



復旦大學

有机磷氧化还原 催化反应研究进展



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指导老师：陆平 教授

汇报时间：2026年3月27日

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4. 有机磷催化的其他反应
5. 总结与展望

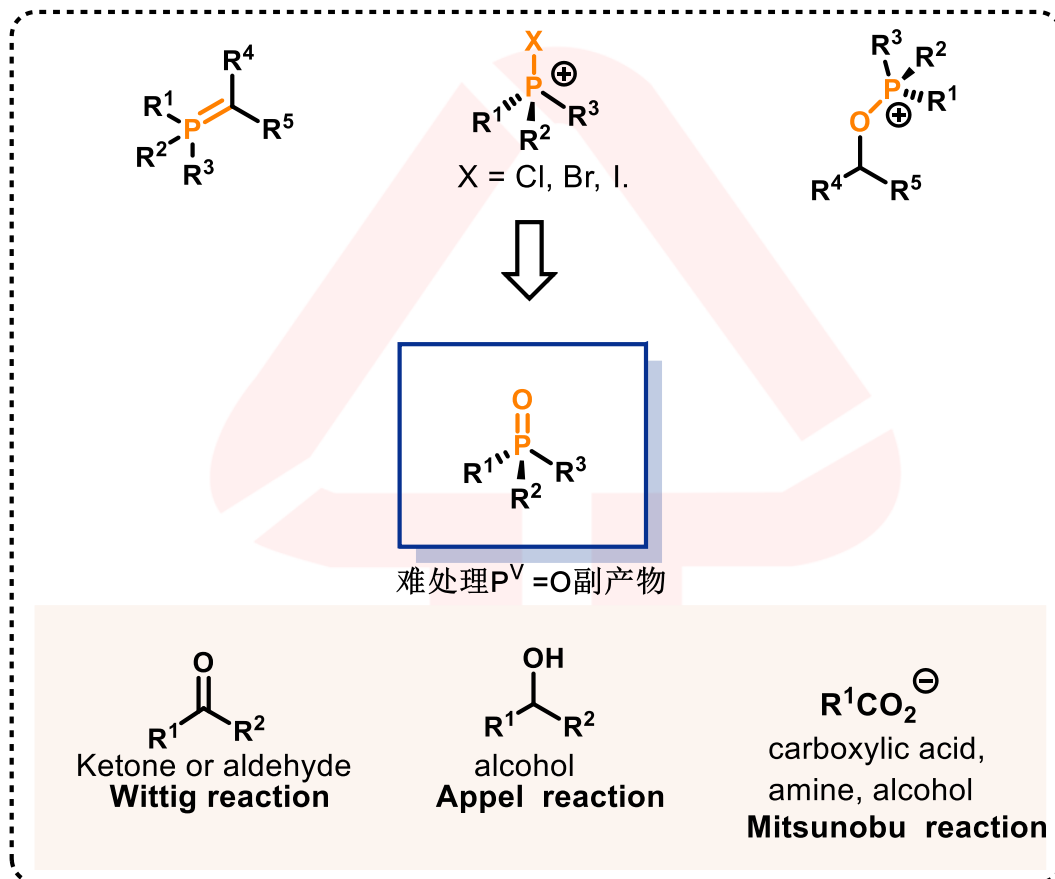


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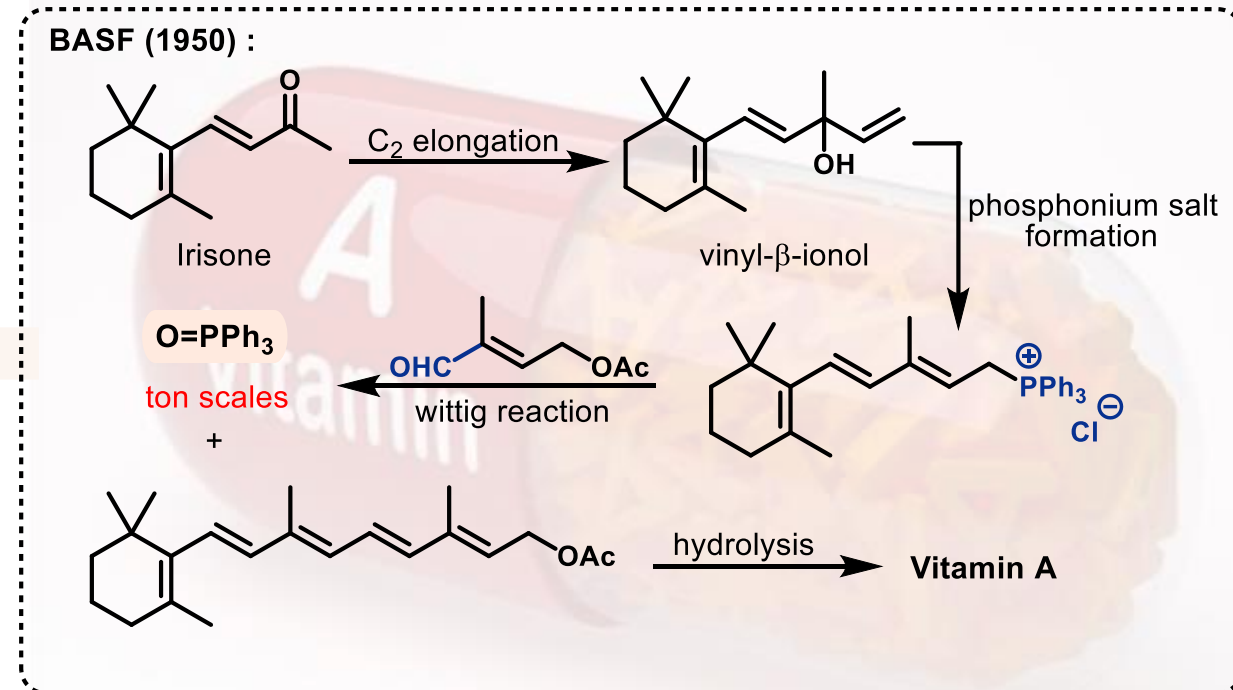
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有机磷参与的经典人名反应



Vitamin A的工业化合路线

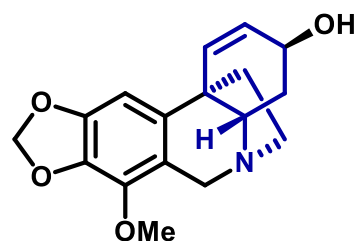


背景

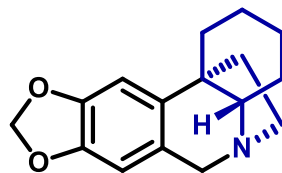


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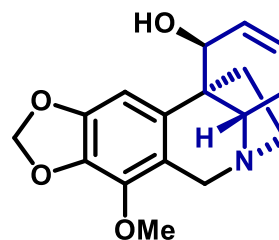
含有顺式-3a-芳基氢化吲哚结构的天然活性分子:



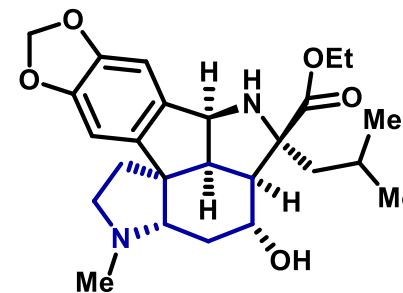
(+)-vittatine : R = H
(+)-powelline : R = OMe



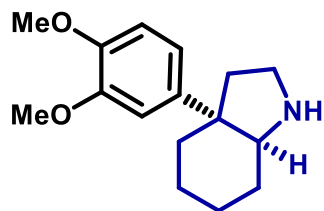
(+)-crinane



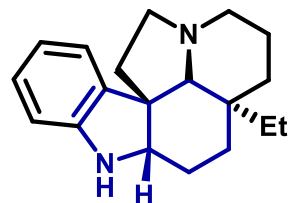
(+)-buphanamine



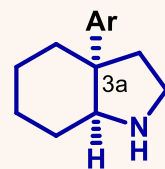
(+)-gracilamine



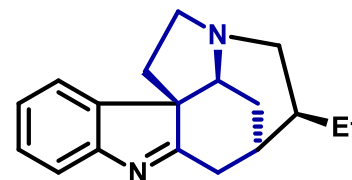
mesembrane



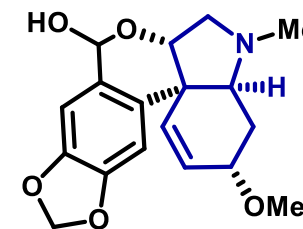
(-)-aspidospermidine



cis-3a-arylhydroindole nucleus

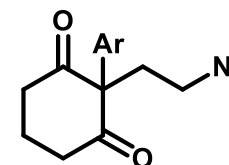
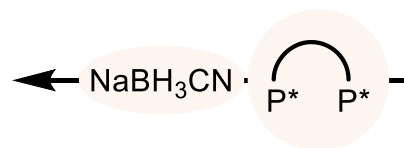
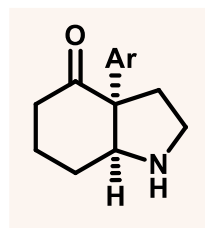
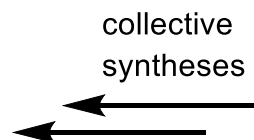
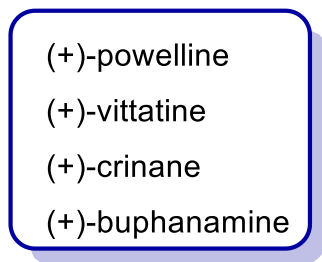


(-)-tubifoline

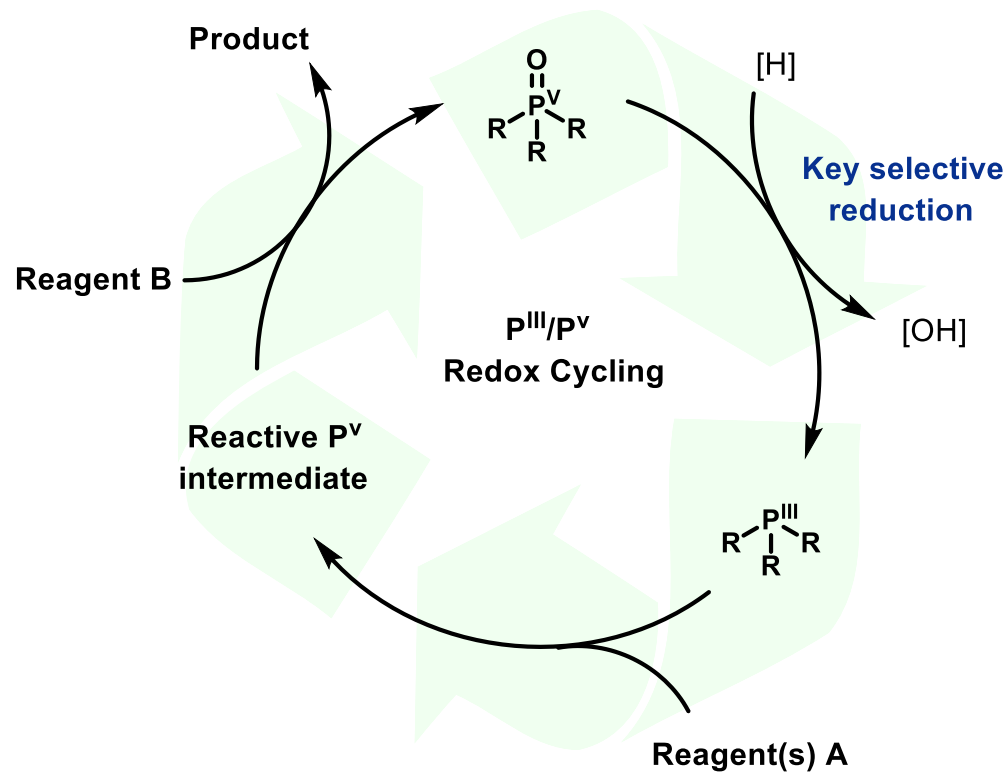


(+)-pretazettine

Asymmetric Staudinger/aza-Wittig Reaction:



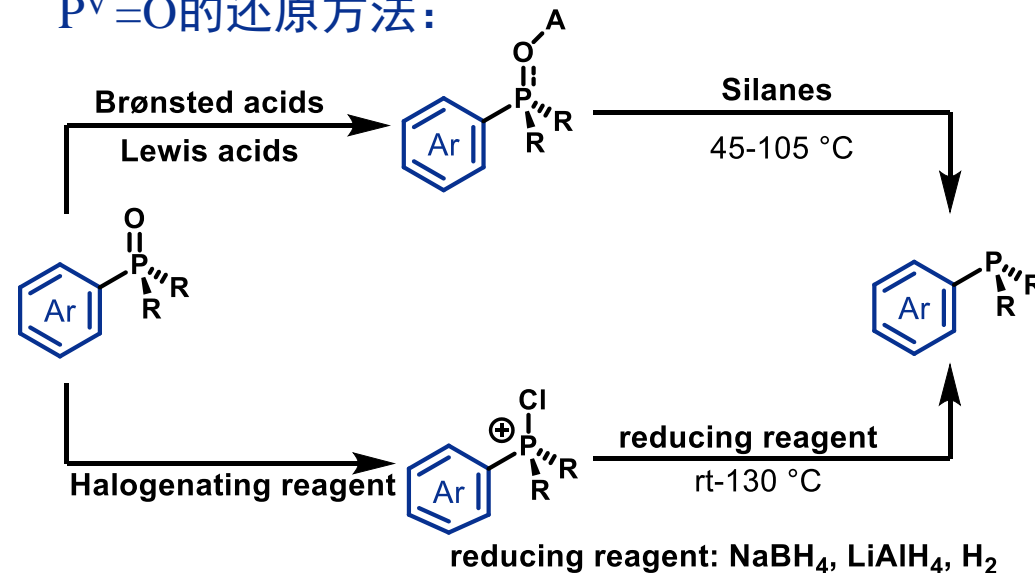
有机磷的氧化还原催化循环:



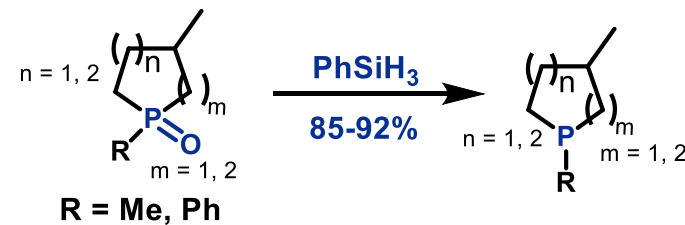
Required features

- Highly efficient reduction
- Chemoselective reduction
- Stereoselective reduction

P^V=O的还原方法:



多芳基取代氧磷化物还原条件较为苛刻



多烷基取代环磷氧化物还原较为容易，用于设计磷催化反应

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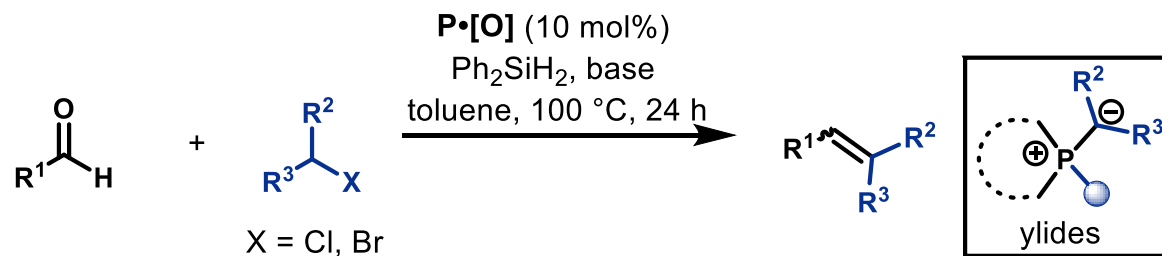


有机磷催化的Wittig 和 Wittig-Type 反应

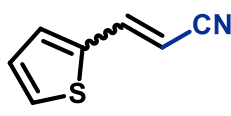
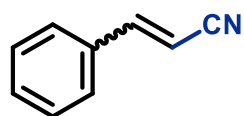
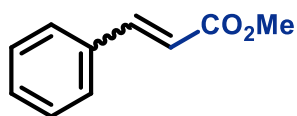
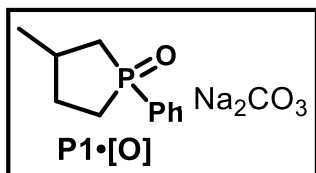


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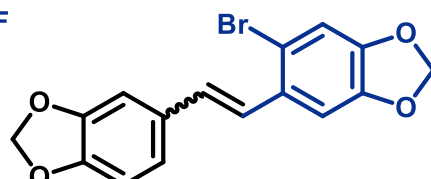
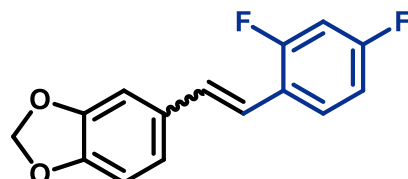
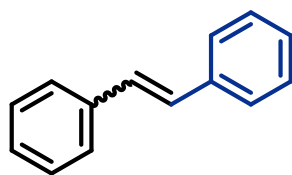
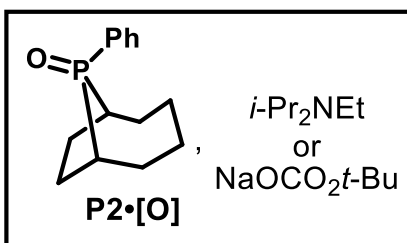
磷催化的wittig反应



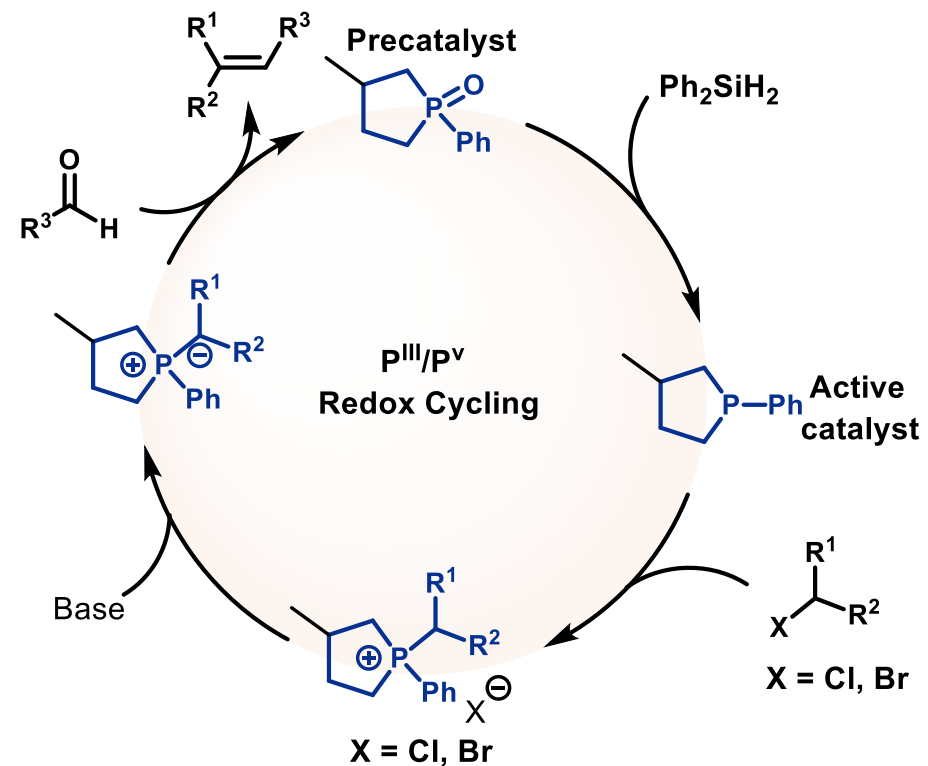
Stabilized ylides



Unstabilized ylides



Possible reaction mechanism:

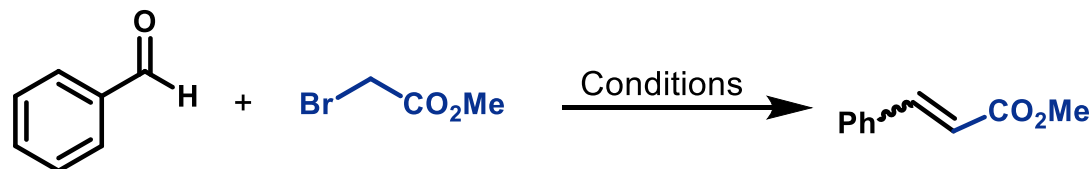


有机磷催化的Wittig 和 Wittig-Type 反应

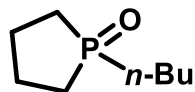


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磷催化的wittig反应



Conditions

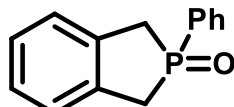


P1•[O]

P1•[O] (10 mol%)
PhSiH₃, *i*-Pr₂NEt
4-NO₂-C₆H₄-CO₂H
27 °C, EtOAc, 24 h

**85%,
86:14 E/Z**

Conditions

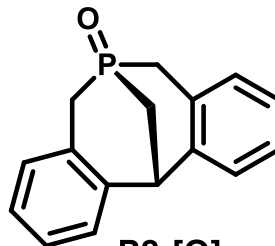


P3•[O]

P2•[O] (10 mol%)
HSi(OMe)₃, Na₂CO₃
150 °C, Toluene, 24 h

**85%,
99:1 E/Z**

Conditions

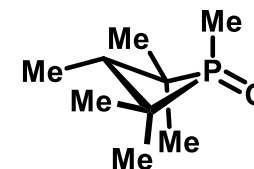


P2•[O]

P2•[O] (5 mol%)
Ph₂SiH₂, *i*-Pr₂NEt
4-NO₂-C₆H₄-CO₂H
100 °C, Toluene, 24 h

**90%,
90:10 E/Z**

Conditions



P4•[O]

