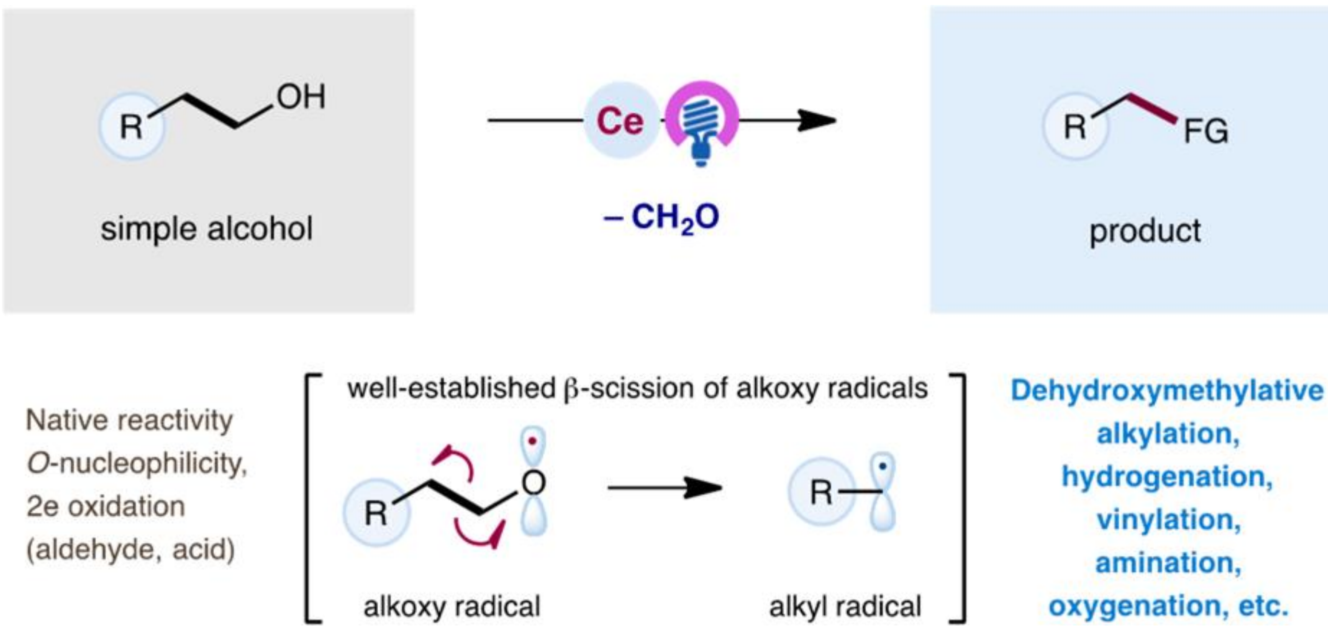
Cerium Catalyzed Functionalization
by Zhiwei Zuo group



Native reactivity
O-nucleophilicity,
2e oxidation
(aldehyde, acid)

Dehydroxymethylative
alkylation,
hydrogenation,
vinylation,
amination,
oxygenation, etc.

LS 2020/0418
D3 Shinsuke Shimizu

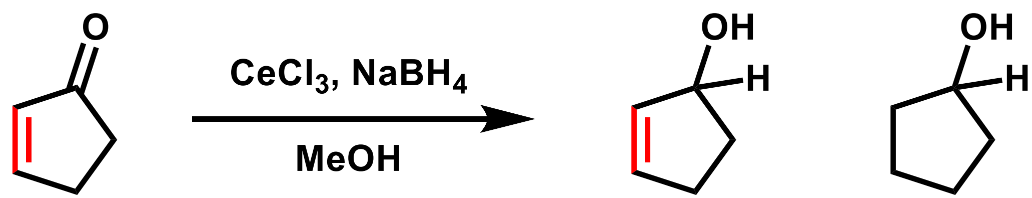
Introduction: Cerium

Features of Ce

*** Earth-abundant lanthanoide**
more abundant than Ru (10^3) and Ir (10^5) in the earth's upper continental crust.

*** Both the Ce(III) and Ce(IV) oxidation states are accessible.**
a unique behaviour among the rare-earth metals.

Ce(III): electrons configuration [Xe](4f)[1]
used as a Lewis acid.



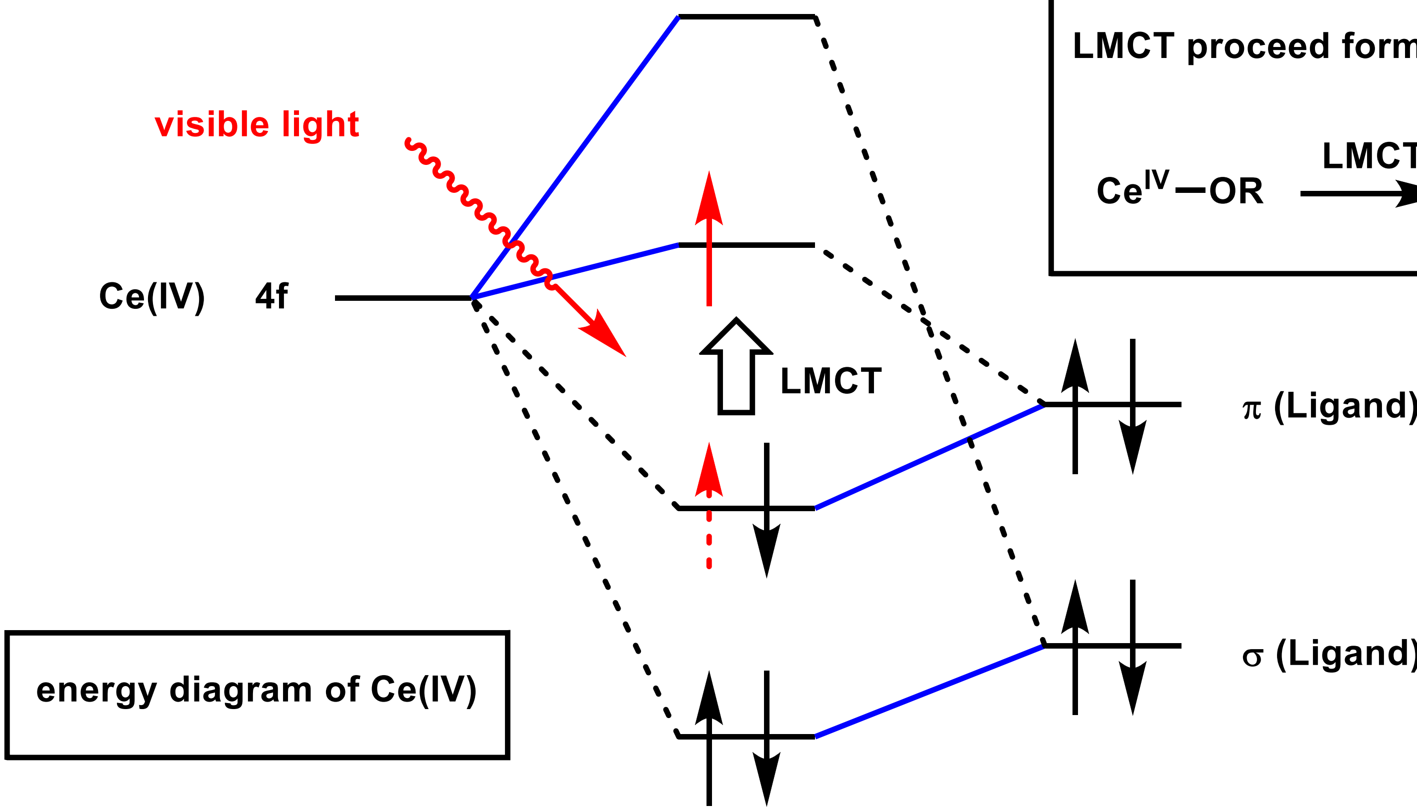
Ce(IV): electrons configuration [Xe]
used as an one electron oxidant (CAN, $(NH_4)_2[Ce(NO_3)_6]$)

1) Qiao, Y.; Schelter, E. J. *Acc. Chem. Res.* **2018**, *51*, 2926. 2) Schelter, E. J. *Nat. Chem.* **2013**, *5*, 348.
3) Brown, H. C.; Hess, H. M. *J. Org. Chem.* **1969**, *34*, 2206.

LMCT: Ligand to Meteal Charge Transfer

LMCT complexes arise from transfer of electrons from MO with ligand-like character to those with metal-like character.
(opposite relationship to MLCT)

*** This type of transfer could occur if complexes have ligands with relatively high-energy lone pairs or if the metal has low-lying empty orbitals.**



LMCT proceed formal reduction of metal

Ce^{IV}—OR $\xrightarrow{\text{LMCT}}$ Ce^{III} •OR

シュライバー・アトキンス無機化学（下） 第4版

Contents

1. Selective functionalization of simple alkanes
   (Zuo’s group, Science, 2018)

2. Dehydroxymethylation of alcohols
   (Zuo's group, main paper, JACS, 2019)

Contents

1. Selective functionalization of simple alkanes
(Zuo’s group, Science, 2018)

2. Dehydroxymethylation of alcohols
(Zuo's group, main paper, JACS, 2019)

Dr. Zhiwei Zuo

2003-2007
B.S. in Chemistry at Nanjing University, School of Chemistry & Chemical Engineering
(Advisor: Prof. Yixiang Chen)

2007-2012
Ph.D. in Organic Chemistry at Shanghai Institute of Organic Chemistry, CAS
(Advisor: Prof. Dawei Ma)

2013-2015
Postdoctoral Fellow at Princeton University, Department of Chemistry;
(Advisor: Prof. David W. C. MacMillan)

2015.9-Present
Assistant Professor (PI) at ShanghaiTech University, School of Physical Sciences and Technology

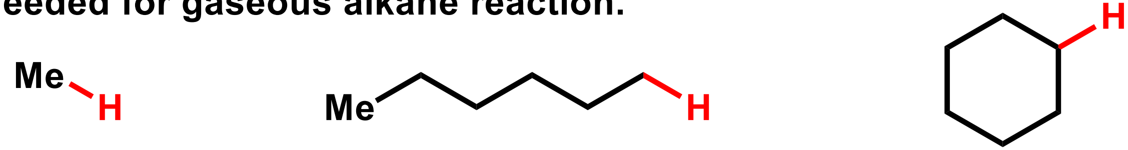
Research Topics

1. **Development of highly efficient catalytic transformations utilizing eco-friendly technologies and abundant functionalities.**
2. **the direct functionalization of carbon frameworks and efficient synthesis of biologically active heterocycles.**

http://hr.shanghaitech.edu.cn/2018/1206/c4789a37852/page.htm

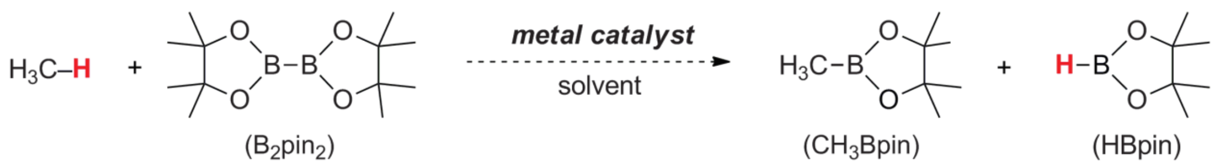
C-H Activation of Simple Alkane

* The C-H bonds of methane are generally more kinetically inert than those of other hydrocarbons, reaction solvents, and methane functionalization products.
* Reaction solvent is needed for gaseous alkane reaction.

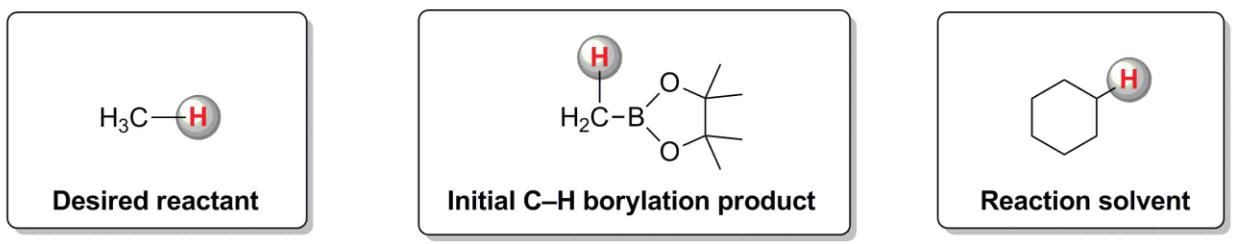


BDE **105 kcal/mol** **101 kcal/mol** **99.5 kcal/mol**

A ***Proposed selective mono-C–H borylation of methane:***



B ***Selectivity challenges:***



sterically activated (most sterically accessible C–H bond)

electronically activated (most acidic C–H bond)

statistically favored (highest concentration C–H bond)

Sanford reported C-H borylation of methane using [Ir], [Rh] or [Ru] catalyst.

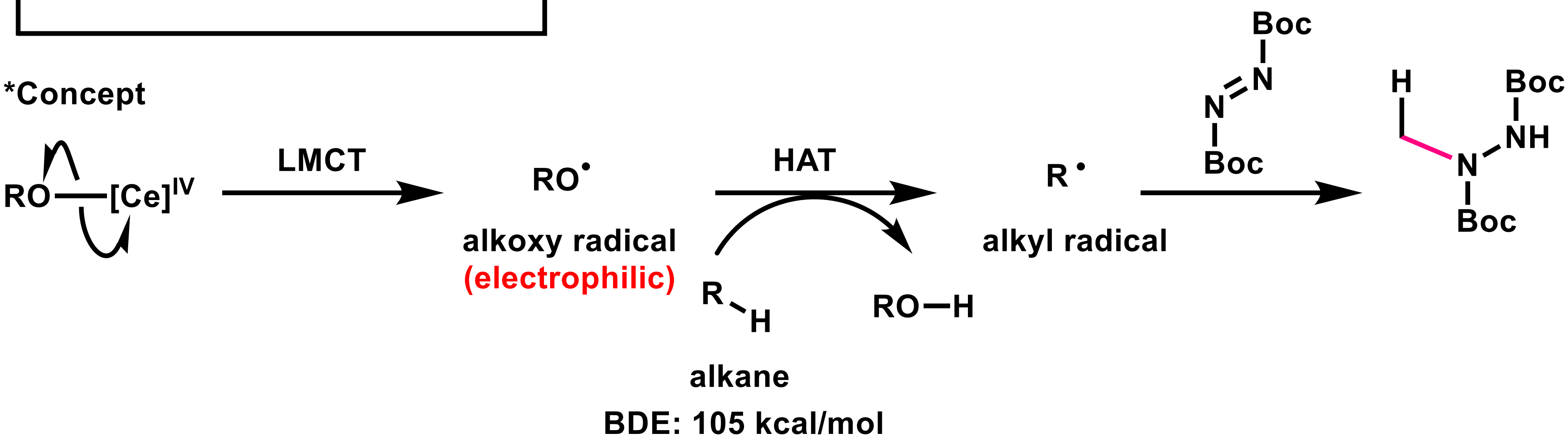
⇨ **chalenge remains to develop efficient Earth-abundant catalytic systems that operate under ambient conditions.**

1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668. 2) Cook, A. K.; Schimler, S. D.; Matzger, A. J.; Sanford, M. S. *Science* **2016**, *351*, 1421. 3) S. J. Blanksby, G. B. Ellison, *Acc. Chem. Res.* **2003**, *36*, 255.

