Photocatalytic [2+2]-Cycloaddition Using StyrenylBpin

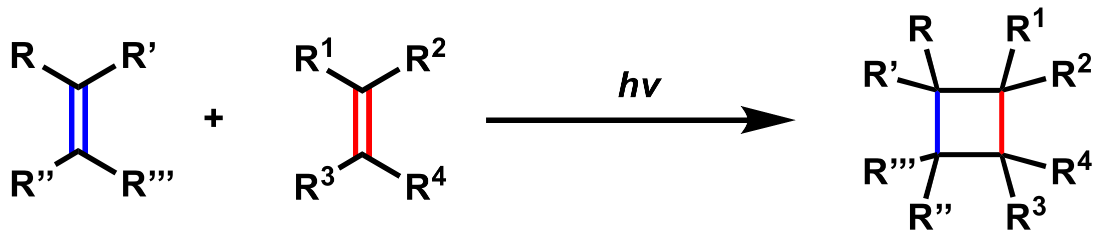
2023.5.20. Literature Seminar

D2 Yuto Hikone

Contents

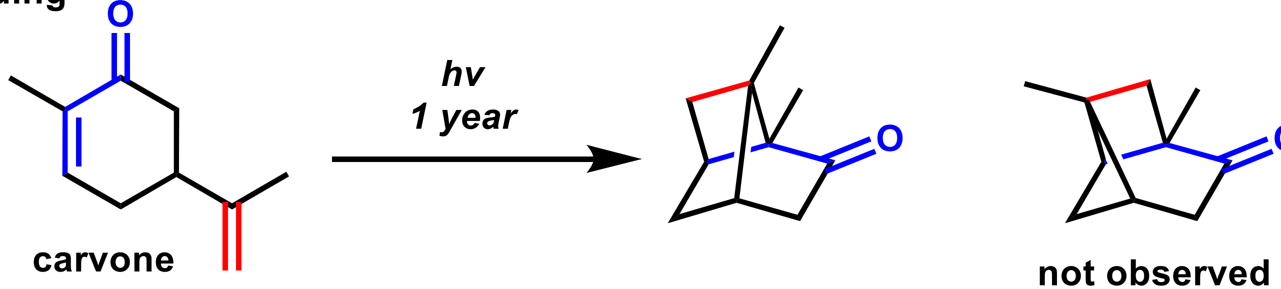
[2+2]-Photocycloaddition: Synthesis of Cyclobutane

[2+2]-photocycloaddition between alkenes

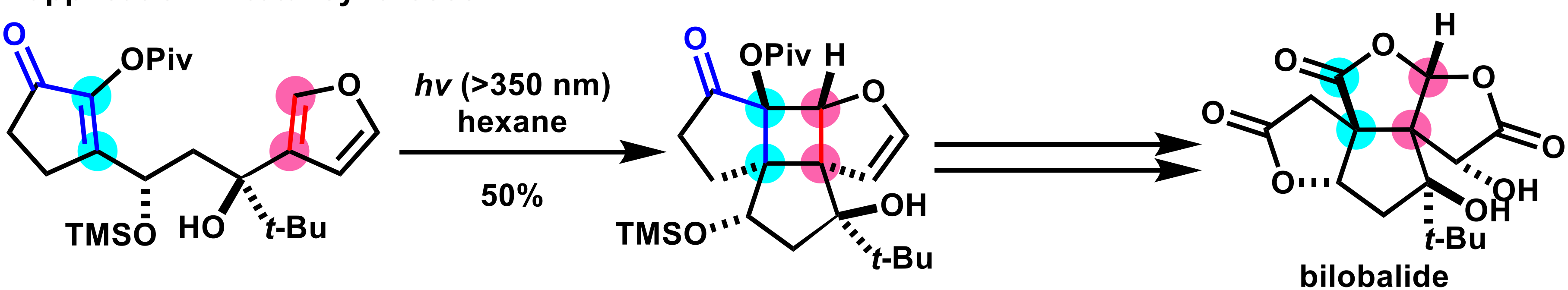


- **generating cyclobutanes**
- **one of the few reliable reactions that enables constructing quaternary carbons**

- **initial finding[1]**



- **application in total syntheses[2]**



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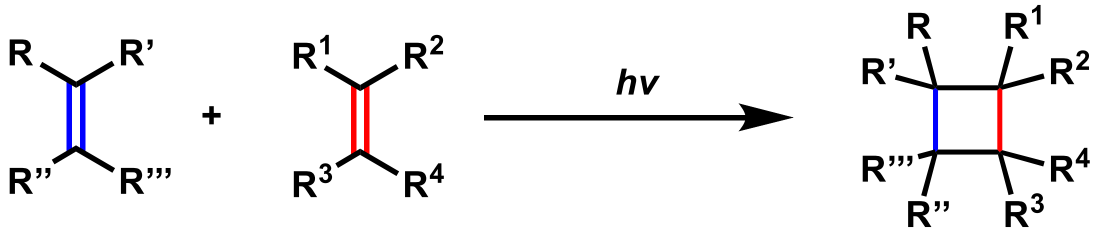
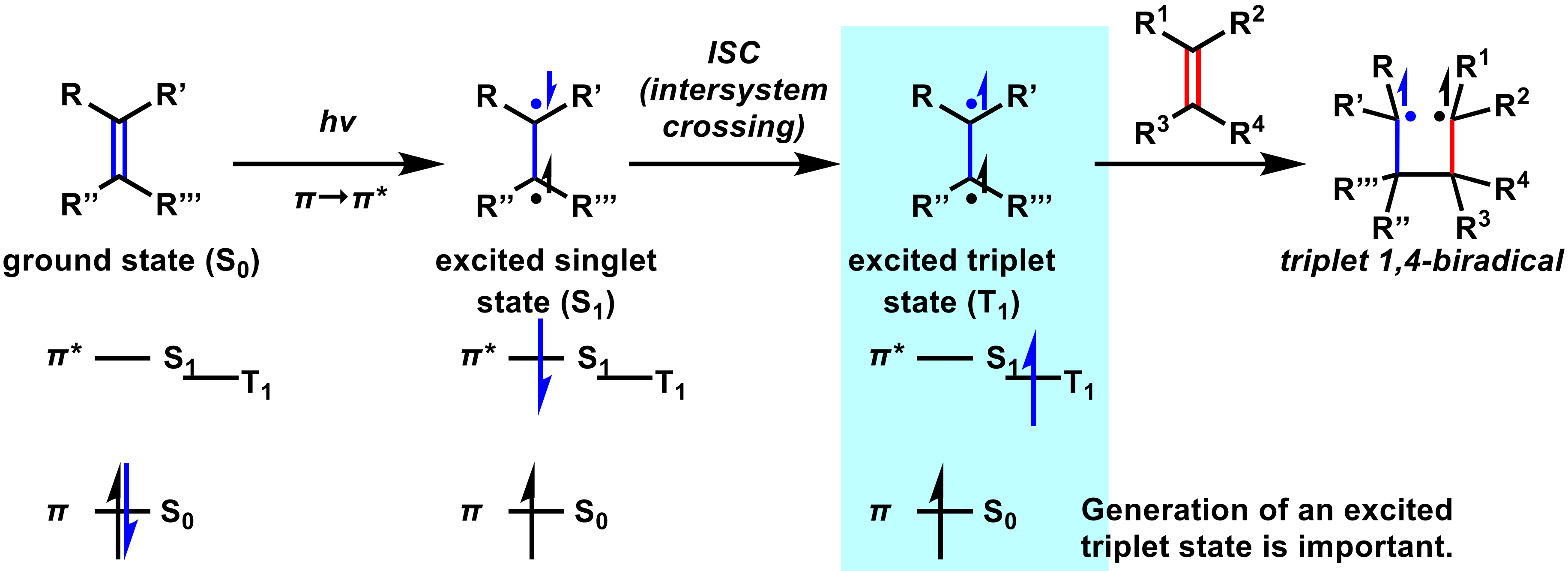
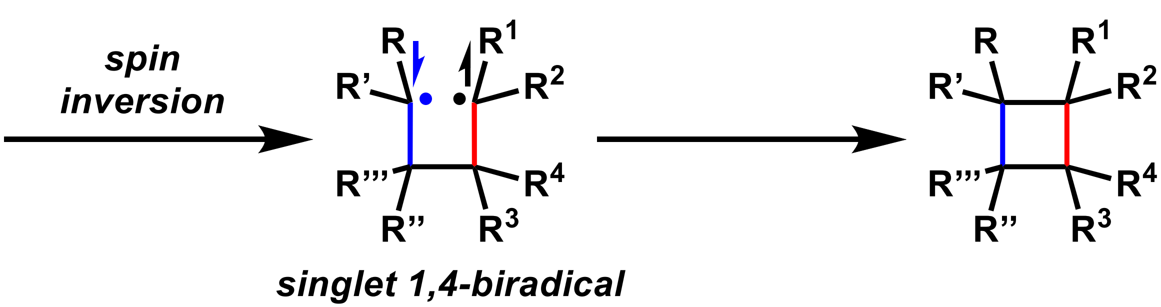
1. Ciamician, G.; Silber, P. Chemische Lichtwirkungen. *Ber. Dtsch. Chem. Ges.* **1908**, *41*, 1928−1935.
2. (a) Corey, E. J.; Su, W.-G. *J. Am. Chem. Soc.* **1987**, *109*, 7534−7536.
   (b) Corey, E. J.; Su, W.-G. *Tetrahedron Lett.* **1988**, *29*, 3423−3426.

[2+2]-Photocycloaddition: Reaction Mechanism



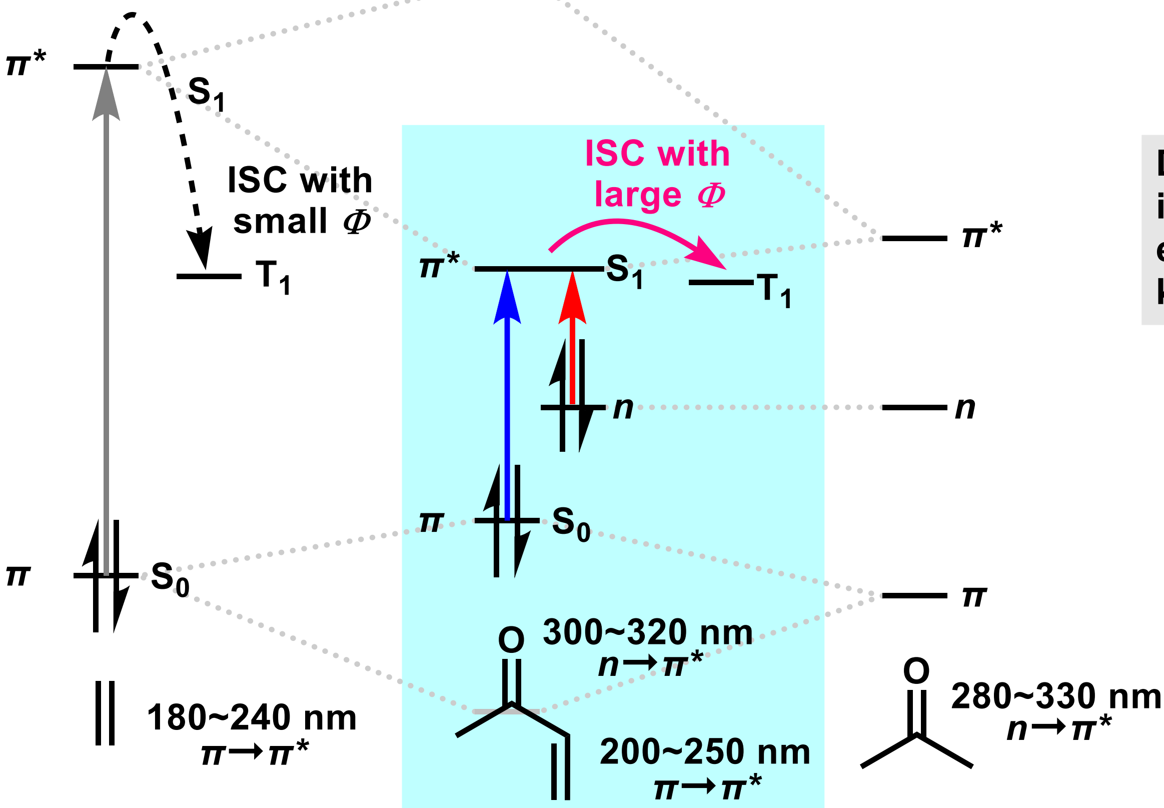


Generation of an excited triplet state is important.



