

C-C Bond Cleavage via Radical-Induced Fragmentations

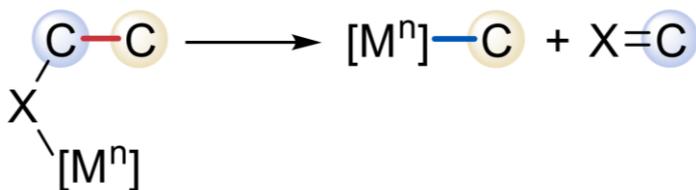
Literature seminar
Yu Zhang

2025.10.30

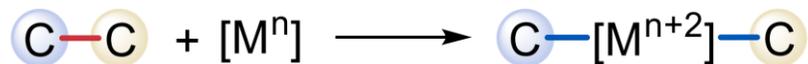
- 01 Strategies for Inert C–C bond Cleavage**
- 02 C-C Bond Cleavage via Alkoxy Radical
- 03 C-C Bond Cleavage via Hidden Alkoxy Radical

Strategies for Inert C–C bond Cleavages—C-C Bond Activation

β -carbon elimination

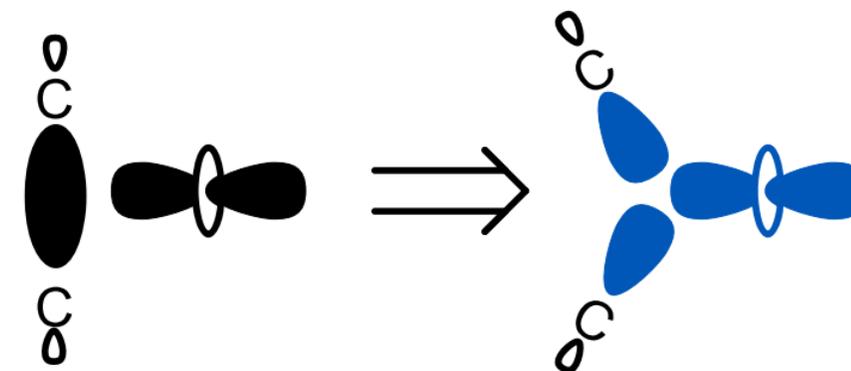


oxidative addition



C–C bond

σ d_{z^2}



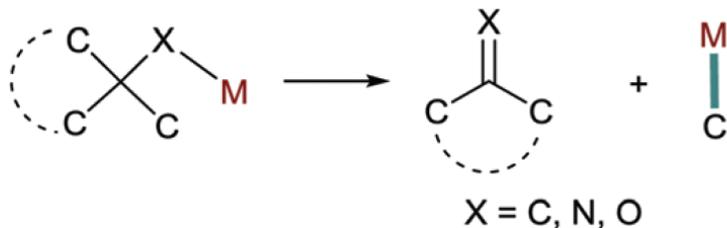
*non-bonding
interaction*

*bonding
interaction*

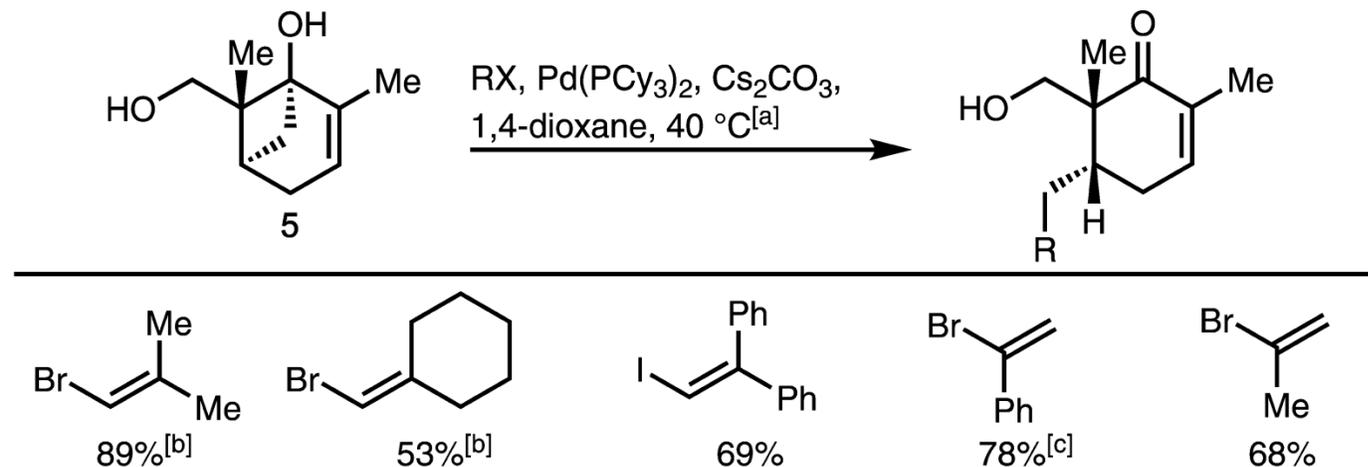
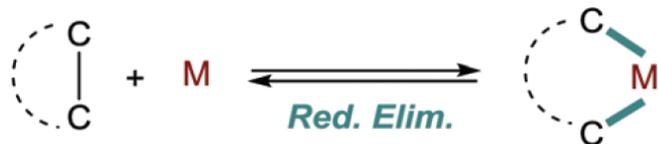
- ◆ *the accessibility of the transition metal center to C–C bonds is generally difficult due to its 'hidden' nature*
- ◆ *relatively high stability of the C–C bond (90 kcal/mol)*

Strategies for Inert C–C bond Cleavages—C-C Bond Activation

(a) β -C Cleavage



(b) Oxidative addition



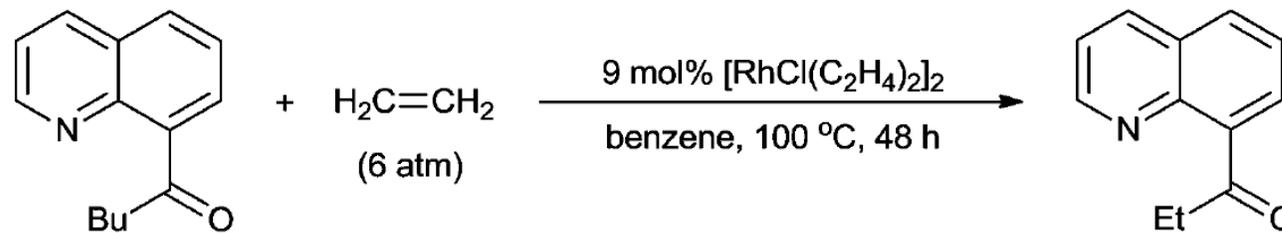
