Seminar

噻蒽鎓盐参与的官能团化反应

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张俊良 教授

2022-04-15

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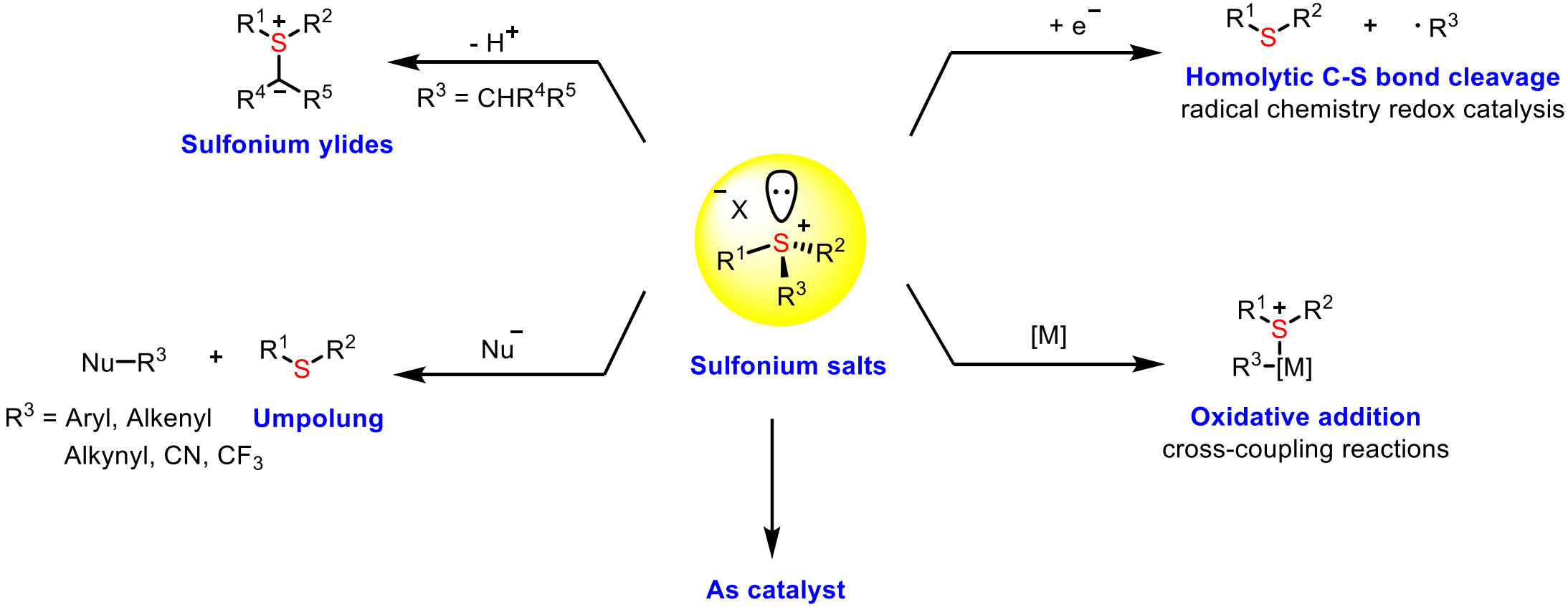
一、背景介绍

硫鎓盐参与的反应：

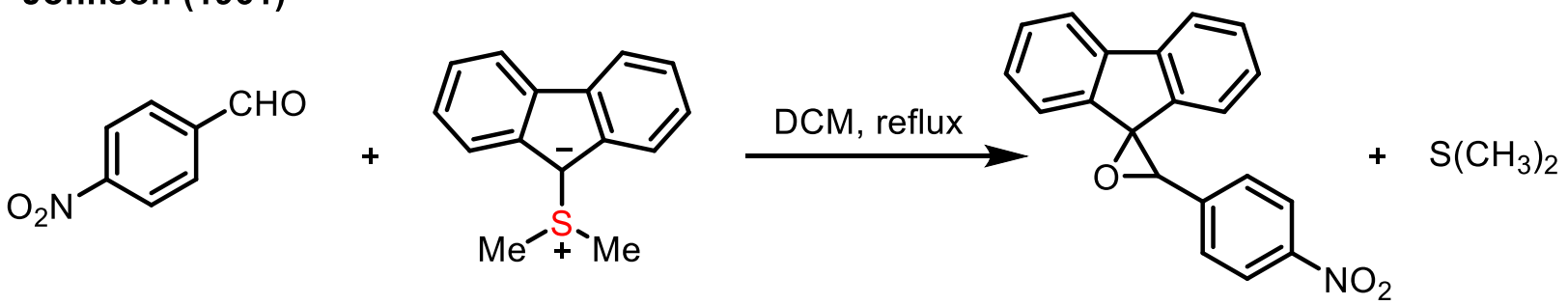


N. Maulide, et al. *Chem. Rev.* **2019**, *119*, 8701-8780;
M. Alcarazo, et al. *Eur. J. Inorg. Chem*. **2020**, *58*, 2486–2500.

一、背景介绍

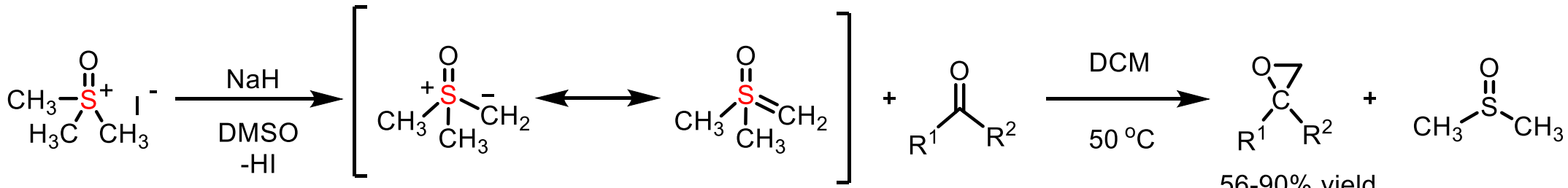
硫鎓盐与硫叶立德的转化：

Johnson (1961)



40% yield

Corey (1962)



dimethylsulfoxonium methylide

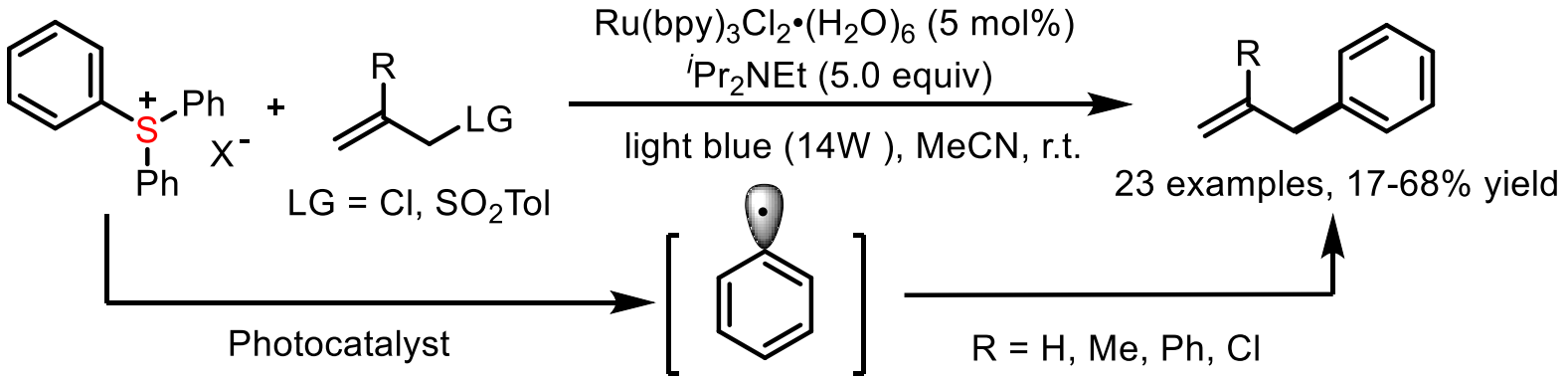
Corey-Chaykovsky Reagent

J. A. Jessop, et al. *J. Chem. Soc.* **1930**, 708-713;
A. W. Johnson, et al. *J. Am. Chem. Soc.* **1961**, *83*, 417-423;
E. J. Corey, et al. *J. Am. Chem. Soc.* **1962**, *84*, 867-868.

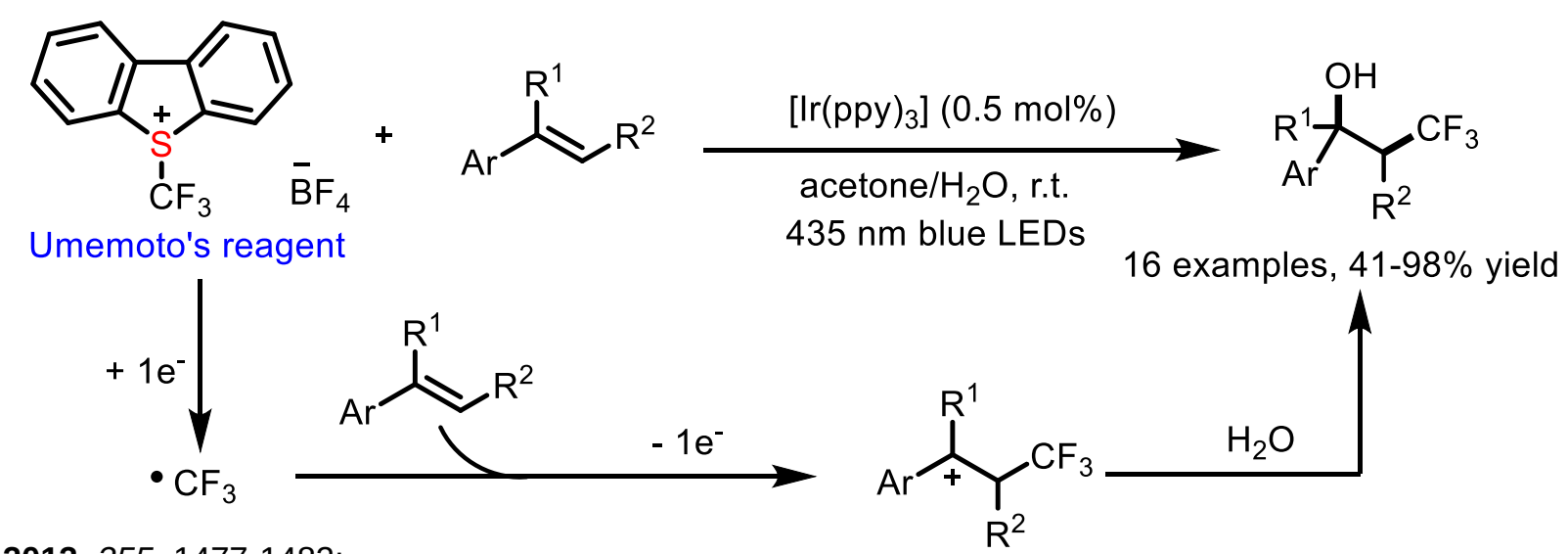
一、背景介绍

硫鎓盐参与的单电子还原反应：

Olivier (2013)



Asiatic (2016)

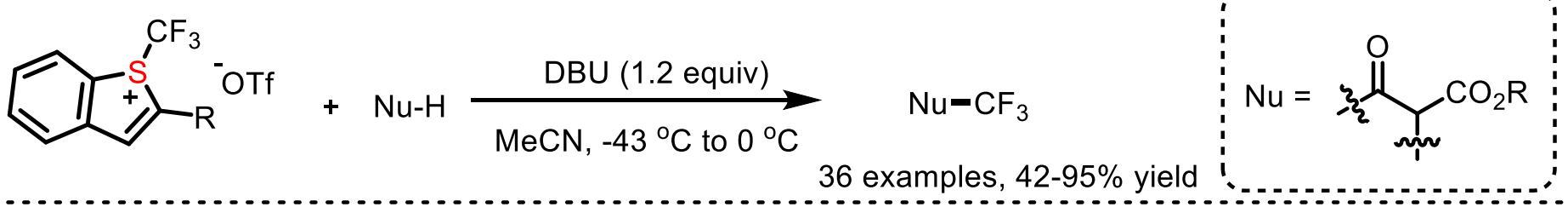


C. Olivier, et al. *Adv. Synth. Catal.* **2013**, *355*, 1477-1482;
M. Asiatic, et al. *Acc. Chem. Res*. **2016**, *49*, 1937-1945.

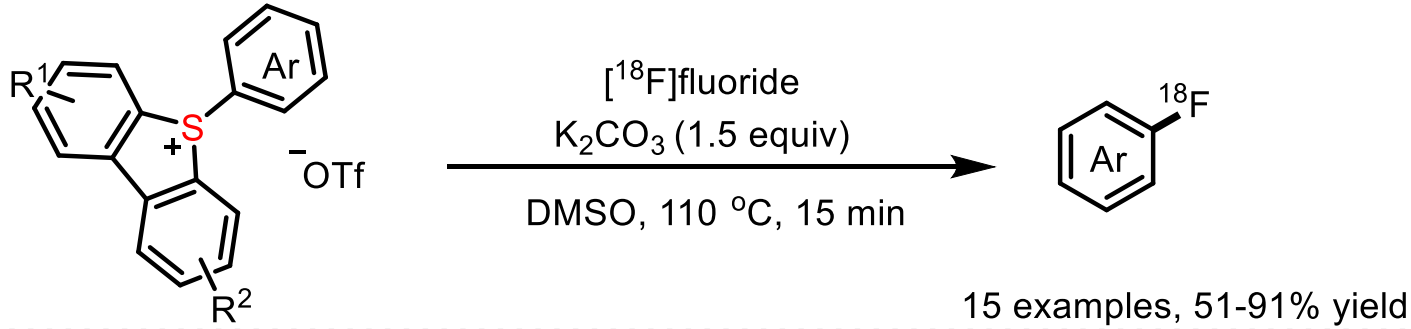
一、背景介绍

硫鎓盐参与的亲核取代反应：

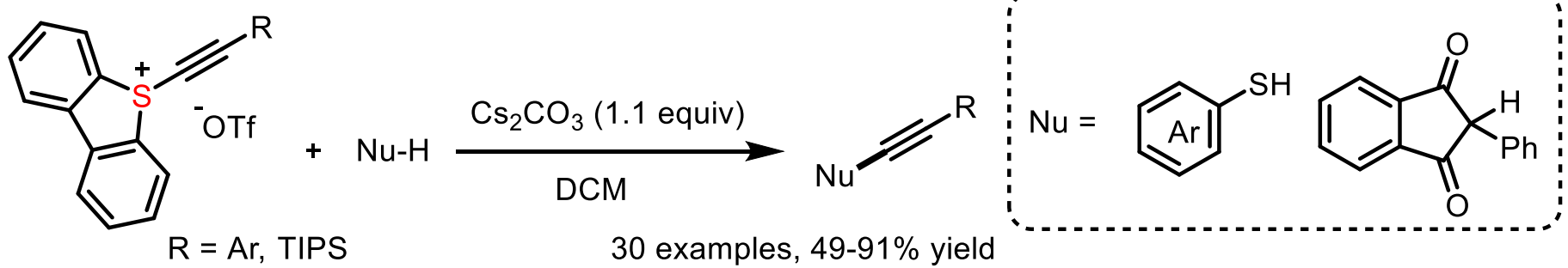
Shibata (2010)



Arshad (2018)



Alcarazo (2019)

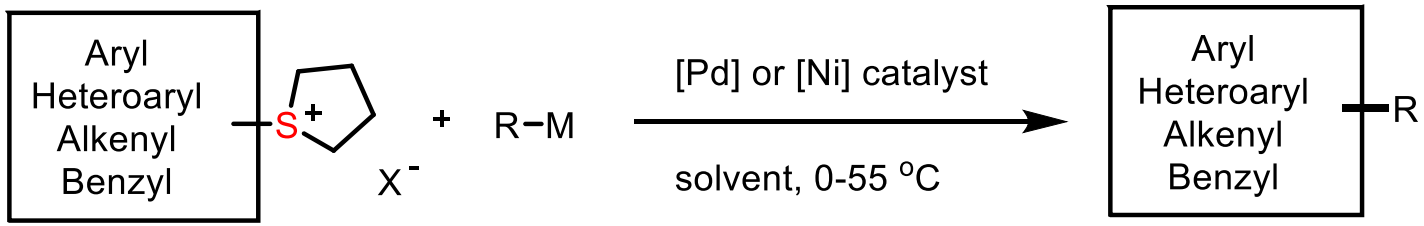


N. Shibata, et al. *Angew. Chem. Int. Ed*. **2010**, *49*, 572-576;
E. Arshad, et al. *J. Am. Chem. Soc.* **2018**, *140*, 11125-11132;
M. Alcarazo, et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 9496-9500.

