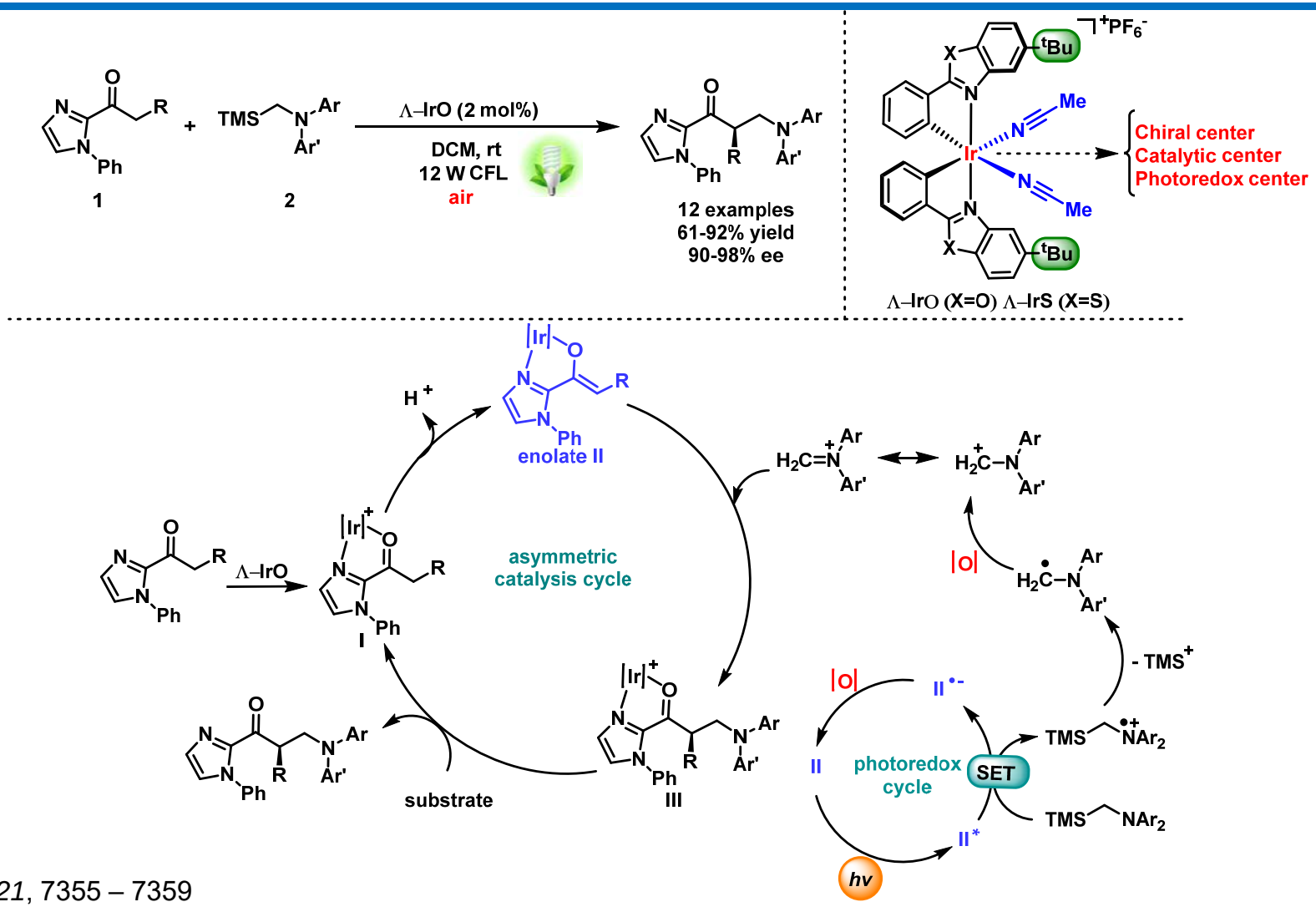
可能的机理



循环伏安法：

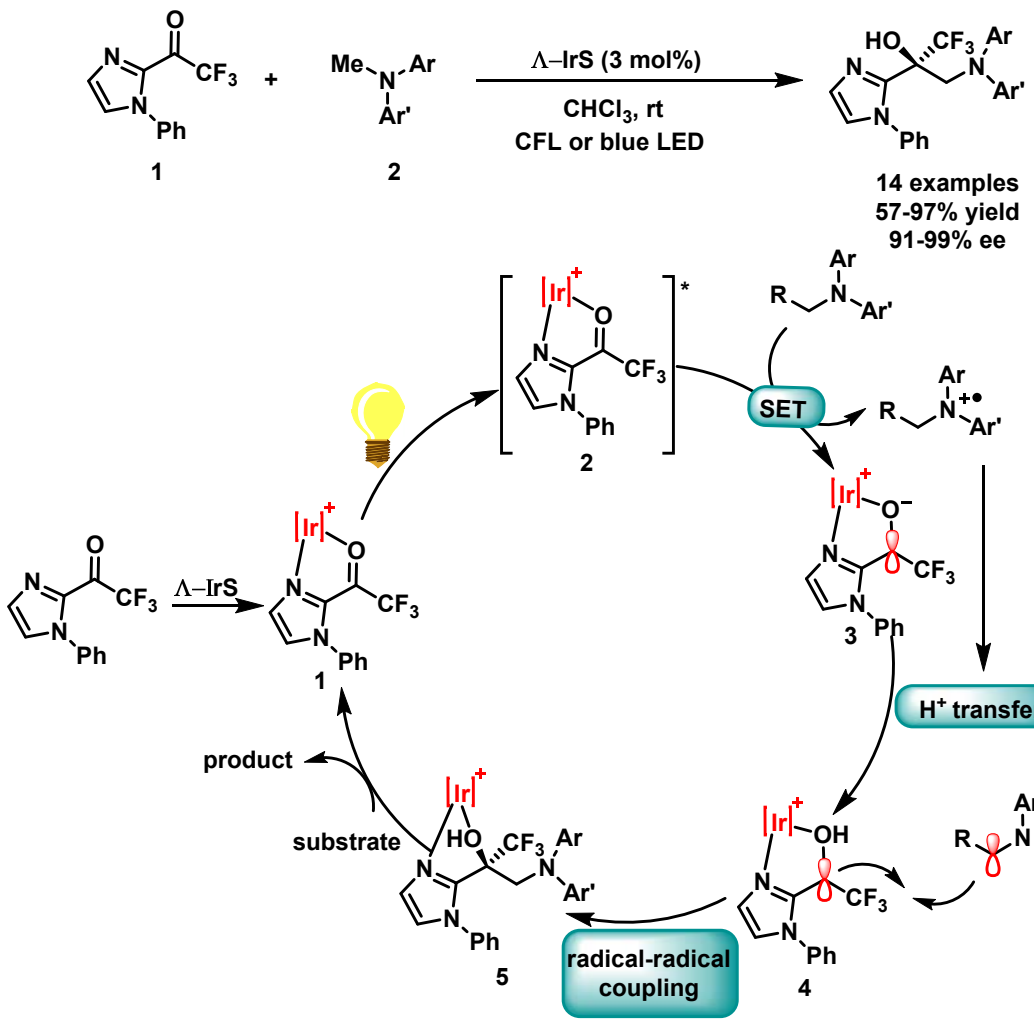
complex	absorbance	emission (E^{00})	$E_{1/2}(PS^+/PS)$	$E_{1/2}(PS^+/PS^*)$
Λ–IrS	425 nm	560 nm (2.21 eV)	> + 1.5 V	> - 0.71 V
enolate II	440 nm	550 nm (2.25 eV)	+ 0.51 V	- 1.74 V