Research Concept

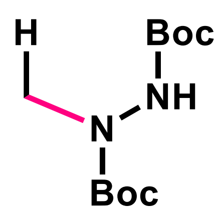
MeO—H BDE: 105 kcal/mol

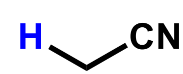
*Concept



* Polarity matched HAT

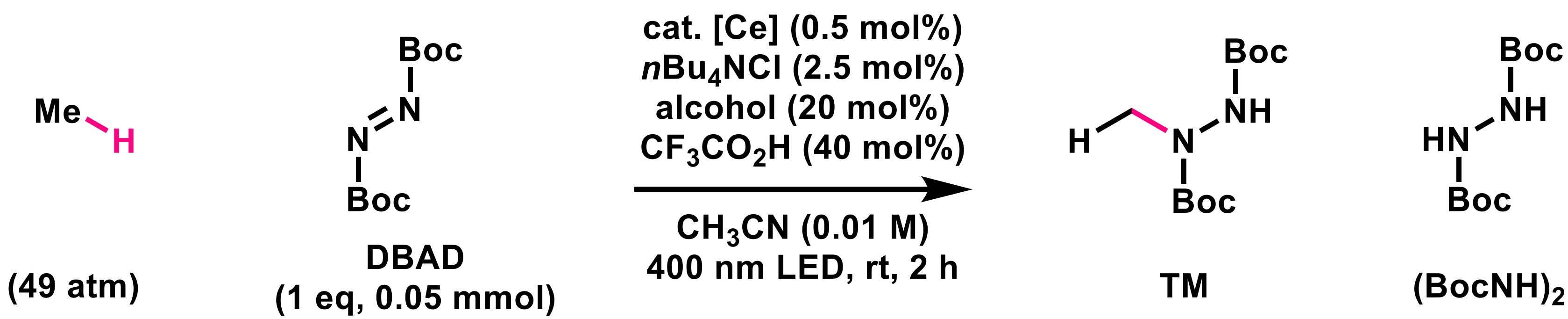
electron deficient
hydrogen atom





1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668. 2) Le, C.; Liang, Y.; Evans, R. W.; Li, X.; MacMillan, D. W. C. *Nature* **2017**, *547*, 79.

Cerium-Catalyzed Amination of Methane

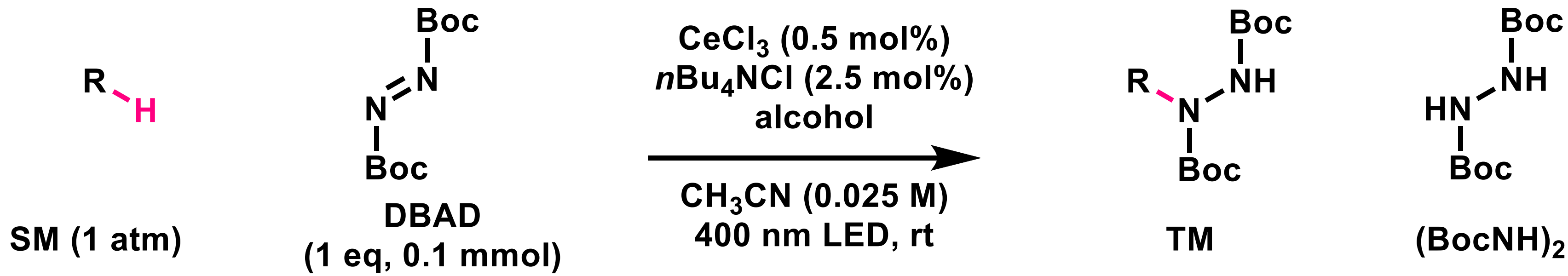


entry	cat. [Ce]	alcohol	conversion	Yield	$(BocNH)_2$	TON
1	$CeCl_3$	CCl_3CH_2OH	89%	39%	33%	78
2	$CeBr_3$	CCl_3CH_2OH	94%	27%	38%	54
3	$Ce(OTf)_3$	CCl_3CH_2OH	92%	20%	39%	40
4	$Ce(OTf)_4$	CCl_3CH_2OH	94%	45%	26%	90
5	$Ce(OTf)_4$	CF_3CH_2OH	60%	21%	28%	42
6	$Ce(OTf)_4$	MeOH	87%	38%	35%	76

Yields were determined by GC analysis of the crude reaction mixtures.

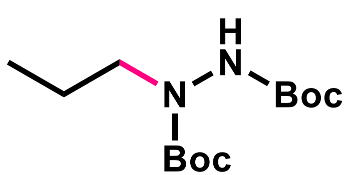
1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Cerium-Catalyzed Amination of Alkanes

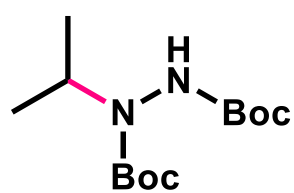


entry	SM	alcohol	time	Yield	statistical	$(BocNH)_2$	TON
1	propane	CCl_3CH_2OH (20 mol%)	9 h	70% (A:B = 1:1)	(A:B = 1:3)	6%	140
2	propane	MeOH (50 mol%)	19 h	39% (A:B = 1:3.9)	(A:B = 1:12)	20%	78
3	propane	*i*PrOH (50 mol%)	19 h	19% (A:B = 1:2.1)	(A:B = 1:6.3)	23%	38
4	propane	*t*BuOH (50 mol%)	19 h	27% (A:B = 1:1.2)	(A:B = 1:3.6)	7%	54
5	*n*-butane	CCl_3CH_2OH (20 mol%)	6 h	76% (C:D = 1:1.7)	(C:D = 1:2.6)	2%	152
6	*n*-butane	MeOH (50 mol%)	18 h	72% (C:D = 1:8)	(C:D = 1:12)	4%	144

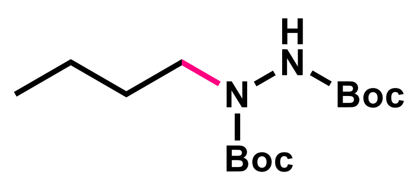
Yields were determined by GC analysis of the crude reaction mixtures.



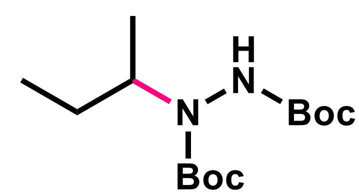
A



B



C

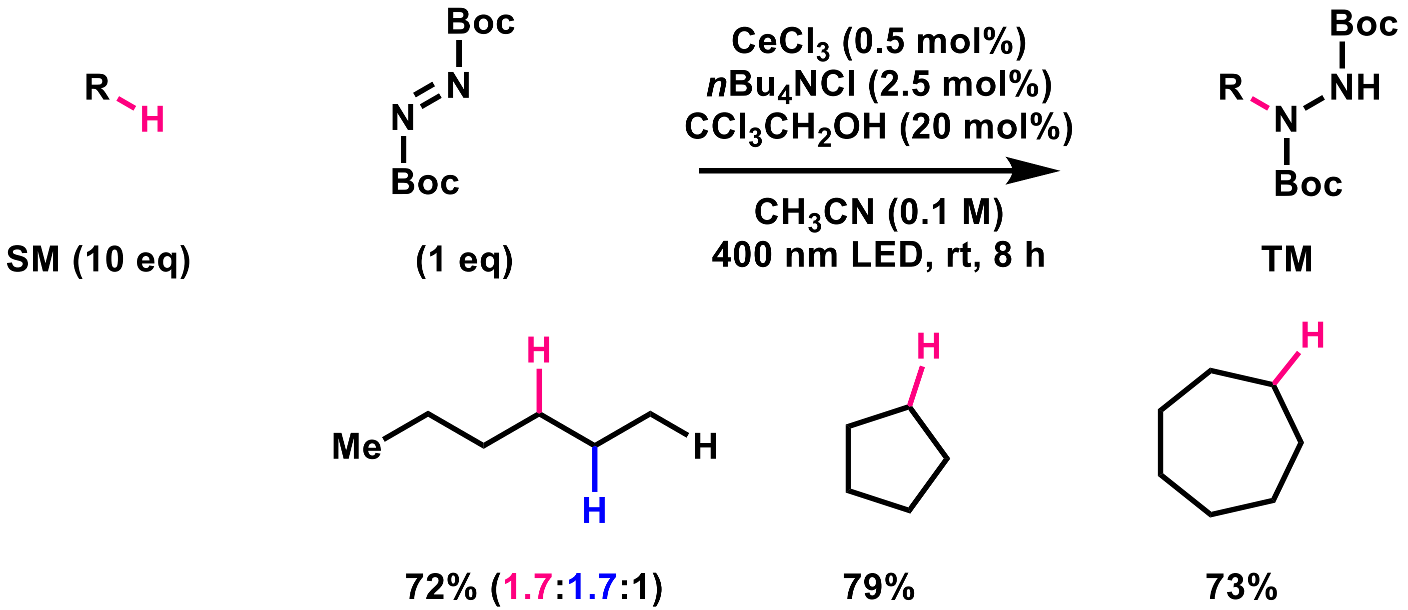


D

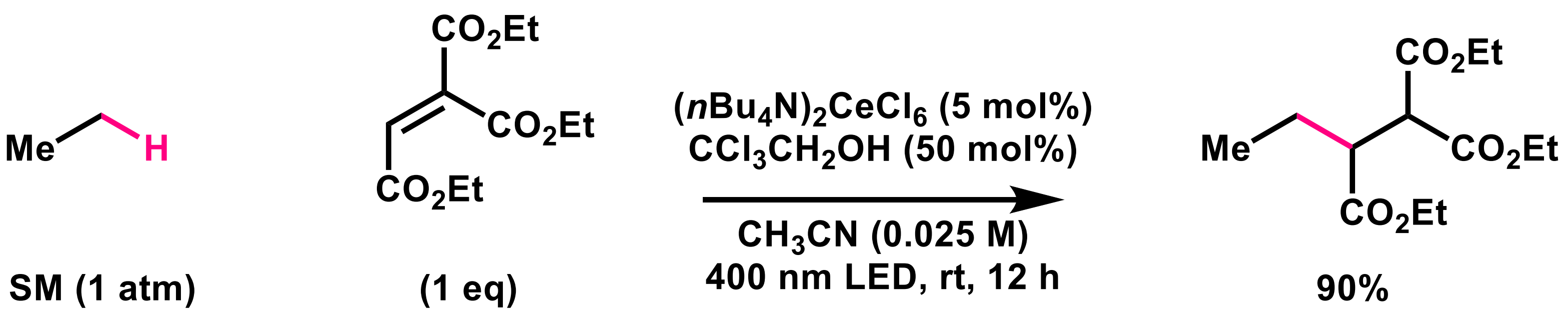
1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Further Applications

a) Substrate scope



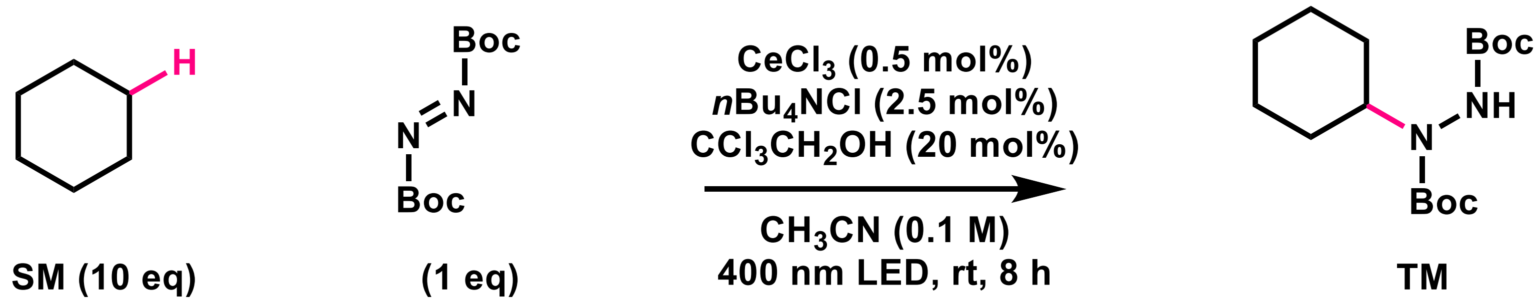
b) Giese reaction



Yields were determined by GC analysis of the crude reaction mixtures.

1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Mechanistic Study (1, control experiments)



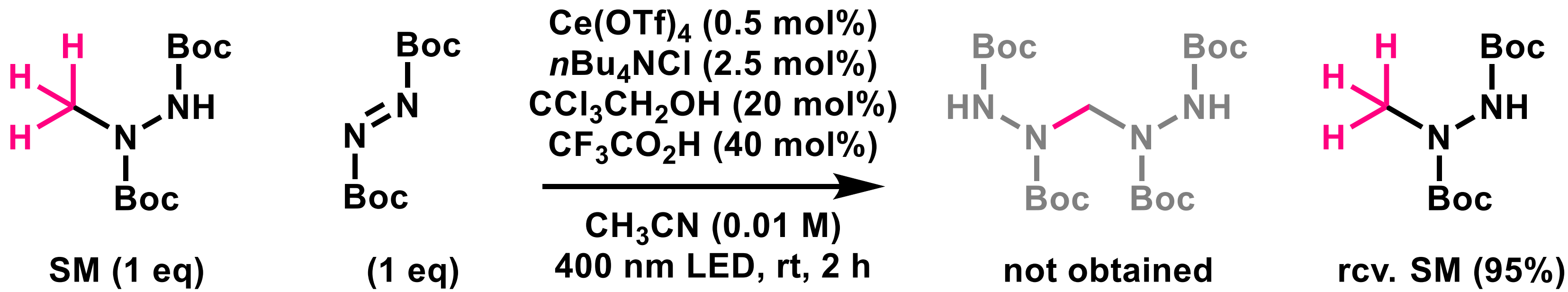
entry	variation from above conditions	Yield
1	none	81%
2	without CC_3CH_2OH	trace
3	without $CeCl_3$, *n*Bu_4NCl	trace
4	without *n*Bu_4NCl	73%
5	without LED	0%

Yields were determined by GC analysis of the crude reaction mixtures.