Sarpong, R. *et al.* *J. Am. Chem. Soc.* **2018**, *140*, 9810.

➤ β -carbon elimination

(Competitive β -H elimination)

➤ direct oxidative addition of C–C bonds

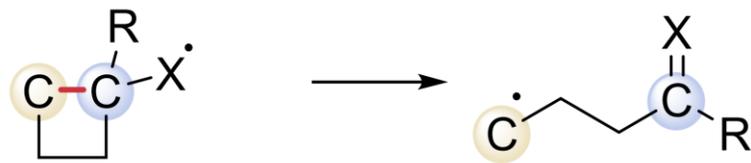
(Requires a directing group)



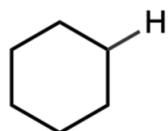
Suggs, J. W. *et al.* *J. Chem. Soc., Chem. Commun.*, **1985**, 92.

Strategies for Inert C–C Bond Cleavages—Radical Fragmentations

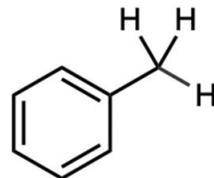
radical fragmentations



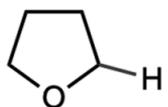
X = O, NR



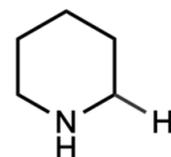
BDE : 99.5



BDE : 90



BDE : 92.1



BDE : 92

| Compound | O–H BDE (kcal mol ⁻¹) | Compound | O–H BDE (kcal mol ⁻¹) |
|----------|--------------------------------------|----------|--------------------------------------|
| | 105.2 ± 0.7 (ref 62) | | 105.4 ± 1.4 (ref 62) |
| | 105.7 ± 0.7 (ref 65) | | 106.8 ± 1.0 (ref 62) |
| | 118.8 ± 0.07 (ref 68) | | 84.8 ± 2.2 (ref 70) |
| | 118.3 (ref 72) | | 69.6 (ref 74) |