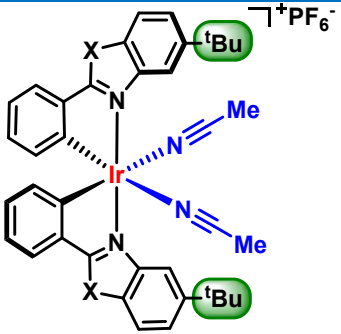
酰基咪唑α-胺烷基化



Chem. Eur. J. **2015**, *21*, 7355 – 7359

酰基咪唑自由基交叉偶联反应





八面体手性铱配合物作用：

- 激发SET
- 稳定酮中间体
- 调控立体化学

Angew. Chem. Int. Ed. **2016**, *55*, 685 –688

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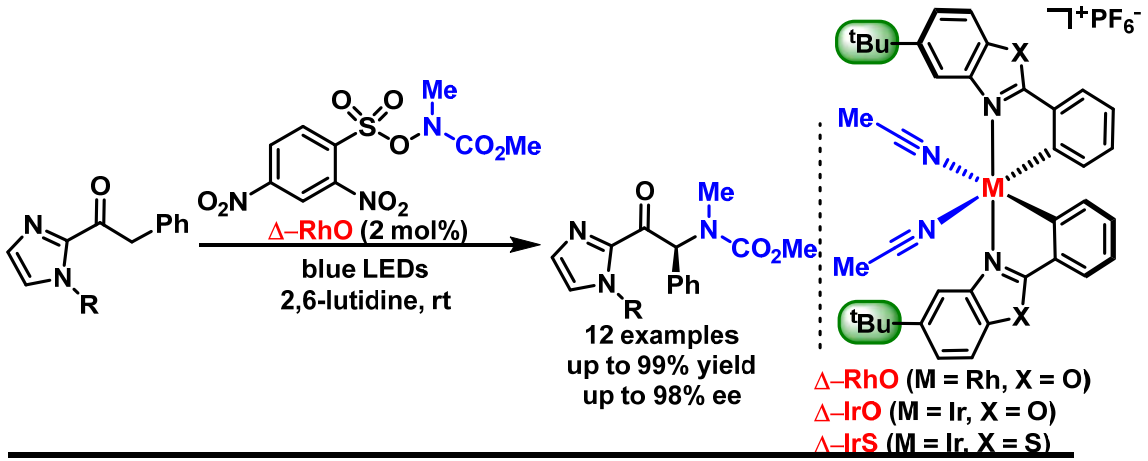
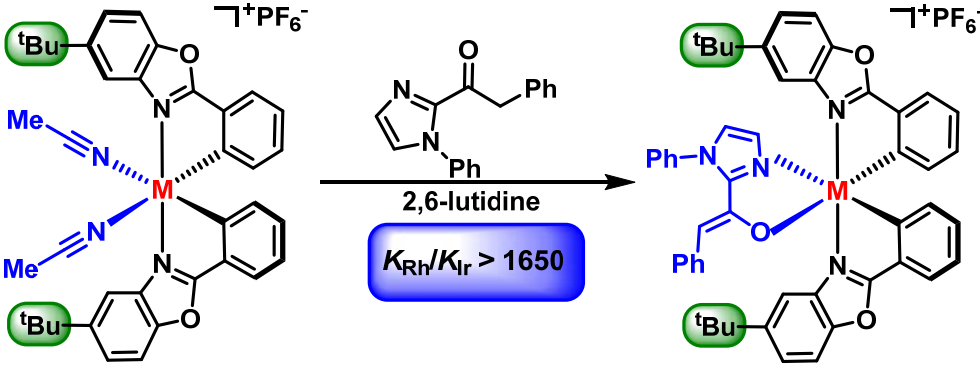
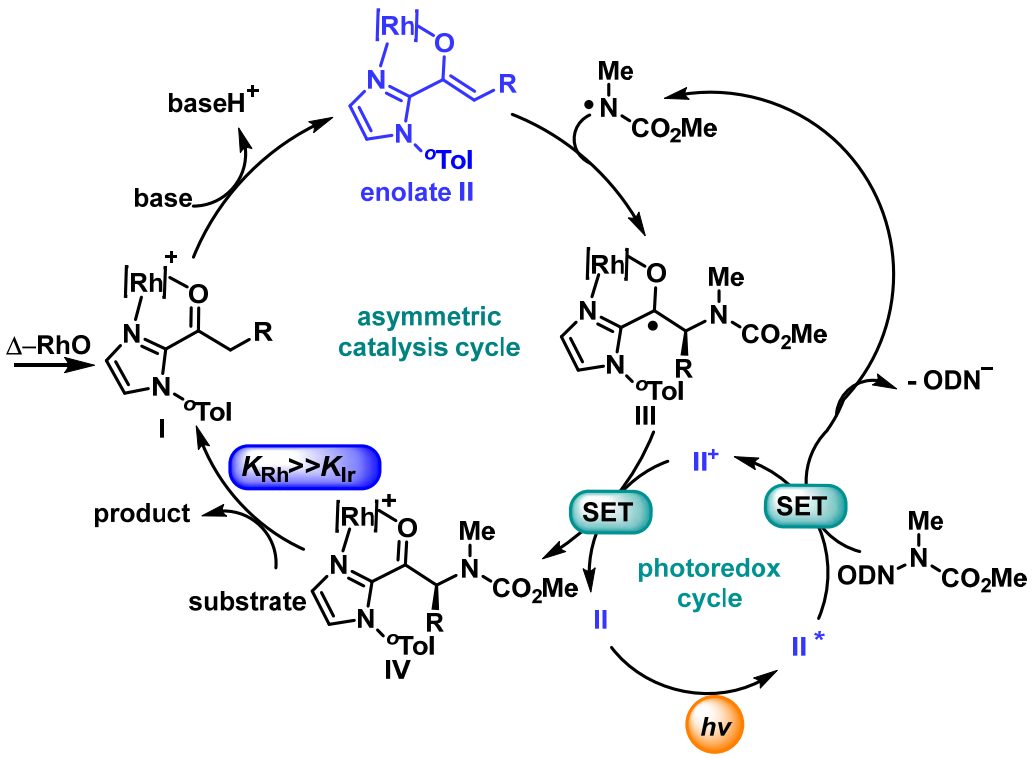
酰基咪唑的α-胺化



entry	catalyst	R	t (h)	yield (%)	ee (%)
1	Δ–IrO (2.0)	^{i}Pr	12	0	N.D.
2	Δ–IrS (2.0)	^{i}Pr	12	0	N.D.
3	Δ–RhO (2.0)	^{i}Pr	12	44	80
4	Δ–RhO (2.0)	Ph	2	93	89
5	Δ–RhO (2.0)	^{o}Tol	2	96	97

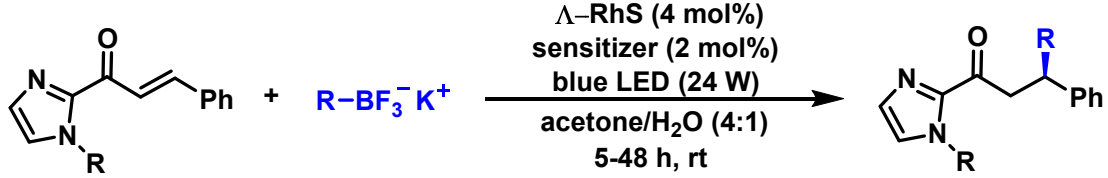


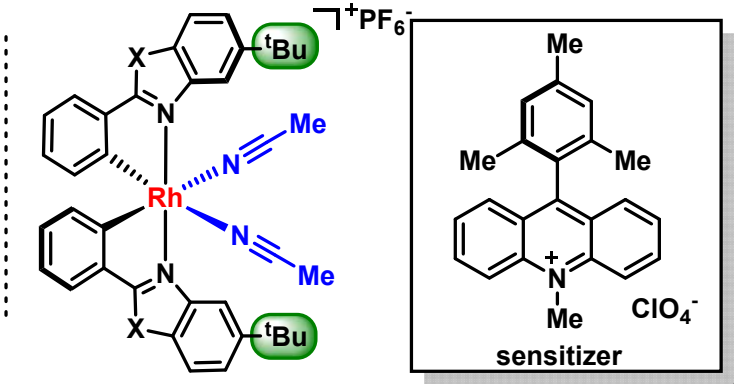


Chem. Eur. J. **2016**, *22*, 9102-9105

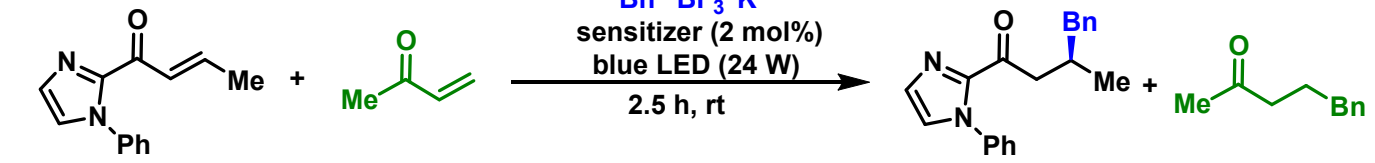
α,β-不饱和酰基咪唑β-烷基化 硼试剂

Meggers (2016)





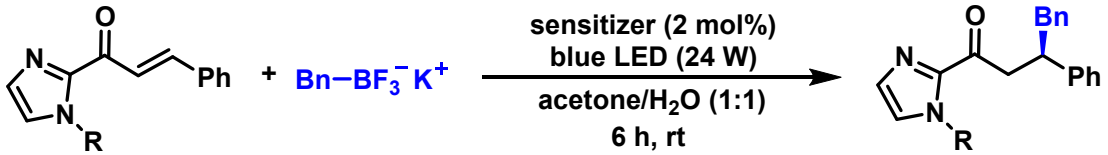
(1)



activated by Rh not activated by Rh

no Rh: 3a:3a' = 0.4
4 mol% Rh: 3a:3a' > 550:1

(2)