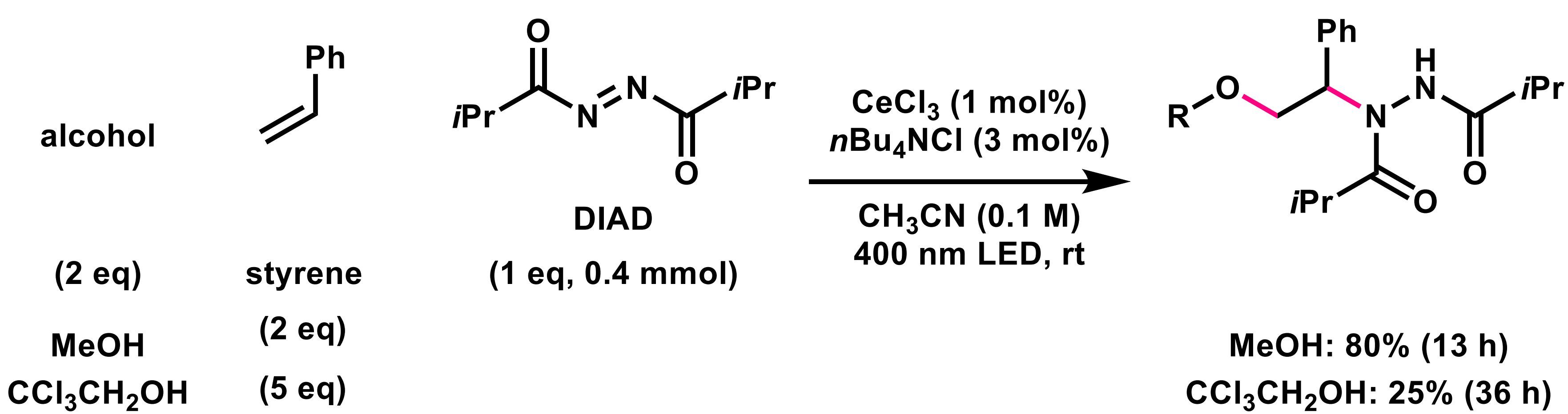
1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Mechanistic Study (2)

a) over-functionalization



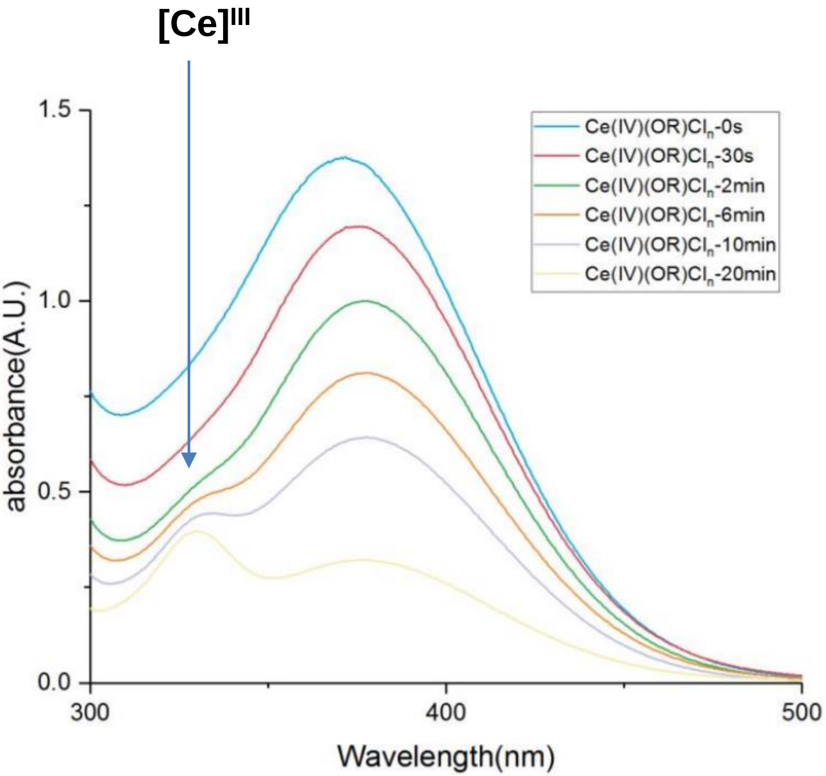
b) radical trapping



Yields were determined by GC analysis of the crude reaction mixtures.

1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Mechanistic Study (3, spectra)



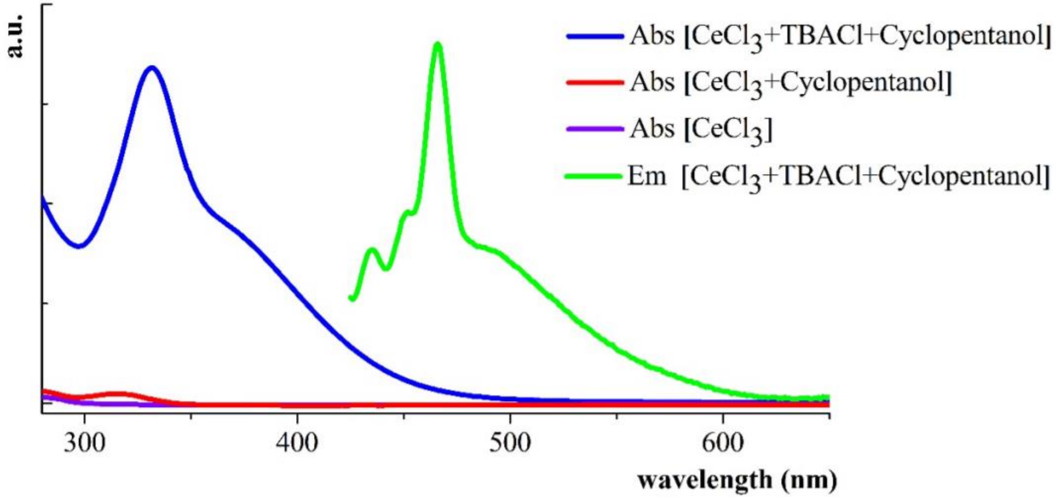


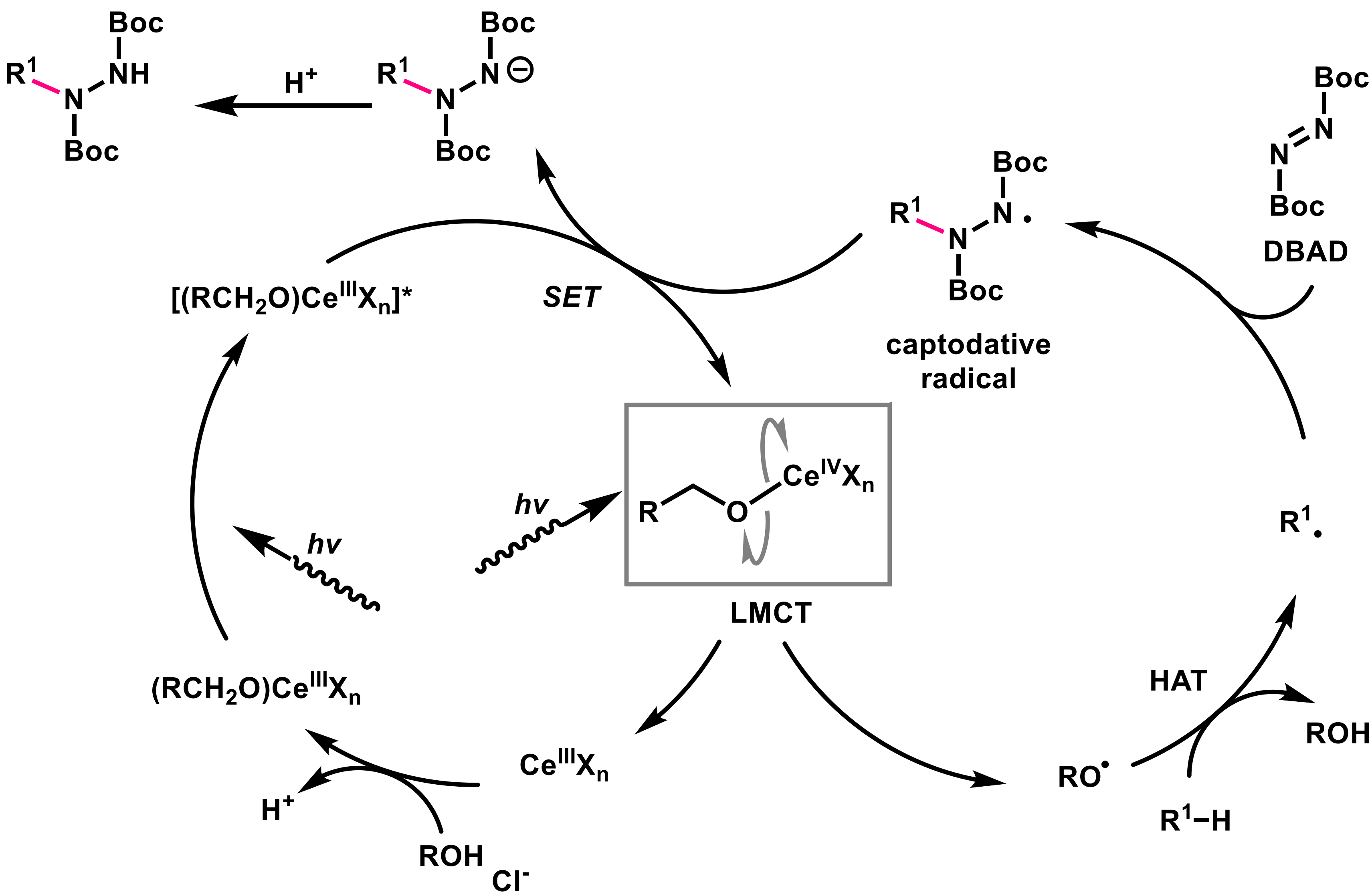
Fig 1. Absorption spectra of solution of $Ce^{IV}(OR)Cl_n$ in CH_3CN under blue light.

(n-$Bu_4N)Ce^{IV}Cl_6$+1-pentanol

Fig 2. Absorption spectra and emission spectra (excited at 408 nm)

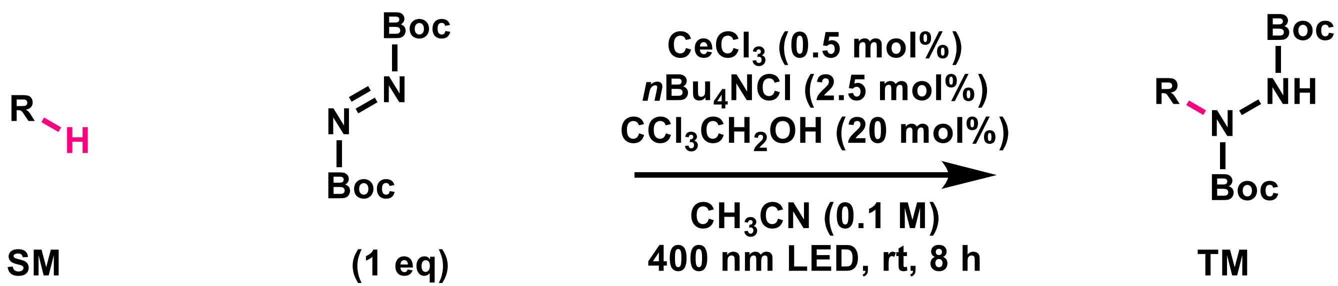
1) Zuo, Z. et. al. *ACIE* **2016**, *55*, 15319. 2) *JACS*, **2018**, *140*, 1612.

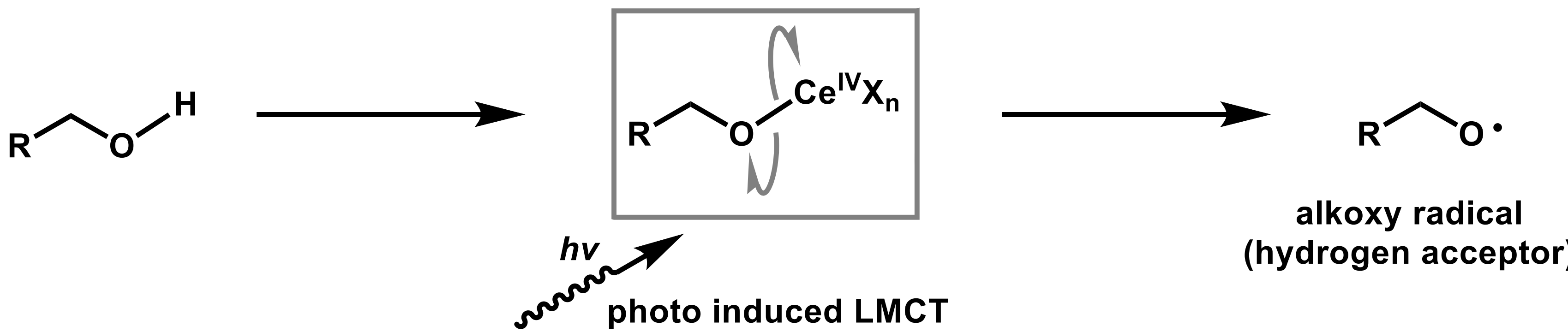
Proposed Mechanism

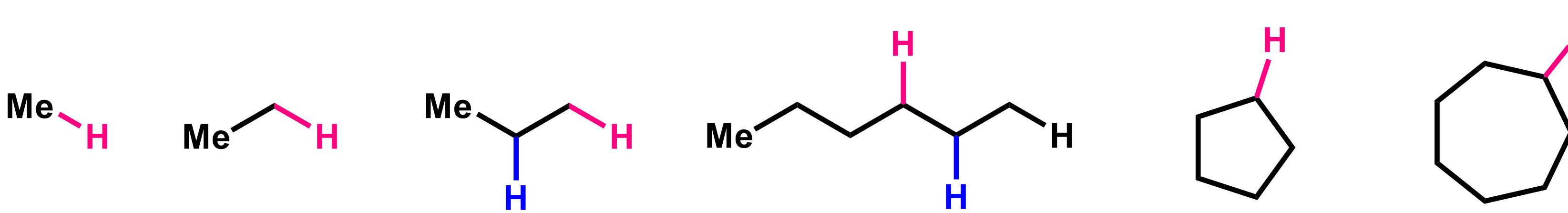


1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Short Summary







(hydrogen donors)

1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.

Contents

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   (Zuo’s group, Science, 2018)

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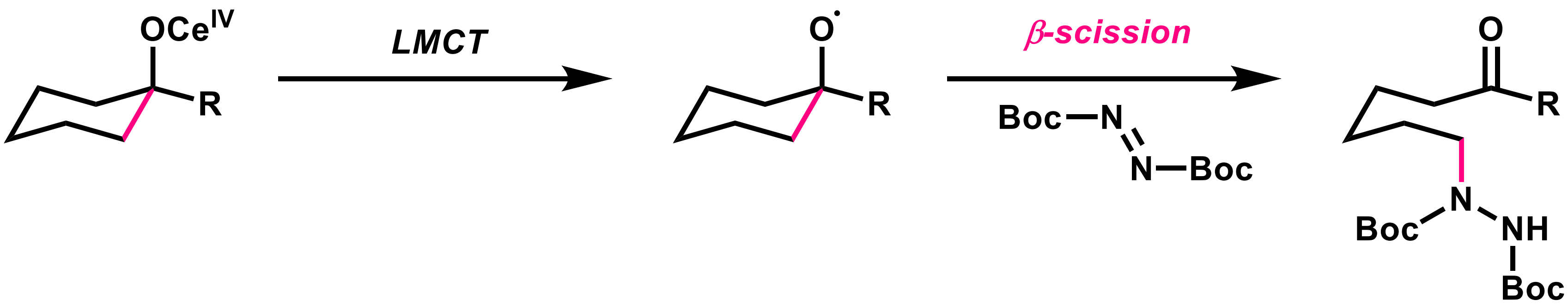
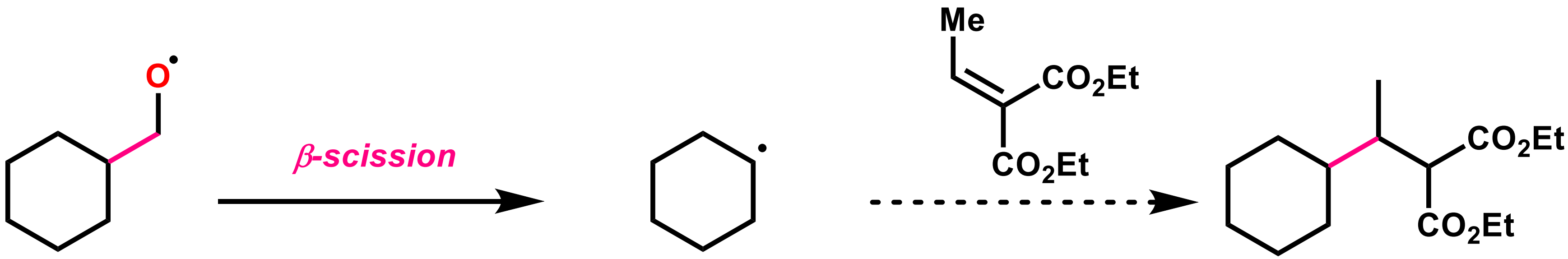
   (Zuo's group, main paper, JACS, 2019)

Research Concept

Zuo, Z. et. al. *Angew. Chem. Int. Ed.* **2016**, *55*, 15319.