一、背景介绍

硫鎓盐参与的过渡金属催化的交叉偶联反应：

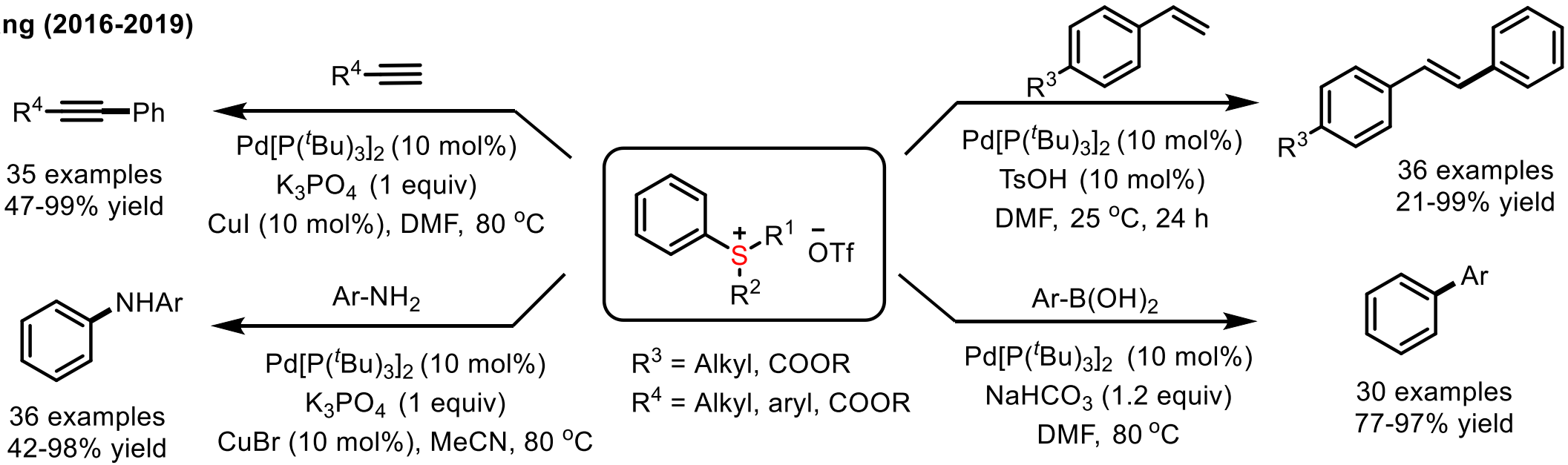
Libeskind (1997)



M = $^{n}Bu_3Sn$, $B(OH)_2$, ZnCl, ZnMe

24 examples, 42-97% yield

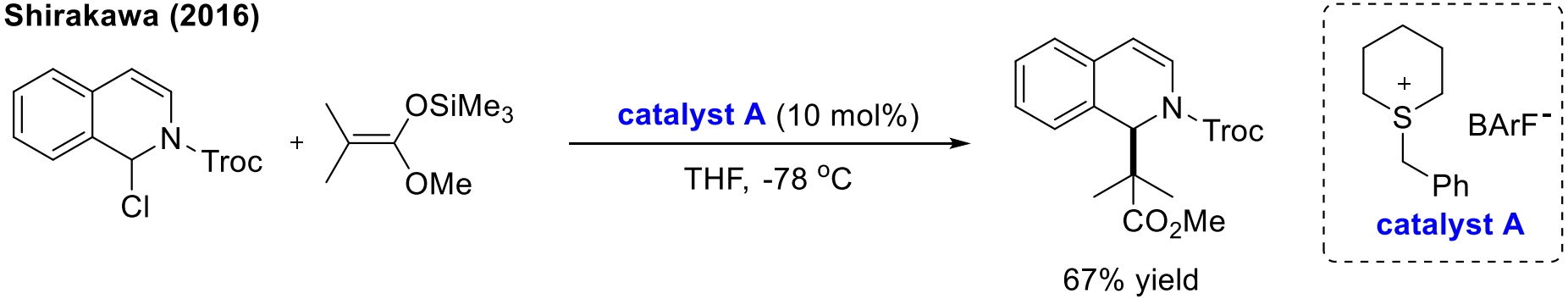
Zhang (2016-2019)



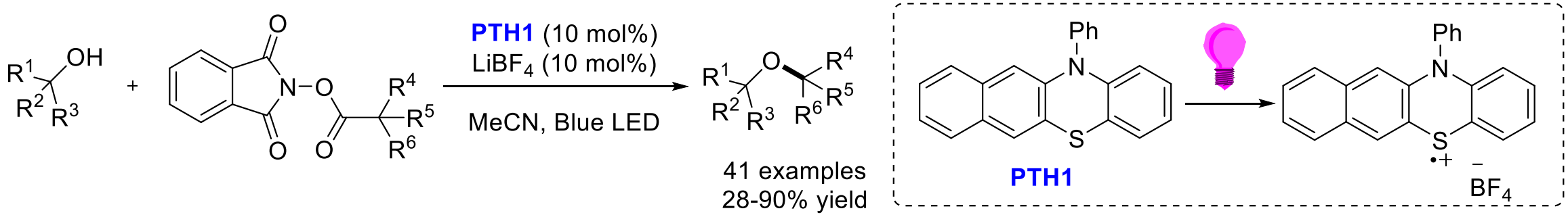
L. Libeskind, et al. *J. Am. Chem. Soc.* **1997**, *119*, 12376-12377;
H. Yoshidab, et al. *Chin. Chem. Lett.* **2021**, *32*, 299-312.

一、背景介绍——硫鎓盐作为催化剂

Shirakawa (2016)



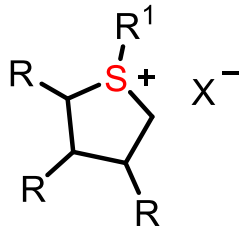
Ohmiya (2020)

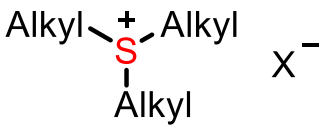


S. Shirakawa, et al. *Chem. Commun.* **2017**, *53*, 119-122;
H. Ohmiya, et al. *J. Am. Chem. Soc*. **2020**, *142*, 1211-1216.

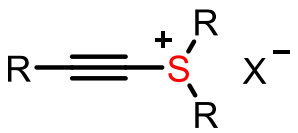
一、背景介绍——硫鎓盐的种类

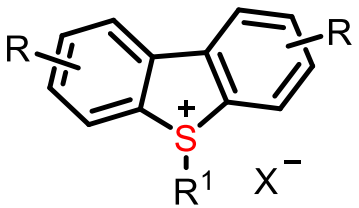
C(sp^3)-Substituted Sulfonium Salts:



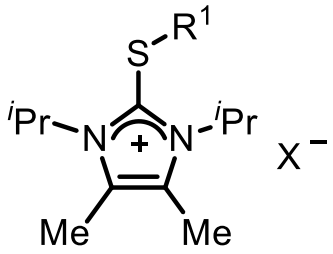


C(sp)-Substituted Sulfonium Salts:



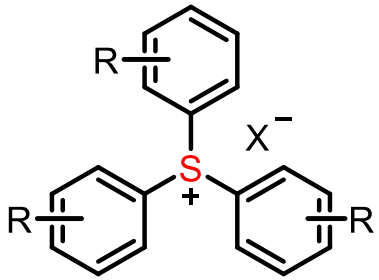


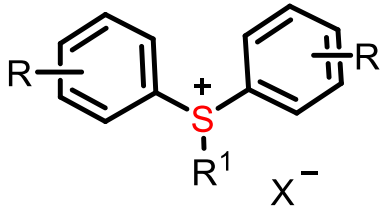
R^1 = CN, Alkyne



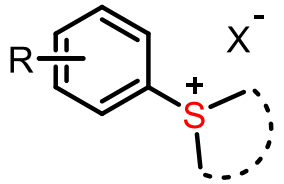
R^1 = CN, Alkyne

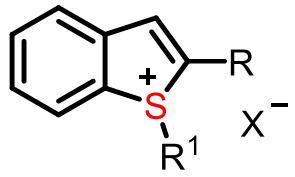
C(sp^2)-Substituted Sulfonium Salts:



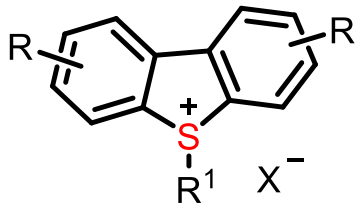


R^1 = Alkyl

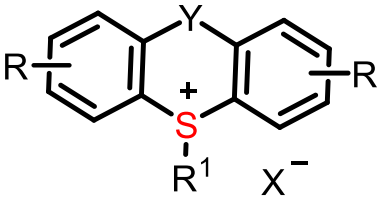




R^1 = Cyclopropyl, Ar

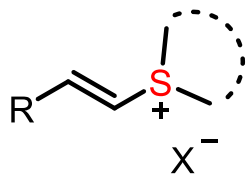


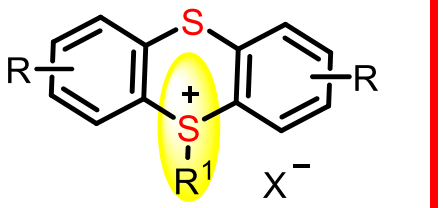
R^1 = Ar, Alkyl



Y = CO, NR, O

R^1 = Ar, Alkyl



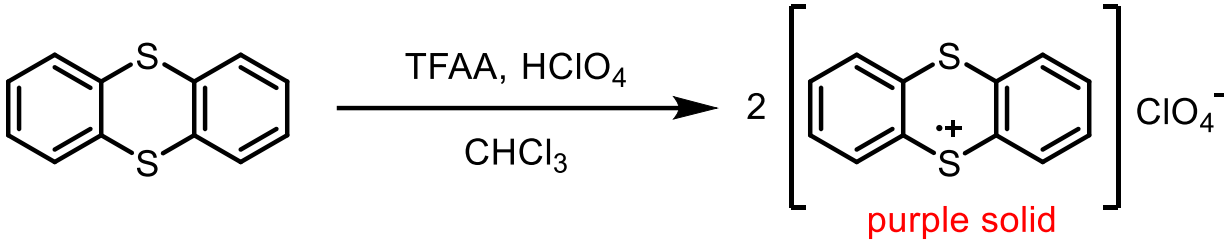


Thianthrenium salts

S. Shirakawa, et al. *Chem. Commun.* **2017**, *53*, 119-122;
H. Ohmiya, et al. *J. Am. Chem. Soc*. **2020**, *142*, 1211-1216.

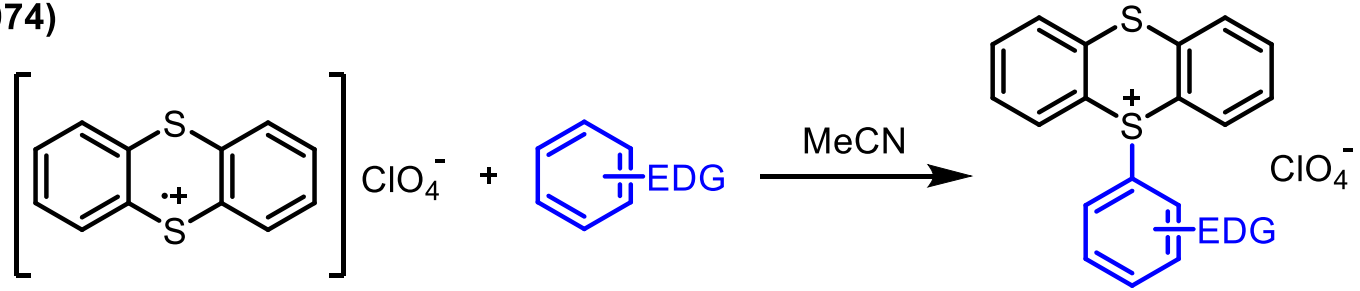
一、背景介绍——噻蒽鎓盐的发展

Lucken (1962)



首次分离
确定结构
溶液中稳定

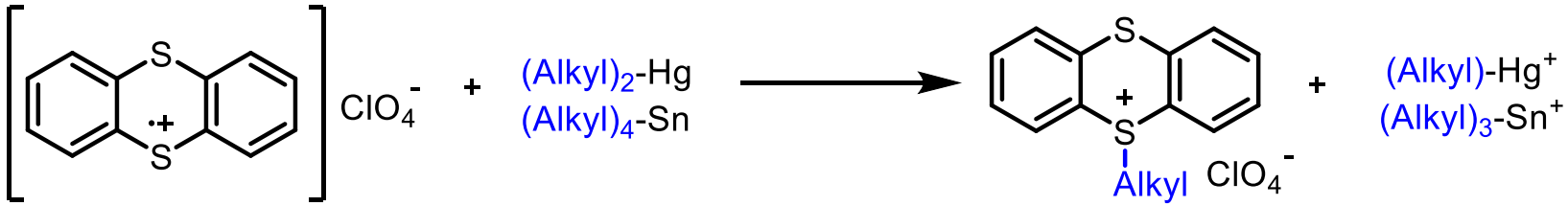
Shine (1971/1974)



32% examples, 53-98% yield

湿敏
不稳定
易爆炸

Shine (1990/1991)



Alkyl = Me, Et, Bu...

E. A. C. Lucken, et al. *J. Am. Chem. Soc.* **1962**, *79*, 4963-4965;
H. J. Shine, et al. *J. Org. Chem.* **1971**, *36*, 2923-2926;
H. J. Shine, et al. *J. Org. Chem.* **1974**, *39*, 2534-2537;
H. J. Shine, et al. *J. Org. Chem.* **1990**, *55*, 2702-2713;
H. J. Shine, et al. *J. Org. Chem.* **1991**, *56*, 914-920.

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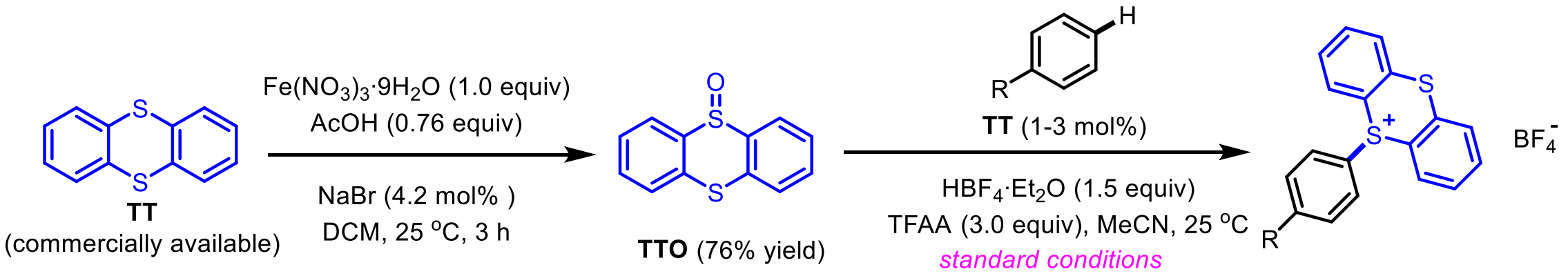
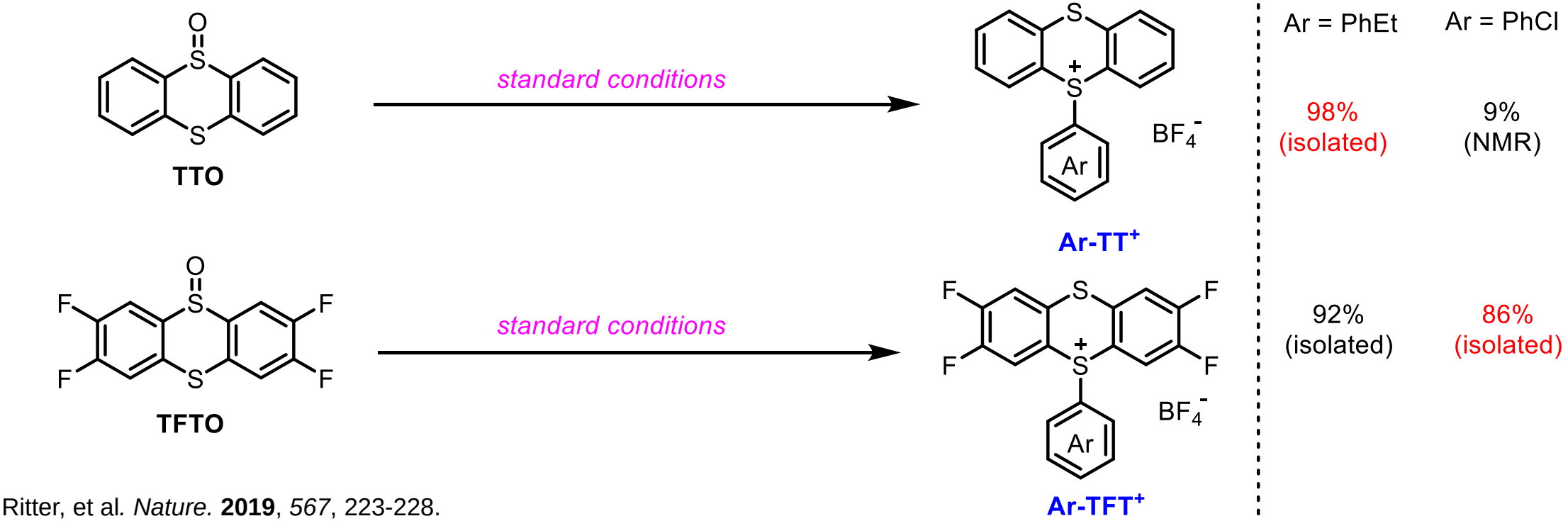
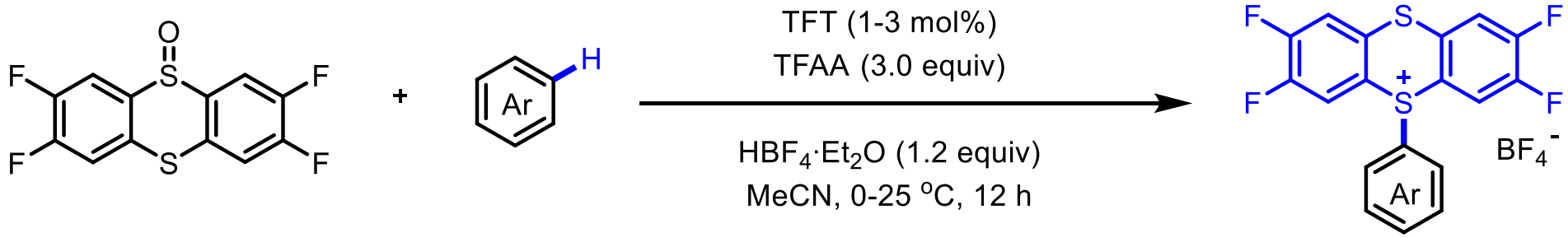
2.1.1 芳基噻蒽鎓盐





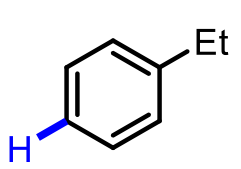
T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.1 芳基噻蒽鎓盐——底物拓展