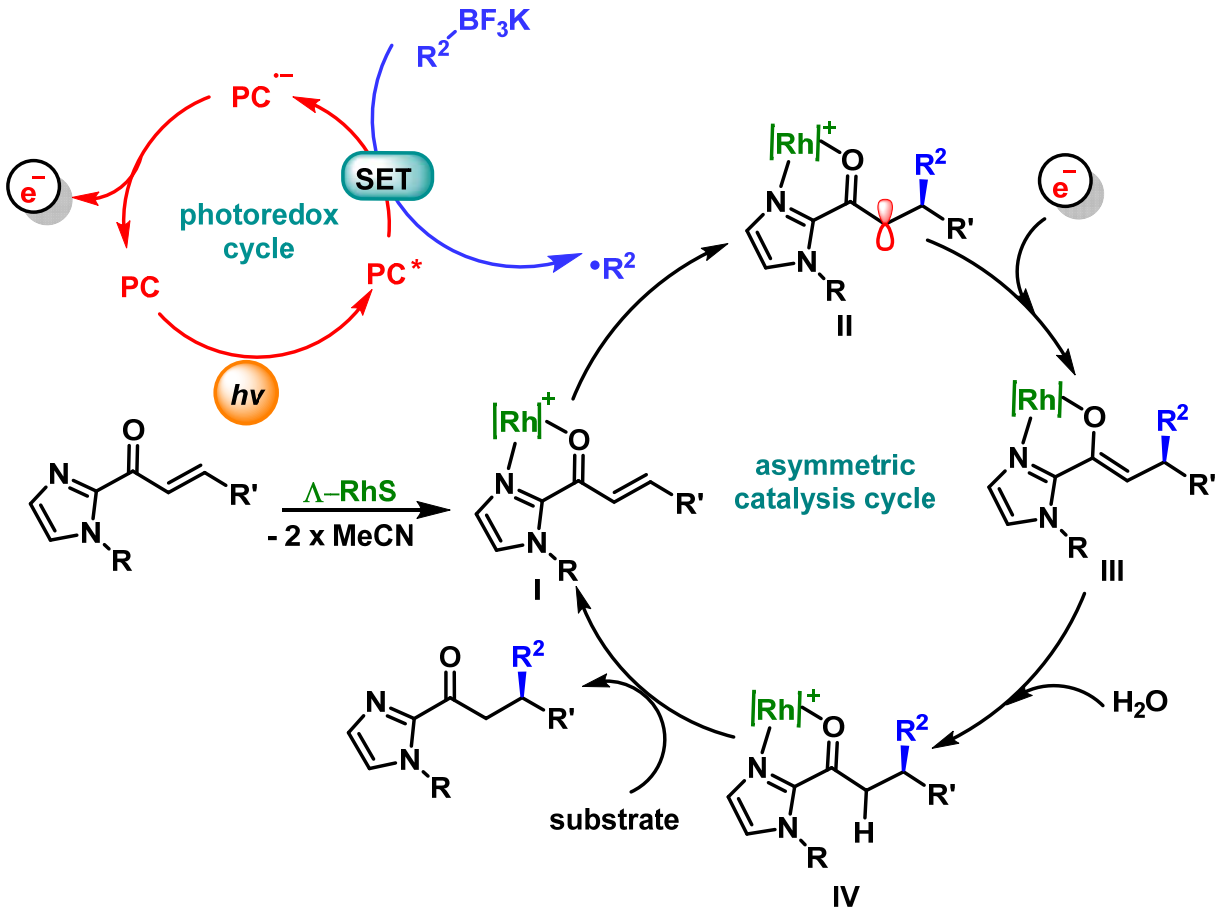


$K_{Rh} : K_{background} > 3 \times 10^4$

no Rh: 29% yield, 0% ee
4 mol% Rh: 73% yield, 96% ee

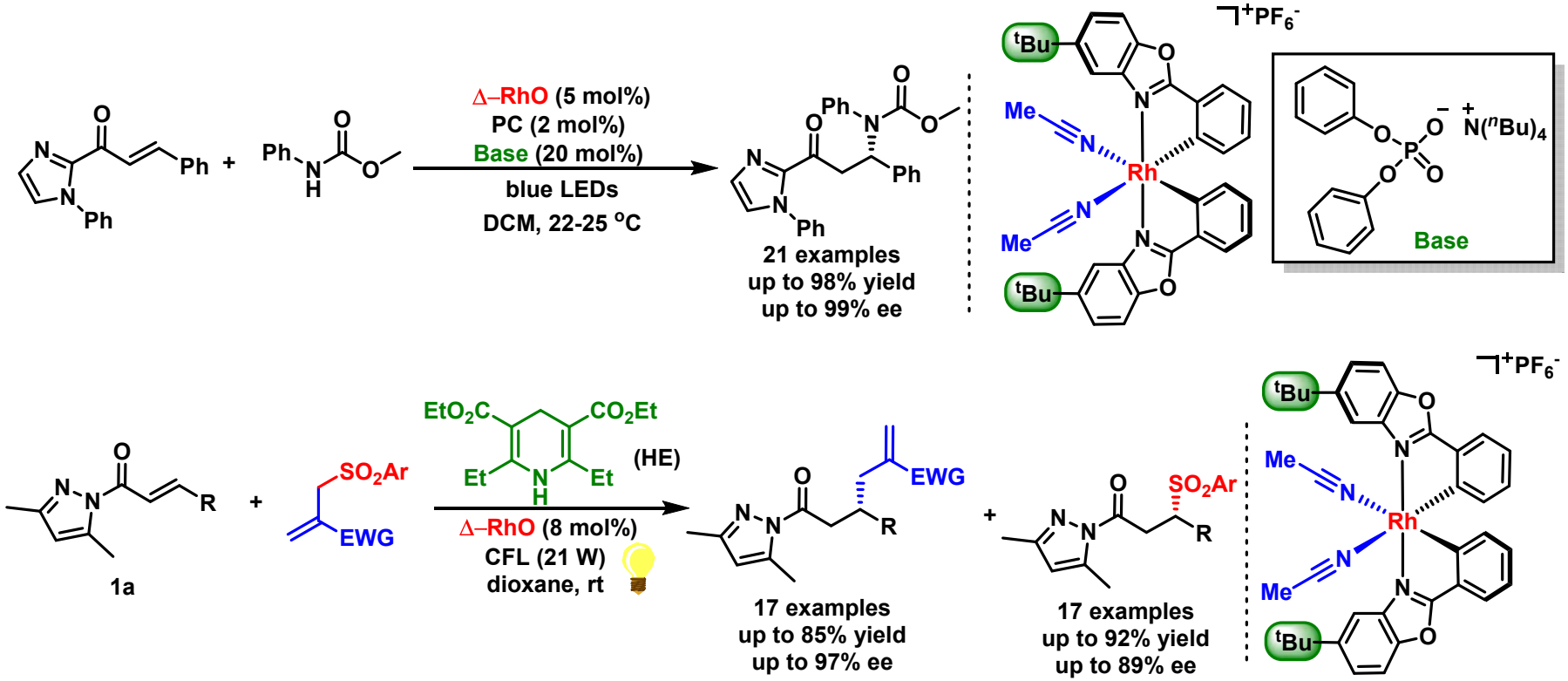
J. Am. Chem. Soc. **2016**, *138*, 6936−6939

可能的机理



J. Am. Chem. Soc. **2016**, *138*, 6936−6939

α,β-不饱和酰基咪唑β-胺化 β-烯丙基化



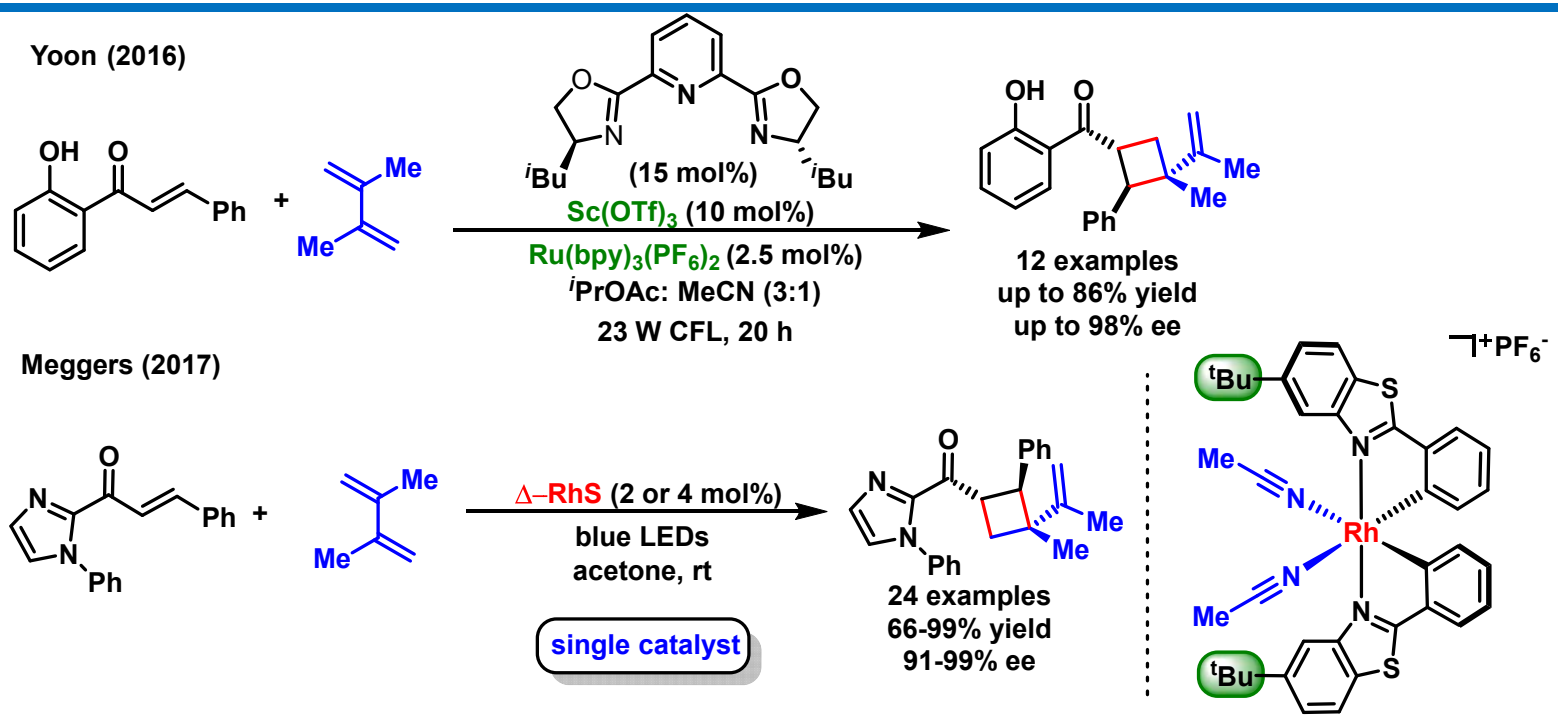
1a: E_p^{red} (-2.59 V *vs.* Fc/Fc$^+$)

RhO-1a: E_p^{red} (-1.62 V *vs.* Fc/Fc$^+$)

HE: E(HE$^{\bullet+}$/HE*) (-2.23 V *vs.* Fc/Fc$^+$)

Chem. Sci., **2017**, *8*, 5757-5763
Chem. Sci., **2017**, *8*, 7126-7131

α,β-不饱和酰基咪唑[2+2]环加成



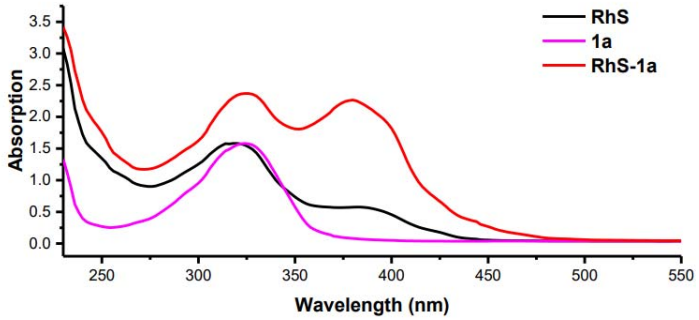
entry	catalyst	condition	t (h)	yield (%)	d.r.	ee (%)
1	Δ–RhS (2.0)	standard	16	99	14:1	99
2	Δ–RhS (0.5)	standard	24	98	12:1	96
3	Δ–RhS (2.0)	air	16	97	14:1	99
4	Δ–RhS (2.0)	air, 1% H_2O	24	96	13:1	99
5	Δ–RhS (2.0)	DMF solvent	16	95	13:1	98
6	Δ–RhS (2.0)	DCM solvent	16	99	14:1	99