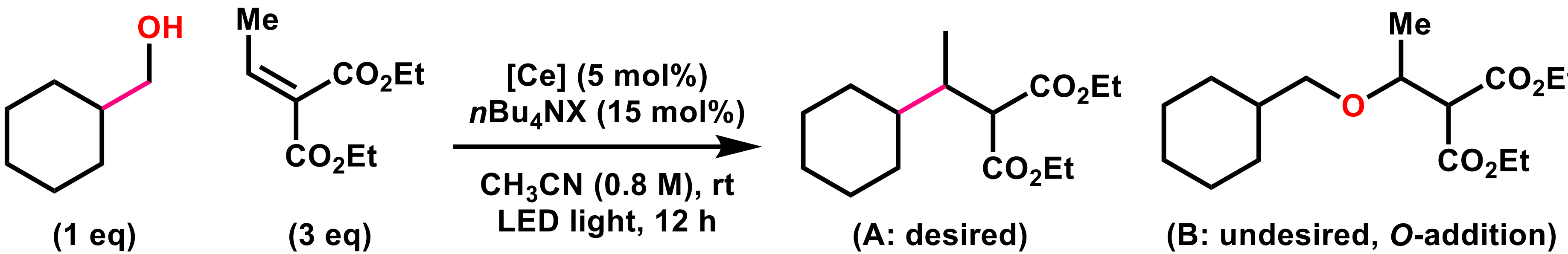


*** Reseach Concept**



1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556. 2) Zuo, Z. et. *al.* *Angew. Chem. Int. Ed.* **2016**, *55*, 15319. 3) Knowles, R. R. *J. Am. Chem. Soc.* **2016**, *138*, 10794.

Optimization of Conditions (1)

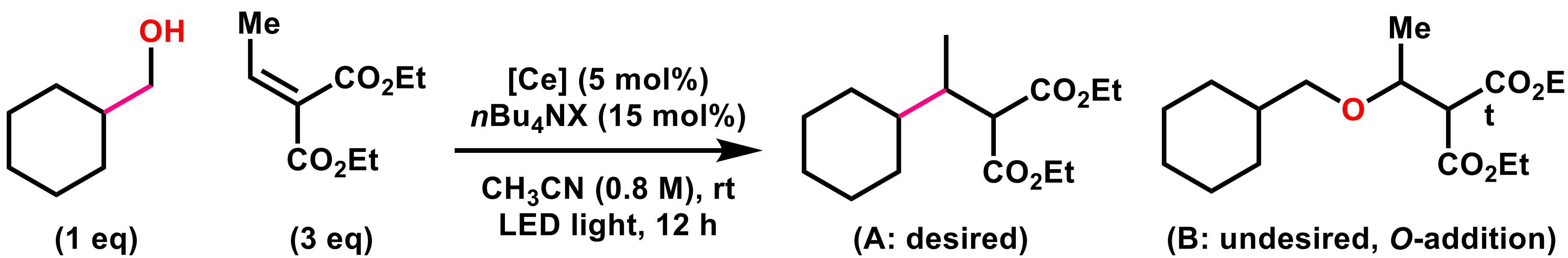


entry	catalysts	light	A: (desired)	B: (undesired)
1	$CeCl_3$, *n*Bu_4NCl	400 nm	2%	6%
2	$CeCl_3$, *n*Bu_4NCl	365 nm	39%	10%
3	$CeCl_3$, *n*Bu_4NBr	400 nm	15%	12%
4	$CeCl_3$, *n*Bu_4NBr	365 nm	85%	trace
5	$CeBr_3$	365 nm	trace	9%
6	*n*Bu_4NBr	365 nm	0%	0%

Yields were determined by GC analysis of the crude reaction mixtures.

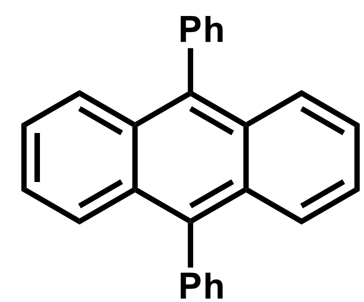
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Optimization of Conditions (2)



entry	catalysts	light	A: (desired)	B: (undesired)
1	$CeCl_3$, $n$$Bu_4NCl$	400 nm	2%	6%
7	$Ce(OTf)_3$	365 nm	trace	34%
8	$Ce(OTf)_3$, $n$$Bu_4NBr$[a]	365 nm	79%	trace
9	$CeBr_3$, $n$$Bu_4NBr$	dark	0%	27%
10	$CeCl_3$, $n$$Bu_4NCl$ DPA (5 mol%)	400 nm	81%	trace

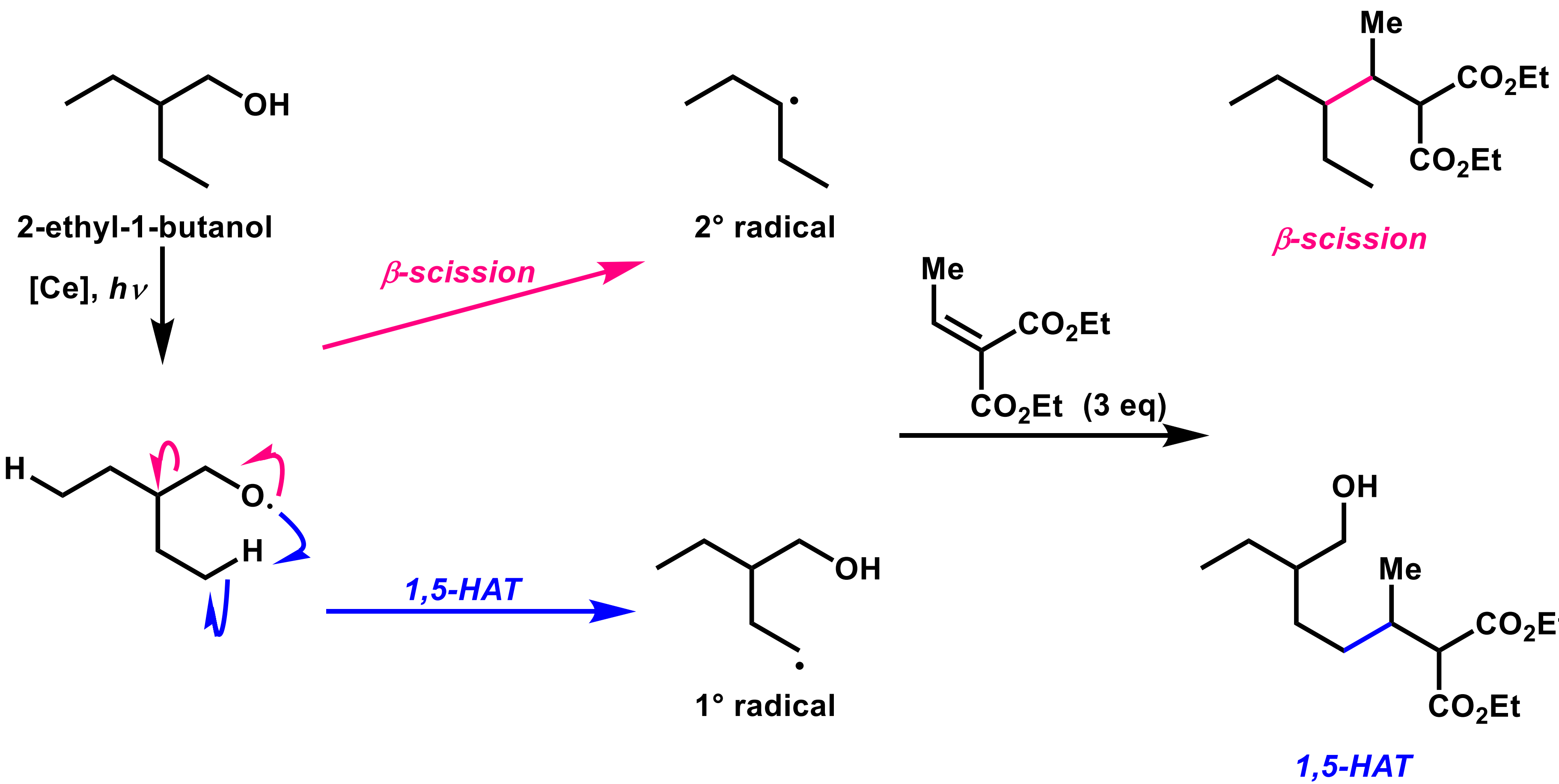
Yields were determined by GC analysis of the crude reaction mixtures.
a: $n$$Bu_4NBr$ (30 mol%)



DPA:
9,10-diphenylanthracene

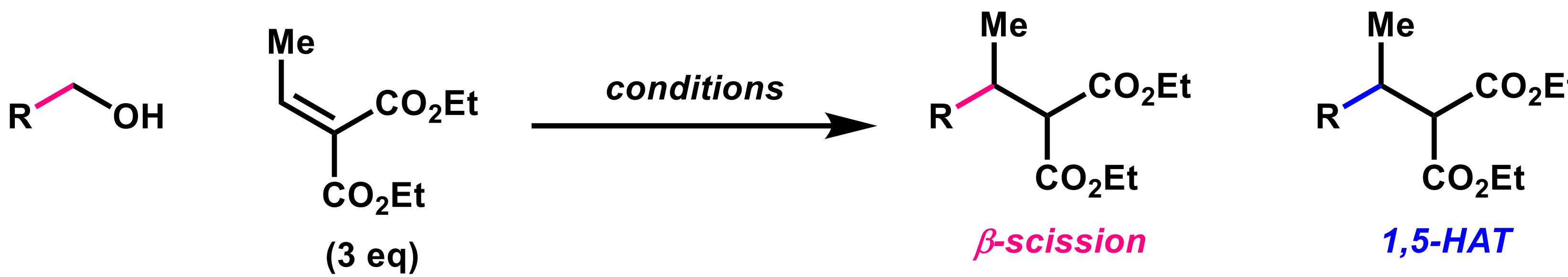
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

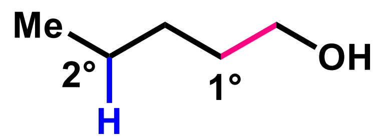
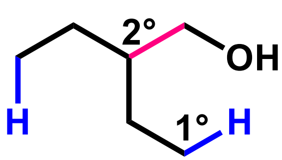
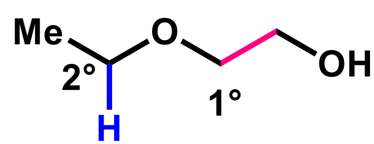
β-scission vs 1,5-HAT (1)



1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

β-scission vs 1,5-HAT (2)

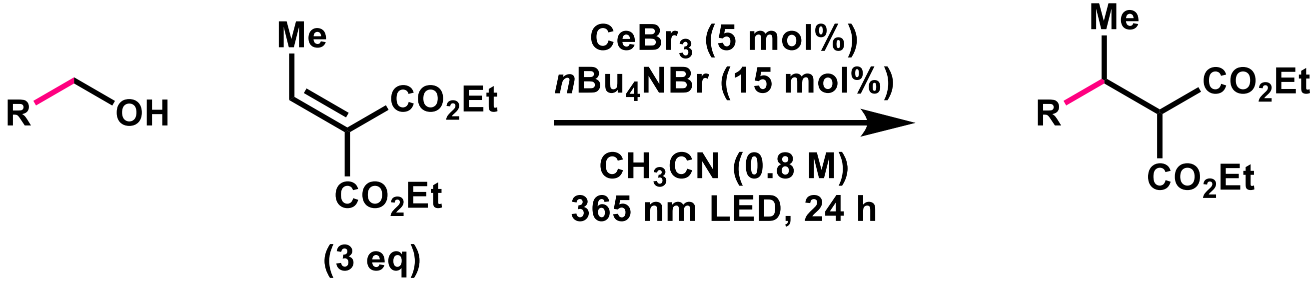


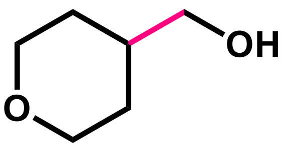
SM	conditions : yields (*β-scission*:*1,5-HAT*)	SM	conditions : yields (*β-scission*:1,5-HAT)
	B: 89% (>20:1) C: 79% (>20:1)		A: 32% (0.3:1) B: 37% (1.2:1)
	B: 90% (>20:1) C: 62% (>20:1)		B: 70% (17:1) C: 89% (15:1)

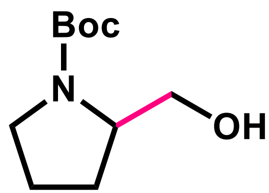
conditions A: $CeCl_3$ (5 mol%), *n*Bu_4NCl (15 mol%), 365 nm, 24 h
conditions B: $CeCl_3$ (5 mol%), *n*Bu_4NBr (15 mol%), 365 nm, 24 h
conditions C: $CeCl_3$ (5 mol%), *n*Bu_4NCl (15 mol%), 9,10-diphenylantracene (5 mol%), 400 nm, 24 h

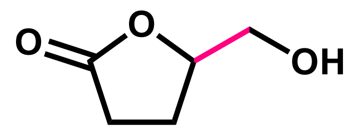
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

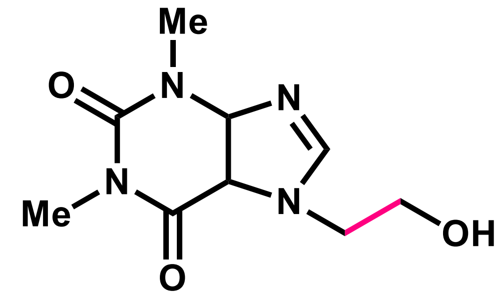
Substrate Scope (alcohol)