Strategies for Inert C–C Bond Cleavages—Radical Fragmentations

| Entry | β -scission | k (s ⁻¹) | E_a (kcal mol ⁻¹) |
|-------|---|------------------------|---------------------------------|
| 1 | $\text{H}_3\text{C}-\text{C}(\text{CH}_3)_2-\text{O}\cdot \longrightarrow \cdot\text{CH}_3 + \text{H}_3\text{C}-\overset{\text{O}}{\parallel}-\text{CH}_3$ | 2.0×10^3 | 22.3 |
| 2 | $\text{H}_3\text{C}-\overset{\text{H}}{\underset{\text{CH}_3}{\text{C}}}-\text{O}\cdot \longrightarrow \cdot\text{CH}_3 + \text{H}-\overset{\text{O}}{\parallel}-\text{CH}_3$ | 1.4×10^2 | 22.9 |
| 3 | $\text{CH}_3\text{CH}_2\text{O}\cdot \longrightarrow \cdot\text{CH}_3 + \text{H}-\overset{\text{O}}{\parallel}-\text{H}$ | 19 | 23.7 |
| 4 | $\text{C}_2\text{H}_5\text{CH}_2\text{O}\cdot \longrightarrow \cdot\text{CH}_2\text{CH}_3 + \text{H}-\overset{\text{O}}{\parallel}-\text{H}$ | 1.7×10^3 | 21.5 |
| 5 | $(\text{CH}_3)_2\text{CHCH}_2\text{O}\cdot \longrightarrow \text{HC}(\cdot)(\text{CH}_3)_2 + \text{H}-\overset{\text{O}}{\parallel}-\text{H}$ | 1.2×10^4 | 19.7 |
| 6 | | 2.2×10^2 | 14.9 |
| | | 1.4×10^5 | 11.7 |

Advantages of Radical Fragmentations

1. Thermodynamically favored

2. Excellent selectivity between C–C and C–H bonds

- 01 Strategies for Inert C–C bond Cleavages
- 02 C-C Bond Cleavage via Alkoxy Radical**
- 03 C-C Bond Cleavage via Hidden Alkoxy Radical