体现反应的普适性和简洁高效性

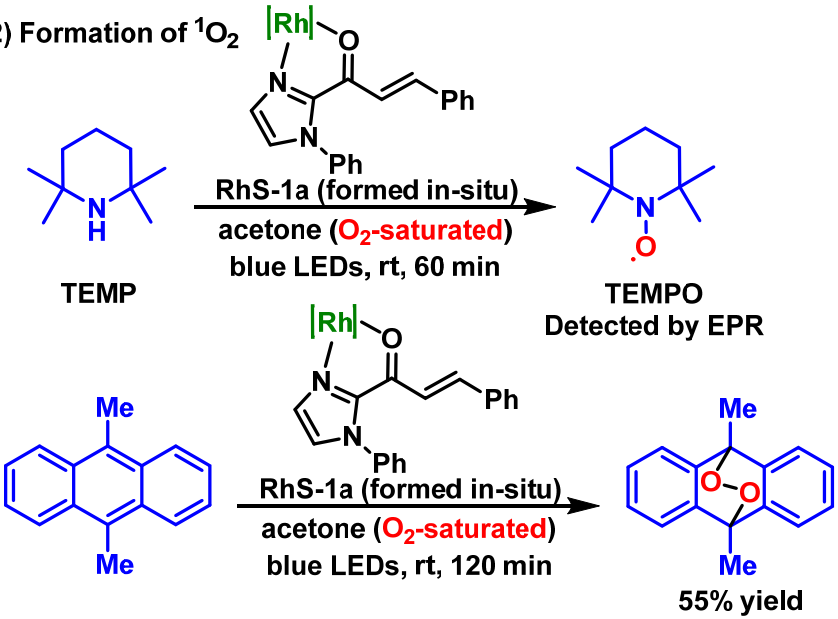
Yoon.; *Science* **2016**, *354*, 1391
Meggers.; *J. Am. Chem. Soc.* **2017**, *139*, 9120

机理验证-三线态中间体

1) UV/Vis absorbance spectra



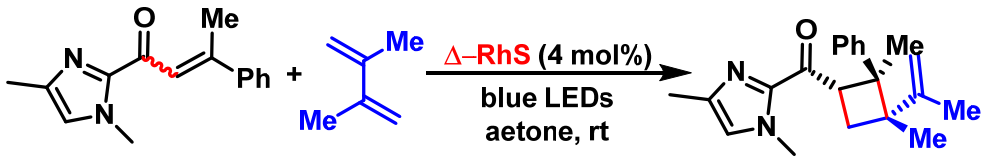
2) Formation of $^1O_2$



3) Control experiments

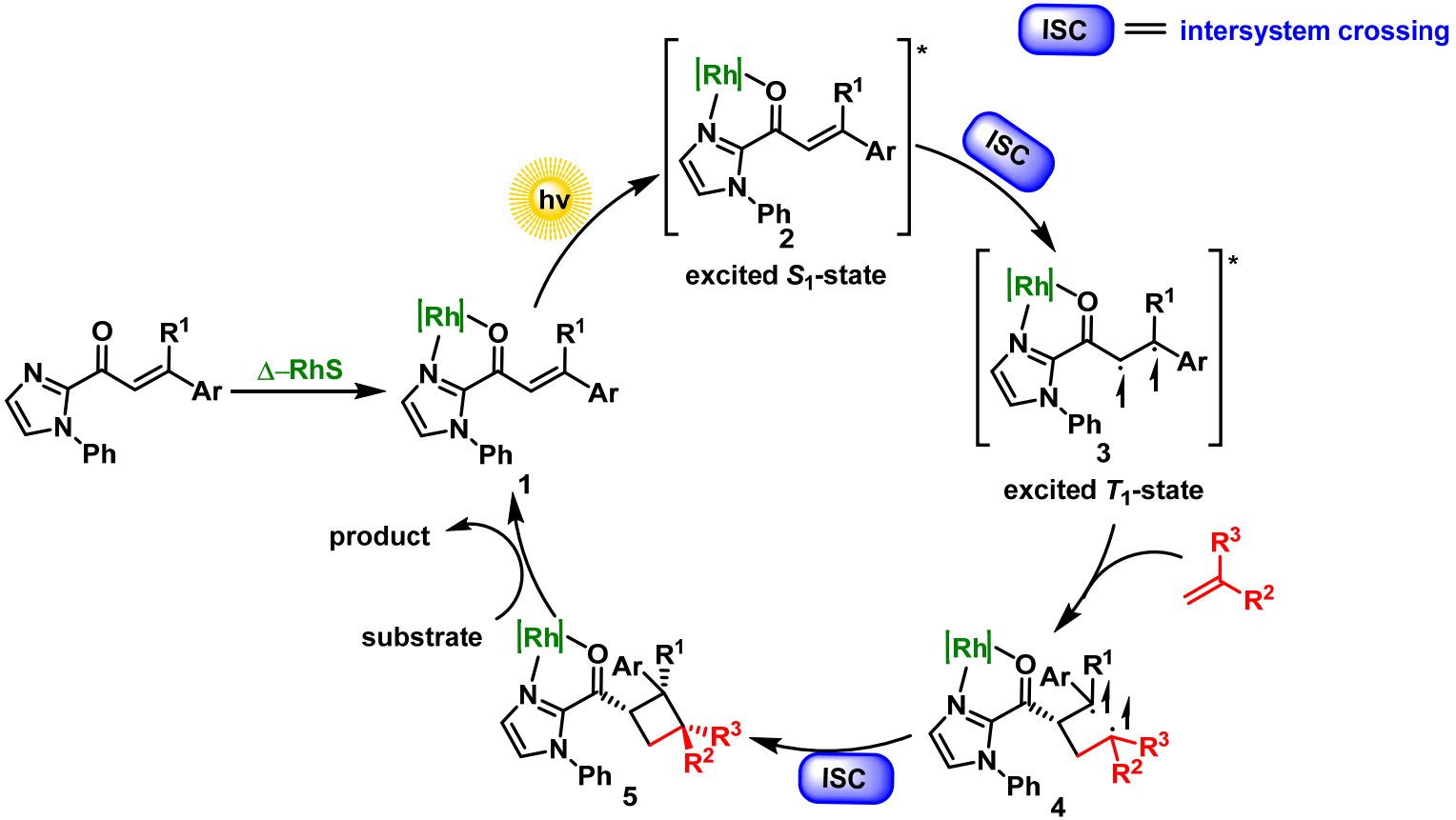
sensitizer	results
Benzil (40 mol%)	68% yield, 5:1 dr
$Ir(ppy)_2(dtbbpy)(PF_6)$ (2.0 mol%)	60% yield, 5:1 dr
$Ir(dFCF_3ppy)_2(bpy)(PF_6)$ (2.0 mol%)	65% yield, 5:1 dr

4) E/Z diastereomer



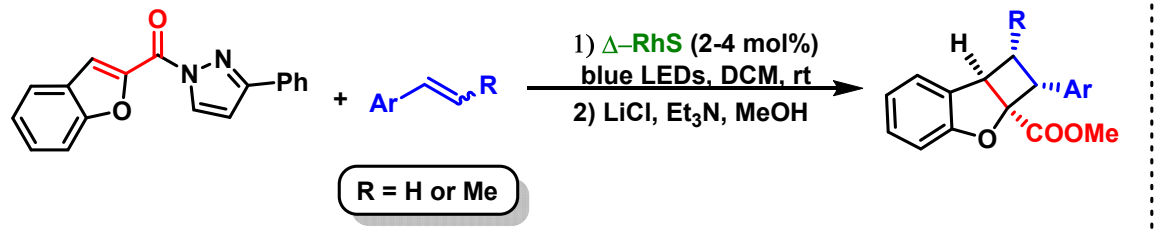
(*E*): 95% yield, 99% ee
(*Z*): 94% yield, 99% ee

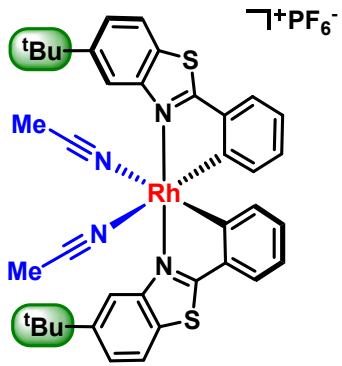
[2+2]环加成反应可能机理

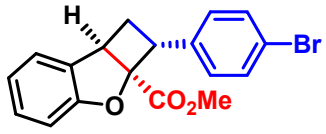


J. Am. Chem. Soc. **2017**, *139*, 9120-9123

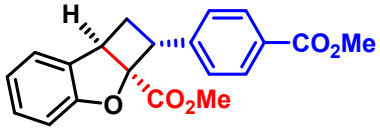
酰基吡唑[2+2]环加成-去芳构化



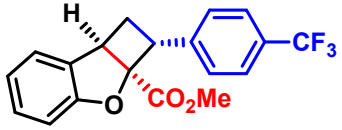




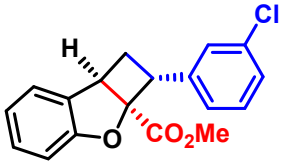
76% yield, 98% ee, 20:1 r.r.



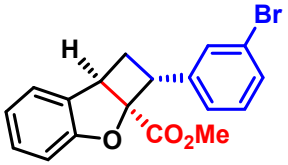
82% yield, 98% ee, 9.0:1 r.r.



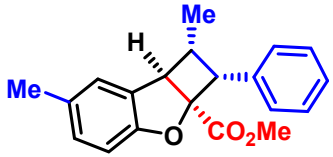
74% yield, 96% ee, 10.5:1 r.r.



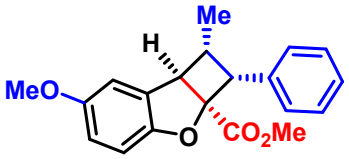
88% yield, 98% ee, 10.1:1 r.r.



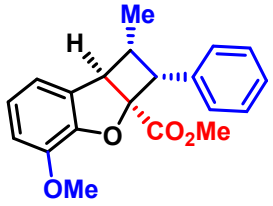
80% yield, 98% ee, 13.0:1 r.r.



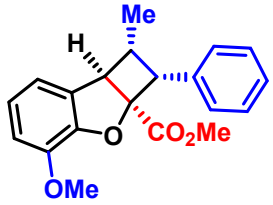
85% yield, 99% ee, >20:1 r.r.



88% yield, 99% ee, >20:1 r.r.