P3•[O] (1.0 mol%)
PhSiH₃, *i*-Pr₂NEt
25 °C, THF, 48 h

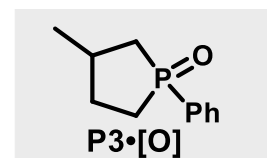
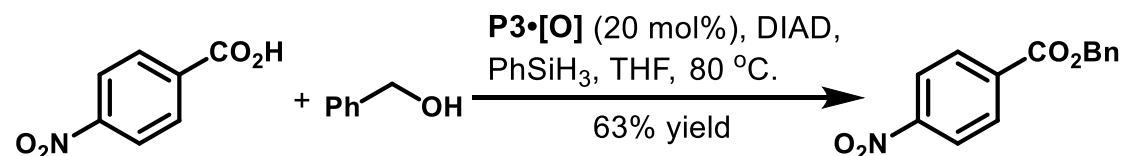
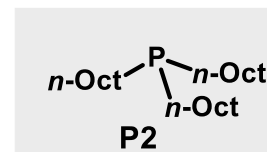
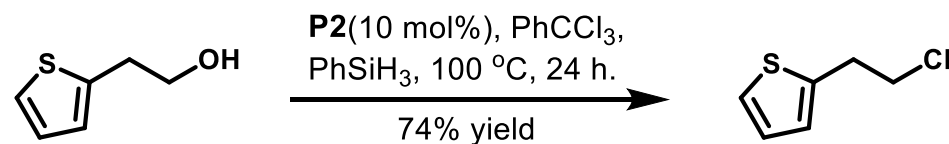
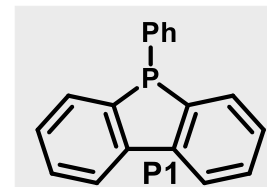
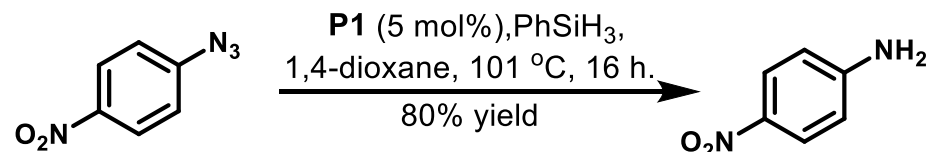
**97%,
97:3 E/Z**

有机磷催化的Wittig 和 Wittig-Type 反应

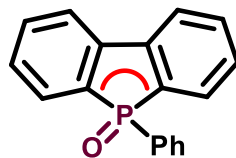
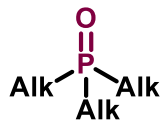
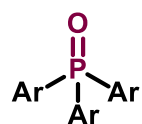


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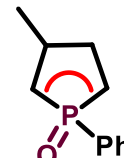
磷催化的其他反应



磷氧化物的还原速率



95.4°



91.5°



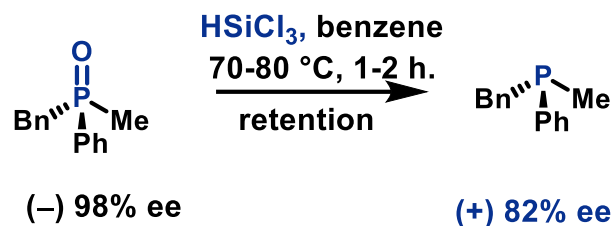
92.4°

有机磷催化的Wittig 和 Wittig-Type 反应

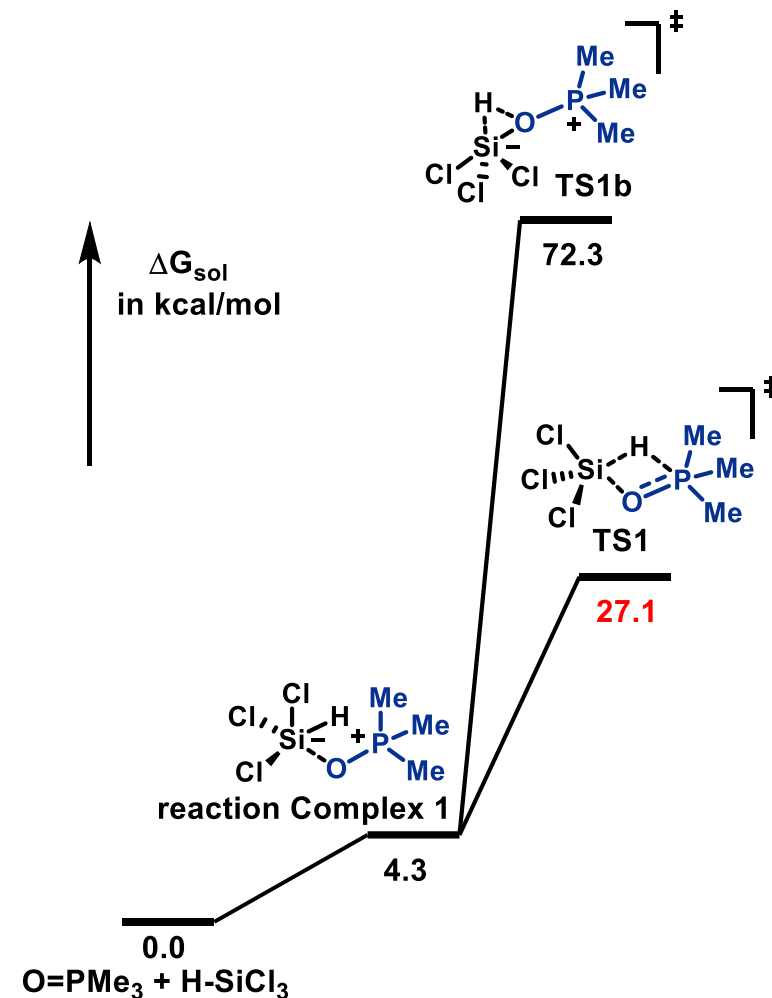
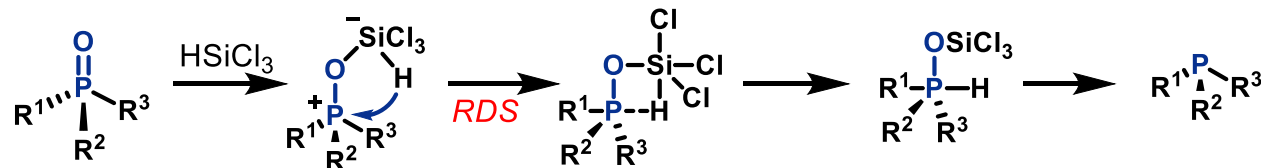


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磷氧化物的还原机理:



$\text{R}_3\text{P=O} + \text{HSiCl}_3$ (Possible reaction mechanism)



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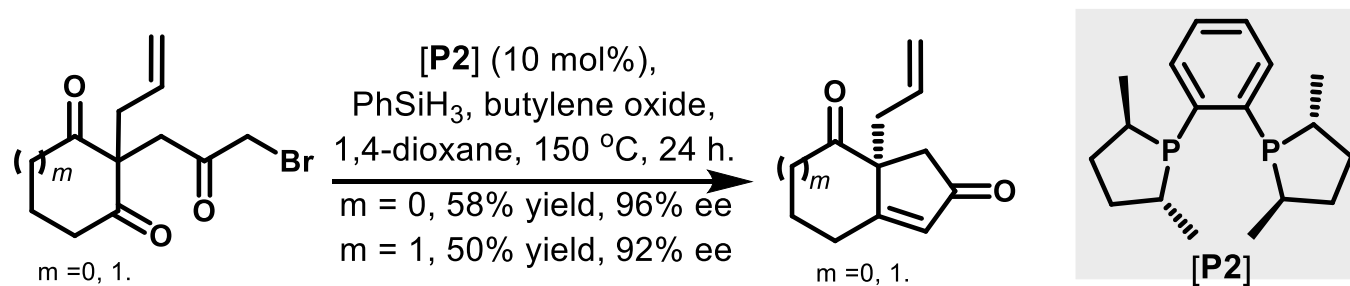
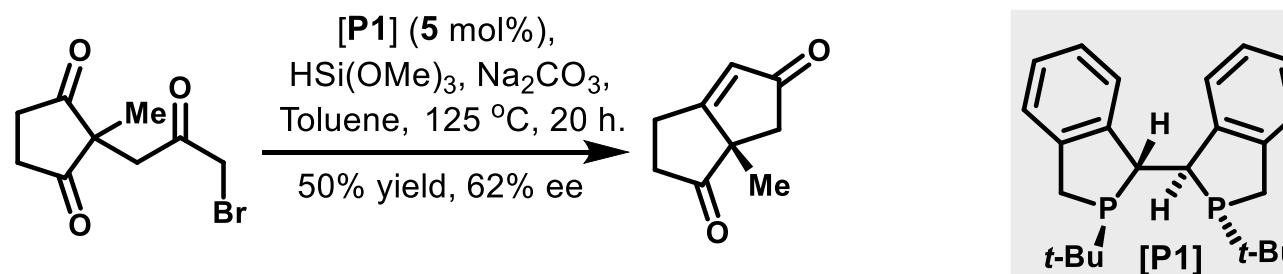
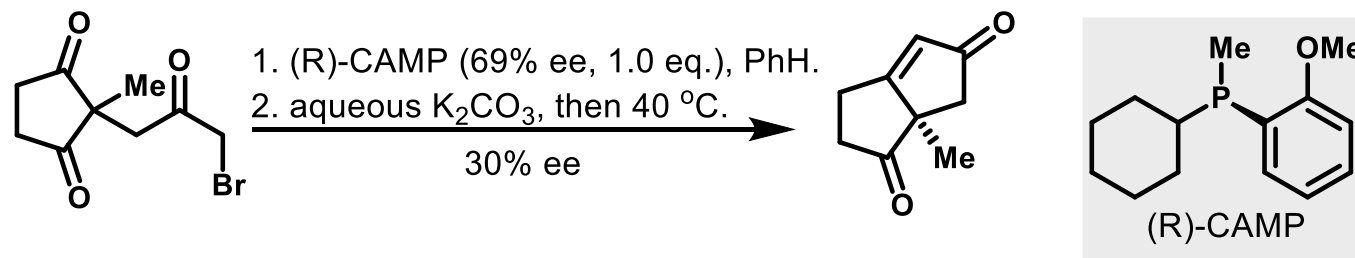


有机磷催化的Wittig和Wittig-Type反应



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磷催化不对称wittig反应的发展

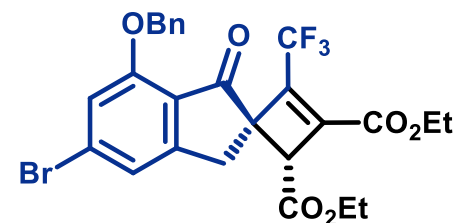
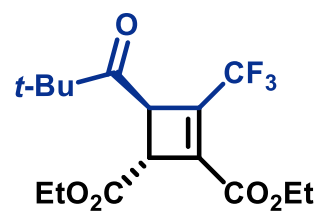
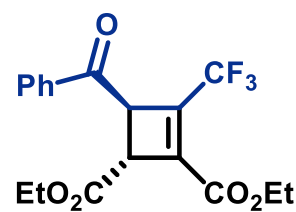
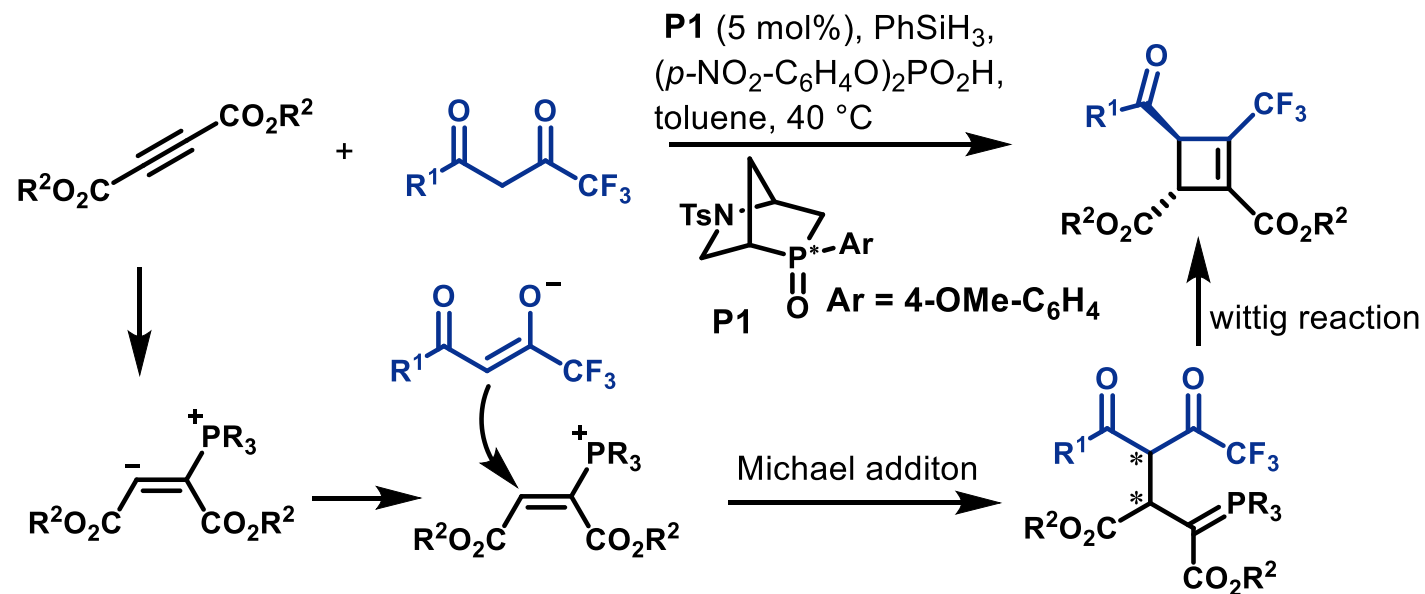


有机磷催化的Wittig和Wittig-Type反应



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磷催化的不对称Michael addition/wittig串联反应:

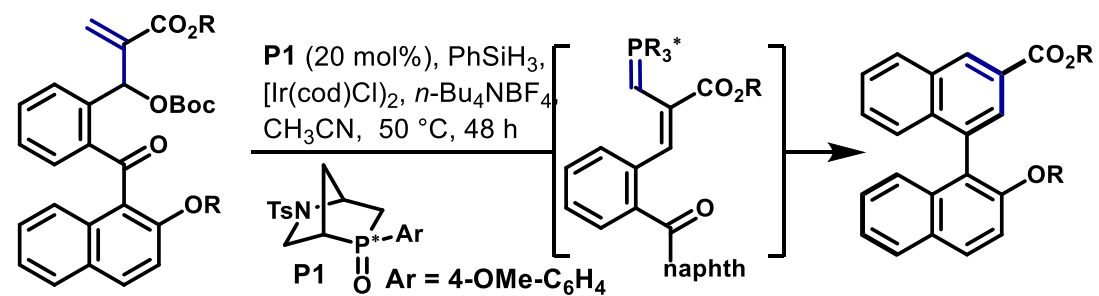


有机磷催化的Wittig 和 Wittig-Type 反应

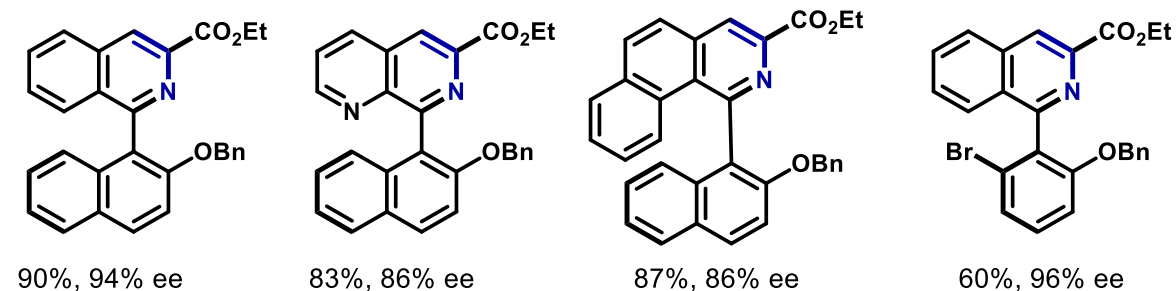
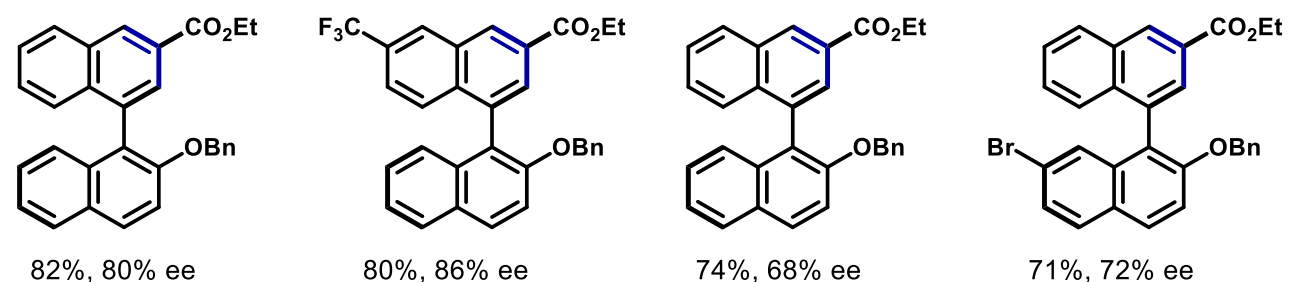
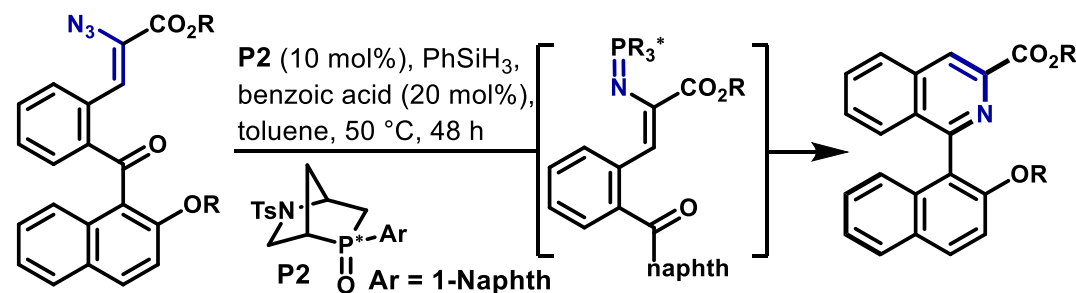


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磷催化的不对称wittig反应



磷催化的不对称Staudinger/aza-Wittig反应



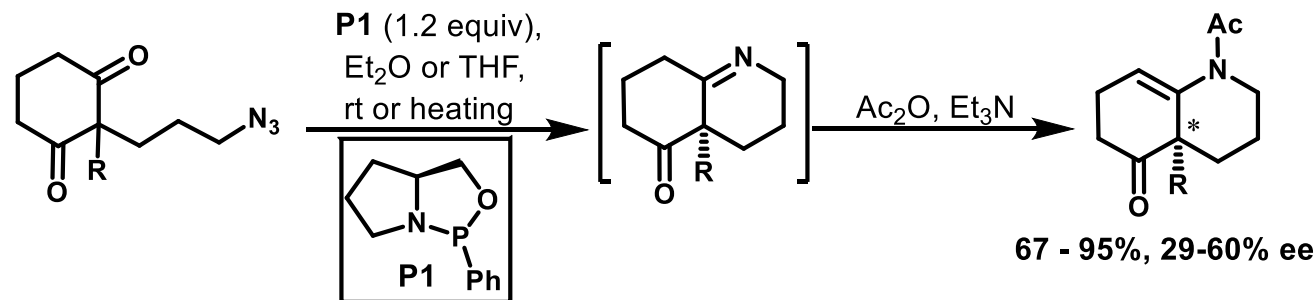
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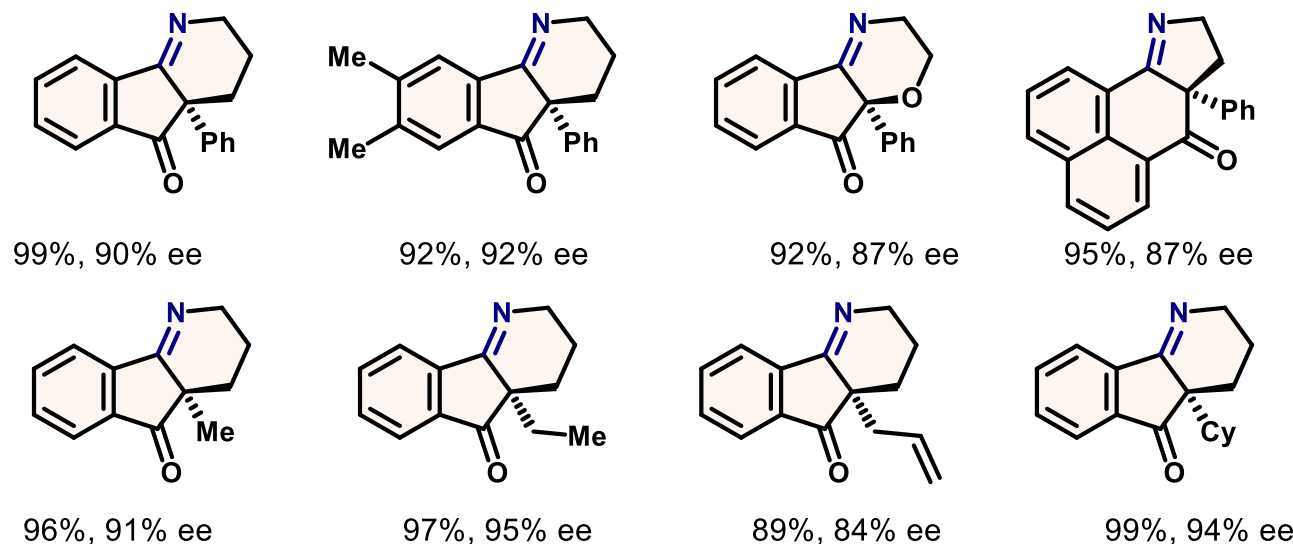
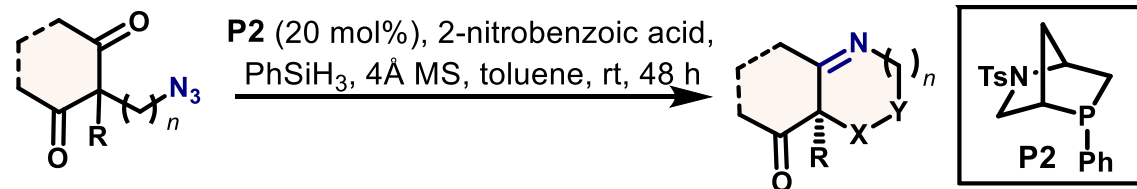
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磷催化的不对称Staudinger Aza-Wittig 反应:

