LMCT Catalysis for Selective Functionalizations of Strong Bonds

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Author Introduction

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ZHIWEI ZUO 左智伟

2020 – PRESENT.	Professor, Shanghai Institute of Organic Chemistry, CAS
2015 – 2020.	Assistant Professor, ShanghaiTech University
2013 – 2015.	Postdoctoral Fellow, Princeton University
	Advisor: Professor David W. C. MacMillan
2007 – 2012.	Ph.D., Chemistry, Shanghai Institute of Organic Chemistry, CAS
	Advisor: Professor Dawei Ma
2003 – 2007	B. S., Chemistry, Nanjing University
	Advisor: Professor Chengjian Zhu and Yixiang Chen

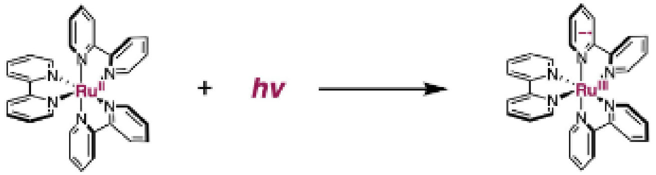
Research Topics:

发展了 铈催化LMCT催化模式(LMCT Catalysis)，通过金属复合物的光促配体到金属的电子跃迁途径，实现有机分子的高效转化。

目 录

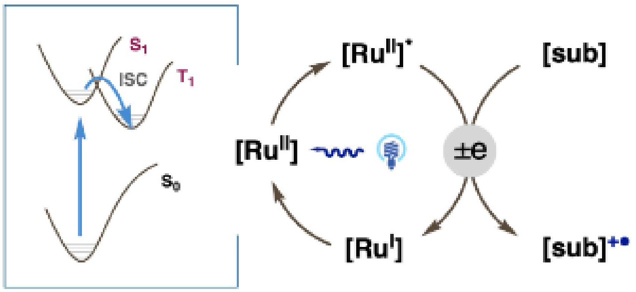
1. 背景

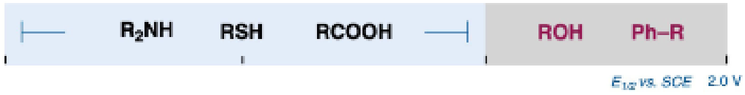
Metal-to-Ligand Charge Transfer excitation



MLCT triplet state: long-lived, redox active

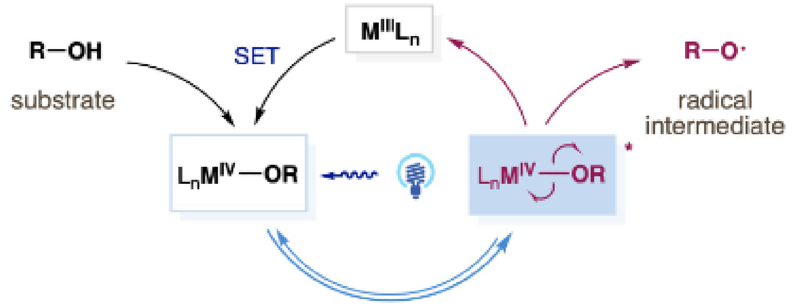
“photoredox catalysis”





Ligand-to-Metal Charge Transfer excitation

- **LMCT catalysis paradigm**

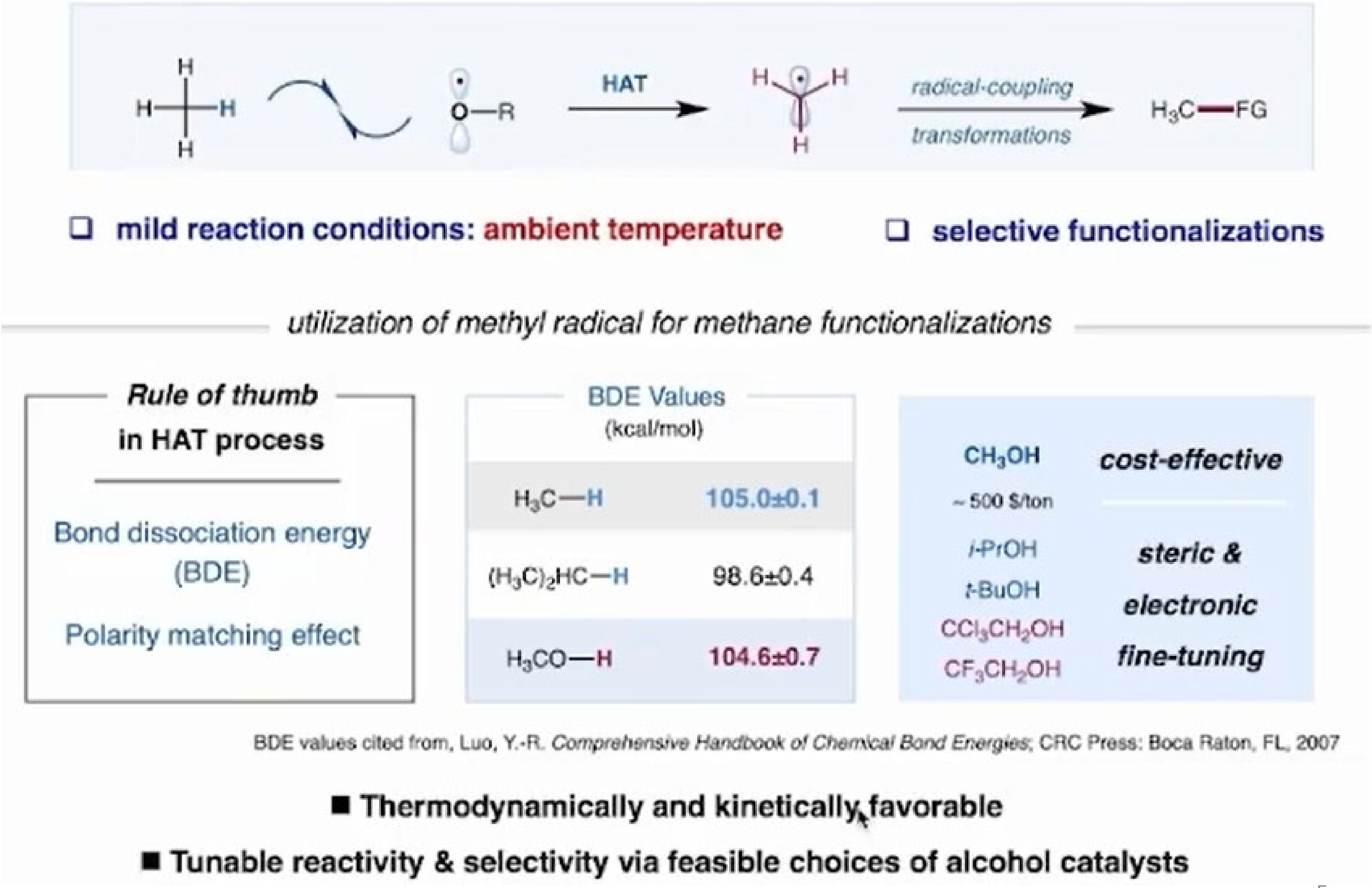


in situ coordination-LMCT-bond homolysis

- concurrent photoexcitation and substrate activation
- photoactive species generated *in situ*
- high valent metal salt as catalyst

- **Metal-to-ligand charge transfer**
- **Metal-to-metal charge transfer**
- **Metal-centered charge transfer**
- **Ligand-to-metal charge transfer**
- **Ligand-to-ligand charge transfer**
- **Intra-ligand charge transfer**

1. 背景



❑ **mild reaction conditions: ambient temperature**

❑ **selective functionalizations**

utilization of methyl radical for methane functionalizations

Rule of thumb
in HAT process

Bond dissociation energy (BDE)

Polarity matching effect

BDE Values (kcal/mol)

H_3C—H	105.0±0.1
$(H_3C)_2HC$—H	98.6±0.4
H_3CO—H	104.6±0.7

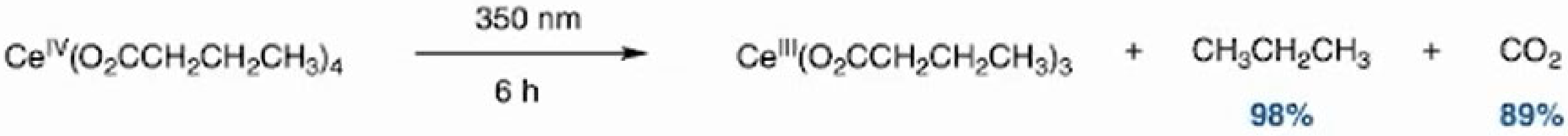
CH_3OH ~ 500 $/ton	***cost-effective***
i-PrOH *t*-BuOH CCl_3CH_2OH CF_3CH_2OH	***steric & electronic fine-tuning***

BDE values cited from, Luo, Y.-R. *Comprehensive Handbook of Chemical Bond Energies*; CRC Press: Boca Raton, FL, 2007

- ■ **Thermodynamically and kinetically favorable**
- ■ **Tunable reactivity & selectivity via feasible choices of alcohol catalysts**

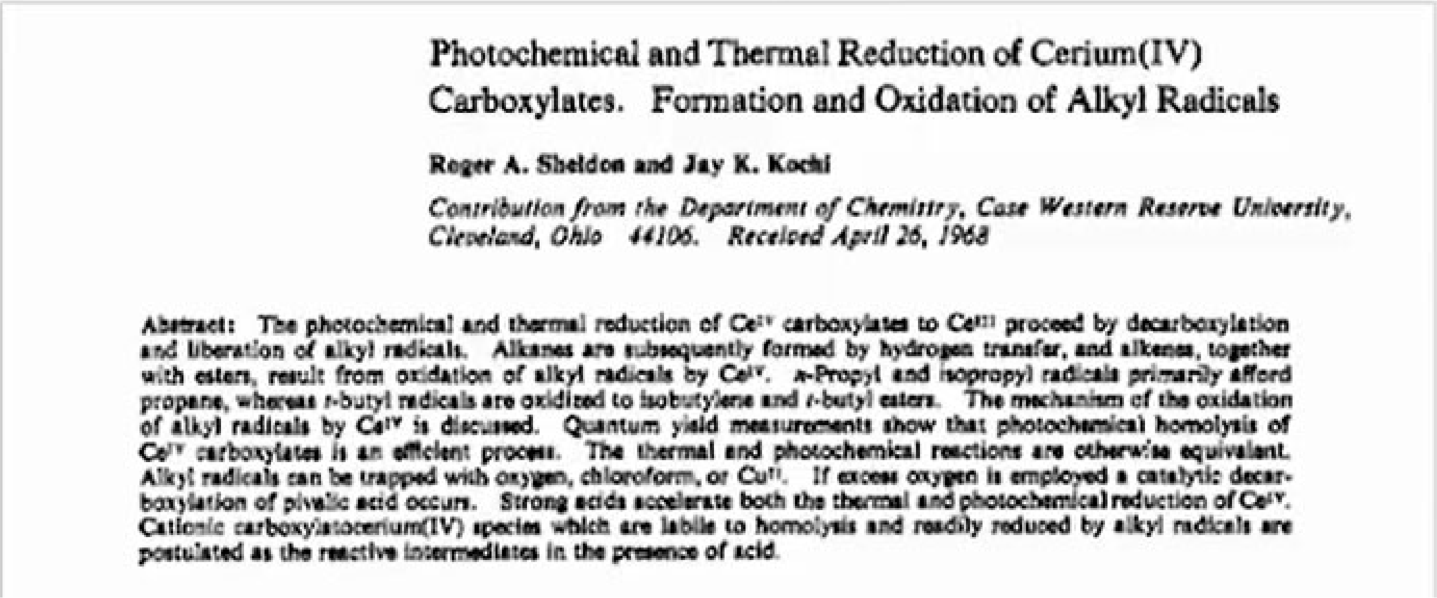
1. 背景

■ Photochemical and thermal reduction of Ce(IV) carboxylates



$$\mathrm{Ce^{IV}(O_2CCH_2CH_2CH_3)_4} \xrightarrow[\text{6 h}]{\text{350 nm}} \mathrm{Ce^{III}(O_2CCH_2CH_2CH_3)_3} + \underset{98\%}{\mathrm{CH_3CH_2CH_3}} + \underset{89\%}{\mathrm{CO_2}}$$

Kochi, J. K. *et al.*, *J. Am. Chem. Soc.* **1968**, *90*, 6688



Photochemical and Thermal Reduction of Cerium(IV) Carboxylates. Formation and Oxidation of Alkyl Radicals

Roger A. Sheldon and Jay K. Kochi

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 26, 1968

Abstract: The photochemical and thermal reduction of Ce^{IV} carboxylates to Ce^{III} proceed by decarboxylation and liberation of alkyl radicals. Alkanes are subsequently formed by hydrogen transfer, and alkenes, together with esters, result from oxidation of alkyl radicals by Ce^{IV}. *n*-Propyl and isopropyl radicals primarily afford propane, whereas *t*-butyl radicals are oxidized to isobutylene and *t*-butyl esters. The mechanism of the oxidation of alkyl radicals by Ce^{IV} is discussed. Quantum yield measurements show that photochemical homolysis of Ce^{IV} carboxylates is an efficient process. The thermal and photochemical reactions are otherwise equivalent. Alkyl radicals can be trapped with oxygen, chloroform, or Cu^{II}. If excess oxygen is employed a catalytic decarboxylation of pivalic acid occurs. Strong acids accelerate both the thermal and photochemical reduction of Ce^{IV}. Cationic carboxylatocerium(IV) species which are labile to homolysis and readily reduced by alkyl radicals are postulated as the reactive intermediates in the presence of acid.

2.1. HAT碳氢键官能化

J|A|C|S JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

Cite This: *J. Am. Chem. Soc.* 2018, 140, 1612−1616

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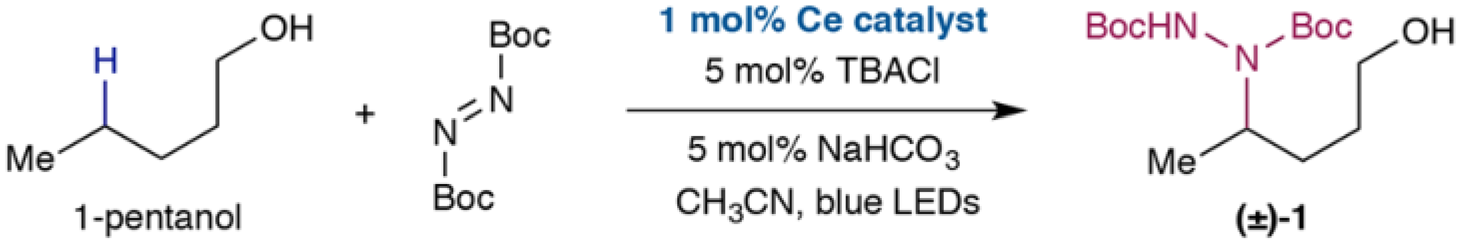
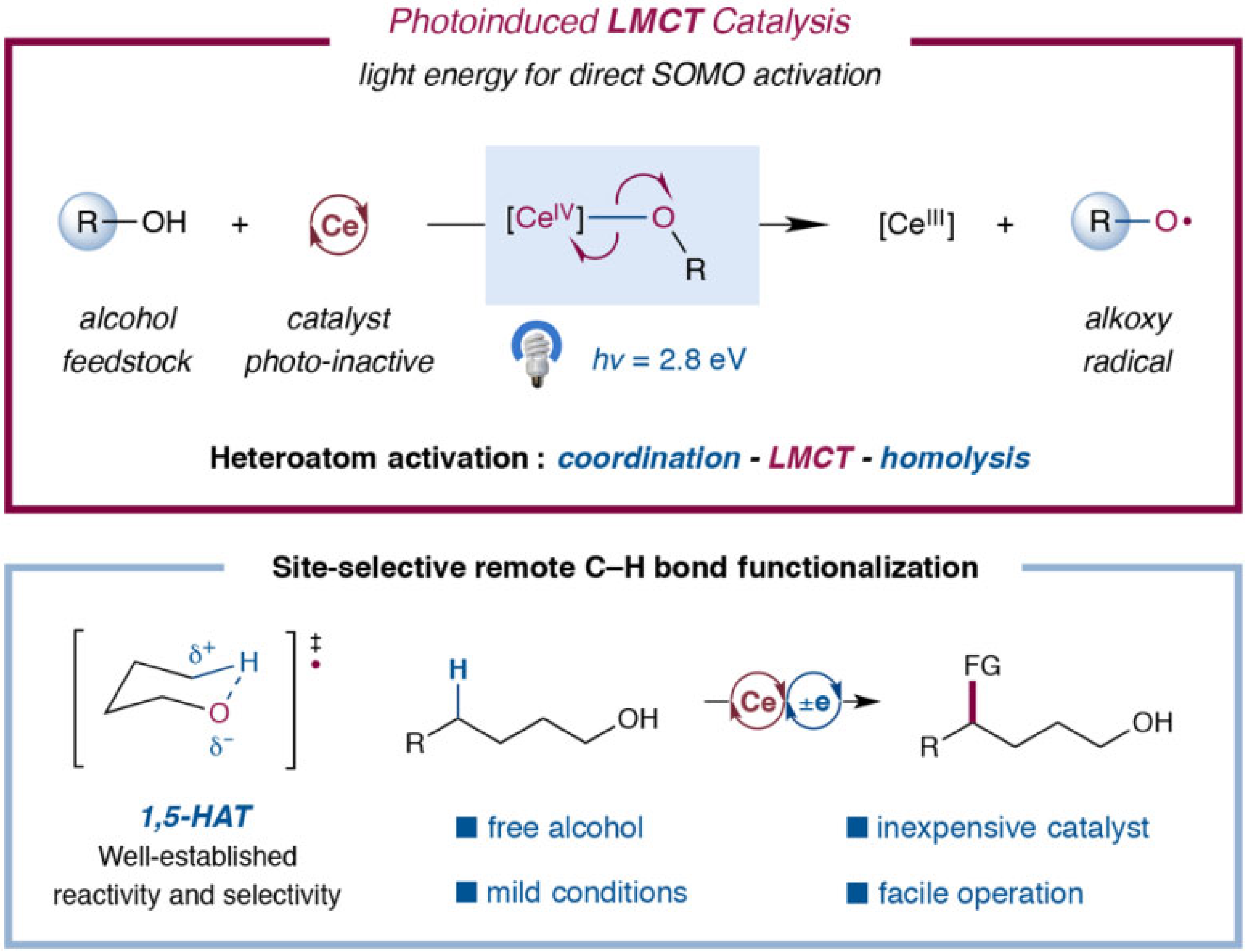
δ-Selective Functionalization of Alkanols Enabled by Visible-Light-Induced Ligand-to-Metal Charge Transfer

Anhua Hu,[†,§] Jing-Jing Guo,[†,§] Hui Pan,[†] Haoming Tang,[†] Zhaobo Gao,[‡] and Zhiwei Zuo*,[†]

[†]School of Physical Science and Technology, ShanghaiTech University, Shanghai 201210, China
[‡]Jiuzhou Pharmaceutical, Zhejiang 318000, China

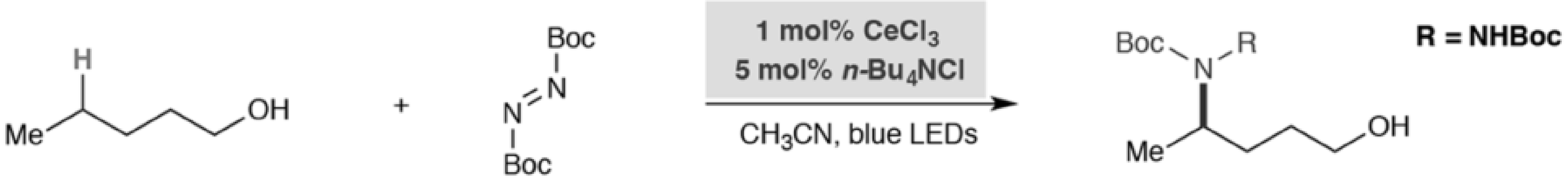


2.1. HAT碳氢键官能化



质子耦合电子转移（**PCET**）催化：一般用于**N–H**键活化，以及富含电子的芳烃取代叔醇中的**O–H**键活化。

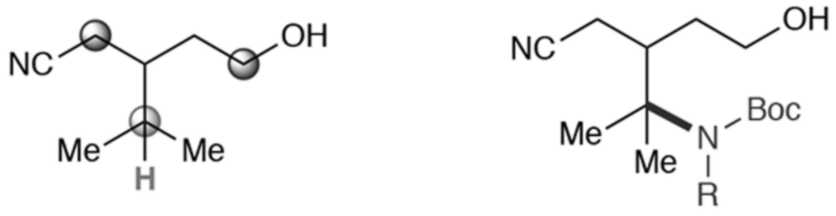
2.1. HAT碳氢键官能化



(±)-1 90% yield

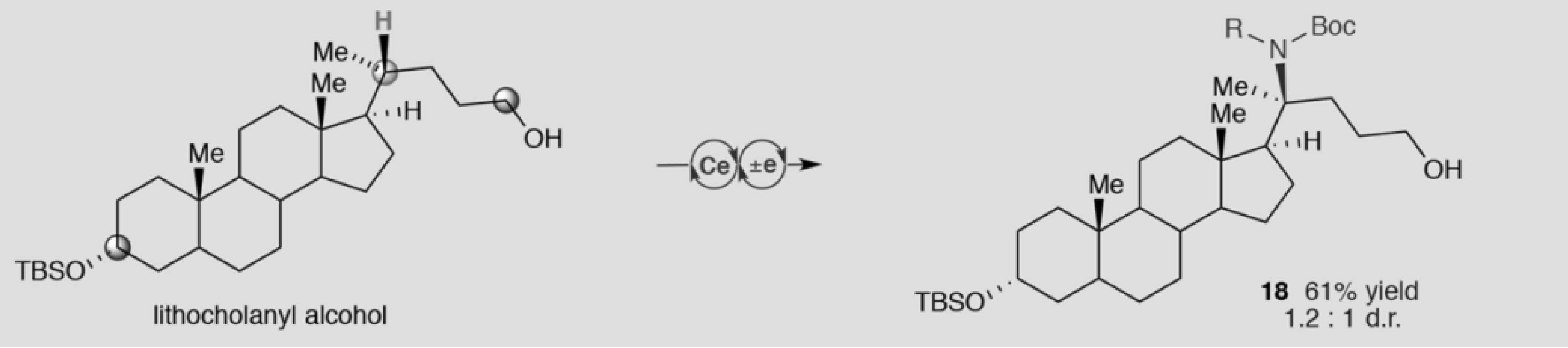
(±)-8 67% yield

证明1,5-HAT机制



(±)-13 78% yield

极性匹配

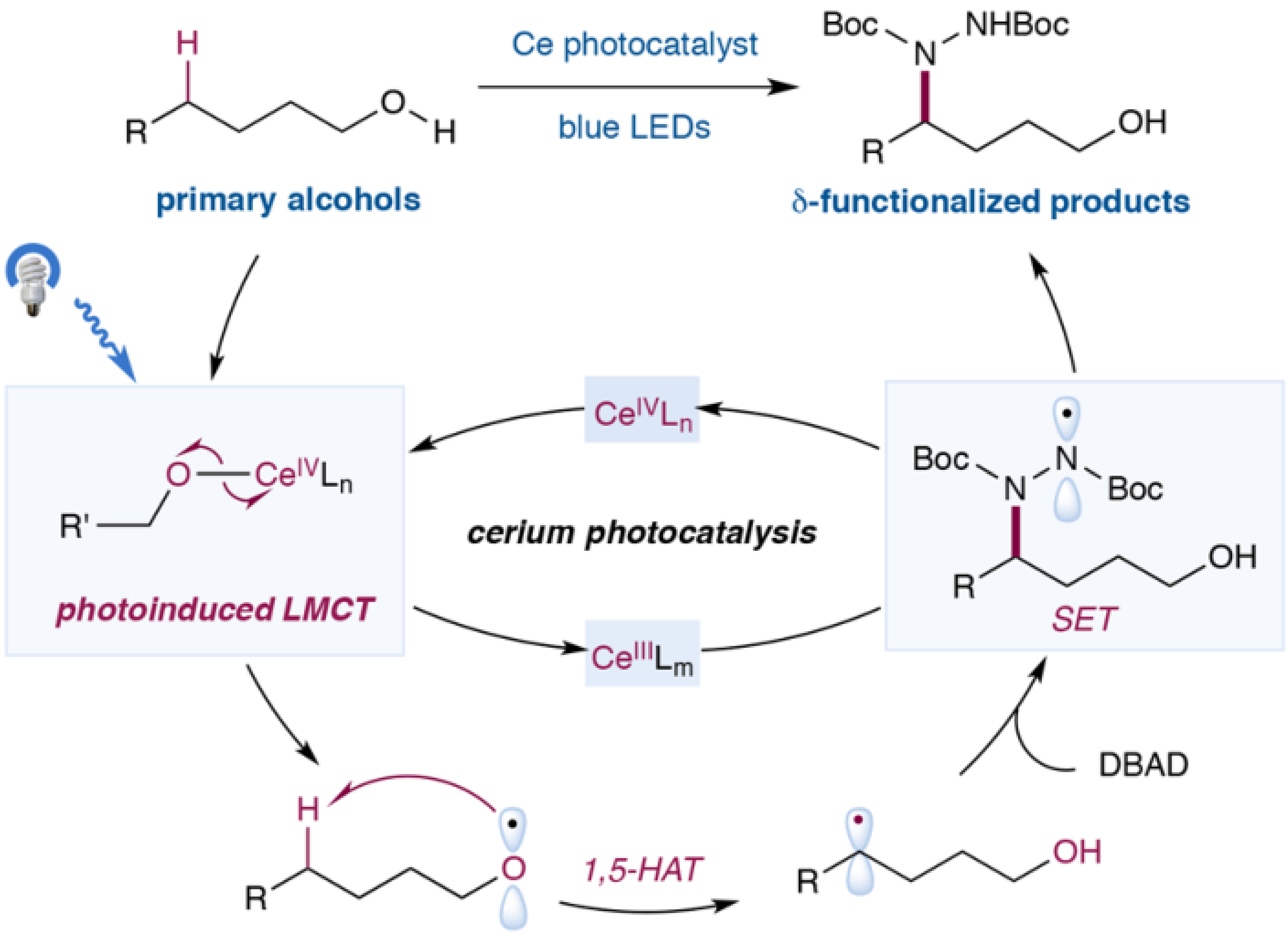


lithocholanyl alcohol

18 61% yield
1.2 : 1 d.r.