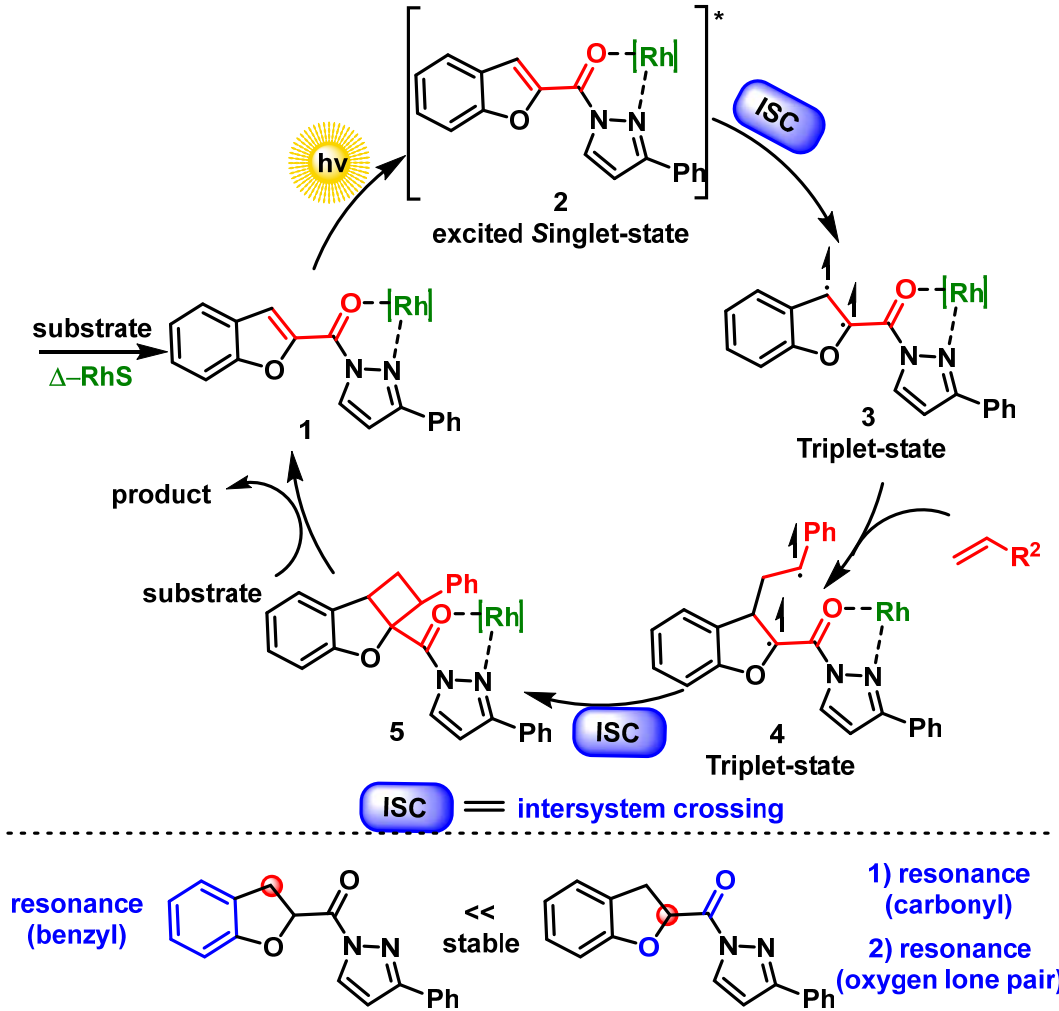
86% yield, 99% ee, >20:1 r.r.

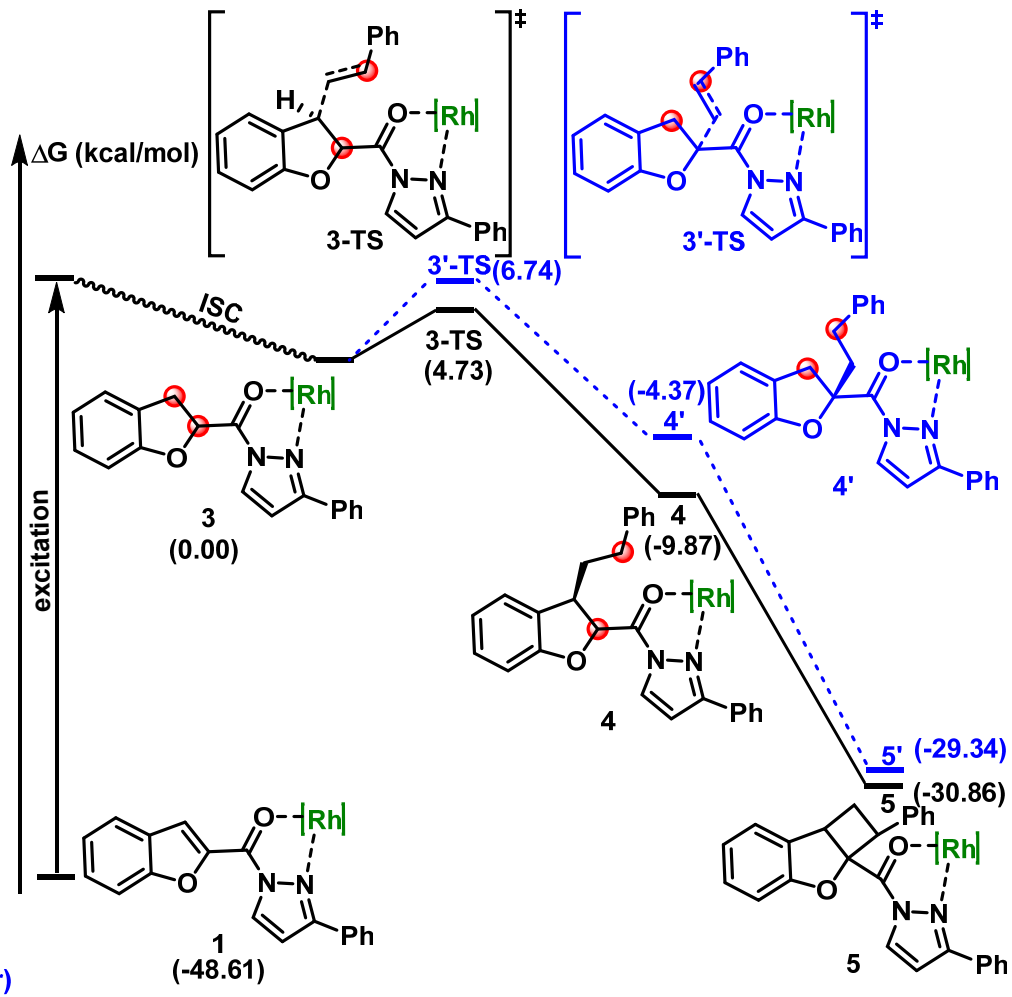


93% yield, 99% ee, >20:1 r.r.

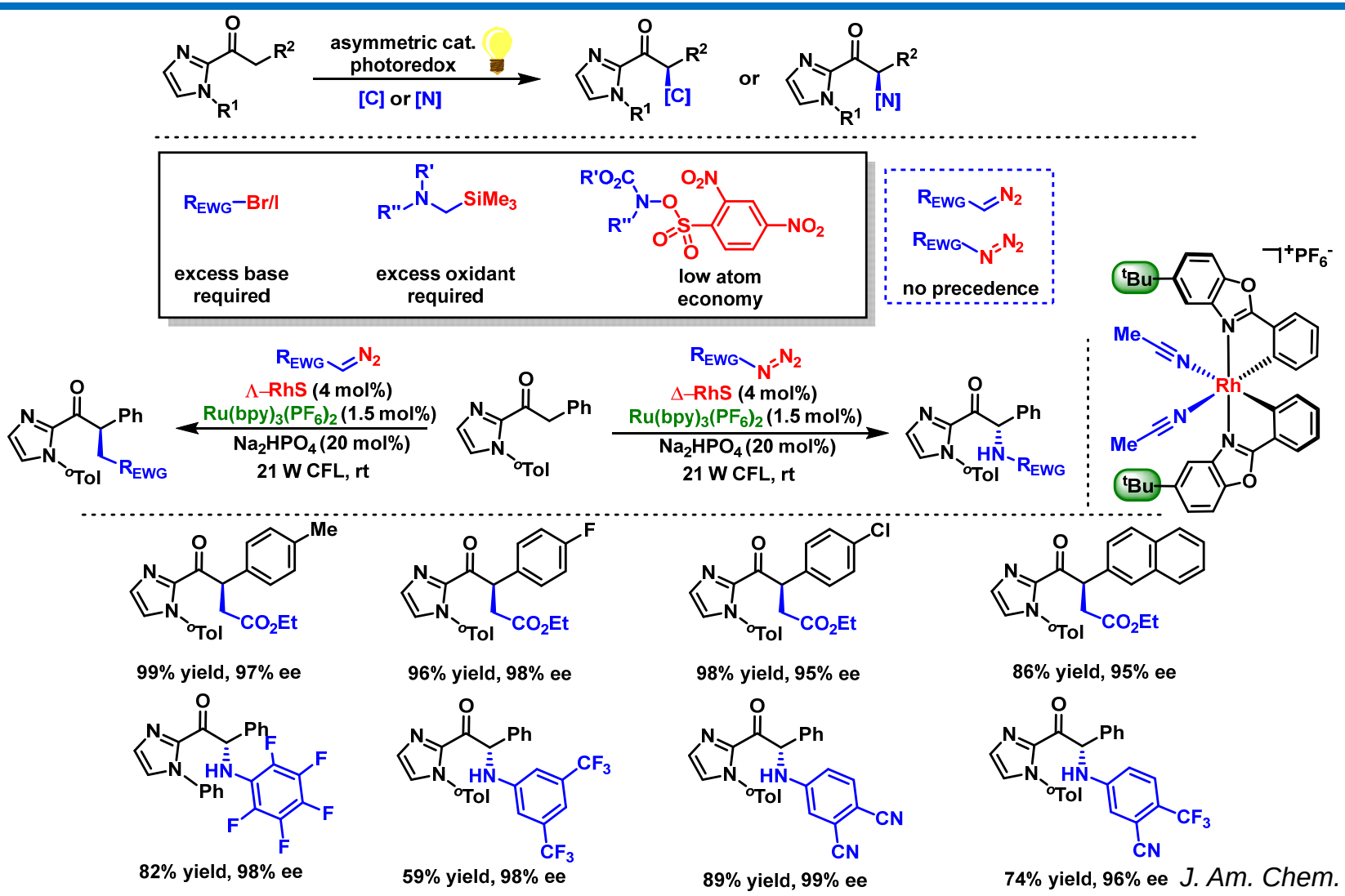
Angew. Chem. Int. Ed. **2018**, *57*, 6242-6246