当量磷试剂使用:



催化量磷试剂使用:

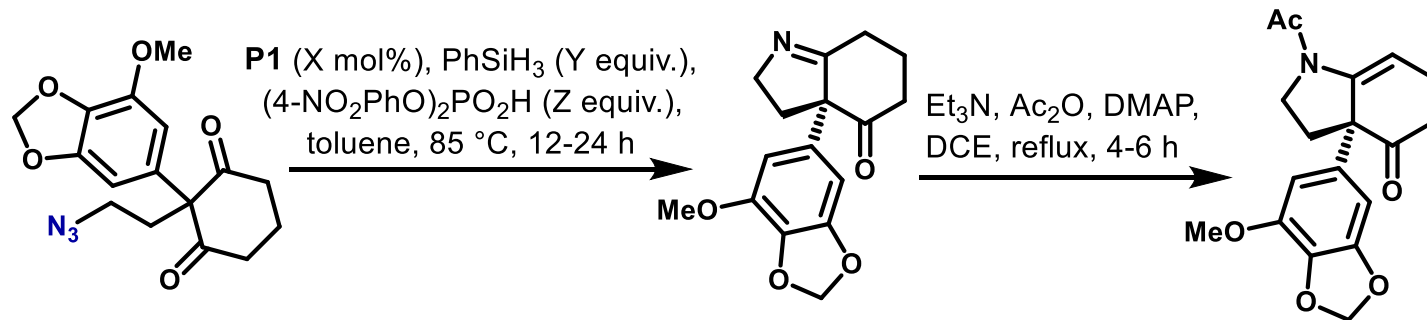


有机磷催化的Wittig 和 Wittig-Type 反应



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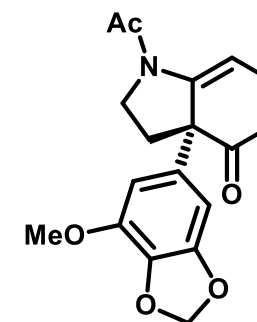
不对称Staudinger Aza-Wittig 反应：



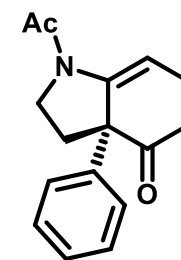
entry	P6 (X)	PhSiH ₃ (Y), acid (Z)	yield (%)	e.r.
1	110	0, 0	>95	98:2
2	50	0, 0	80	92.5:7.5
3	20	4.0, 0	40	97.5:2.5
4	20	4.0, 0.2	34	87.5:12.5
5	20	4.0, 0.2 DIPEA (0.2)	95	95:5
6	15	4.0, 0.15 DIPEA (0.75)	95	96:4

酸的加入可提高PhSiH₃的还原能力

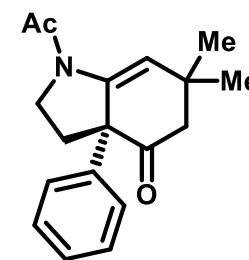
Selected substrates:



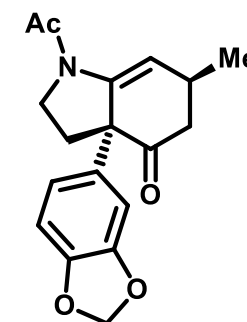
95% yield
e.r. = 96:4



94% yield
e.r. = 92:8



94% yield
e.r. = 89:11



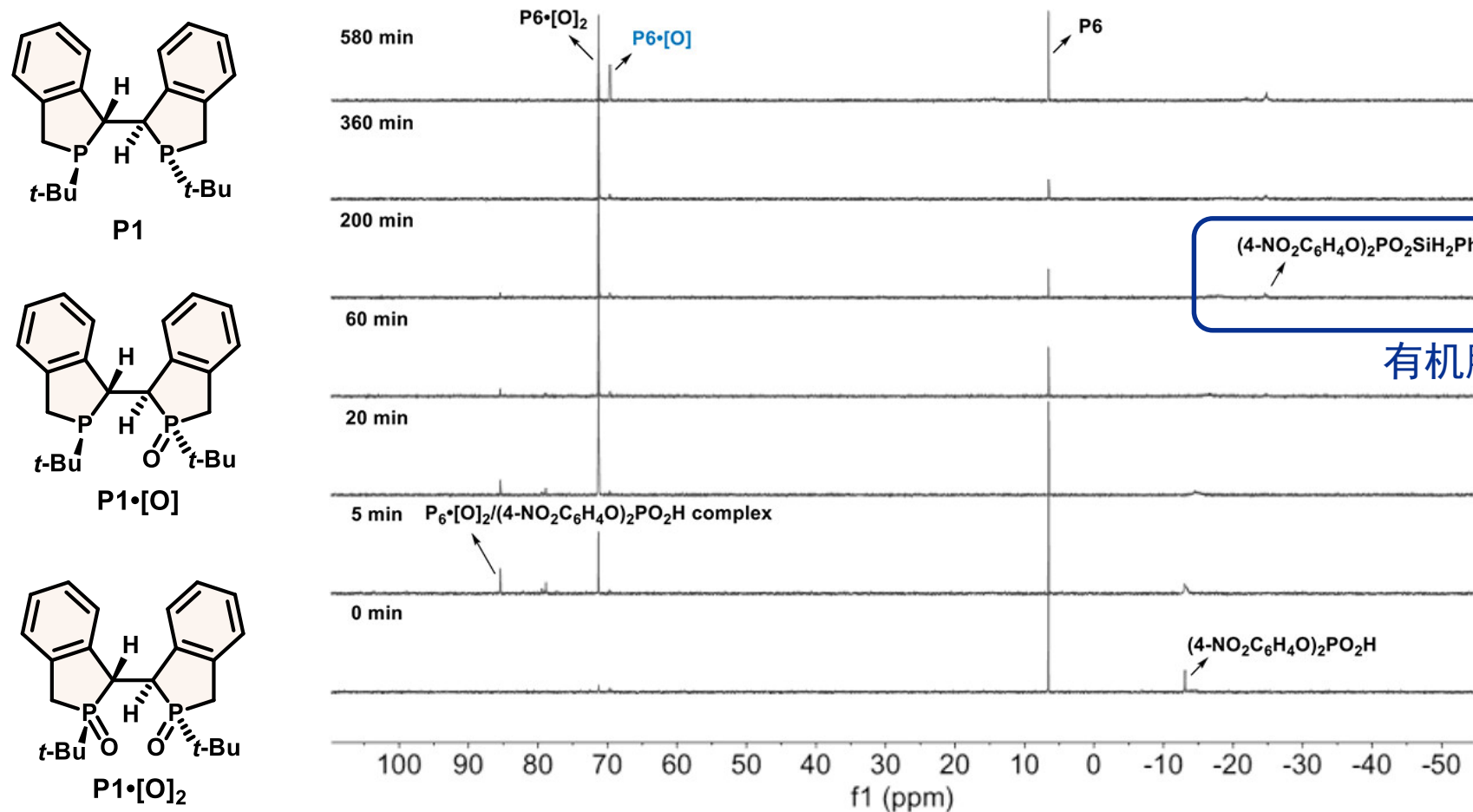
67% yield
e.r. = 96:4

有机磷催化的Wittig 和 Wittig-Type 反应



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Time-stacked in situ ^{31}P NMR of stoichiometric reaction of **P6** at 40 °C.



有机磷酸与PhSiH₃生成硅酯

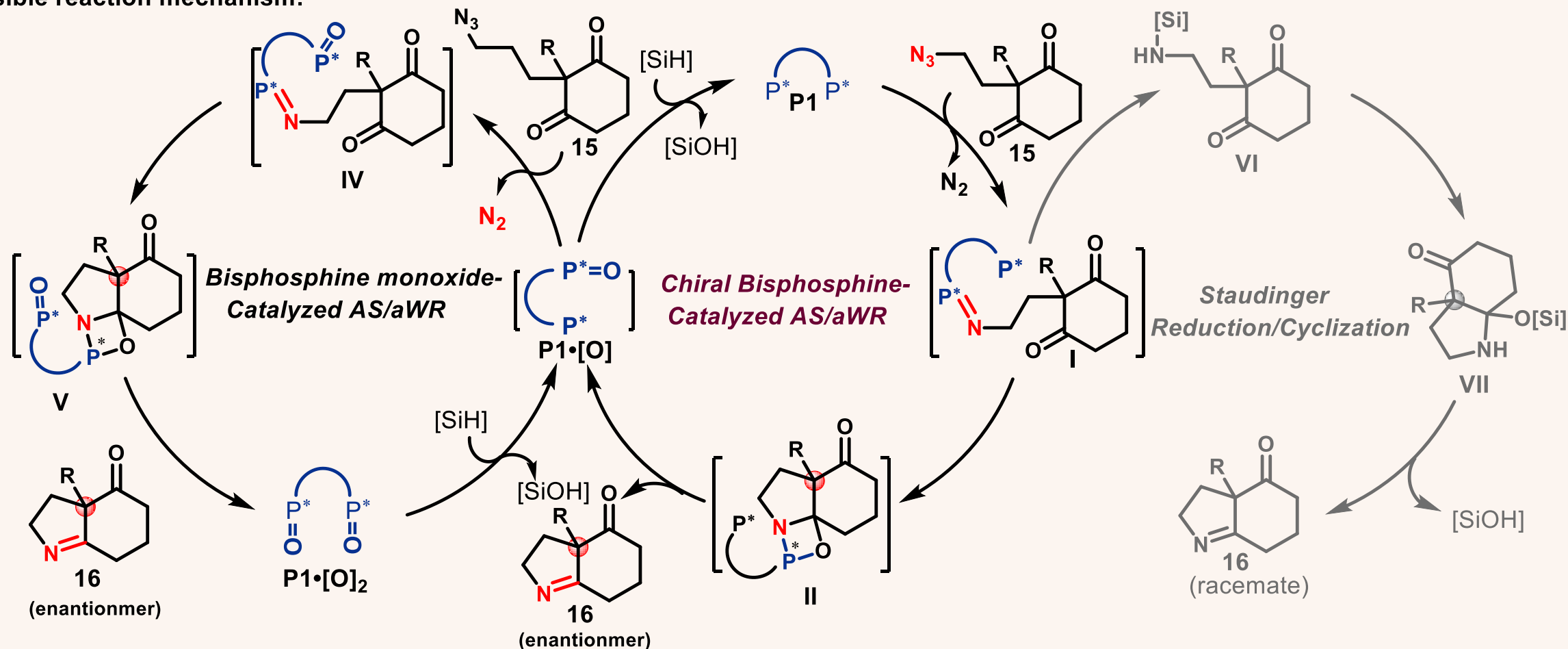
双磷单氧化物与双磷双氧化物均可参与催化循环

有机磷催化的Wittig 和 Wittig-Type 反应



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Possible reaction mechanism:

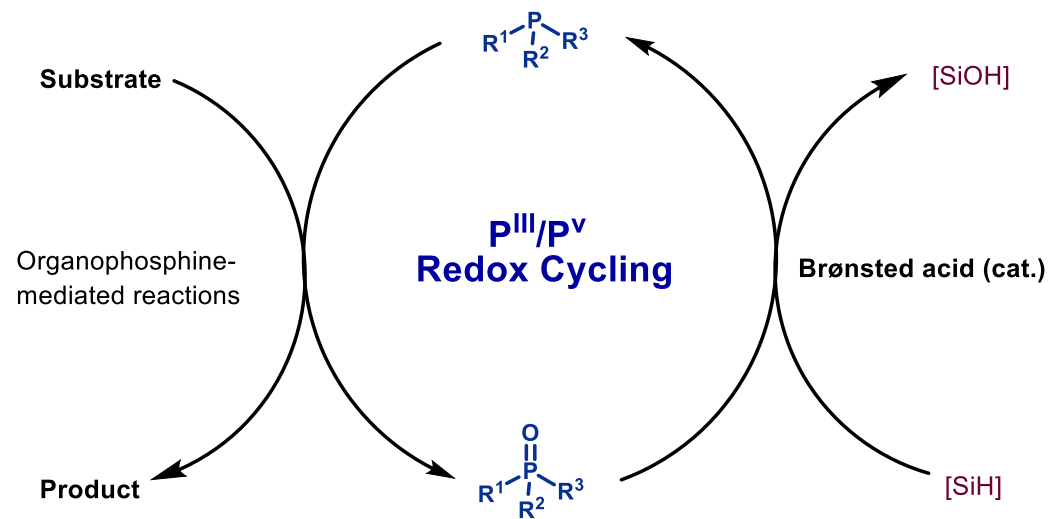


有机磷催化的Wittig 和 Wittig-Type 反应



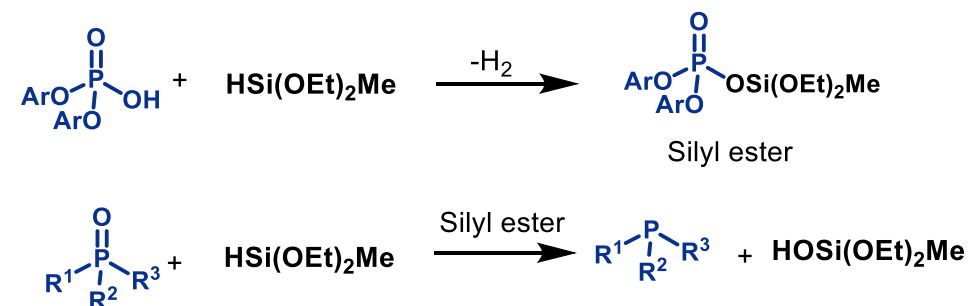
復旦大學

Brønsted acid 及硅烷参与的 P=O 键还原机理探究:

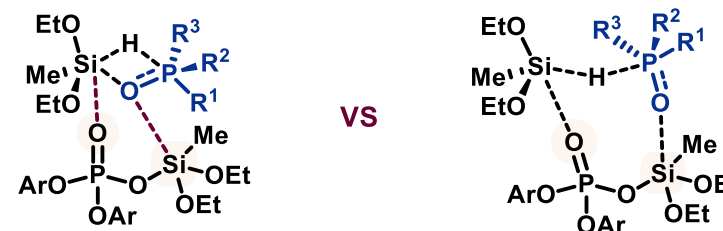


- 2012 Beller ● (EtO)₂MeSiH/PhSiH₃, (PhO)₂P(O)OH (15%), toluene, 110 °C, 24 h
- 2013 O'Brien ● PhSiH₃, 4-NO₂PhCO₂H (1.0 eq.), DIPEA (14 eq.), toluene, 100 °C, 20 min
- 2015 Voituriez ● PhSiH₃, (4-NO₂PhO)₂P(O)OH (5%), DIPEA (5%), toluene, 90 °C, 3.5 h
- 2016 Werner ● PhSiH₃, CF₃SO₃H (1%), toluene, 70 °C, 24 h
- 2017 Aldrich ● DPDS, (4-NO₂PhO)₂P(O)OH (20%), EtOAc, 23 °C, 48 h

Beller等人提出的反应可能经历的过渡态:



Presumed activation modes

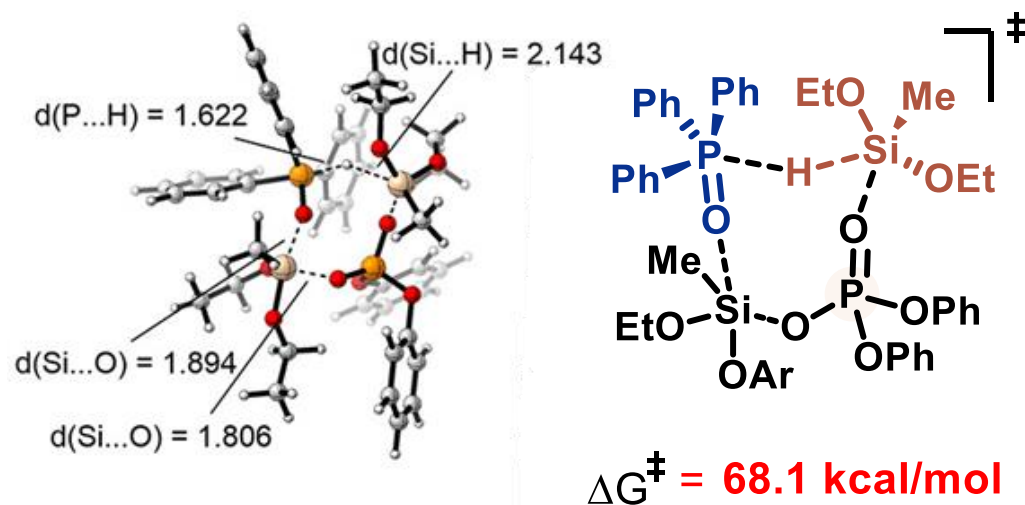
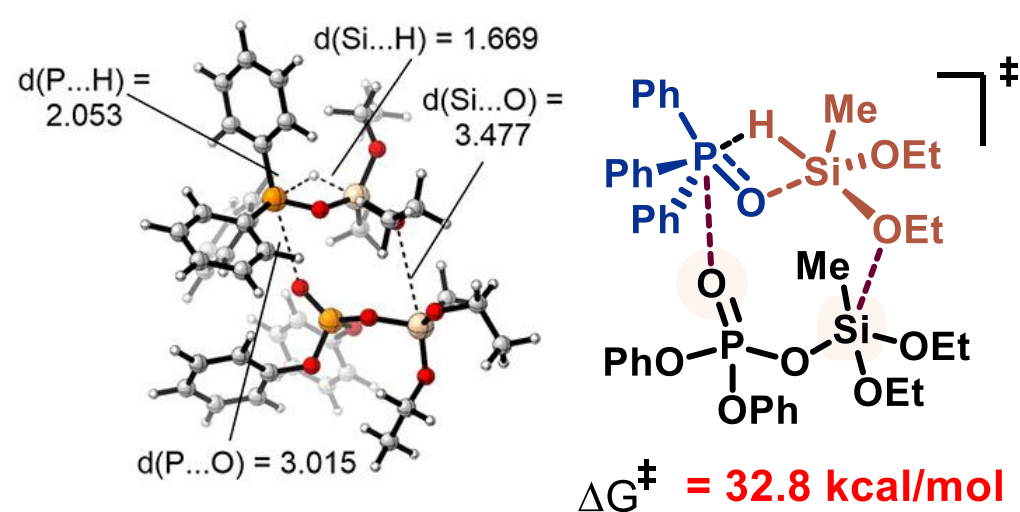
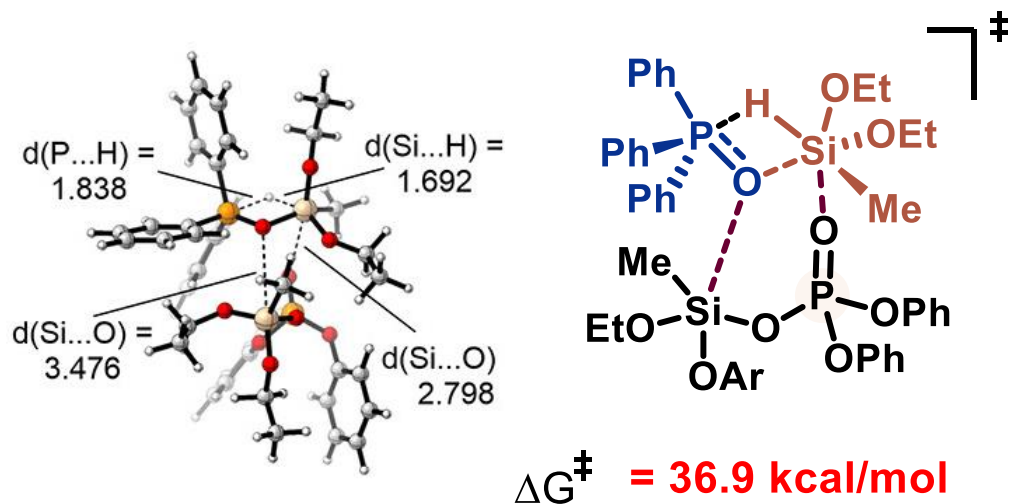


有机磷催化的Wittig和Wittig-Type反应



復旦大學

猜想的过渡态结构能量计算:



对于改变反应历程，不走四元环过渡态机理，能量会变得尤其高

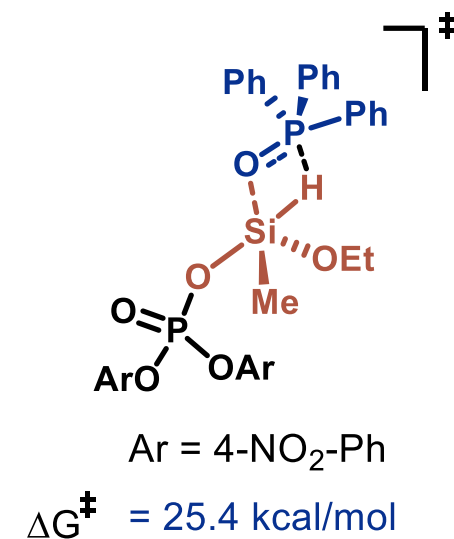
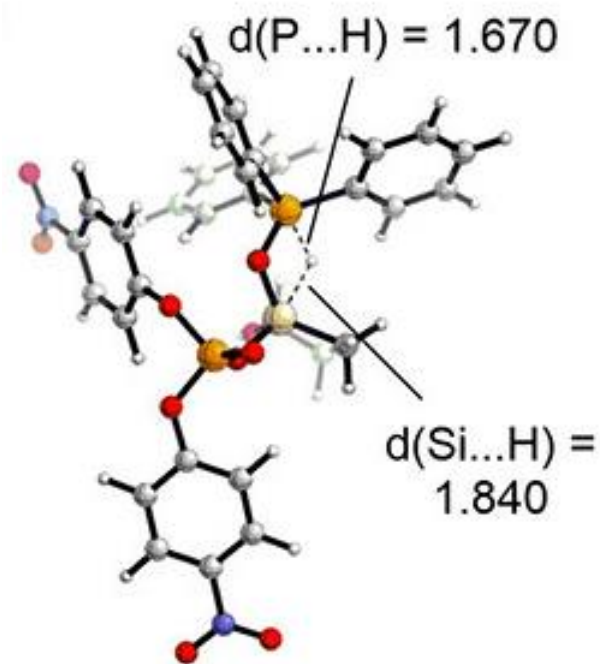
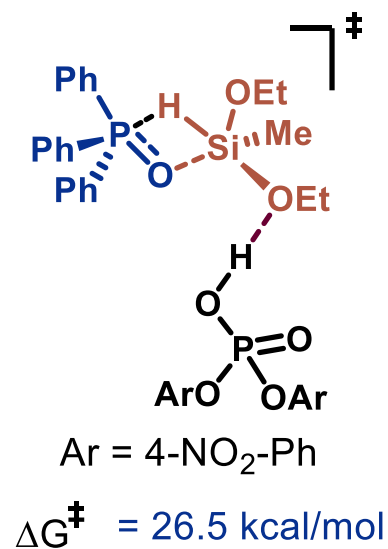
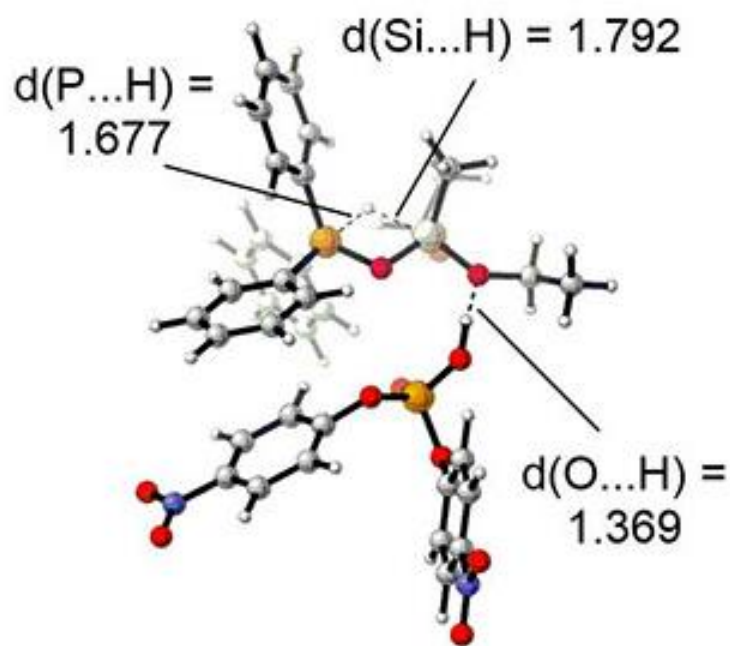
猜想的过渡态结构经计算能量过高，非反应中真实经历的过渡态

有机磷催化的Wittig 和 Wittig-Type 反应



復旦大學

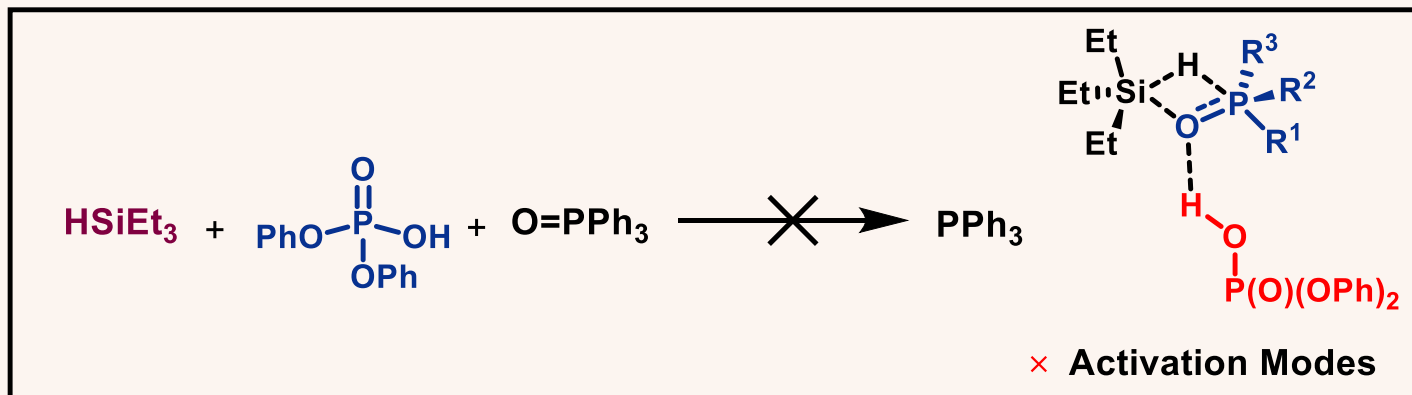
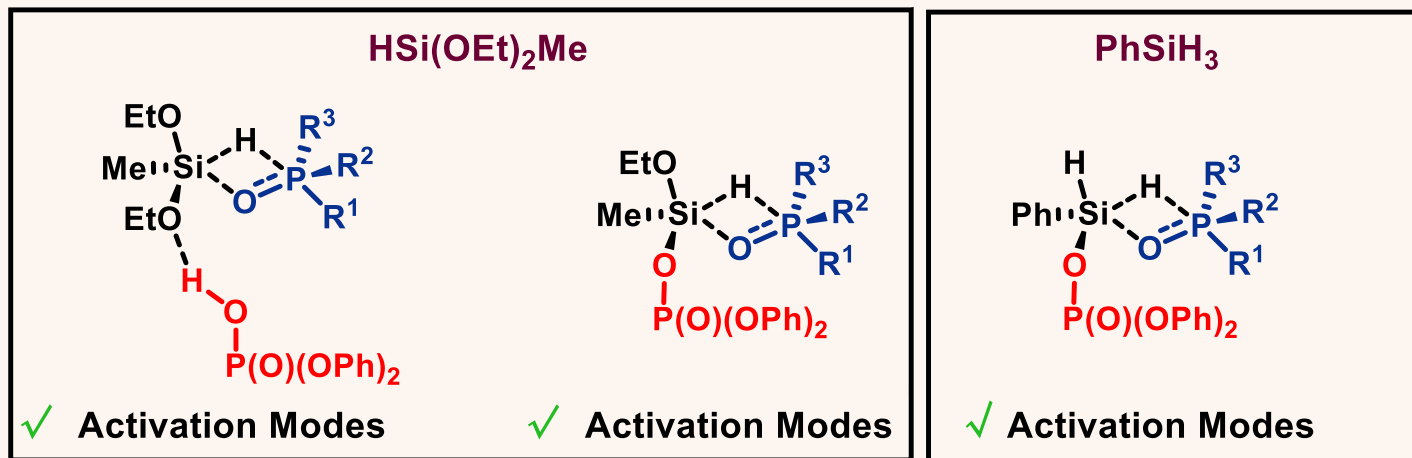
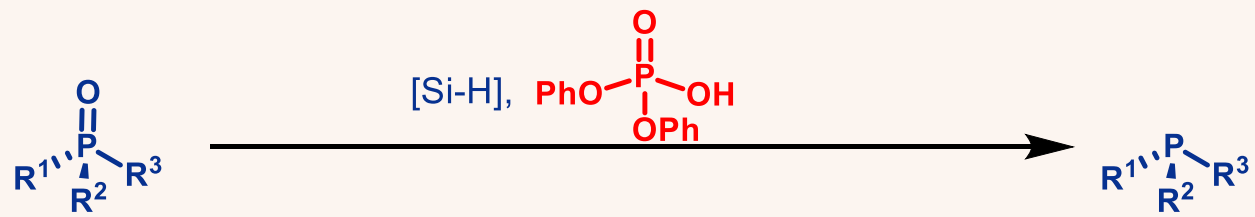
可能经历的过渡态结构:



有机磷催化的Wittig 和 Wittig-Type 反应



復旦大學



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1. 背景
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 - 2.1 消旋反应
 - 2.2 手性反应
3. **有机磷催化的硝基化合物还原反应**
4. 有机磷催化的其他反应
5. 总结与展望

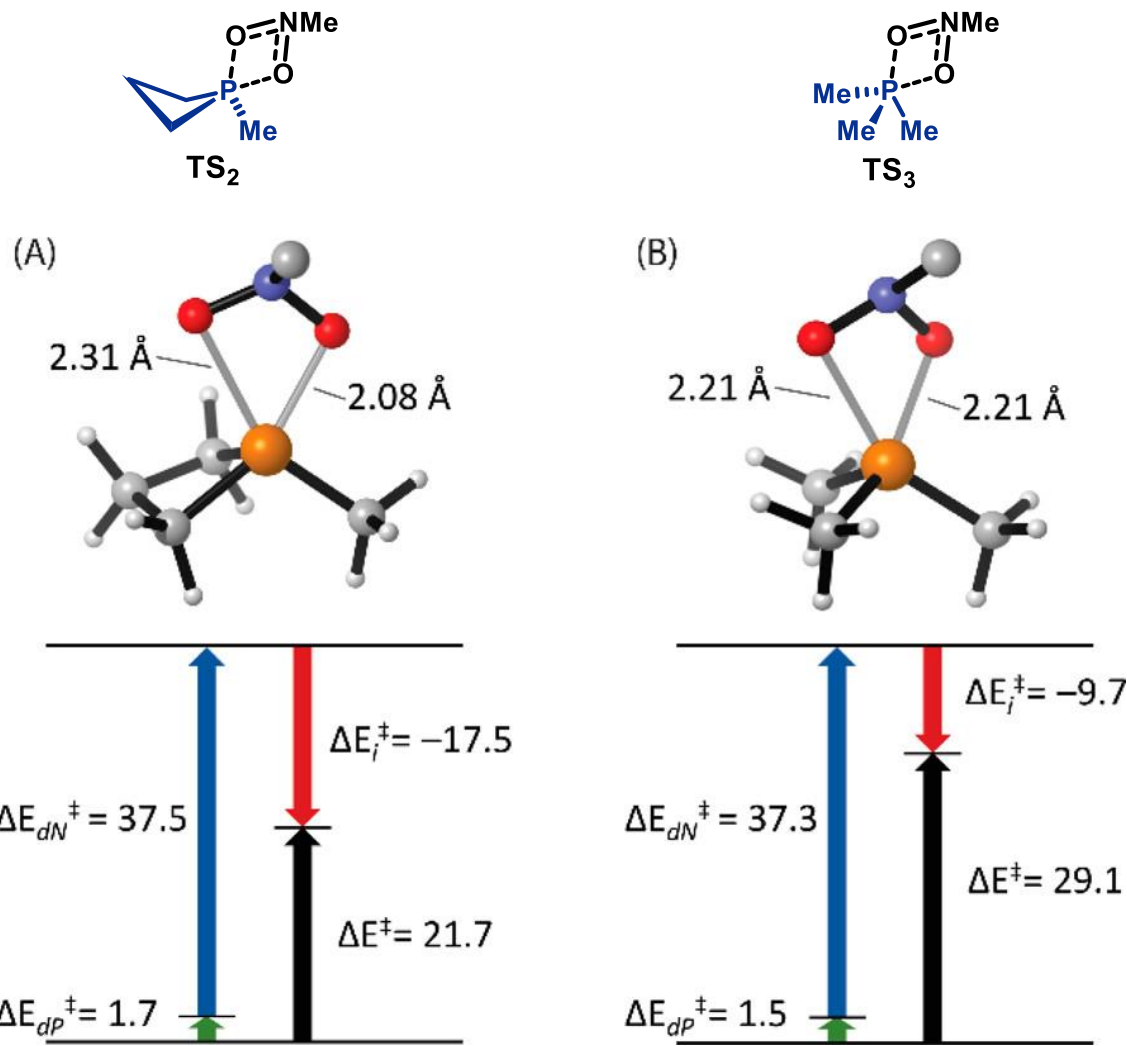
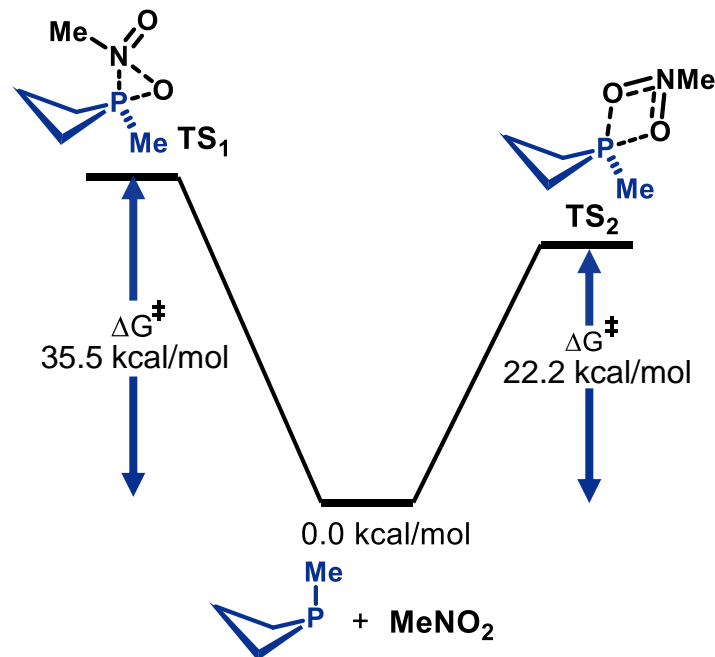
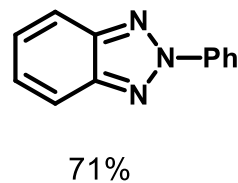
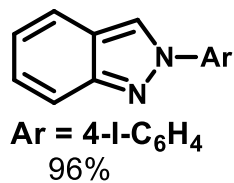
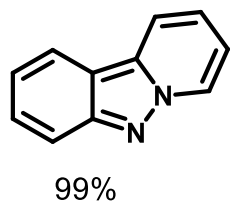
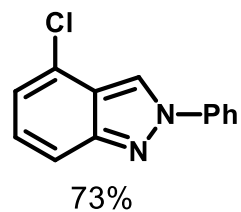
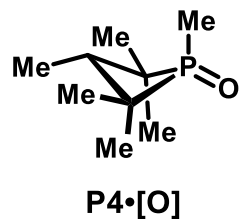
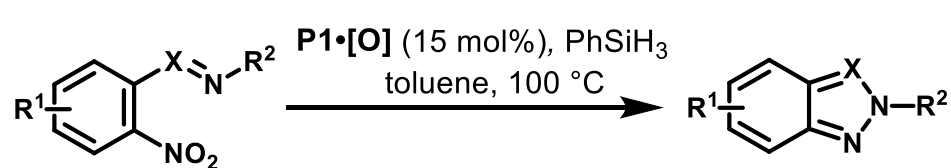


膦催化的硝基化合物还原反应



復旦大學

分子内的Cadogan–Sundberg环化反应

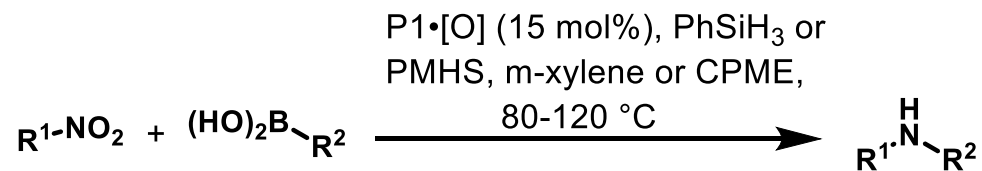


膦催化的硝基化合物还原反应

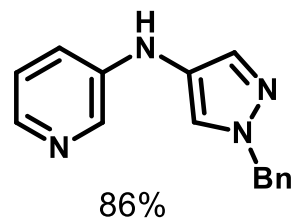
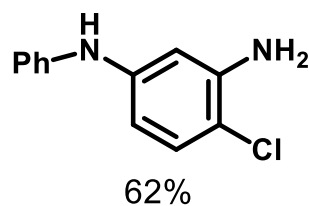
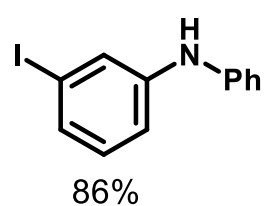


復旦大學

硝基化合物与硼酸的分子间还原型碳-氮交叉偶联反应

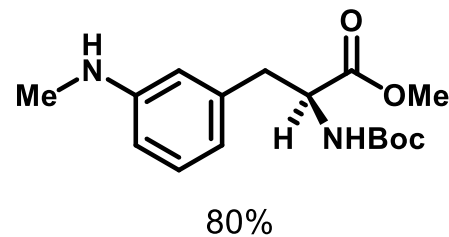
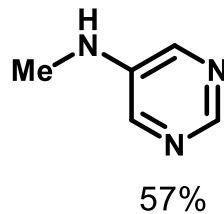
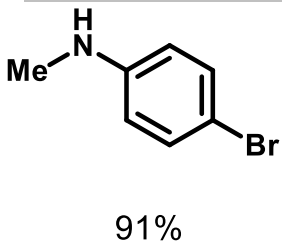


$R^1 = (\text{hetero})\text{aryl}$

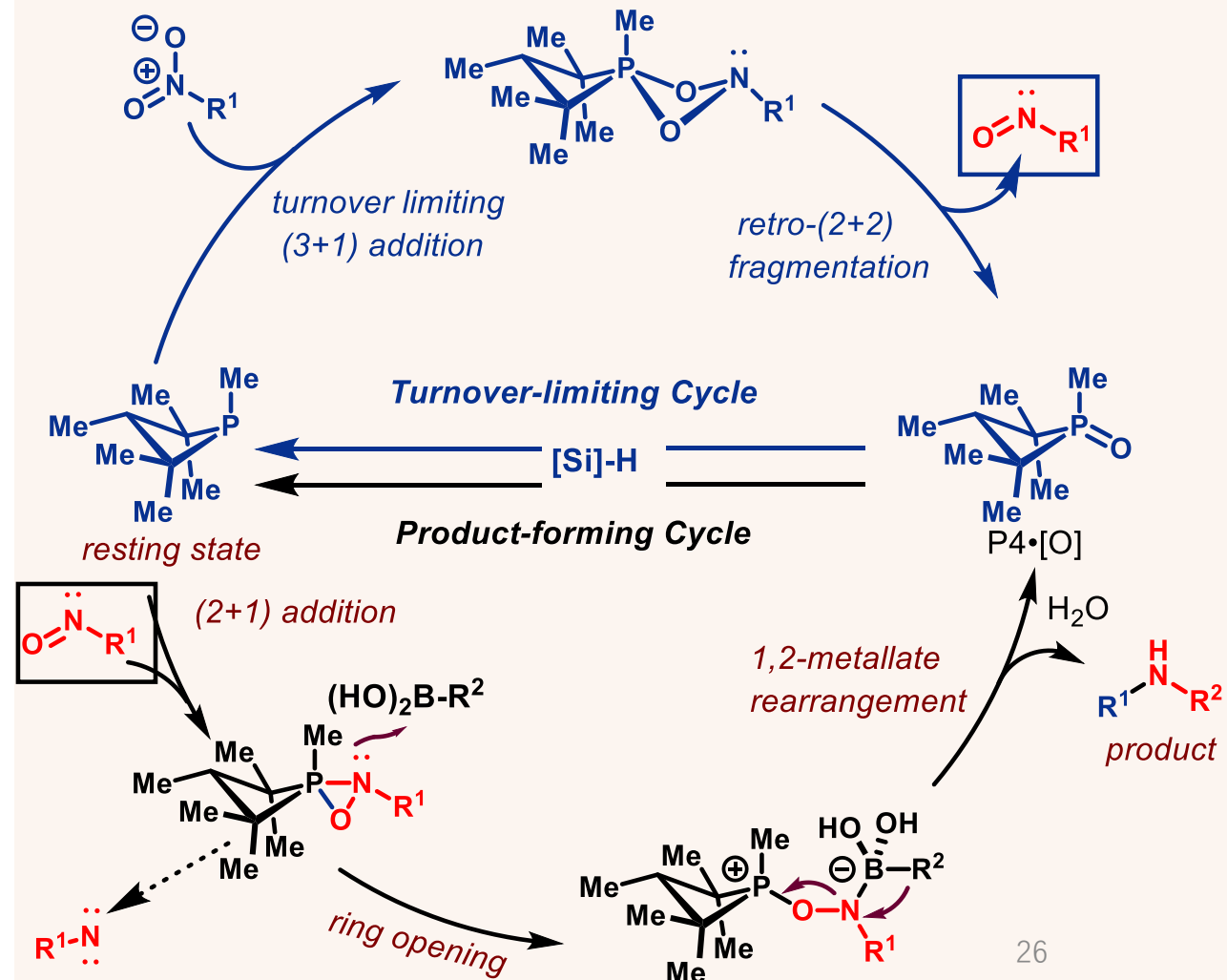


$R^1 = \text{methyl}$

with boronic ester



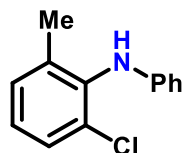
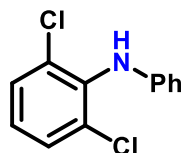
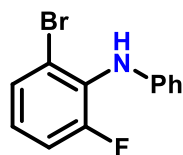
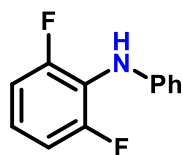
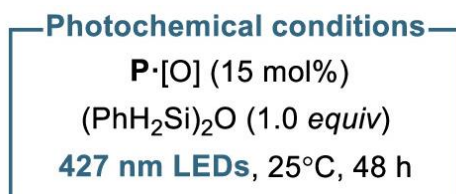
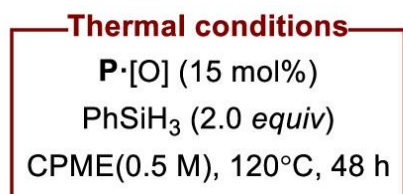
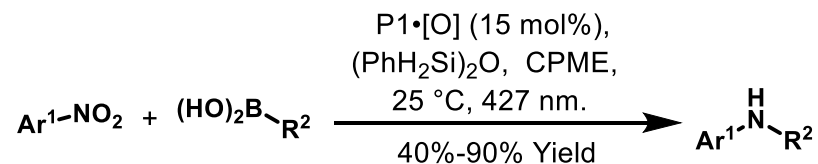
Possible reaction mechanism:



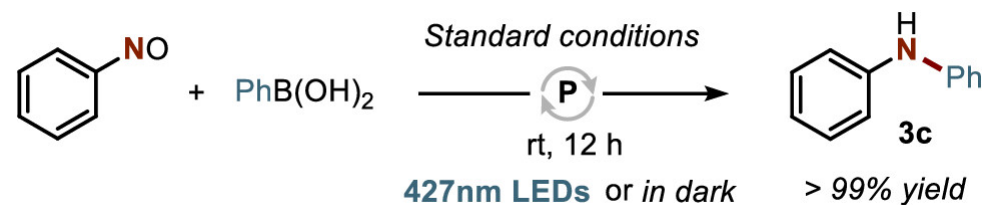
磷催化的硝基化合物还原反应



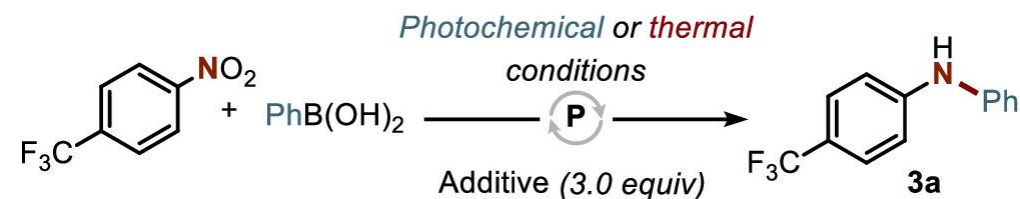
復旦大學



关键中间体验证:



自由基抑制实验:



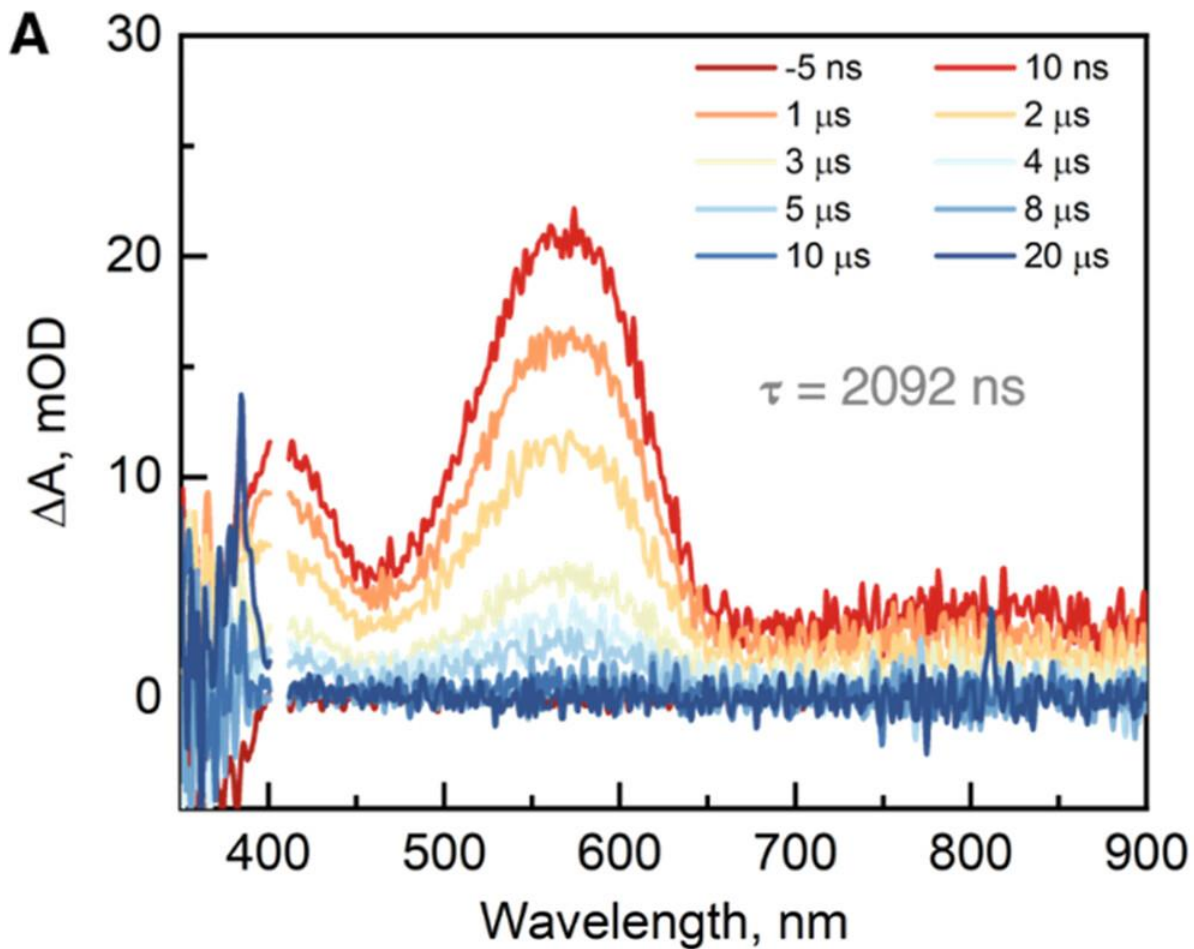
Additive	Photochemical	Thermal
None	>95%	>95%
BHT	67%	>95%
PBN	15%	>95%

膦催化的硝基化合物还原反应



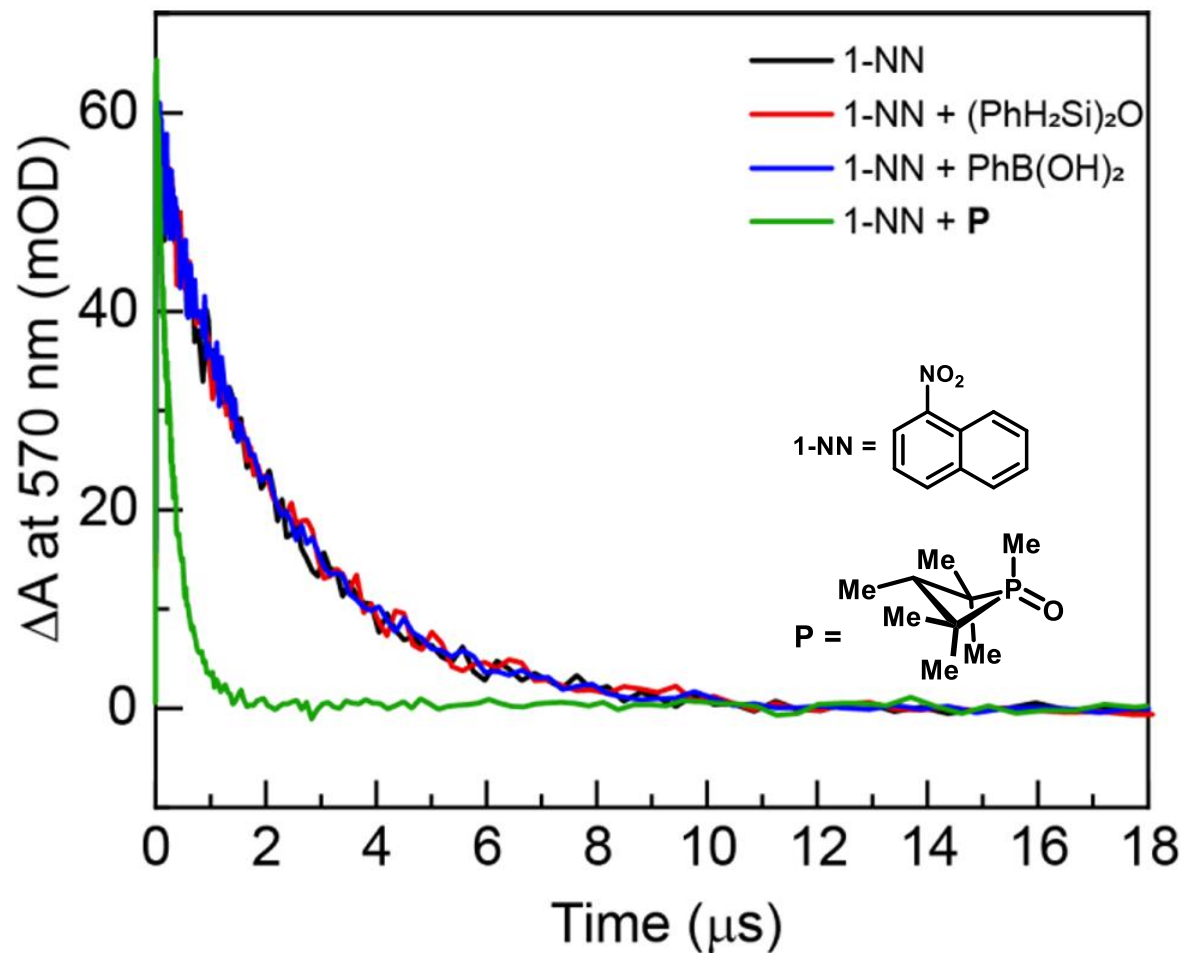
復旦大學

瞬态吸收光谱



激发态吸收波长为410 nm, 570 nm, 800 nm, 激发态寿命约为2.12 μ s.

淬灭实验



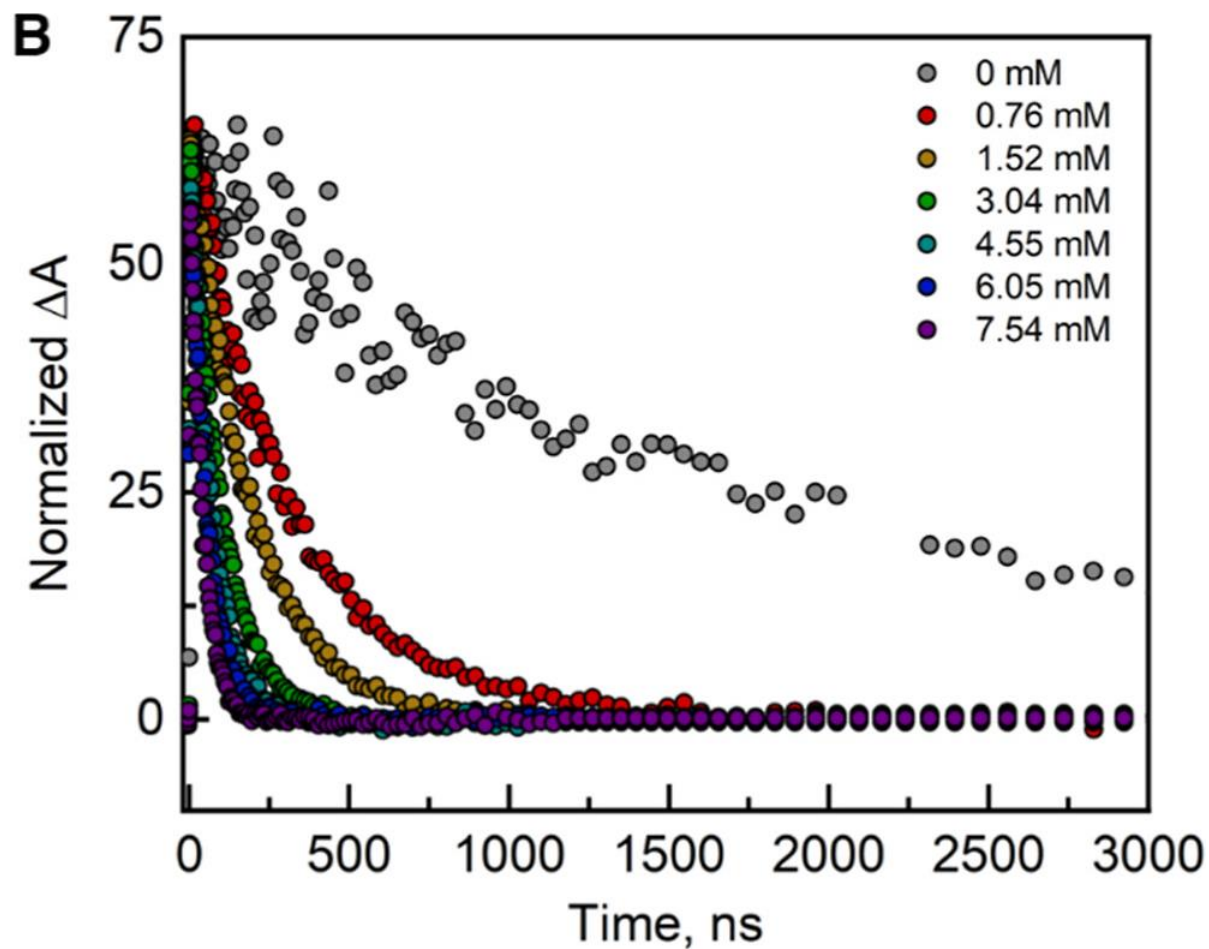
反应物中, 对激发态硝基化合物寿命产生明显影响的是膦催化剂

膦催化的硝基化合物还原反应



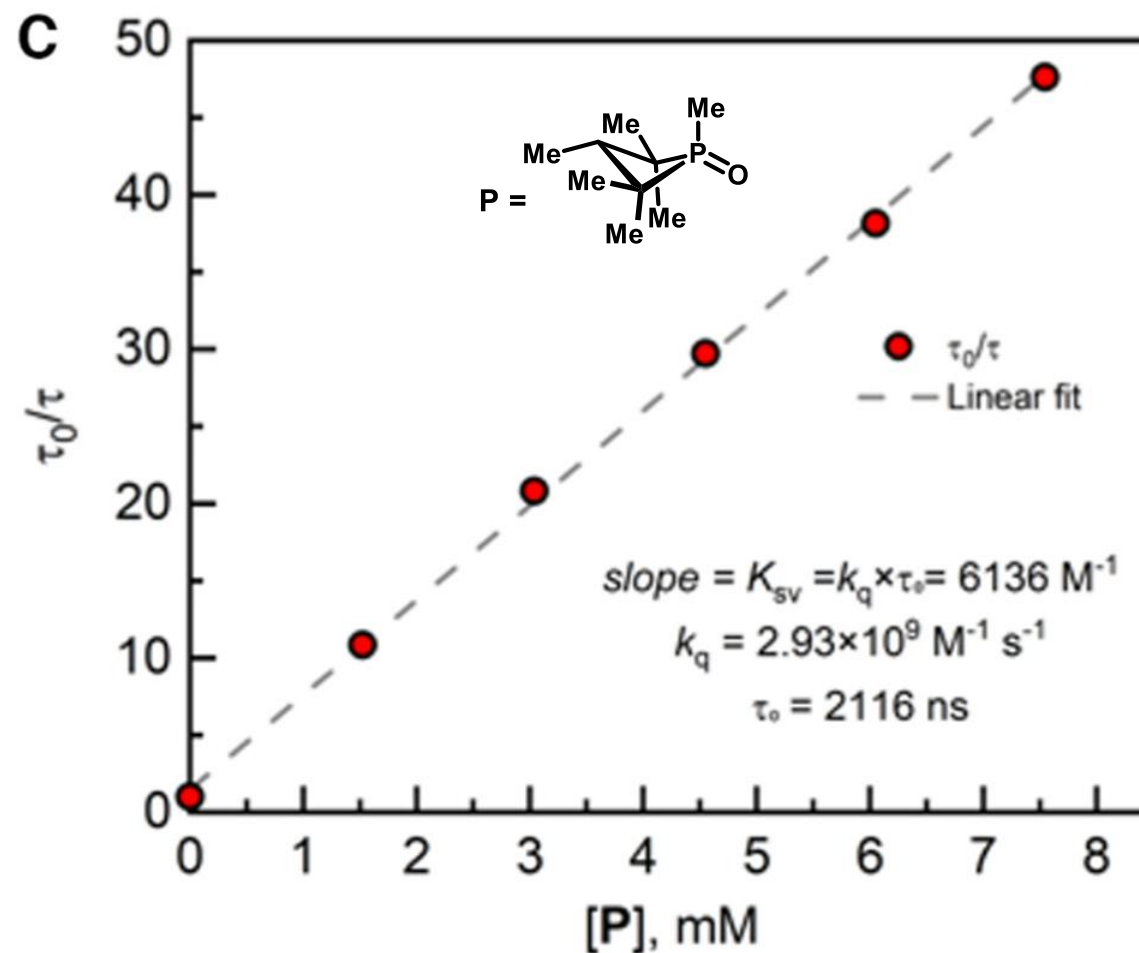
復旦大學

归一化动力学曲线



不同浓度膦催化剂下，激发态硝基化合物寿命比较

Stern-Volmer淬灭曲线

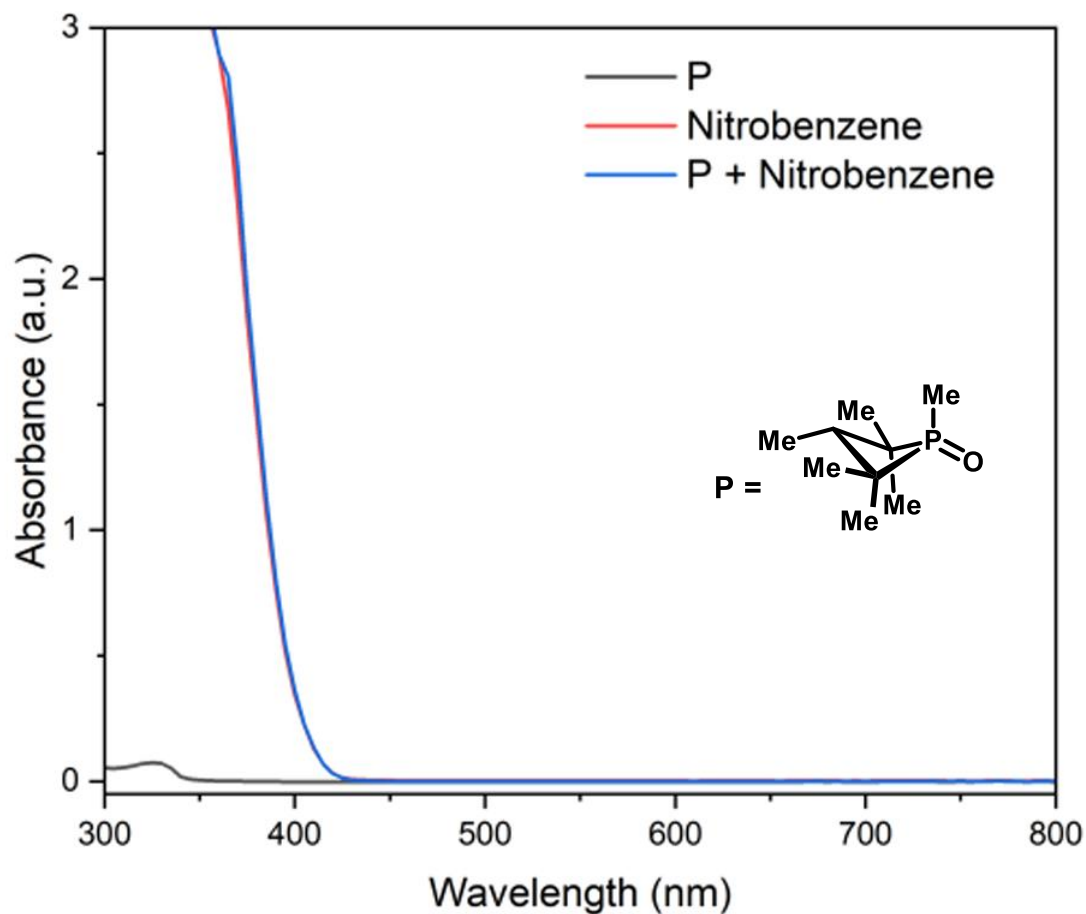


膦催化的硝基化合物还原反应



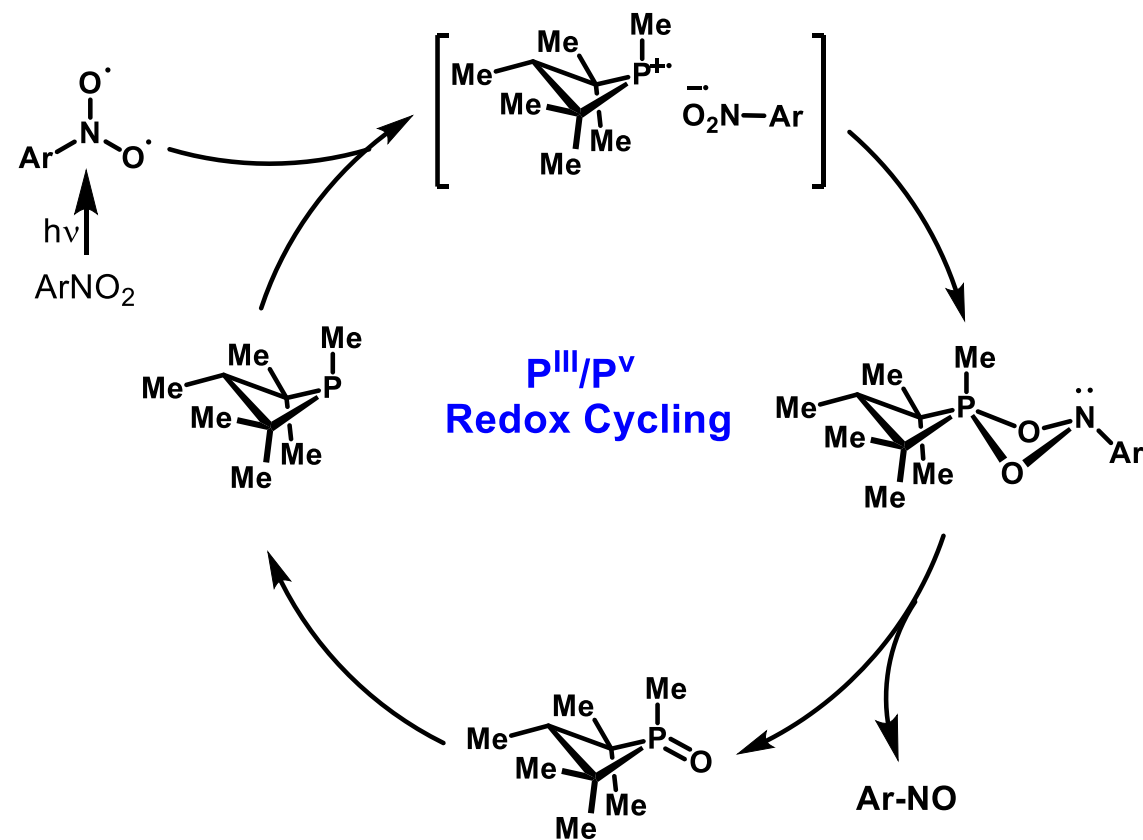
復旦大學

紫外吸收实验



硝基化合物与膦催化剂混合后没有观察到明显的红移或蓝移

Possible reaction mechanism:

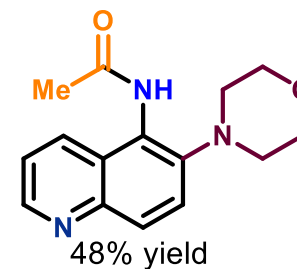
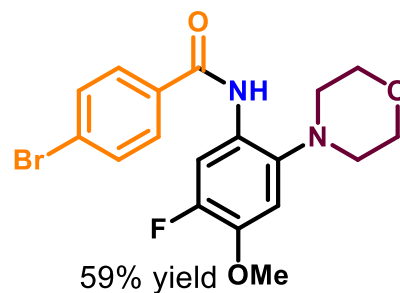
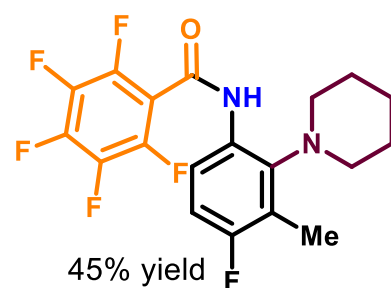
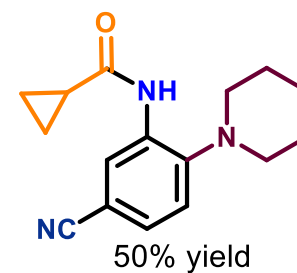
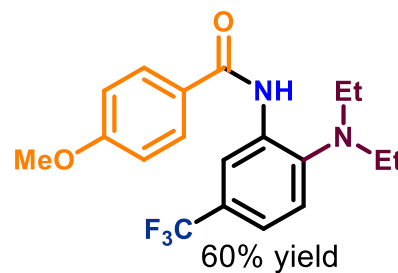
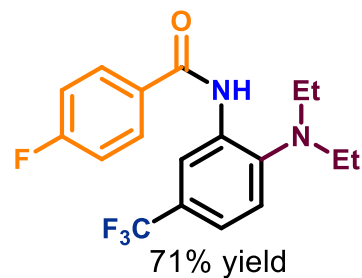
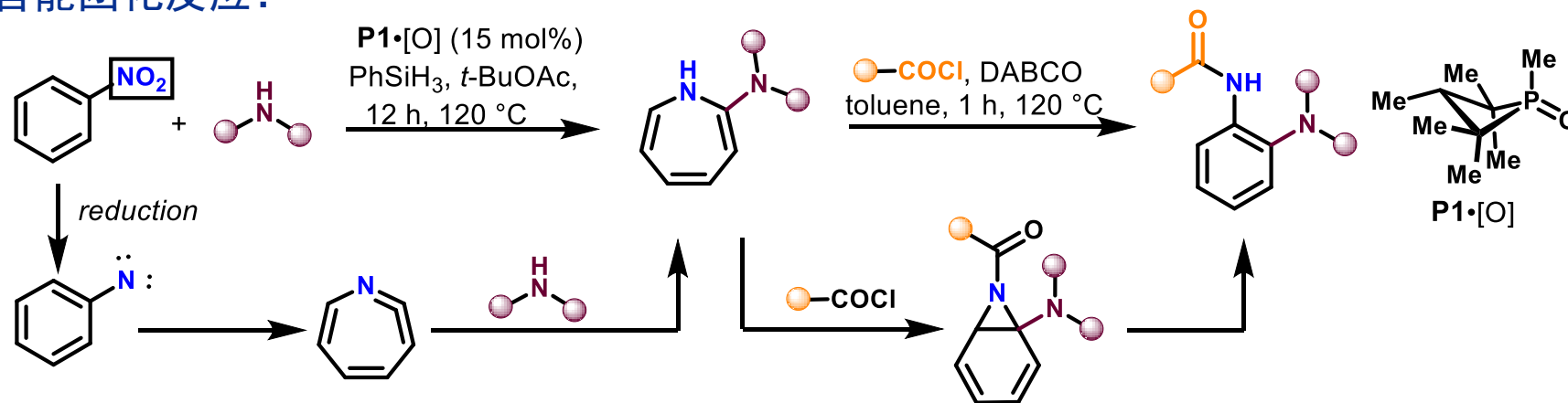


膦催化的硝基化合物还原反应



復旦大學

硝基芳烃的碳/氮双官能团化反应:

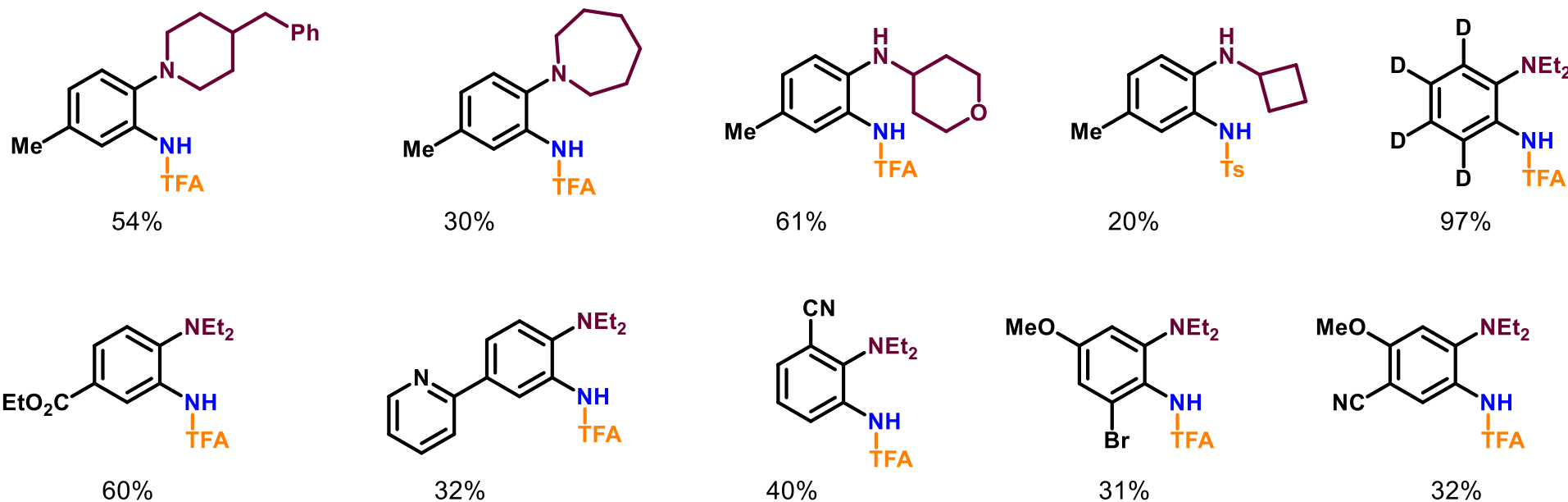
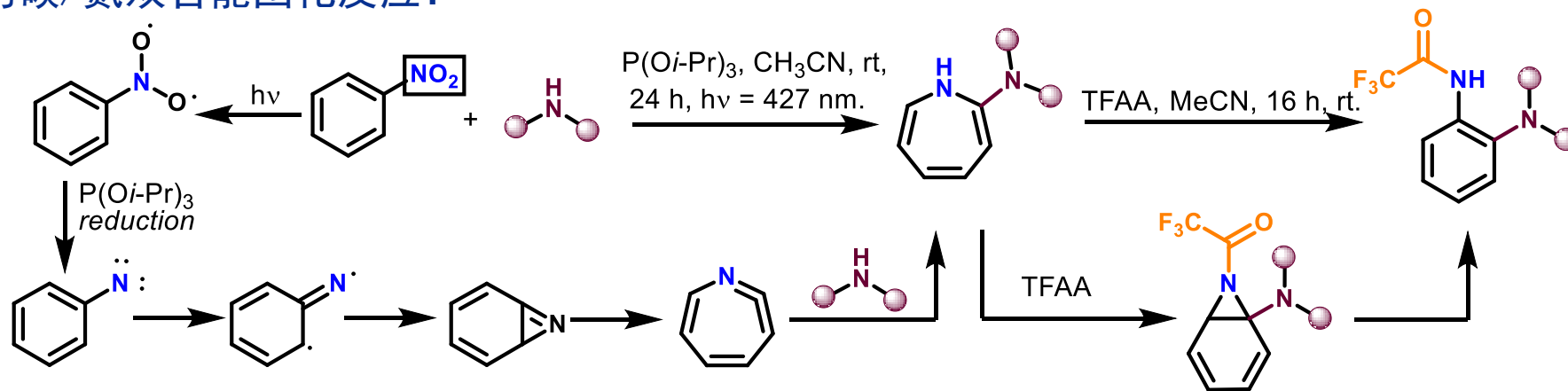


磷催化的硝基化合物还原反应



復旦大學

硝基芳烃的碳/氮双官能团化反应:



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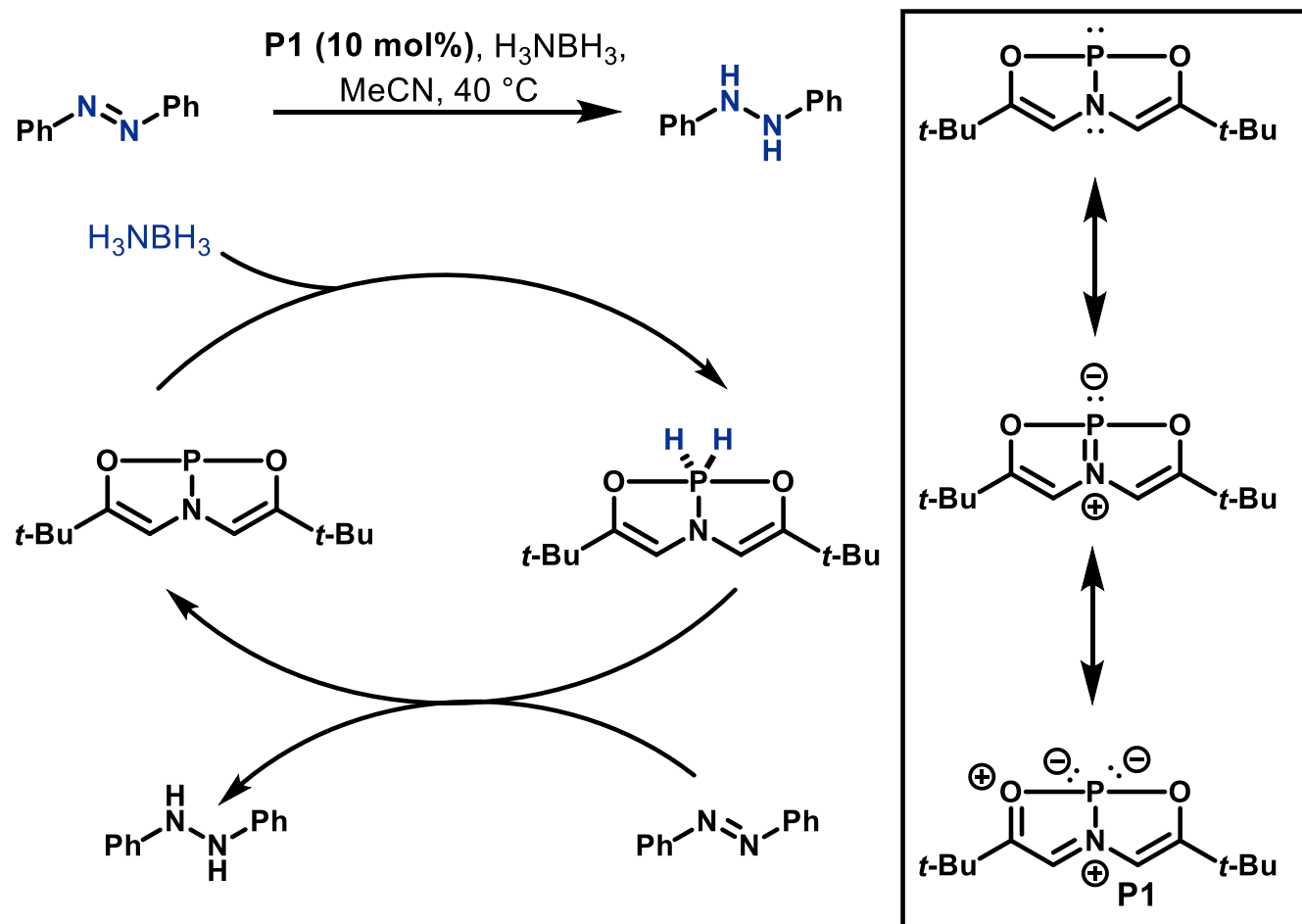


Catalytic Hydride and Hydrogen Transfer

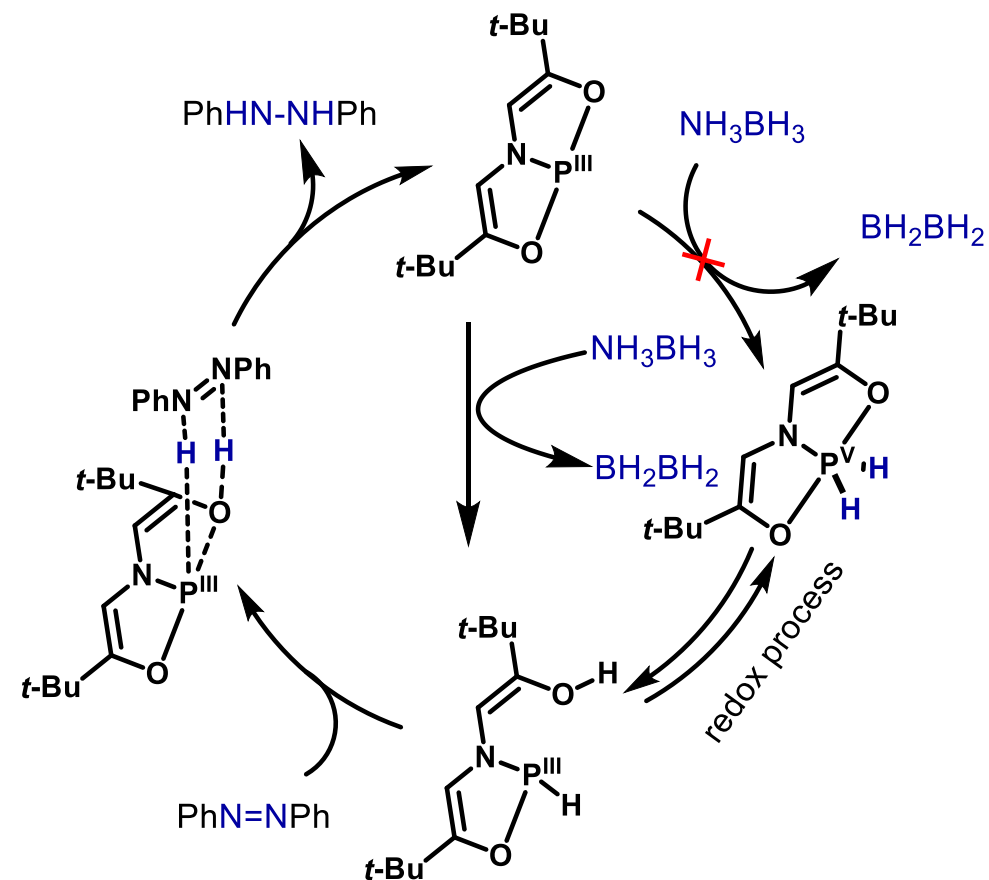


復旦大學

磷催化的氢原子转移反应



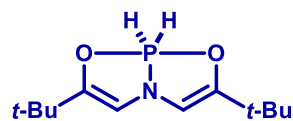
Controversial mechanism



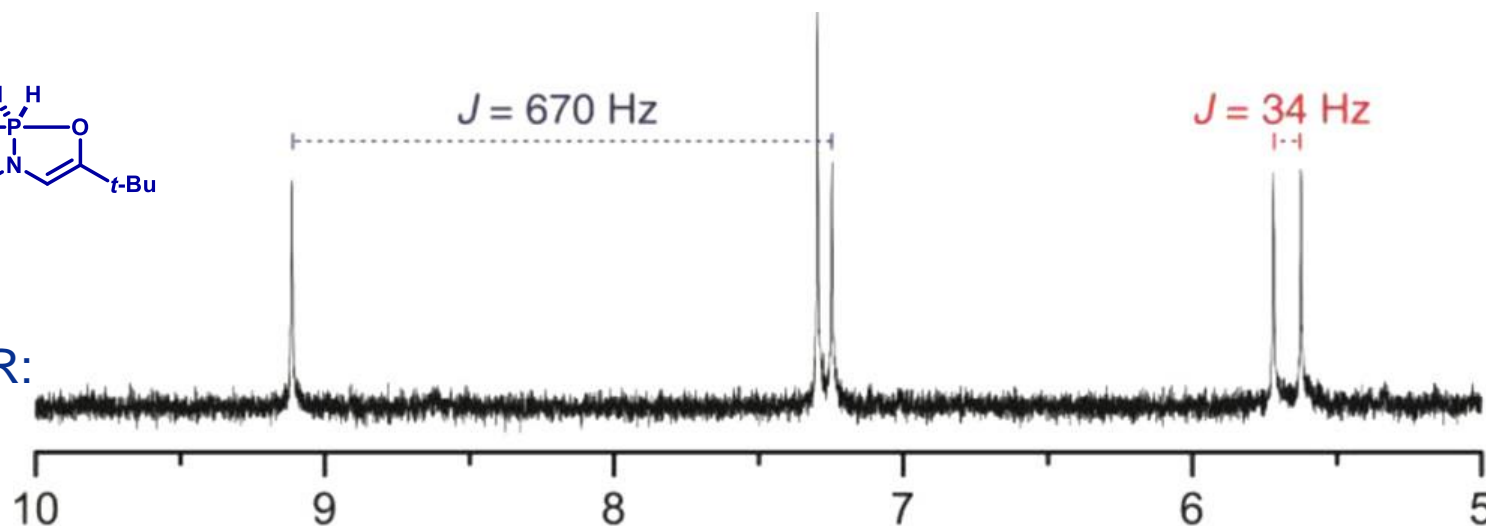
Catalytic Hydride and Hydrogen Transfer



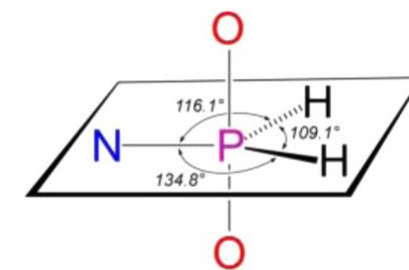
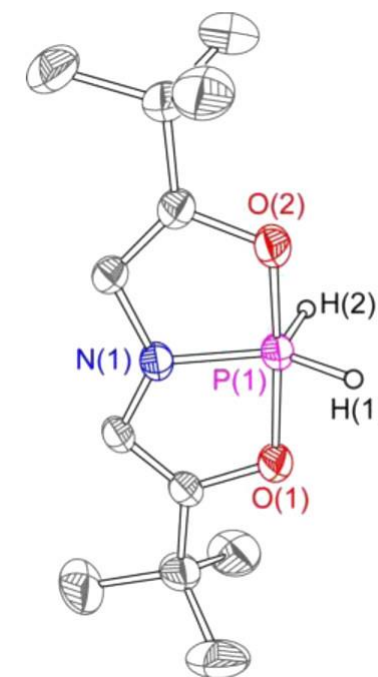
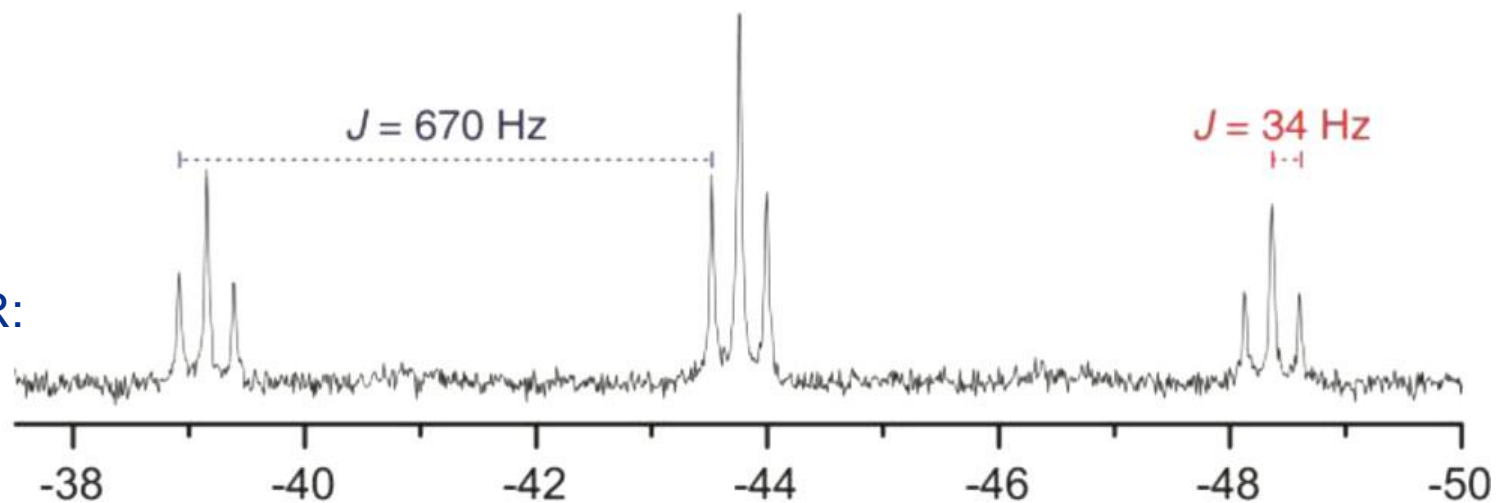
復旦大學