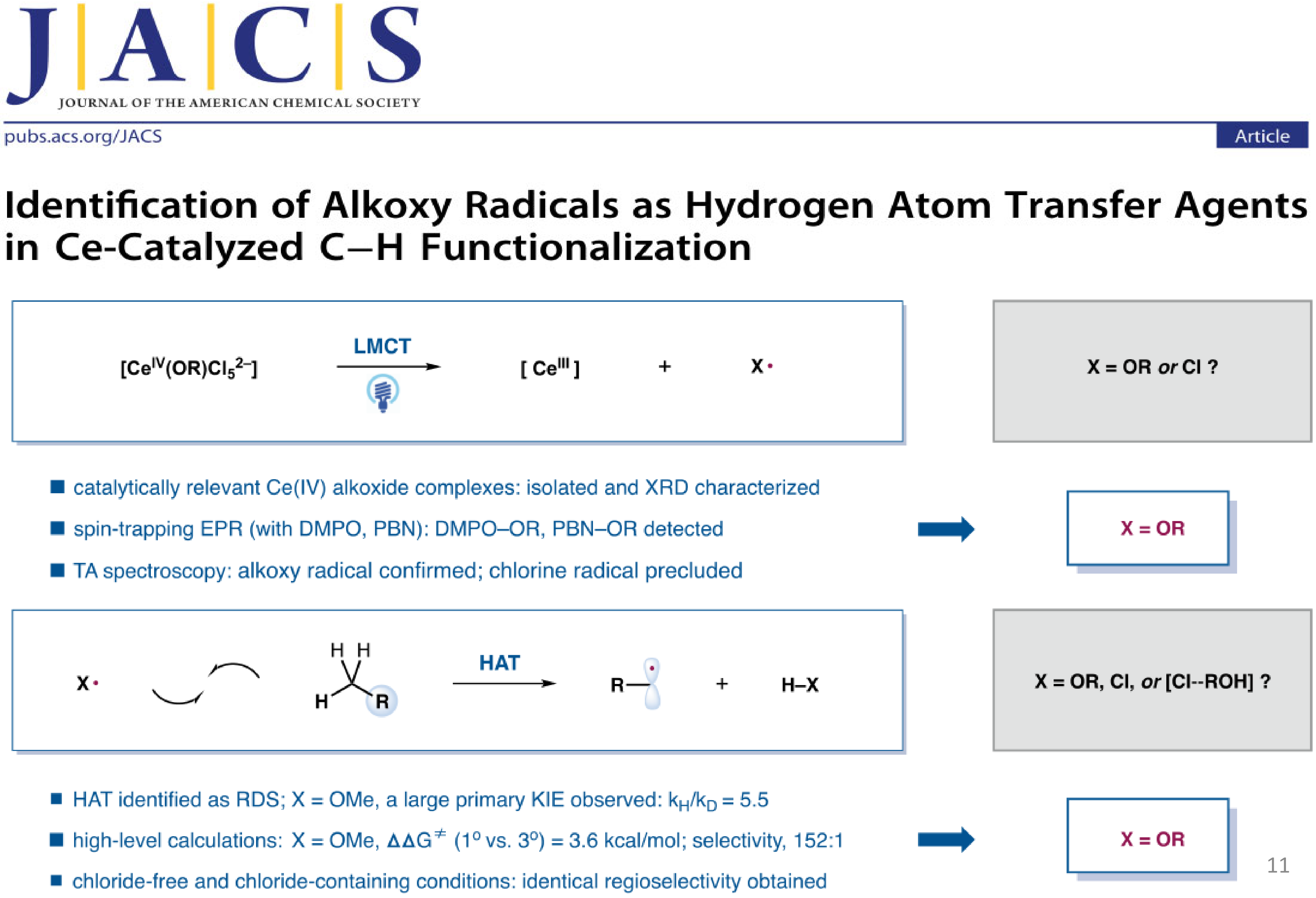
石胆醇

2.1. HAT碳氢键官能化



2.2. HAT碳氢键官能化

Zuo, Z. J. Am. Chem. Soc. 2023, 145, 359



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Article

Identification of Alkoxy Radicals as Hydrogen Atom Transfer Agents in Ce-Catalyzed C–H Functionalization

$[Ce^{IV}(OR)Cl_5^{2-}] \xrightarrow{LMCT} [Ce^{III}] + X\cdot$

X = OR *or* Cl ?

- catalytically relevant Ce(IV) alkoxide complexes: isolated and XRD characterized
- spin-trapping EPR (with DMPO, PBN): DMPO–OR, PBN–OR detected
- TA spectroscopy: alkoxy radical confirmed; chlorine radical precluded

X = OR

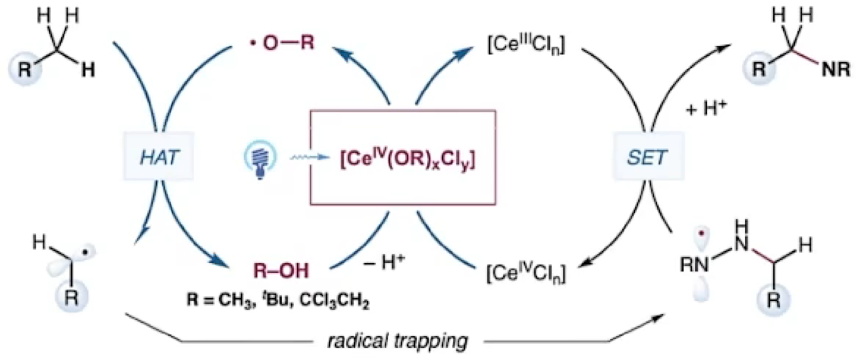
X = OR, Cl, *or* [Cl--ROH] ?

- HAT identified as RDS; X = OMe, a large primary KIE observed: $k_H/k_D = 5.5$
- high-level calculations: X = OMe, $\Delta\Delta G^{\neq}$ (1^o vs. 3^o) = 3.6 kcal/mol; selectivity, 152:1
- chloride-free and chloride-containing conditions: identical regioselectivity obtained

X = OR

机理实验

Ce-catalyzed selective C(sp³)–H functionalizations: mechanistic investigations



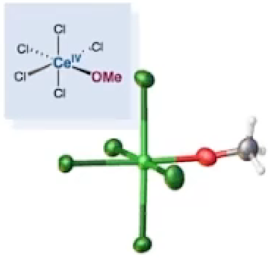
- proposed catalytic cycle

✓ [Ce(OR)Cl$_5$] complex as photoactive species

✓ selective generation of alkoxy radical in LMCT-homolysis

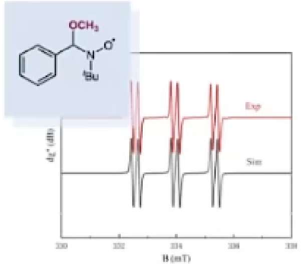
✓ alkoxy radical-mediated HAT for selective cleavage of C–H bond

● XRD



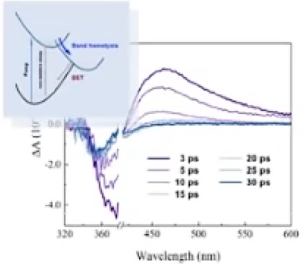
[Ce(OR)Cl$_5$] complexes isolated and characterized

● EPR



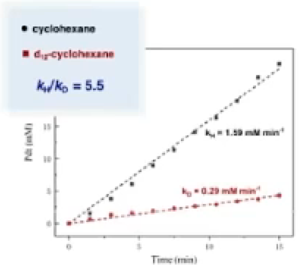
alkoxy radicals spin-adduct detected, Cl• precluded

● TrA



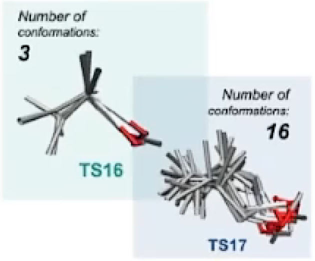
LMCT kinetic process established, BET identified

● KIE



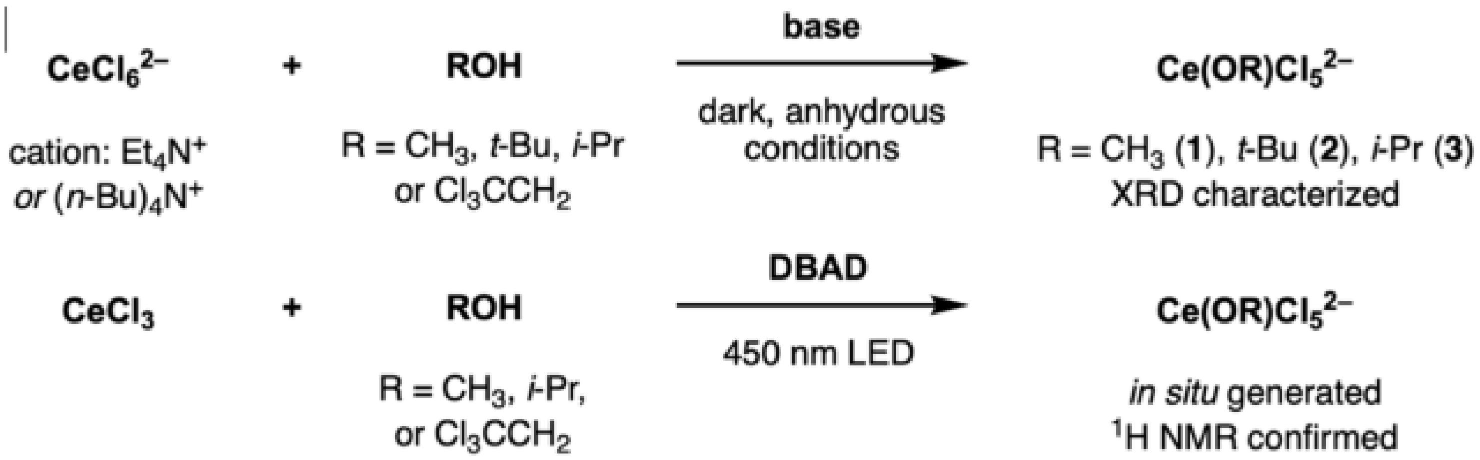
RO• mediated HAT validated as rate-determining step

● DFT



regioselectivity and KIE investigated via DFT

2.2.1. 中间体制备和表征



$CeCl_6^{2-} + ROH \xrightarrow[\text{dark, anhydrous conditions}]{\text{base}} Ce(OR)Cl_5^{2-}$

cation: Et_4N^+ *or* $(n\text{-}Bu)_4N^+$

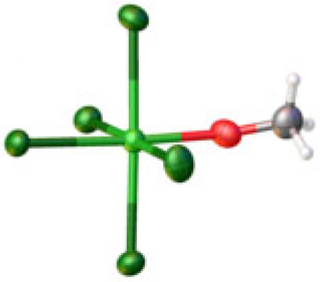
R = CH_3, *t*-Bu, *i*-Pr or Cl_3CCH_2

R = CH_3 (**1**), *t*-Bu (**2**), *i*-Pr (**3**)
XRD characterized

$CeCl_3 + ROH \xrightarrow[\text{450 nm LED}]{\text{DBAD}} Ce(OR)Cl_5^{2-}$

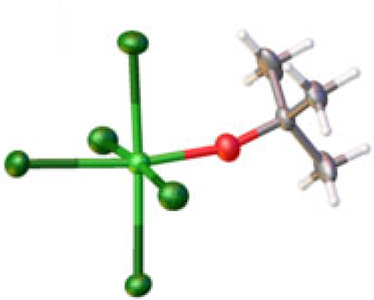
R = CH_3, *i*-Pr, or Cl_3CCH_2

in situ generated
^1H NMR confirmed



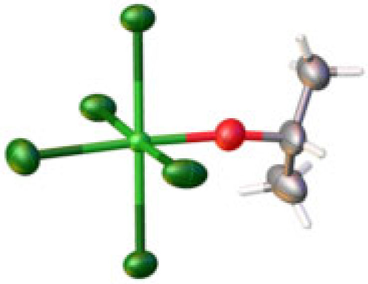
1

$Ce(OMe)Cl_5^{2-}$



2

$Ce(O^tBu)Cl_5^{2-}$



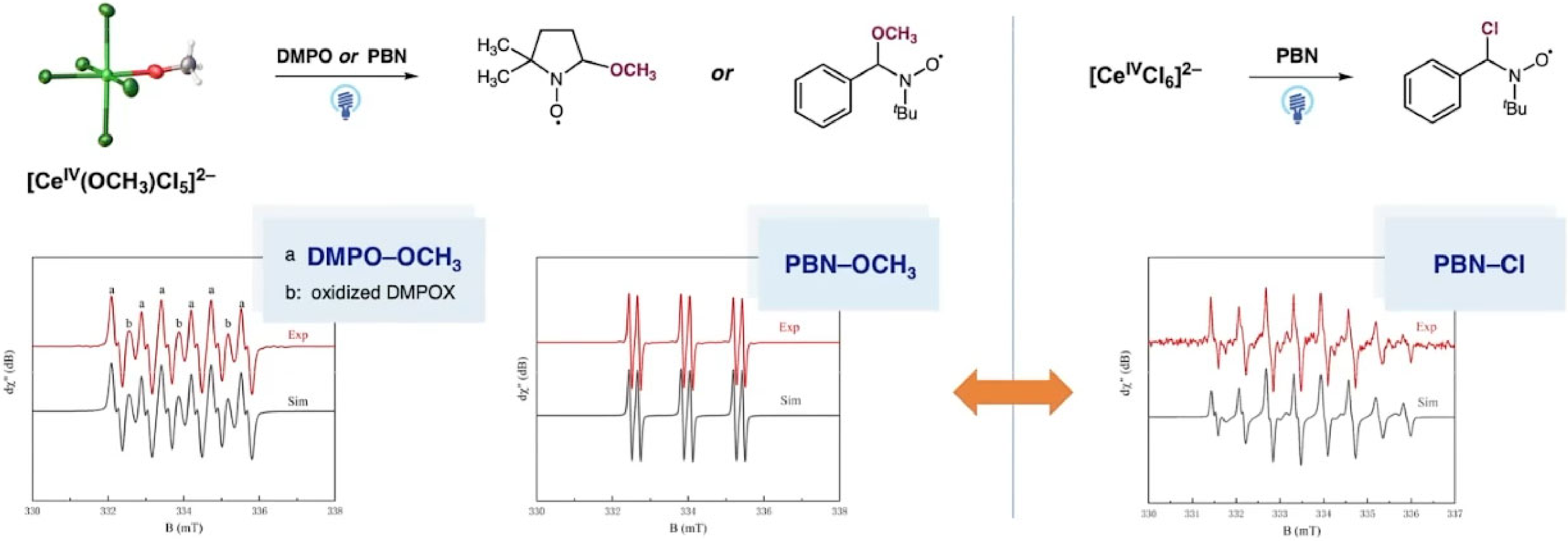
3

$Ce(O^iPr)Cl_5^{2-}$

2.2.2. 电子顺磁共振(EPR)实验

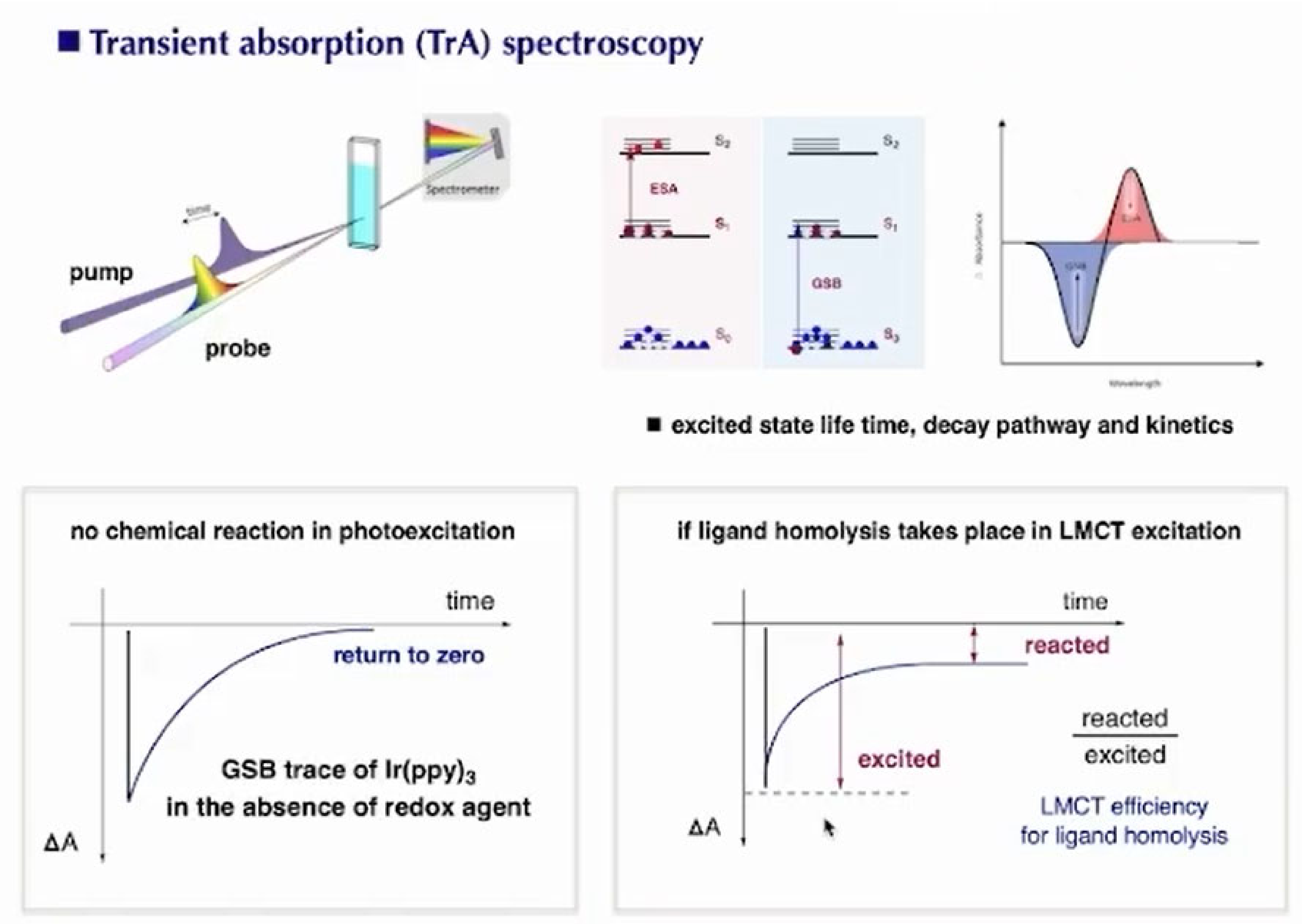
DMPO **PBN**

- Operando EPR validates the exclusive generation of alkoxy radical in the LMCT excitation of $[Ce(OR)Cl_5]^{2-}$



- characteristic spectrum of spin adduct of $^tBuO\cdot$, $^iPrO\cdot$, $Cl_3CH_2O\cdot$, $CF_3CH_2O\cdot$, $(CF_3)_2CHO\cdot$ obtained
- exclusive generation of alkoxy radical in the LMCT-homolysis, precluding the generation of chlorine radical

2.2.3. 瞬态吸收光谱 (Transient Absorption)研究



■ Transient absorption (TrA) spectroscopy

■ excited state life time, decay pathway and kinetics

no chemical reaction in photoexcitation

GSB trace of $Ir(ppy)_3$
in the absence of redox agent

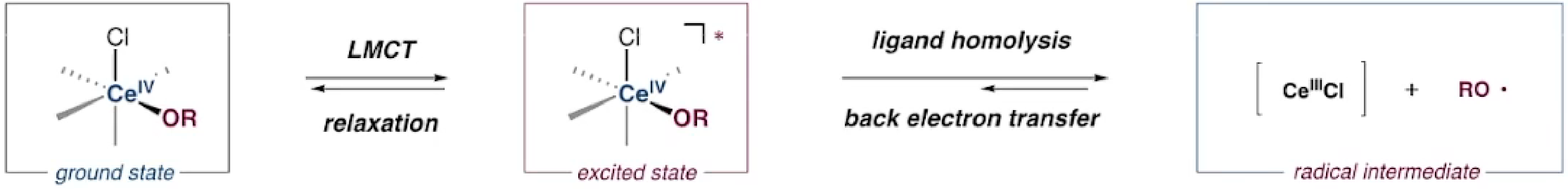
if ligand homolysis takes place in LMCT excitation

$\frac{\text{reacted}}{\text{excited}}$

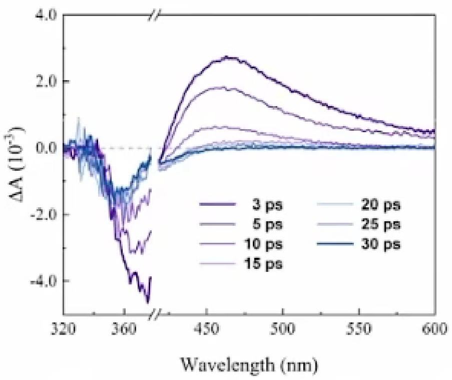
LMCT efficiency
for ligand homolysis

2.2.3. 瞬态吸收光谱 (Transient Absorption)研究

- TA spectroscopy experiment of $[Ce(OCH_3)Cl_5]^{2-}$: probe the LMCT process at fs timeframe

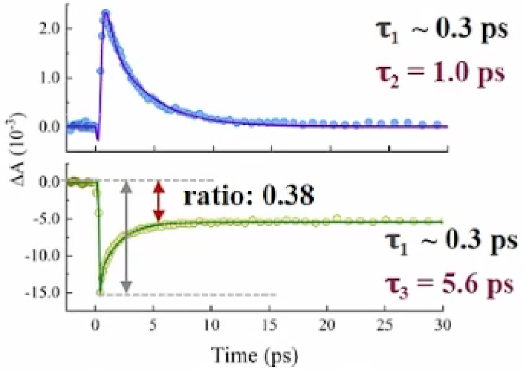


● TA spectra of $[Ce(OCH_3)Cl_5]^{2-}$



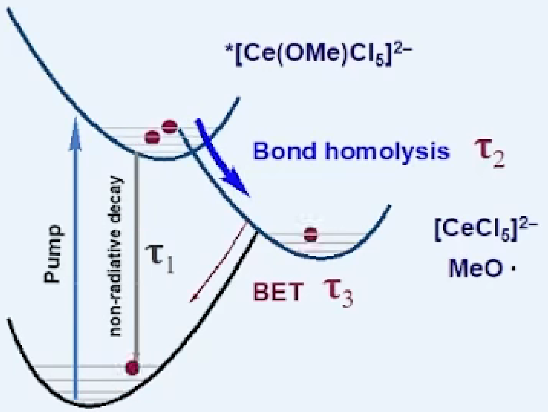
no absorption in the range of 320-350 nm, precludes the generation of Cl·