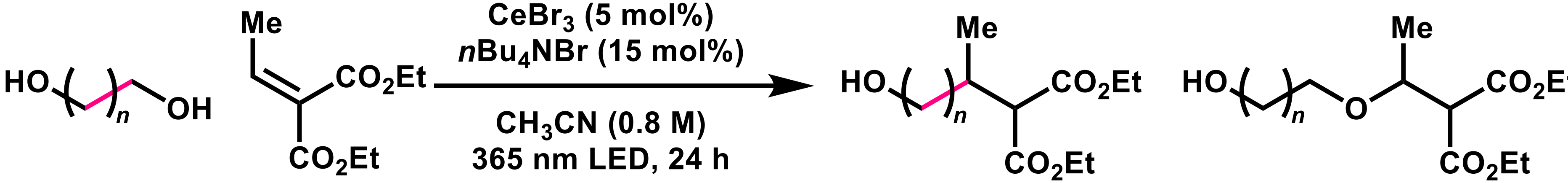








70% | 95% (dr 4.5:1) | 76% (dr 1.2:1) | 67% (138 hours)



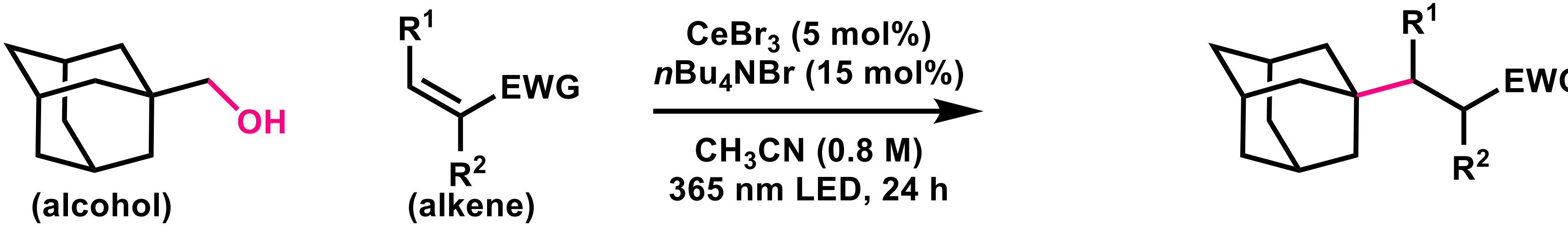
(0.4 mmol) (3 eq)

n = 1	0%	0%
n = 2	0%	37%
n = 4	12%	23%
n = 5	9%	32%

** chelation inhibit dehydroxymethylation?*

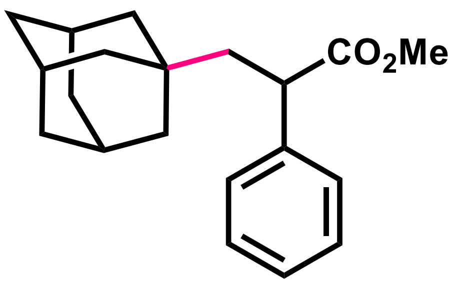
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Substrate Scope (alkene)

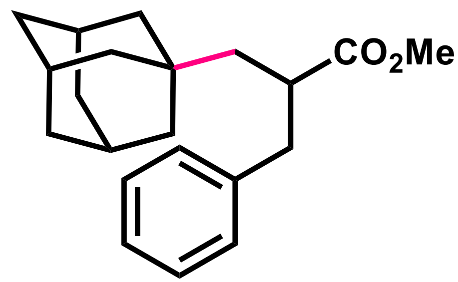


*** conditions A**

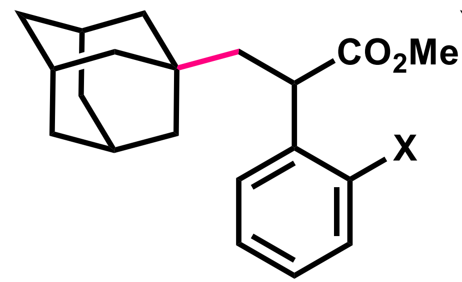
alcohol (1 eq), alkene (3 eq), diphenylanthracene (5 mol%)
$CeCl_3$ (5 mol%), *n*Bu_4NCl (15 mol%), CH_3CN (0.05 M), 400 nM LED, 24 h.



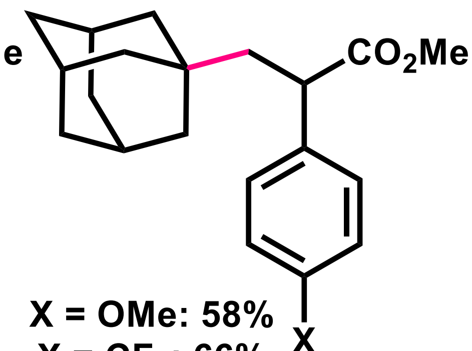
84%



69%



X = Me: 78%
X = OMe: 62%
X = Cl: 65%

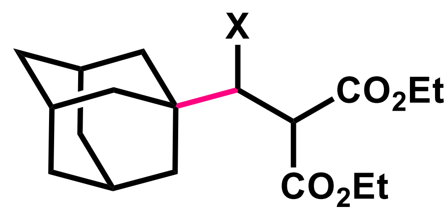


X = OMe: 58%
X = CF_3: 66%

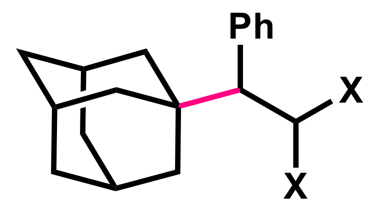
*** conditions B**

alcohol (3 eq), alkene (1 eq), $CeBr_3$ (5 mol%)
nBu_4NBr (15 mol%), CH_3CN, 365 nm LED.

high concentration of alkene would give undesired reduction and dimerization.



X = CF_3: 85%
X = CO_2Et: 75%
X = cyclohexyl: 42%

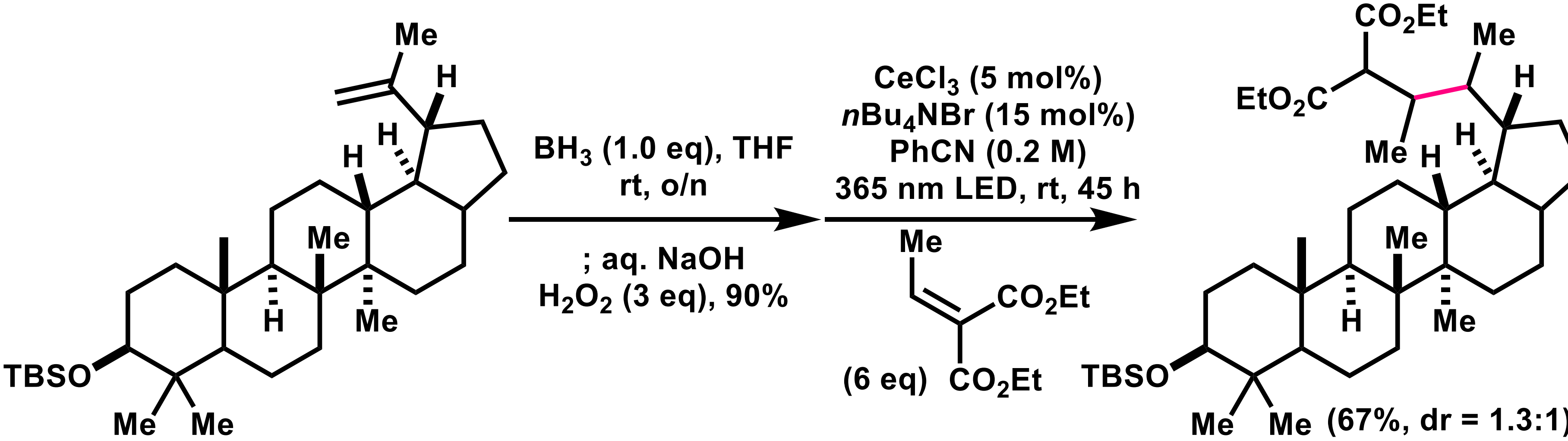


X = CO_2Me: 68%
X = CN: 69%

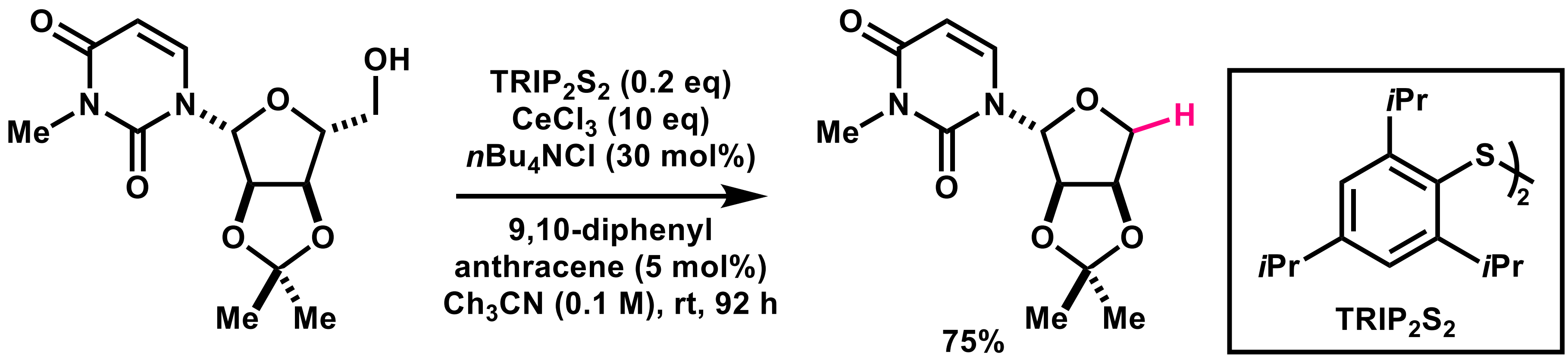
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Application of This Transformation

a) Formal C=C bond cleavage and alkylation



b) Reductive dehydroxymethylation



1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Mechanistic Study

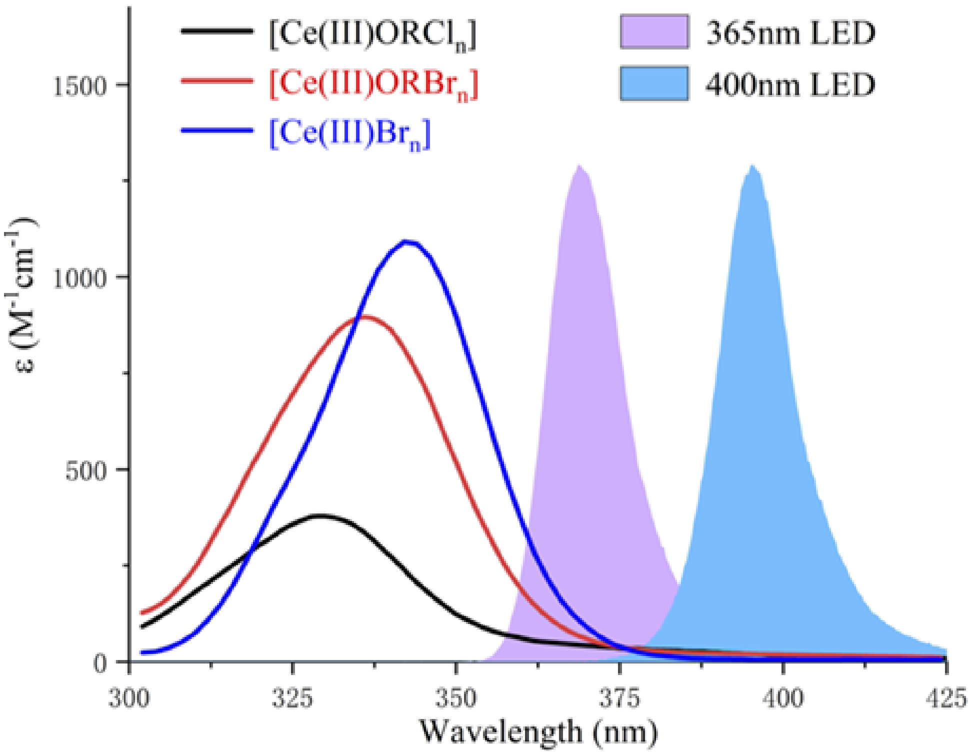


Fig. (A) UV-Vis absorption spectra of in situ formed cerium complexes.