^1H NMR:



^{31}P NMR:

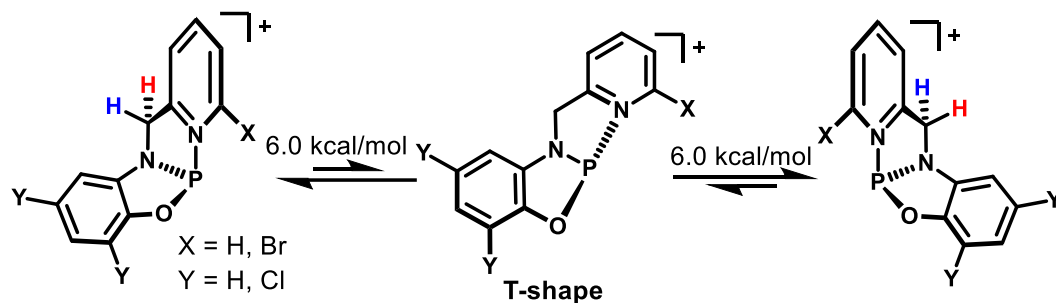


Catalytic Hydride and Hydrogen Transfer

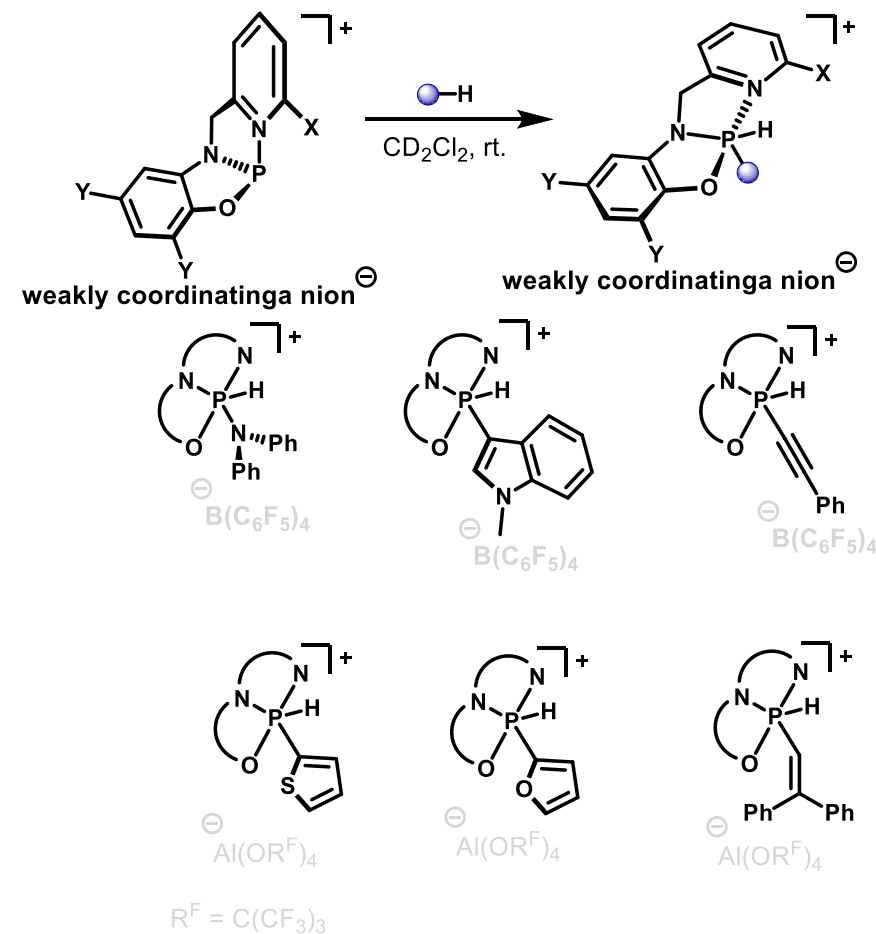
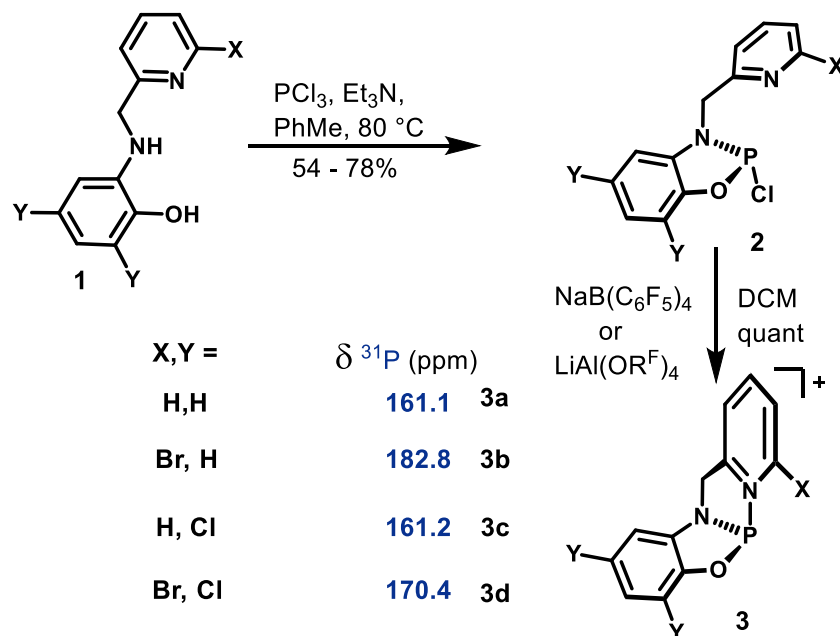


復旦大學

C-H bond activation reaction



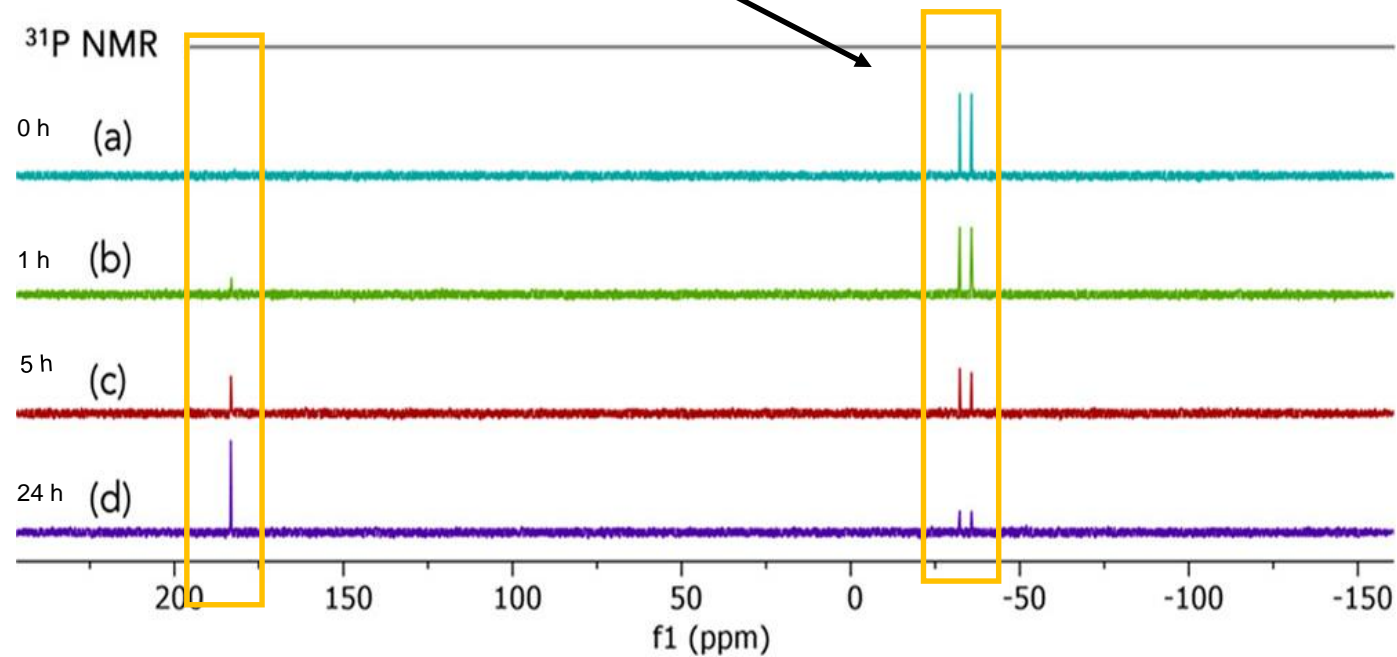
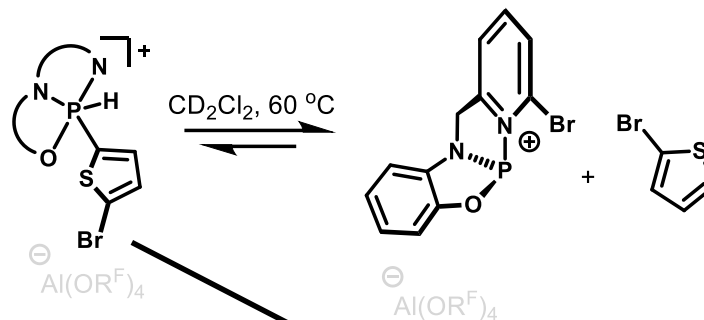
low-barrier isomerization to reactive T-shaped isomer.



Catalytic Hydride and Hydrogen Transfer



復旦大學

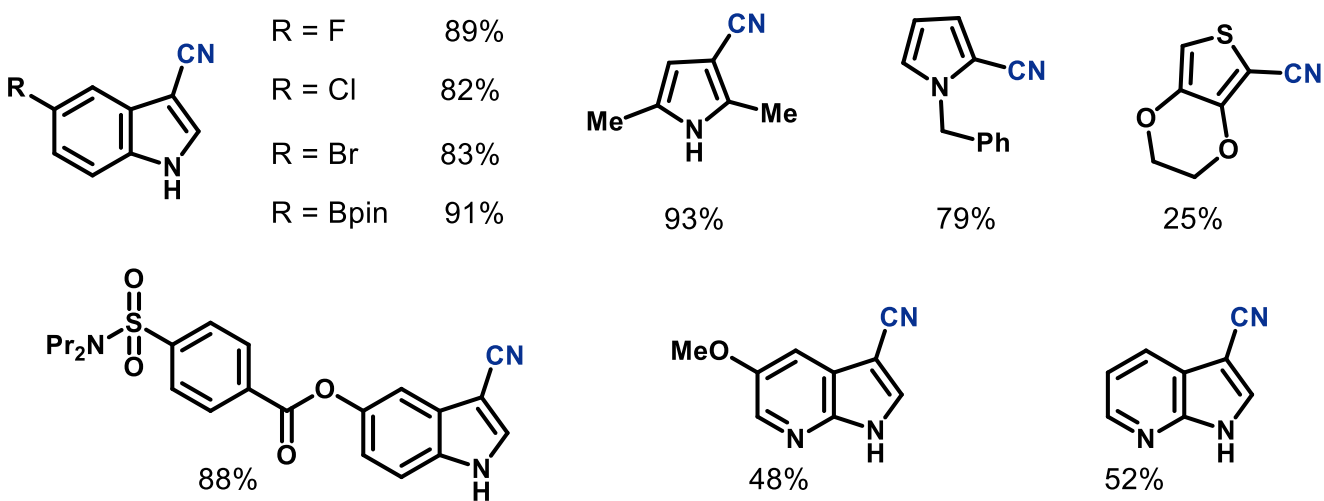
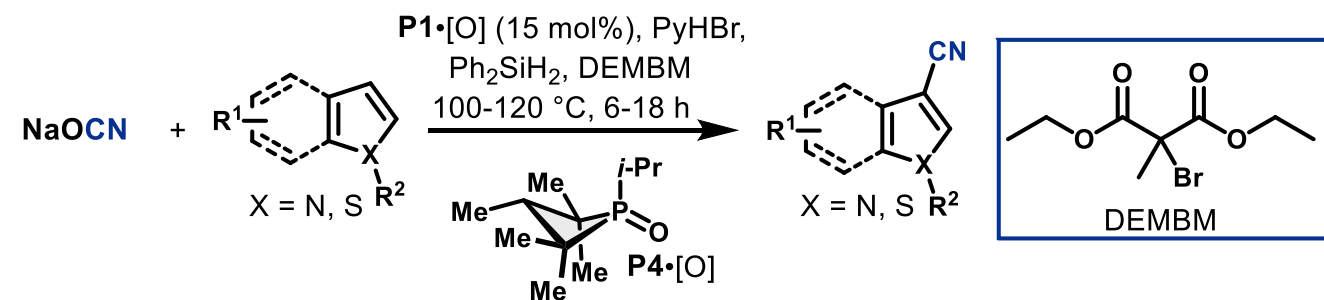


磷催化的其他反应

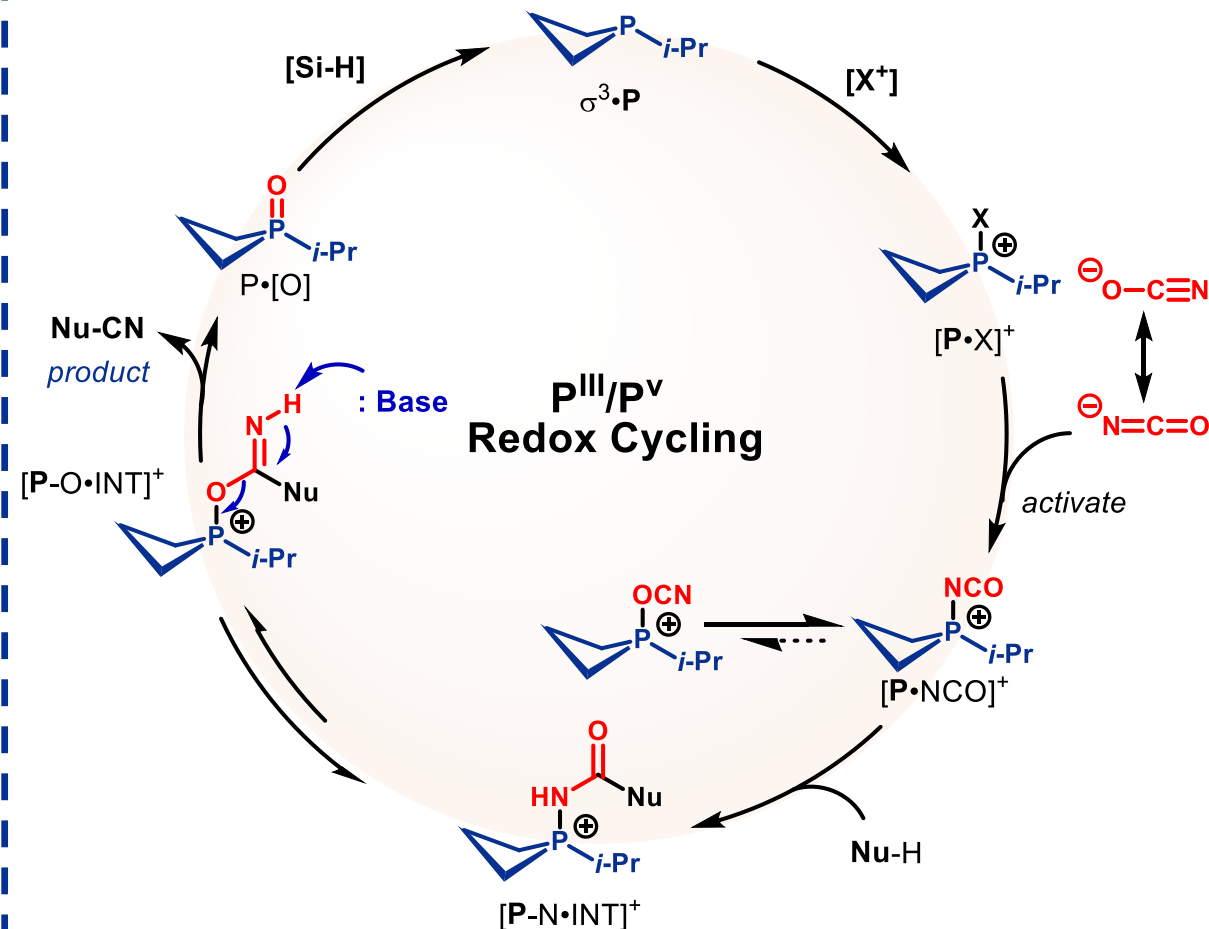


復旦大學

通过氰酸钠 (NaOCN) 活化实现的亲电氰基化反应



Possible reaction mechanism:

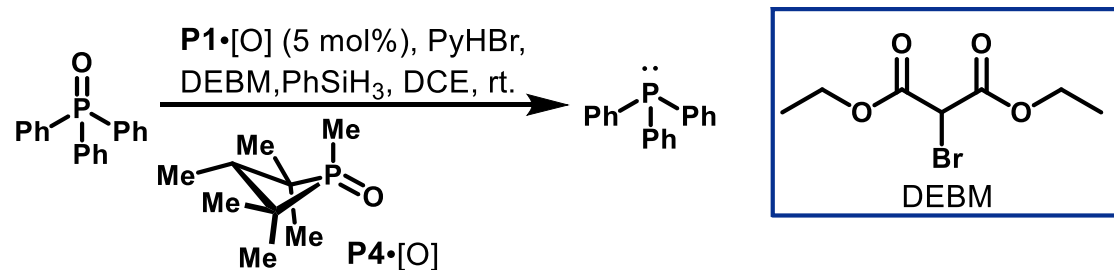


磷催化的其他反应

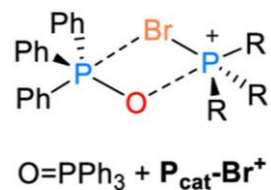
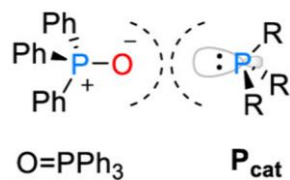
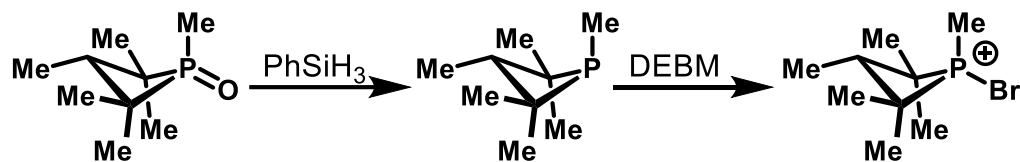