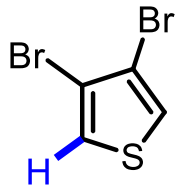


TFTO

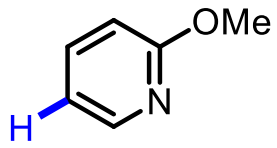
30 examples, 20-95% yield



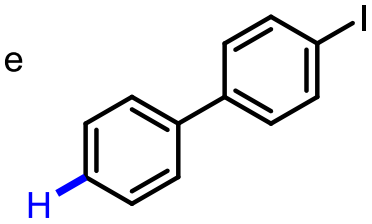
92%



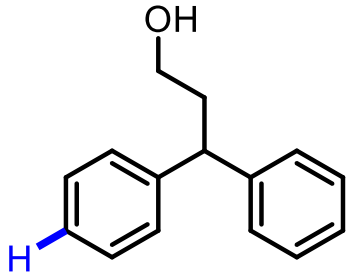
68%



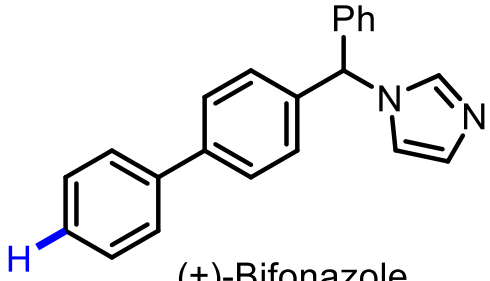
87%



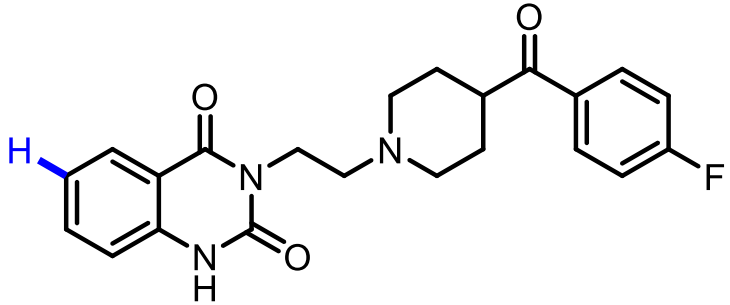
59%



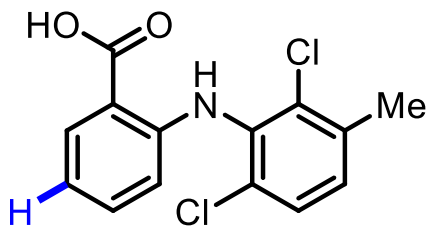
76%



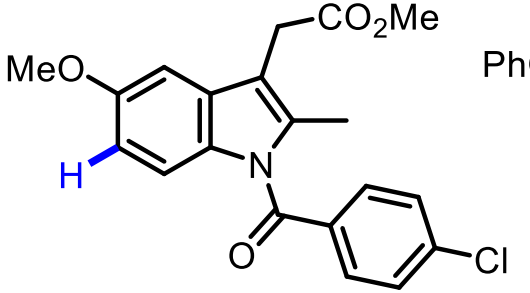
(±)-Bifonazole
67%



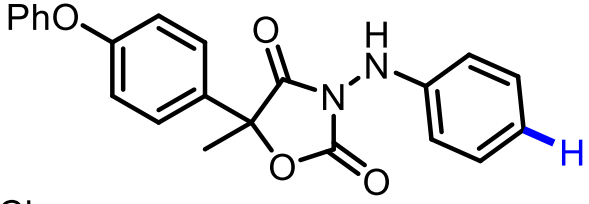
Ketanserin
84%



Meclofenamic acid
87%



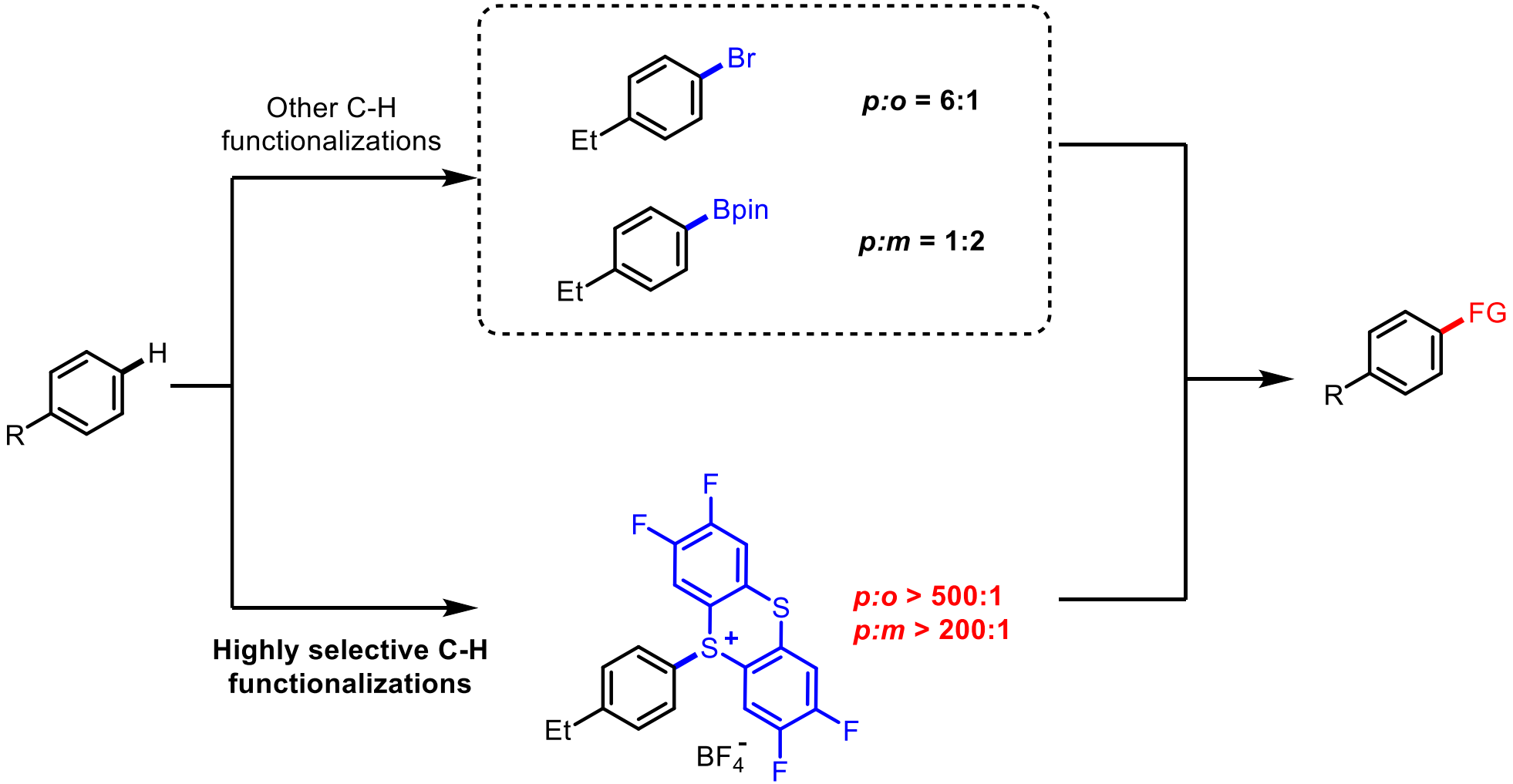
Indometacin methylester
85%



(±)-Famoxadone
81%

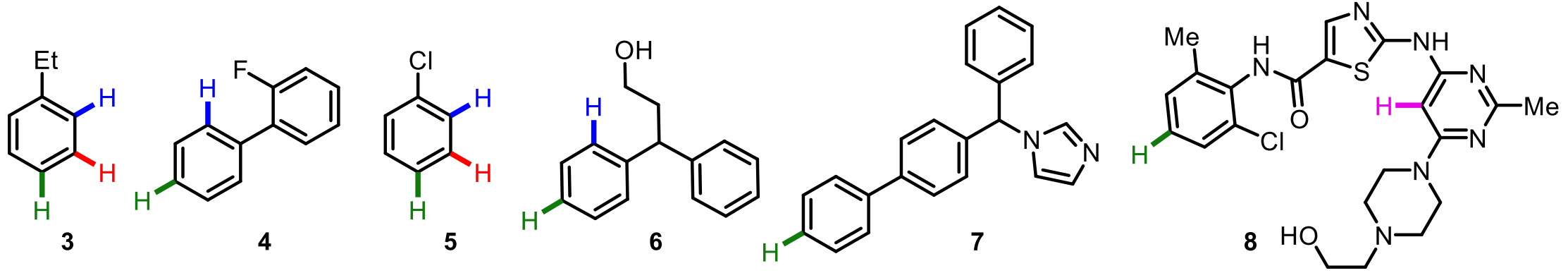
T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.1 芳基噻蒽鎓盐——区域选择性



T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.1 芳基噻蒽鎓盐——区域选择性



	Ar-TFT$^+$	$FeCl_3$ Br_2	$AuCl_3$ NBS	NBS HFIP	Ph_3PS NBS
3	●	◔	◔	◔	○
4	●	◔	◔	◔	○
5	●	○	◔	○	○
6	●	○	◔	◔	○
7	●	🌈	🌈	🌈	🌈
8	●	●	●	●	●

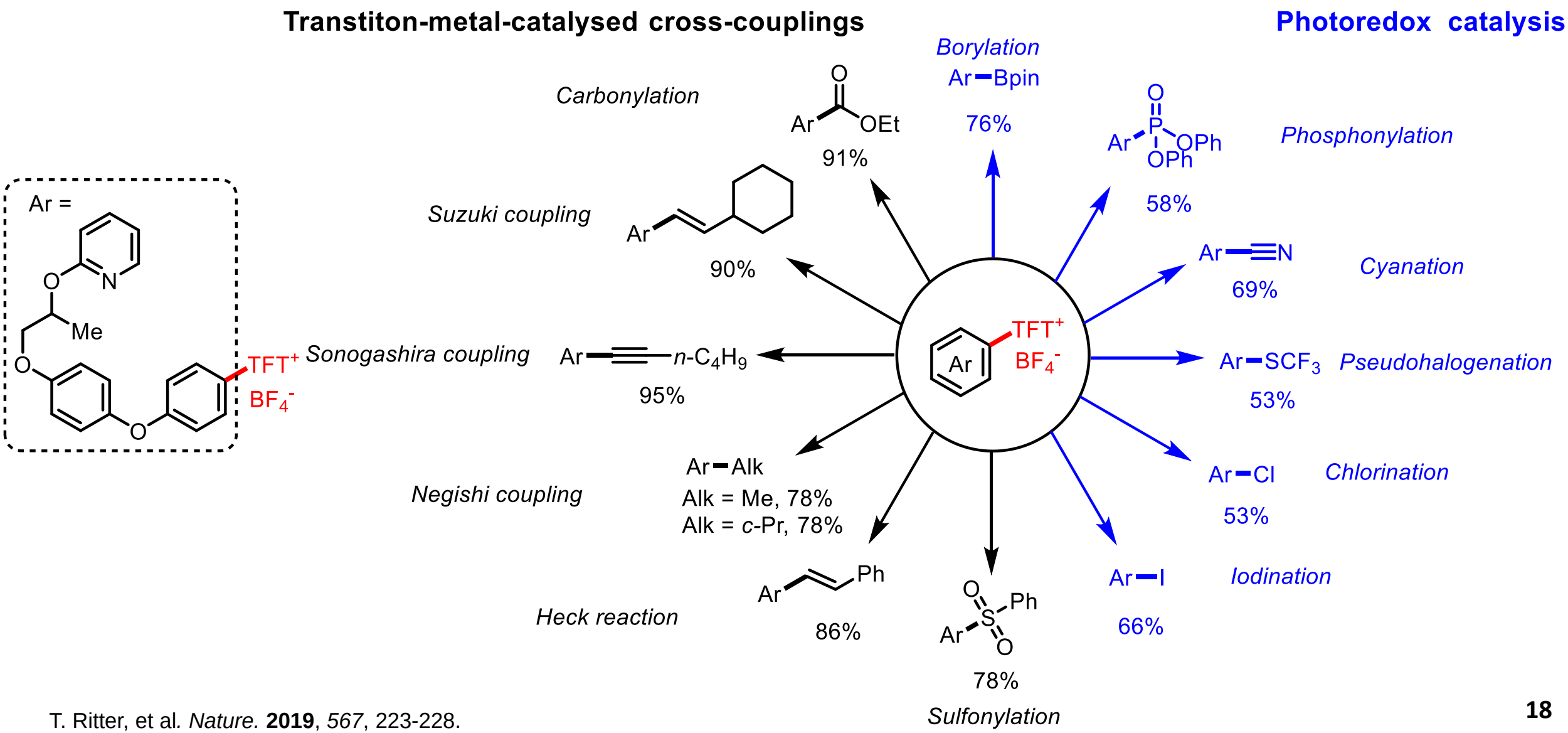
● position of reaction *p* • *o*/*m* •••

🌈 complex mixture

○ no reaction

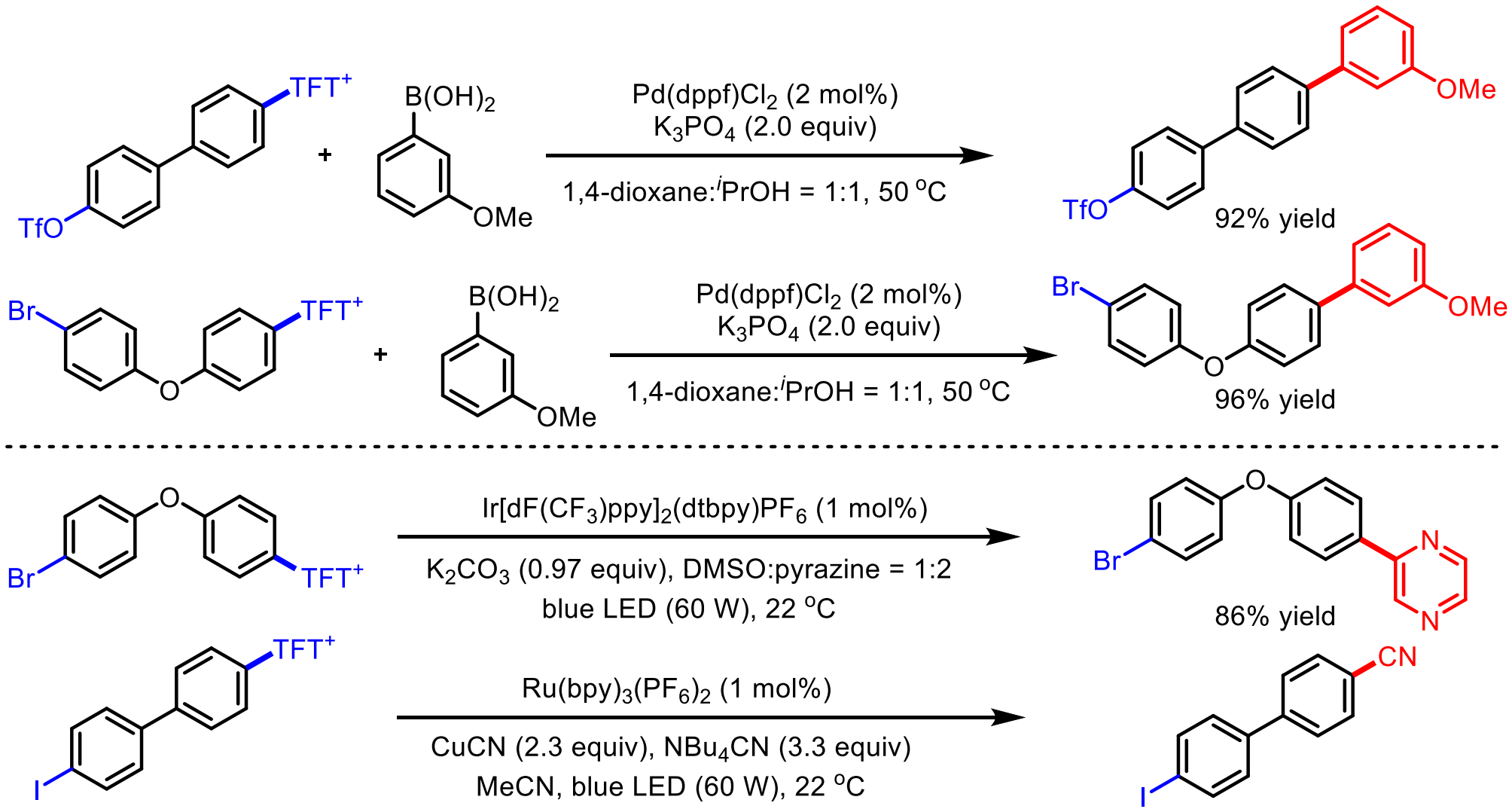
T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.1 芳基噻蒽鎓盐——官能团转化的初步探究



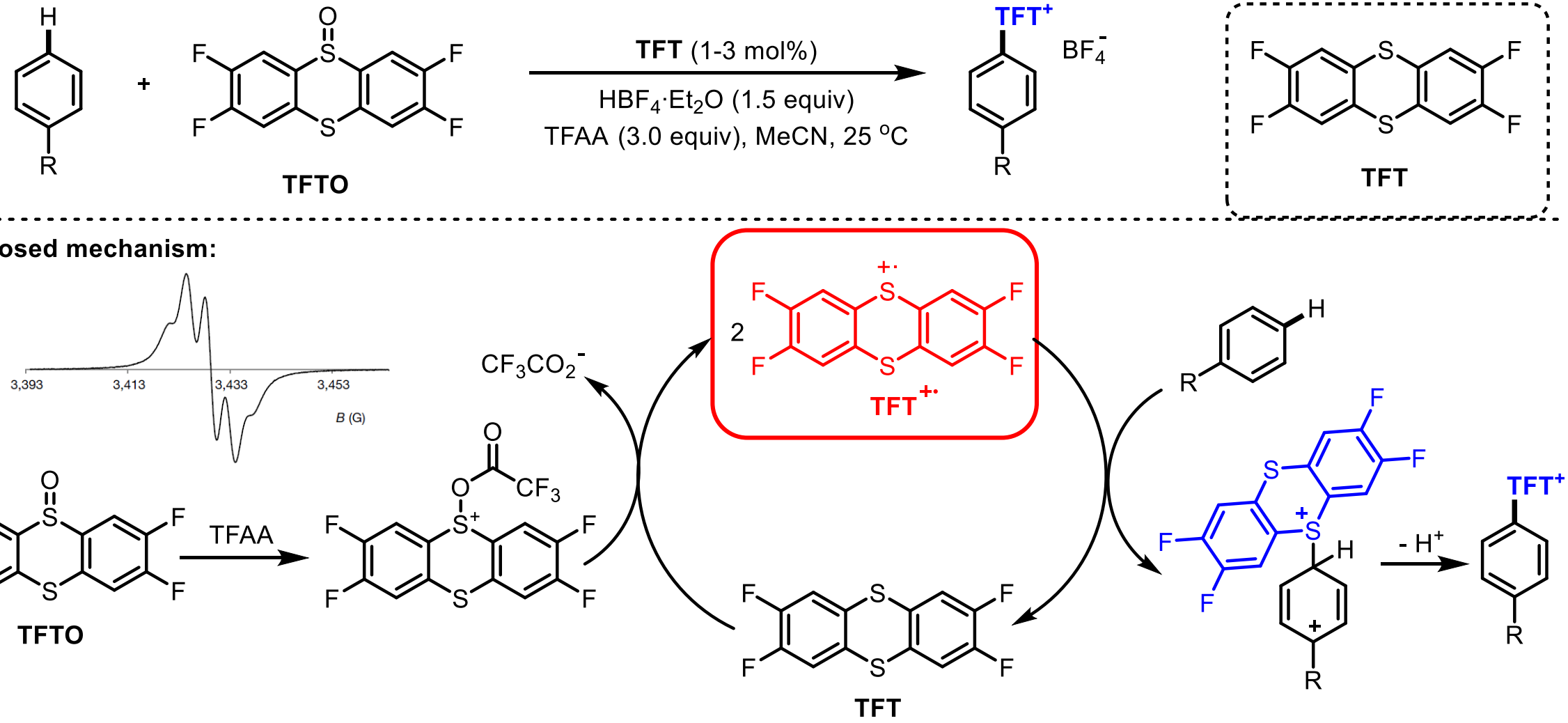
T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.1 芳基噻蒽鎓盐——官能团转化的初步探究