Methods to Generate Excited Triplet State

- Direct photoexcitation approach

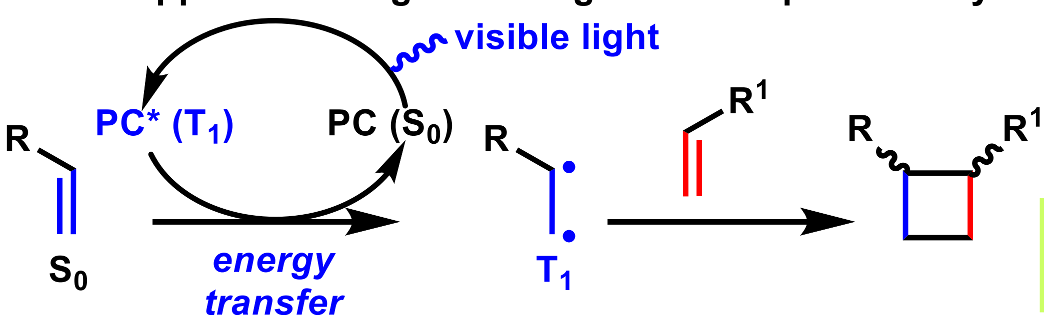


Direct photoexcitation approch is applicable to limited substrates, especially, enone (α,β-unsaturated ketone).

advantages of enone:
- small energy gap between π and π* orbitals
- n→π* transition

-> easily excited by light with higher wavelength
- efficient ISC (high Φ)

- Indirect approach using visible-light-excited photocatalyst

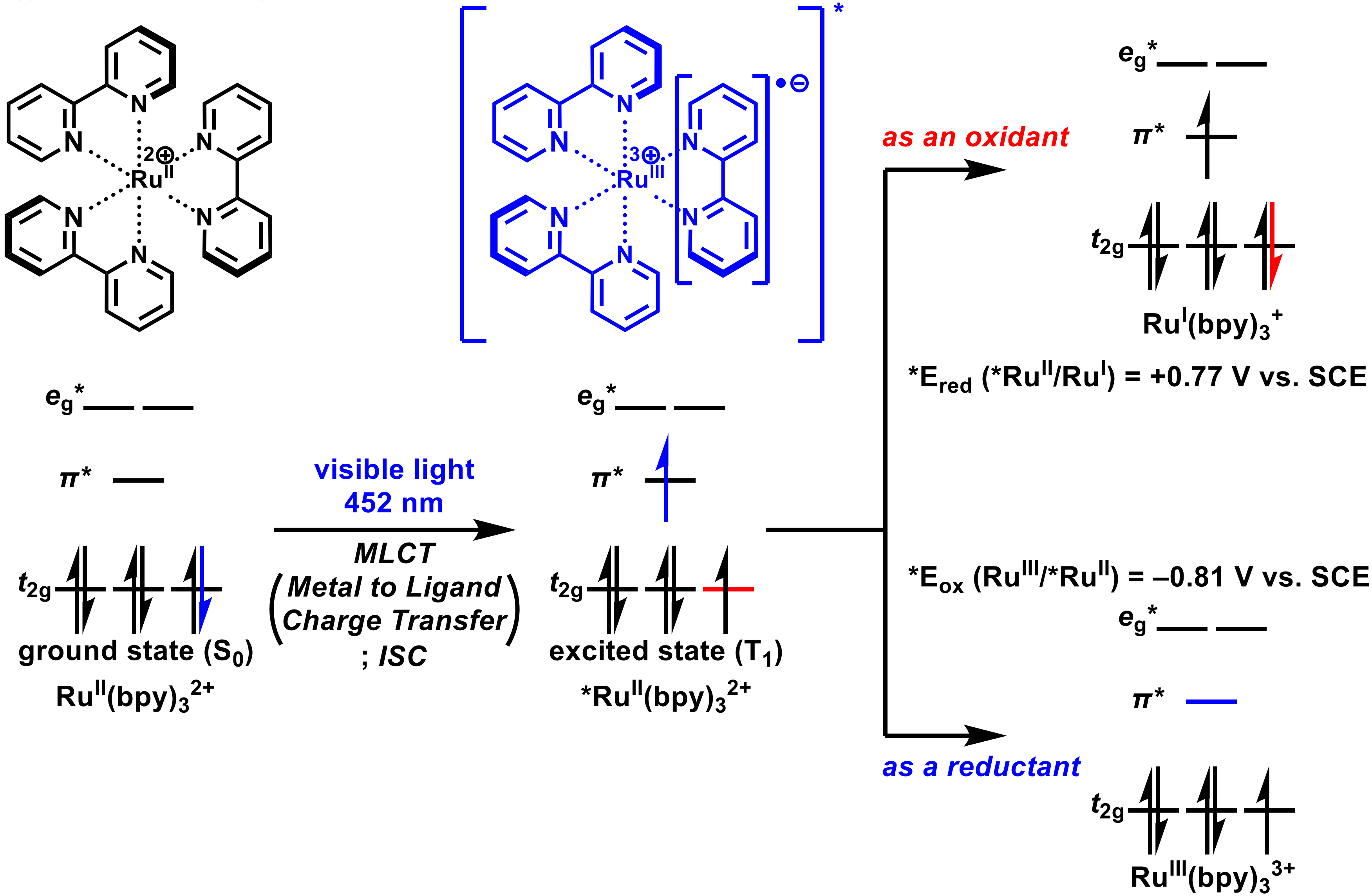


In certain conditions, energy transfer between ground state (S_0) substrate and excited triplet state (T_1) photocatalyst occurs to exchange their quantum states.

-> generation of triplet substrate with the aid of low energy visible light

Electron Transfer

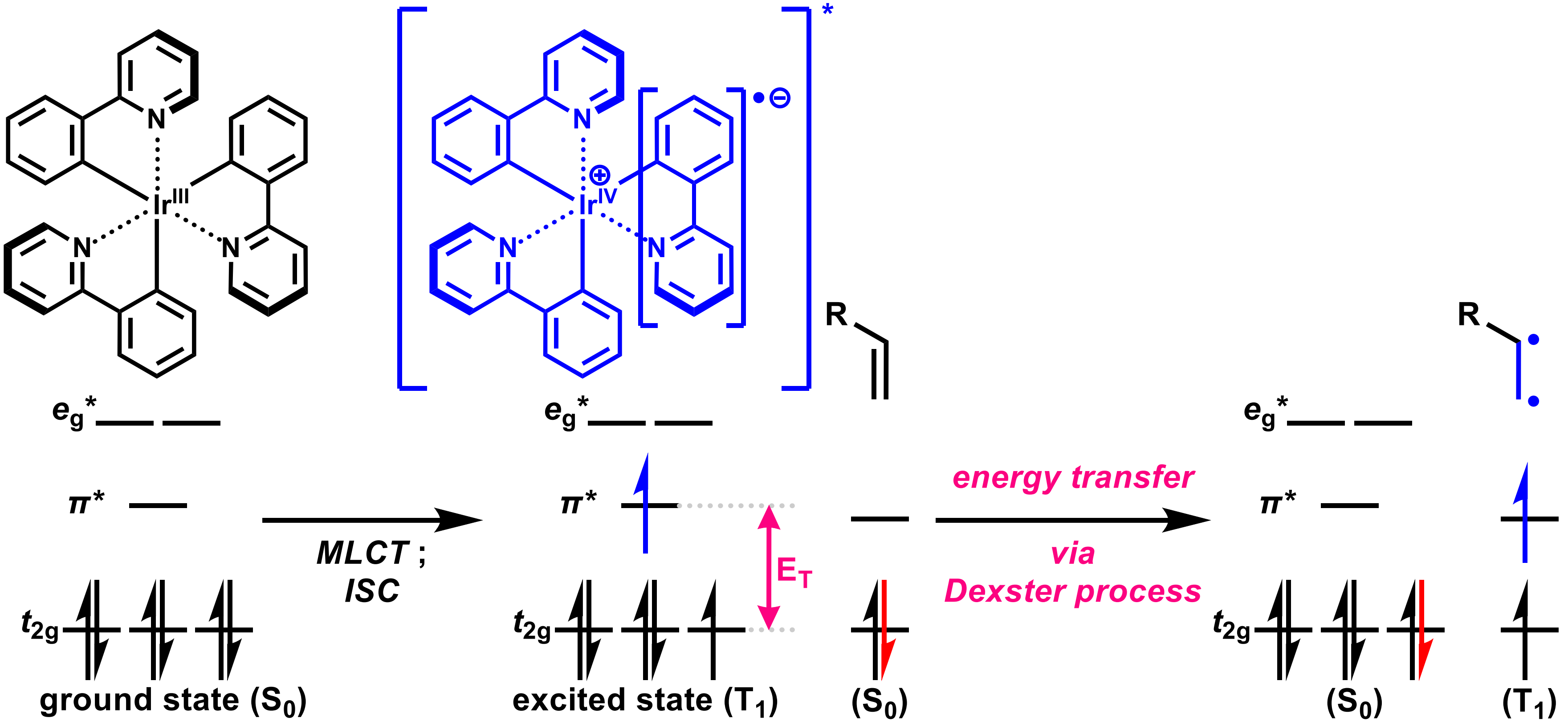
Ru (group 8, period 5): $[Kr]4d^7 5s^1$



Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322– 5363.

Energy Transfer

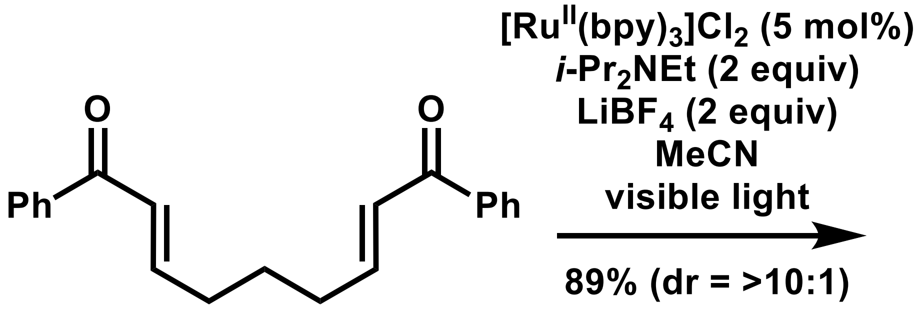
Ir (group 9, period 6): [Xe]4f^{14}5d^{7}6s^{2}

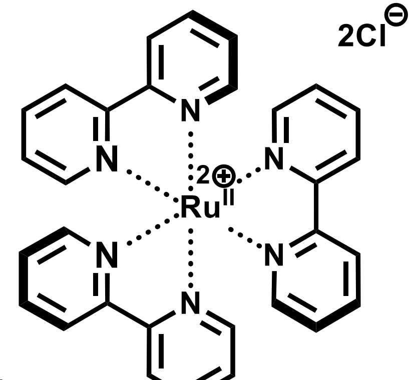


An excited photocatalyst, which does not posess a sufficient excited state oxidation/reduction potential, but has an larger T_1-S_0 energy gap (E_T) than that of substrates, can sensitize the substrates via energy transfer.

1. Chen, B. B.; Wang, S.; Jiang, S. W.; Yu, Z. G.; Wan, X. G.; Ding, H. F.; Wu, D. *New J. Phys.* **2015**, *17*, 013004.
2. Strieth-Kalthoff, F.; James, M. J.; Teders, M.; Pitzer, L.; Glorius, F. *Chem. Soc. Rev.* **2018**, *47*, 7190–7202.