酰基吡唑[2+2]环加成-去芳构化





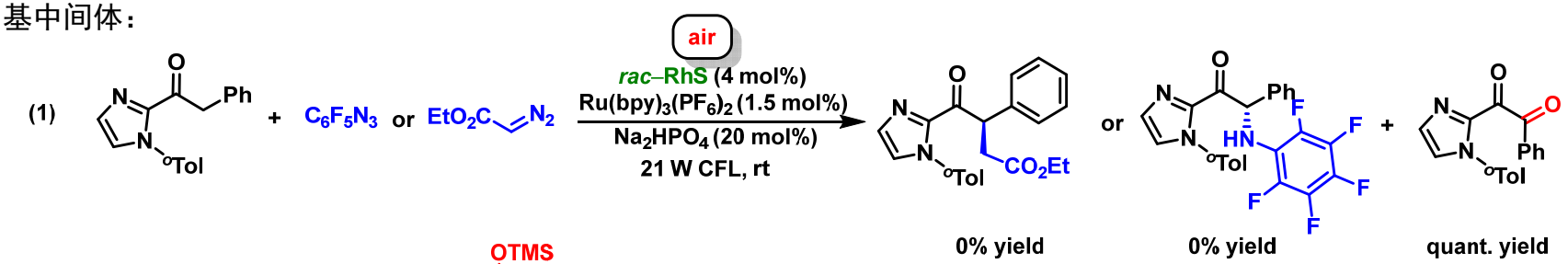
酰基咪唑α-烷基化 α-胺化

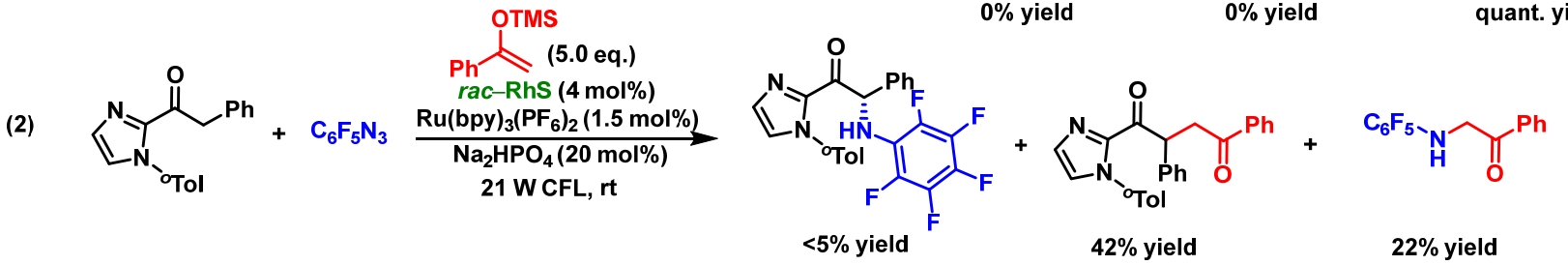


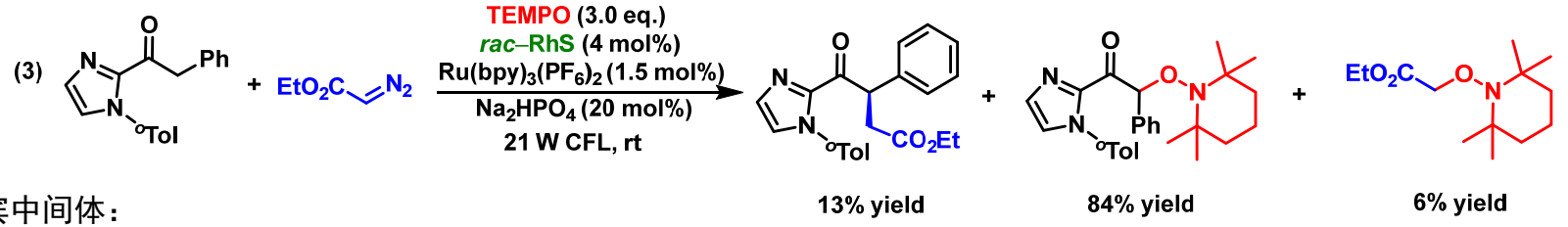
J. Am. Chem. Soc. **2016**, *138*, 12636-12642

机理验证

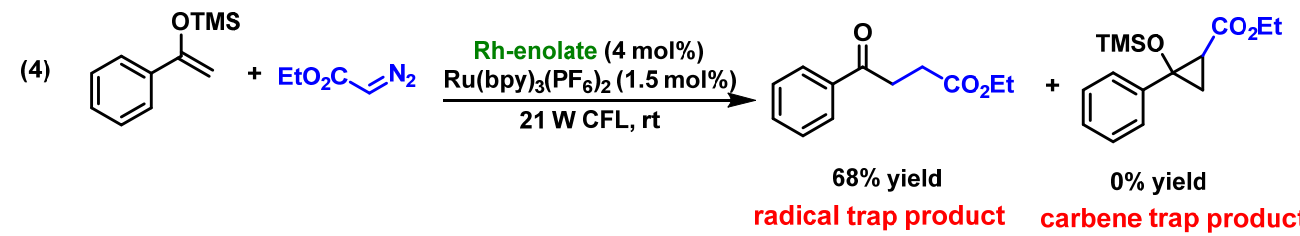
探究自由基中间体：





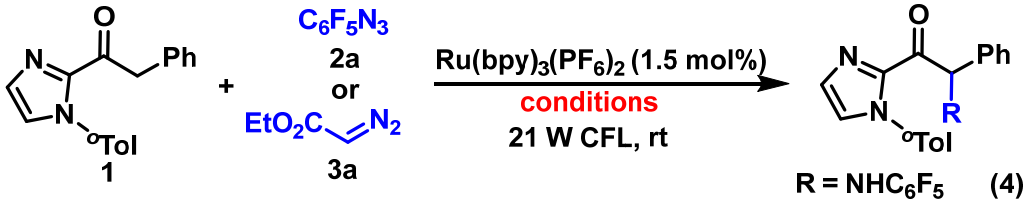


排除卡宾中间体：

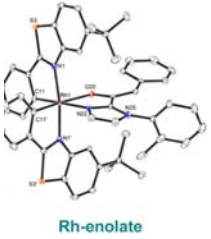


机理验证及可能的机理

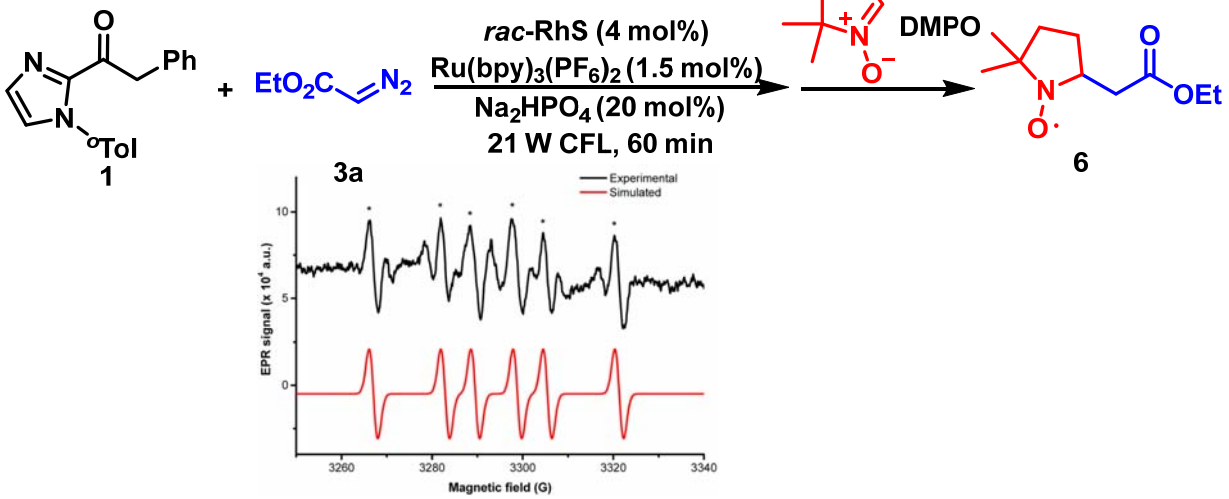
验证烯醇铑为反应中间体：

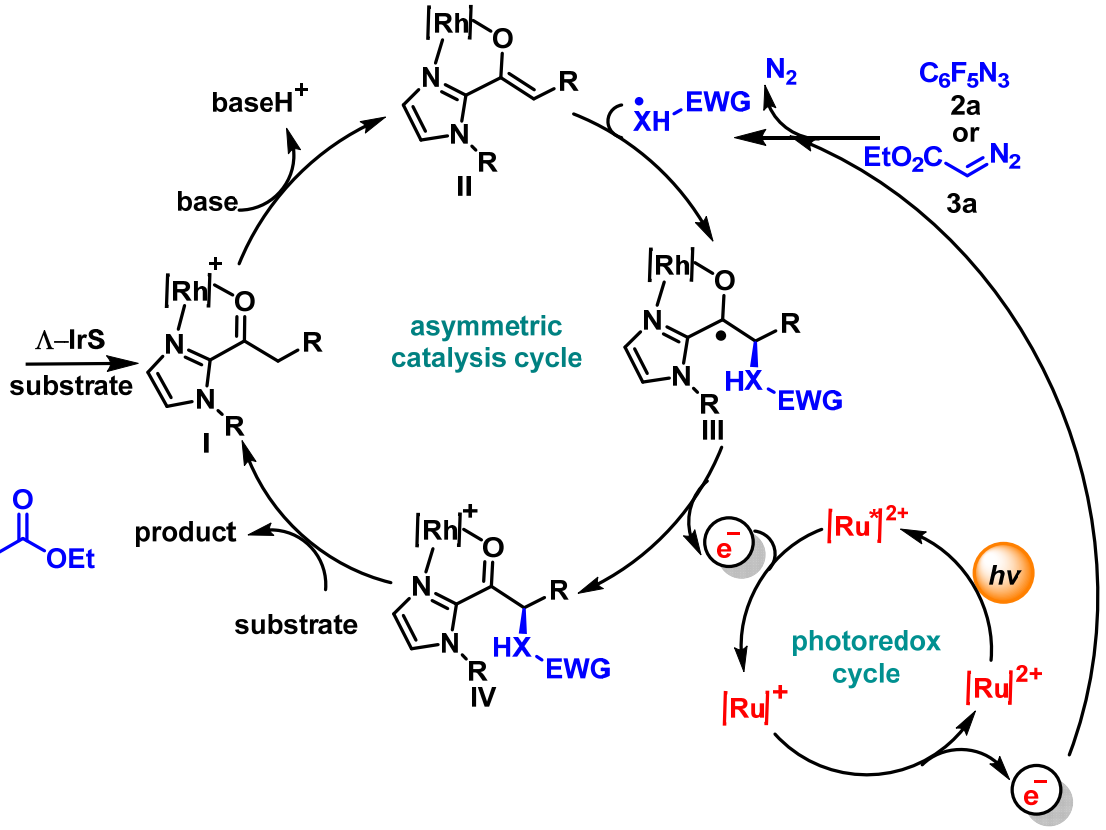


reagent	conditions	products
2a	RhS + Na_2HPO_4	4, 79%
2a	Rh-enolate	4, 74%
3a	RhS + Na_2HPO_4	5, 99%
3a	Rh-enolate	5, 99%