T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

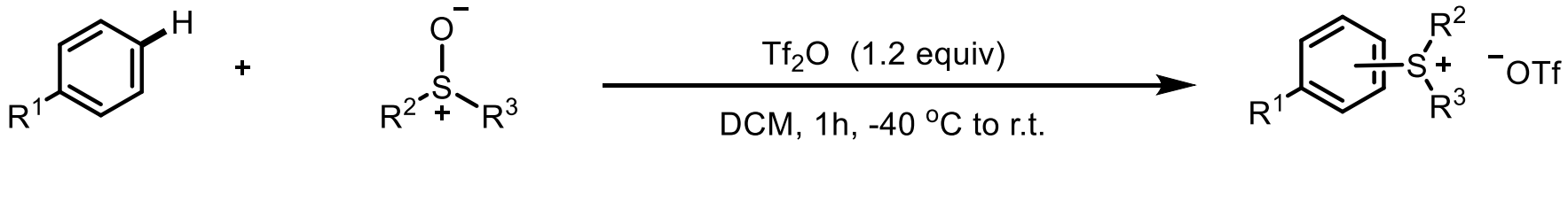
2.1.1 芳基噻蒽鎓盐——机理的初步探究

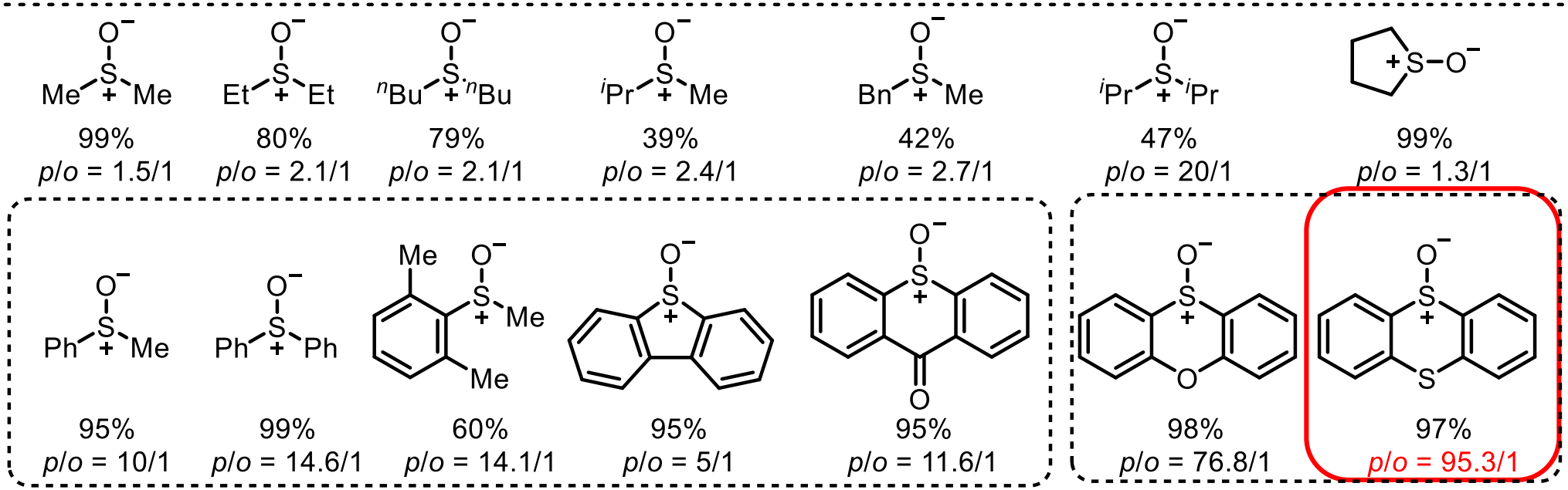


T. Ritter, et al. *Nature.* **2019**, *567*, 223-228.

2.1.2 芳基噻蒽鎓盐——构建C-B键

Wang (2020)





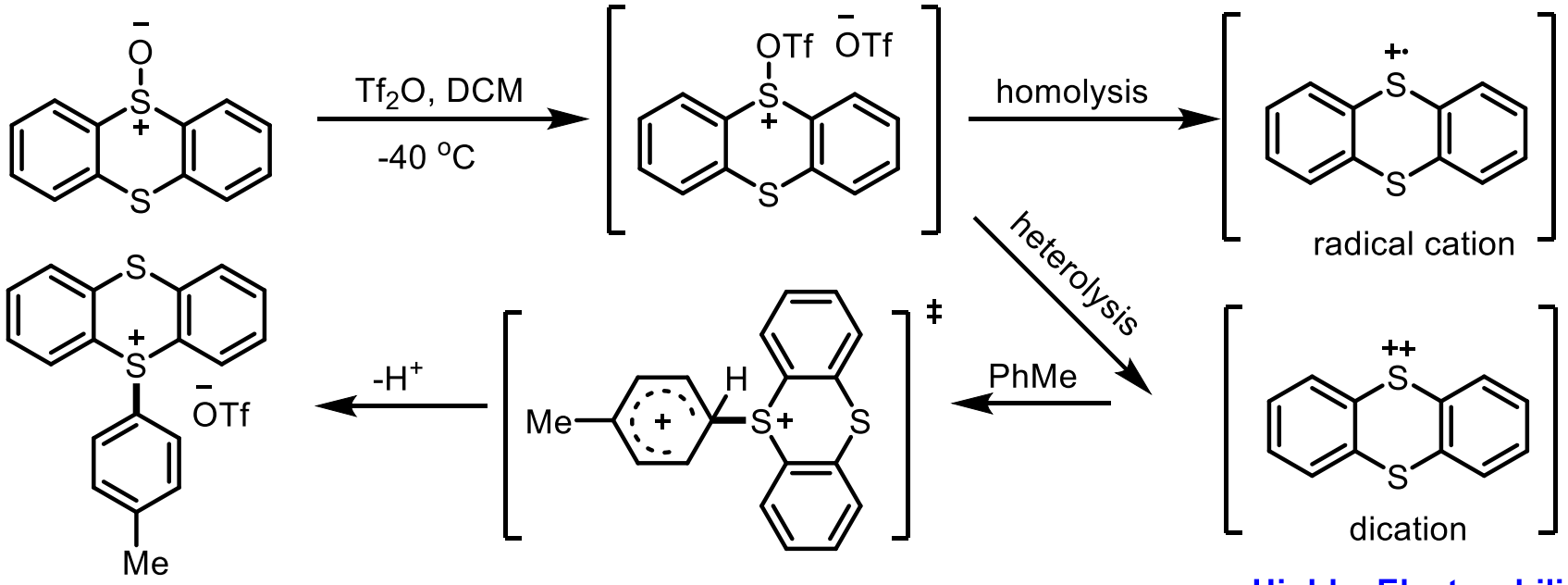
SEAr Process (EPR Slience)

Radical Cation Detected

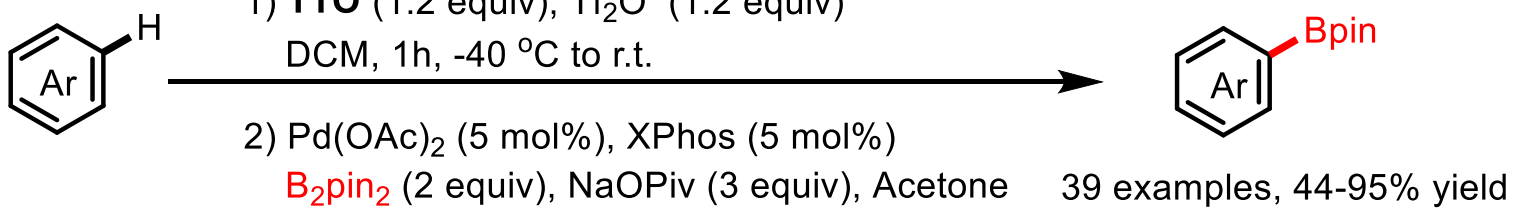
P. Wang, et al. *Sci. China Chem.* **2020**, *63*, 336-340;

2.1.2 芳基噻蒽鎓盐——构建C-B键

Proposed mechanism:



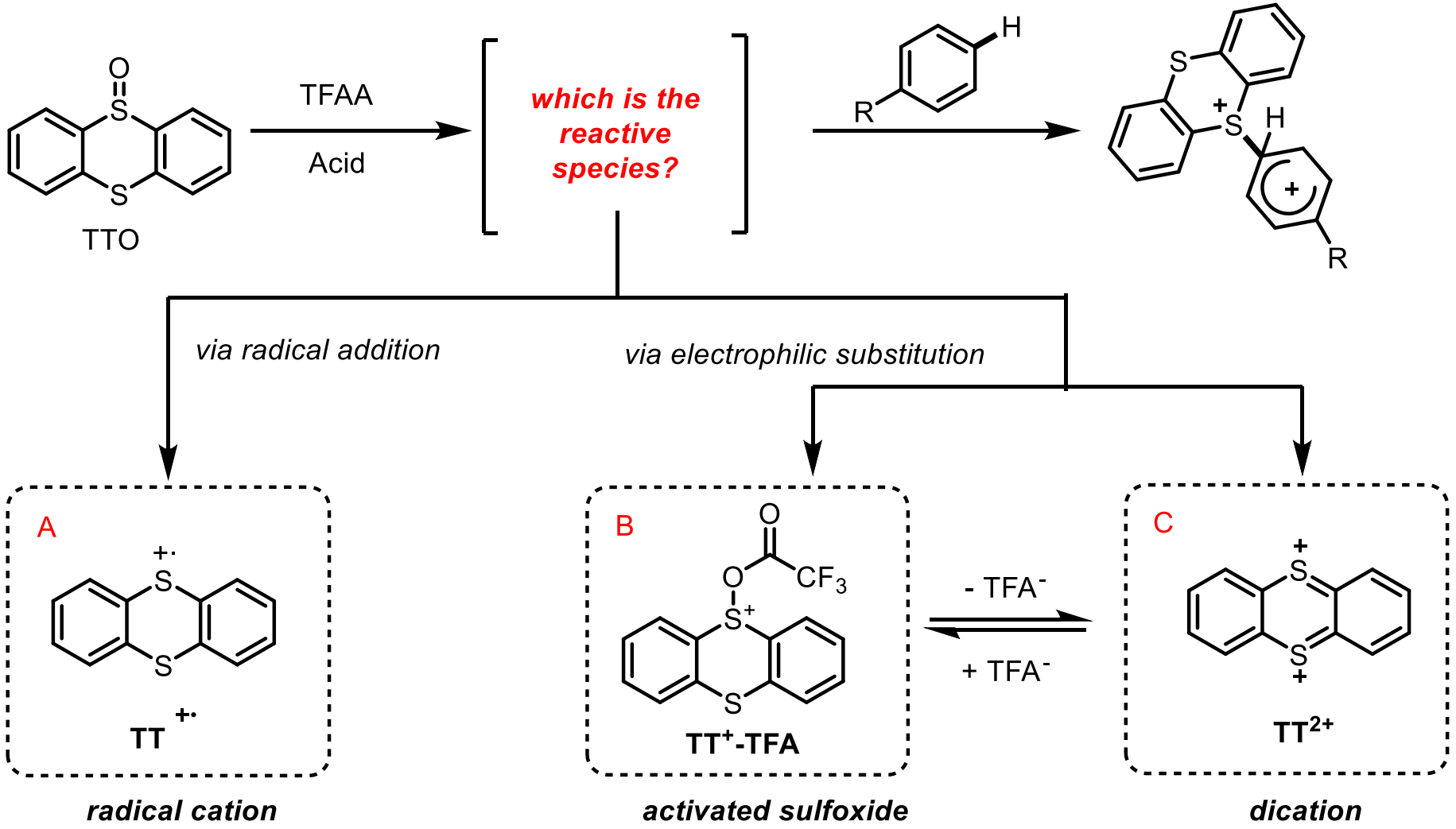
Wang (2020)



without removal of acid and solvent

P. Wang, et al. *Sci. China Chem.* **2020**, *63*, 336-340;
P. Wang, et al. *Chin. J. Chem.* **2020**, *38*, 1269-1272.

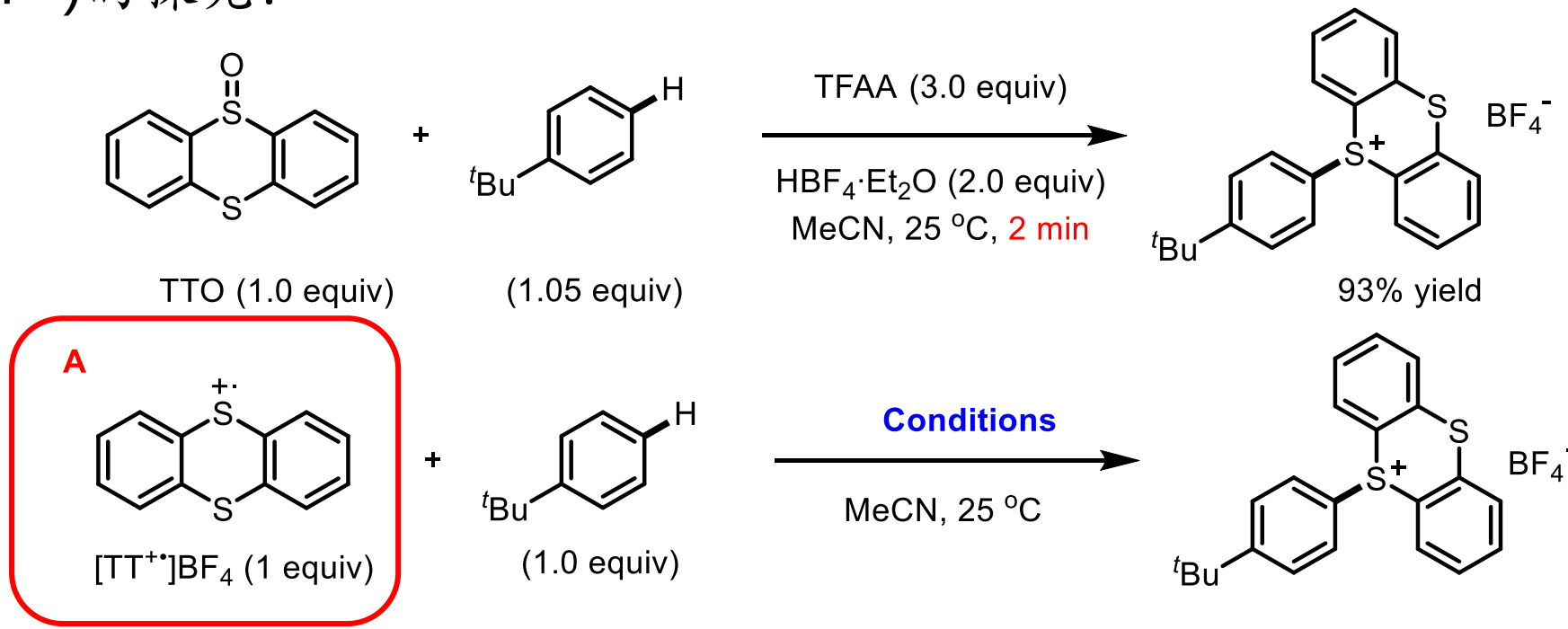
2.1.3 芳基噻蒽鎓盐——机理的进一步探究



T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 16041-16054.

2.1.3 芳基噻蒽鎓盐——机理的进一步探究

对中间体A($TT^{+\cdot}$)的探究：



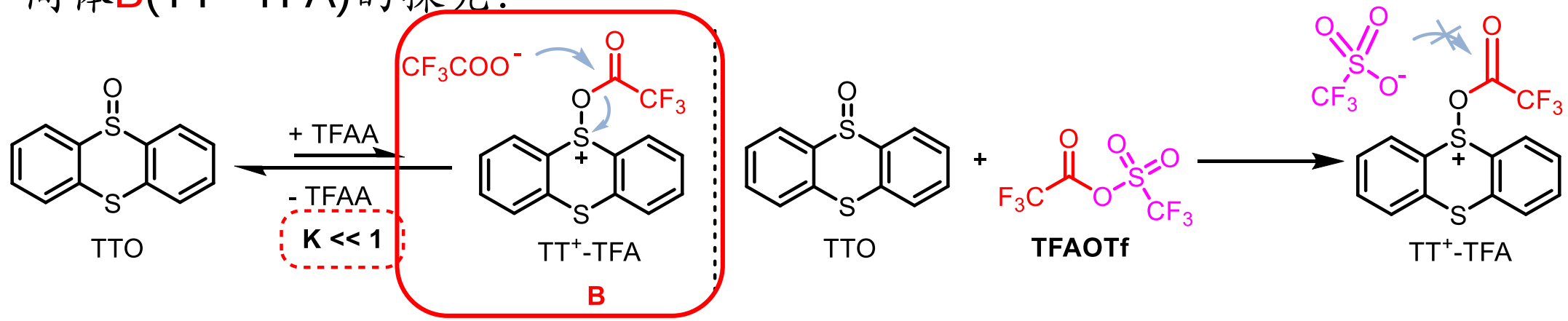
Entry	Conditions	Yield after 2 min	Yield after 24 h
1	no additives	n.d.	8%
2	TFAA (3 equiv), $HBF_4 \cdot Et_2O$ (2 equiv)	n.d.	11%

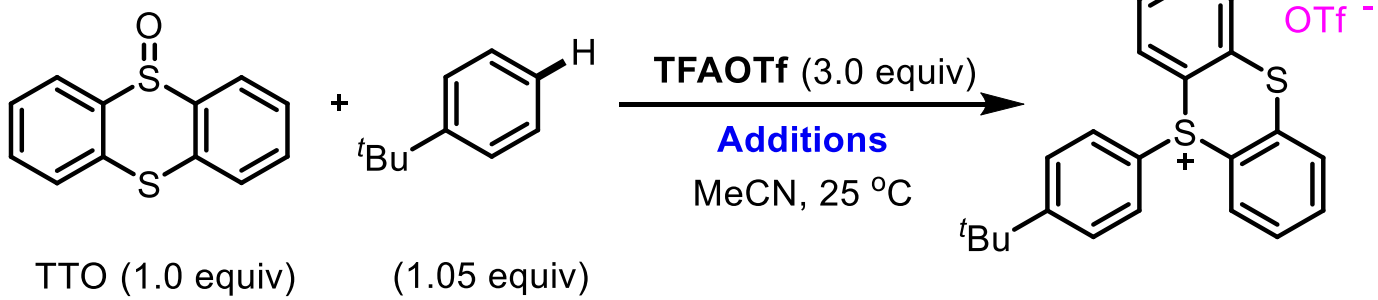
结论：中间体A不是活性中间体

T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 16041-16054.

2.1.3 芳基噻蒽鎓盐——机理的进一步探究

对中间体B(TT$^+$-TFA)的探究：





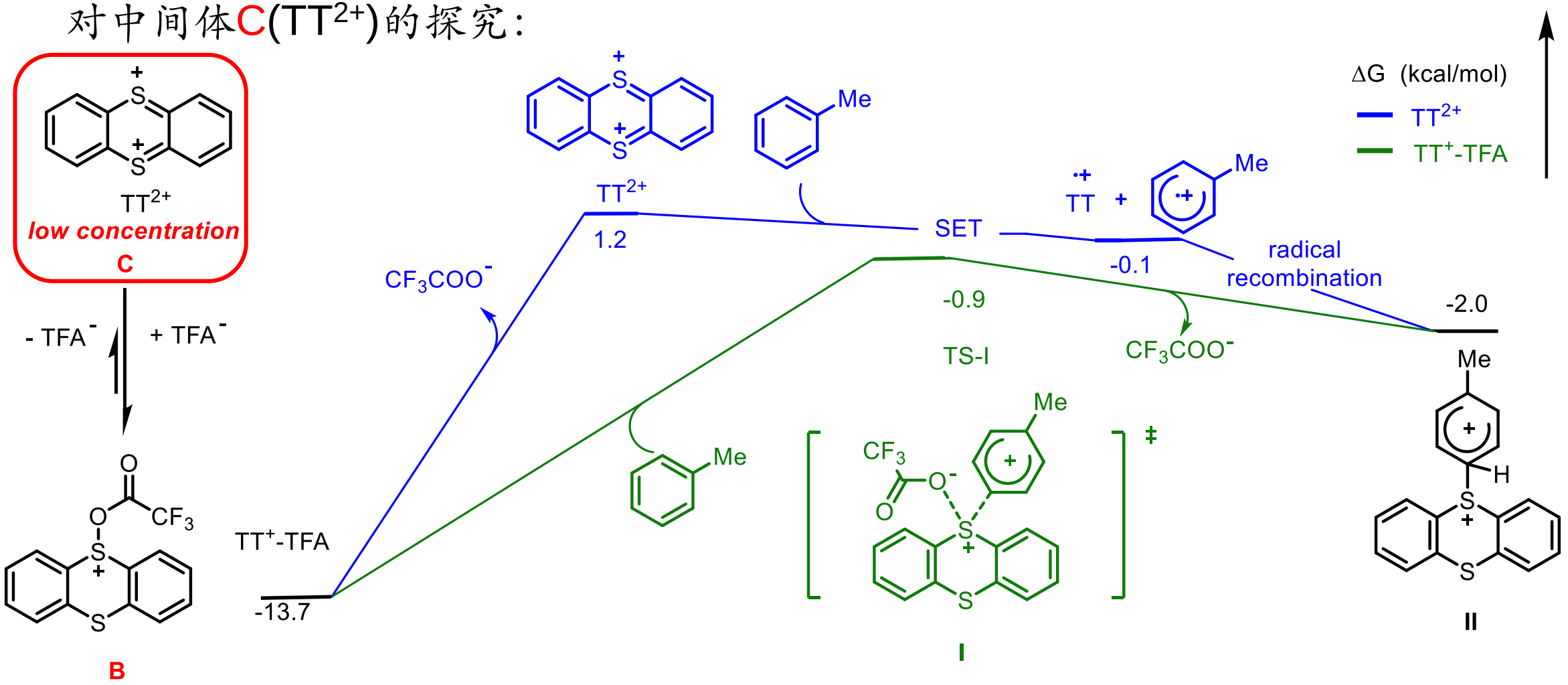
Entry	Additions	Yield
1	none	95%
2	TFAOTf (1.2 equiv)	89%
3	+ K_2CO_3 (3.5 equiv)	78%
4	+ 2,6-^{t}Bu$_2$py (3.5 equiv)	71%

结论：中间体B是活性中间体

T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 16041-16054.