Traditional Method for the Generation of Alkoxy Radicals

Classic Precursors for Alkoxy Radical Generation



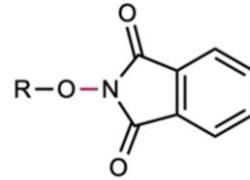
hydroperoxide



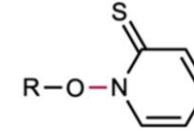
Barton nitrite ester



alkoxy hypochlorite



N-alkoxy phthalimides



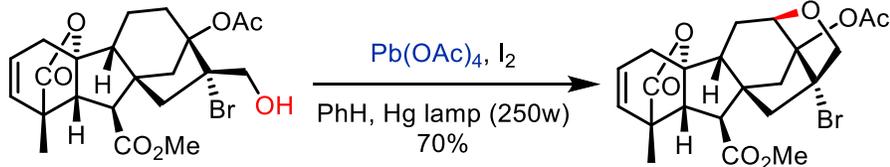
N-alkoxy pyridinethiones



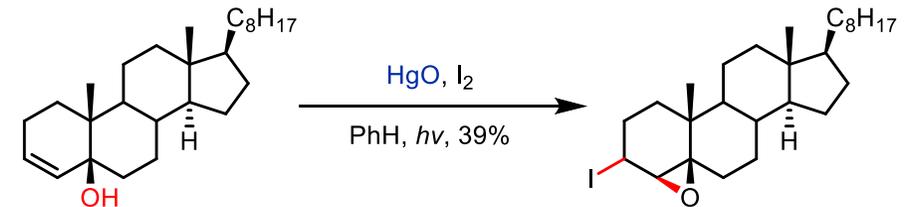
alkyl 4-nitrobenzenesulfonates

Direct Oxidation of Alcohols into Alkoxy Radicals

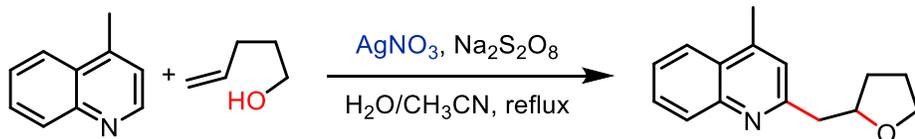
Pb(OAc)₄/I₂ system



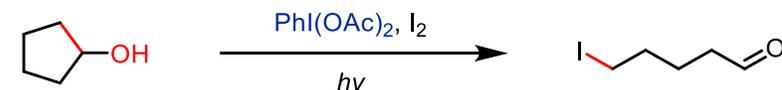
HgO / I₂ system



AgNO₃/Na₂S₂O₈ system



PhI(OAc)₂/I₂ system



左智伟

- 2007, Nanjing University, B. S., Advisor: 朱成建教授, 成义祥教授;
- 2012, Shanghai Institute of Organic Chemistry, PhD., Advisor: 马大为教授;
- 2013-2015, Princeton University, Postdoctoral Fellow,
Advisor: Prof. David W. C. MacMillan;
- 2015-2020, Shanghai Tech University, Assistant Professor;
- 2020-present, Shanghai Institute of Organic Chemistry, Professor;



PhD work on total synthesis of communesins:

J. Am. Chem. Soc. **2010**, *132*, 13226–13228.
Angew. Chem. Int. Ed. **2011**, *50*, 12008–120011.

Postdoctoral work on photocatalysis:

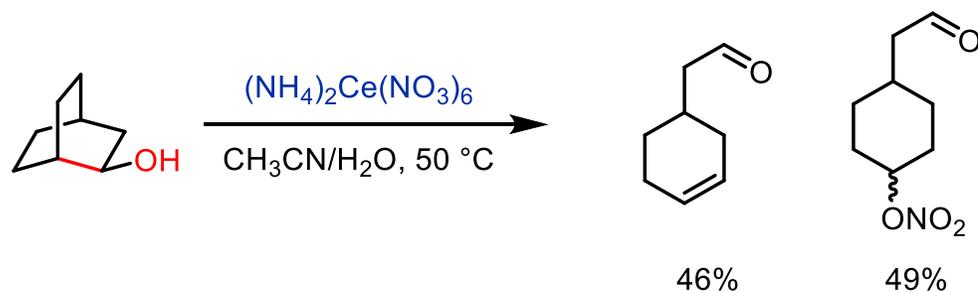
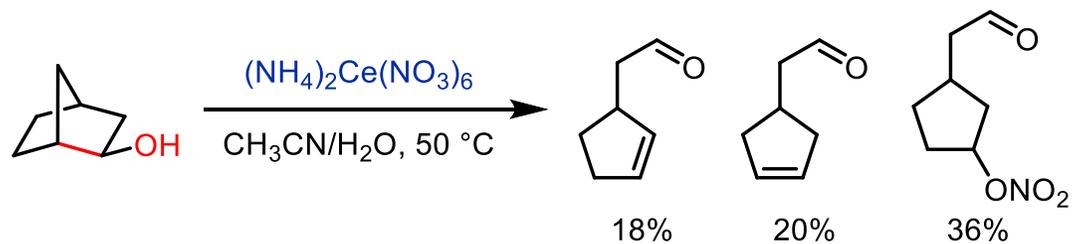
Science **2014**, *345*, 437–440.
J. Am. Chem. Soc. **2014**, *136*, 5257–5260.
J. Am. Chem. Soc. **2014**, *136*, 10886–10889.
J. Am. Chem. Soc. **2016**, *138*, 1832–1835.