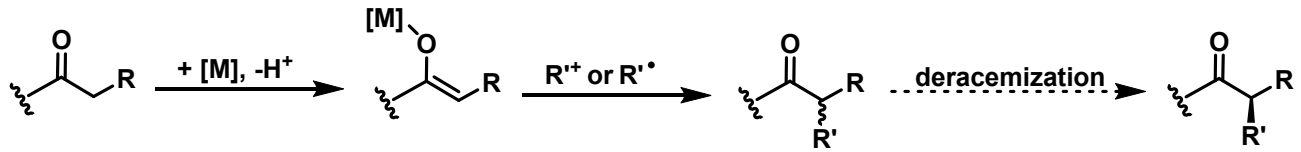


EPR自由基捕获实验：

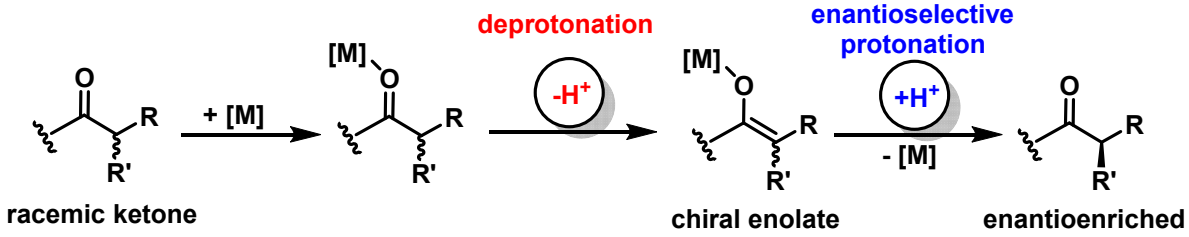


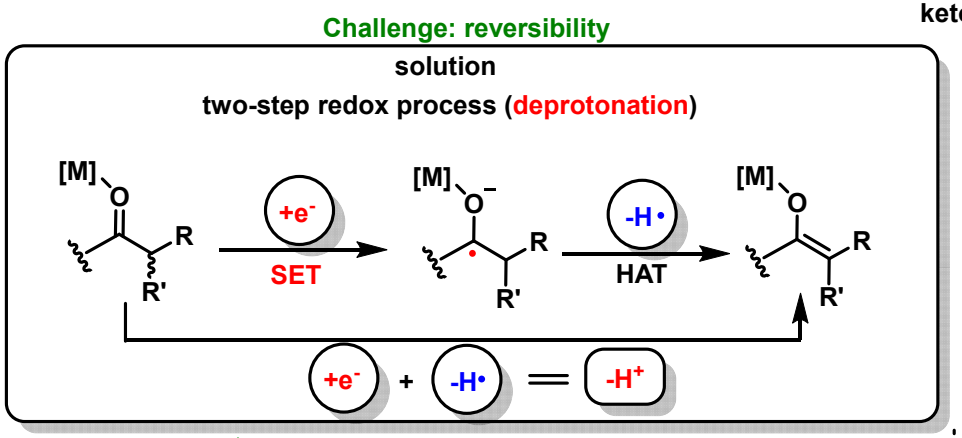


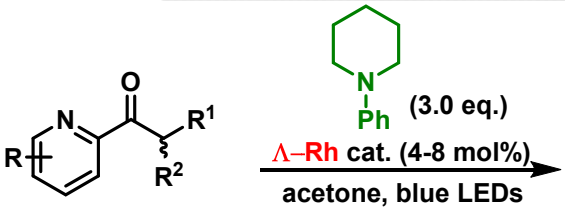
羰基吡啶去消旋化



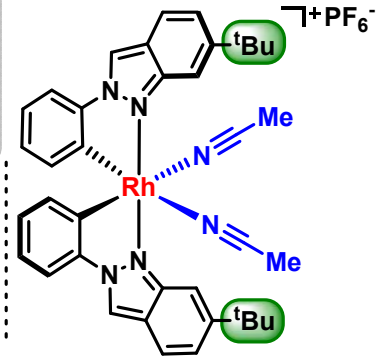
策略：通过形成手性烯醇铑实现去消旋化





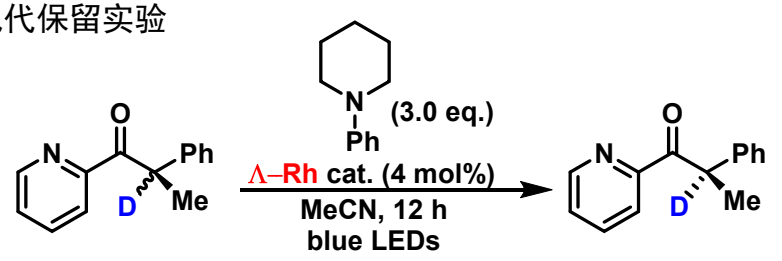


36 examples
up to 98% yield
up to 97% ee

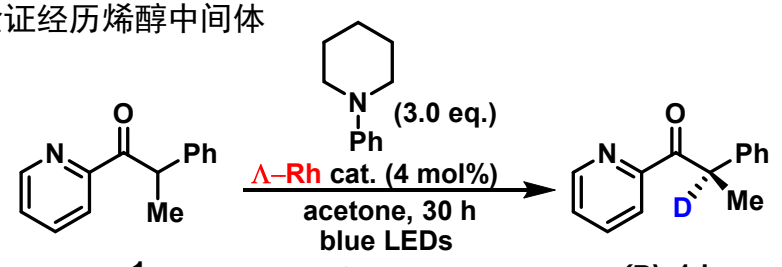


羰基吡啶去消旋化控制实验

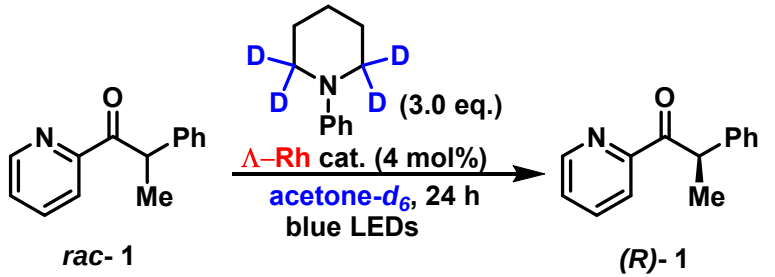
1、氘代保留实验



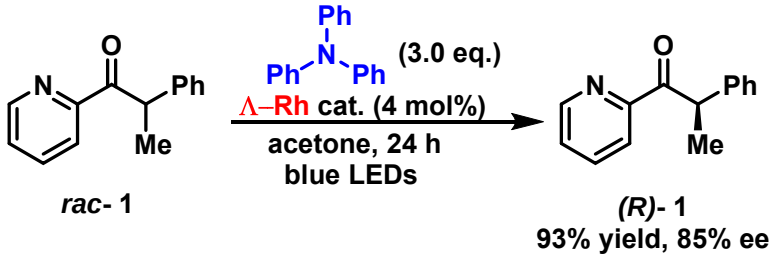
2、验证经历烯醇中间体



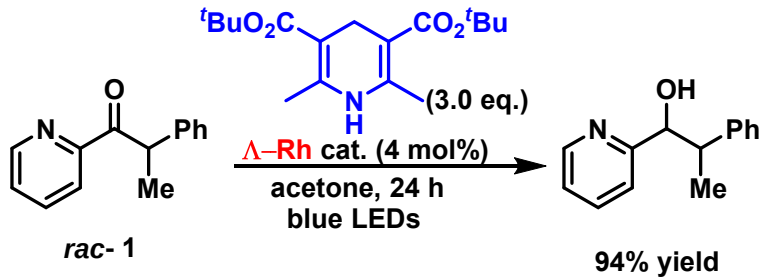
3、氘代叔胺氘代溶剂排除其他质子源



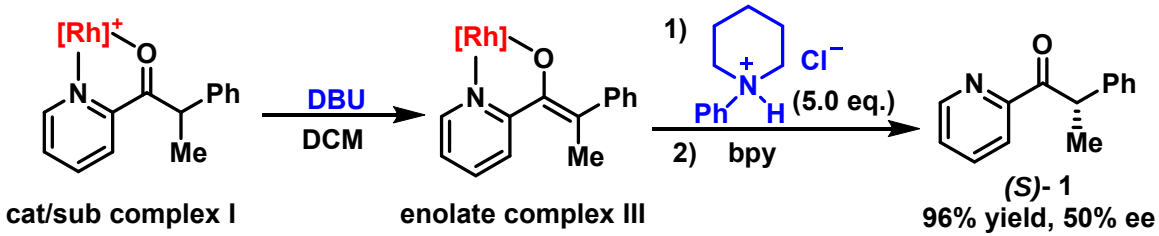