復旦大學

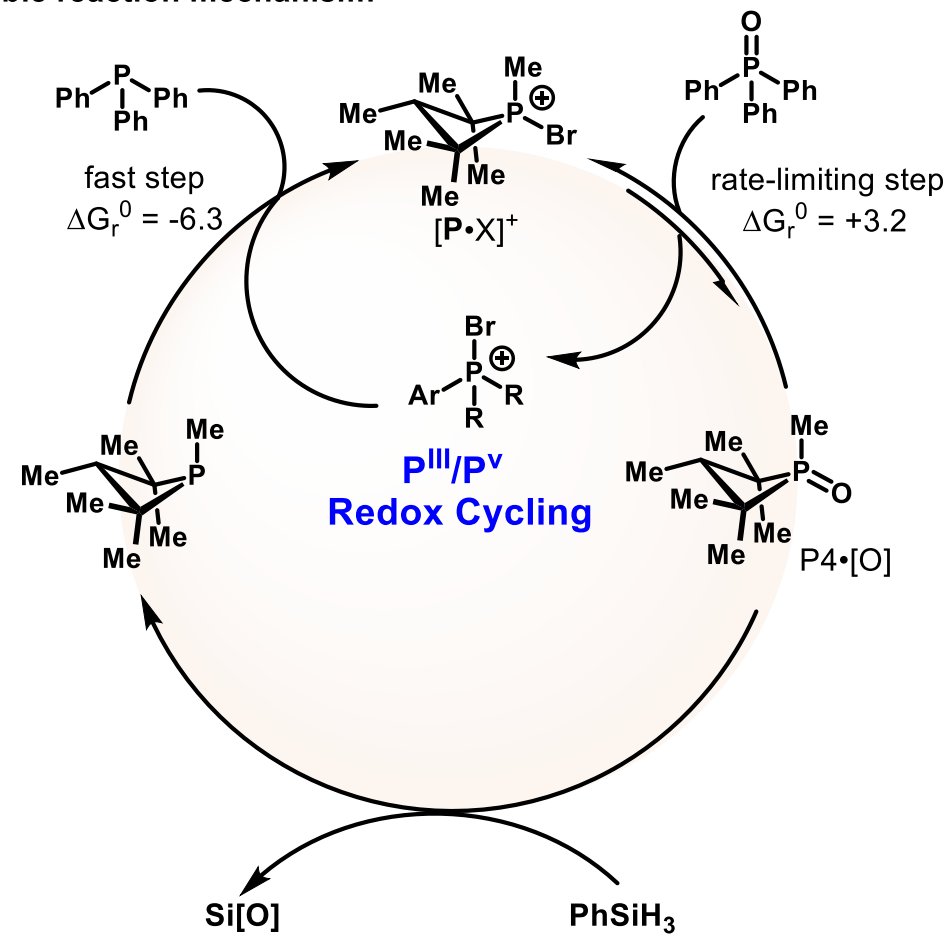
通过等键反应实现三苯基氧磷还原



Reaction Design



Possible reaction mechanism:

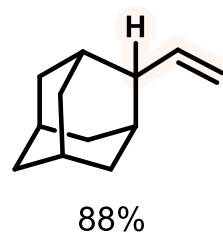
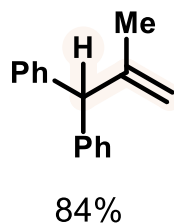
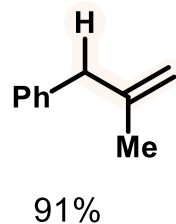
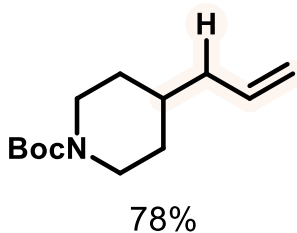
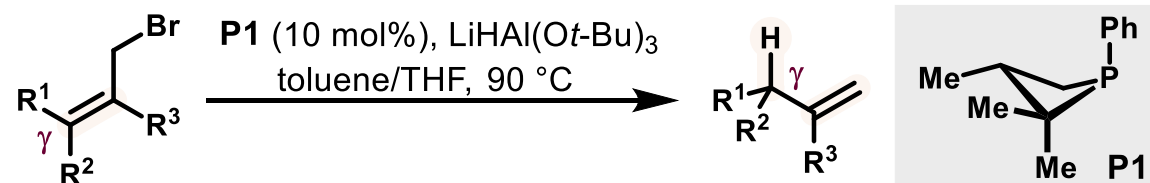


磷催化的其他反应

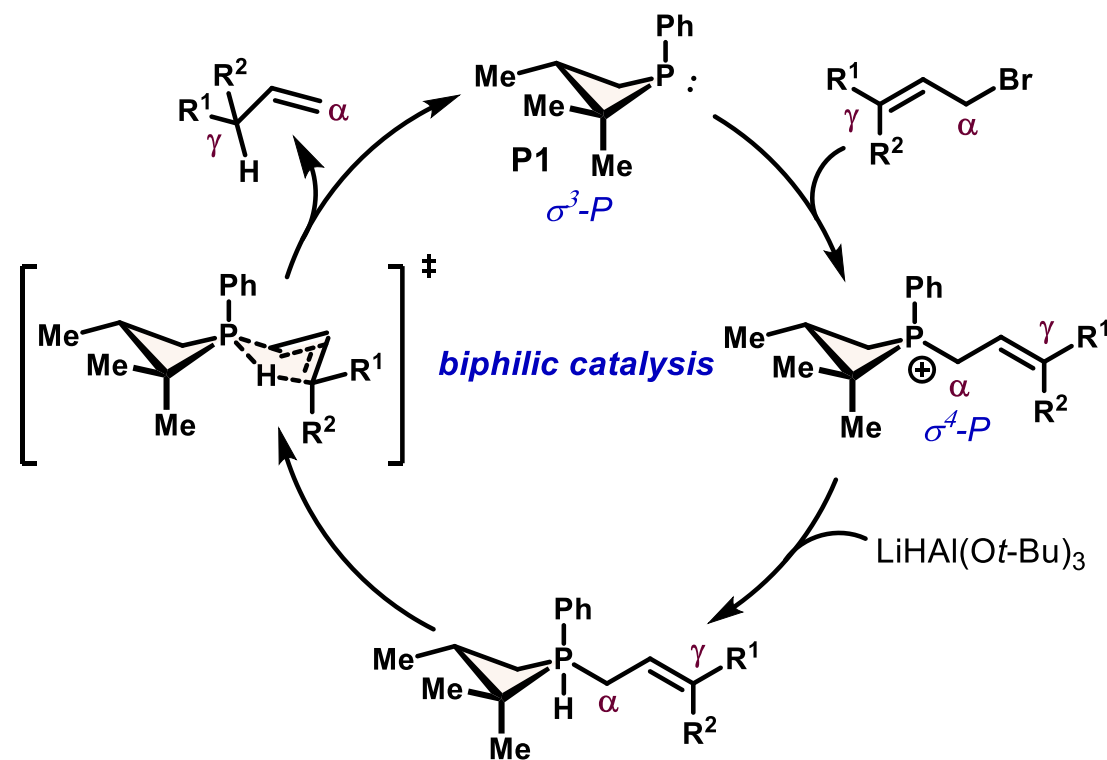


復旦大學

烯丙基溴的区域选择性还原:



Possible reaction mechanism:

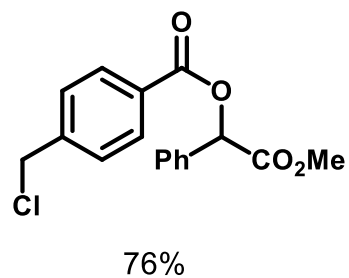
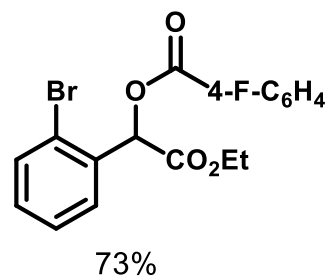
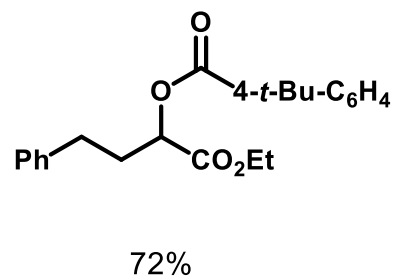
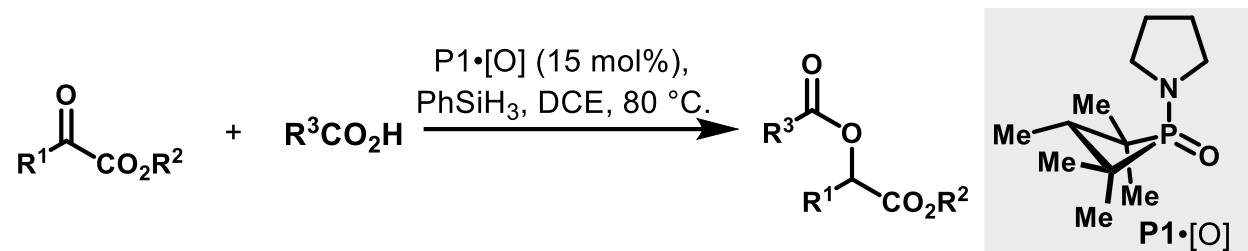


磷催化的其他反应

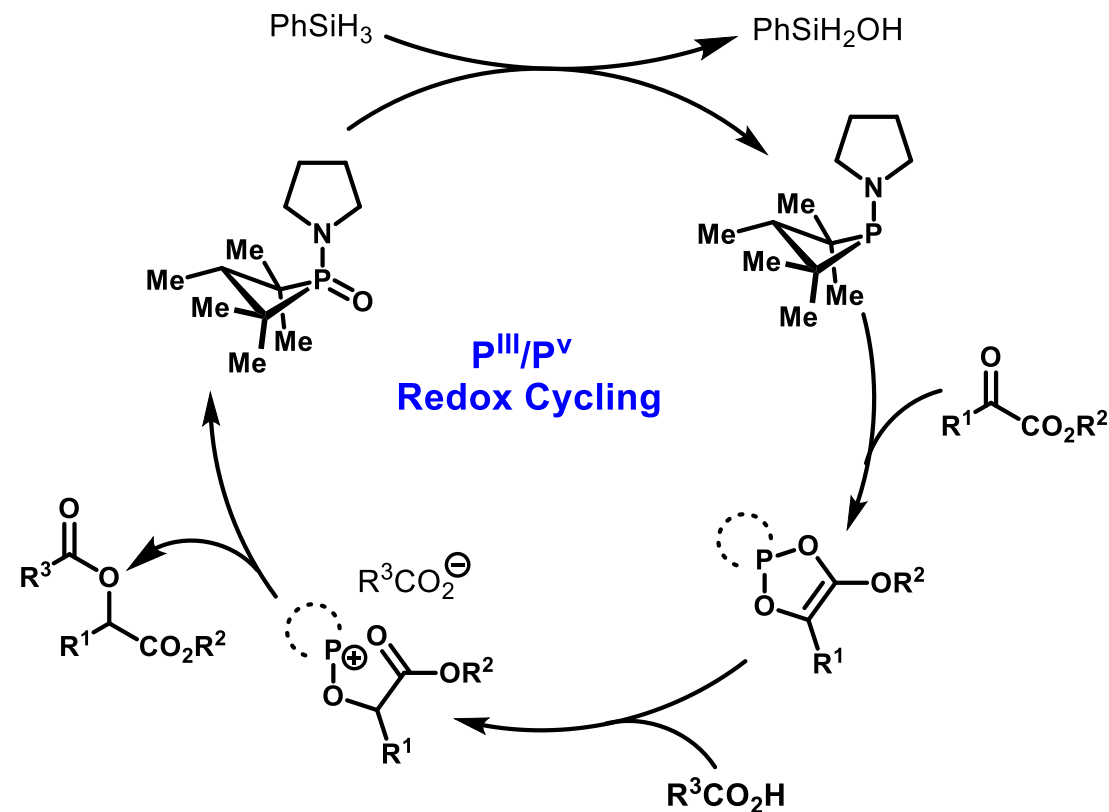


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磷催化的 α - 氧代羧酸酯与羧酸的脱氧缩合反应



Possible reaction mechanism:



目录

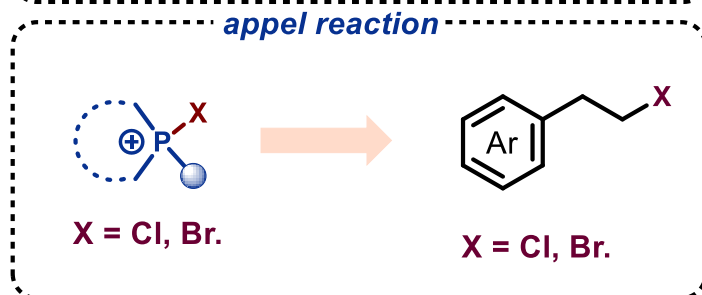
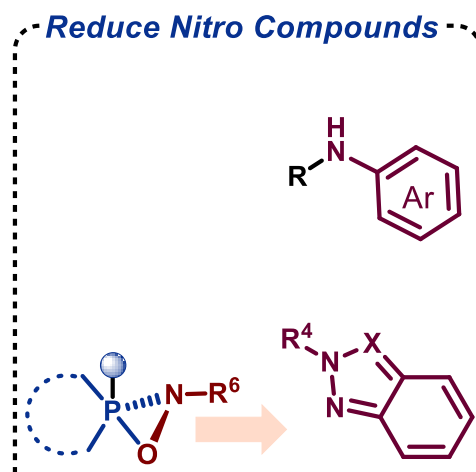
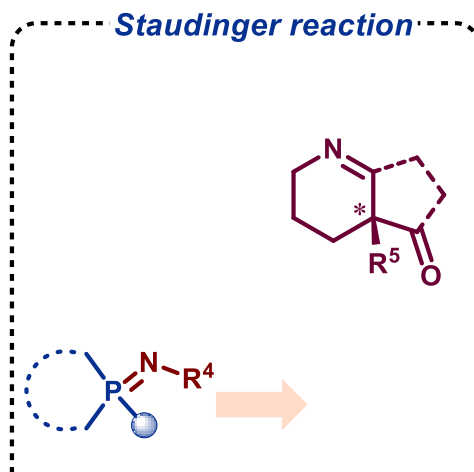
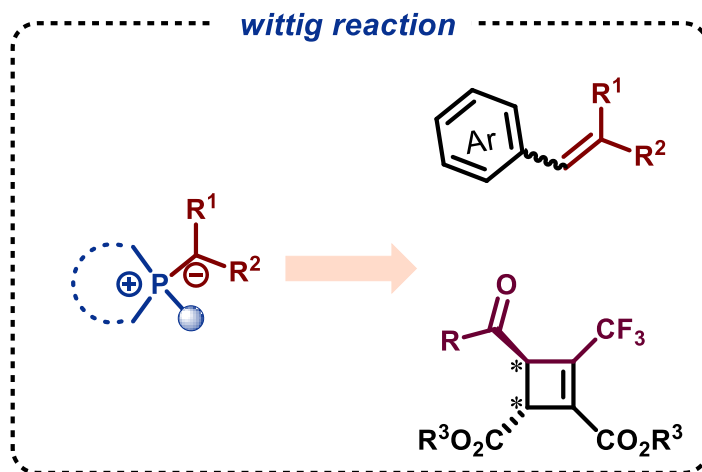
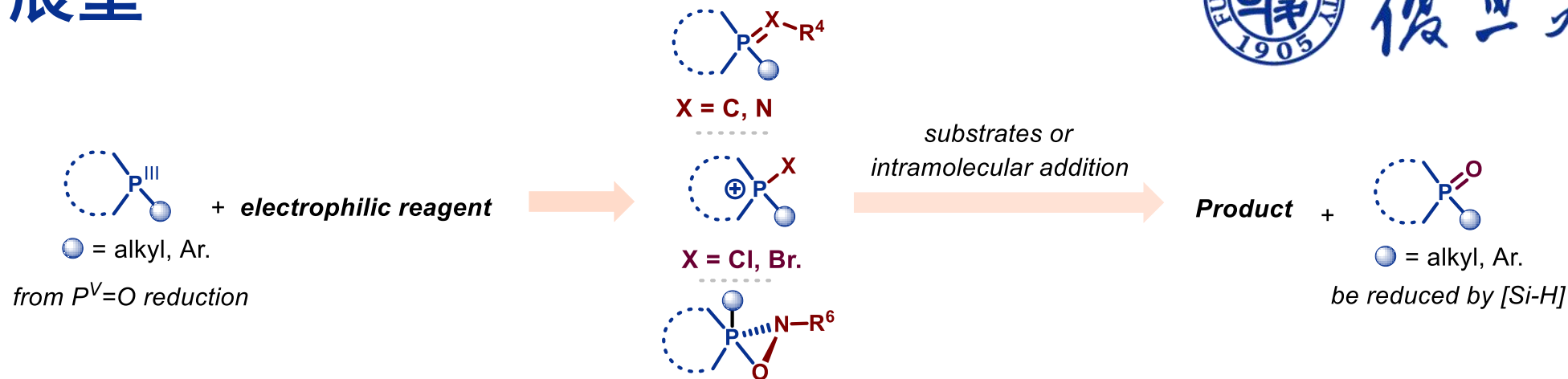
1. 背景
2. 有机磷催化的Wittig 和 Wittig-Type 反应
 - 2.1 消旋反应
 - 2.2 手性反应
3. 有机磷催化的硝基化合物还原反应
4. 有机磷催化的其他反应
5. **总结与展望**



总结与展望



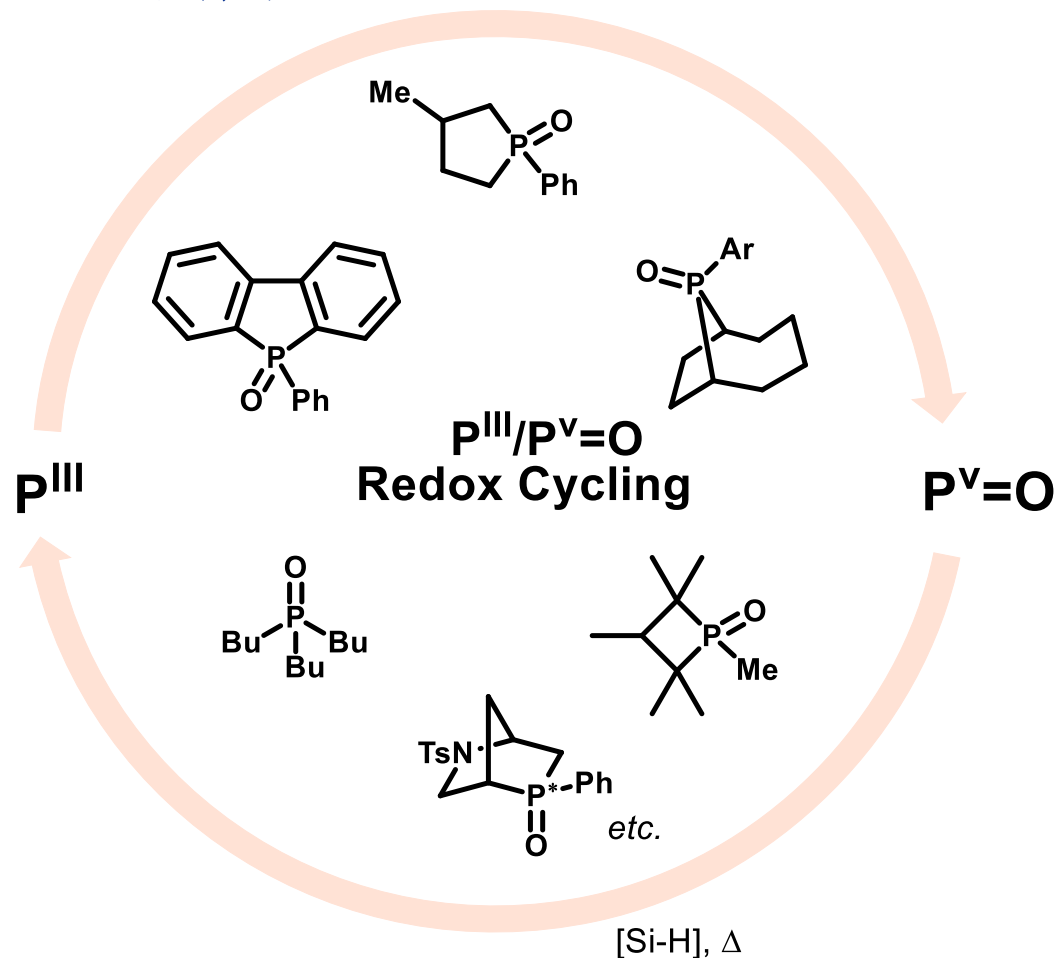
復旦大學



总结与展望



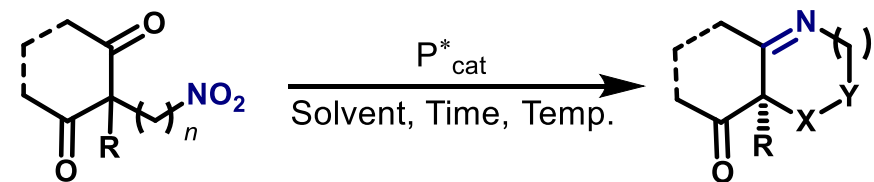
復旦大學



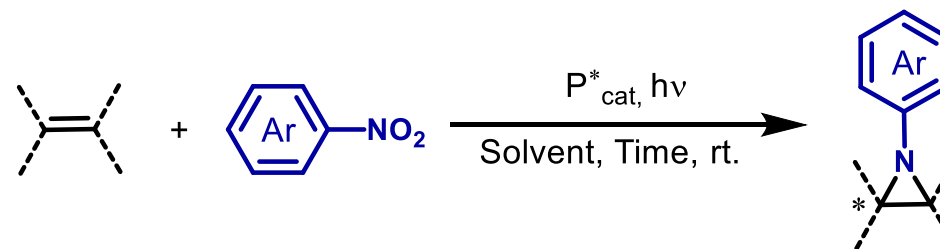
限制:

- ➡ 对磷的结构要求较高, 需要烷基取代的磷
- ➡ 目前对P^V=O的还原绝大部分集中在硅氢试剂
- ➡ 反应所需温度较高, 造成许多敏感性官能团不耐受

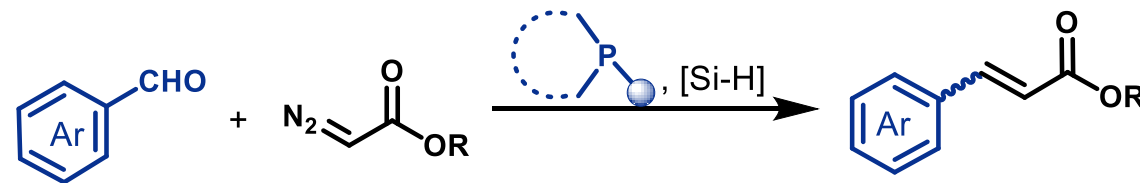
展望:



以硝基化合物完成不对称Staudinger Aza-Wittig 反应



以硝基化合物做为氮卡宾前体来实现氮杂环丙烷的合成



利用全烷基取代磷化合物高度亲电性, 拓宽Wittig反应应用范围



復旦大學

THANKS