● Kinetic trace at 580 nm and 370 nm

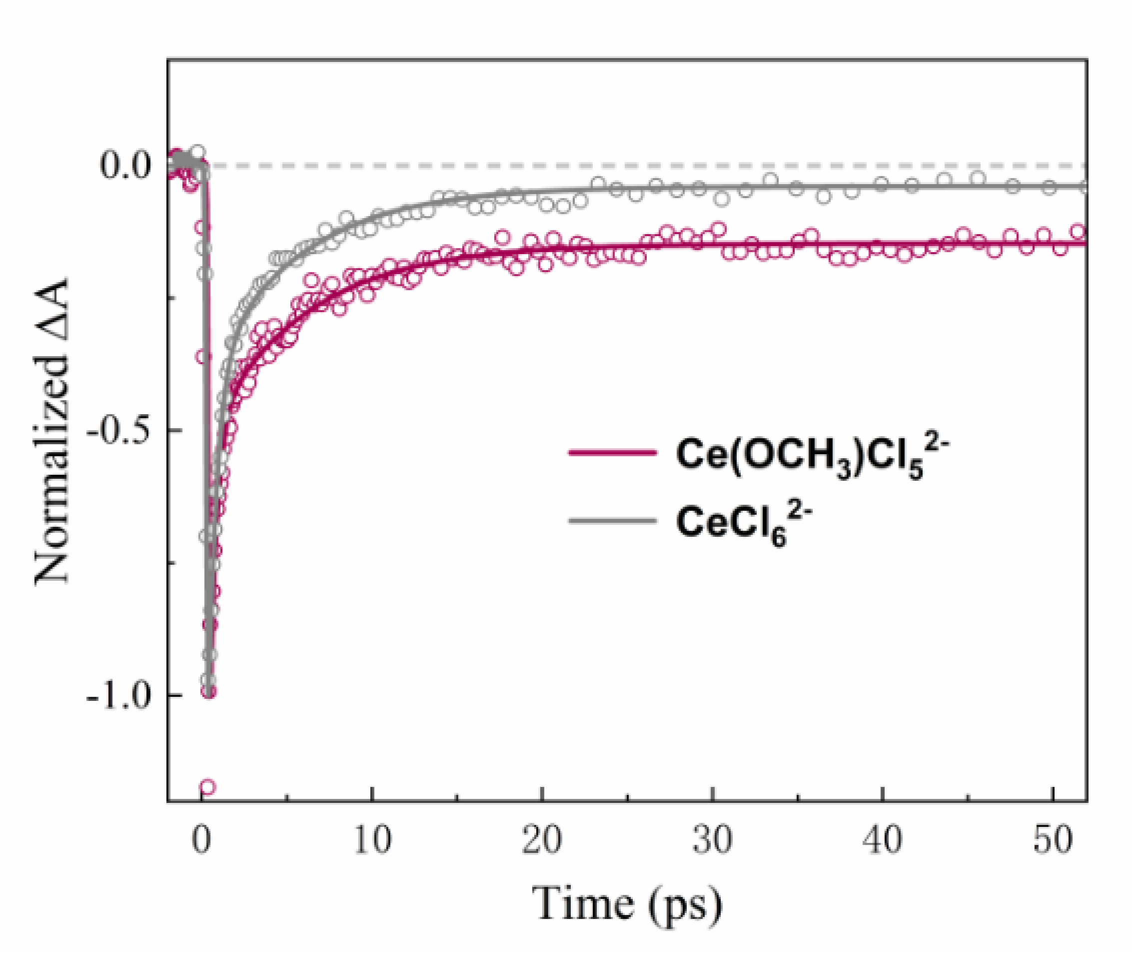


ligand homolysis efficiency: 38%
back electron transfer (BET) validated

● simplified diagram of LMCT excitation

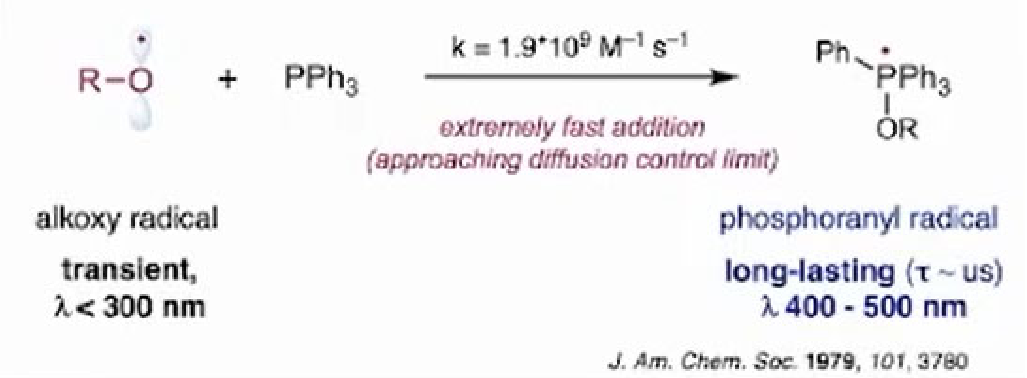


2.2.3. 瞬态吸收光谱 (Transient Absorption)研究



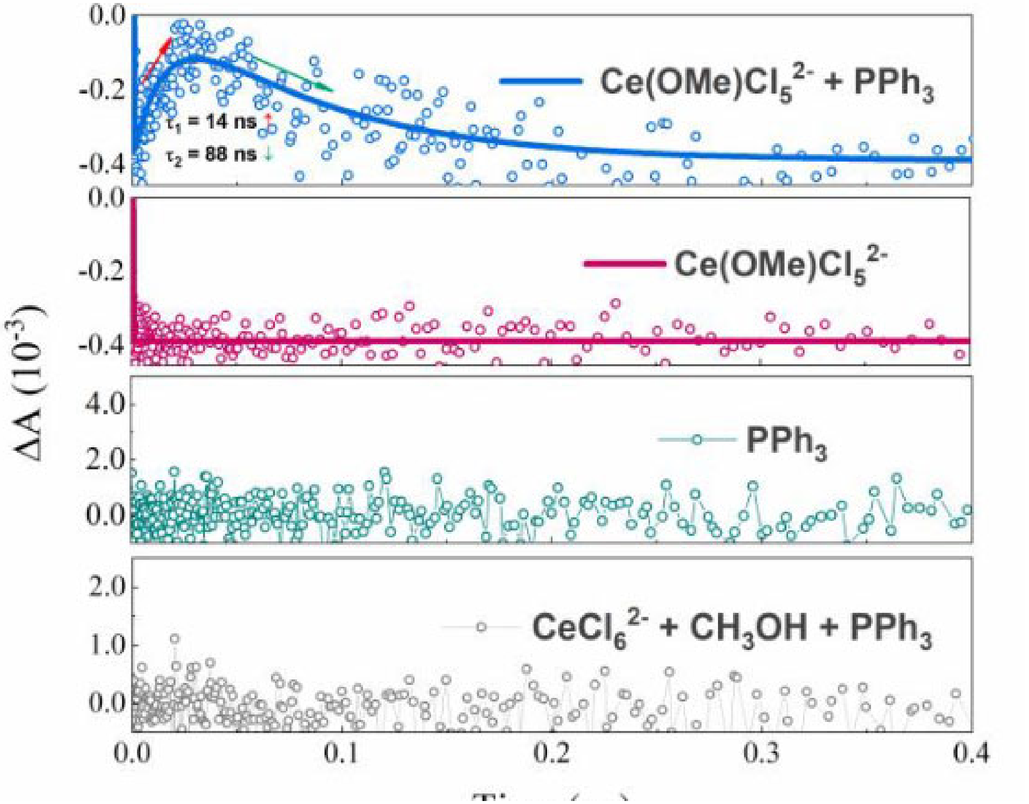
Ratio:0.05
vs
Ratio:0.38

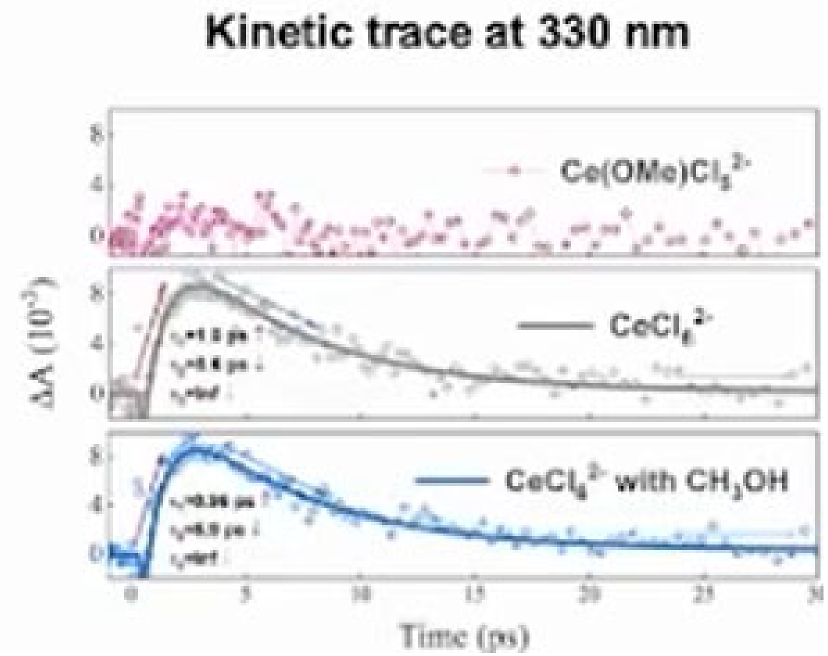
2.2.3. 瞬态吸收光谱 (Transient Absorption)研究



J. Am. Chem. Soc. **1979**, *101*, 3780

430 nm





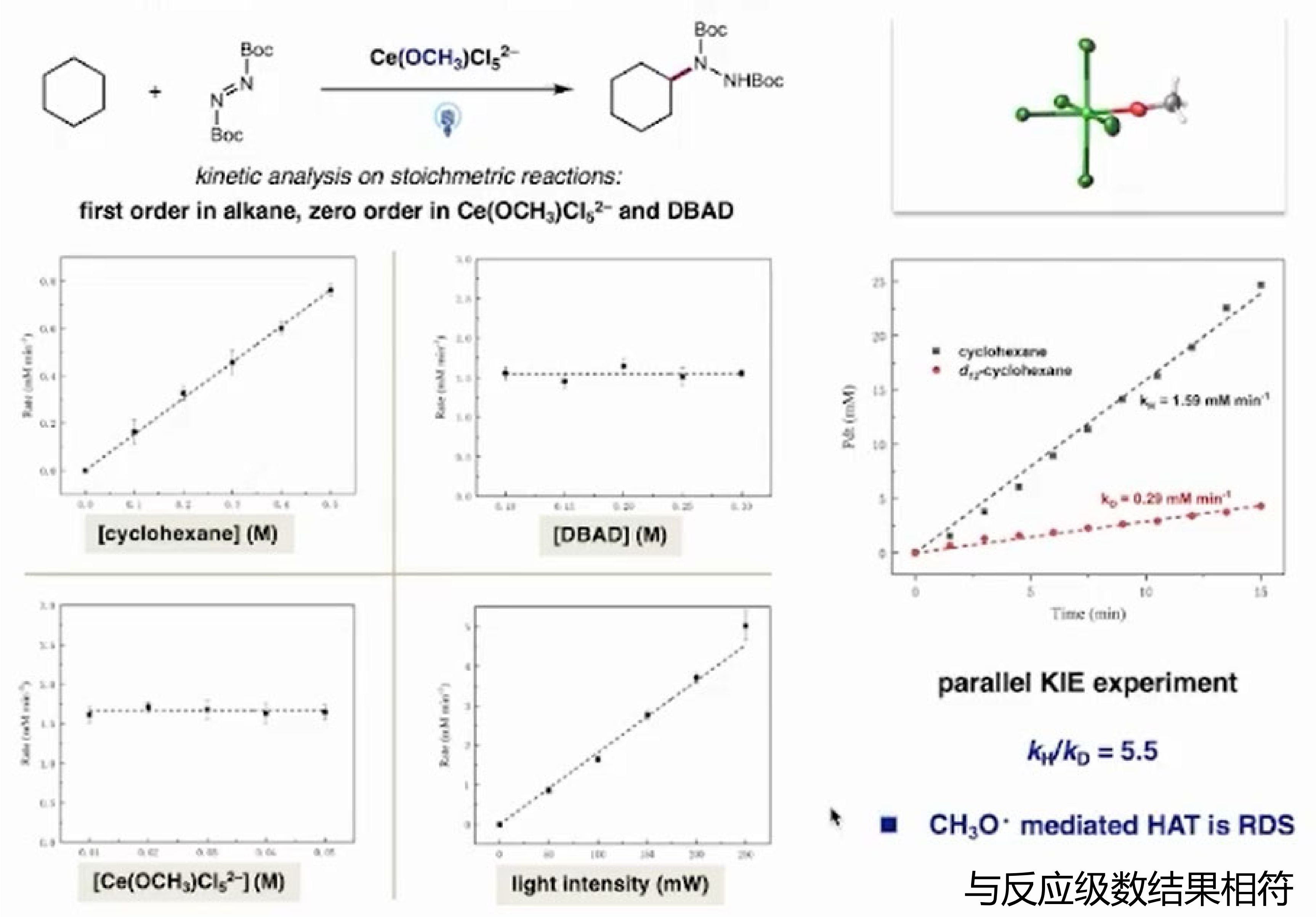
chlorine radical - CH_3CN charge transfer band (320-370 nm)

J. Chem. Phy. **2001**, *115*, 9361; *Chem. Rev.* **2019**, *119*, 4628

Photoexcitation of $Ce(OCH_3)Cl_5^{2-}$ does not generate Cl·

Cl· does not form any complex with alcohol

2.2.4. Parallel KIE experiments



kinetic analysis on stoichmetric reactions:

first order in alkane, zero order in Ce(OCH$_3$)Cl$_5^{2-}$ and DBAD

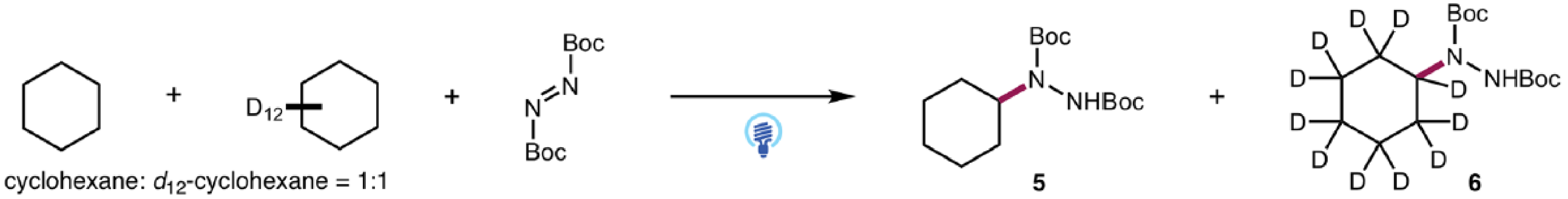
parallel KIE experiment

$k_H/k_D = 5.5$

- CH$_3$O· mediated HAT is RDS

与反应级数结果相符

2.2.4. Intermolecular competition KIE experiments

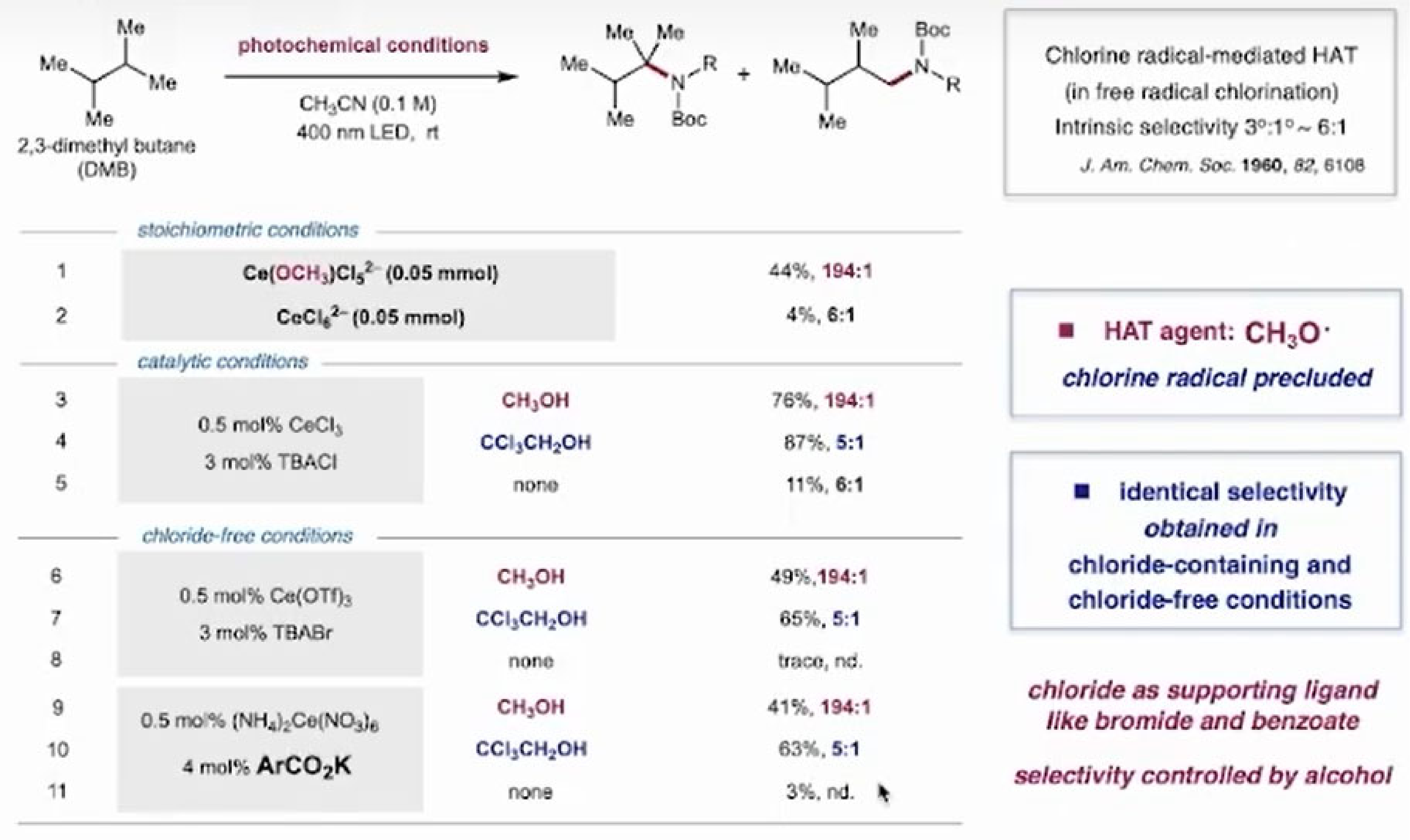


cyclohexane: d_{12}-cyclohexane = 1:1

	premade complex 0.1 mmol Ce(IV) complex	**KIE** **[5]:[6]**	yield
1	**$Ce(OMe)Cl_5^{2-}$**	**5.1**	26%
2	**$CeCl_6^{2-}$**	**1.1**	12%

	original conditions **0.5 mol% $CeCl_3$, 2.5 mol% TBACl**	**KIE** **[5]:[6]**	yield
3	with 20 mol% **MeOH**	**5.1**	19%
4	without alcohol	**1.1**	9%

2.2.5.区域选择性控制实验



2,3-dimethyl butane (DMB)

photochemical conditions

CH_3CN (0.1 M)
400 nm LED, rt

Chlorine radical-mediated HAT
(in free radical chlorination)
Intrinsic selectivity 3°:1° ~ 6:1
J. Am. Chem. Soc. **1960**, *82*, 6108

stoichiometric conditions			
1	**$Ce(OCH_3)Cl_5^{2-}$ (0.05 mmol)**		44%, 194:1
2	**$CeCl_6^{2-}$ (0.05 mmol)**		4%, 6:1
catalytic conditions			
3	0.5 mol% $CeCl_3$ 3 mol% TBACl	CH_3OH	76%, 194:1
4		CCl_3CH_2OH	87%, 5:1
5		none	11%, 6:1
chloride-free conditions			
6	0.5 mol% $Ce(OTf)_3$ 3 mol% TBABr	CH_3OH	49%,194:1
7		CCl_3CH_2OH	65%, 5:1
8		none	trace, nd.
9	0.5 mol% $(NH_4)_2Ce(NO_3)_6$ 4 mol% $ArCO_2K$	CH_3OH	41%, 194:1
10		CCl_3CH_2OH	63%, 5:1
11		none	3%, nd.

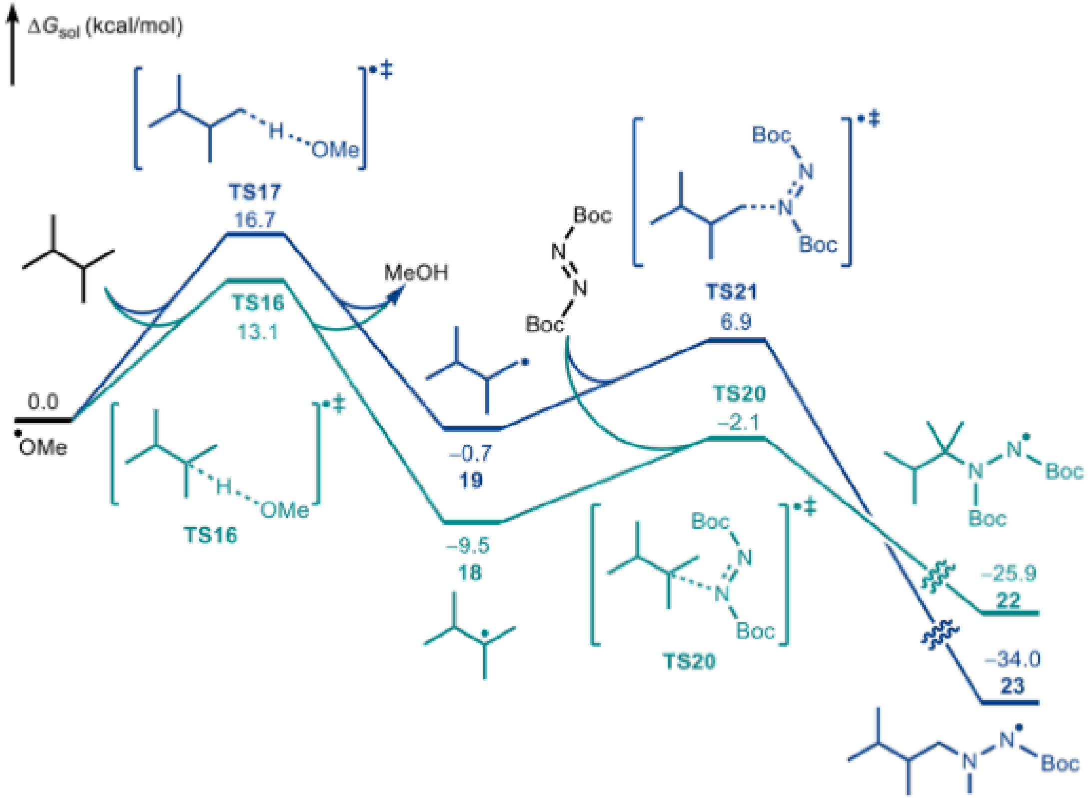
- **HAT agent: $CH_3O\cdot$**
  chlorine radical precluded

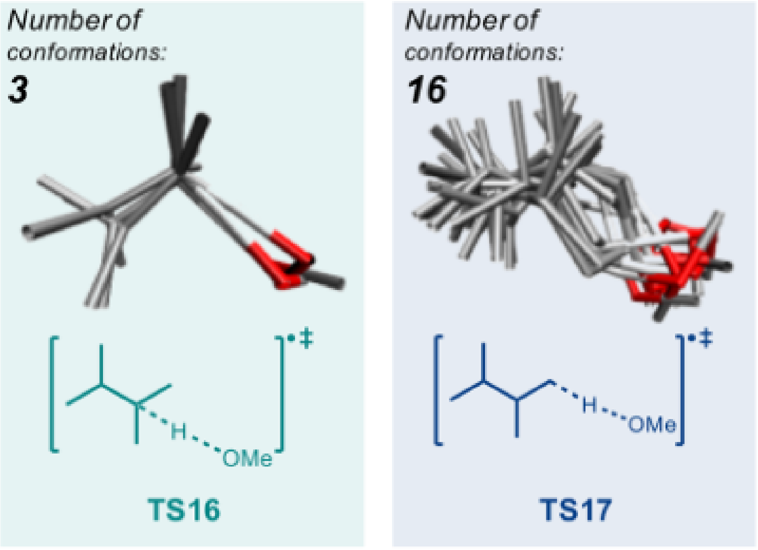
- **identical selectivity *obtained in* chloride-containing and chloride-free conditions**

chloride as supporting ligand like bromide and benzoate

selectivity controlled by alcohol

2.2.6. DFT calculations





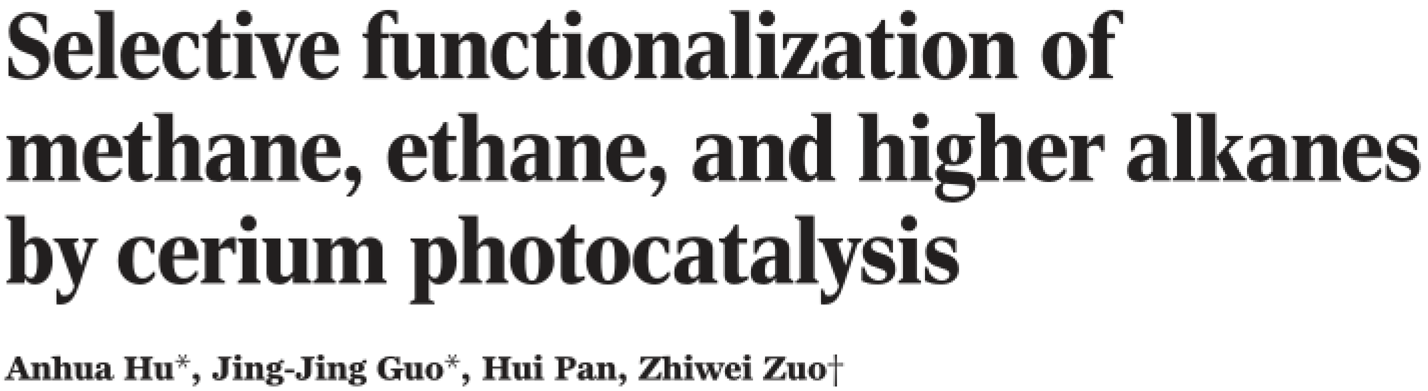
selectivity(calc.): ***152 : 1***

selectivity(exp.): ***194 : 1***

总结：LMCT过程产生单一的烷氧基自由基，而不是氯自由基。

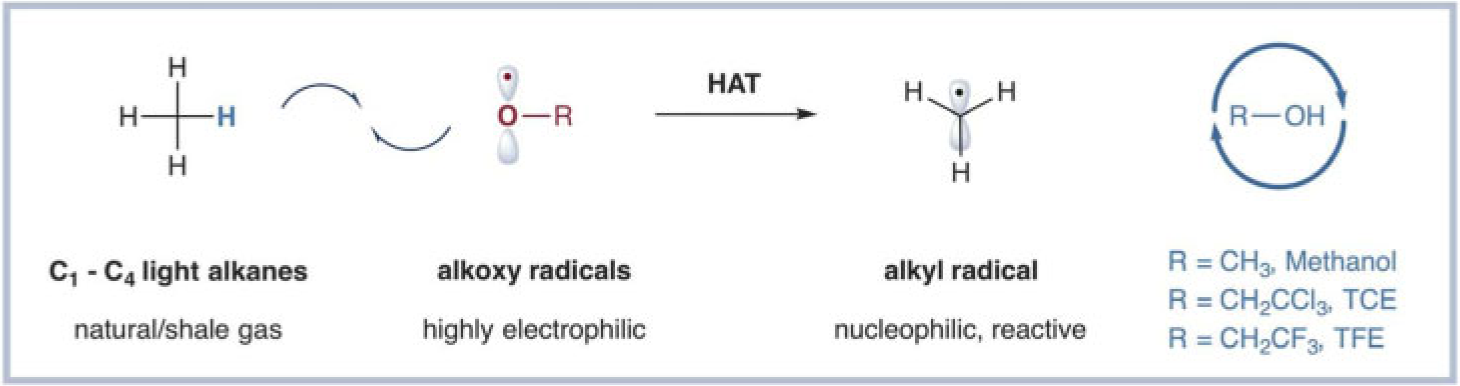
2.3. HAT碳氢键官能化

Zuo, Z. Science 2018, 361, 668



Selective functionalization of methane, ethane, and higher alkanes by cerium photocatalysis

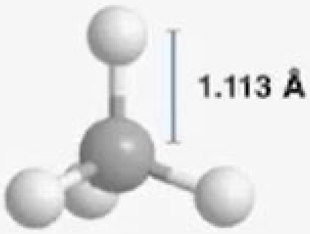
Anhua Hu*, Jing-Jing Guo*, Hui Pan, Zhiwei Zuo†



2.3. HAT碳氢键官能化

Methane functionalization

- ☐ "Grand challenge"
- ☐ Low intrinsic reactivity
- ☐ Selectivity and efficiency



BDE 105 kcal/mol

Ionization potential 12.6 ev

Proton affinity 5.3 ev

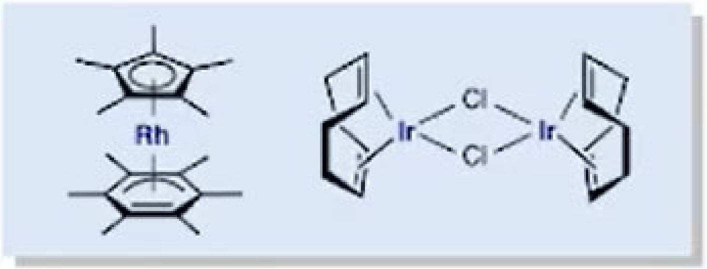
■ Homogeneous catalysts for methane activation

Pt Pd Rh Ru Ir etc...