via Electron Transfer

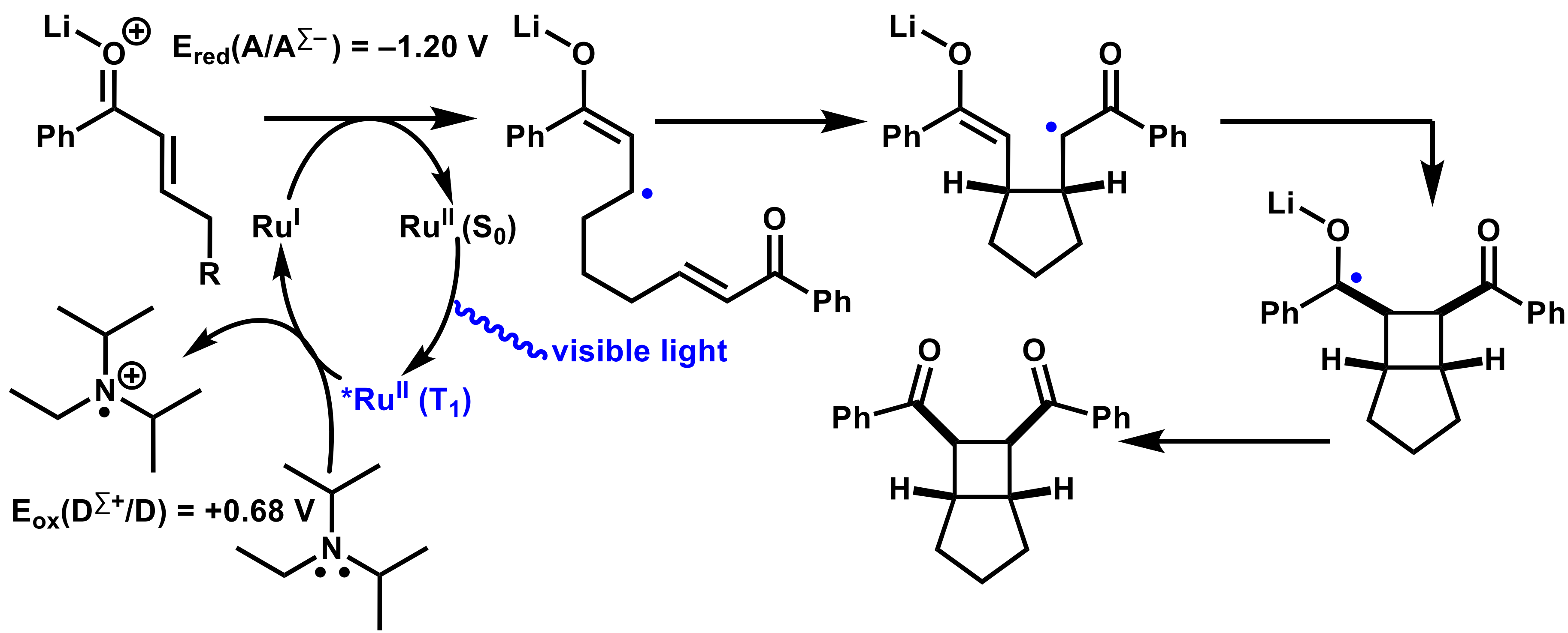




$[Ru^{II}(bpy)_3]Cl_2$

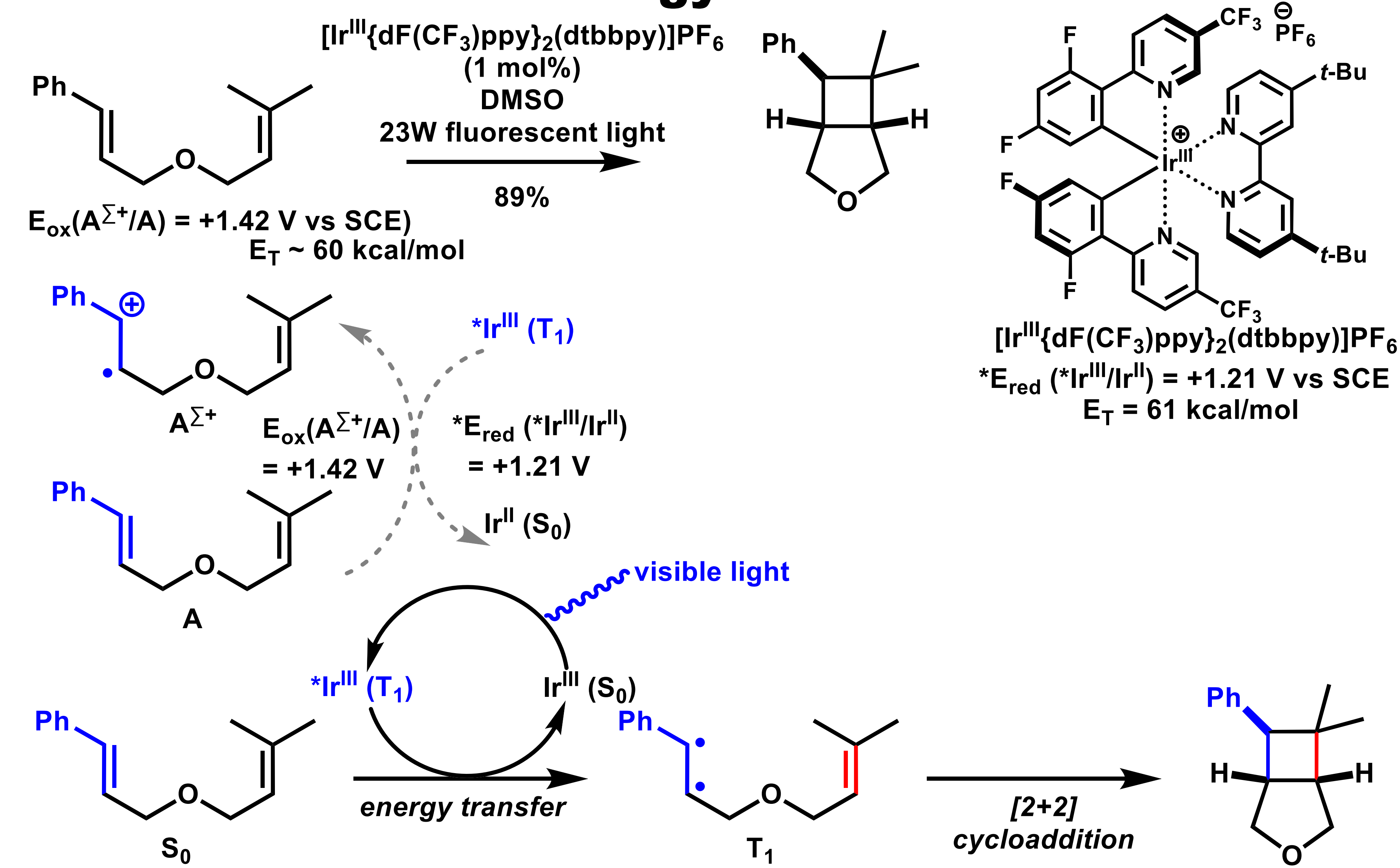
$*E_{red}$ ($*Ru^{II}/Ru^{I}$) = +0.77 V vs SCE

E_{red} (Ru^{II}/Ru^{I}) = –1.33 V vs SCE



Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 12886–12887.

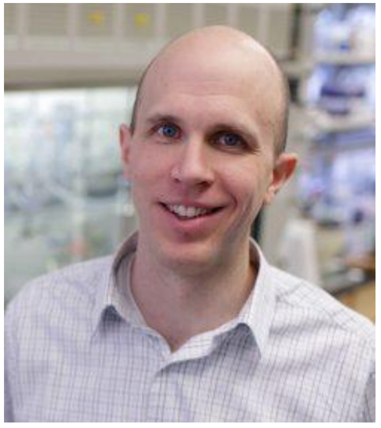
via Energy Transfer



1. Lu, Z.; Yoon, T. P. *Angew. Chem. Int. Ed*. **2012**, *51*, 10329–10332.
2. Lowry, M. S.; Goldsmith, J. I.; Slinker, J. D.; Rohl, R.; Pascal, R. A.; Malliaras, G. G.; Bernhard, S. *Chem. Mater.* **2005**, *17*, 5712−5719.

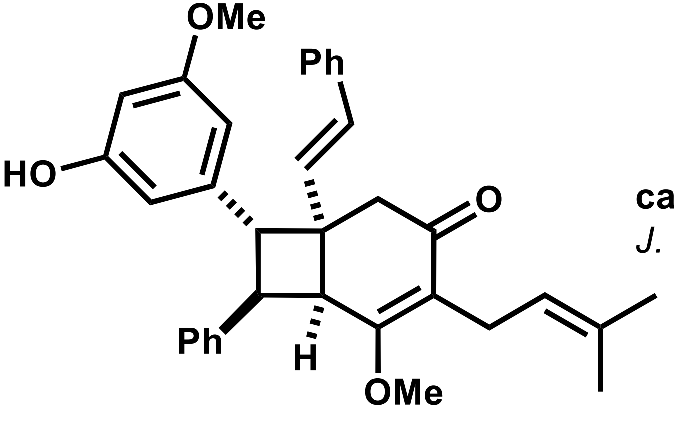
Contents

Prof. M. Kevin Brown



Career:
1998-2002 : B.S. @ Hamilton College
2002-2008 : Ph.D. @ Boston College (Prof. Amir H. Hoveyda)
2008-2011 : National Institutes of Health Postdoctoral Fellow @Harvard University (Prof. E. J. Corey)
2011-2017 : Assistant Professor @ Indiana University
2017-2021 : Associate Professor @Indiana University
2021- : James F. Jackson Professor @ Indiana University

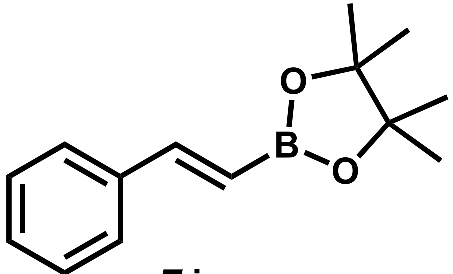
Research interests:
Discovery and development of novel and widely applicable stereoselective chemical reactions
1. methods development: transition-metal catalyzed reactions, cycloaddition processes
2. mechanistic studies
3. synthesis of complex natural products using methods developed in his lab



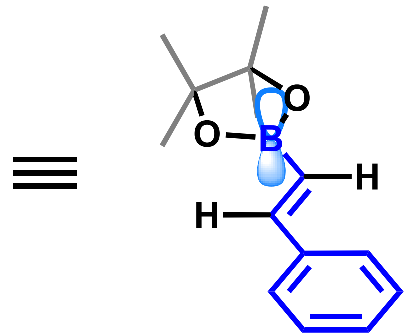
cajanusine
J. Am. Chem. Soc. **2020**, *142*, 5002.

StyrenylBpin

- styrenylBpin

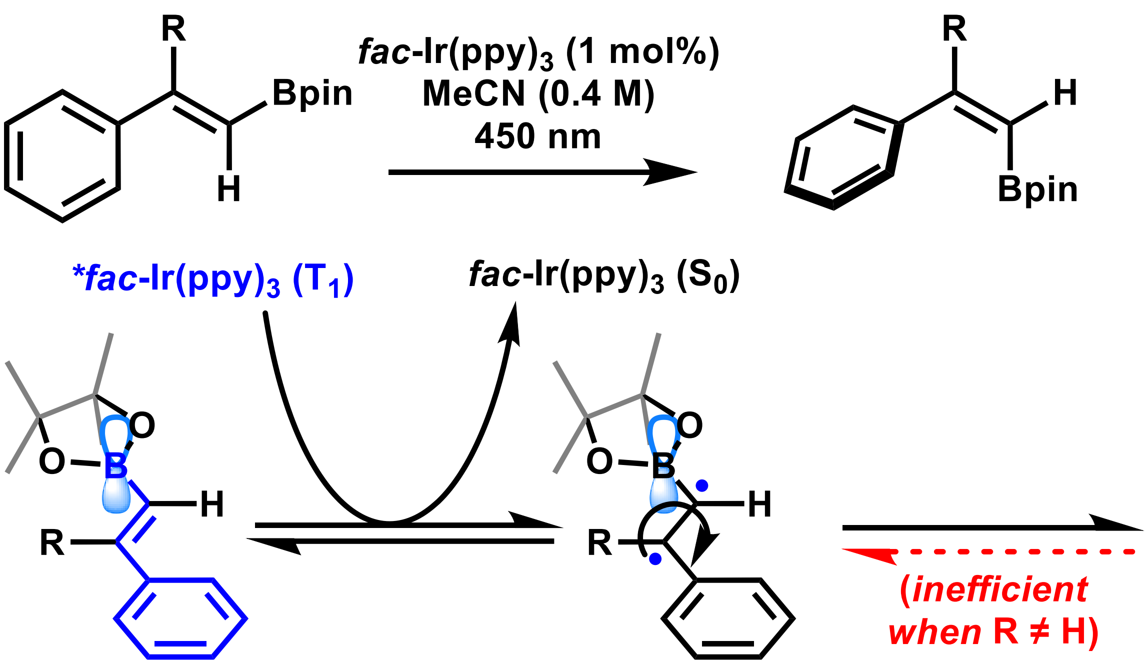


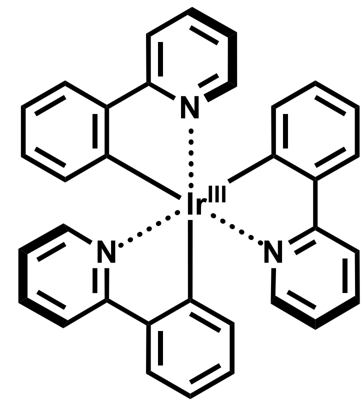
E isomer



interaction of vacant p orbital of boron with π-system of styrene
-> increasing electron deficiency (= lowering *π**)
-> more easily sensitized than styrene with lower energy?

- Photocatalytic E/Z isomerization of styrenylBpin[1]



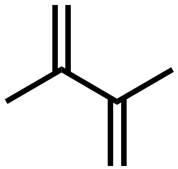


fac-Ir(ppy)$_3$

1. Molloy, J. J.; Metternich, J. B.; Daniliuc, C. G.; Watson, A. J. B.; Gilmour, R. *Angew. Chem., Int. Ed.* **2018**, *57*, 3168−3172.

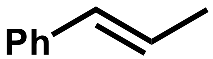
Triplet Energy Based Reaction Design

- **comparison of triplet energy**

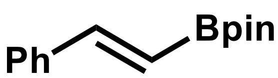


E_T = 60.5 kcal/mol (exp.)
56.3 kcal/mol (calc.)*

E_T = 60.8 kcal/mol (exp.)
56.2 kcal/mol (calc.)*



E_T = 59.5 kcal/mol (exp.)
55.4 kcal/mol (calc.)*



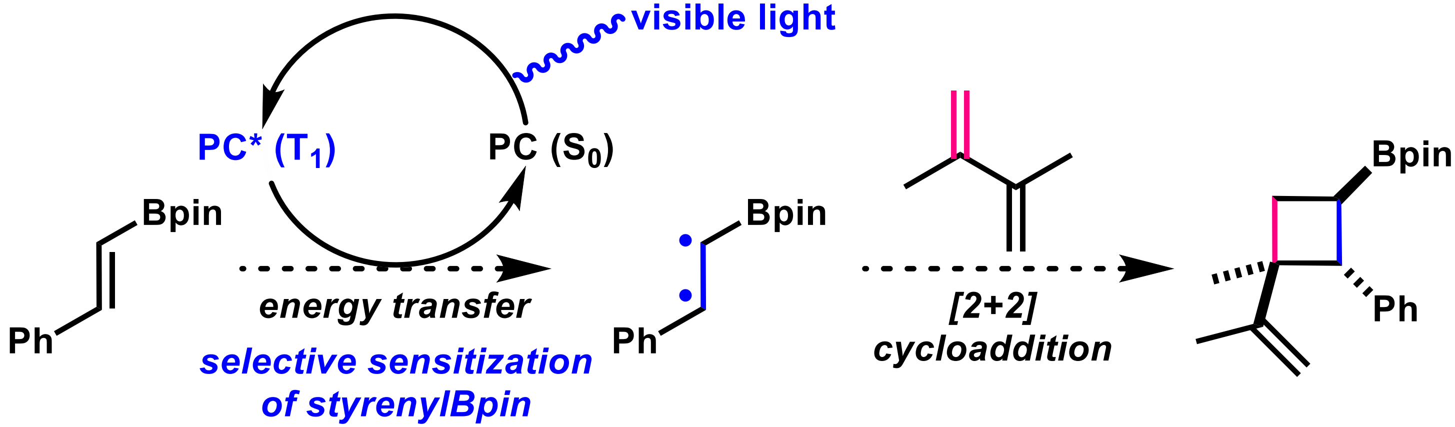
E_T = n/d (exp.)
51.8 kcal/mol (calc.)*

Calculation showed that styrenylBpin has the lowest triplet energy to be sensitized.