2.1.3 芳基噻蒽鎓盐——机理的进一步探究

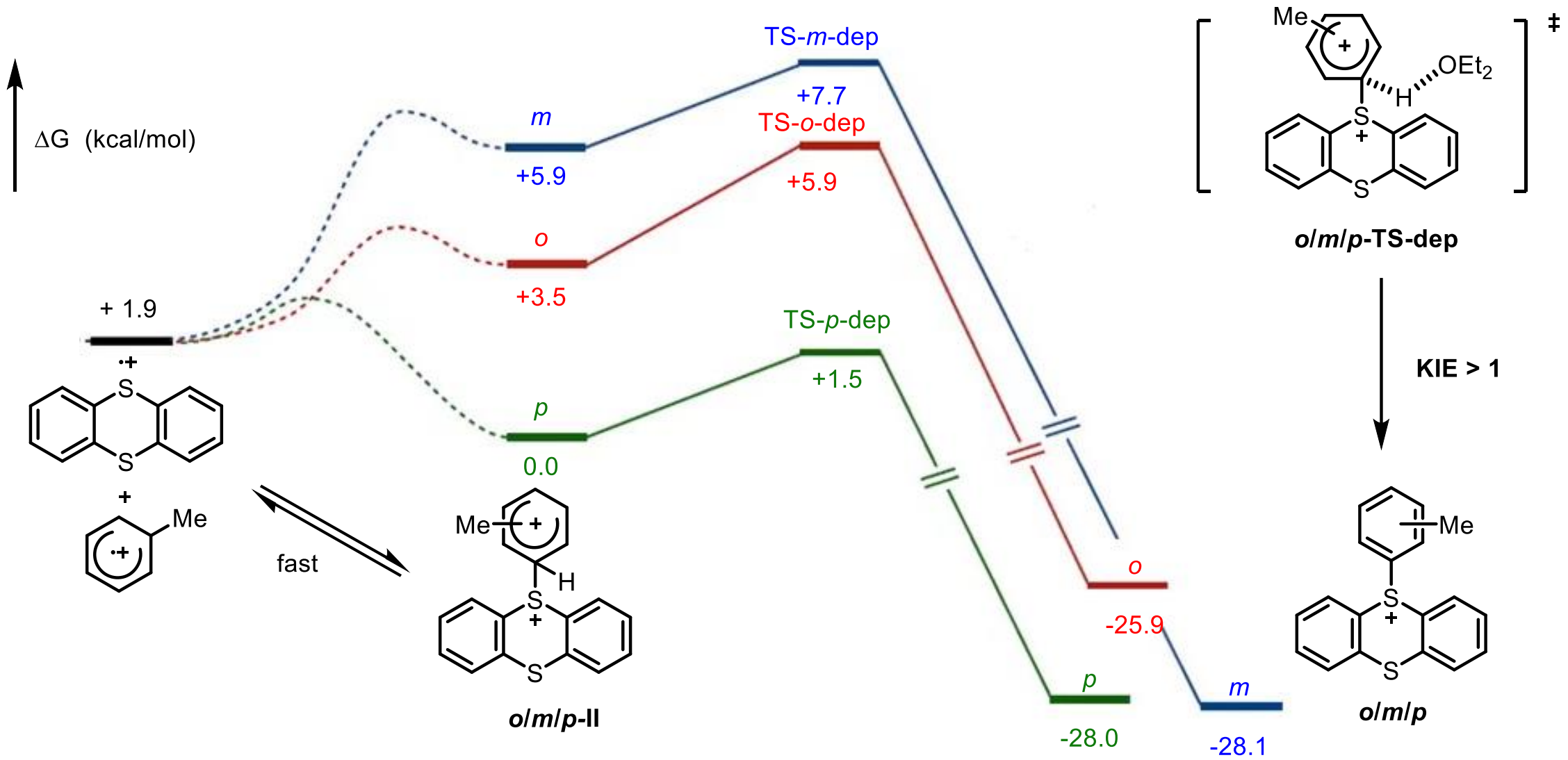
对中间体C(TT^{2+})的探究：



结论：中间体C也是活性中间体

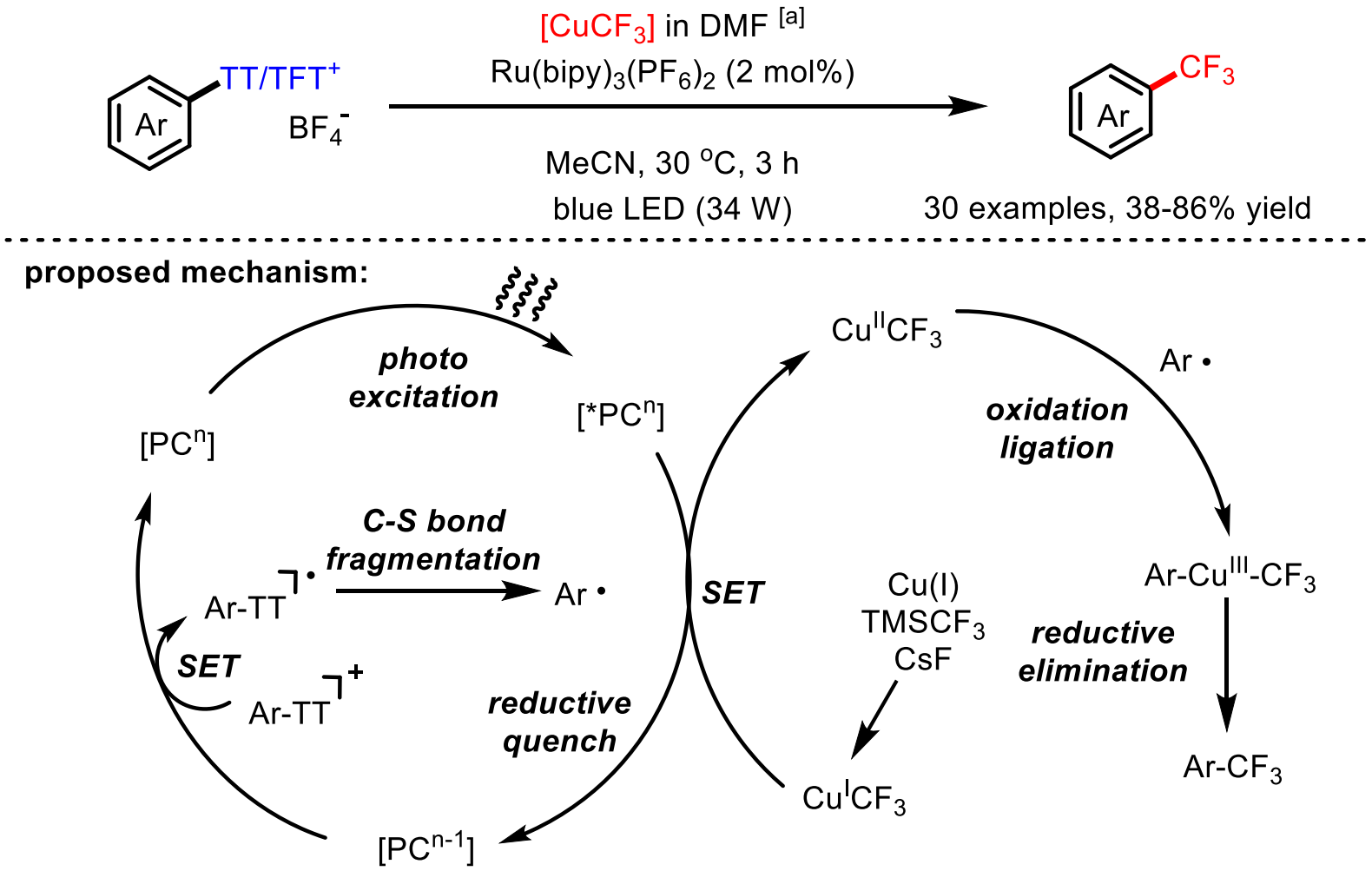
T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 16041-16054.

2.1.3 芳基噻蒽鎓盐——机理的进一步探究



T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 16041-16054.

2.1.4 芳基噻蒽鎓盐——构建C-CF_3键

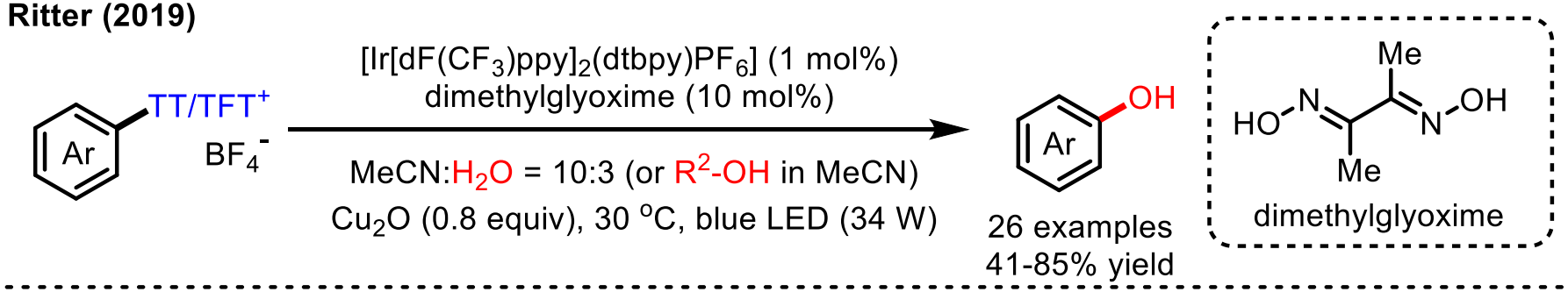


[a] CuSCN (1.5 equiv), CsF (2.0 equiv), $TMSCF_3$ (1.5 equiv) in DMF at 23 °C for 30 min

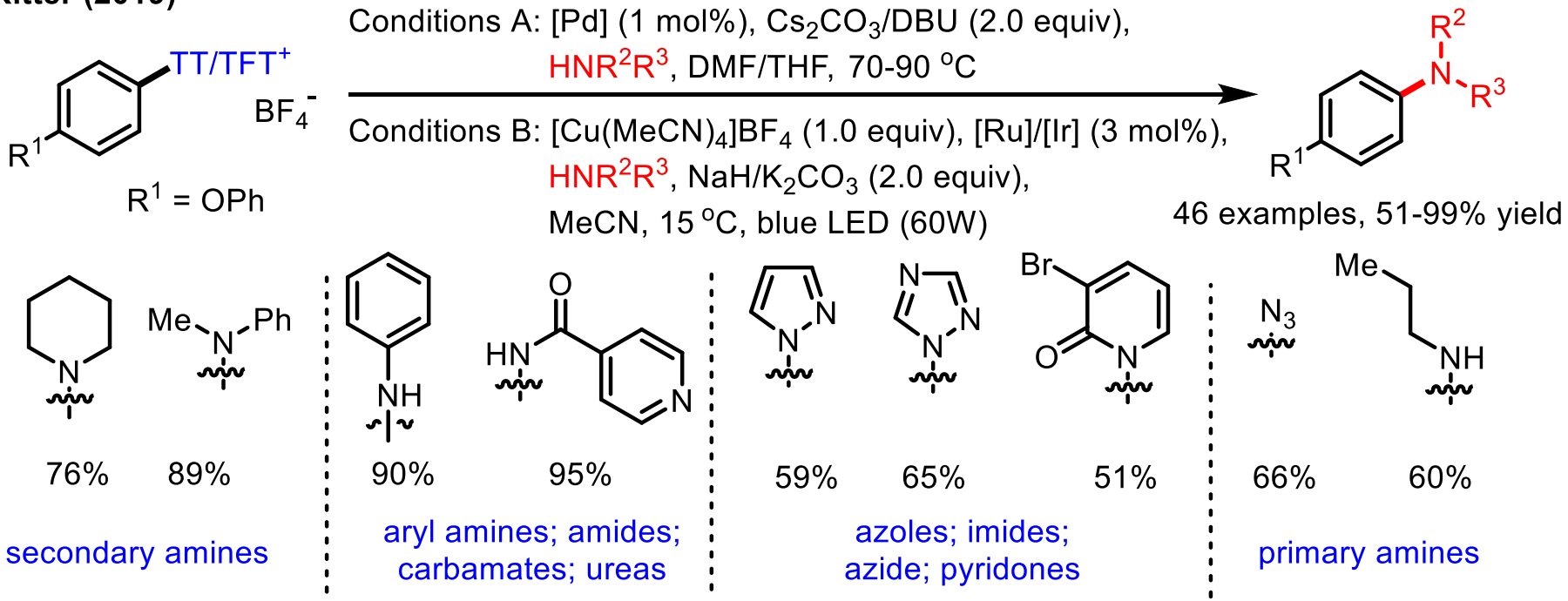
T. Ritter, et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 14615-14619.

2.1.5 芳基噻蒽鎓盐——构建C-O/C-N键

Ritter (2019)



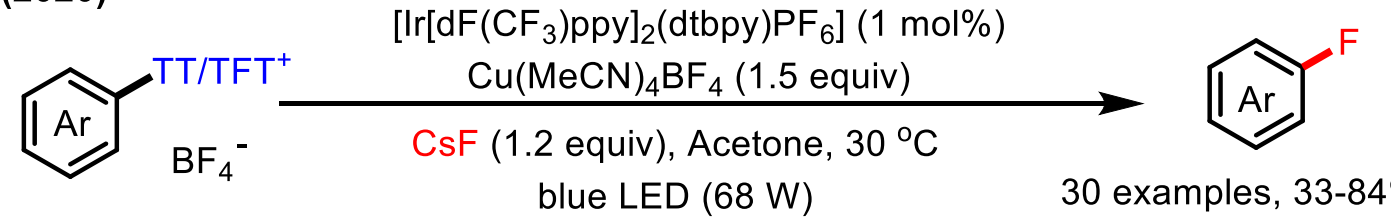
Ritter (2019)



T. Ritter, et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 16161-16166;
T. Ritter, et al. *J. Am. Chem. Soc.* **2019**, *141*, 13346-13351.

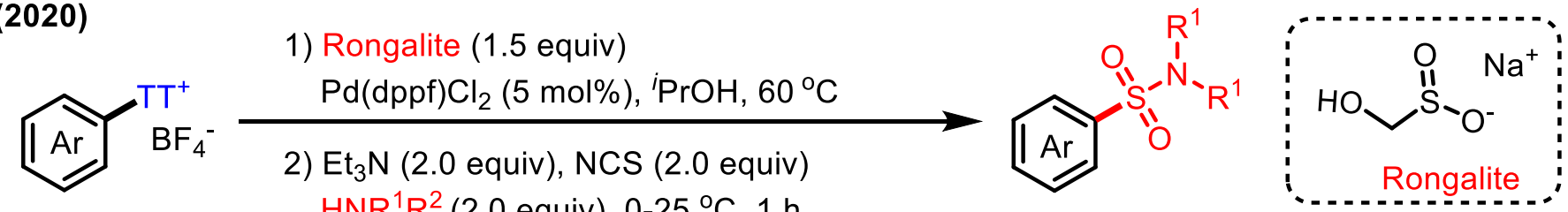
2.1.6 芳基噻蒽鎓盐——构建C-F/C-S/C-Ge键

Ritter (2020)



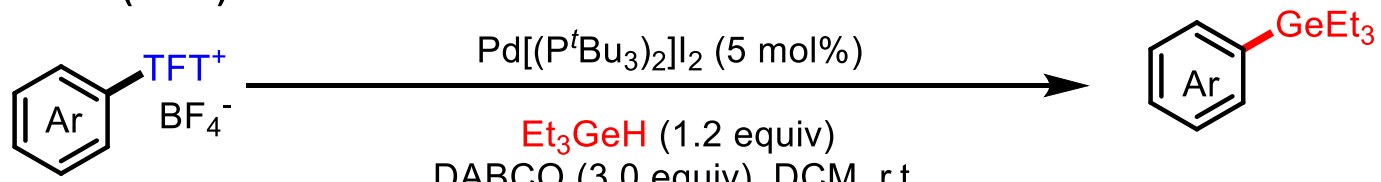
30 examples, 33-84% yield

Ritter (2020)



36 examples, 32-91% yield

Schoenebeck (2020)

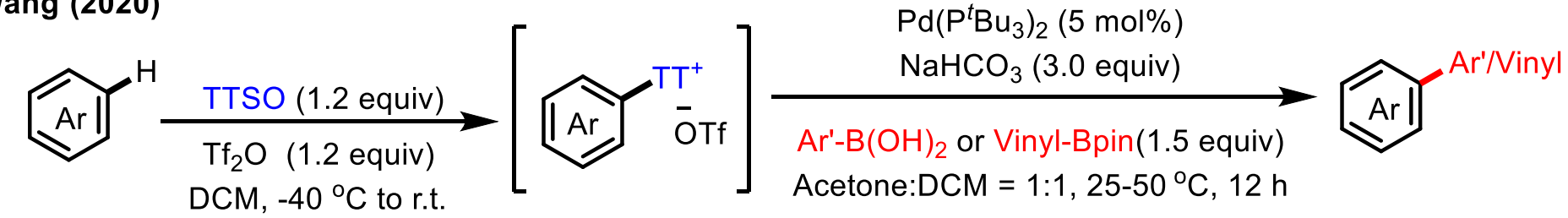


20 examples, 30-72% yield

T. Ritter, et al. *Nat. Chem.* **2020**, *12*, 56-62;
T. Ritter, et al. *Org. Lett.* **2020**, *22*, 4593-4596;
F. Schoenebeck, et al. *Org. Lett.* **2020**, *22*, 4802-4805.