Shilov, A. E. et al. *Chem. Rev.* **1997**, 97, 2879
Periana, R. A. et al. *Chem. Rev.* **2017**, 117, 8521

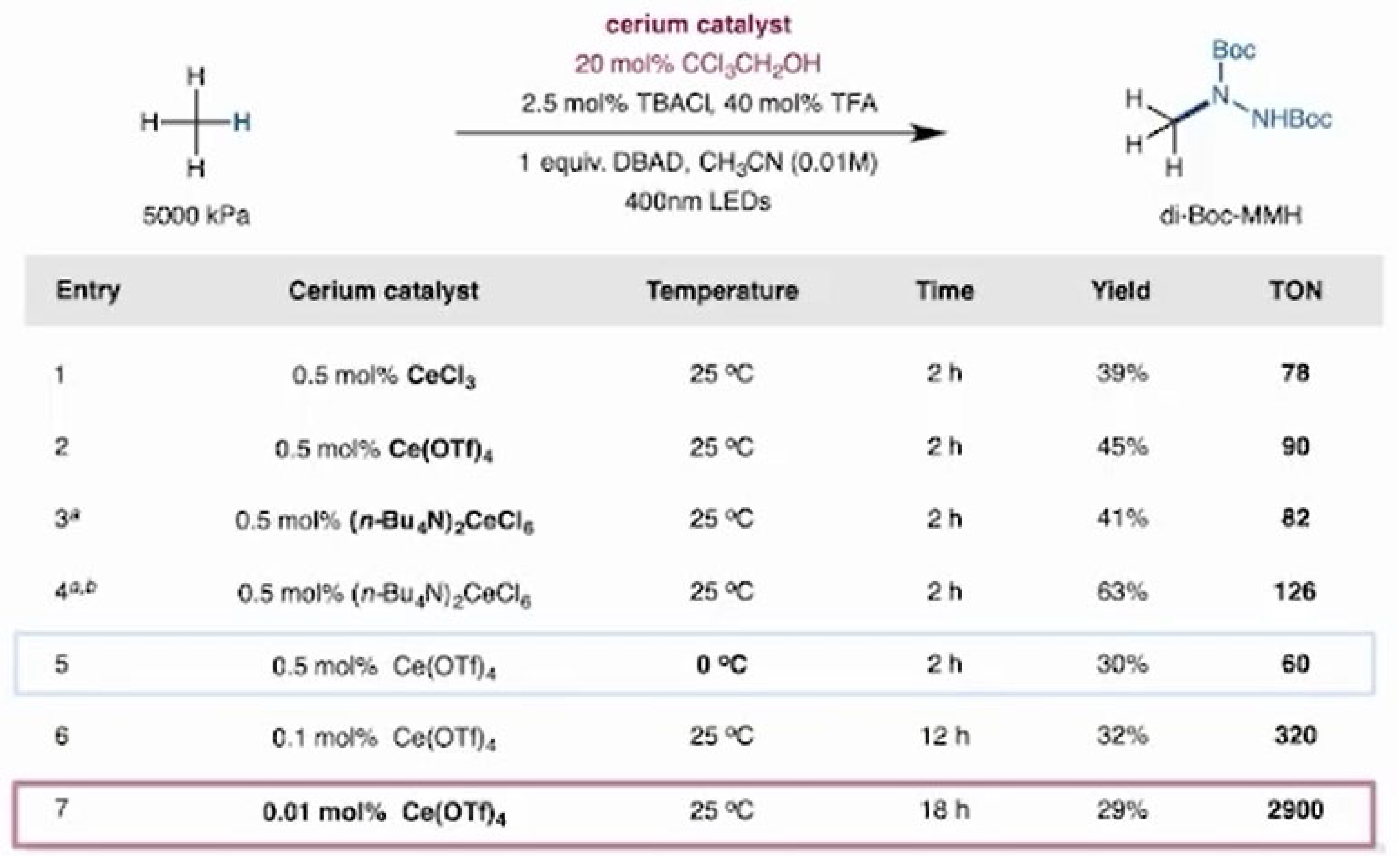
$$H_3C\text{—}H + B_2pin_2 \xrightarrow[c\text{-}C_6H_{12}]{\text{catalyst}} H_3C\text{—}Bpin$$

3500 kPa; 150 °C; 52% yield, TON 104

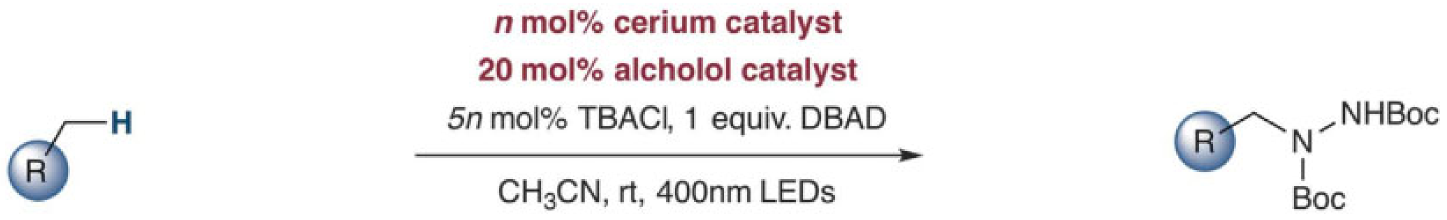


Sanford, M. S. et al. Science **2016**, *351*, 1421   *Mindiola, D. J. et al. Science* **2016**, *351*,1424

2.3. HAT碳氢键官能化



Entry	Cerium catalyst	Temperature	Time	Yield	TON
1	0.5 mol% **$CeCl_3$**	25 °C	2 h	39%	**78**
2	0.5 mol% **$Ce(OTf)_4$**	25 °C	2 h	45%	**90**
3[a]	0.5 mol% **(n-$Bu_4N)_2CeCl_6$**	25 °C	2 h	41%	**82**
4[a,b]	0.5 mol% (n-$Bu_4N)_2CeCl_6$	25 °C	2 h	63%	**126**
5	0.5 mol% $Ce(OTf)_4$	**0 °C**	2 h	30%	**60**
6	0.1 mol% $Ce(OTf)_4$	25 °C	12 h	32%	**320**
7	**0.01 mol% $Ce(OTf)_4$**	25 °C	18 h	29%	**2900**



Alkane	Entry	Cerium catalyst	Loading (*n*)	Alcohol catalyst	Time	Yield	TON
R = H[*] **Methane** (5000 kPa)	1	$Ce(OTf)_4$	0.5	CCl_3CH_2OH	2 h	45%	**90**
	2[†]	$(n\text{-}Bu_4N)_2CeCl_6$	0.5	CCl_3CH_2OH	2 h	63%	**126**
	3	$Ce(OTf)_4$	0.01	CCl_3CH_2OH	18 h	29%	**2900**
R = Me[‡] **Ethane** (101 kPa)	4	$CeCl_3$	0.5	CCl_3CH_2OH	4 h	74%	**148**
	5[§]	$CeCl_3$	0.01	CCl_3CH_2OH	4 h	97%	**9700**
R = Et **Propane** (101 kPa)	6	$CeCl_3$	0.5	CCl_3CH_2OH	9 h	70% (1:1 r.r.)	**140**
	7	$CeCl_3$	0.5	CF_3CH_2OH	12 h	61% (1:1 r.r.)	**122**
	8[‖]	$CeCl_3$	0.5	CH_3OH	19 h	39% (1:3.9 r.r.)	**78**
R = Pr **Butane** (101 kPa)	9	$CeCl_3$	0.5	CCl_3CH_2OH	6 h	76% (1:1.7 r.r.)	**152**
	10	$CeCl_3$	0.5	$(CH_3)_2CHOH$	18 h	40% (1:4 r.r.)	**80**
	11[‖]	$CeCl_3$	0.5	CH_3OH	18 h	72% (1:8 r.r.)	**144**
Cyclohexane	12	$CeCl_3$	0.5	CCl_3CH_2OH	16 h	81%	**162**

2.3. HAT碳氢键官能化

Gas input (G)

compressed gaseous alkane

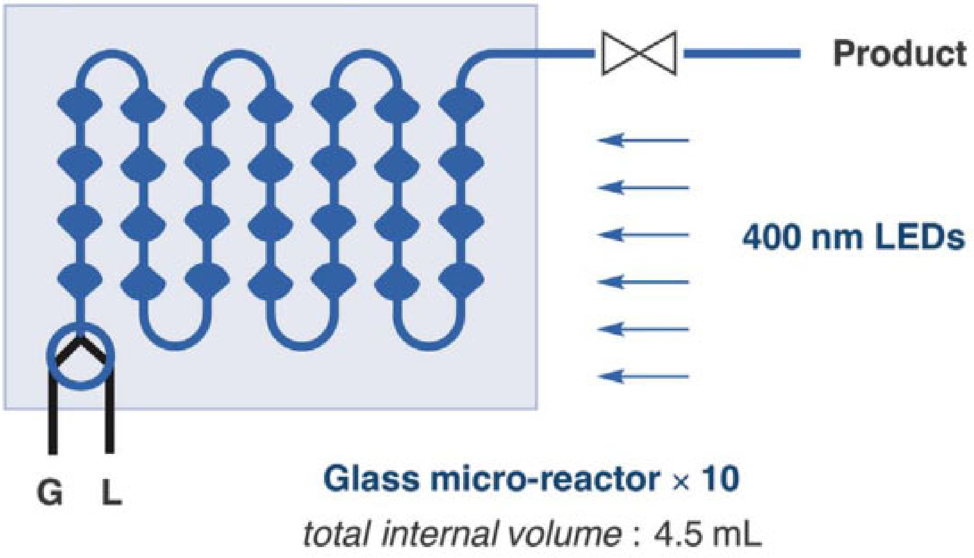
Liquid input (L)

(n-$Bu_4N)_2CeCl_6$ (42 mg, 1 mol%)

CCl_3CH_2OH (149 mg, 20 mol%)

DBAD (1.15 g, 5 mmol)

CH_3CN (100 mL)



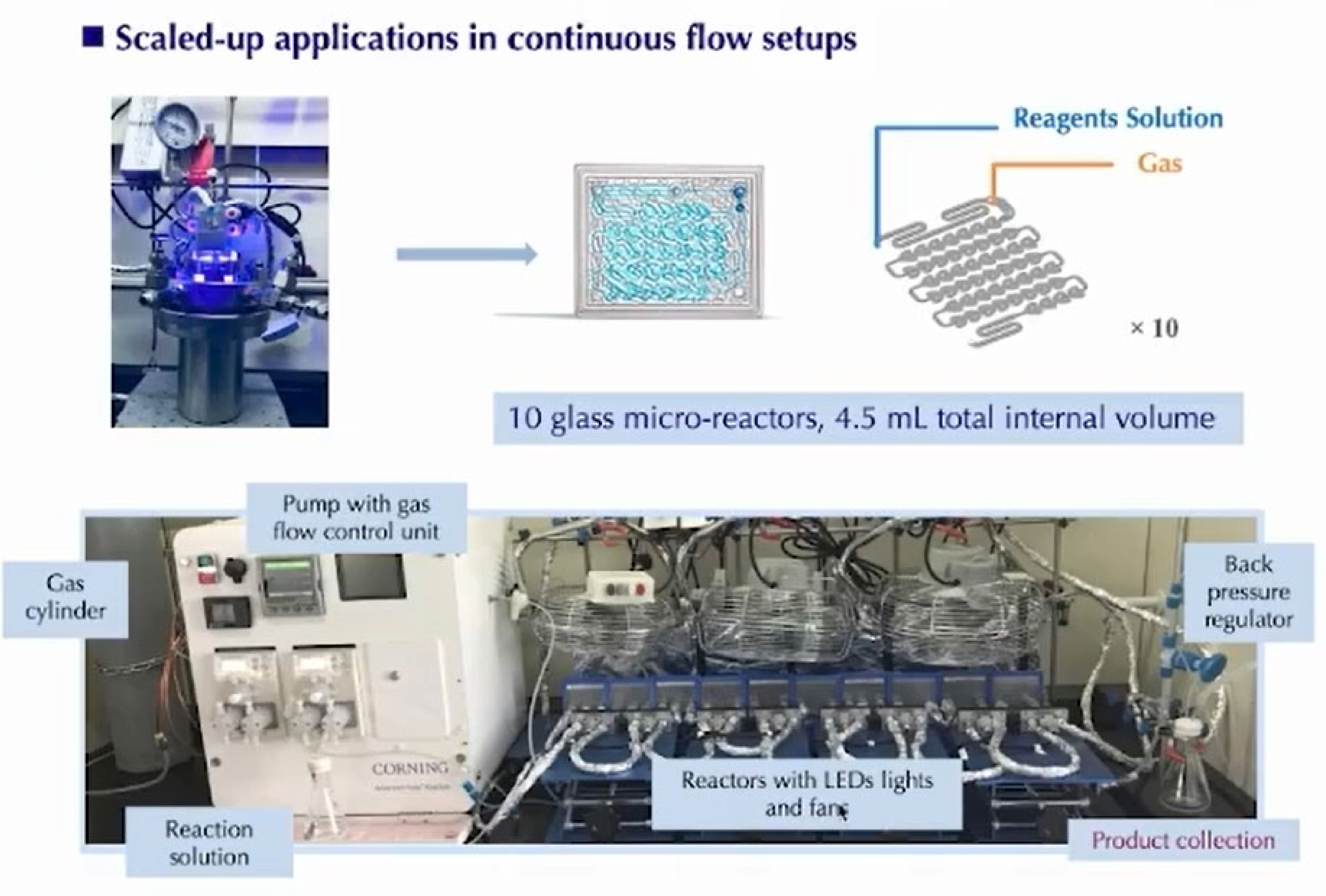
Glass micro-reactor × 10

total internal volume : 4.5 mL

Entry	Alkane	Flow rate	Residence time	Yield	Productivity
1^*	methane (1800 kPa)	0.3 mL/min	**15 min**	15%	0.6 mmol/d
$2^\dagger$	ethane (1500 kPa)	0.75 mL/min	**6 min**	90%	2.0 mmol/h
3	propane (800 kPa)	0.75 mL/min	**6 min**	76%	1.7 mmol/h
4	butane (400 kPa)	0.75 mL/min	**6 min**	56%	1.3 mmol/h
$5^\ddagger$	cyclohexane (22 mL)	0.5 mL/min	**9 min**	70%	4.2 mmol/h

反应在玻璃微通道反应器中高效进行，使工业化生产成为可能。

2.3. HAT碳氢键官能化



■ Scaled-up applications in continuous flow setups

Reagents Solution

Gas

× 10

10 glass micro-reactors, 4.5 mL total internal volume

Pump with gas flow control unit

Gas cylinder

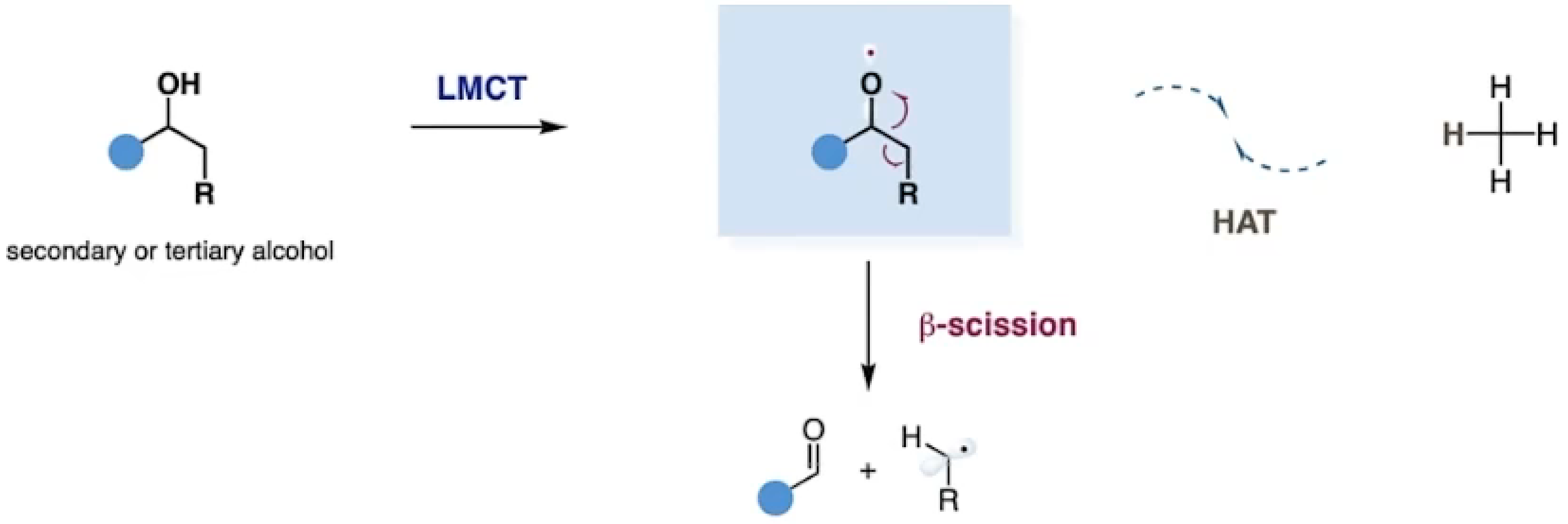
Back pressure regulator

Reactors with LEDs lights and fans

Reaction solution

Product collection

Alkoxy radicals: HAT vs. β-scission



3.1. β-scissions断裂碳碳键

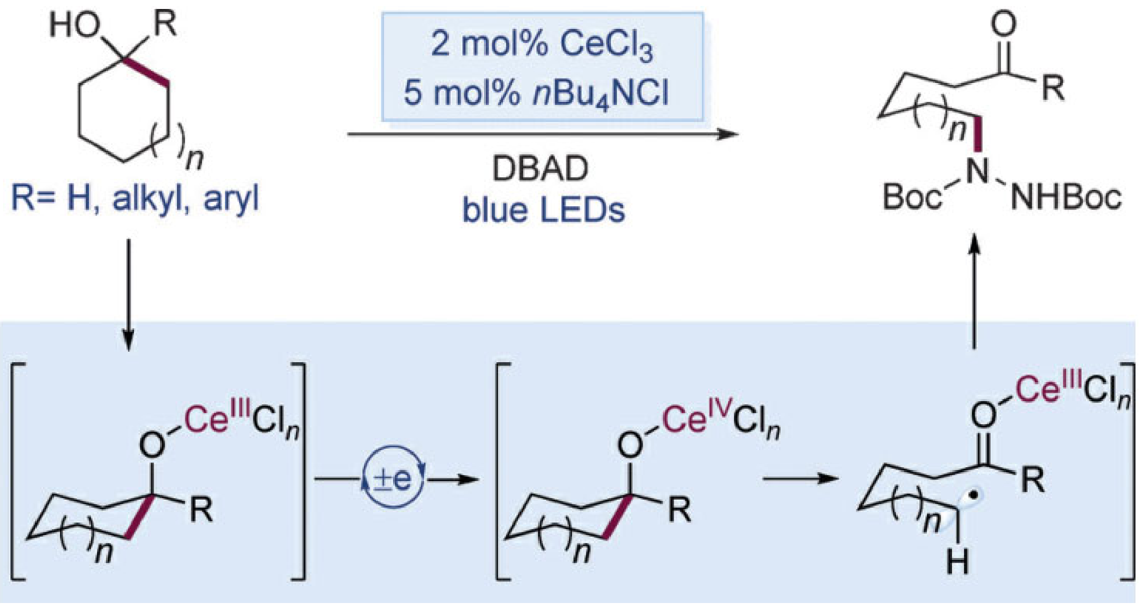
GDCh **Communications** Angewandte Chemie International Edition

Photochemistry

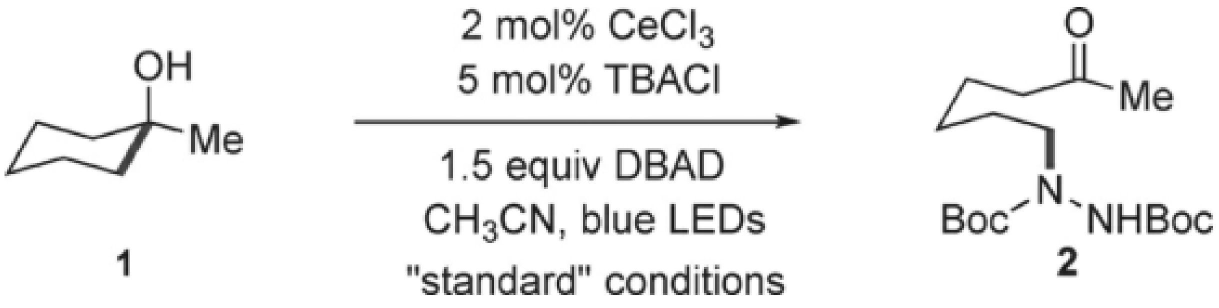
International Edition: DOI: 10.1002/anie.201609035
German Edition: DOI: 10.1002/ange.201609035

Photocatalytic C−C Bond Cleavage and Amination of Cycloalkanols by Cerium(III) Chloride Complex

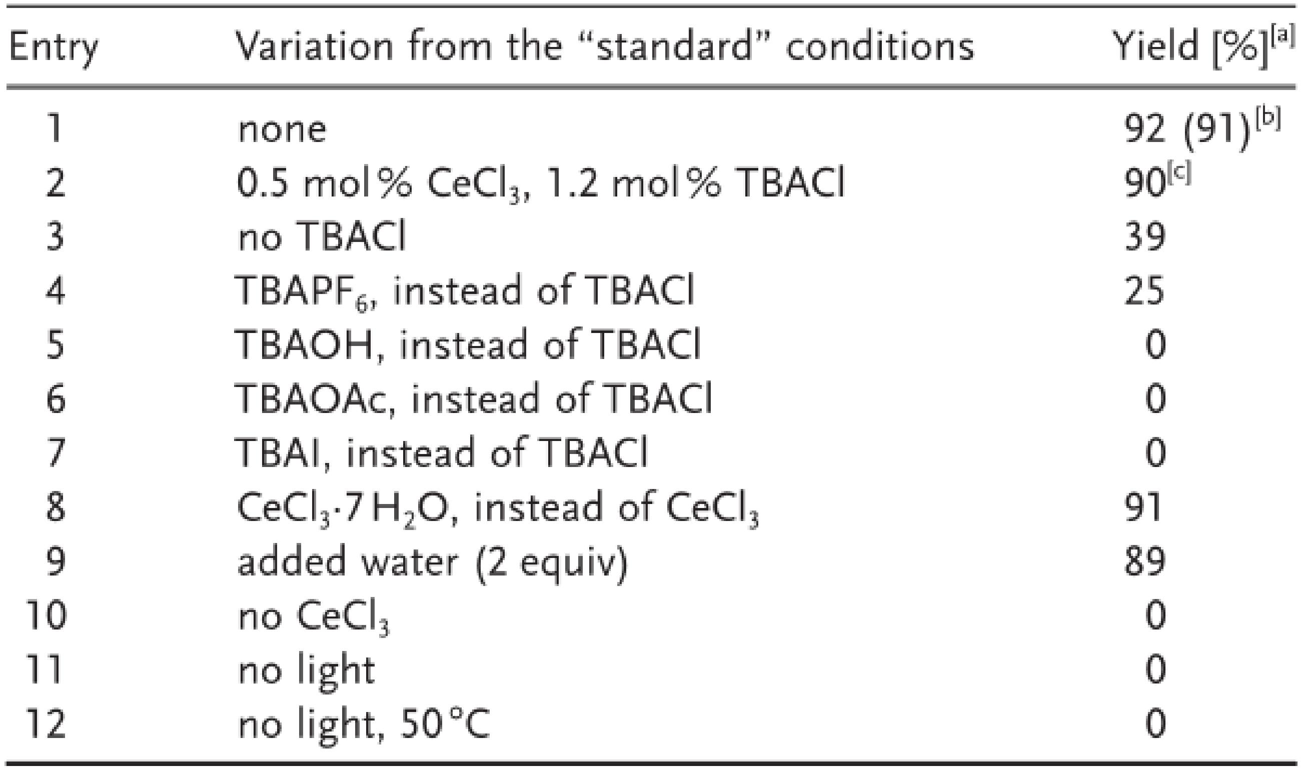
*Jing-Jing Guo[+], Anhua Hu[+], Yilin Chen, Jianfeng Sun, Haoming Tang, and Zhiwei Zuo**



3.1. β-scissions断裂碳碳键

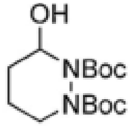
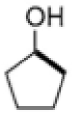
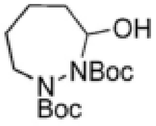
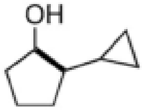
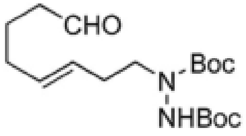
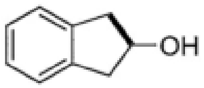
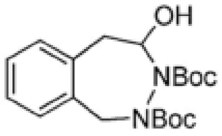
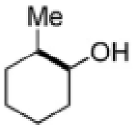
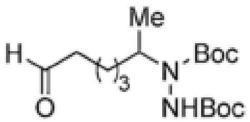
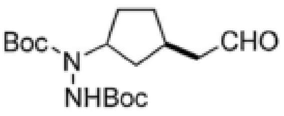


1 → 2

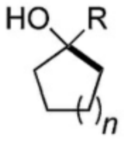
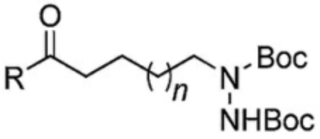
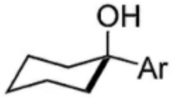
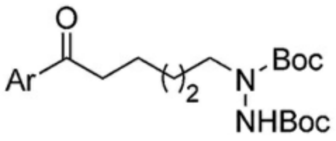
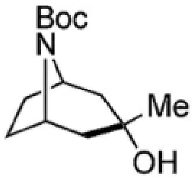
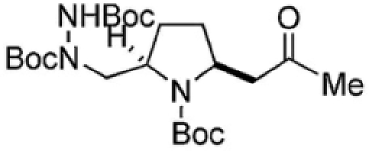
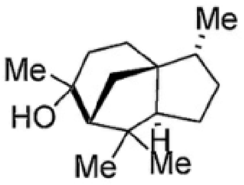
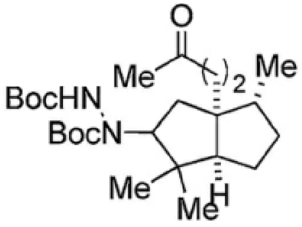


Entry	Variation from the “standard” conditions	Yield [%][a]
1	none	92 (91)[b]
2	0.5 mol% $CeCl_3$, 1.2 mol% TBACl	90[c]
3	no TBACl	39
4	$TBAPF_6$, instead of TBACl	25
5	TBAOH, instead of TBACl	0
6	TBAOAc, instead of TBACl	0
7	TBAI, instead of TBACl	0
8	$CeCl_3{\cdot}7H_2O$, instead of $CeCl_3$	91
9	added water (2 equiv)	89
10	no $CeCl_3$	0
11	no light	0
12	no light, 50 °C	0

3.1. β-scissions断裂碳碳键

Secondary cycloalkanols	Product	
		**19**, 98%
		**20**, 73%
		**21**, 98%
		**22**, 68%
		**23**, 68%
		**24**, 97% 2.4:1 d.r.