-> Selective triplet energy transfer to styrenylBpin can be plausible.

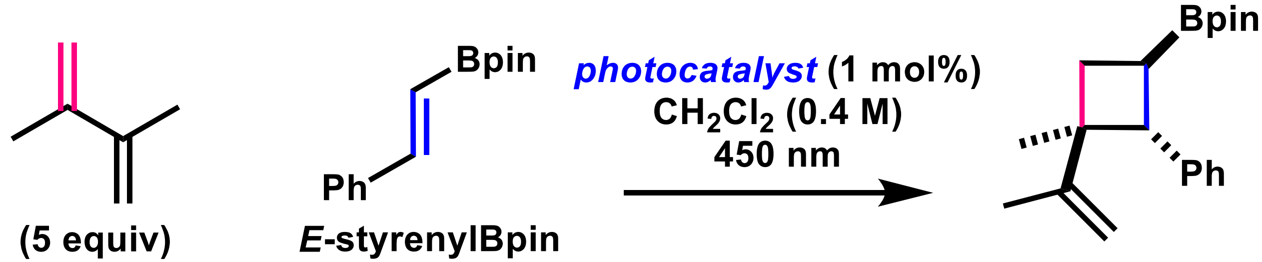
***ωB97XD/aug-cc-pVDZ level of theory**
CH_2Cl_2 as a solvent

- **Design of reaction system**



Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K.
Angew. Chem., Int. Ed. **2022**, *61*, No. e202200725.

Optimization

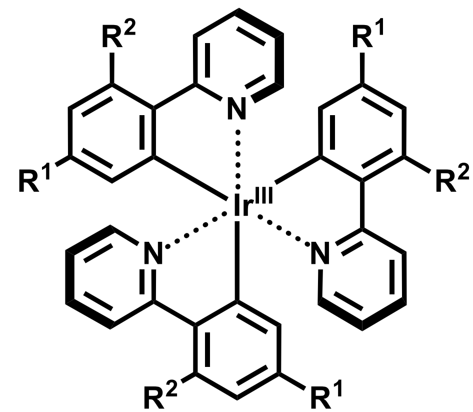


(5 equiv)
E_T = 60.5 (exp.)
56.3 (calc.)

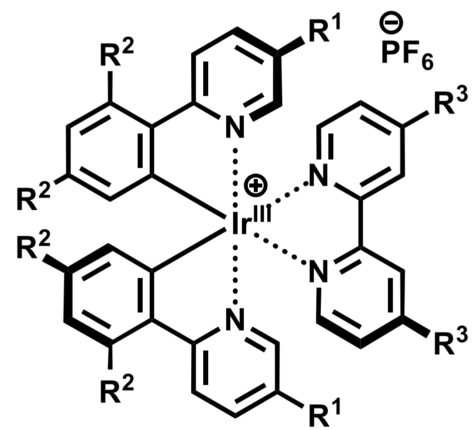
E-styrenylBpin
E_T = n/d (exp.)
51.8 (calc.)

photocatalyst	E_T [kcal/mol]	yield
[Ir^{III}{dF(CF$_3$)ppy}$_2$(bpy)]PF$_6$ (1)	60.4	38
[Ir^{III}{dF(CF$_3$)ppy}$_2$(dtbbpy)]PF$_6$ (2)	60.2	45
fac-Ir(dFppy)$_3$ (3)	60.1	49
fac-Ir(*p*-CF$_3$ppy)$_3$ (4)	58.6	60
[Ir^{III}(dFppy)$_2$(dtbbpy)]PF$_6$ (5)	55.4	41
fac-Ir(ppy)$_3$ (6)	55.2	71
[Ir^{III}(ppy)$_2$(dtbbpy)]PF$_6$ (7)	49.2	28
fac-Ir(ppy)$_3$ (6)	55.2	82%[a]
fac-Ir(ppy)$_3$ (6)	55.2	82%[b]

[a] CH_2Cl_2 (0.8 M) [b] *Z*-styrenylBpin was used



(R^1, R^2)
(3) : (F, F)
(4) : (CF_3, H)
(6) : (H, H)



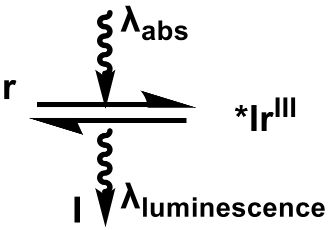
(R^1, R^2, R^3)
(1) : (CF_3, F, H)
(2) : (CF_3, F, *t*-Bu)
(5) : (F, F, H)
(7) : (H, H, *t*-Bu)

Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.

Mechanistic Investigation (1)

Stern-Volmer quenching

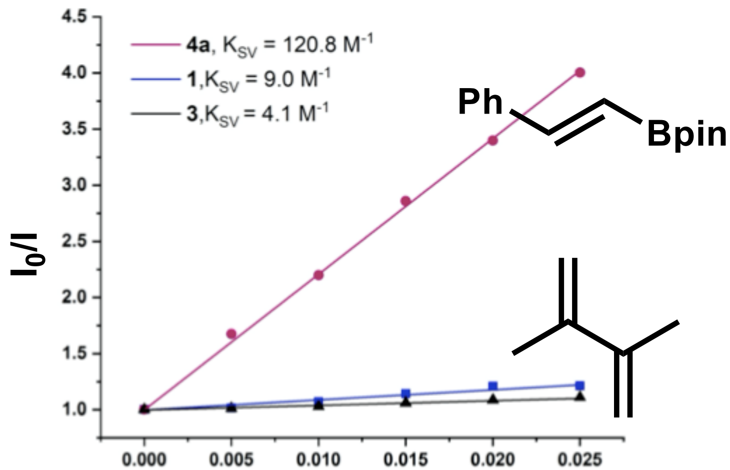
Ir^{III} photocatalyst (0.3 mM CH_2Cl_2) + various quencher (0-25 mM)

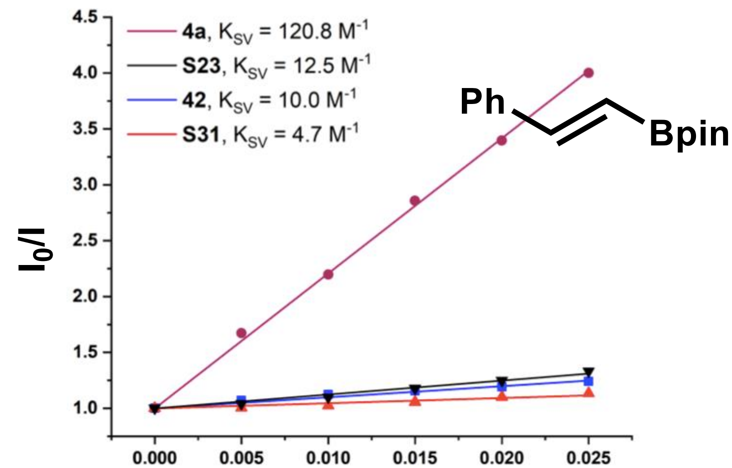


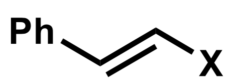
$^{*}Ir^{III}$

I_0 : emission intensity without quencher
I : emission intensity with quencher
Good quencher shows large I_0/I.

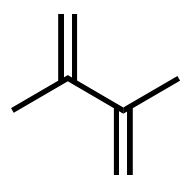
- quenching of *fac*-Ir(ppy)$_3$ with various styrenyl derivatives and diene



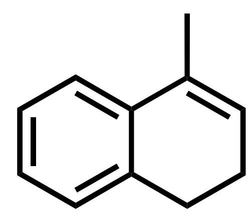




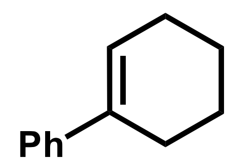
4a : X = Bpin
3 : X = H



1



S23



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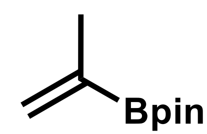


S31

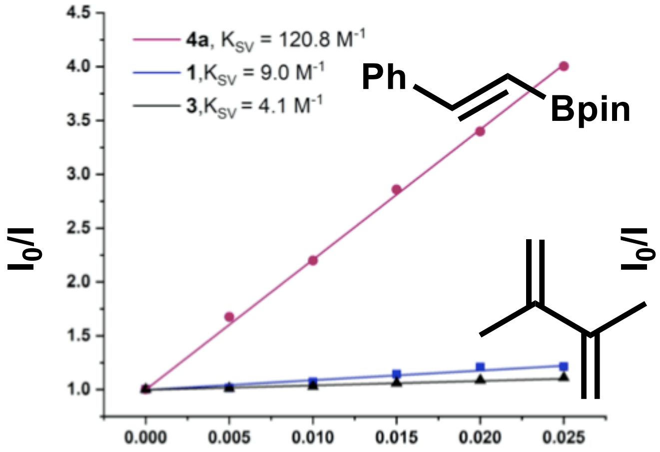
StyreneylBpin is selectively sensitized by excited Ir catalyst.

Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.

Mechanistic Investigation

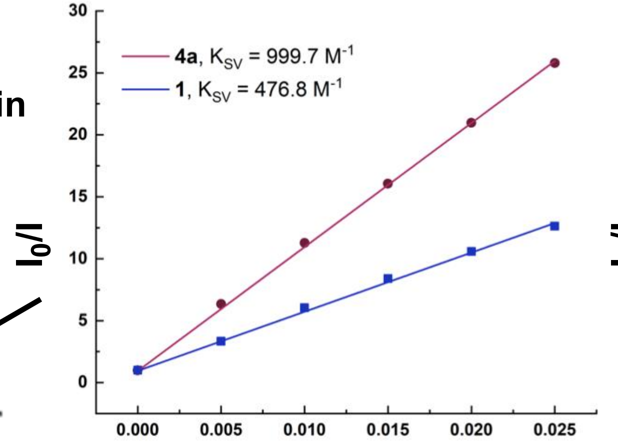
Stern-Volmer quenching

- **equeching of various Ir photocatalysts with styrenylBpin (4a) and 2,3-dimethylbutadiene (1)**



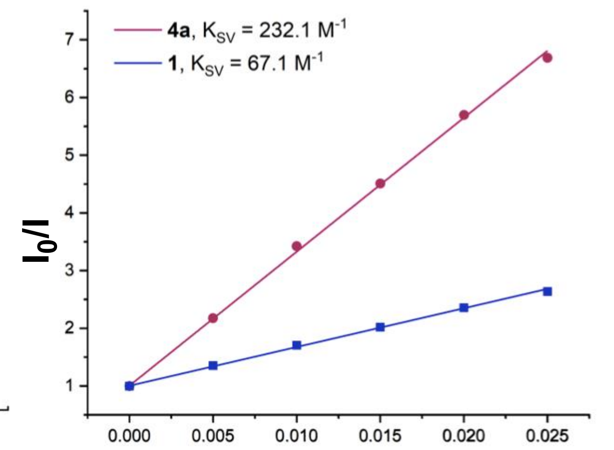
concentration (M)

***fac*-Ir(ppy)$_3$**



concentration (M)

***fac*-Ir(dFppy)$_3$**



concentration (M)

[Ir^{III}(dFppy)$_2$(dtbbpy)]PF_6

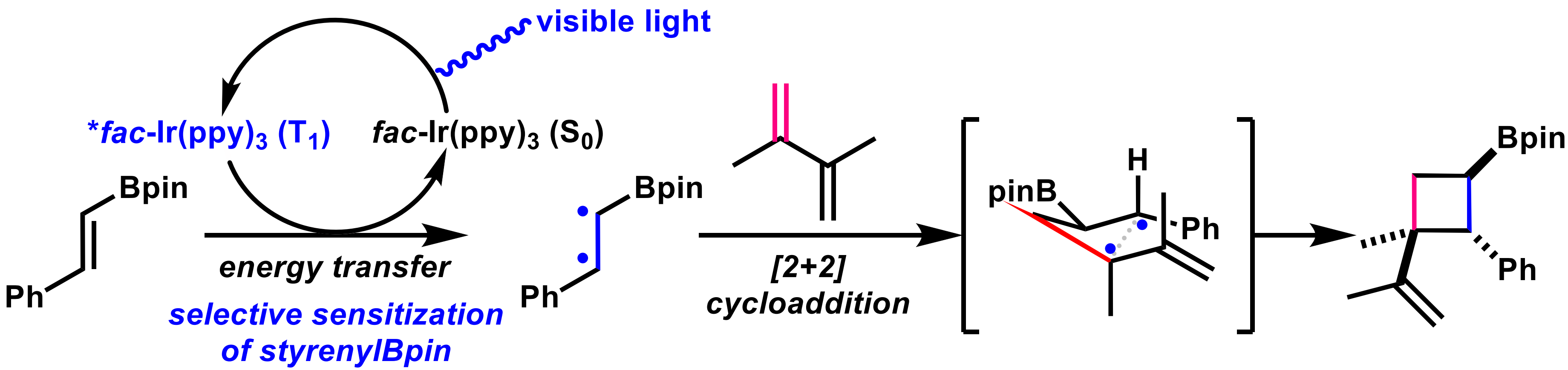
Among three Ir photocatalysts, only *fac*-Ir(ppy)$_3$ can selectively sensitize styrenylBpin without exciting 2,3-dimethylbutadiene.