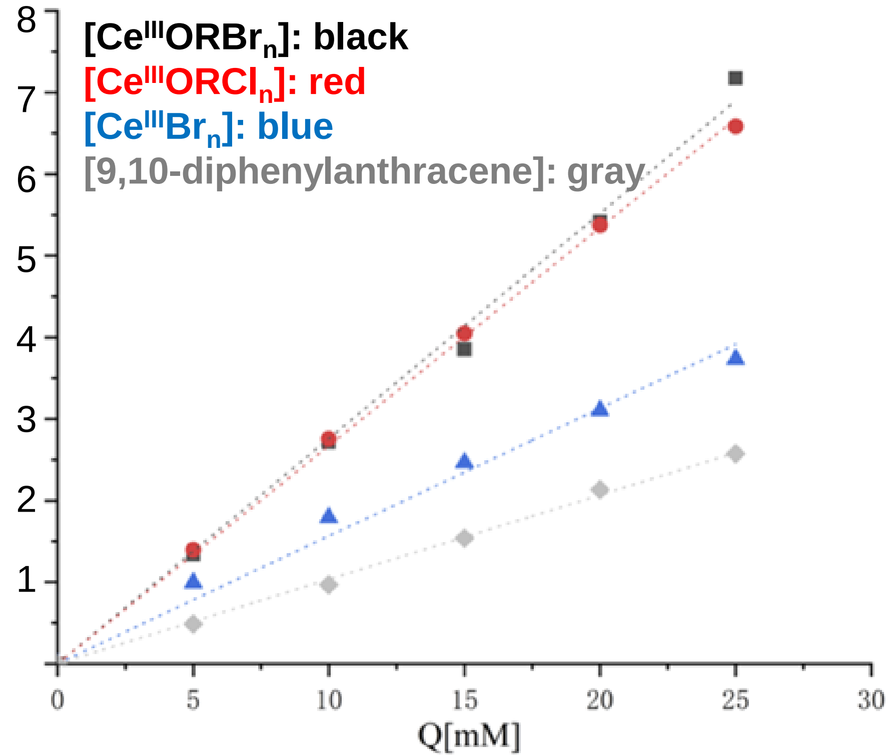
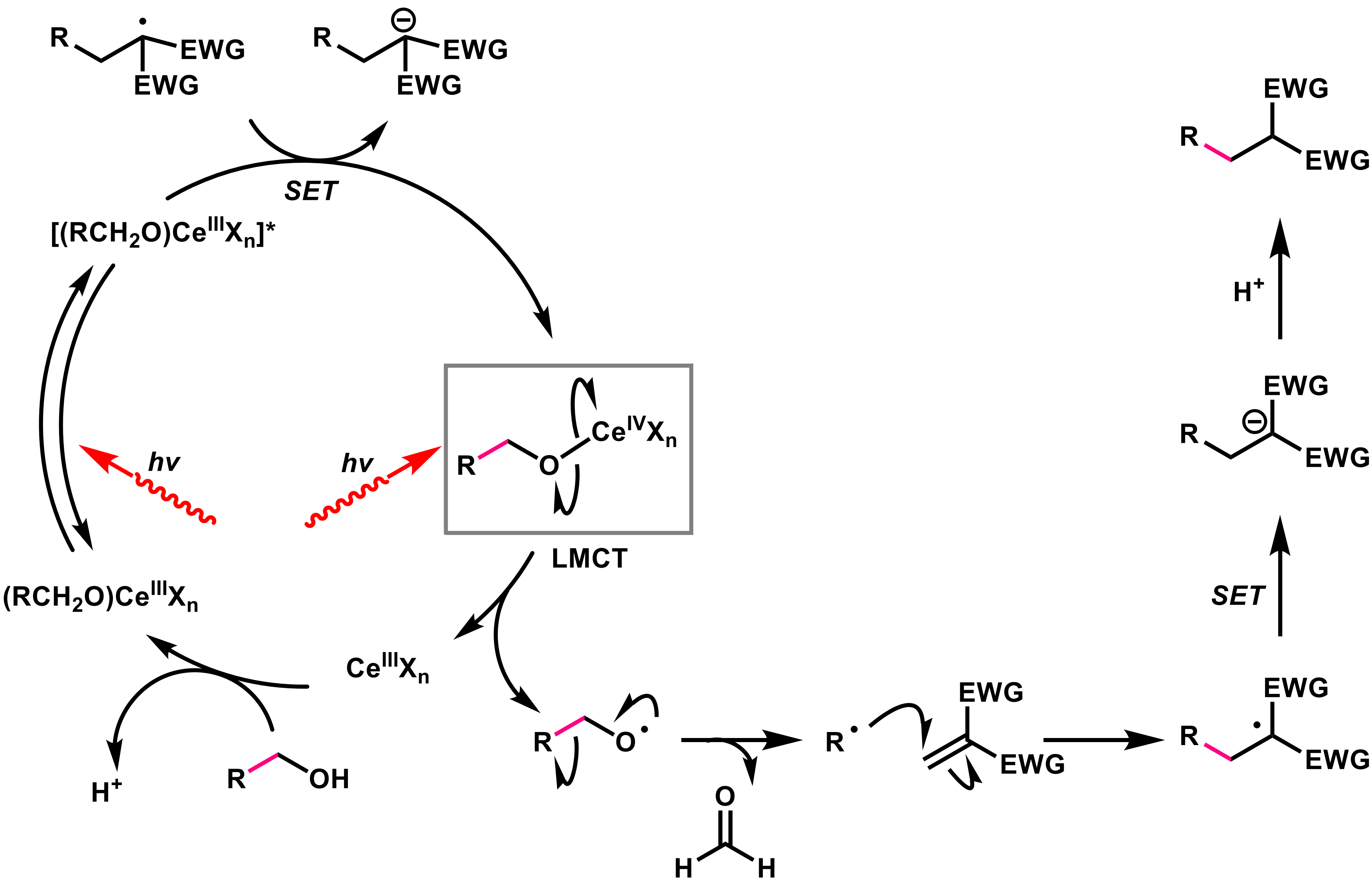


Fig. (B) Stern-Volmer quenching experiments by an electron-deficient alkene of cerium complexes at 330 nm (DPA: 370 nm).

In each conditions, *n*Bu$_4$NX was added.

1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Proposed Mechanism

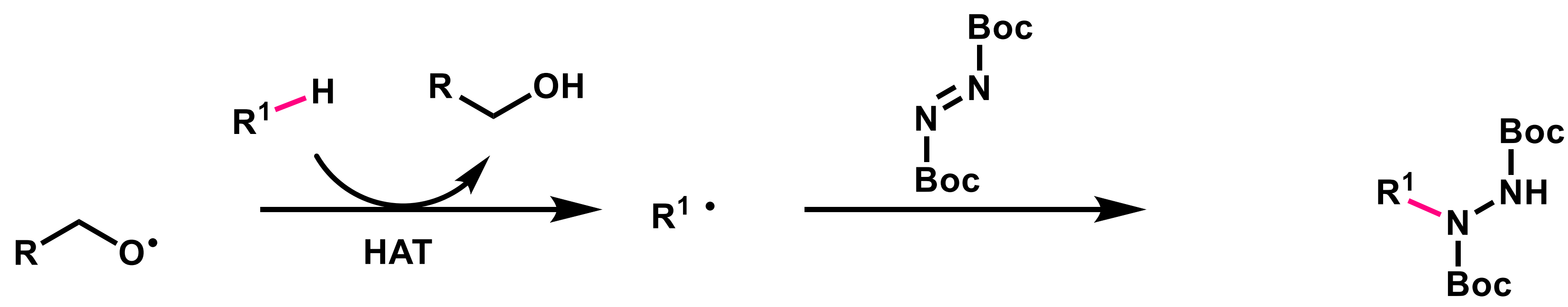


1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

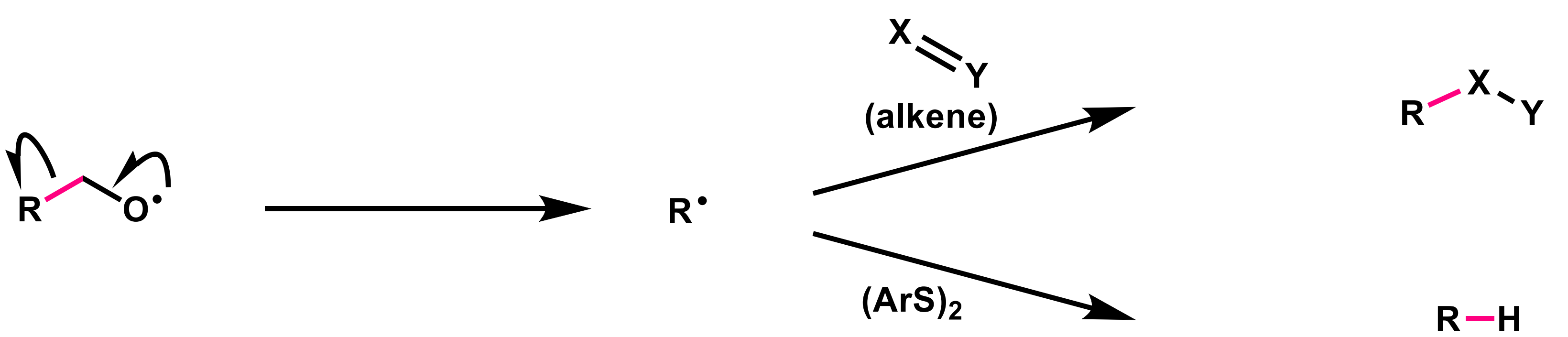
Summary

a) generation of alkoxy radidcal

b) intermolecular HAT



c) β-scission and functionalization



1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.
2) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Appendix

Introduction: Cerium

Z	名称	元素記号	M^{3+} の電子配置	$E^{\ominus}$/V	$r(M^{3+})$/pm†1	酸化数†2
57	ランタン	La	[Xe]	−2.38	116	2(n), **3**, 4
58	セリウム	Ce	[Xe] $(4f)^1$	−2.34	114	2(n), **3**, 4
59	プラセオジム	Pr	[Xe] $(4f)^2$	−2.35	113	2(n), **3**, 4
60	ネオジム	Nd	[Xe] $(4f)^3$	−2.32	111	2(n), **3**
61	プロメチウム	Pm	[Xe] $(4f)^4$	−2.29	109	**3**
62	サマリウム	Sm	[Xe] $(4f)^5$	−2.30	108	2(n), **3**
63	ユウロピウム	Eu	[Xe] $(4f)^6$	−1.99	107	2, **3**
64	ガドリニウム	Gd	[Xe] $(4f)^7$	−2.28	105	**3**
65	テルビウム	Tb	[Xe] $(4f)^8$	−2.31	104	**3**, **4**
66	ジスプロシウム	Dy	[Xe] $(4f)^9$	−2.29	103	2(n), **3**
67	ホルミウム	Ho	[Xe] $(4f)^{10}$	−2.33	102	**3**
68	エルビウム	Er	[Xe] $(4f)^{11}$	−2.32	100	**3**
69	ツリウム	Tm	[Xe] $(4f)^{12}$	−2.32	99	2(n), **3**
70	イッテルビウム	Yb	[Xe] $(4f)^{13}$	−2.22	99	2, **3**
71	ルテチウム	Lu	[Xe] $(4f)^{14}$	−2.30	98	**3**

†1 配位数＝8のときのイオン半径〔R. D. Shannon, *Acta Cryst.*, **A32**, 751(1976) より〕.
†2 太字の酸化数は最も安定な状態を示す．(n) はその状態が，非水溶液中という条件のみで安定であることを意味している．

シュライバー・アトキンス無機化学（下） 第4版

BDE of Alcohols

	$C_2H_5O{-}H$	$H_3CO{-}H$	$F_3CH_2CO{-}H$	$HOH_2C{-}H$
BDE	105 kcal/mol	105 kcal/mol	106.6 kcal/mol	95.7 kcal/mol

photoexcited cerium chloride/alchol complex: $[E_{1/2}\ (Ce^{IV}/{}^{*}Ce^{III})] = -2.2$ V

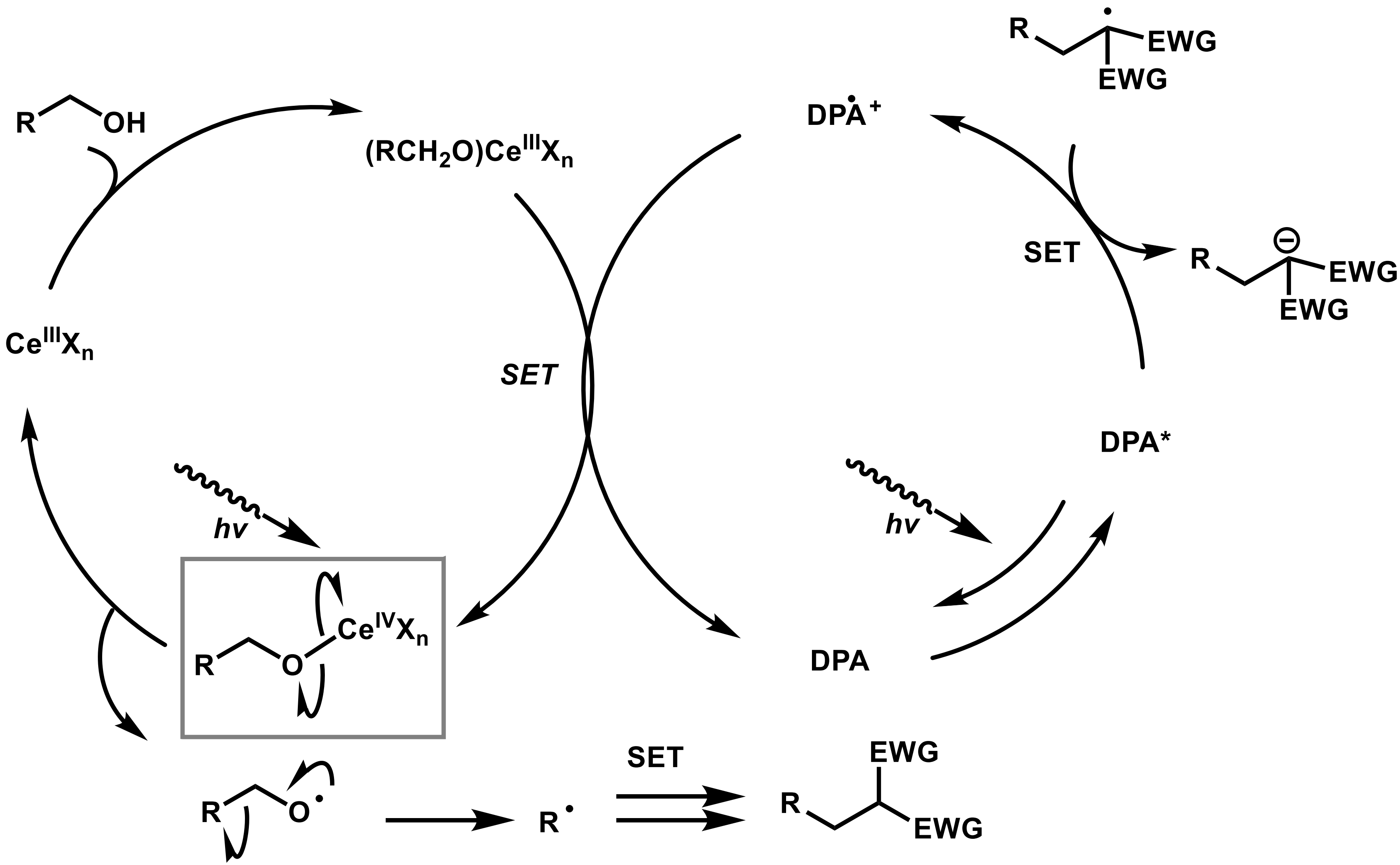
ground state $[E_{1/2}\ (Ce^{IV}/Ce^{III})] = 0.4$ V

photoexcited $[Ce^{III}Cl_6]^{3-}$: $E_{1/2} = -3.07$ V

DBAD: $E_{1/2}(red) = -0.7$ V

1) Luo, Y. R., Comprehensive Handbook of Chemical Bond Energies, CRC Press, Boca Raton, FL, **2007**.

Proposed Mechanism



1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Mechanistic Study

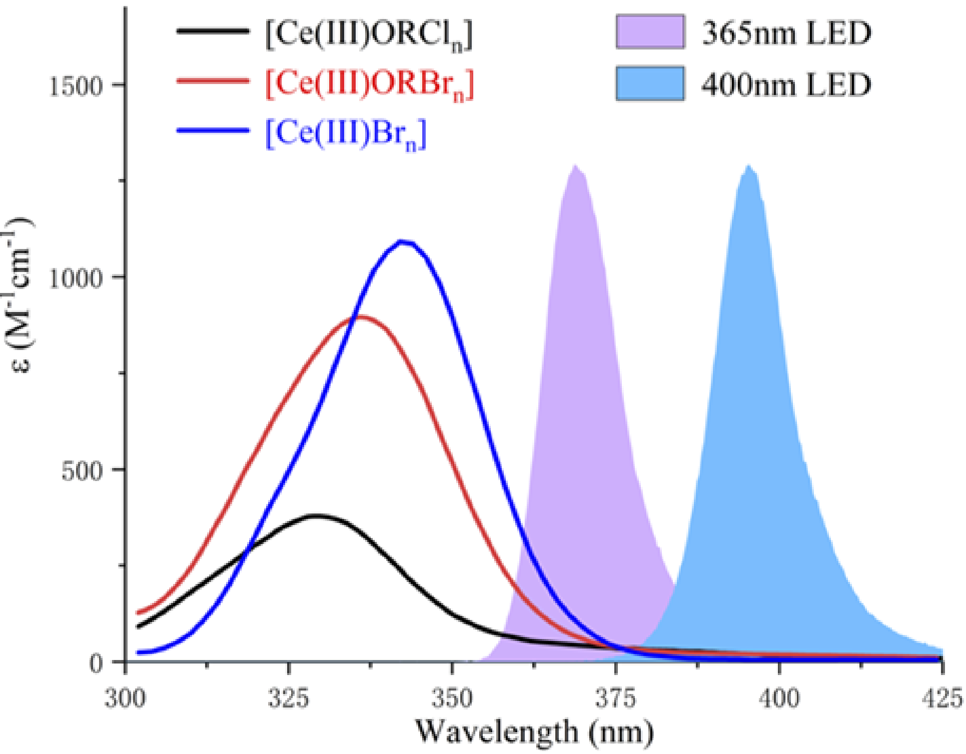


Fig. (A) UV-Vis absorption spectra of in situ formed cerium complexes.