对于四元和五元的仲醇底物，在完成碳氮键构筑后倾向于环化生成六元和七元化合物

Tertiary cycloalkanols	Product	
		**3** n = 0, R = Ph, 97% **4** n = 1, R = Me, 84% **5** n = 3, R = Me, 80% **6** n = 4, R = Ph, 77%
		**7** Ar = Ph, 83% **8** Ar = 4-MeC$_6$H$_4$, 89% **9** Ar = 4-FC$_6$H$_4$, 84% **10** Ar = 4-ClC$_6$H$_4$, 86% **11** Ar = 4-BrC$_6$H$_4$, 97%
		**14**, 78%[b]
		**15**, 70% 2:1 d.r.[b]

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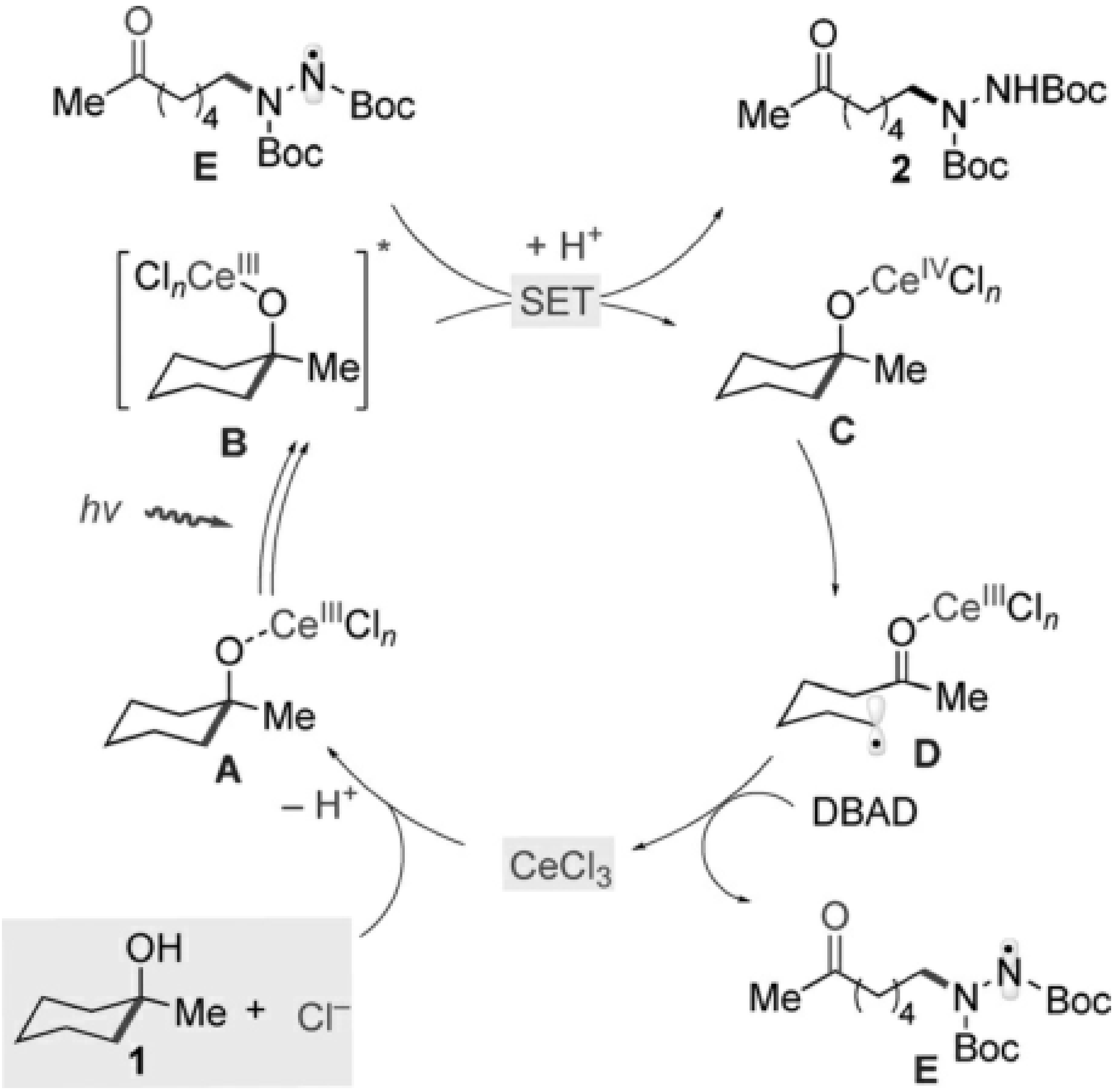
[a] All reactions are run on 0.4 mmol scale under the optimized reaction conditions. Yield is that of the isolated product. Diastereoselectivity was determined by either ^{1}H NMR or HPLC analysis. See the Supporting Information for experimental details. [b] Reaction performed with 10 mol% CeCl$_3$ and 25 mol% TBACl.

3.1. β-scissions断裂碳碳键



3.2. β-scissions断裂碳碳键

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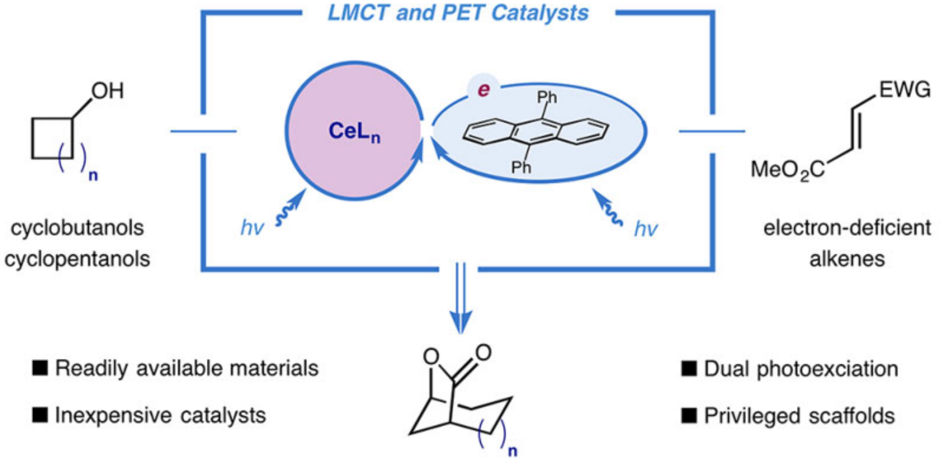
Communication
Cite This: *J. Am. Chem. Soc.* 2018, 140, 13580−13585
pubs.acs.org/JACS

Cerium-Catalyzed Formal Cycloaddition of Cycloalkanols with Alkenes through Dual Photoexcitation

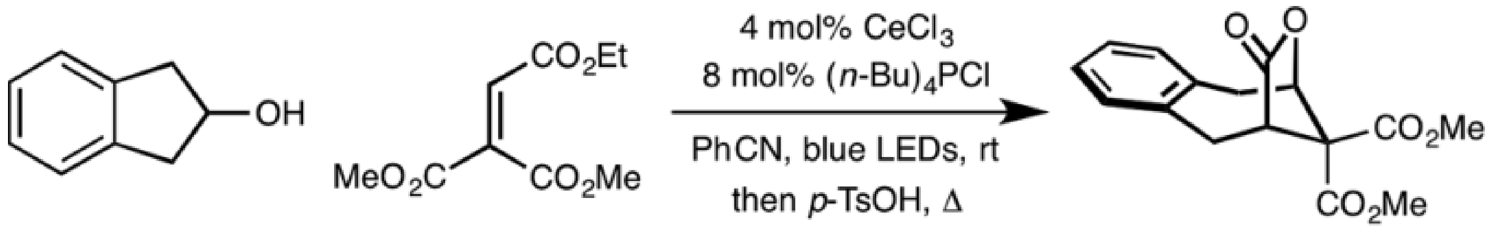
Anhua Hu,† Yilin Chen,† Jing-Jing Guo, Na Yu, Qing An, and Zhiwei Zuo*



配体-金属电荷转移（LMCT）+光诱导电子转移（PET）

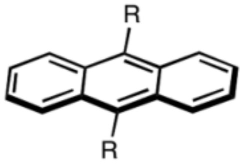
环烷醇与烯烃的形式环加成反应

3.2. β-scissions断裂碳碳键

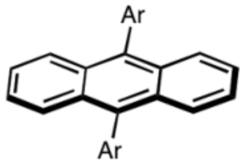


1 1.0 equiv. **2** 1.5 equiv. **3**

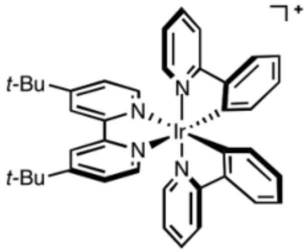
Entry	Additives	Light	Yield (%)[a]
1	none	blue LEDs	8
2	2 mol% anthracene	blue LEDs	19
3	2 mol% DBA	blue LEDs	32
4	2 mol% DMA	blue LEDs	56
5	2 mol% DCA	blue LEDs	10
6	2 mol% DPA	blue LEDs	82
7	2 mol% **4**	blue LEDs	78
8	2 mol% **5**	blue LEDs	42
9	2 mol% Ir(ppy)$_2$(dtbbpy)PF$_6$	blue LEDs	48



R = Br, **DBA**
R = OMe, **DMA**
R = CN, **DCA**



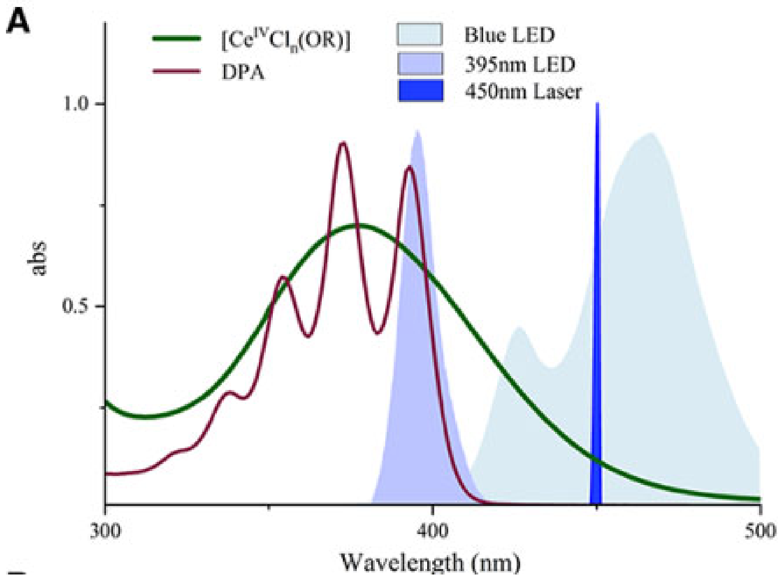
Ar = Ph, **DPA**
Ar = 2,4-di-F-C_6H_3, **4**
Ar = 3,4-di-OMe-C_6H_3, **5**



Ir(ppy)$_2$(dtbbpy)PF$_6$

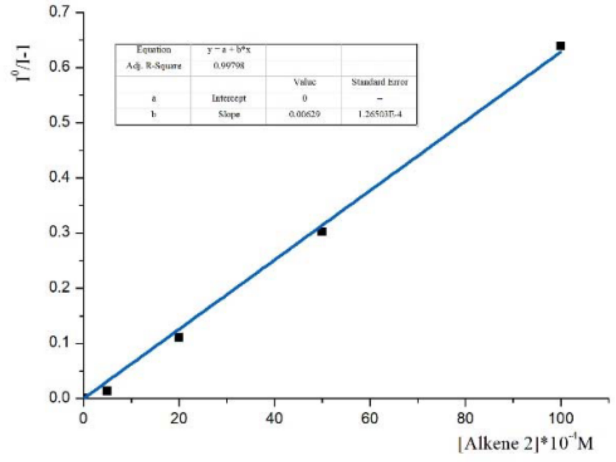
蒽类化合物，尤其是DPA对该反应有明显的加速效应。

3.2. β-scissions断裂碳碳键

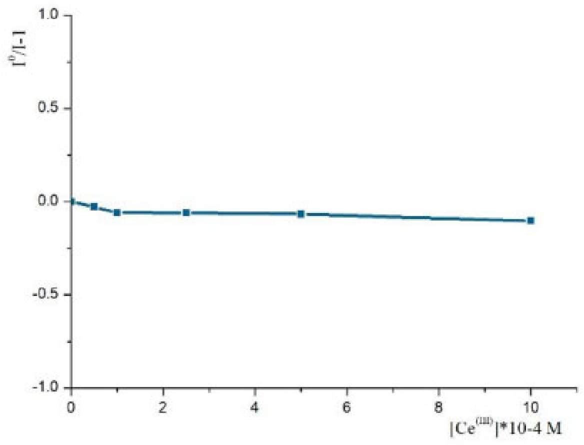


Light	PET catalyst	Yield
395 nm LED LMCT ON PET ON	DPA	50%
	none	6%
450 nm Laser LMCT ON PET OFF	DPA	9%
	none	8%

激发的DPA起到了催化作用

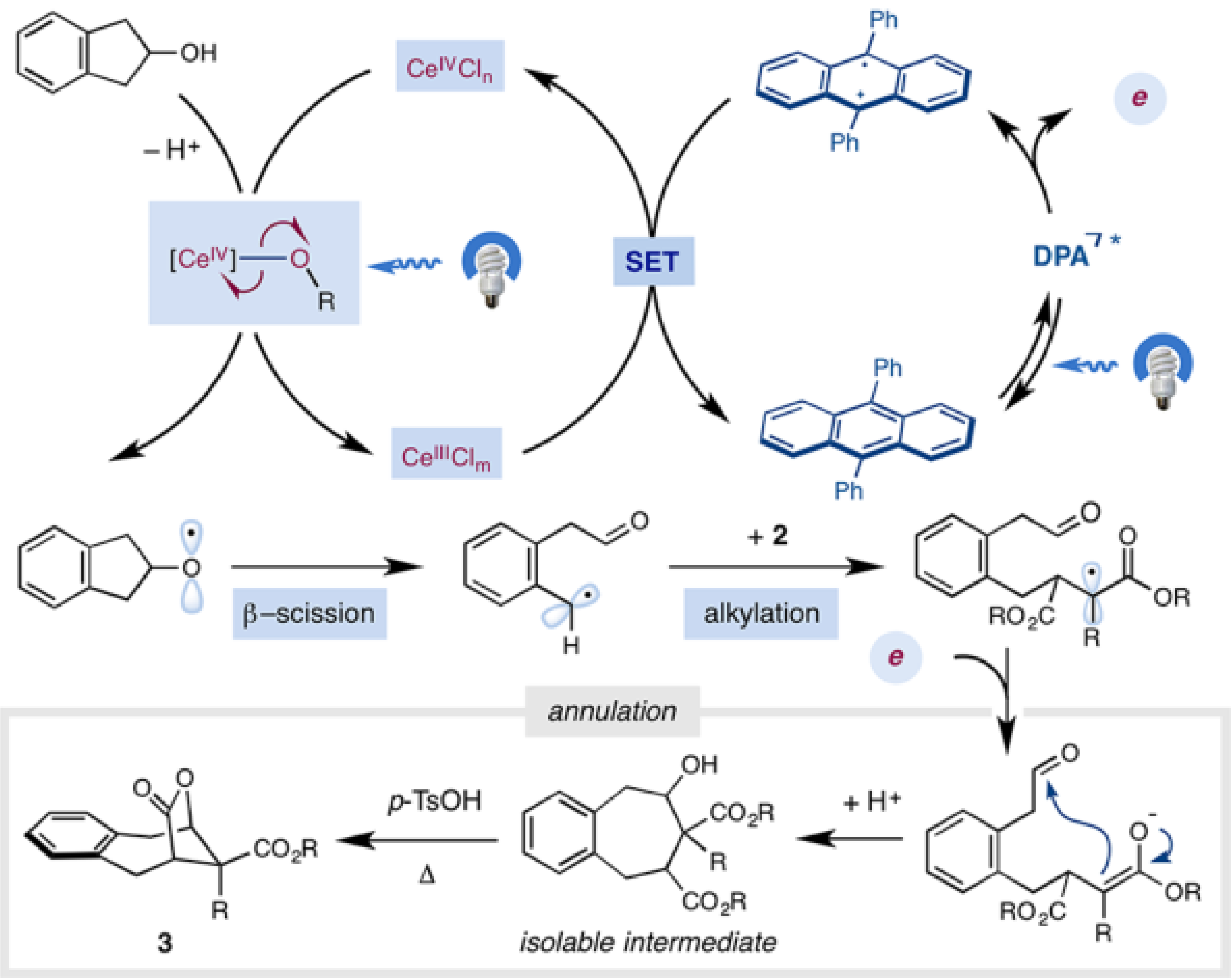


Stern-Volmer quenching studies of DPA by alkene 2.



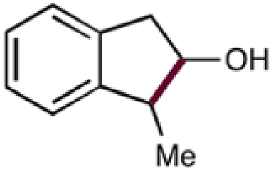
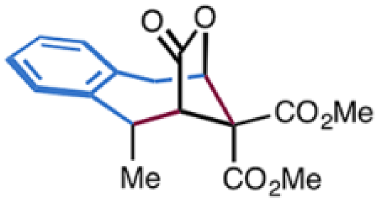
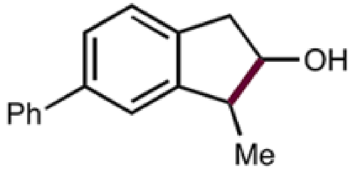
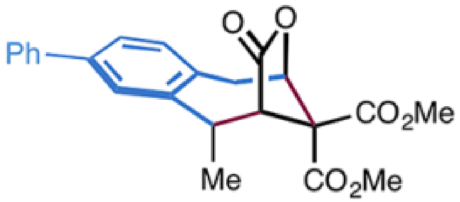
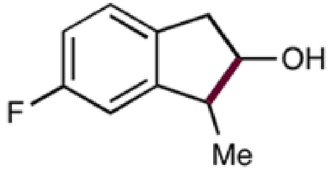
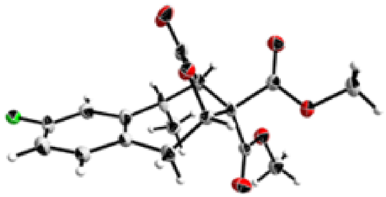
Stern-Volmer quenching studies of DPA by $Ce^{(III)}Cl_n(OC_5H_9)$.

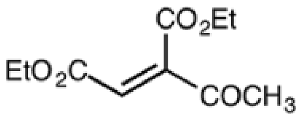
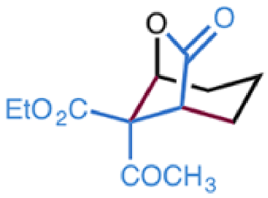
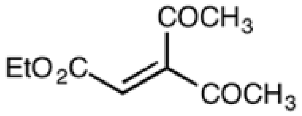
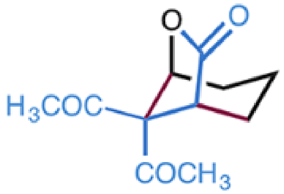
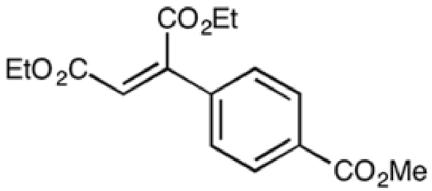
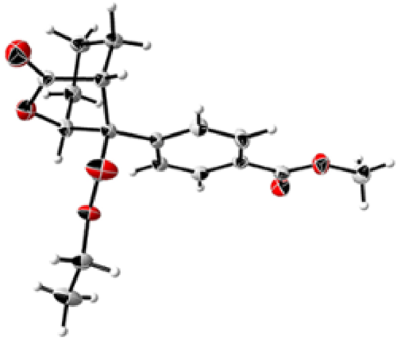
3.2. β-scissions断裂碳碳键



光诱导电子转移(PET)：在光的诱导下，电子进行分子内或分子间转移的现象。

3.2. β-scissions断裂碳碳键

cycloalkanols	products [a]
	 **6** 12 h, 69% yield 1.4 : 1 d.r.
	 **9** 14 h, 65% yield 1.5 : 1 d.r.
	 **12** 15 h, 79% yield 1.7 : 1 d.r.

alkenes	products [b]
	 **21** 18 h, 88% yield 1.2 : 1 d.r.
	 **24** 18 h, 86% yield
	 **27** 18 h, 72% yield 1.6 : 1 d.r.