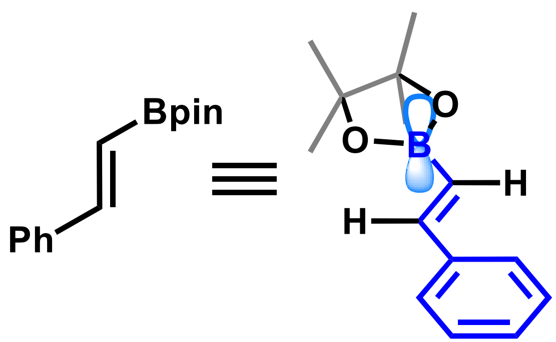
i. **Difference between *fac*-Ir(ppy)$_3$ and *fac*-Ir(dFppy)$_3$**
   Order of E_T is important:
   55.2 (*fac*-Ir(ppy)$_3$) < 56.3 (2,3-dimethylbutadiene (1)) < 60.1 (*fac*-Ir(dFppy)$_3$)

ii. **Difference between *fac*-Ir(ppy)$_3$ and [Ir^{III}(dFppy)$_2$(dtbbpy)]PF_6**
   E_Ts are almost same (55.2 vs 55.4). Does the size of photocatalyst play an important role during Dexster energy transfer?

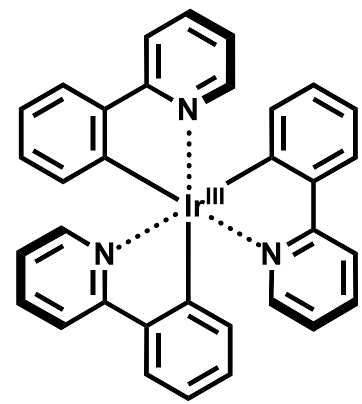
Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.

Proposed Mechanism





vacant p orbital of Boron
-> lower $\pi \rightarrow \pi^*$ transition than
general styrene derivatives or dienes



fac-Ir(ppy)$_3$

adequate E_T that can excite
strenylBpin selectively

Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K.
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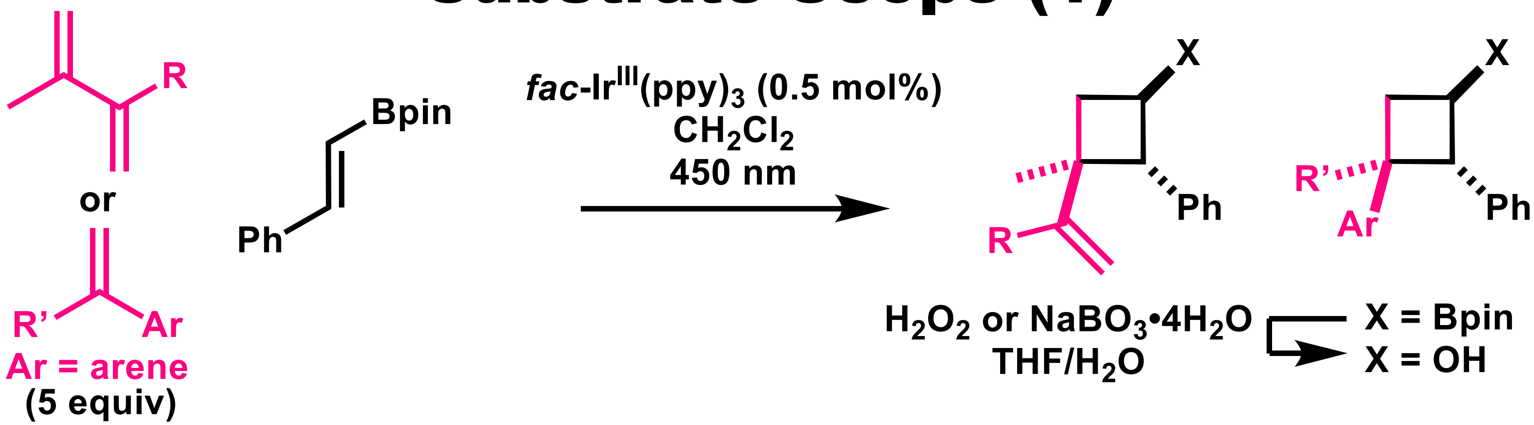
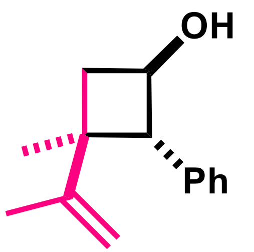
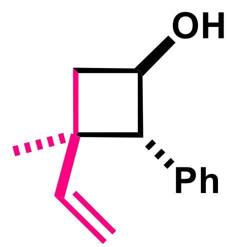
Substrate Scope (1)

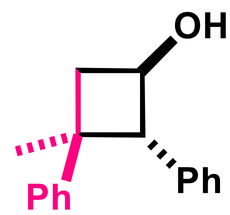




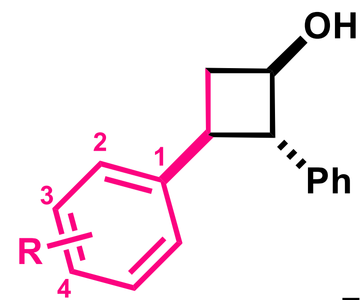
65%, dr = 10:1



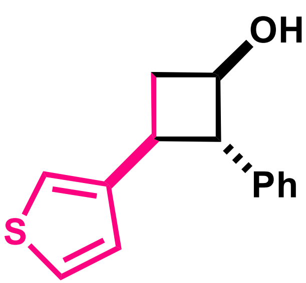
57%, dr = 3:1, rr = 3:1



63%, dr = 5:1



R = H 74%, dr = 5:1
R = 2-Me 62%, dr = 4:1
R = 4-OMe 69%, dr = 4:1



56%, dr = 4:1

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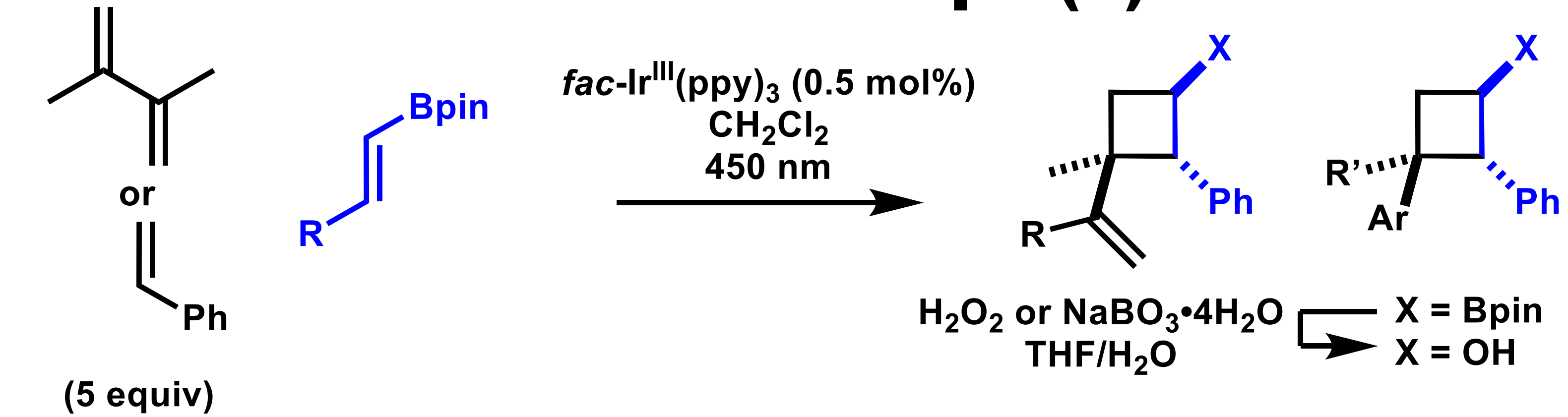
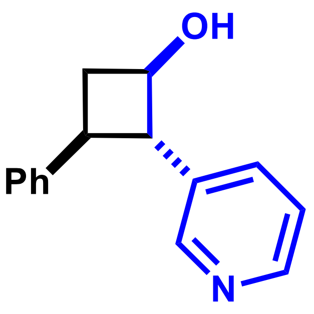
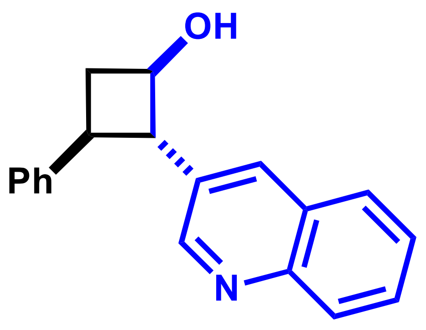
Substrate Scope (2)

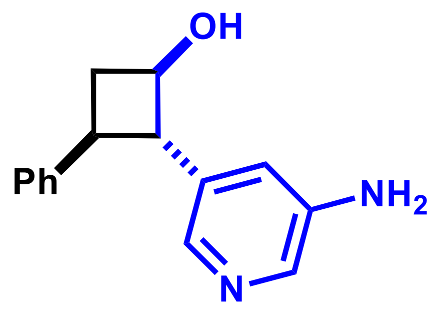




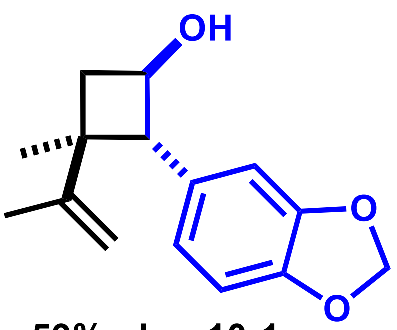
65%, dr = 12:1



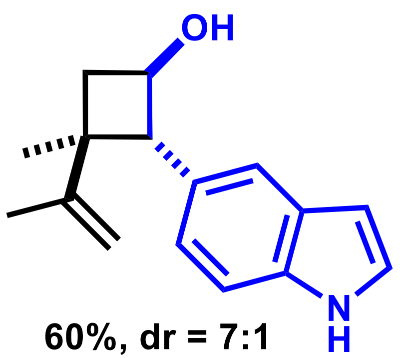
59%, dr = 10:1



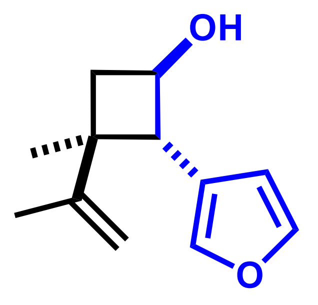
55%, dr = 6:1



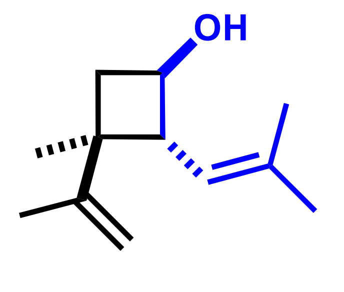
59%, dr = 10:1



60%, dr = 7:1



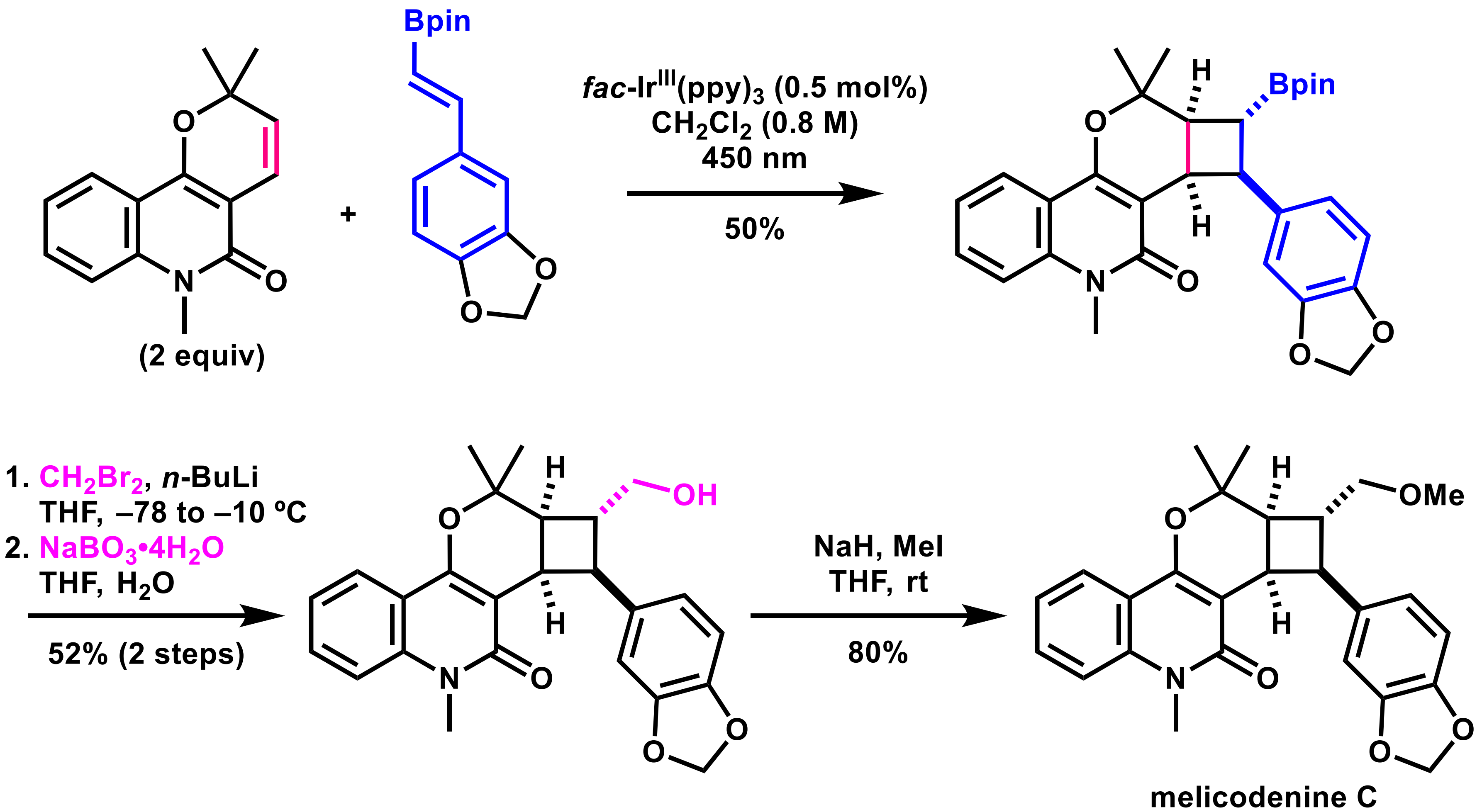
49%, dr = 7:1



39%, dr = 10:1

Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.