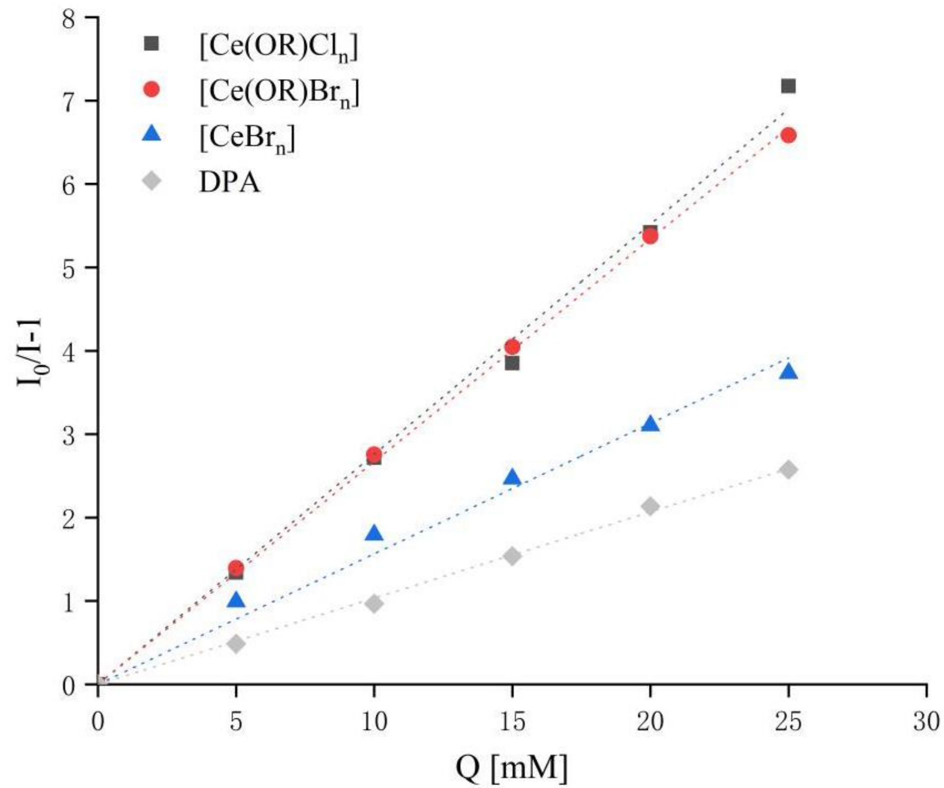
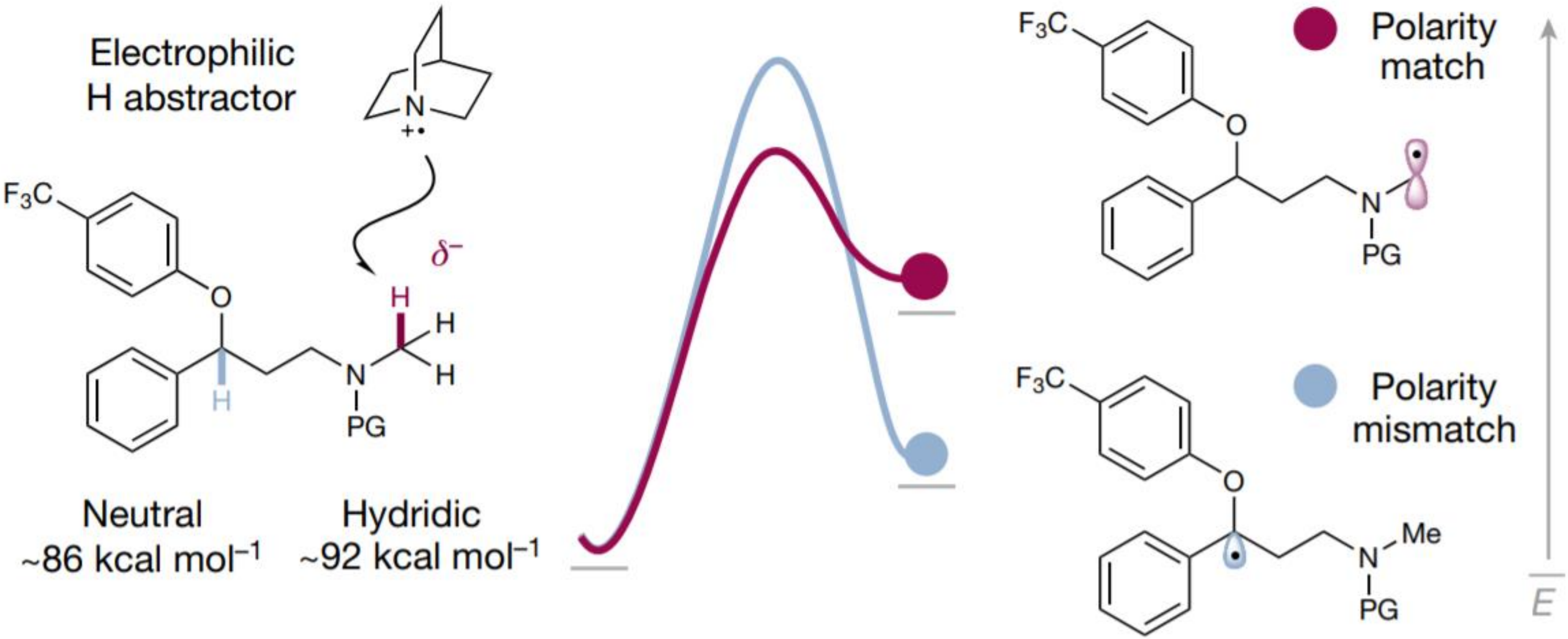


Fig. (B) Stern-Volmer quenching experiments by an electron-deficient alkene of cerium complexes.

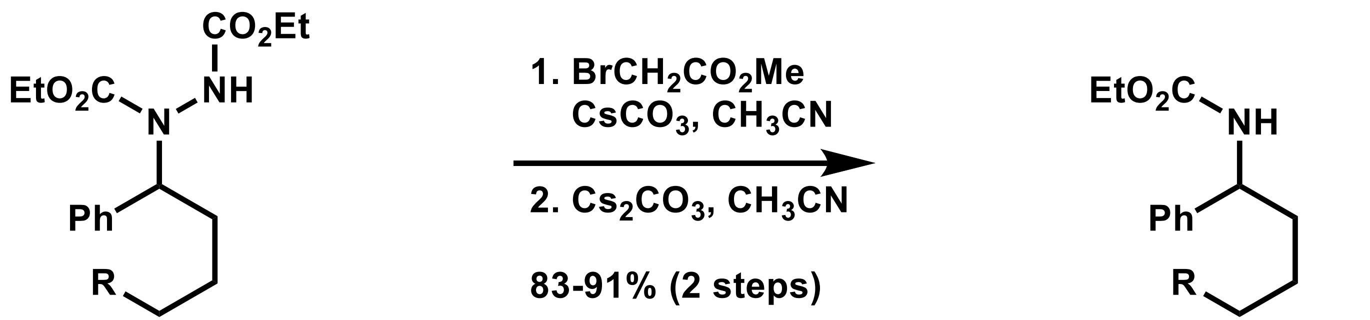
1) Zhang, K.; Chang, L.; An, Q.; Wang, X.; Zuo, Z. *J. Am. Chem. Soc.* **2019**, *141*, 10556.

Polarity Matched HAT

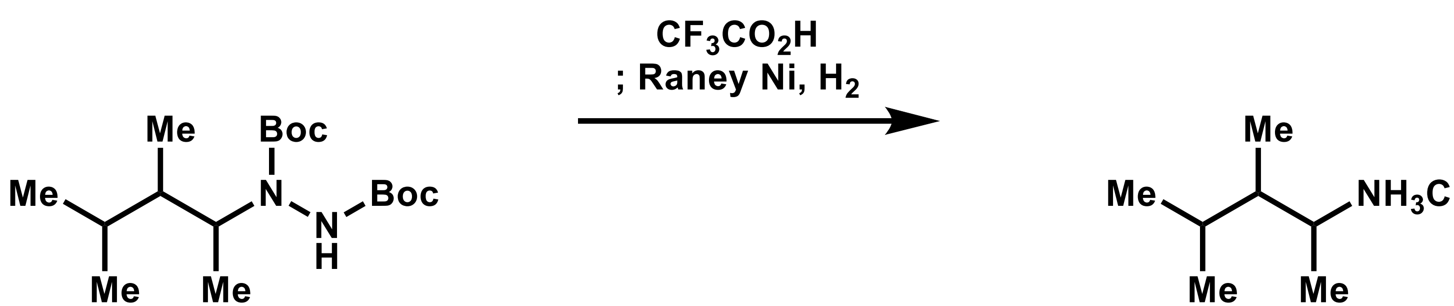


1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668. 2) Le, C.; Liang, Y.; Evans, R. W.; Li, X.; MacMillan, D. W. C. *Nature* **2017**, *547*, 79.

Conversion of Hydrazine Derivative

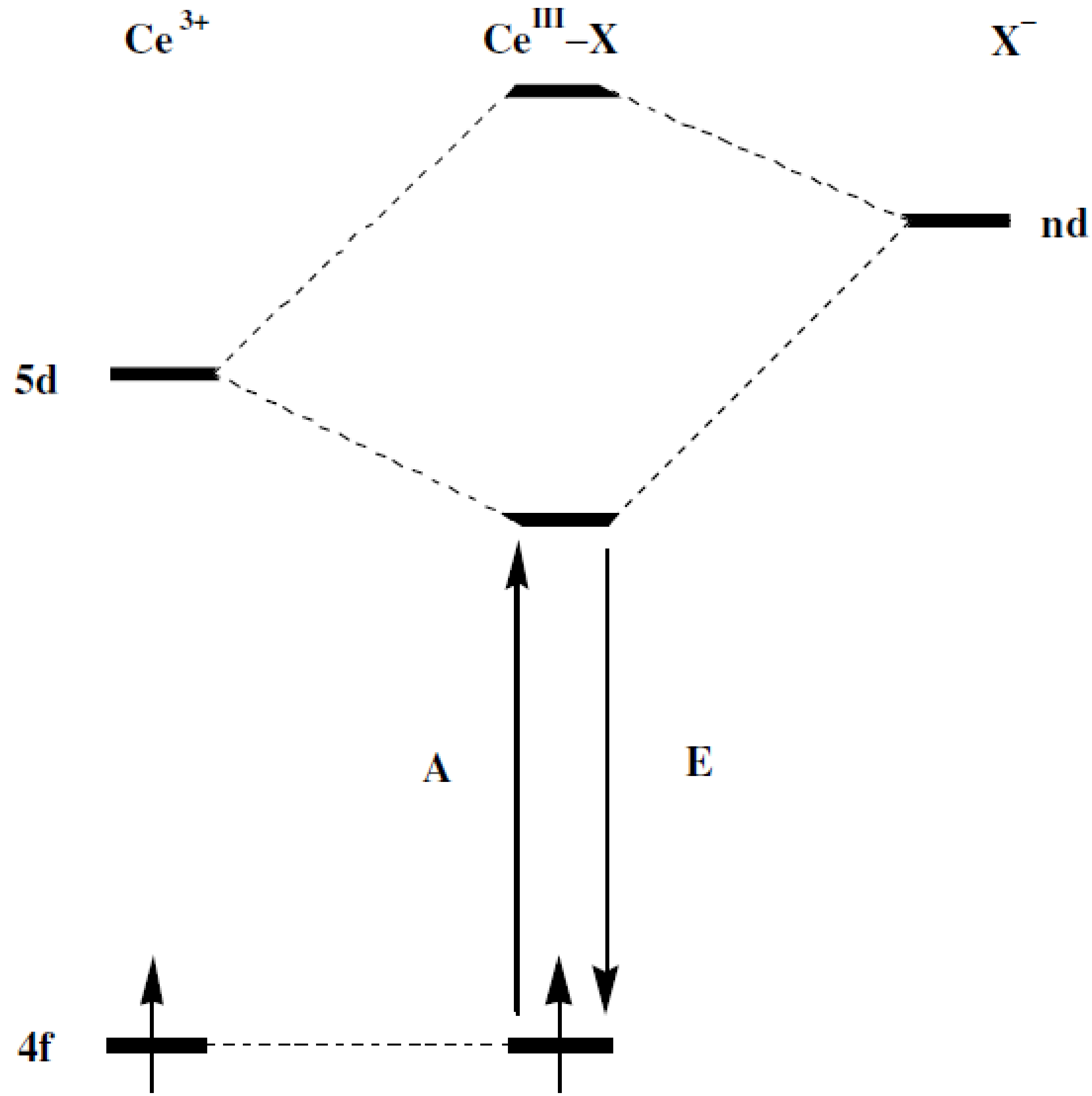


R = H, OTBDPS, CN   R = H, OTBDPS, CN



1) Magnus, P.; Garizi, N.; Seibert, K. A.; Ornholt, A. *Org. Lett.* **2009**, *11*, 5646. 2) Inoue, M. et. al. *J. Org. Chem.* 2012, *77*, 9959. 3) Zuo, Z. et. al. *J. Am. Chem. Soc.* **2020**, *142*, 6216.

Effect of Chloride Anione



Volger, A.; Kunkely, H. *Inorg. Chim. Acta.* **2006**, *138*, 5984.