4、三苯胺排除胺自由基阳离子脱质子的参与



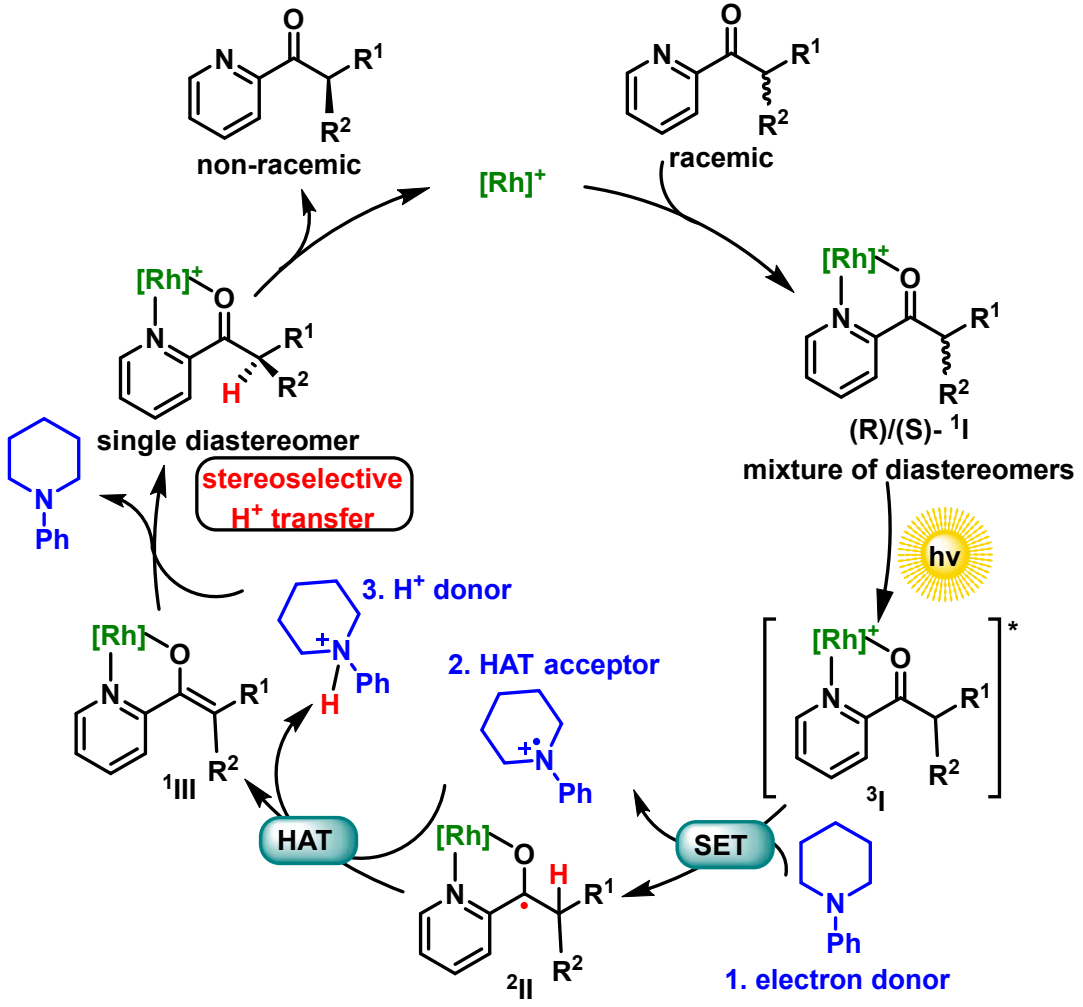
5、HE作为还原试剂



5、去质子化和不对称质子化分步进行

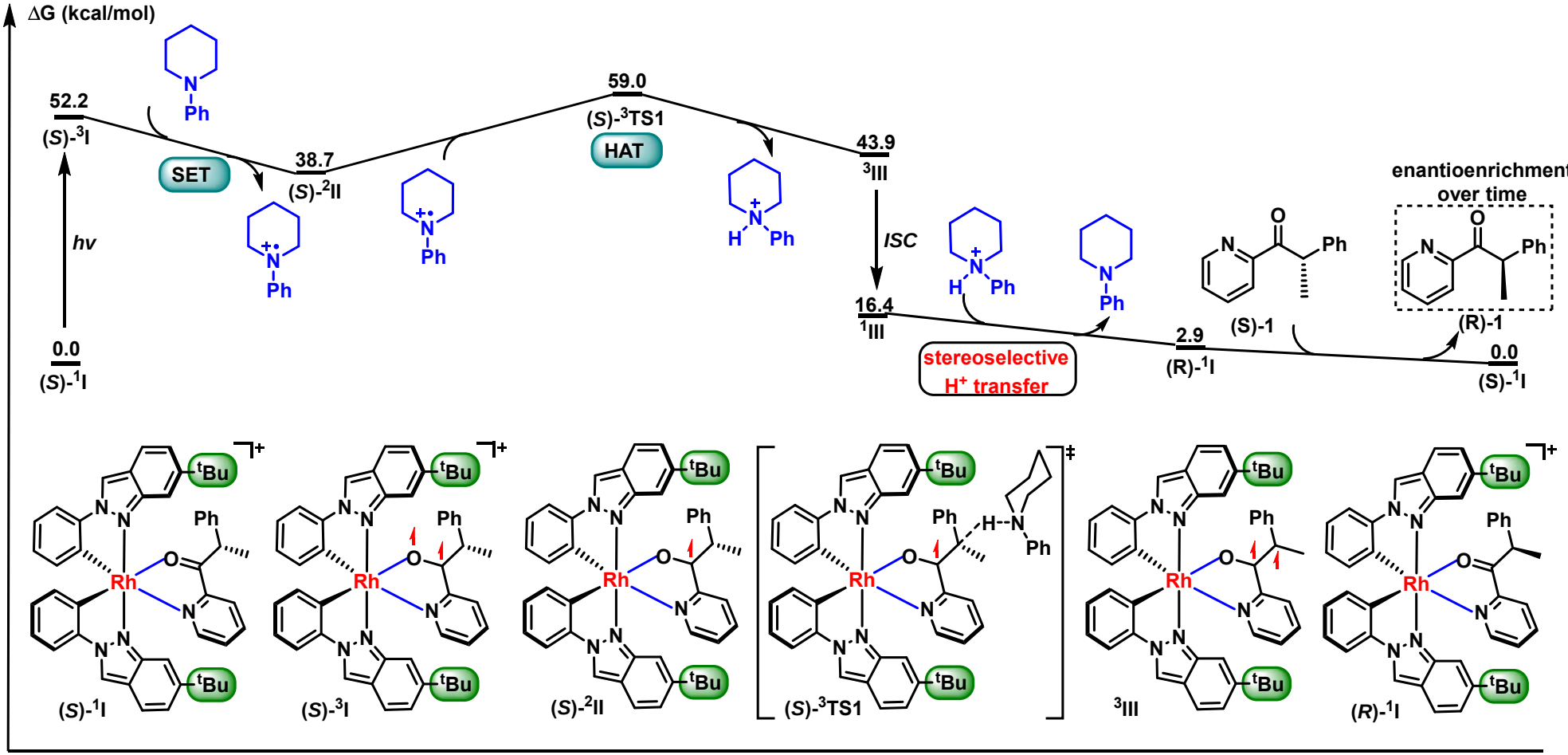


羰基吡啶去消旋化机理



J. Am. Chem. Soc. **2021**, *143*, 13393-13400

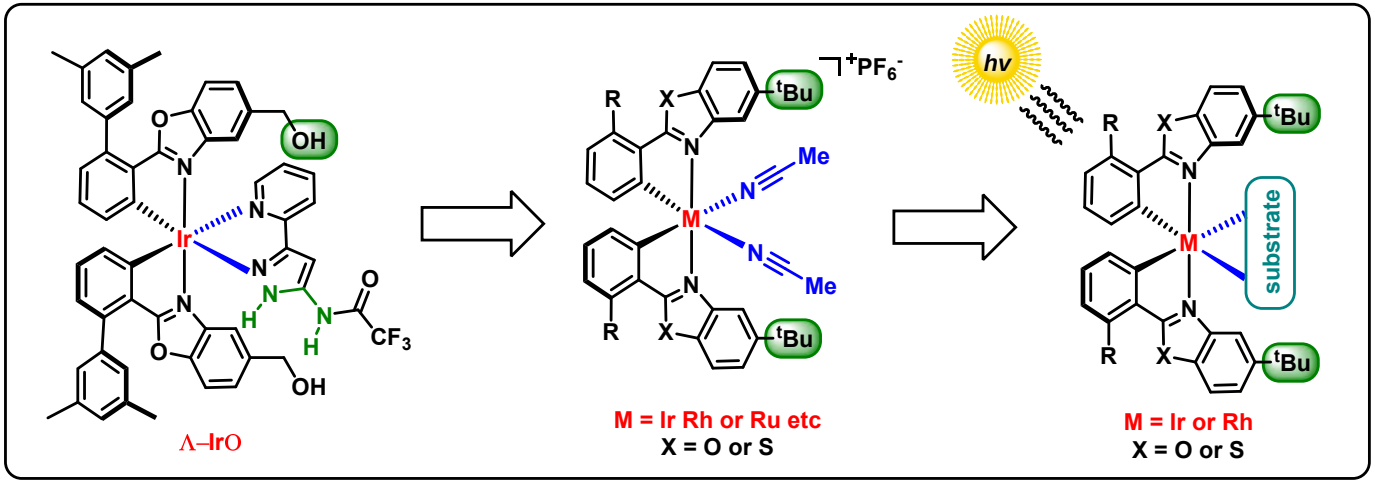
羰基吡啶去消旋化DFT计算



目录

三、总结与展望

总结：



分子间相互作用(氢键)
应用范围有限

手性路易斯酸
应用范围得到拓展

手性路易斯酸
光氧化还原催化剂
成为不对称光催化领域
一面旗帜

优点：

- 结构稳定、易制备、易储存
- 应用面广、催化多种类型反应构建C-C键、 C-N键、C-X键
- 高活性、高对映选择性，操作便捷

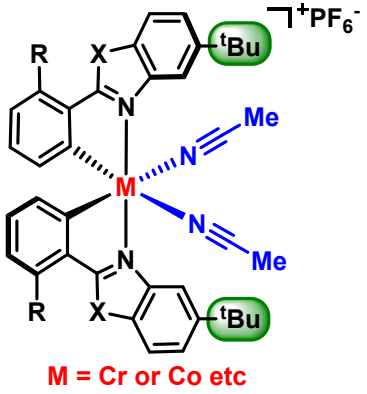
缺点：

- 使用酰基咪唑或酰基吡唑作为底物，不利于原子经济性

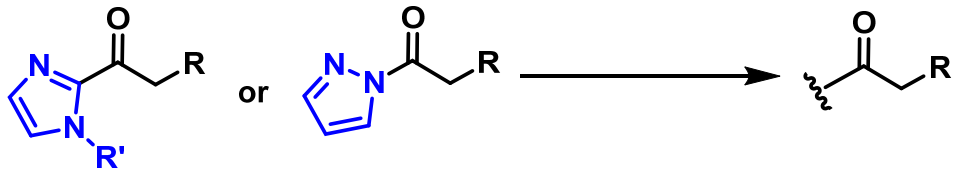
三、总结与展望

展望：

- 发展更多不同类别的八面体手性金属配合物(M =铬, 钴…)及其应用



- 使用更加一般性的底物，同样实现高收率高对映选择性合成



敬请各位老师同学
批评指正