Synthesis of Melicodenine C

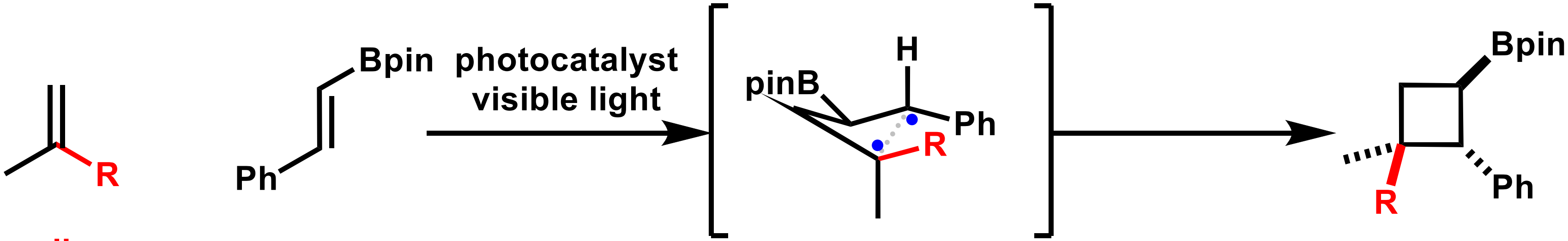


Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.

Contents

Outline

Drawbacks of previous reaction[1]



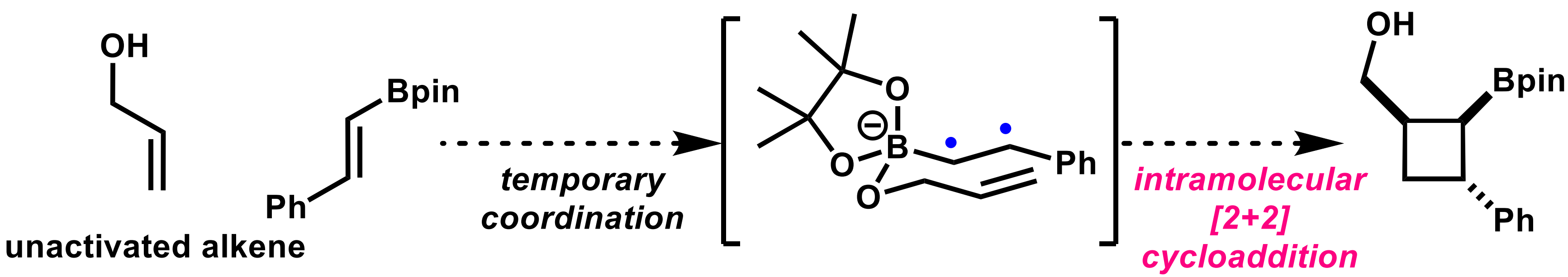
R = alkene or arene

stabilized by neighboring R

To stabilize 1,4-biradical intermediate, acceptors should have conjugated systems.

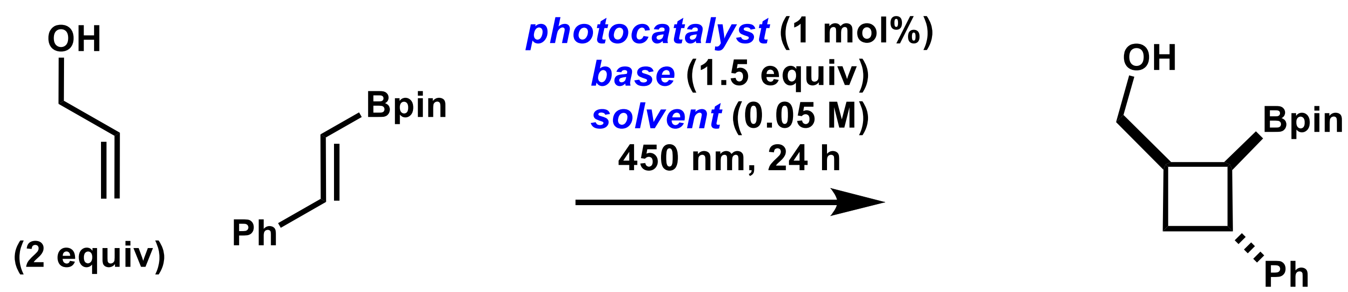
New strategy[2]

temporary coordination of unactivated allylic alcohol to Bpin unit
-> intramolecular [2+2]-cycloaddition



1. Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.
2. Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.

Optimization



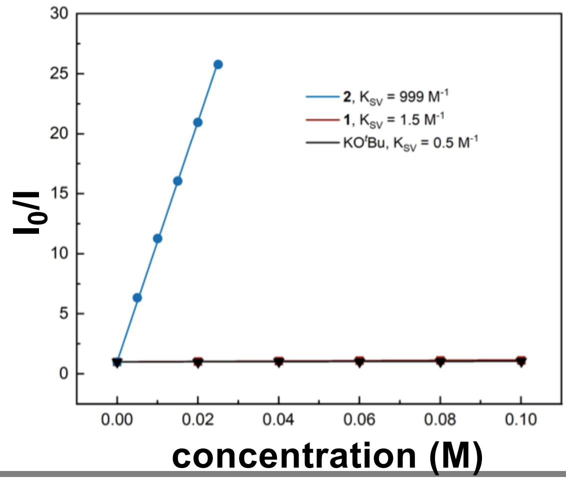
entry	*photocatalyst*	*base*	*solvent*	rcv. SM	yield
1	**fac-Ir(ppy)$_3$**	**t-BuOK**	CH_2Cl_2	**76**	**14**
2	**fac-Ir(dFppy)$_3$**	**t-BuOK**	CH_2Cl_2	**18**	**55**
3	**none**	**t-BuOK**	CH_2Cl_2	**81**	**<2**
4	**fac-Ir(dFppy)$_3$**	**t-BuONa**	CH_2Cl_2	**35**	**45**
5	**fac-Ir(dFppy)$_3$**	**t-BuOLi**	CH_2Cl_2	**80**	**4**
6	**fac-Ir(dFppy)$_3$**	**DBU**	CH_2Cl_2	**80**	**<2**
7	**fac-Ir(dFppy)$_3$**	**none**	CH_2Cl_2	**92**	**<2**
8*	**fac-Ir(dFppy)$_3$**	**t-BuOK (2 equiv)**	CH_2Cl_2	**26**	**64**
9*	**fac-Ir(dFppy)$_3$**	**t-BuOK (2 equiv)**	**THF**	**74**	**14**
10*	**fac-Ir(dFppy)$_3$**	**t-BuOK (2 equiv)**	CH_3CN	**79**	**<2**
11*	**fac-Ir(dFppy)$_3$**	**t-BuOK (2 equiv)**	**toluene**	**18(<2)**	**68(78**)**

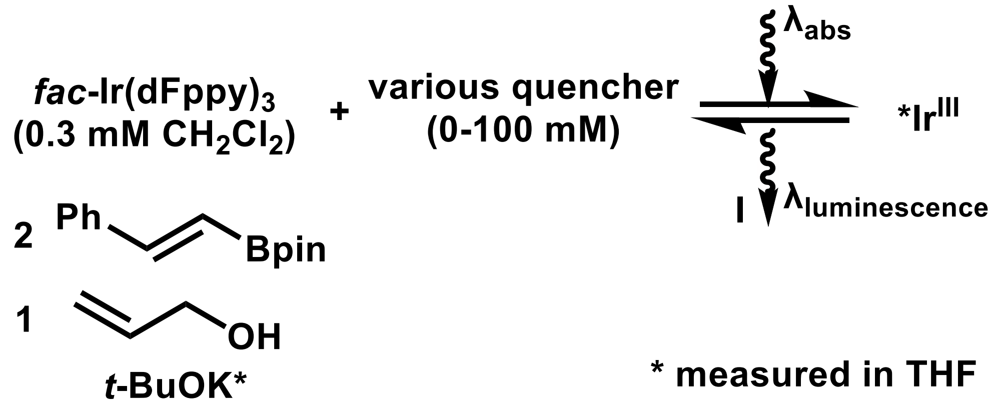
*** 3 equiv of allyl alcohol ** 0.02 M**

Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.