2.1.7 芳基噻蒽鎓盐——构建C-C键

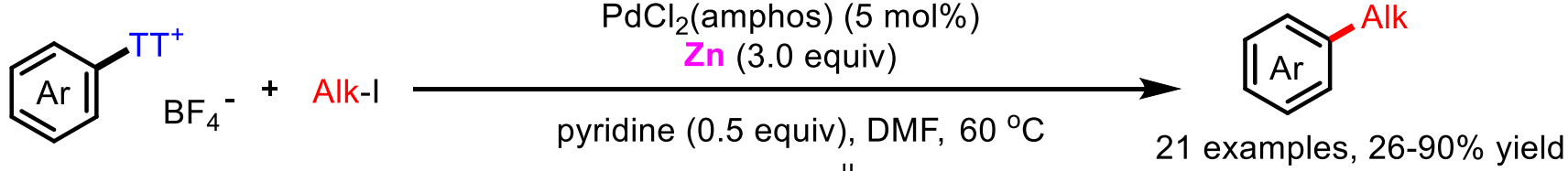
Wang (2020)



without removal of acid and solvent

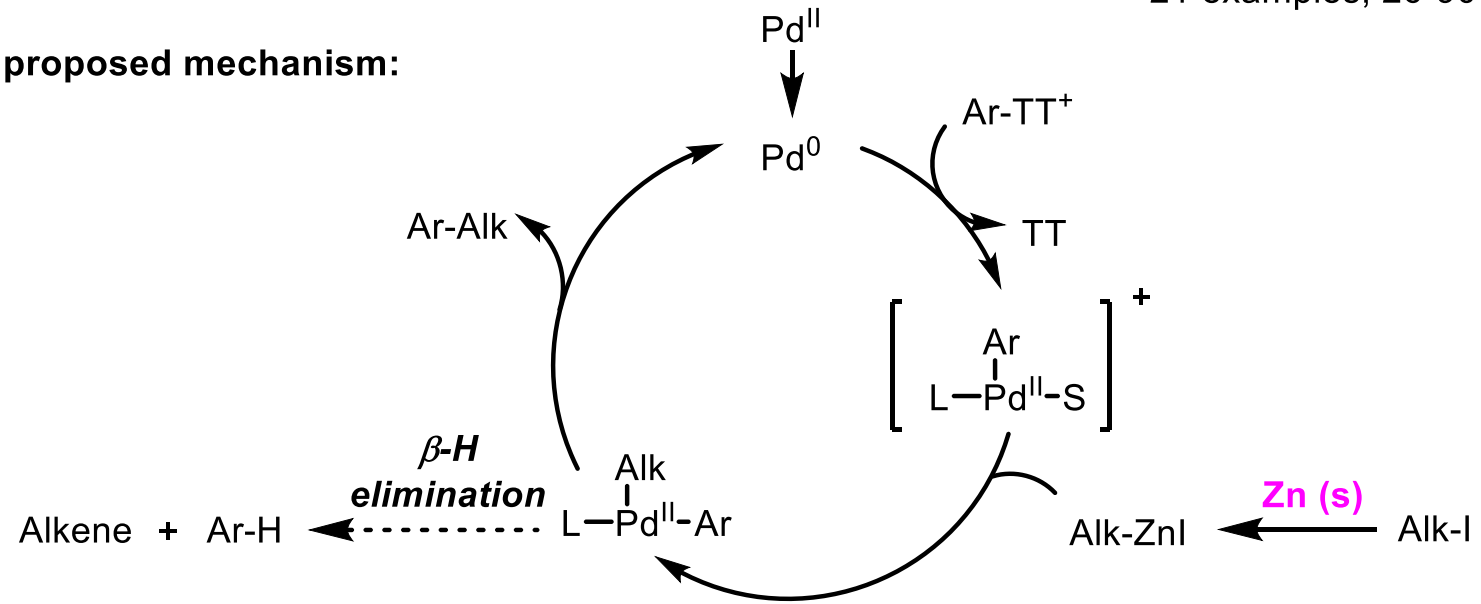
89 examples, 50-99% yield

Ritter (2021)



21 examples, 26-90% yield

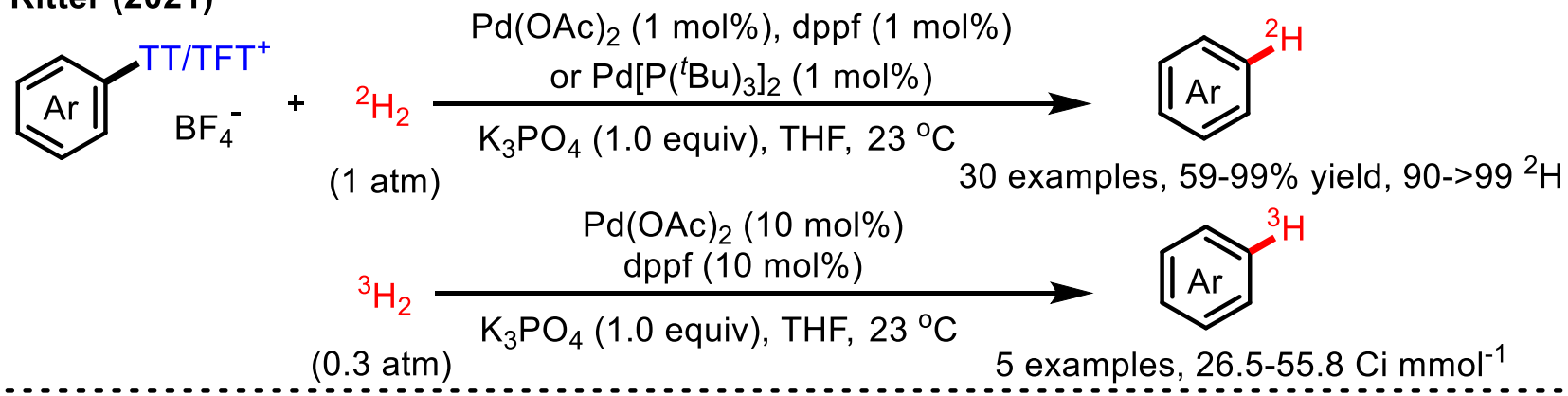
proposed mechanism:



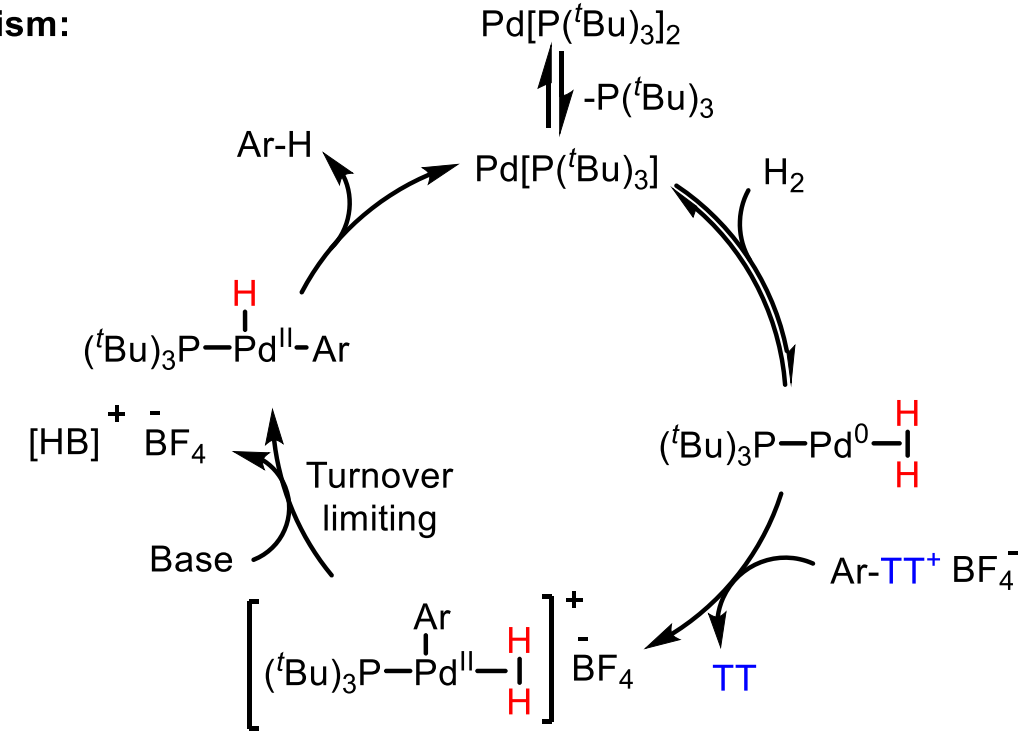
P. Wang, et al. *Chem. Commun.* **2020**, *56*, 5058-5061;
T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 7909-7914.

2.1.8 芳基噻蒽鎓盐——构建C-^{2}H/^{3}H键

Ritter (2021)



proposed mechanism:



T. Ritter, et al. *Nature* **2021**, *600*, 444-449.

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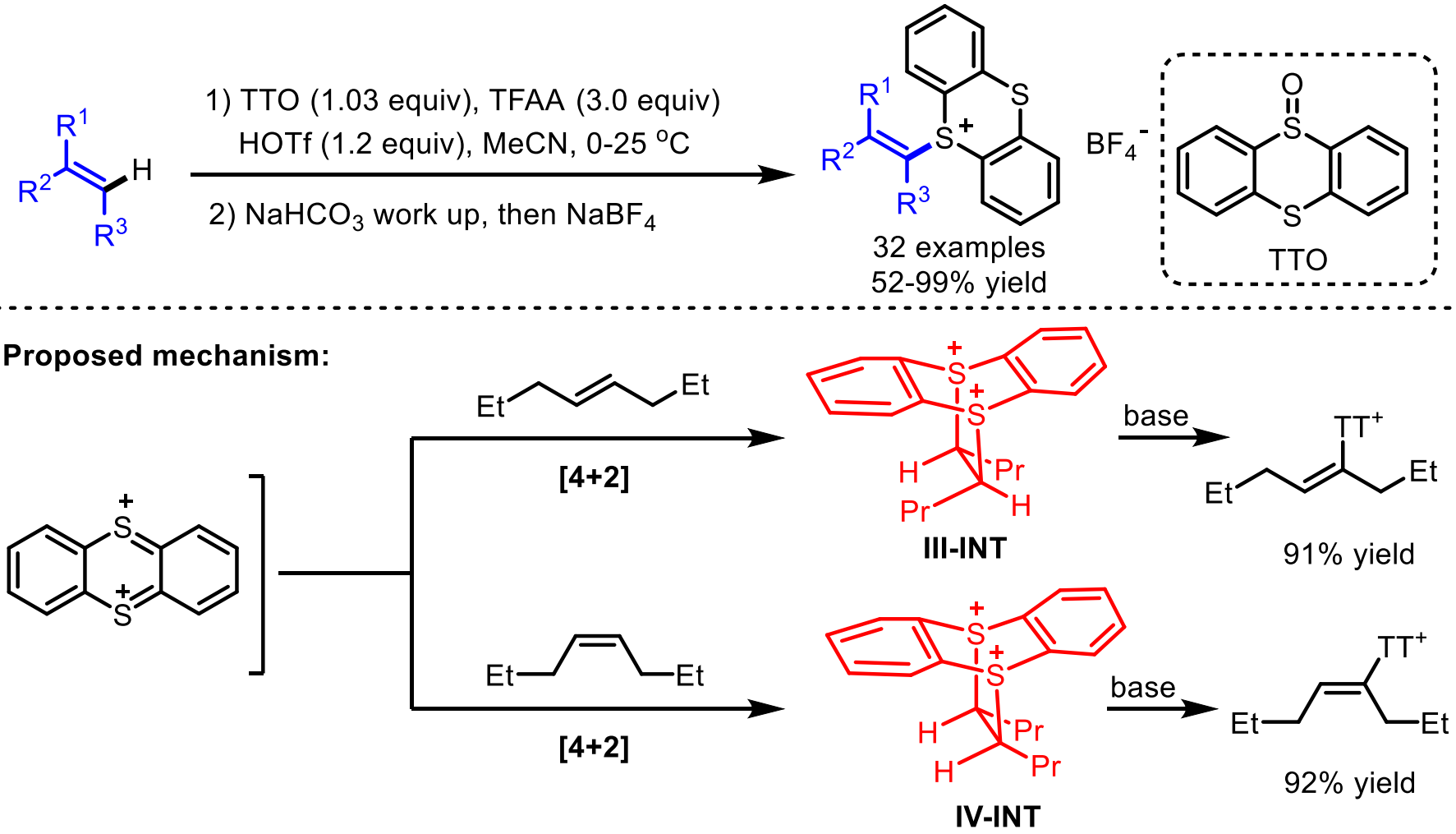
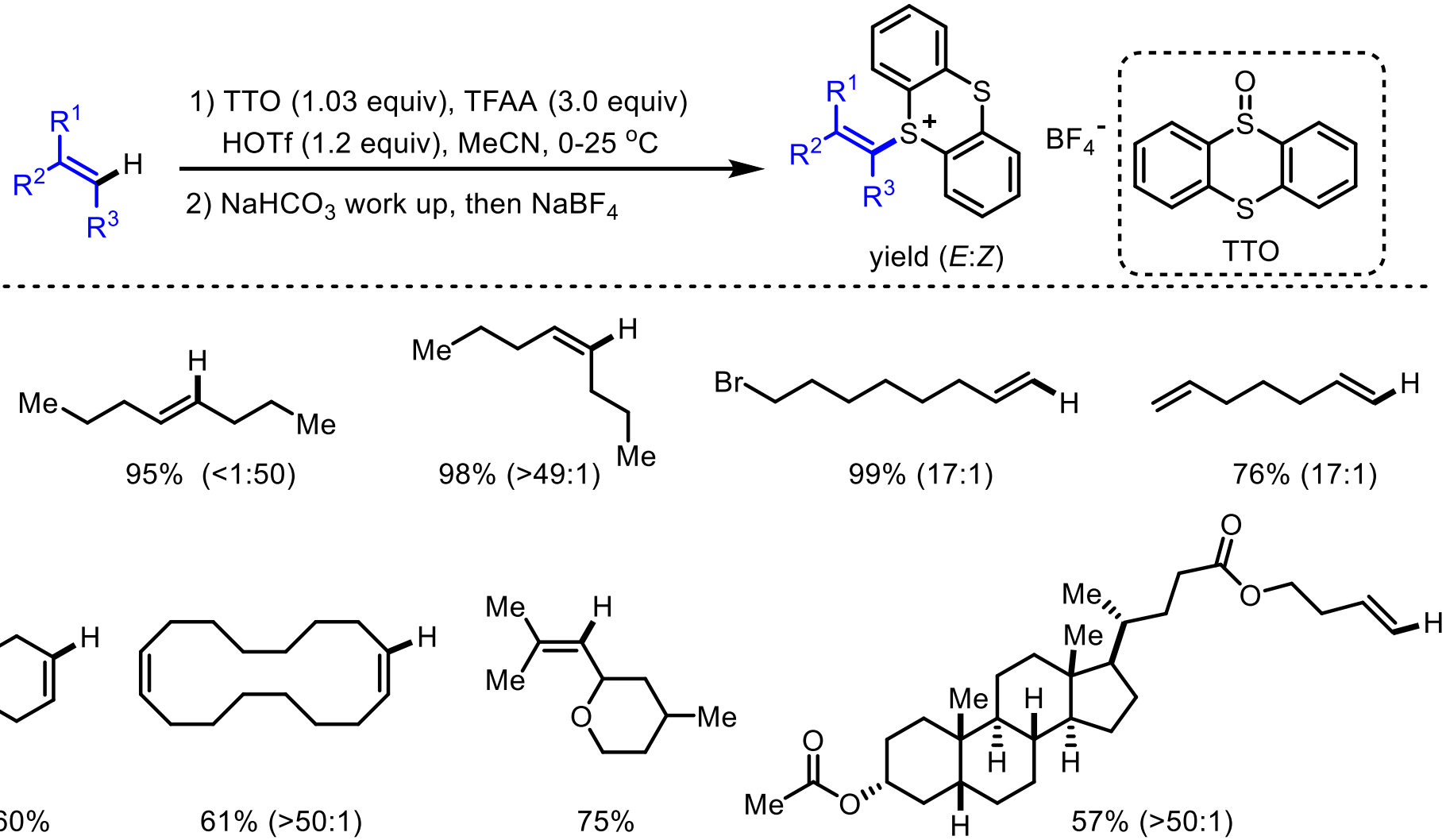
2.2.1 烯基噻蒽鎓盐——烯基亲电试剂



T. Ritter, et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 5616-5620.

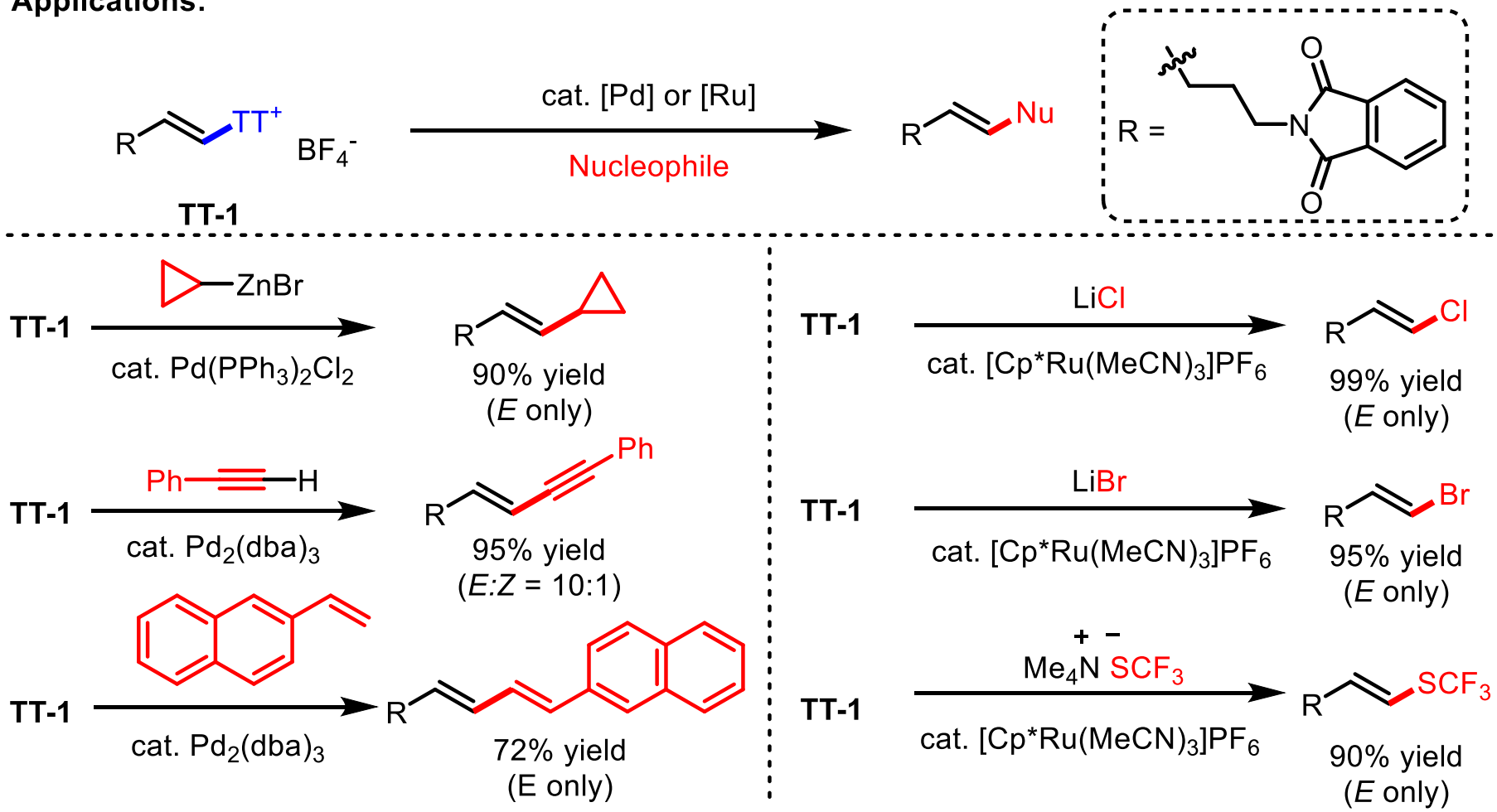
2.2.1 烯基噻蒽鎓盐——烯基亲电试剂



T. Ritter, et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 5616-5620.

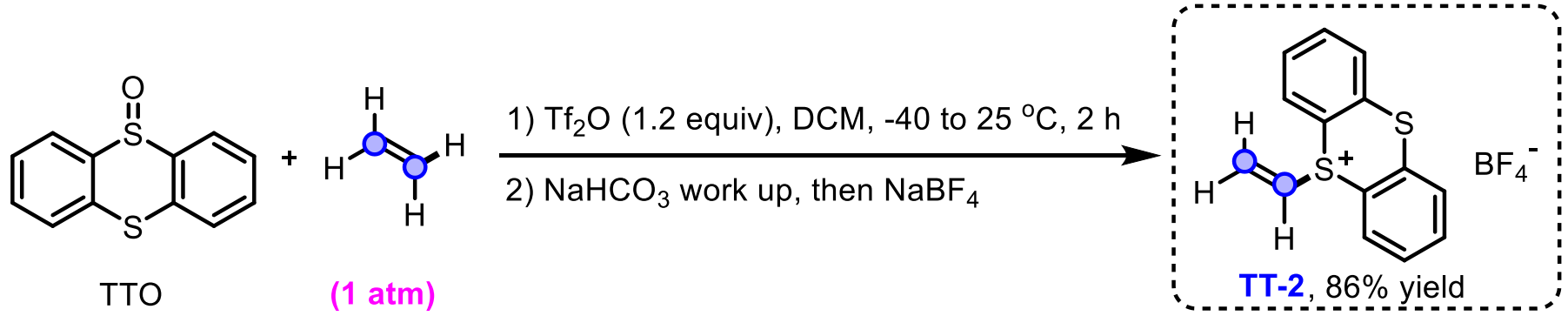
2.2.1 烯基噻蒽鎓盐——烯基亲电试剂

Applications:

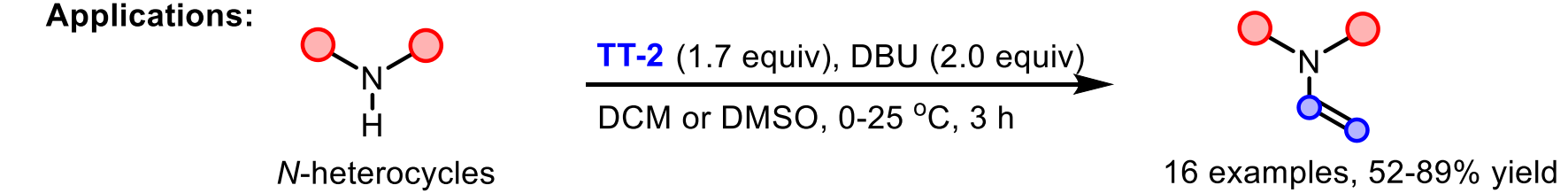


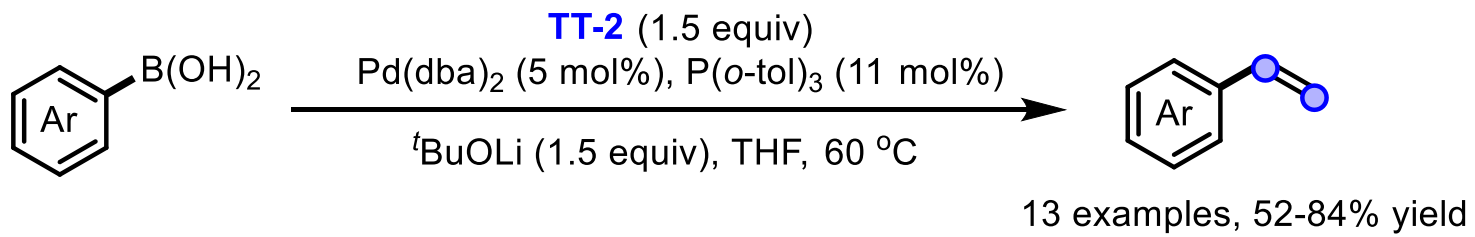
T. Ritter, et al. *Angew. Chem., Int. Ed.* **2020**, *59*, 5616-5620.

2.2.1 烯基噻蒽鎓盐——烯基亲电试剂



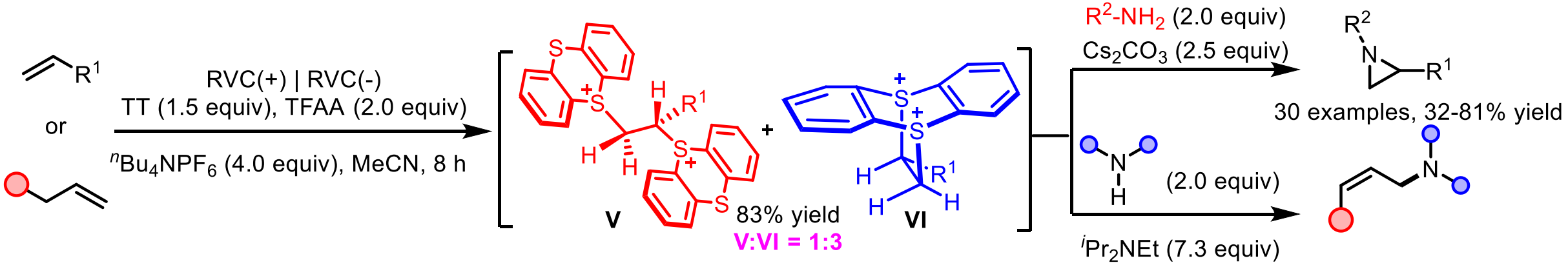
Applications:

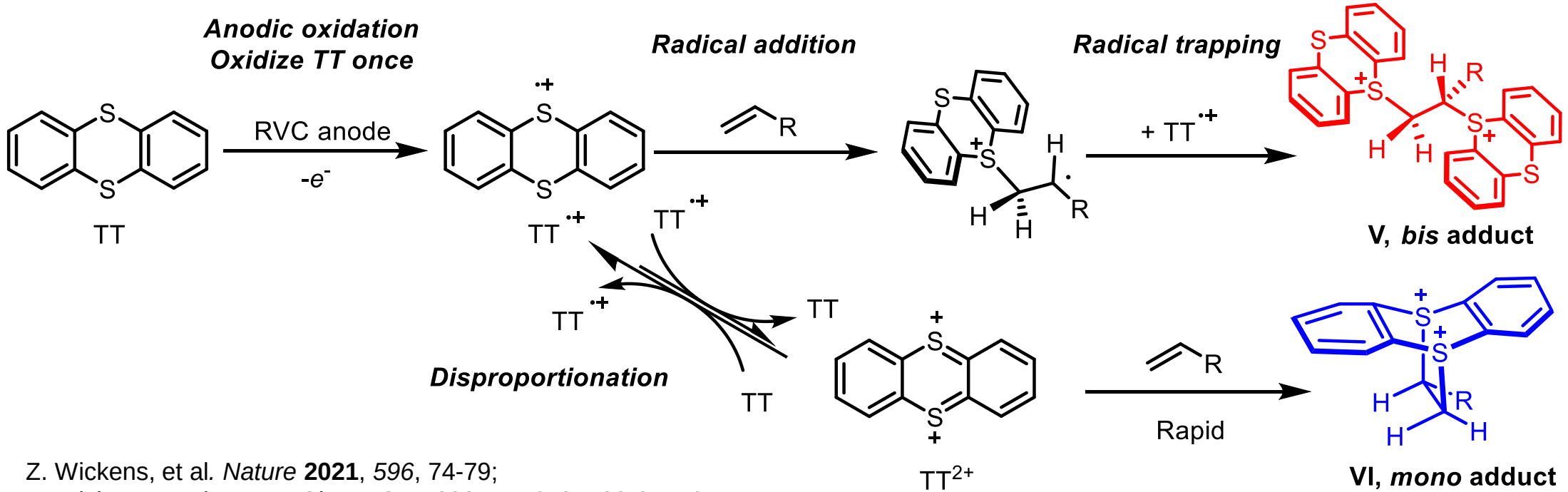




T. Ritter, et al. *J. Am. Chem. Soc.* **2021**, *143*, 12992-12998.

2.2.2 烯基噻蒽鎓盐——合成氮杂环丙烷/烯丙基胺

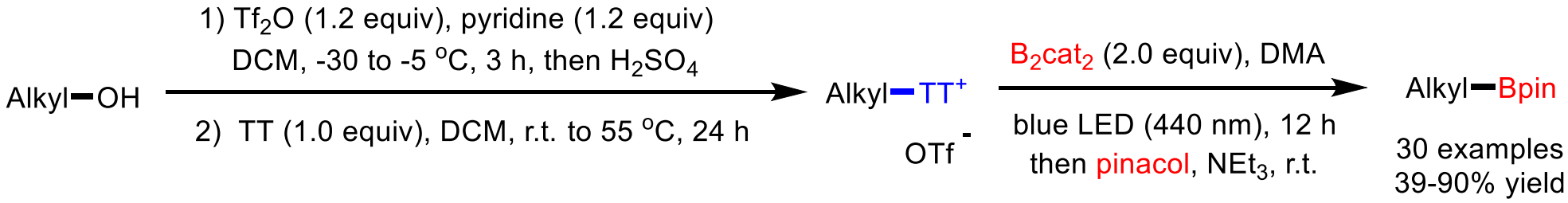




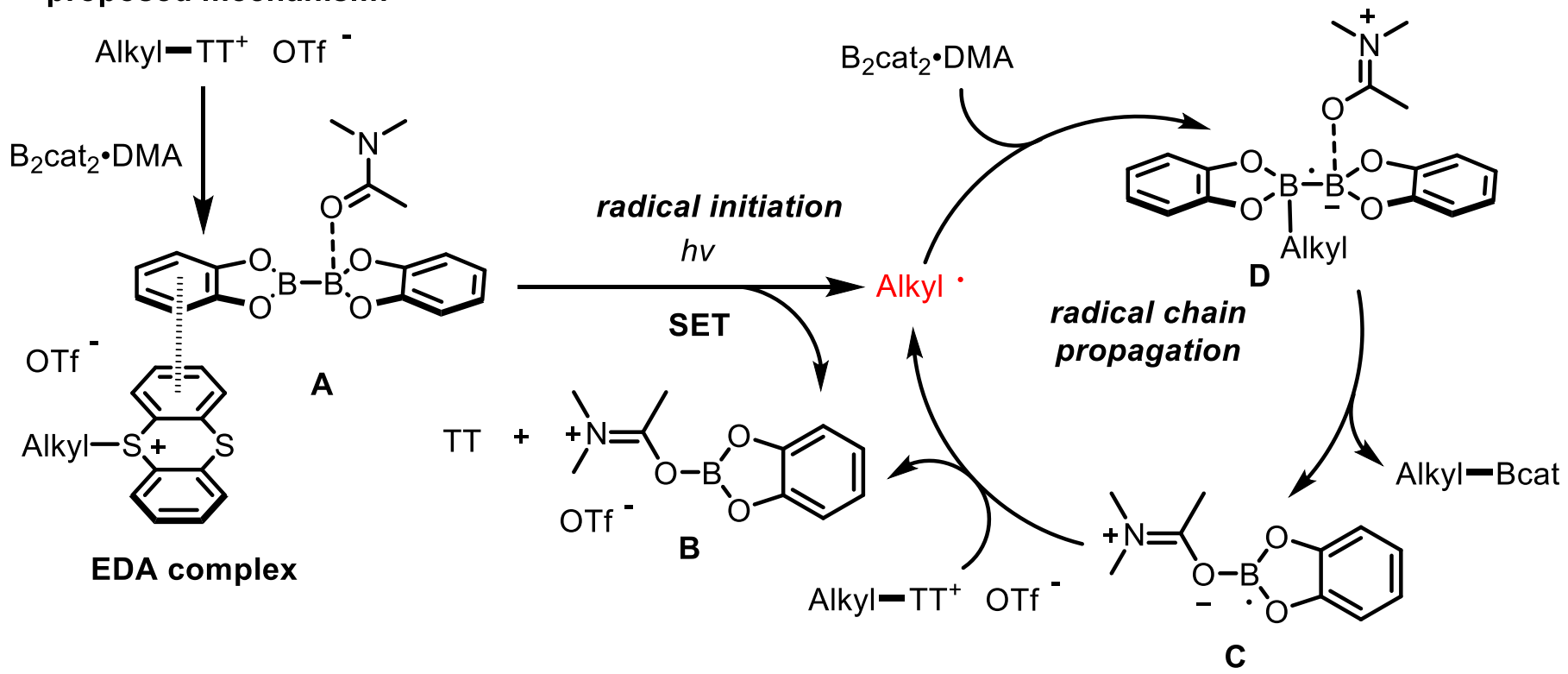
Z. Wickens, et al. *Nature* **2021**, *596*, 74-79;
Z. Wickens, et al. *J. Am. Chem. Soc.* **2021**, *143*, 21503-21510.

目录

2.3.1 烷基噻蒽鎓盐——构建C-B/C-C键



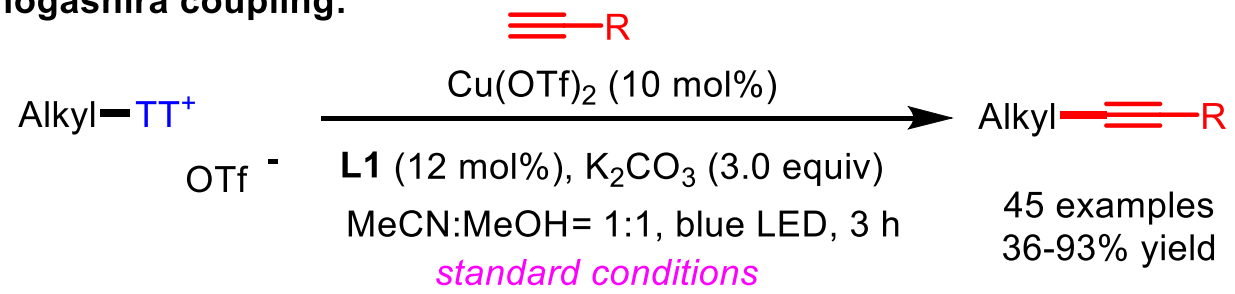
proposed mechanism:

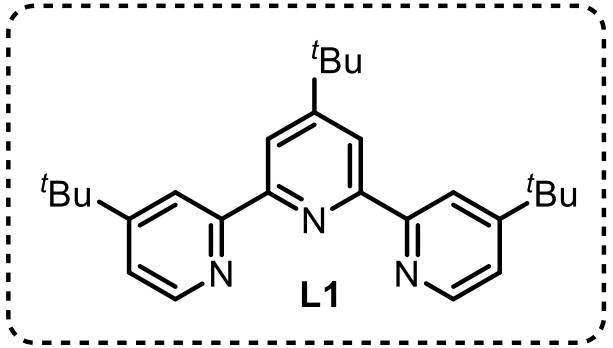


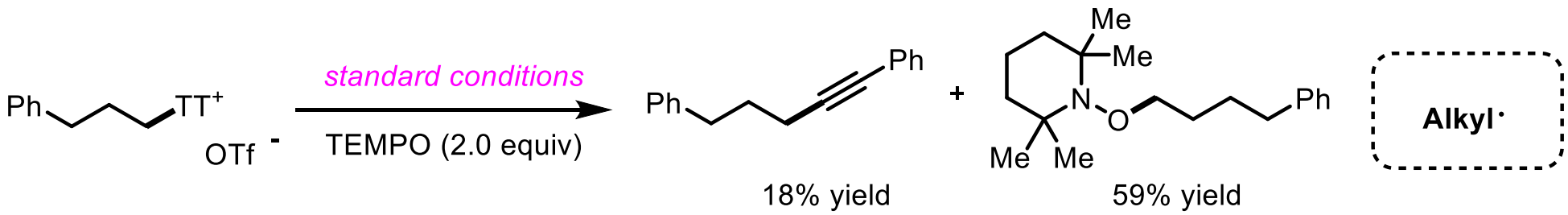
Z. Shi, et al. *Nat. Commun.* **2021**, *12*, 4526-4534.