Stern-Volmer study

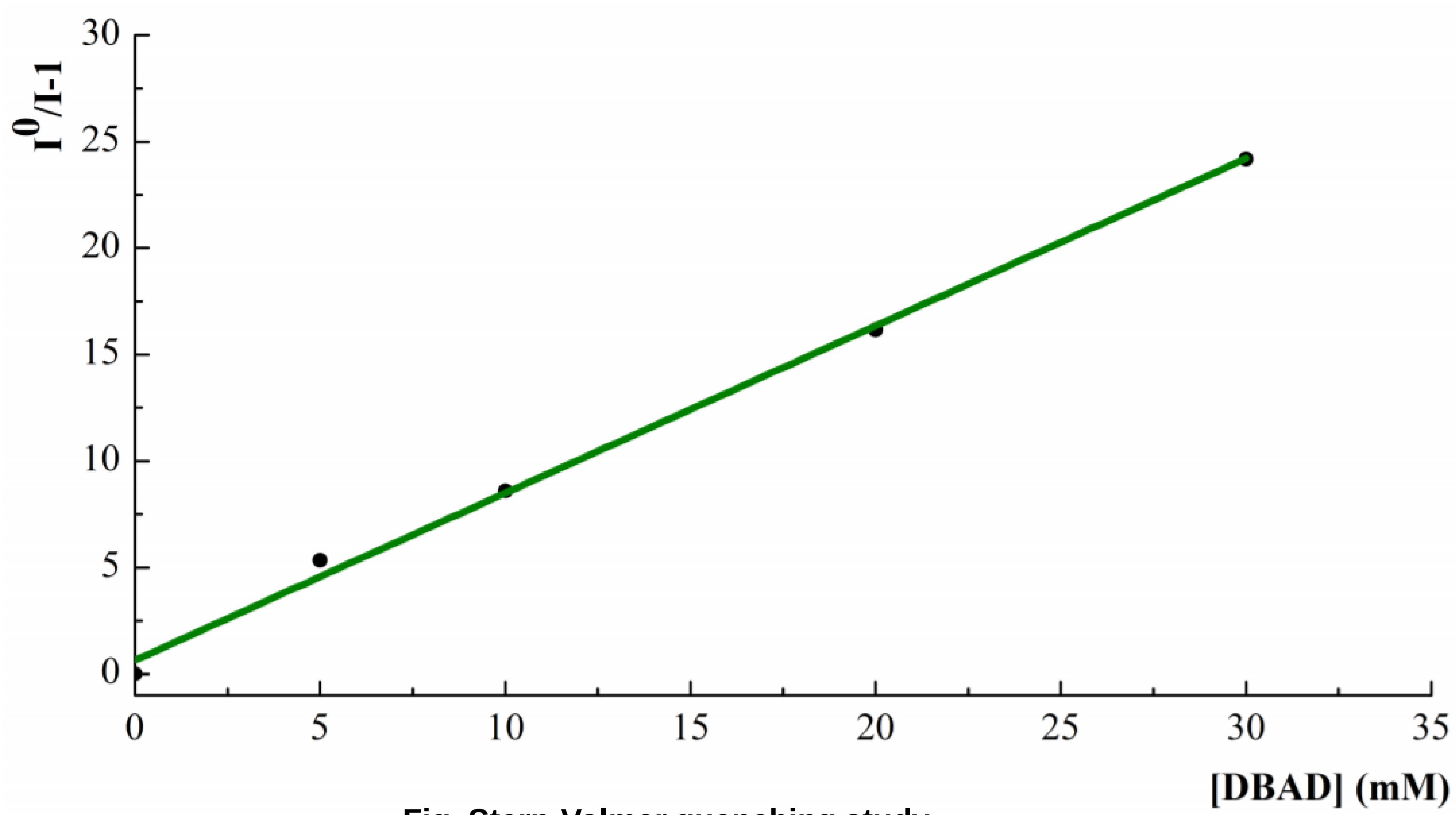


Fig. Stern-Volmer quenching study.
[$CeCl_3$+cyclopentanol+DBAD]

Zuo, Z. et. al. *ACIE* **2016**, *55*, 15319.

Effect of Chloride Anione

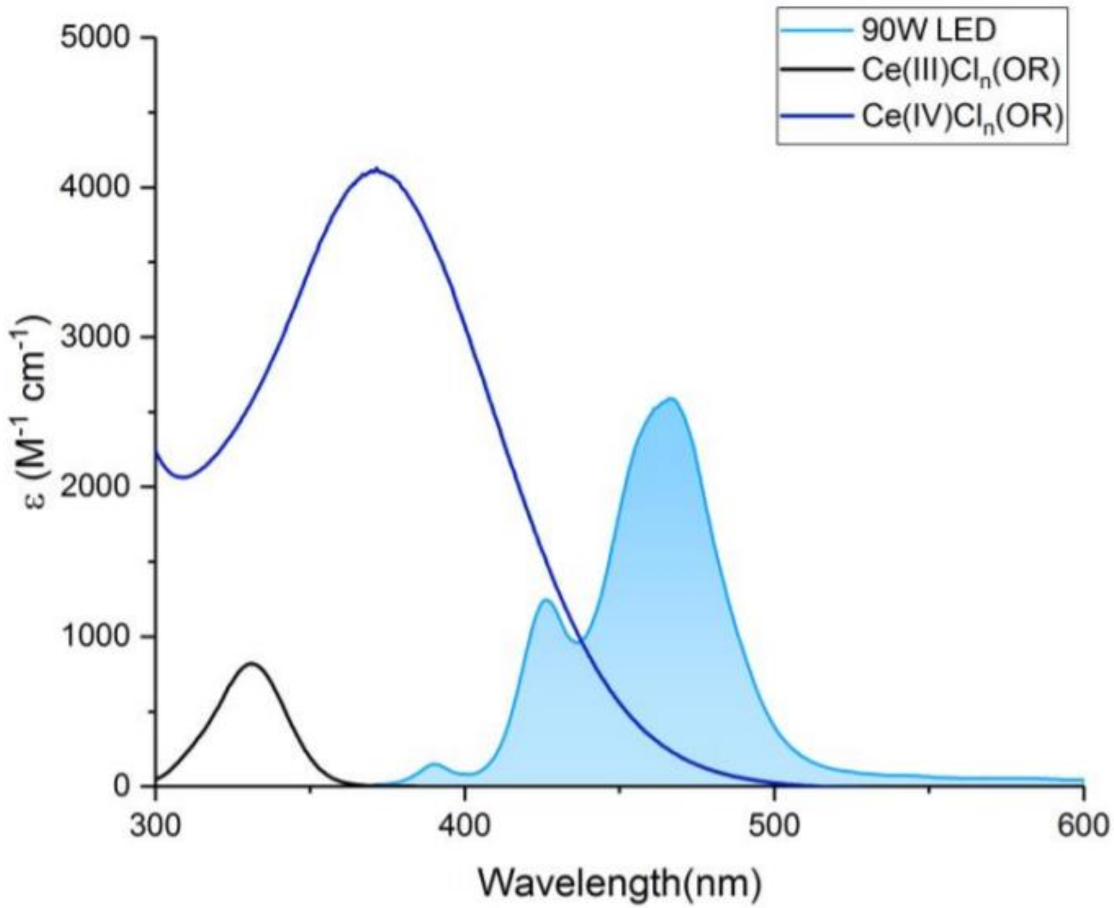
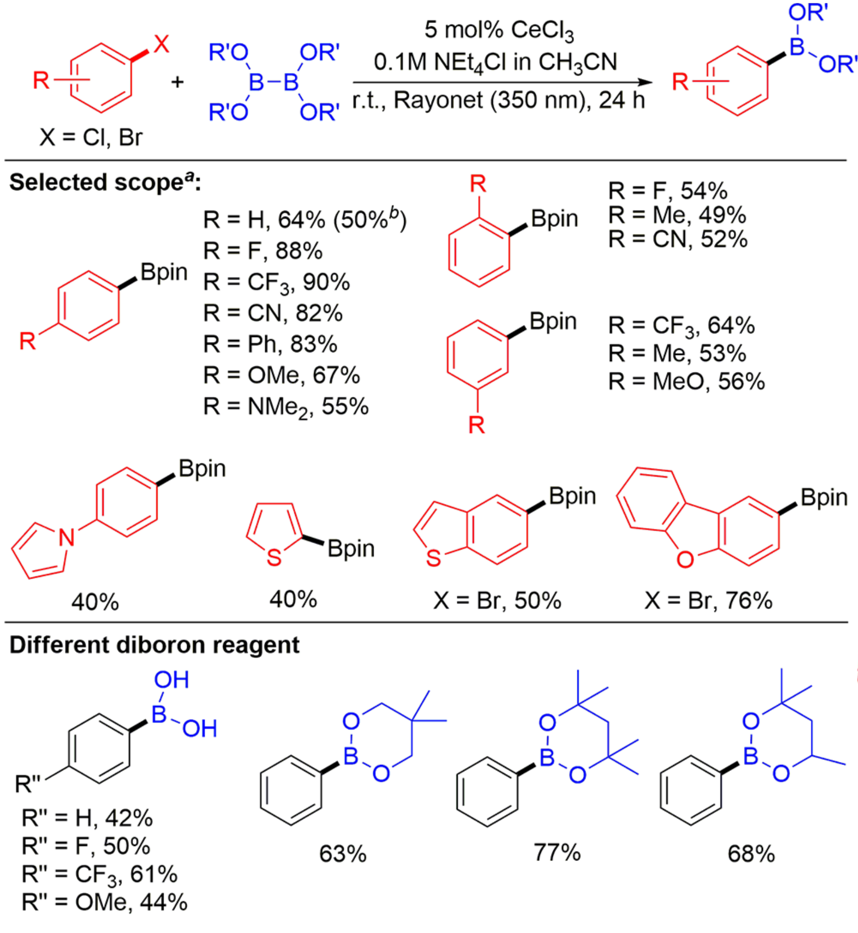
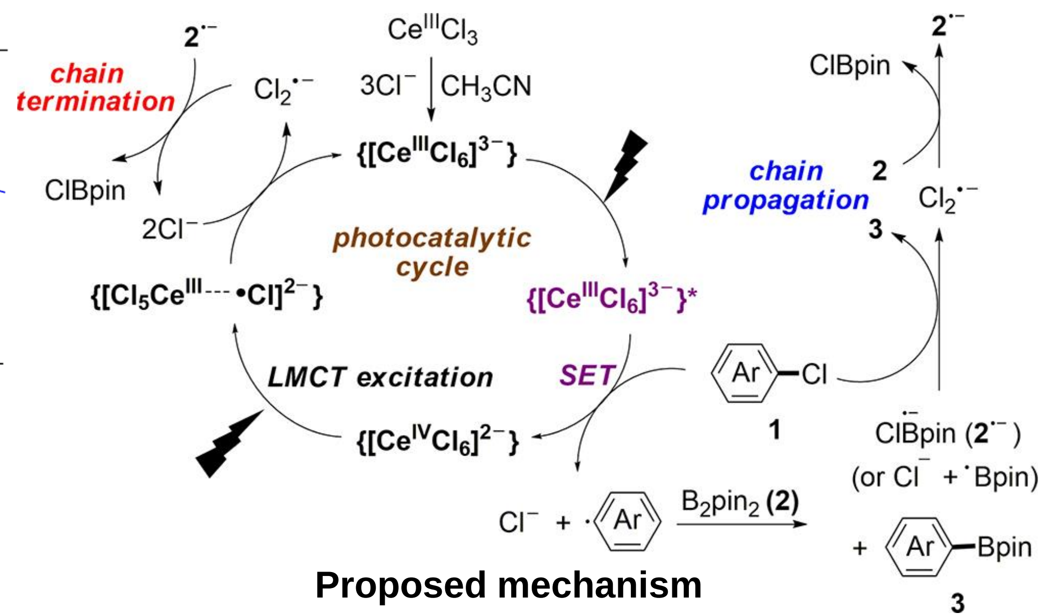


Fig. Absorption spectra of Ce^{IV}(OR)Cl$_n$ and Ce^{III}(OR)Cl$_n$ complexes

Zuo, Z. et. al. *JACS* **2018**, *140*, 1612.

Generation of $[Ce^{III}Cl_6]^{3-}$

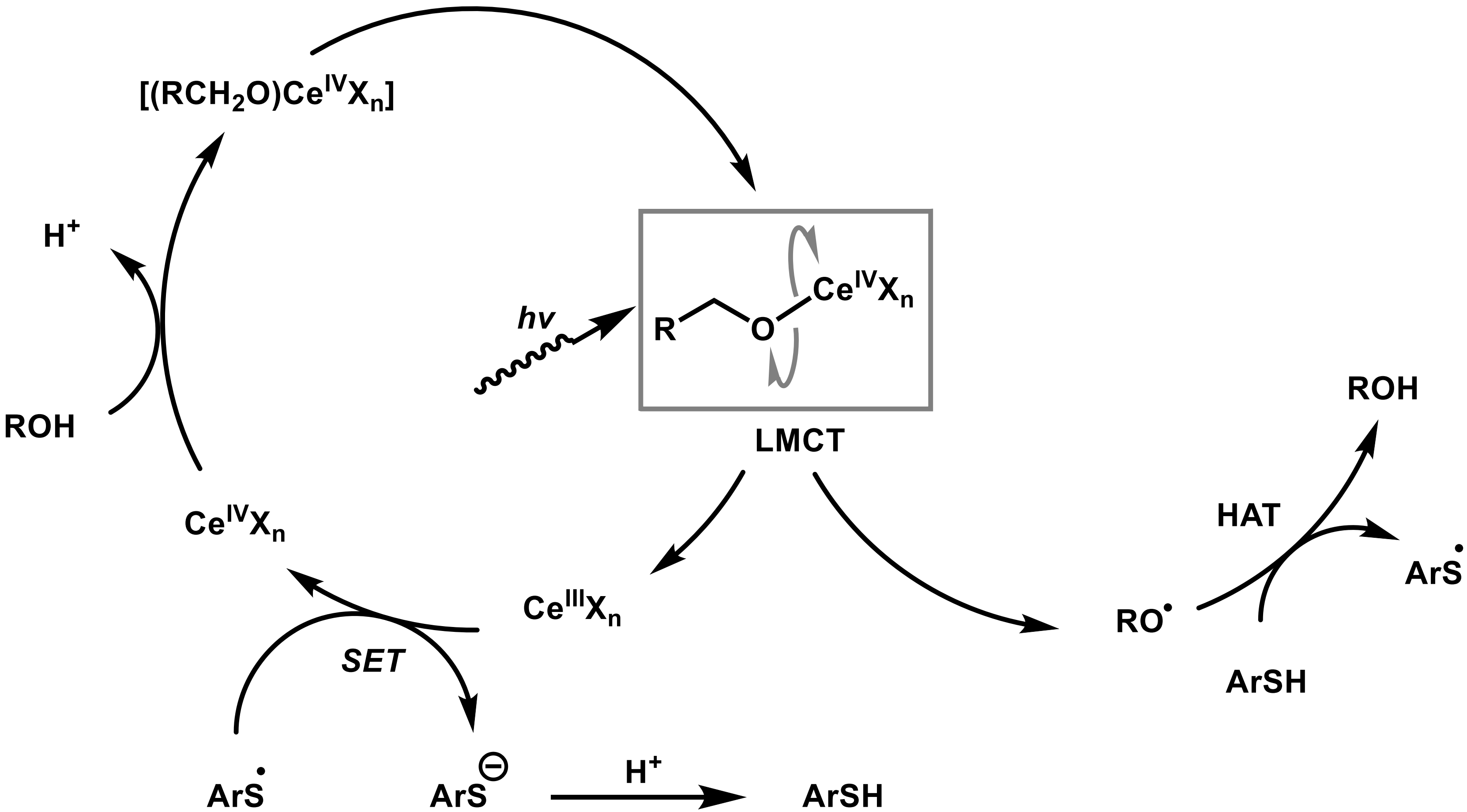




Proposed mechanism

Qiao, Y. Schelter, E. J. *Acc. Chem. Res.* **2018**, *51*, 2926.

Proposed Mechanism ($TRIP_2S_2$)



1) Hu, A.; Guo, J.-J.; Pan, H.; Zuo, Z. *Science* **2018**, *361*, 668.