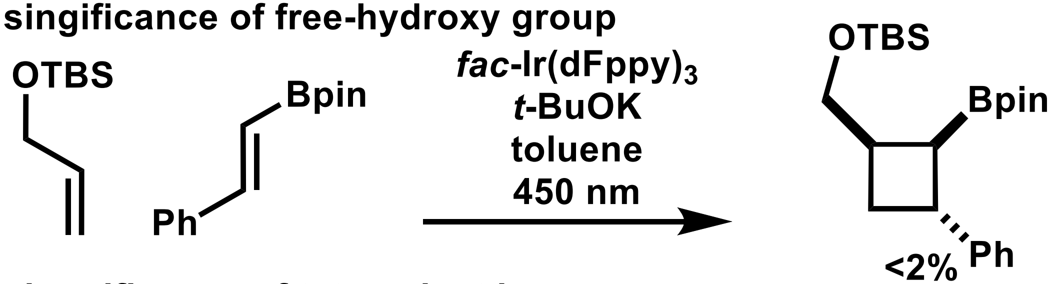
Mechanistic Study

Stern-Volmer quenching

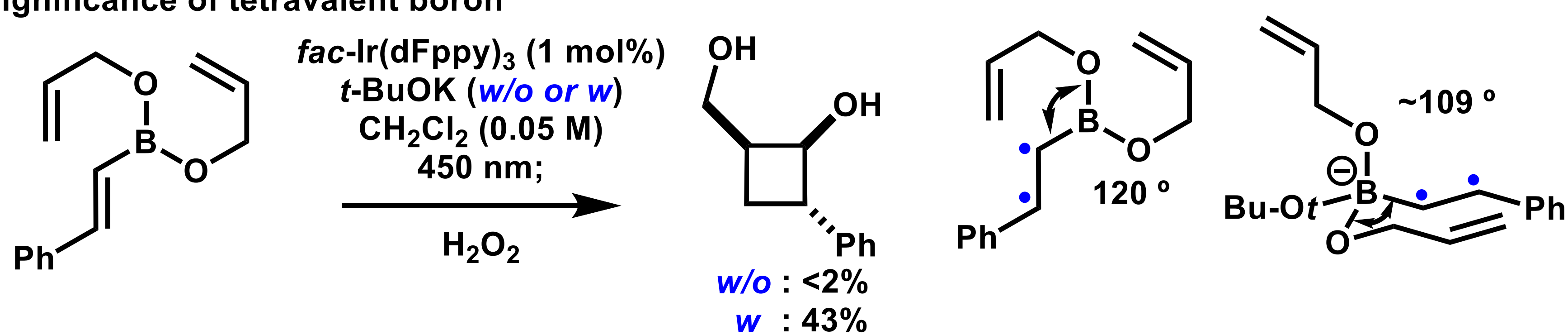




singificance of free-hydroxy group



singnificance of tetravalent boron



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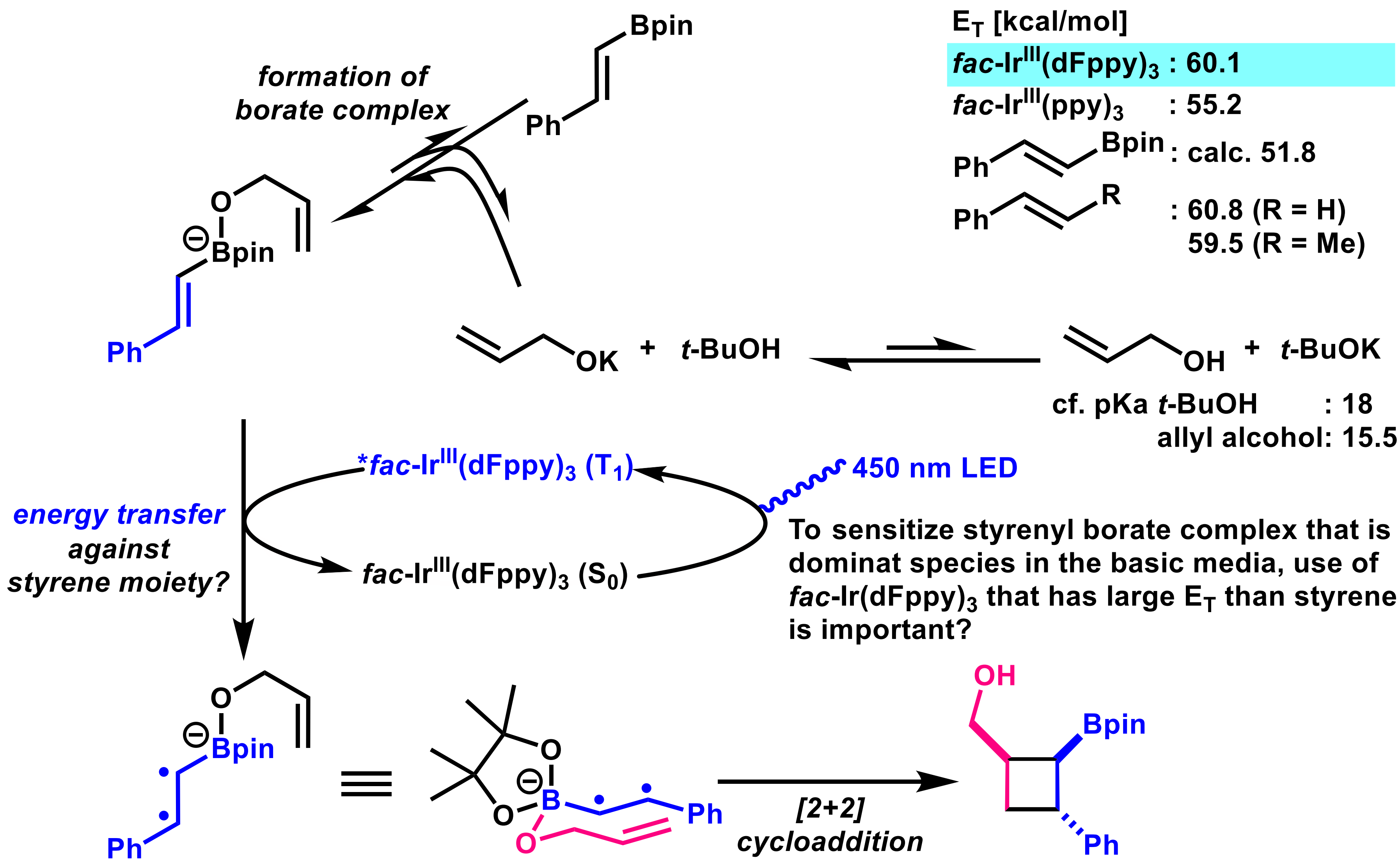
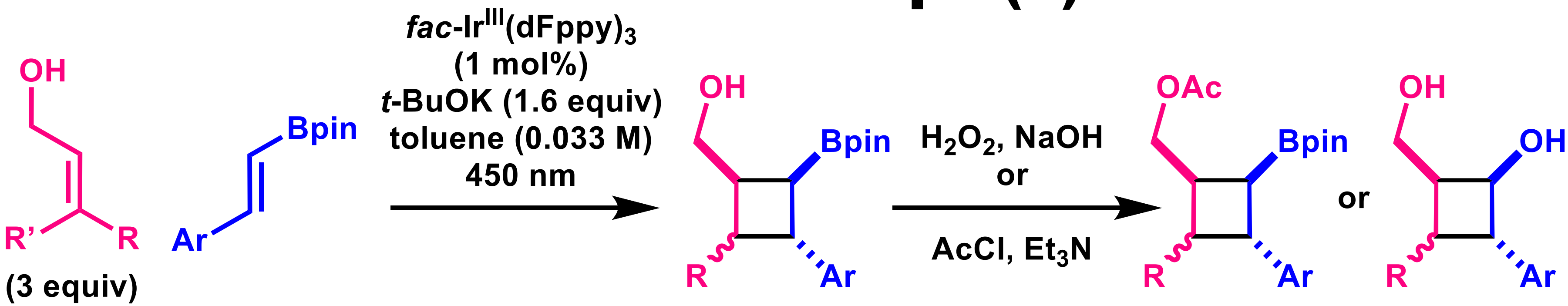
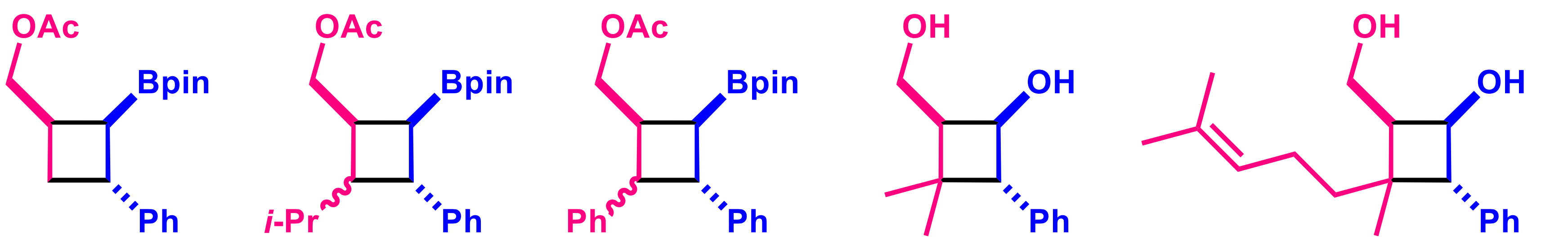
Proposed Mechanism



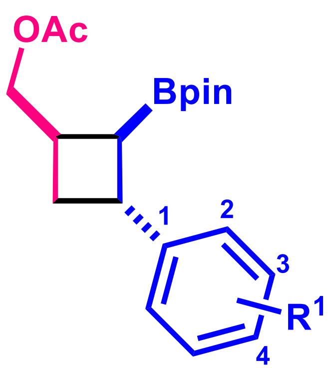
Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.

Substrate Scope (1)

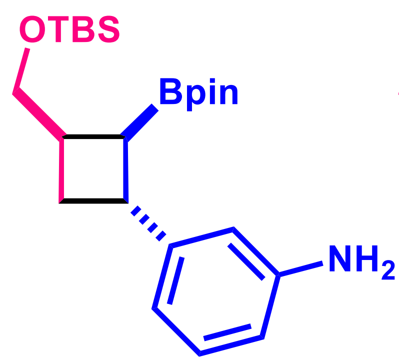




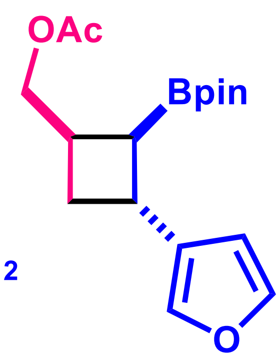
83%, dr = >20:1 | 73%, dr = 1:1 | 44%, syn to Ph; 28%, anti to Ph | 58%, dr = >20:1 | 56%, dr = 1:1



R^1 = 2-Me	69%, dr = >20:1
R^1 = 3-F	66%, dr = >20:1
R^1 = 4-OMe	70%, dr = >20:1
R^1 = 4-CF_3	71%, dr = >20:1
R^1 = 4-Br	54%, dr = >20:1
R^1 = 4-CO_2*t*-Bu	54%, dr = >20:1*



52%**, dr = >20:1



65%***, dr = >20:1

* CH_2Cl_2 ** primary alcohol protected by TBS group. *** 2 mol% of *fac*-Ir(dFppy)$_3$

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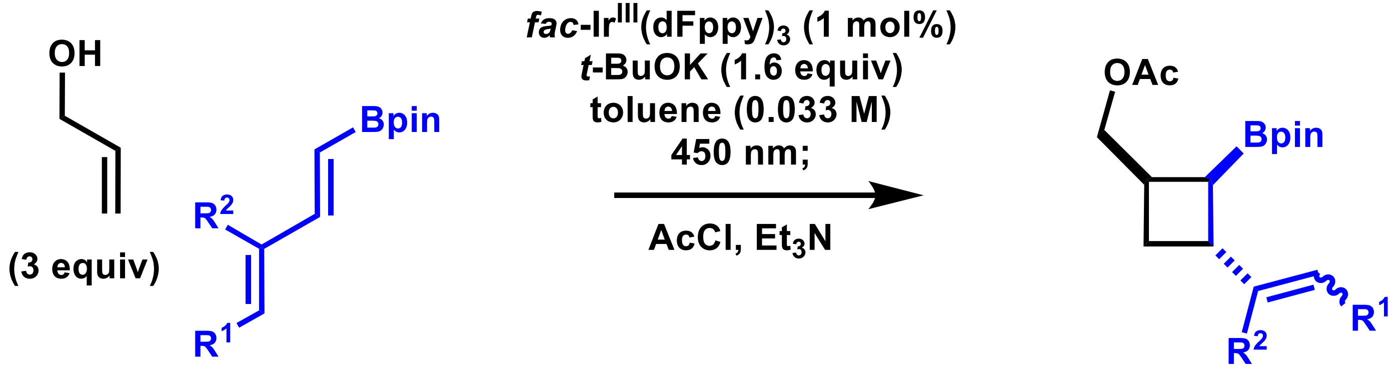
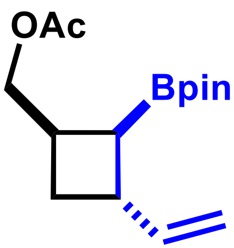
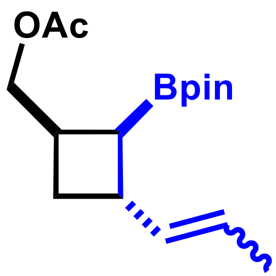
Substrate Scope (2)