3.2. β-scissions断裂碳碳键

Reactant solution

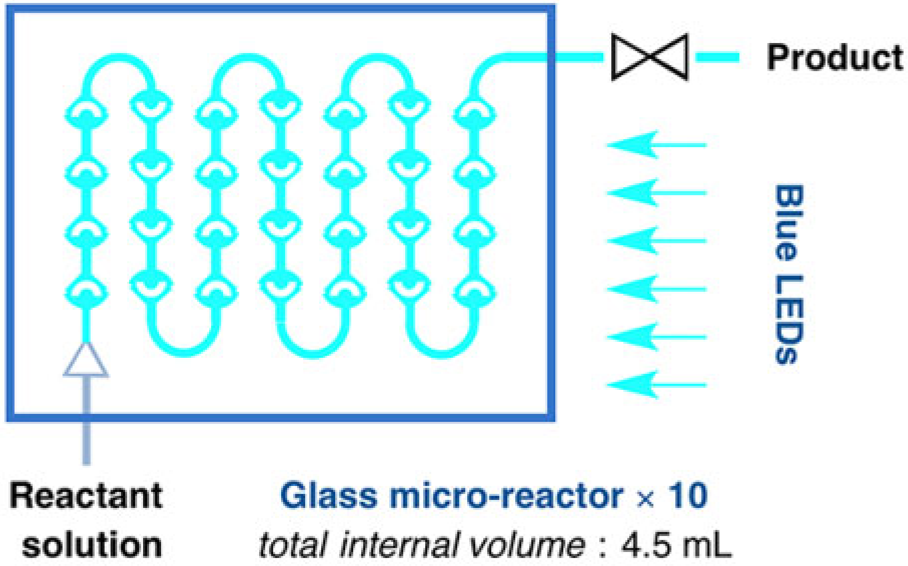
cyclobutanol (1.44 g), **2** (6.48 g)

$CeCl_3$ (49 mg), DPA (66 mg)

Bu_4PCl (118 mg), PhCN (50 mL)

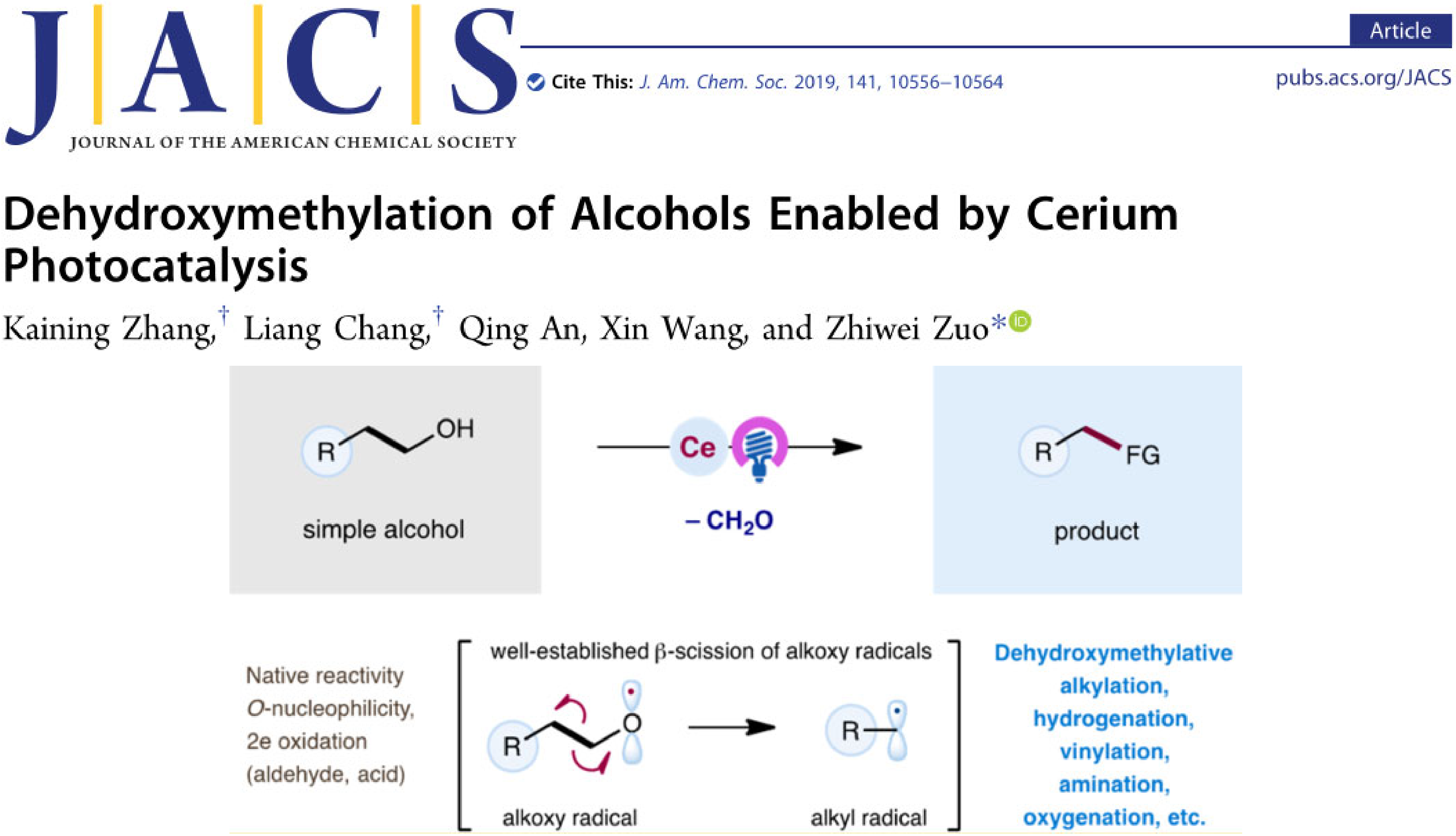
Product output

4.6 g, 80% yield, 5 mmol/h



使用连续流动技术进行了100倍放大的反应。采用平行的10个玻璃微反应器（4.5mL总内部体积）以确保最大限度地利用光子以实现高效率。在闭环模式下以5mmol/h的显著生产率生产所需的环加成产物。

3.3. β-scissions断裂碳碳键



JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

Cite This: *J. Am. Chem. Soc.* 2019, 141, 10556−10564

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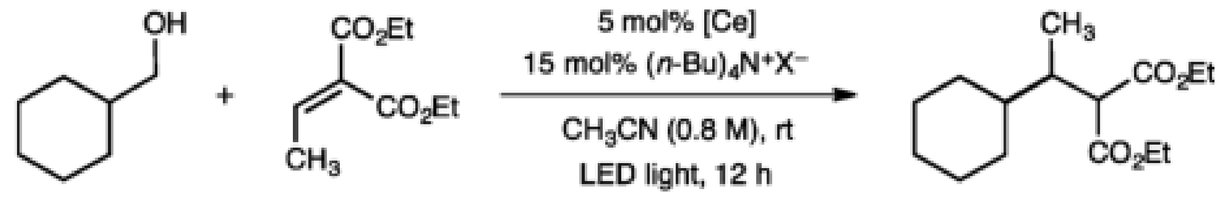
Dehydroxymethylation of Alcohols Enabled by Cerium Photocatalysis

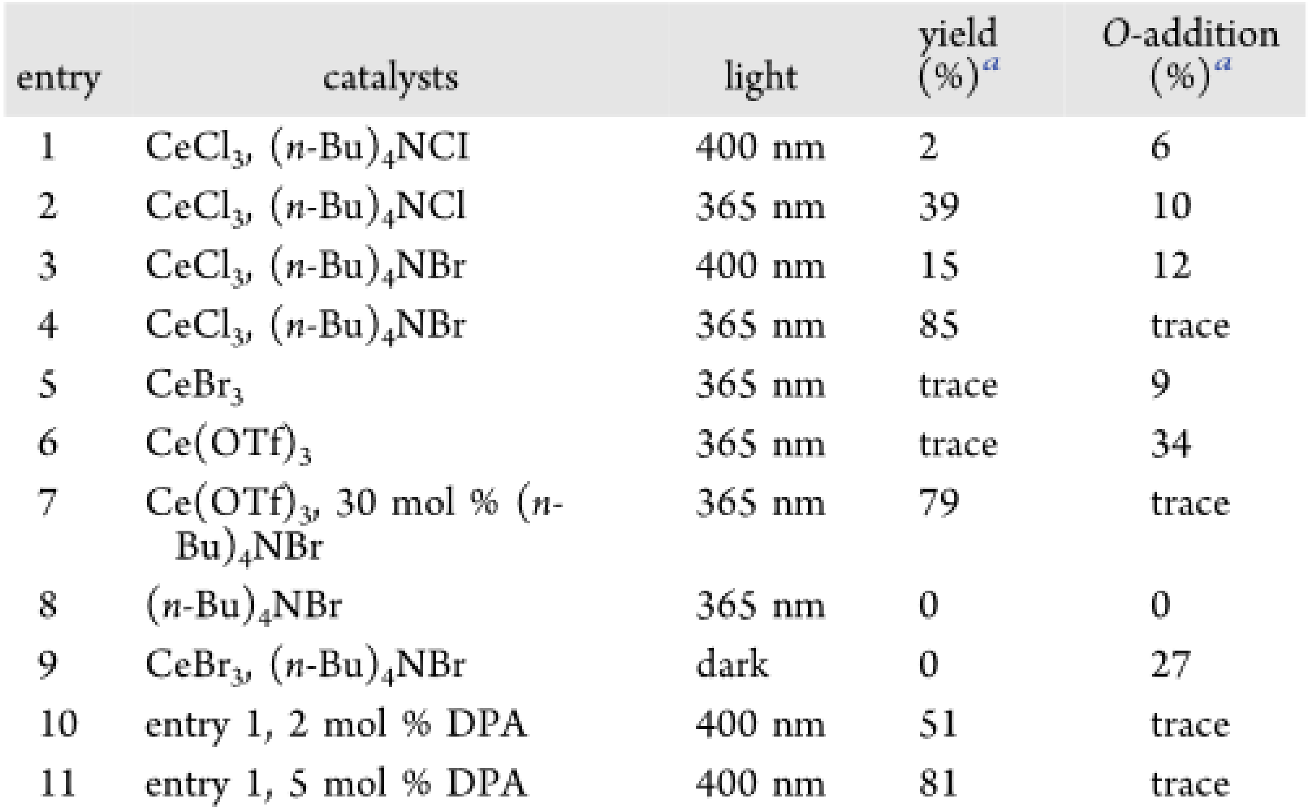
Kaining Zhang,† Liang Chang,† Qing An, Xin Wang, and Zhiwei Zuo*

脱氢甲基化将醇原料直接转化为少含一个碳原子的烷基合成子，后续有望实现多种官能化。

3.3. β-scissions断裂碳碳键



1 (1.0 equiv.) **2** (3.0 equiv.) **3**



entry	catalysts	light	yield (%)[a]	*O*-addition (%)[a]
1	$CeCl_3$, $(n\text{-}Bu)_4NCl$	400 nm	2	6
2	$CeCl_3$, $(n\text{-}Bu)_4NCl$	365 nm	39	10
3	$CeCl_3$, $(n\text{-}Bu)_4NBr$	400 nm	15	12
4	$CeCl_3$, $(n\text{-}Bu)_4NBr$	365 nm	85	trace
5	$CeBr_3$	365 nm	trace	9
6	$Ce(OTf)_3$	365 nm	trace	34
7	$Ce(OTf)_3$, 30 mol % $(n\text{-}Bu)_4NBr$	365 nm	79	trace
8	$(n\text{-}Bu)_4NBr$	365 nm	0	0
9	$CeBr_3$, $(n\text{-}Bu)_4NBr$	dark	0	27
10	entry 1, 2 mol % DPA	400 nm	51	trace
11	entry 1, 5 mol % DPA	400 nm	81	trace

3.4. β-scissions断裂碳碳键

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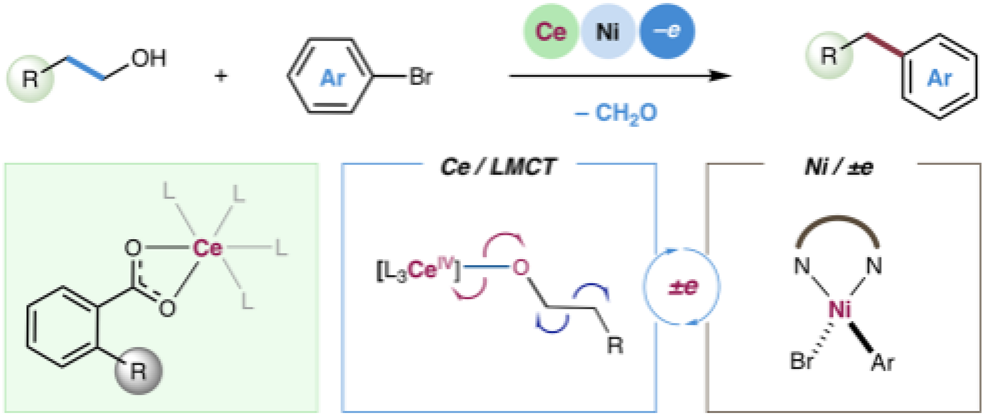
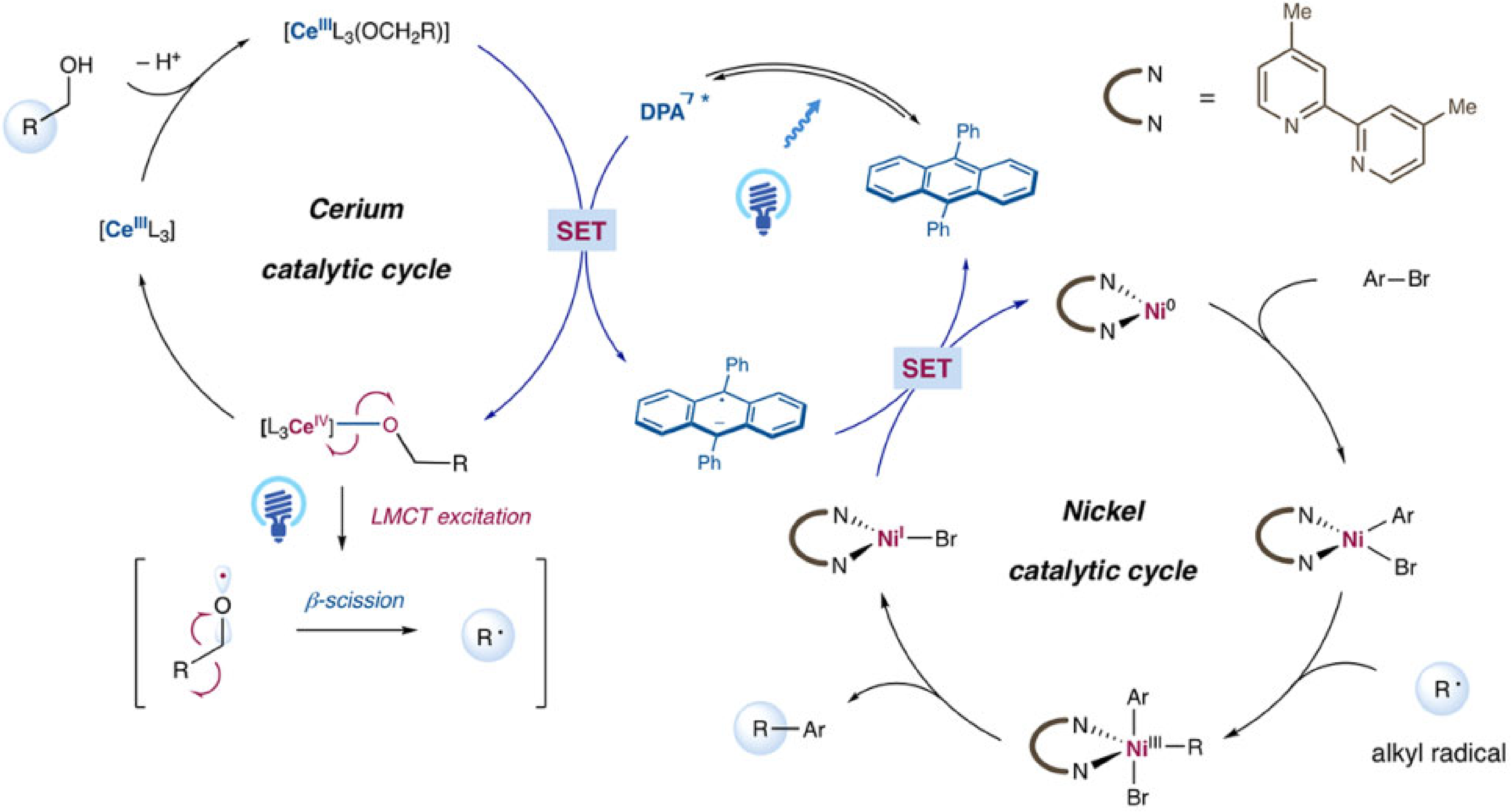
Communication

Photocatalytic Dehydroxymethylative Arylation by Synergistic Cerium and Nickel Catalysis

Yuegang Chen, Xin Wang, Xu He, Qing An, and Zhiwei Zuo*

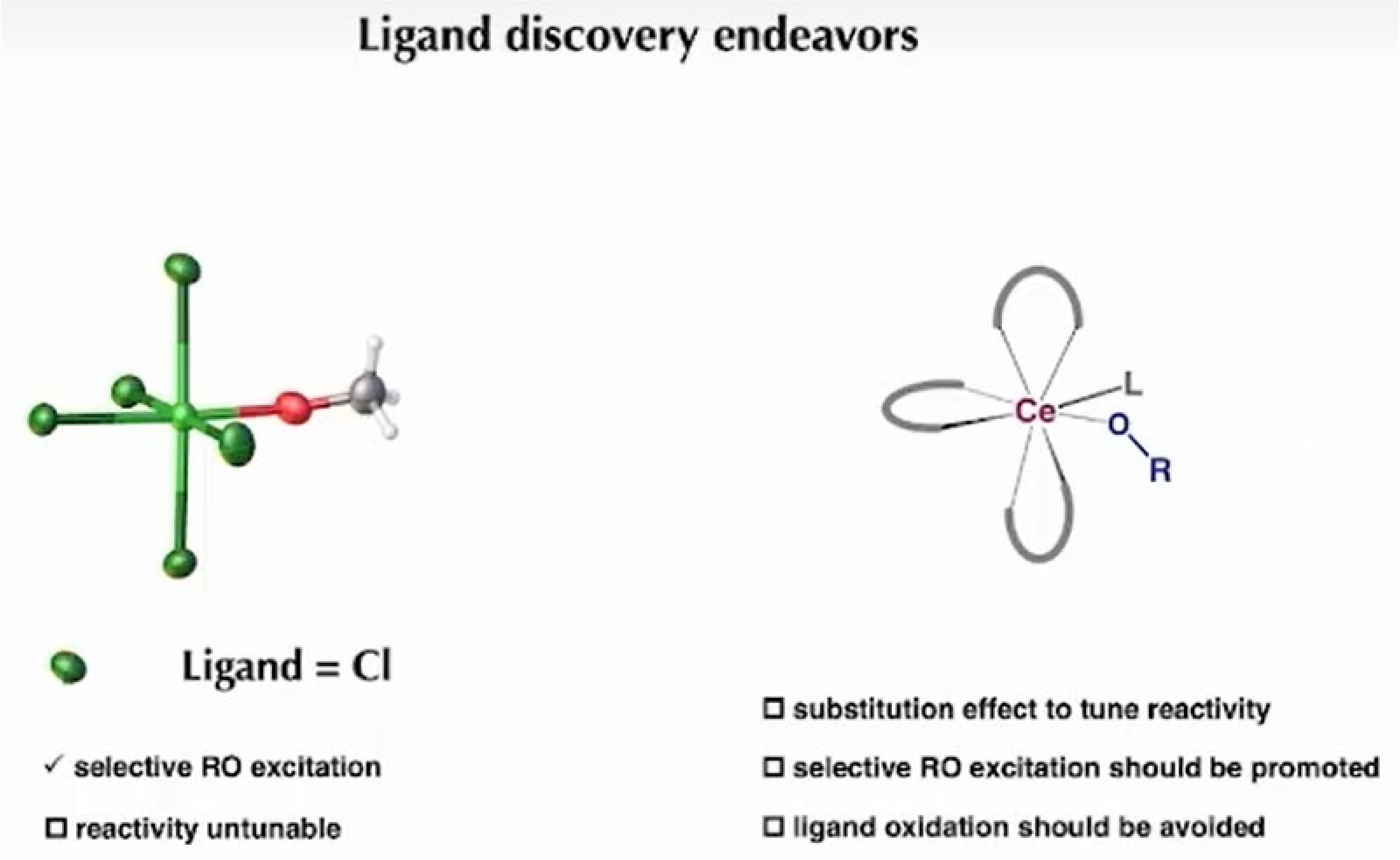


3.4. β-scissions断裂碳碳键



联吡啶配体会毒化铈催化剂

3.4. β-scissions断裂碳碳键



Ligand discovery endeavors

● Ligand = Cl

✓ selective RO excitation

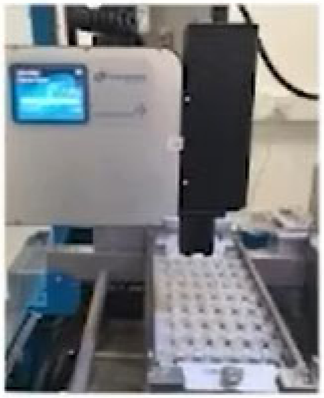
☐ reactivity untunable

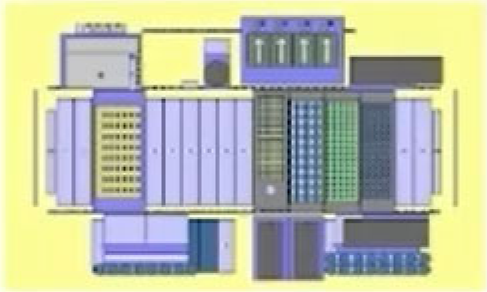
☐ substitution effect to tune reactivity

☐ selective RO excitation should be promoted

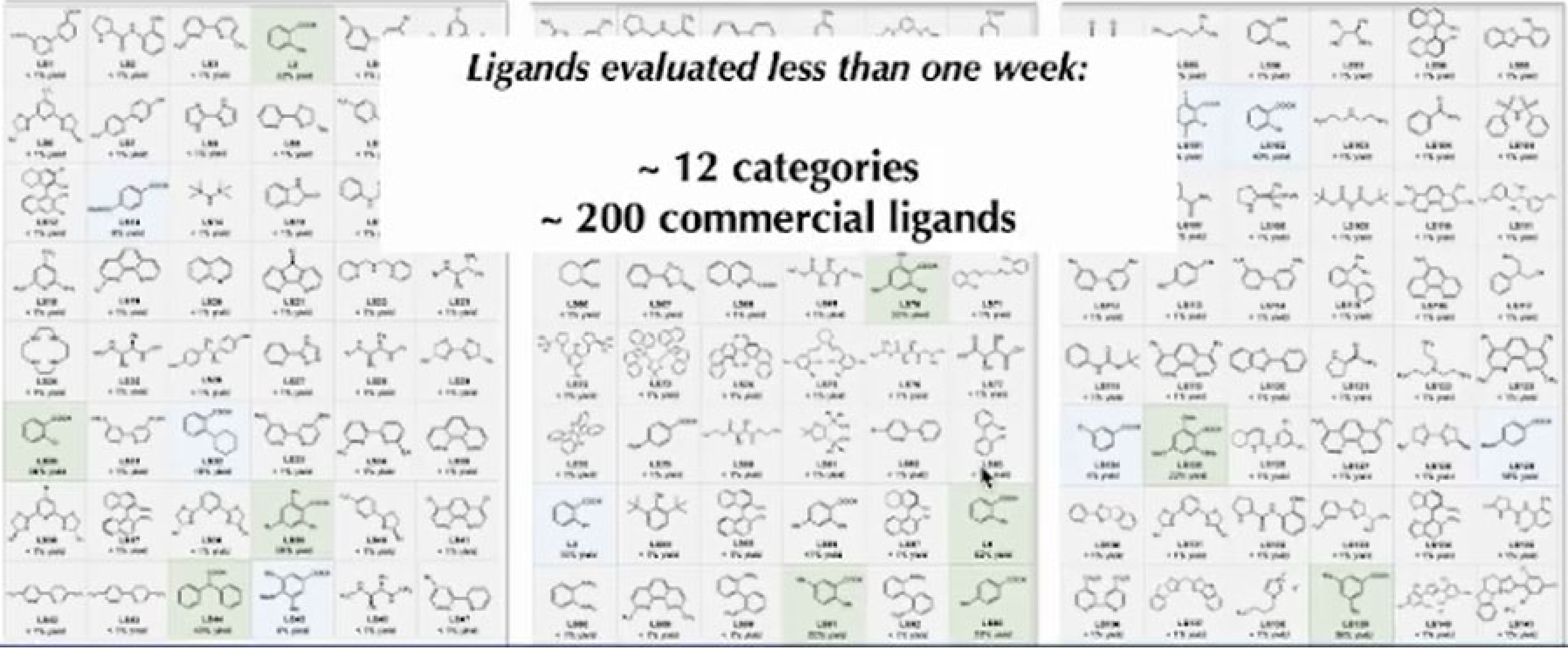
☐ ligand oxidation should be avoided

High-throughput ligand evaluation performed by automated system





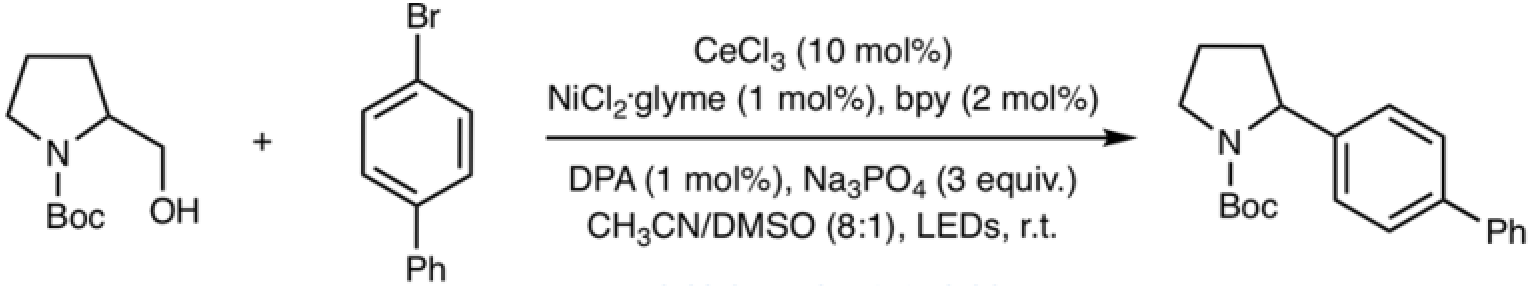
CHEMSPEED



Ligands evaluated less than one week:

~ 12 categories
~ 200 commercial ligands

3.4. β-scissions断裂碳碳键

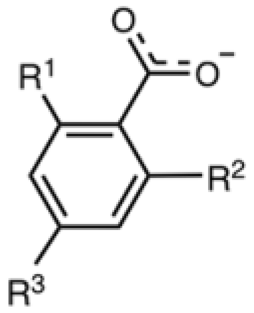


1 + 2 → 3

$CeCl_3$ (10 mol%)
$NiCl_2$·glyme (1 mol%), bpy (2 mol%)
DPA (1 mol%), Na_3PO_4 (3 equiv.)
CH_3CN/DMSO (8:1), LEDs, r.t.