2.3.1 烷基噻蒽鎓盐——构建C-B/C-C键

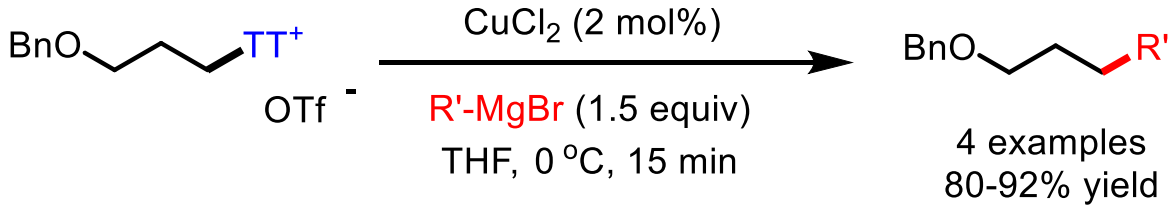
Sonogashira coupling:

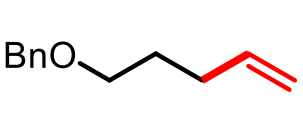


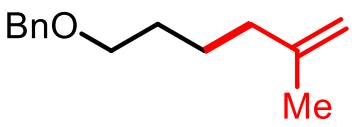




Kumada coupling:







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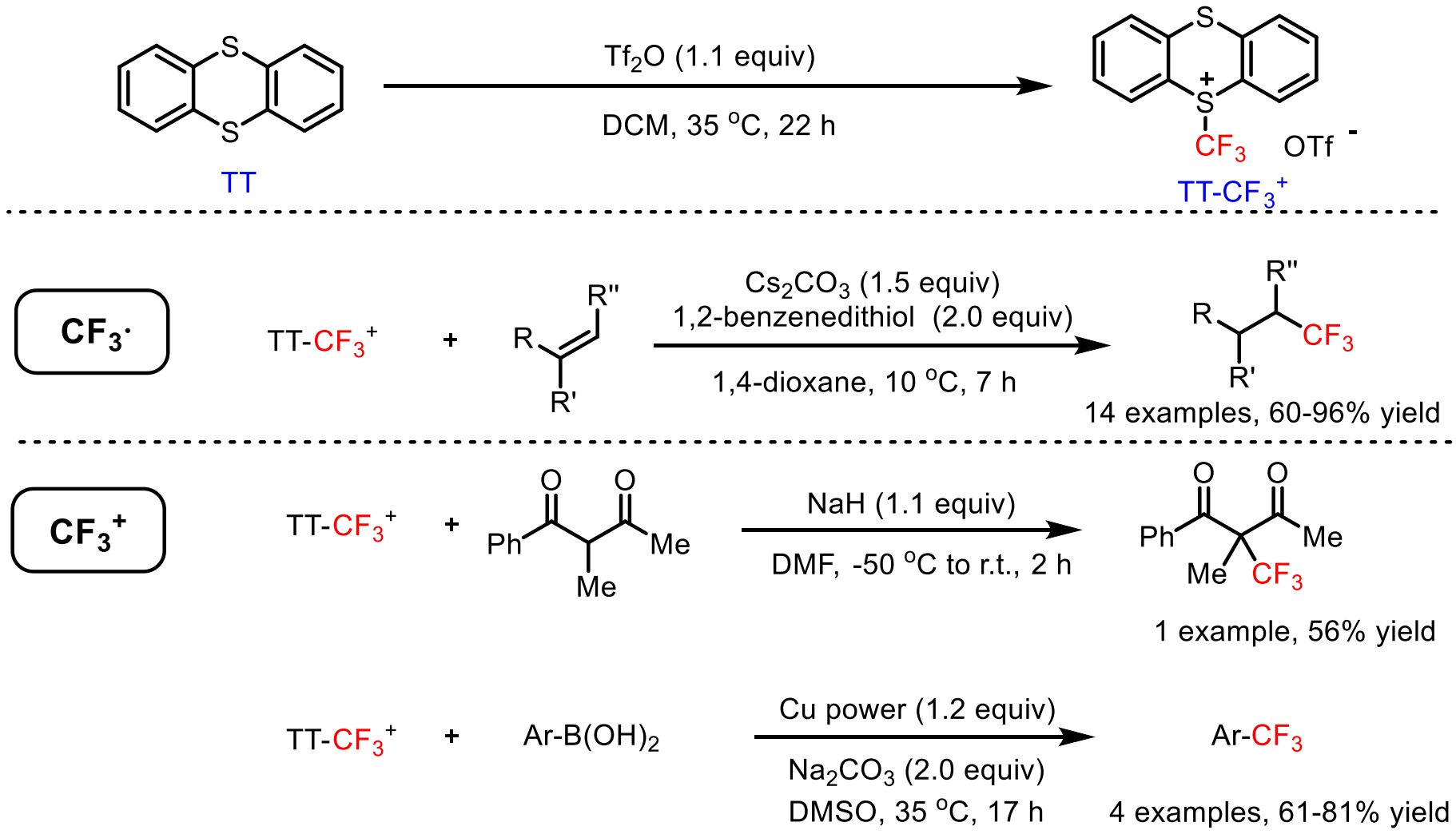
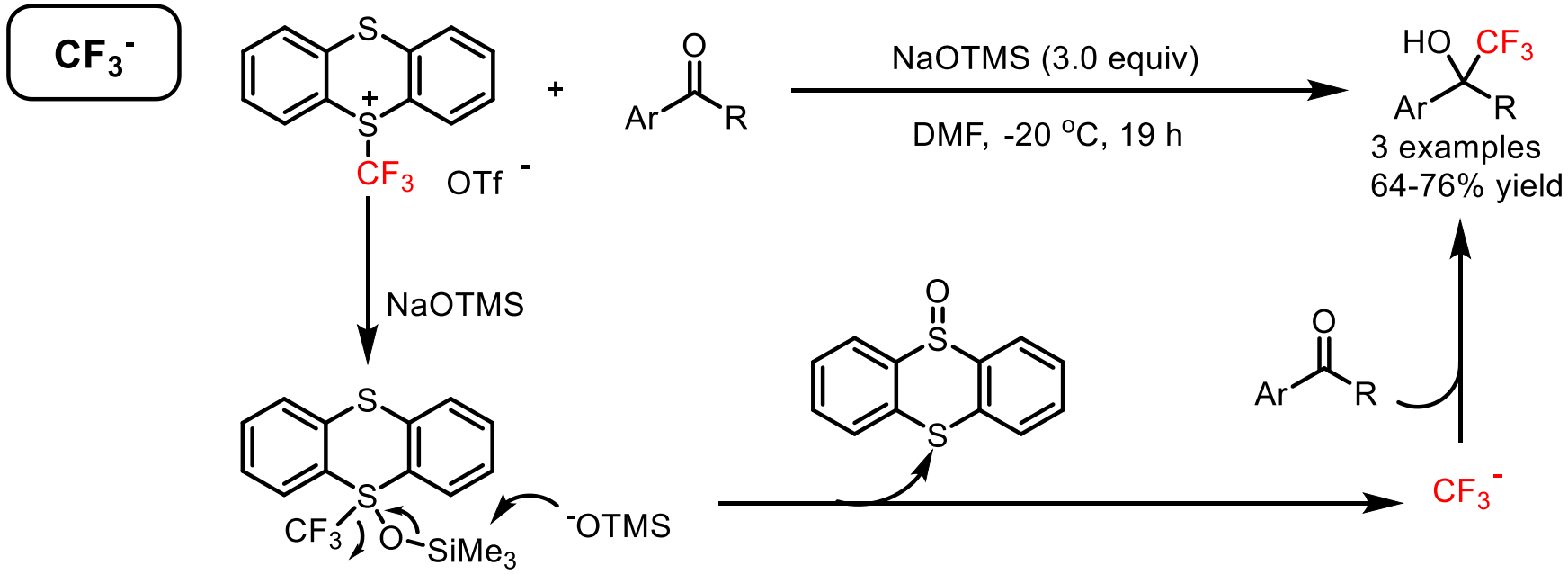
2.3.2 烷基噻蒽鎓盐——三氟甲基试剂



T. Ritter, *et al. J. Am. Chem. Soc.* **2021**, *143*, 7623-7628.

2.3.2 烷基噻蒽鎓盐——三氟甲基试剂



结论：同时具有亲电、亲核、自由基的反应性

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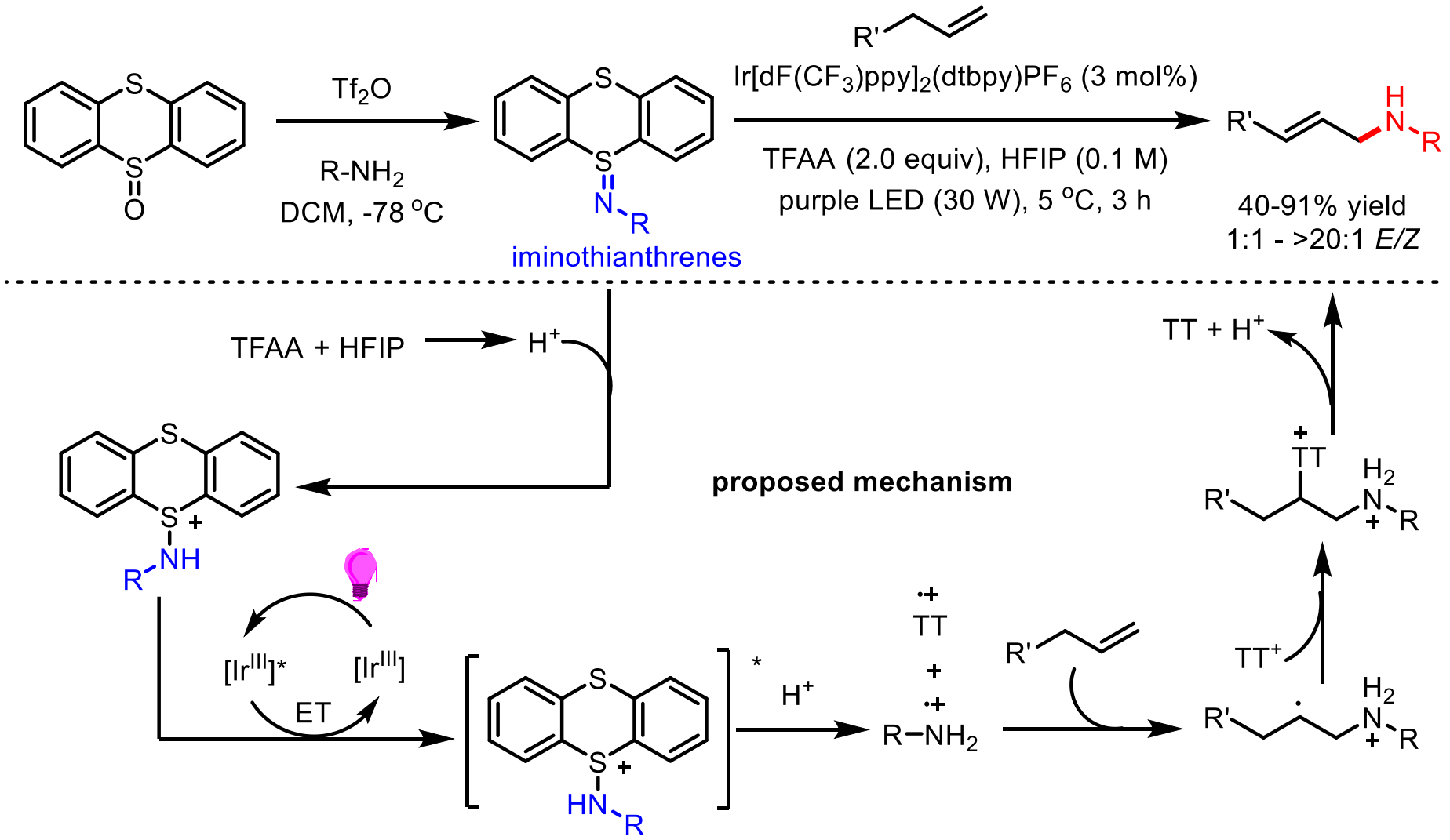
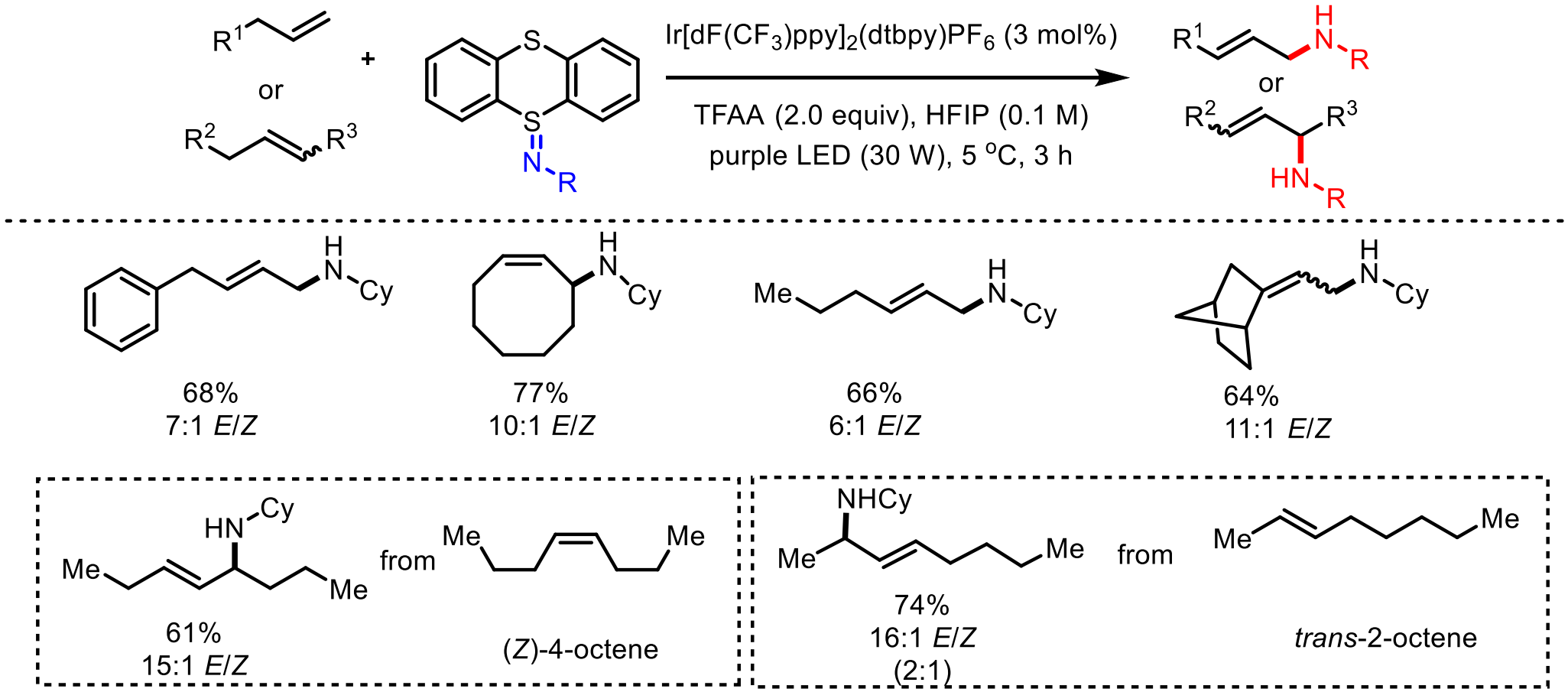
2.4 新型亚胺基噻蒽鎓盐



T. Ritter, et al. *J. Am. Chem. Soc.* **2020**, *142*, 17287-17293.

2.4 新型亚胺基噻蒽鎓盐



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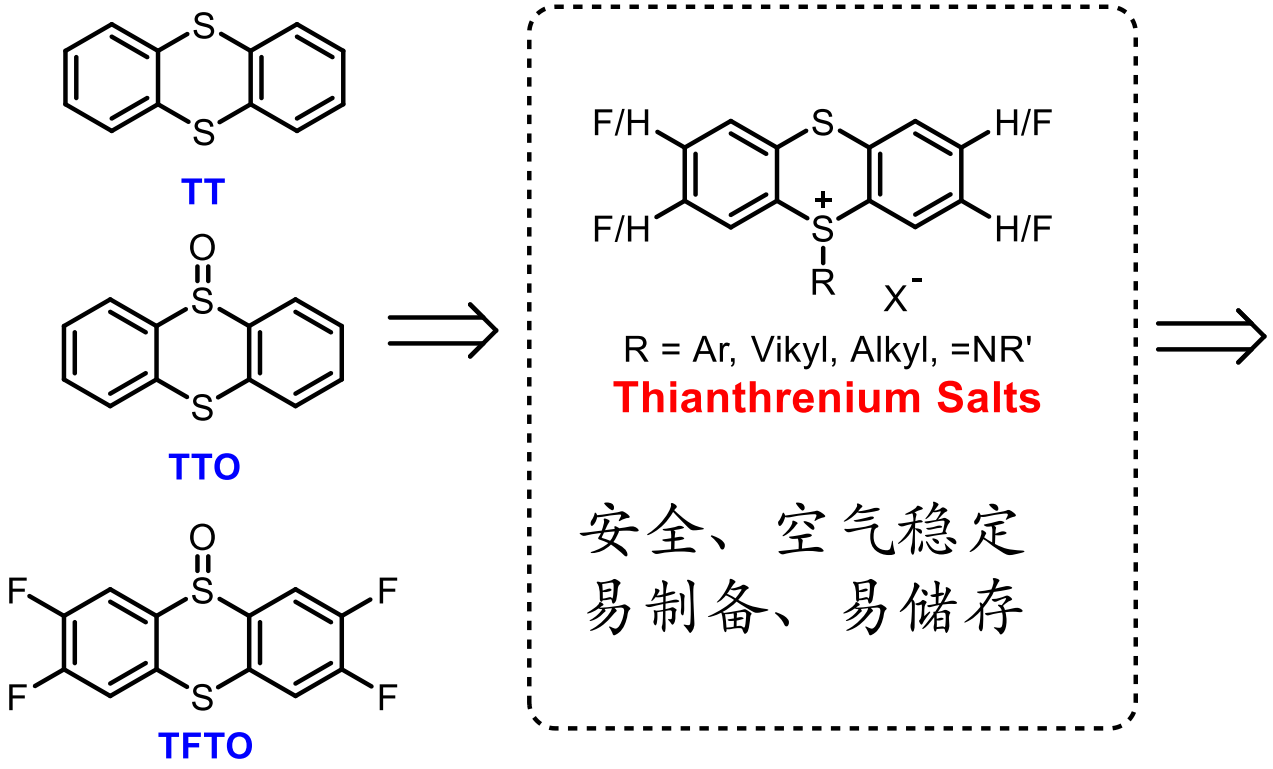
三、总结与展望

总结：



优点：

- 构建C-C键、C-X键
  (X = F/O/N/Ge/B/^{2}H/^{3}H)
- 高活性、高区域选择性，利于后期官能团化反应

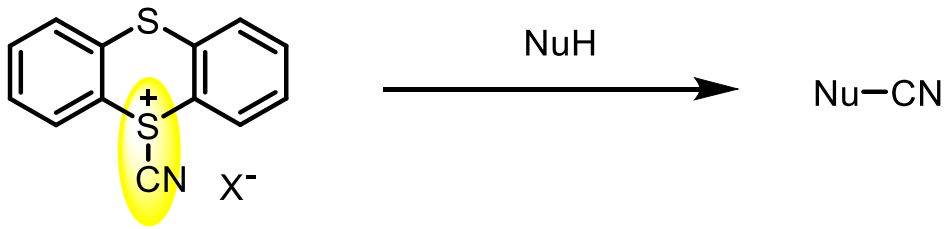
缺点：

- 使用当量的噻蒽鎓盐作为底物，不利于原子经济性

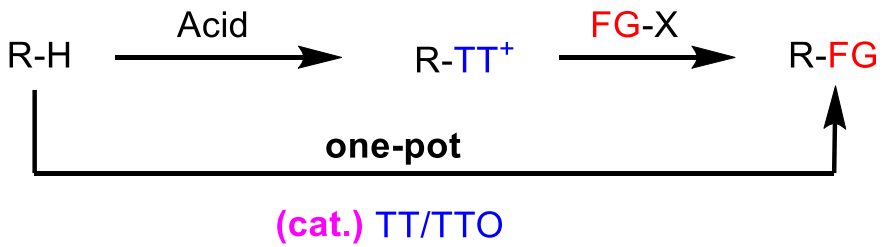
三、总结与展望

展望：

- 发展更多不同类别的噻蒽鎓盐 (R = 炔基,氰基, CD_3 …)及其应用

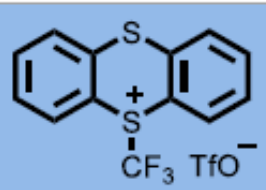
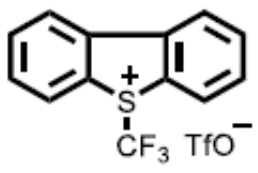
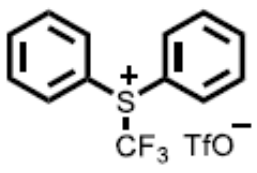
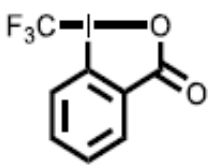
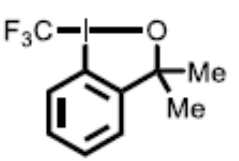


- 使用催化量的噻蒽鎓盐，一锅法实现高产率高区域选择性合成



THANK YOU

Table 1. Thermochemical and Electrochemical Properties of Common CF_3 Reagents

					
Decomposition temperature (°C)[48]	142	128	168	149	135
Enthalpy of first transition[48]	endothermic[a]	endothermic[a]	endothermic[a]	exothermic	exothermic
Cathodic peak potential E_{red} (V *vs* Cp_2Fe)[51]	−0.99	−0.87	−1.31	−1.49	−1.34

[a]For detailed DSC-TGA analysis, see Supporting Information Figures S15–S17.

Z. Shi, *et al. Nat. Commun.* **2021**, *12*, 4526-4534.