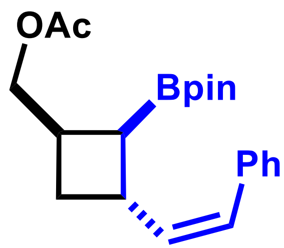




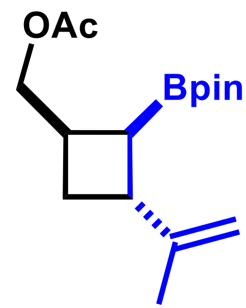
66%, dr = >20:1



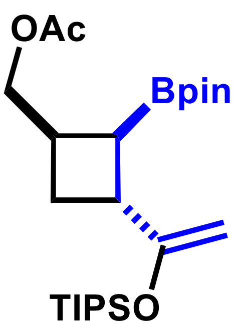
79%, dr = >20:1, E/Z = 1:1



71%*, dr = >20:1, E/Z = 1:8



71%, dr = >20:1



52%, dr = >20:1

* 1 mol% of *fac*-Ir(ppy)$_3$

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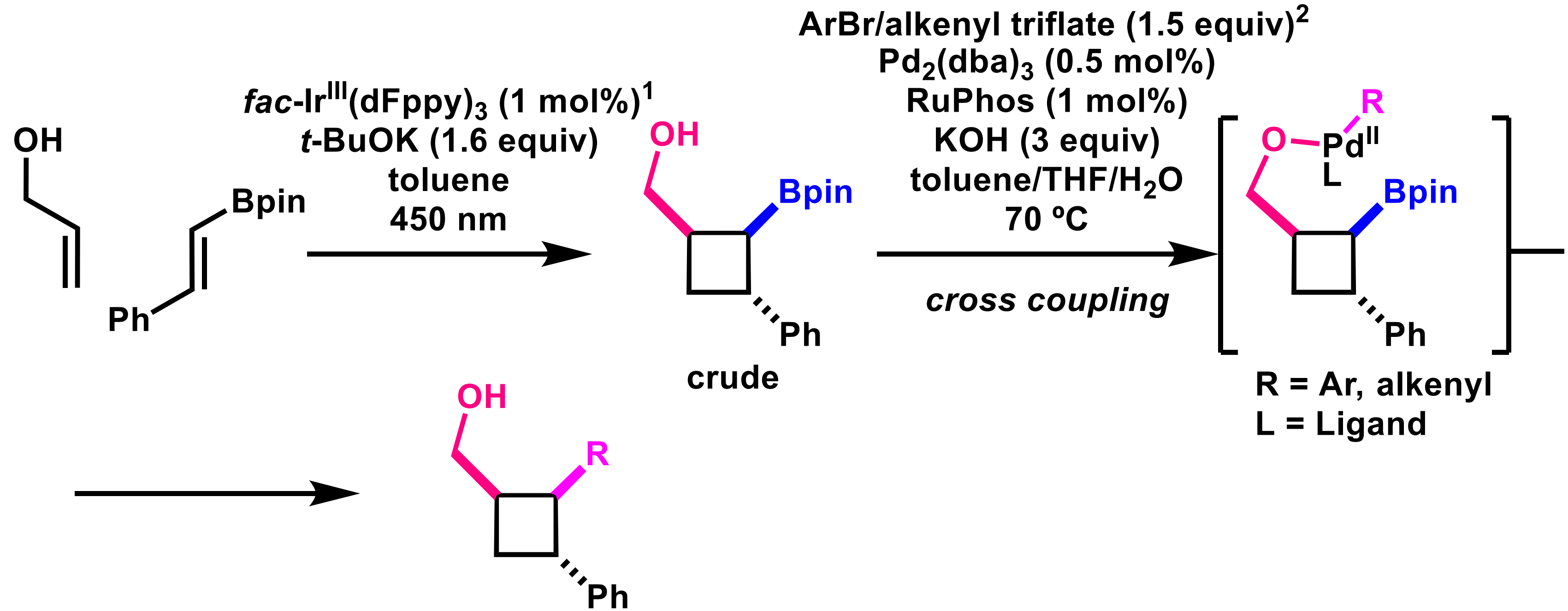
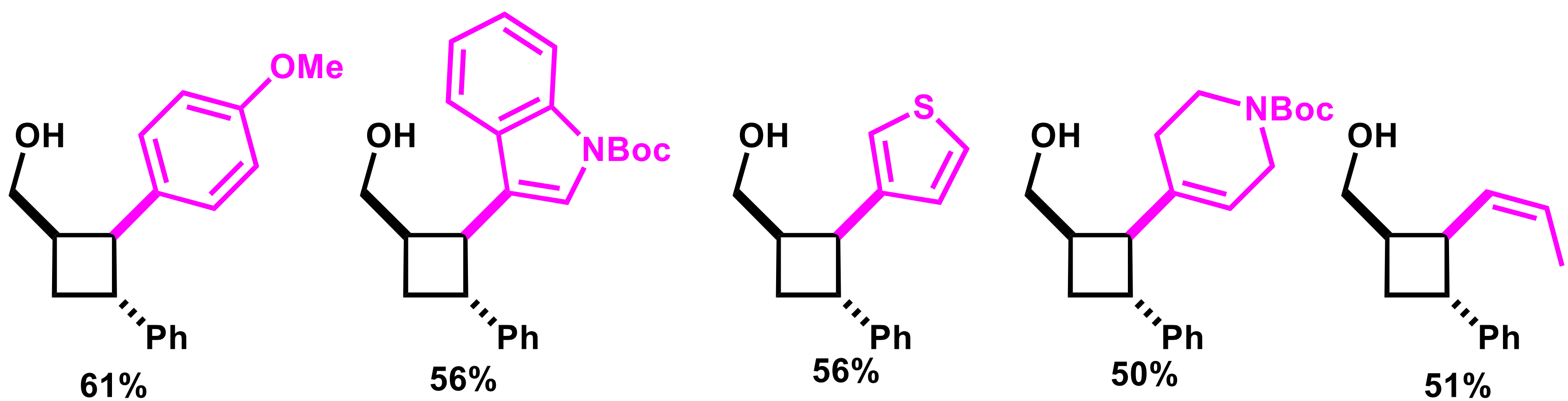
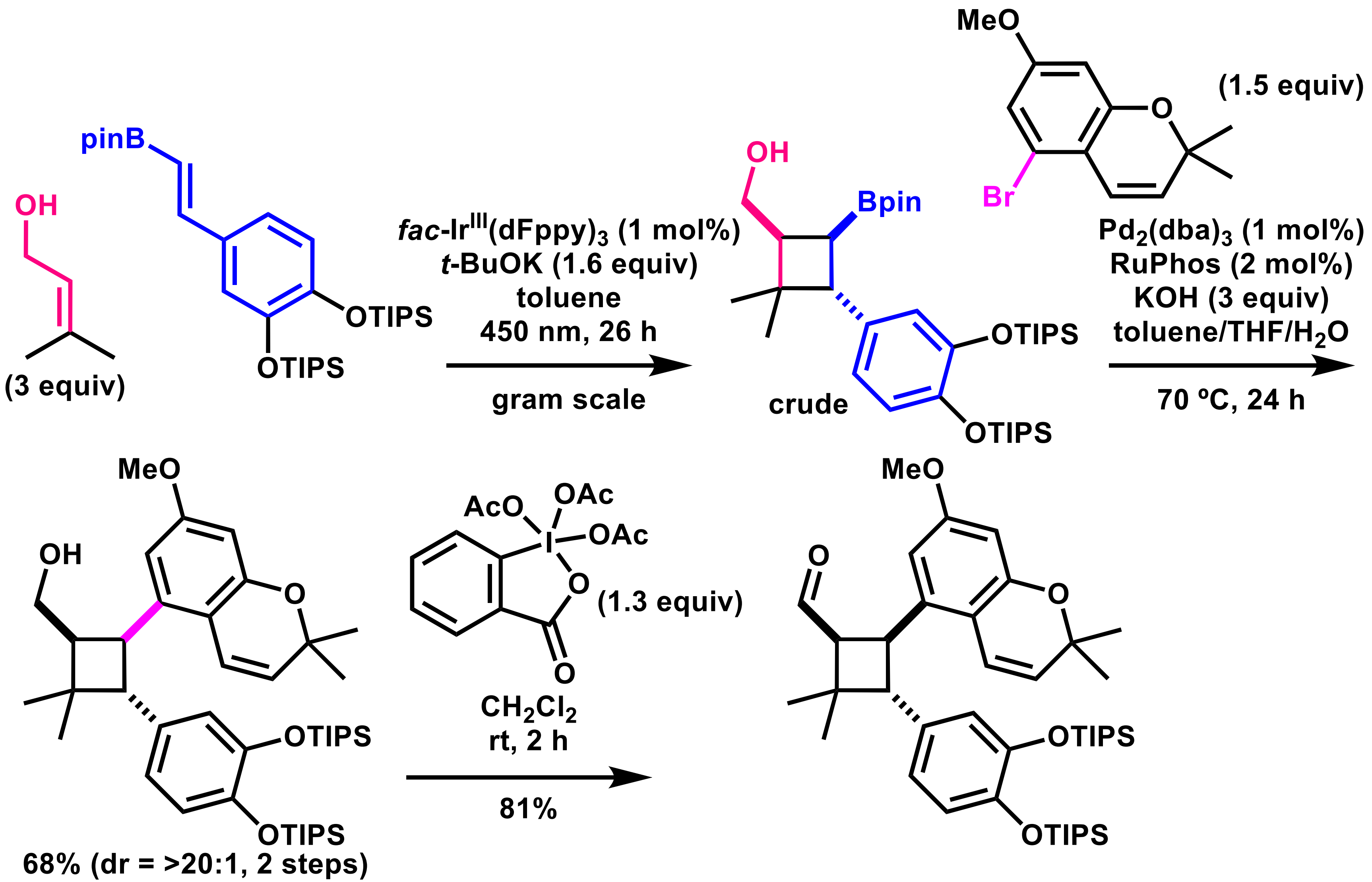
Cross coupling





1. Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.
2. Blaisdell, T. P.; Morken, J. *J. Am. Chem. Soc.* **2015**, *137*, 8712– 8715.

Synthesis of Artochamin J (1)



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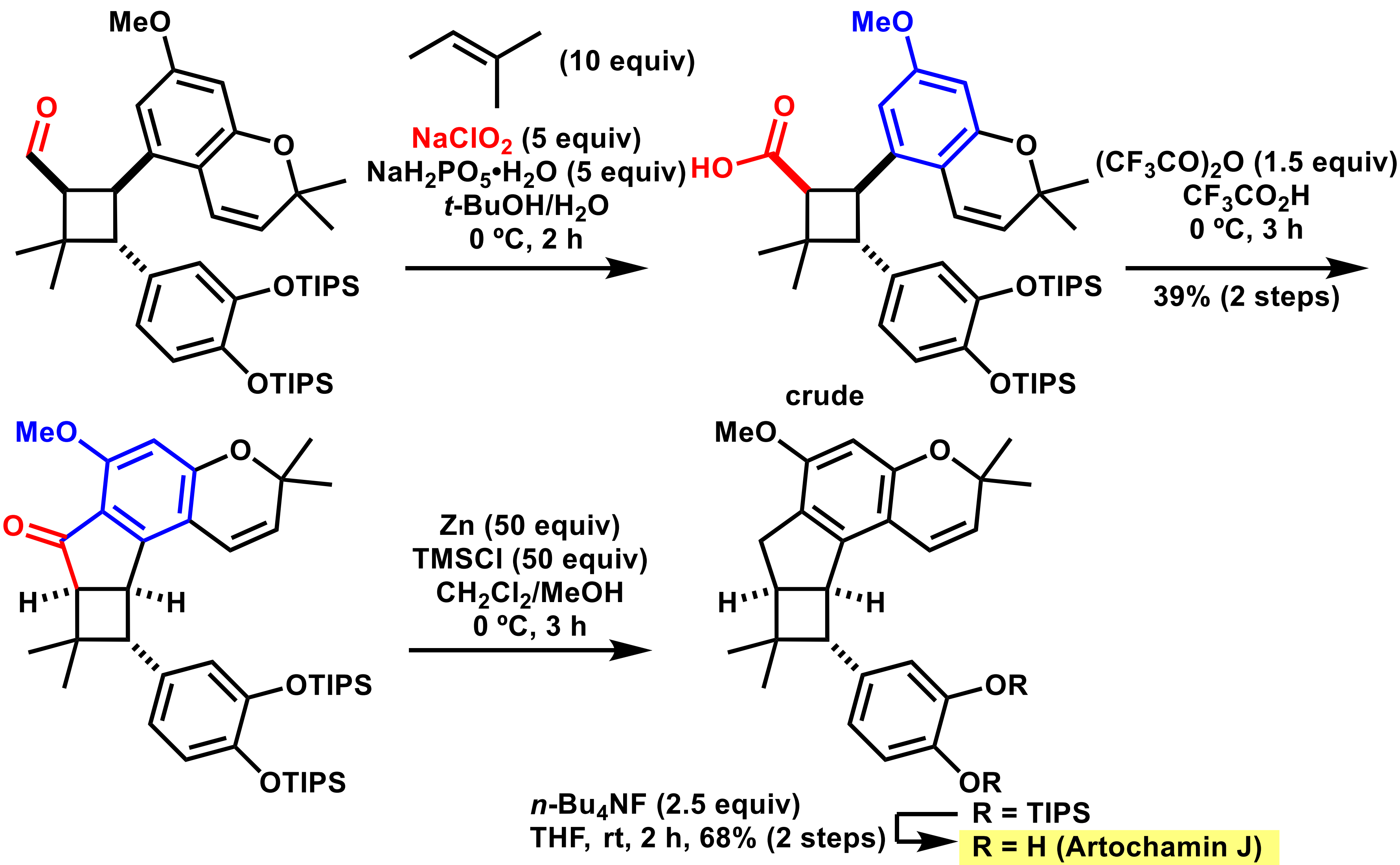
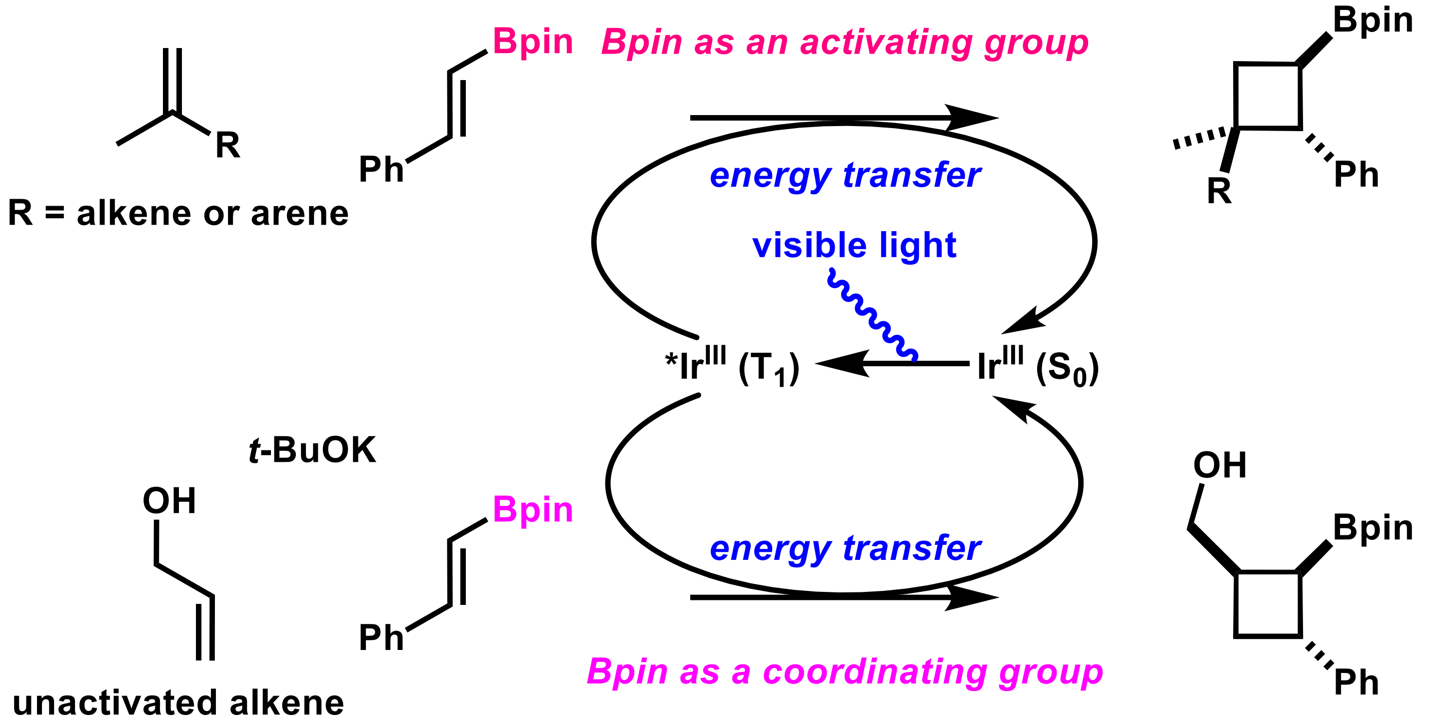
Synthesis of Artochamin J (2)



Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.

Summary



1. Liu, Y.; Ni, D.; Stevenson, B. G.; Tripathy, V.; Braley, S. E.; Raghavachari, K.; Swierk, J. R.; Brown, M. K. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202200725.
2. Liu, Y.; Ni, D.; Brown, B. *J. Am. Chem. Soc.* **2022**, *144*, 18790–18796.