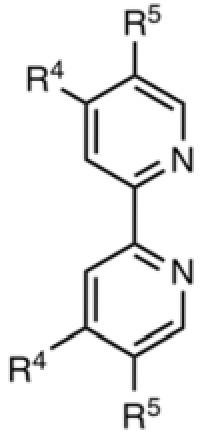
initial result: 0% yield

benzoate ligand for Ce



R^1, R^2, R^3 = H, **L1**
R^1, R^3 =H, R^2 = Me, **L2**
R^1, R^3 =H, R^2 = *i*-Pr, **L3**
R^1, R^2, R^3 = *i*-Pr, **L4**
R^1, R^3 =H, R^2 = pyrrolyl, **L5**
R^1, R^3 =H, R^2 = Ph, **L6**
R^1, R^3 =H, R^2 = Mes, **L7**

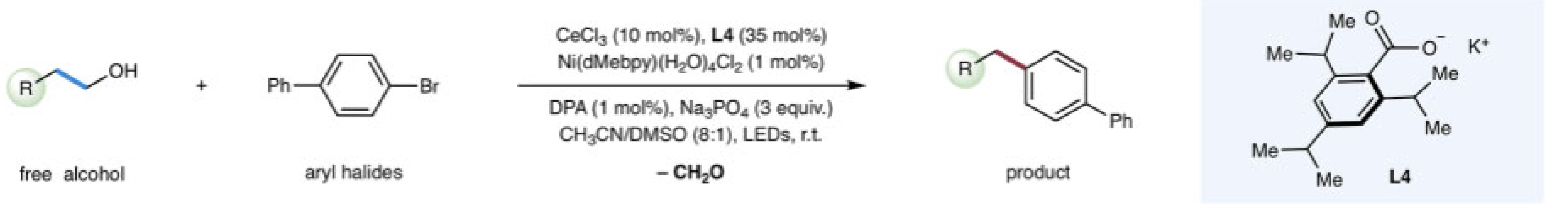
well-established ligand for Ni



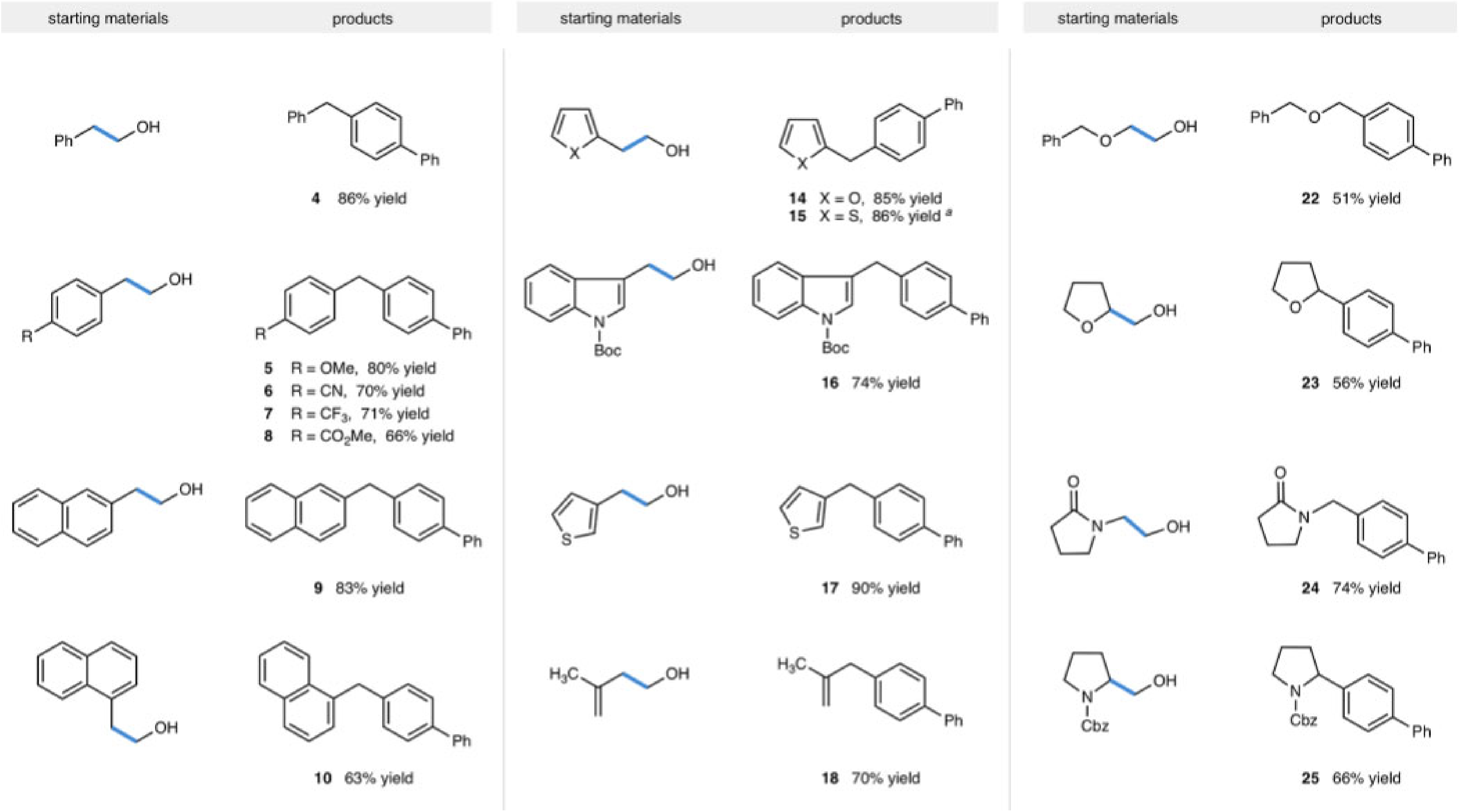
R^4 = *t*-Bu, R^5 = H, **L8**
R^4 = OMe, R^5 = H, **L9**
R^4 = Me, R^5 = H, **L10**
R^4 = H, R^5 = Me, **L11**
R^4 = H, R^5 = OMe, **L12**

Optimal yield:
93%

3.4. β-scissions断裂碳碳键



CeCl$_3$ (10 mol%), **L4** (35 mol%)
Ni(dMebpy)(H$_2$O)$_4$Cl$_2$ (1 mol%)
DPA (1 mol%), Na$_3$PO$_4$ (3 equiv.)
CH$_3$CN/DMSO (8:1), LEDs, r.t.
– CH$_2$O



4 86% yield

5 R = OMe, 80% yield
6 R = CN, 70% yield
7 R = CF$_3$, 71% yield
8 R = CO$_2$Me, 66% yield

9 83% yield

10 63% yield

14 X = O, 85% yield
15 X = S, 86% yield [a]

16 74% yield

17 90% yield

18 70% yield

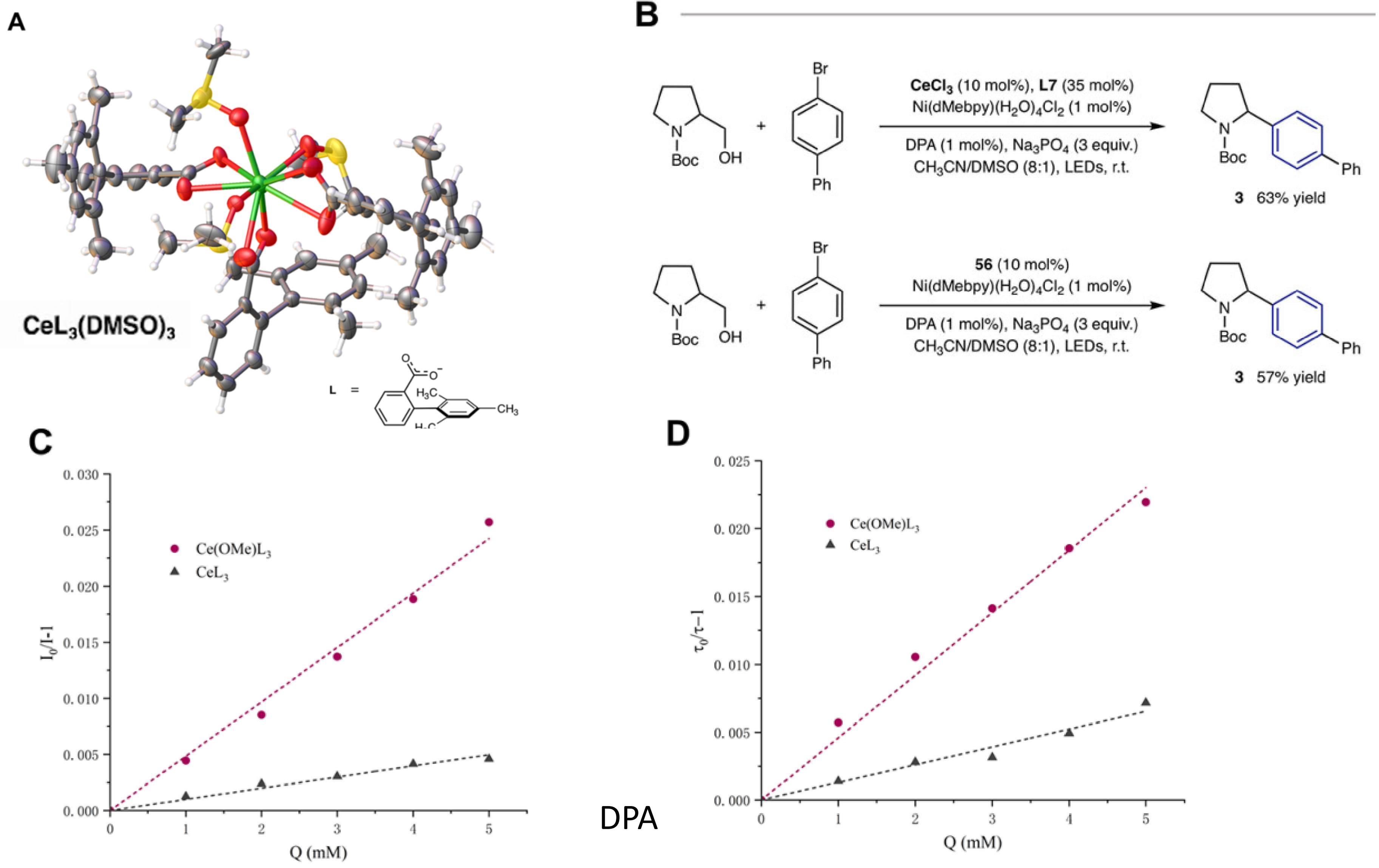
22 51% yield

23 56% yield

24 74% yield

25 66% yield

3.4. β-scissions断裂碳碳键



DPA

Figure 3. Mechanistic studies. (A) Molecular structure of **56** with 30% probability ellipsoids. (B) Evaluation of the catalytic efficiency of the cerium complex. (C) Stern−Volmer plot based on the steady-state emission experiment. (D) Stern−Volmer plot based on the time-resolved emission experiment. See the Supporting Information for a detailed description. (E) Proposed catalytic cycle.

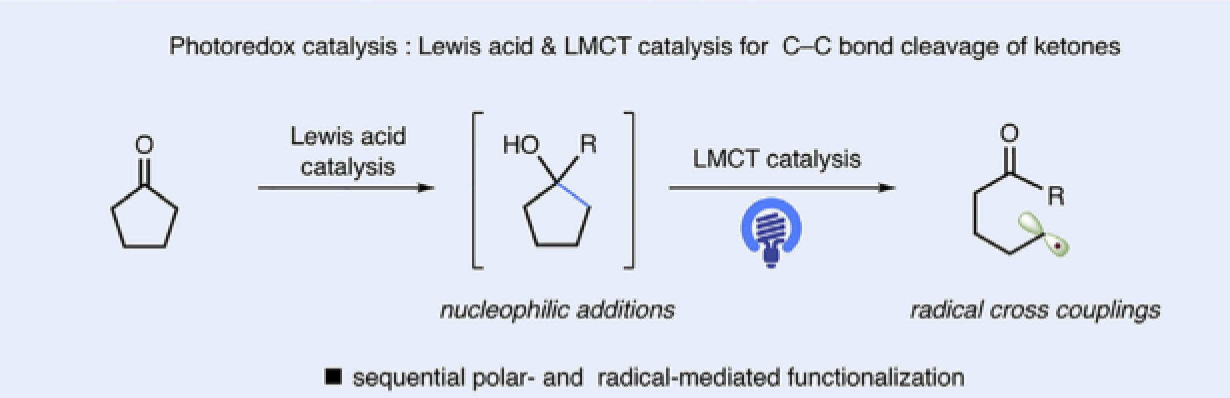
3.5. β-scissions断裂碳碳键

Chem

CellPress

Article

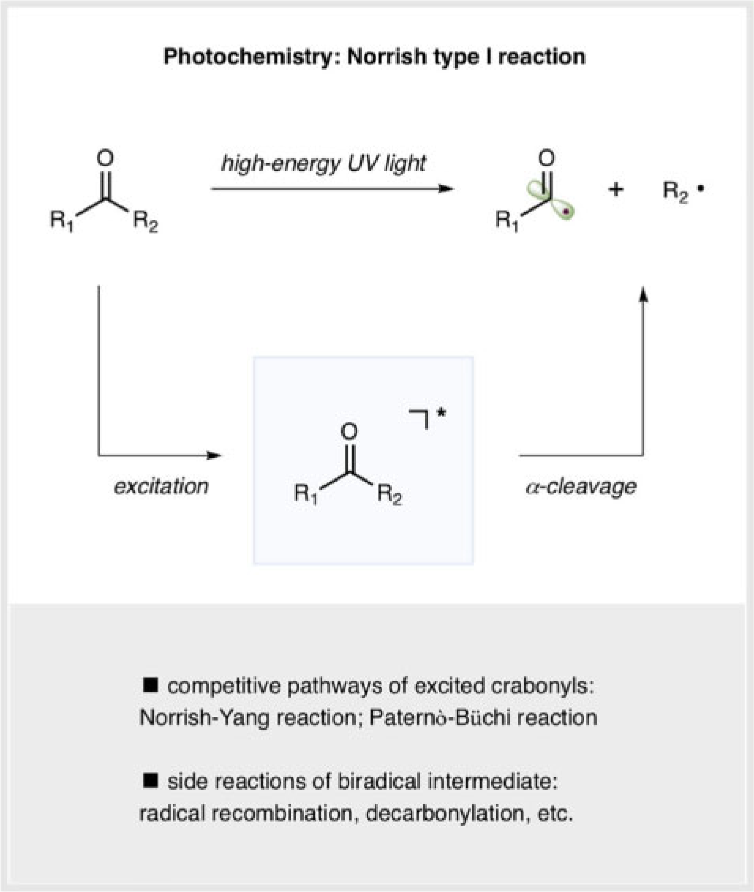
Selective C-C Bond Scission of Ketones via Visible-Light-Mediated Cerium Catalysis


Photoredox catalysis : Lewis acid & LMCT catalysis for C–C bond cleavage of ketones

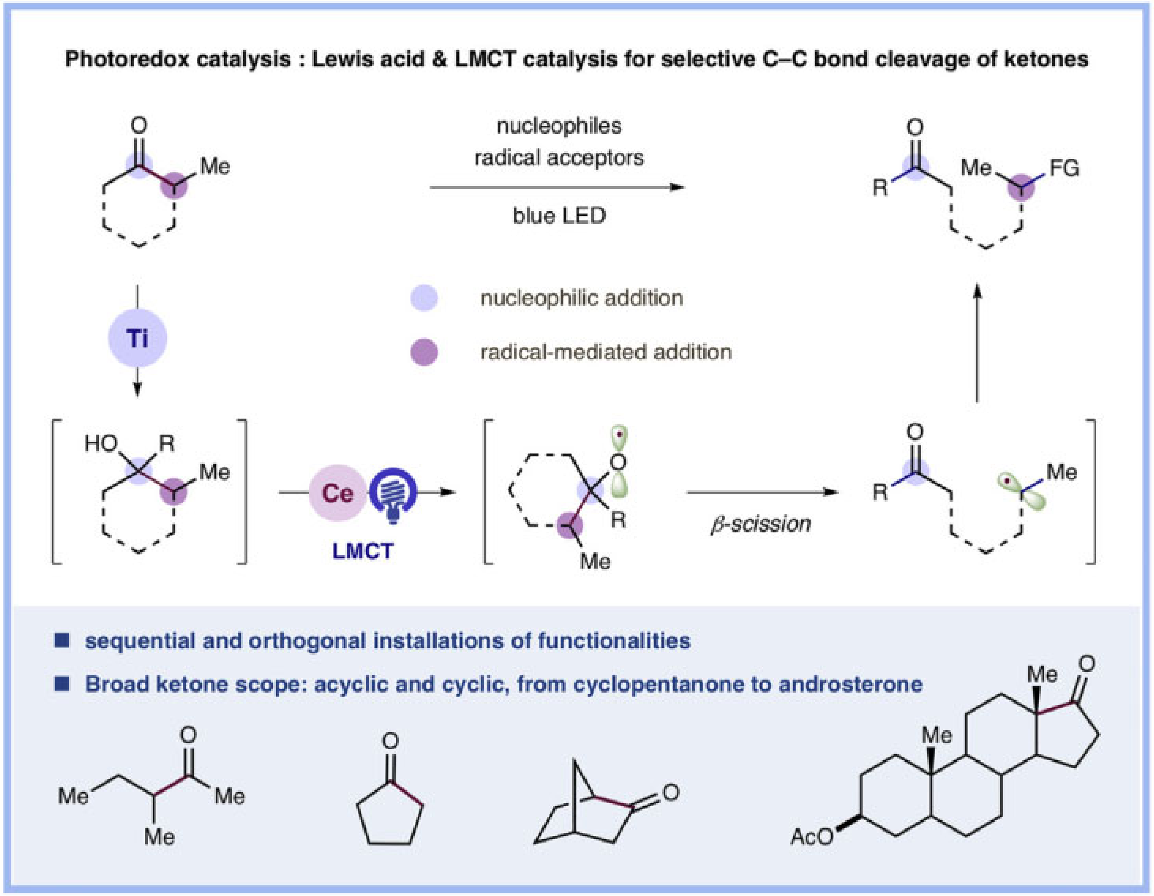
■ sequential polar- and radical-mediated functionalization

通过路易斯酸催化和LMCT协同催化，选择性地裂解酮的C–C键，从而能够通过顺序和正交的方式在裂解的C–C键的每个碳上安装不同的官能团。

3.5. β-scissions断裂碳碳键


Photochemistry: Norrish type I reaction

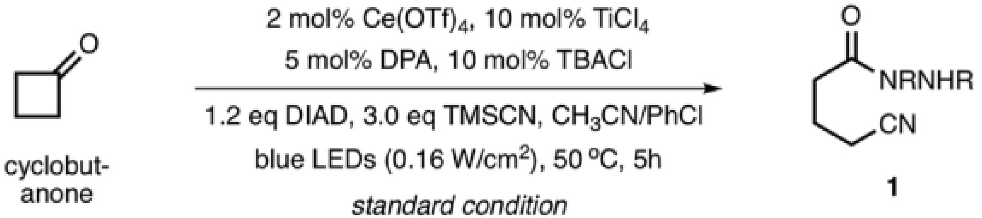
- competitive pathways of excited crabonyls: Norrish-Yang reaction; Paternò-Büchi reaction
- side reactions of biradical intermediate: radical recombination, decarbonylation, etc.


Photoredox catalysis : Lewis acid & LMCT catalysis for selective C–C bond cleavage of ketones

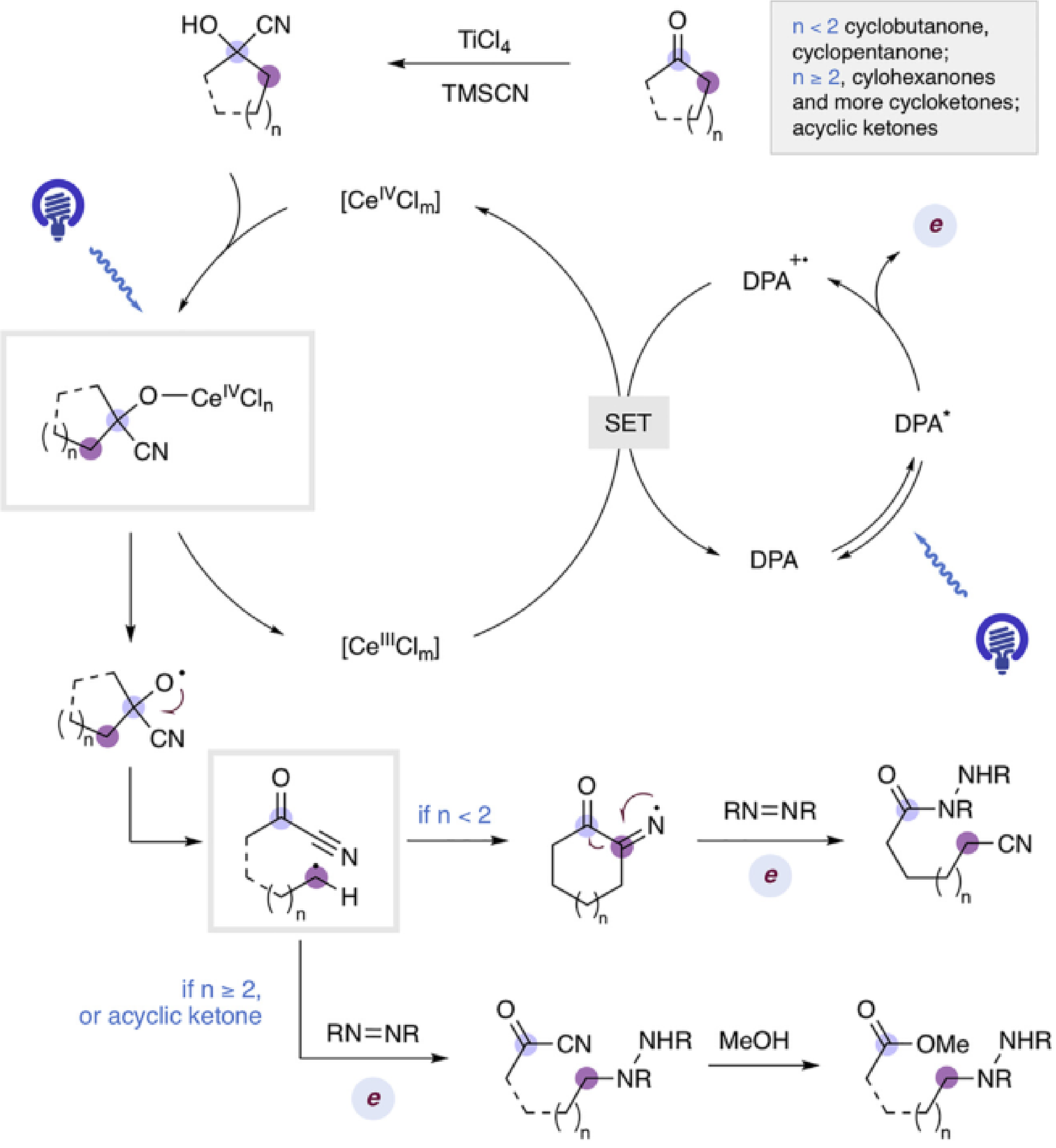
- sequential and orthogonal installations of functionalities
- Broad ketone scope: acyclic and cyclic, from cyclopentanone to androsterone

Norrish I型反应是一种切割酮的C–C键的强大方法，但由于选择性和实用性问题，使得合成应用受到限制。

3.5. β-scissions断裂碳碳键

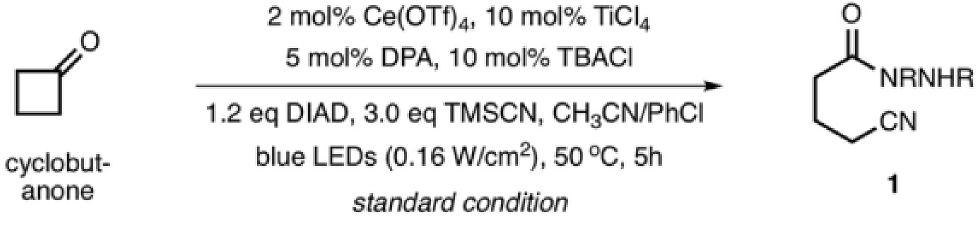


1



n < 2 cyclobutanone,
cyclopentanone;
n ≥ 2, cylohexanones
and more cycloketones;
acyclic ketones

3.5. β-scissions断裂碳碳键



cyclobut-anone

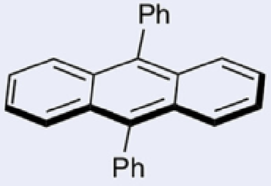
2 mol% $Ce(OTf)_4$, 10 mol% $TiCl_4$
5 mol% DPA, 10 mol% TBACl

1.2 eq DIAD, 3.0 eq TMSCN, $CH_3CN/PhCl$
blue LEDs (0.16 W/cm^2), 50 °C, 5h
standard condition

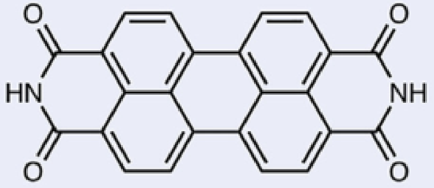
1

Entry	variations from standard condition	**Yield (%)**[a]
1	none	92
2	without $TiCl_4$	0
3	$AlEtCl_2$ instead of $TiCl_4$	9
4	$BF_3 \cdot OEt_2$ instead of $TiCl_4$	0
5	$AlCl_3$ instead of $TiCl_4$	5
6	$ZnCl_2$ instead of $TiCl_4$	10
7	without DPA	48
8	PDI instead of DPA	82
9	$Ir(ppy)_3$ instead of DPA	88
10	without $Ce(OTf)_4$	0
11	without 100 Wblue LED	0

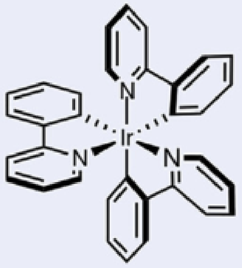
体系中自由基物种可以氧化三价铈



DPA

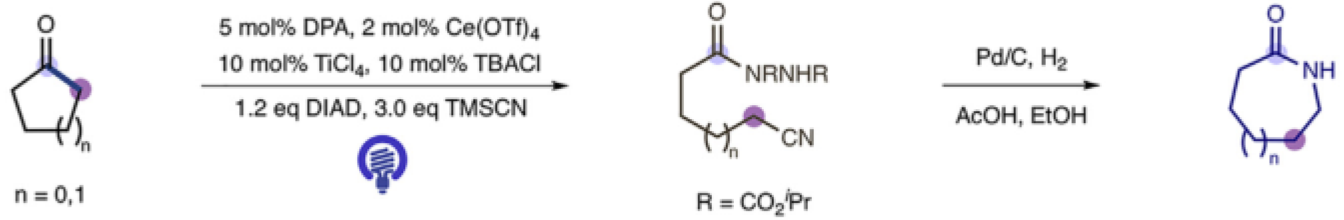


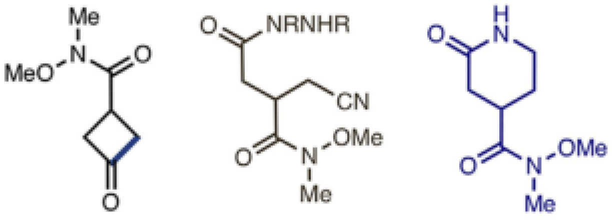
PDI



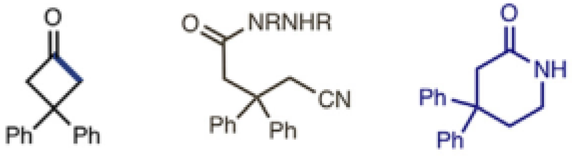
***fac*-Ir(ppy)$_3$**

3.5. β-scissions断裂碳碳键

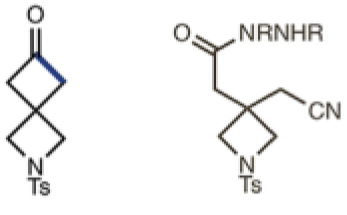




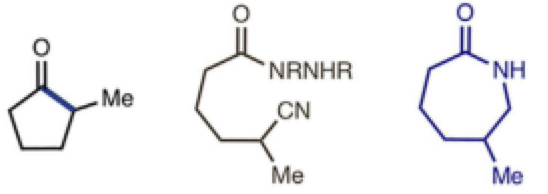
4a 67% yield **4b** 50% yield



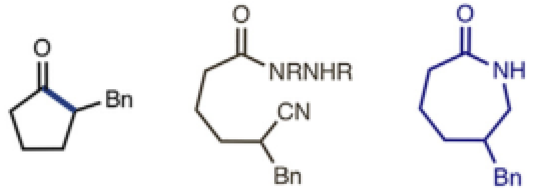
5a 97% yield **5b** 87% yield



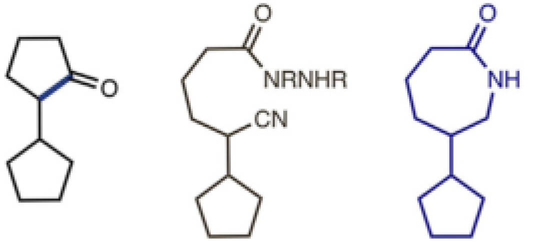
6a 86% yield **6b** 40% yield



8a 70% yield **8b** 70% yield



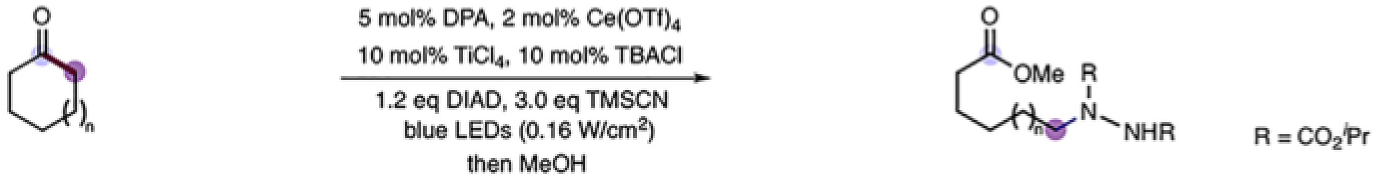
9a 73% yield **9b** 71% yield

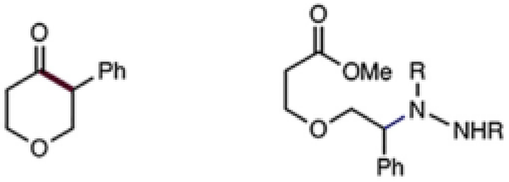


10a 51% yield **10b** 48% yield

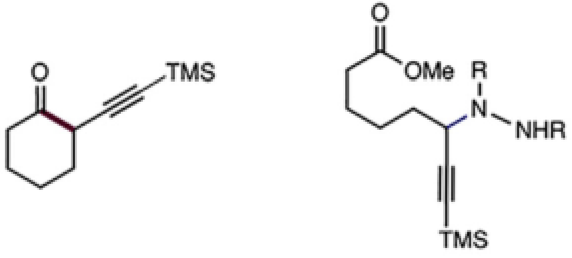
3.5. β-scissions断裂碳碳键

环状



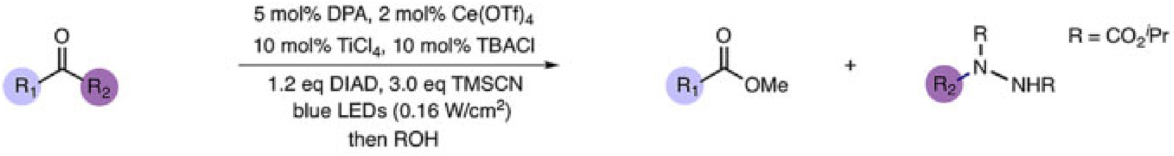


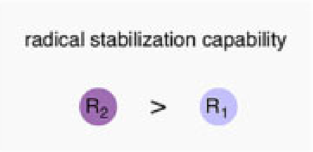
22 68% yield

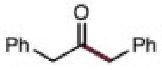
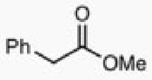
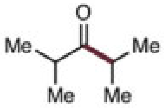
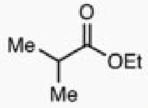
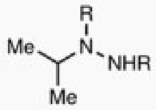
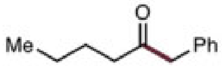


27 50% yield

链状





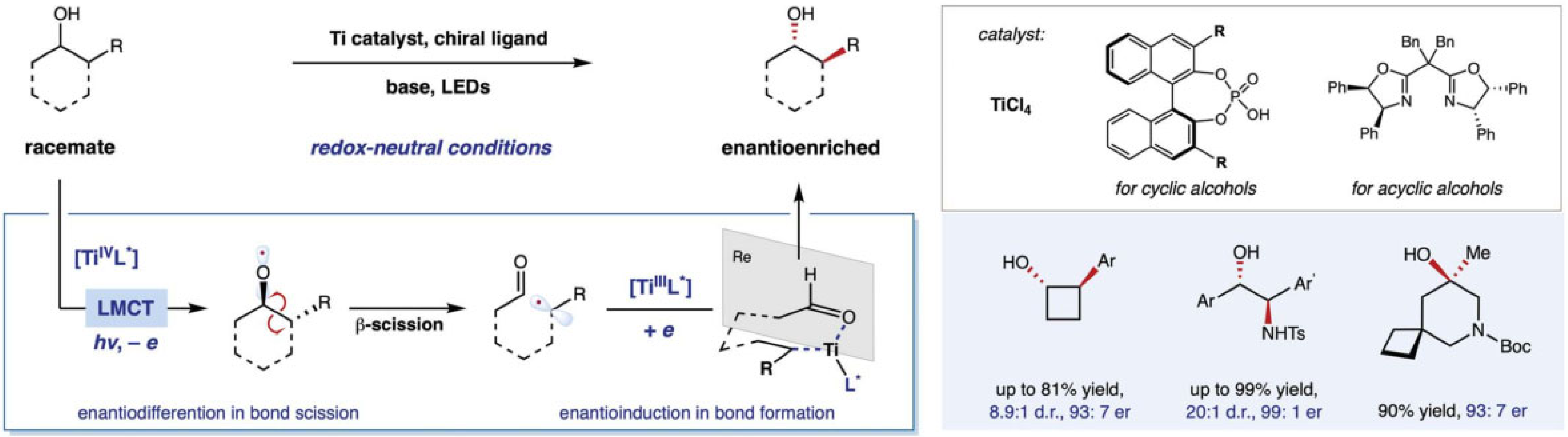
ketone	product	ketone	product	ketone	product
	 **34** 65% yield [a]  **35** 76% yield		 **36** 90% yield [a]  **37** 87% yield		 **38** 75% yield [a]  **35** 71% yield

3.6. β-scissions断裂碳碳键

ORGANIC CHEMISTRY

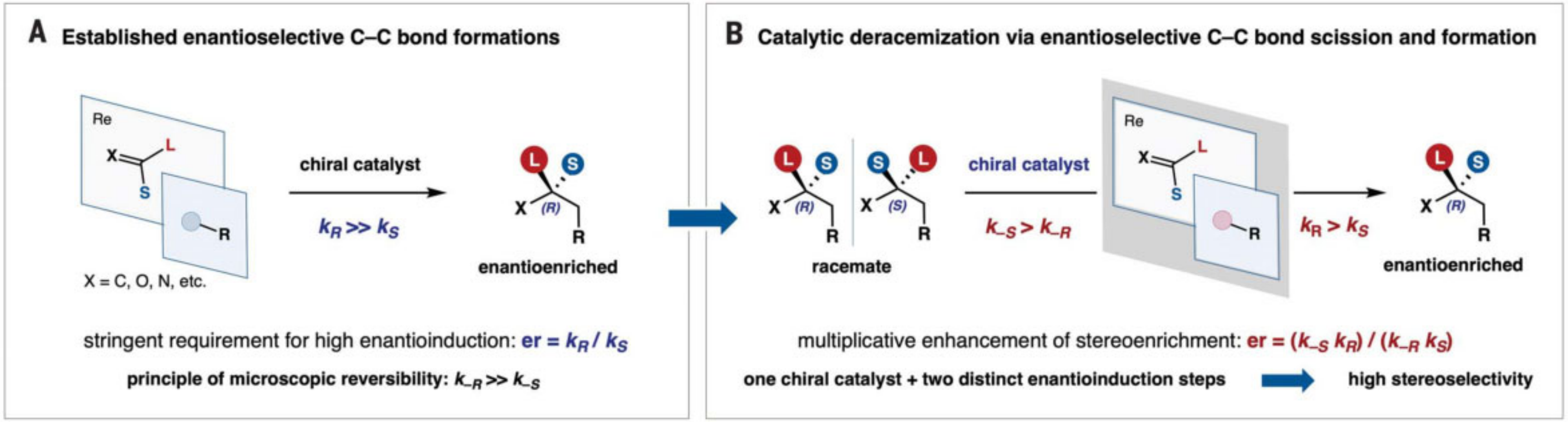
Multiplicative enhancement of stereoenrichment by a single catalyst for deracemization of alcohols

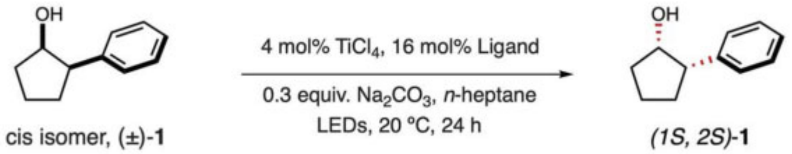
Lu Wen†, Jia Ding†, Lingfei Duan†, Shun Wang, Qing An, Hexiang Wang, Zhiwei Zuo*



利用配体金属电荷转移催化（LMCT catalysis）策略，首次实现了非张力碳碳键断裂-立体重组，建立了手性放大和手性富集的新过程。

3.6. β-scissions断裂碳碳键

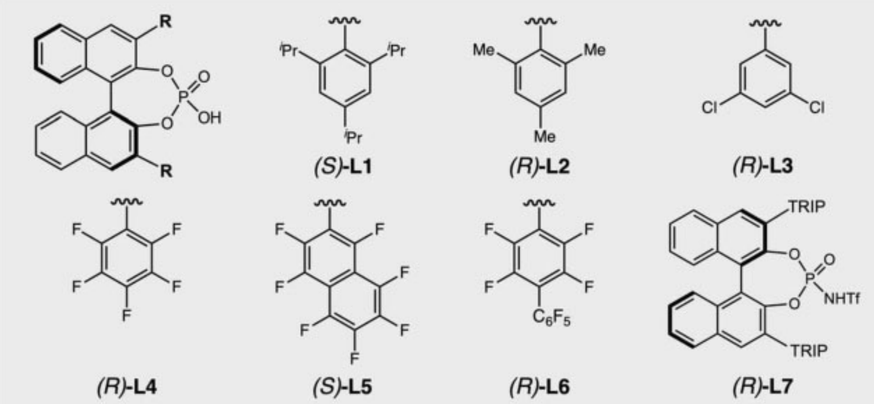




cis isomer, (±)-**1**

(1S, 2S)-**1**

entry	ligand	yield (%)	d.r.	er
1	*(S)*-**L1**	93	8.8:1	99:1
2	*(R)*-**L2**	94	2.2:1	13:87
3	*(R)*-**L3**	96	1:1	62:38
4	*(R)*-**L4**	99	1:1	41:59
5	*(S)*-**L5**	97	1.6:1	44:56
6	*(R)*-**L6**	94	1.2:1	66:34
7	*(R)*-**L7**	99	3.2:1	21:79
8	*(S)*-**L1**, $EtN(^iPr)_2$ instead of Na_2CO_3	99	3.9:1	93:7
9	*(R)*-**L1**	99	8.8:1	1:99

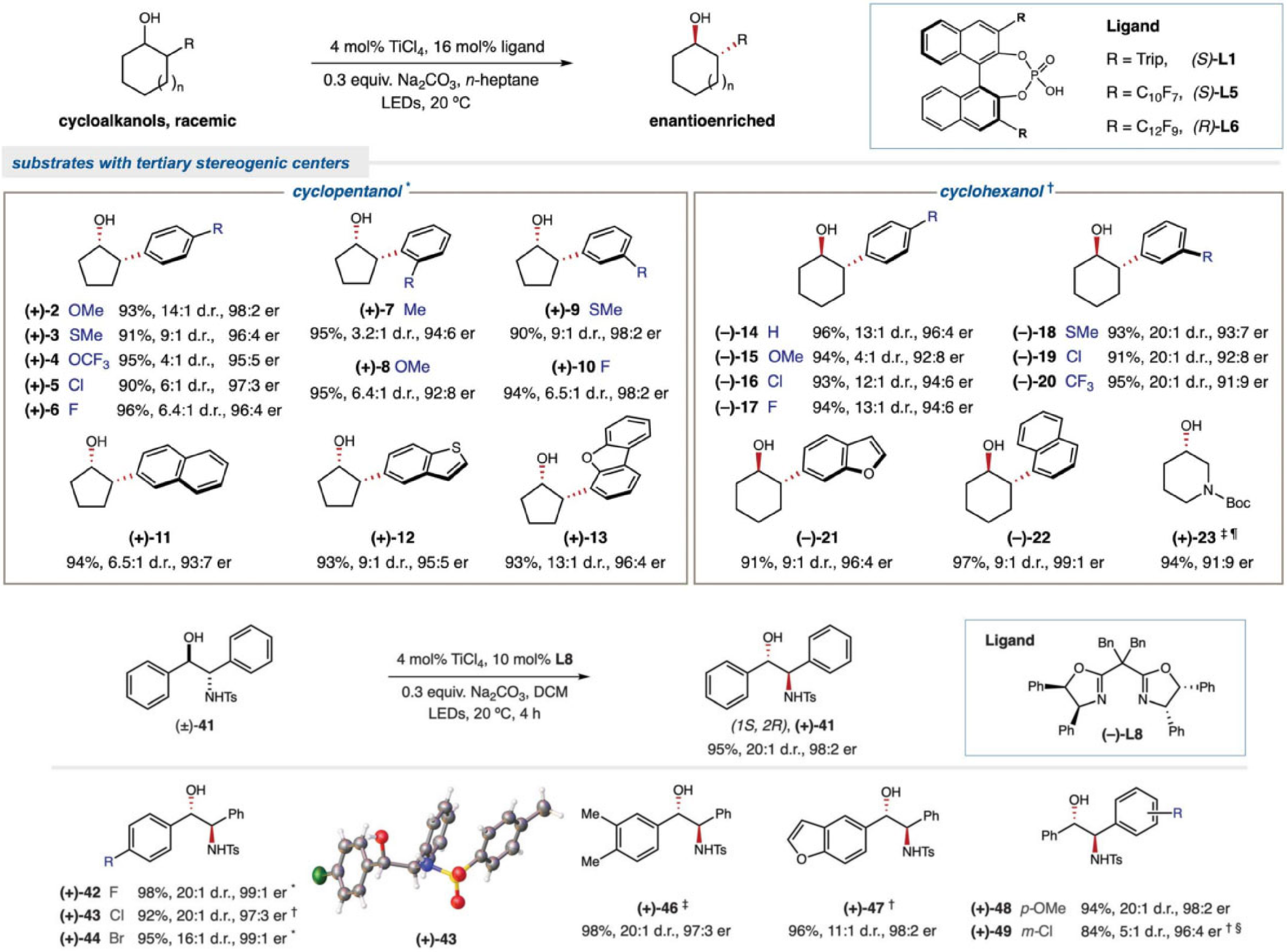


(S)-**L1** *(R)*-**L2** *(R)*-**L3**

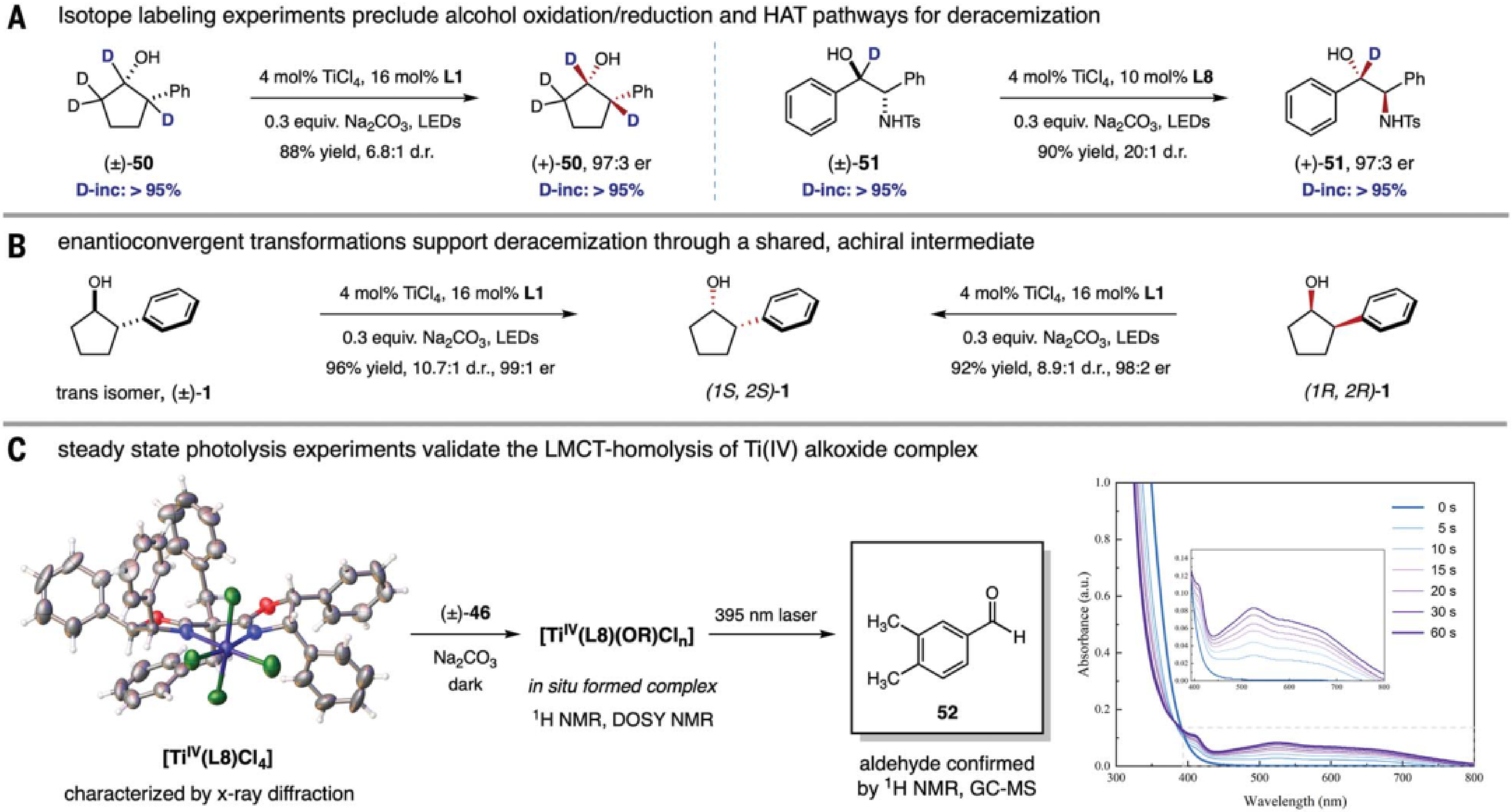
(R)-**L4** *(S)*-**L5** *(R)*-**L6** *(R)*-**L7**

entry	control experiments of entry 1	yield (%)	d.r.	er
10	$CeCl_3$ instead of $TiCl_4$	97	>20:1	50:50
11	$FeCl_3$ instead of $TiCl_4$	95	>20:1	50:50
12	no *(S)*-**L1**	95	1:1.2	50:50
13	no $TiCl_4$	>99	>20:1	50:50
14	dark	>99	>20:1	50:50

3.6. β-scissions断裂碳碳键



3.6. β-scissions断裂碳碳键

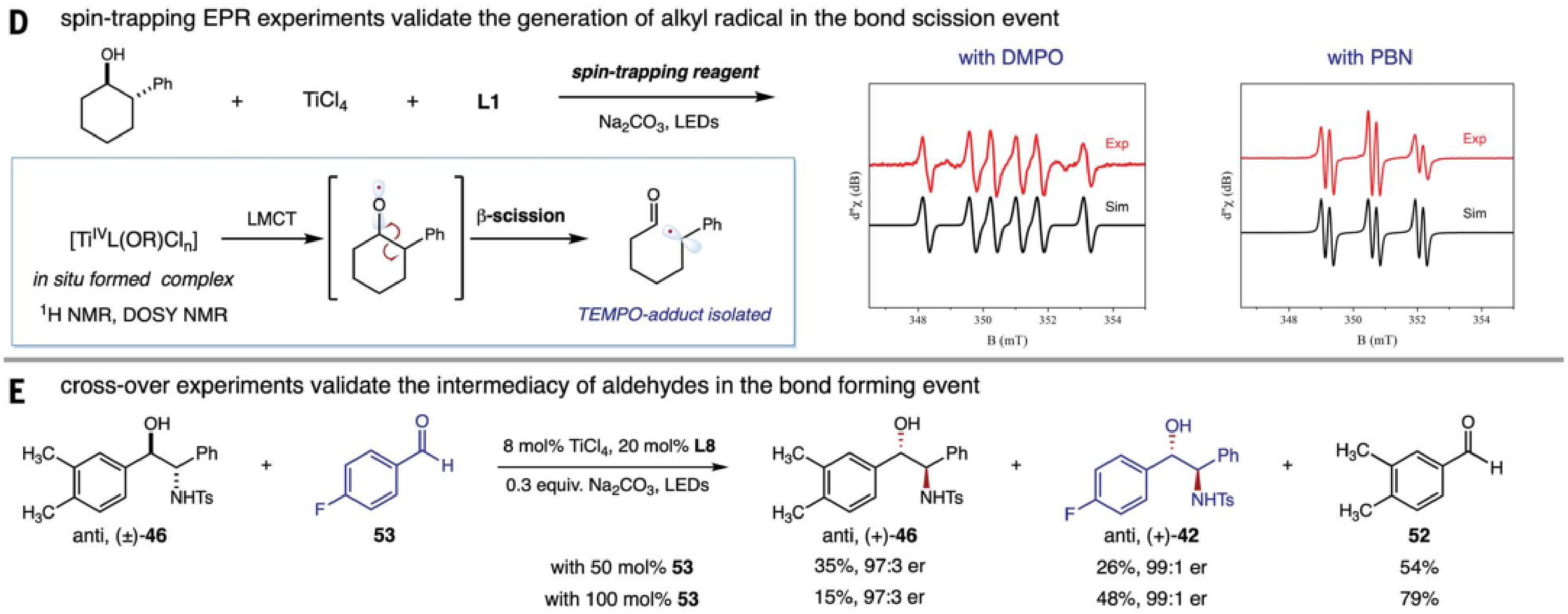


A. 排除了HAT或串联的氧化还原过程作为去消旋化途径

B. 由C–C键断裂生成了共同的前手性中间体

C. 验证了Ti(IV)配合物的LMCT均裂过程

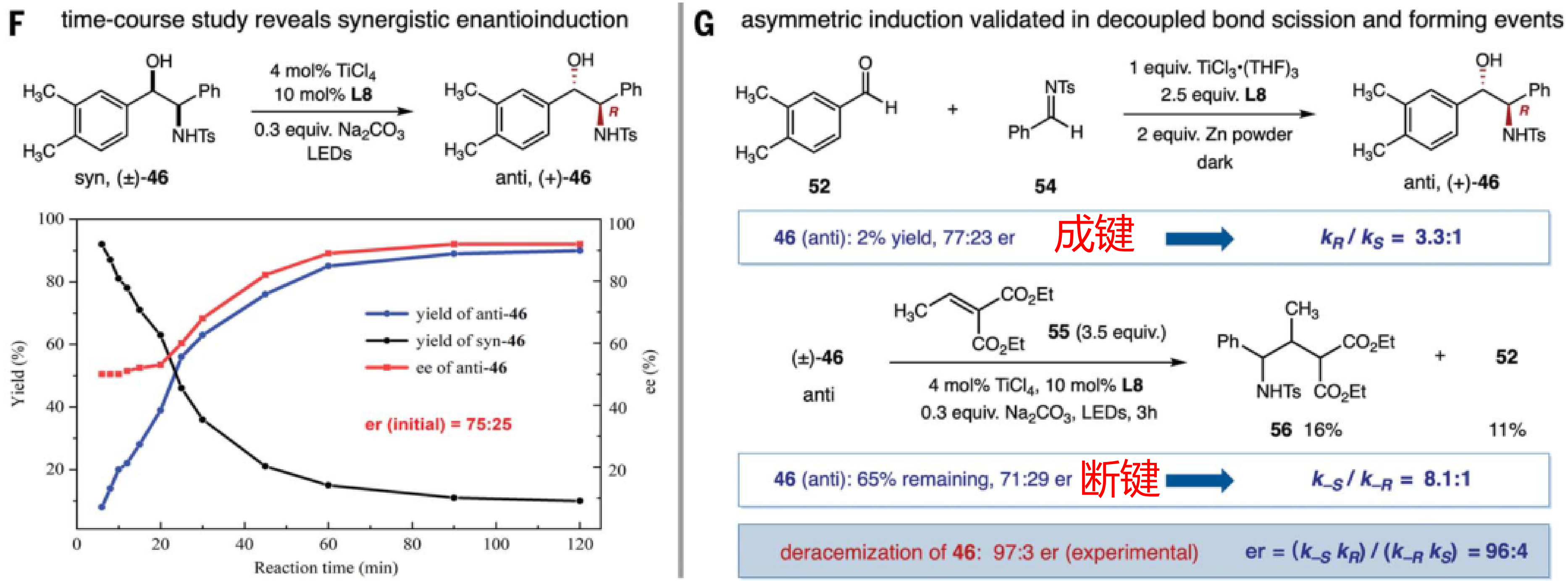
3.6. β-scissions断裂碳碳键



D. 证明了反应过程中烷基自由基的存在

E. 加入活性更高的对氟苯甲醛，新的对氟取代氨基醇的生成明确支持了醛和*β*-断裂产生的碳中心自由基作为去消旋化反应中的共同中间体

3.6. β-scissions断裂碳碳键



通过立体选择性乘积公式 (er = kRk-S/kSk-R)，预测达到平衡时产物的立体选择性为96:4 er，这与去消旋化反应的实验值(er 97:3)基本一致，验证了去消旋化反应中催化剂手性放大的倍增效应。

Thanks!