左智伟

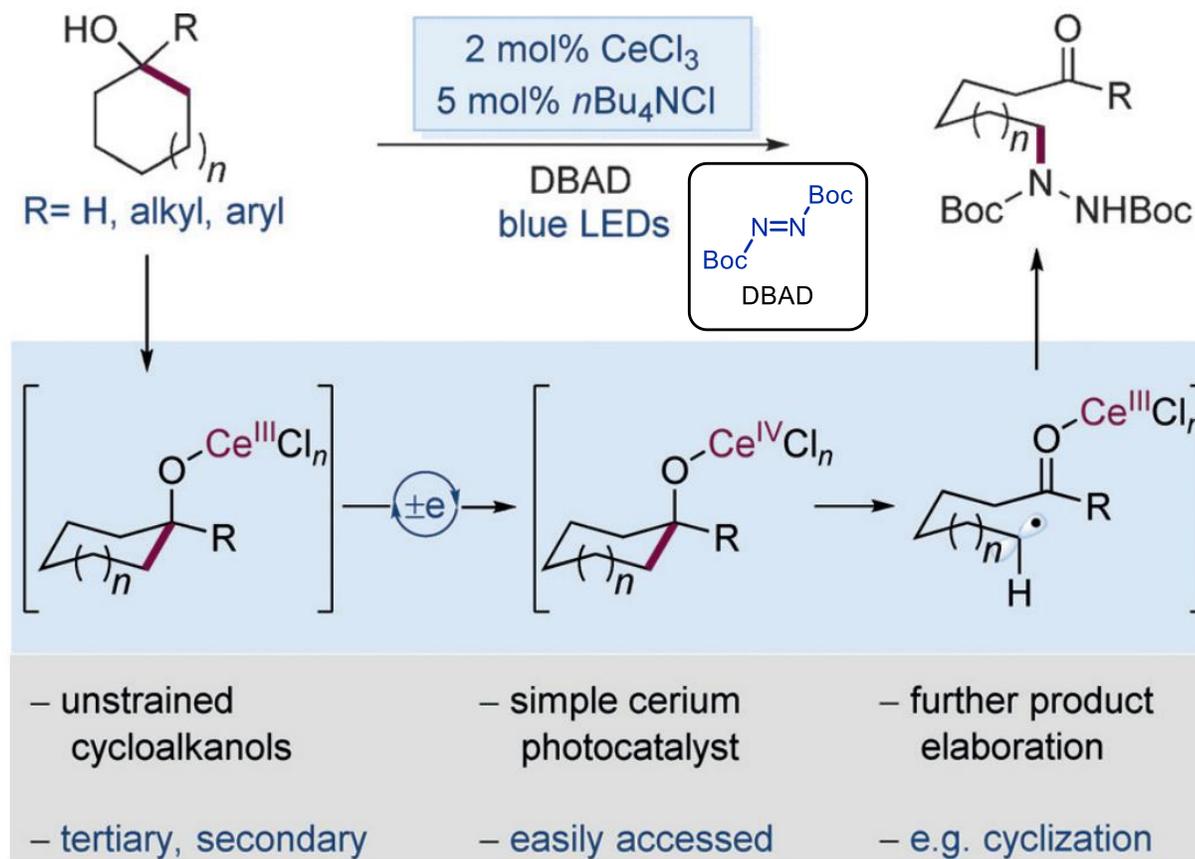
Alkoxy Radicals from visible-light-induced photoredox catalysis



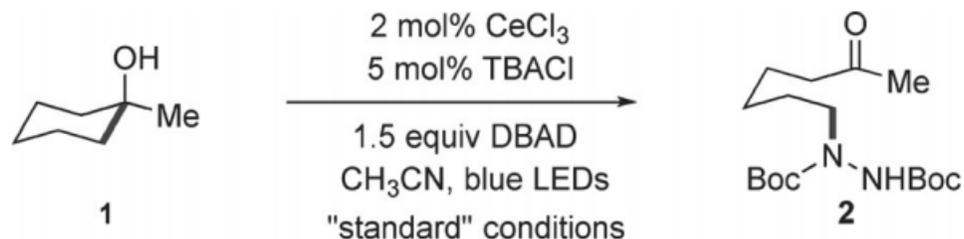
Kochi, J. K. *et al. J. Am. Chem. Soc.* **1968**, *90*, 6688–6698.



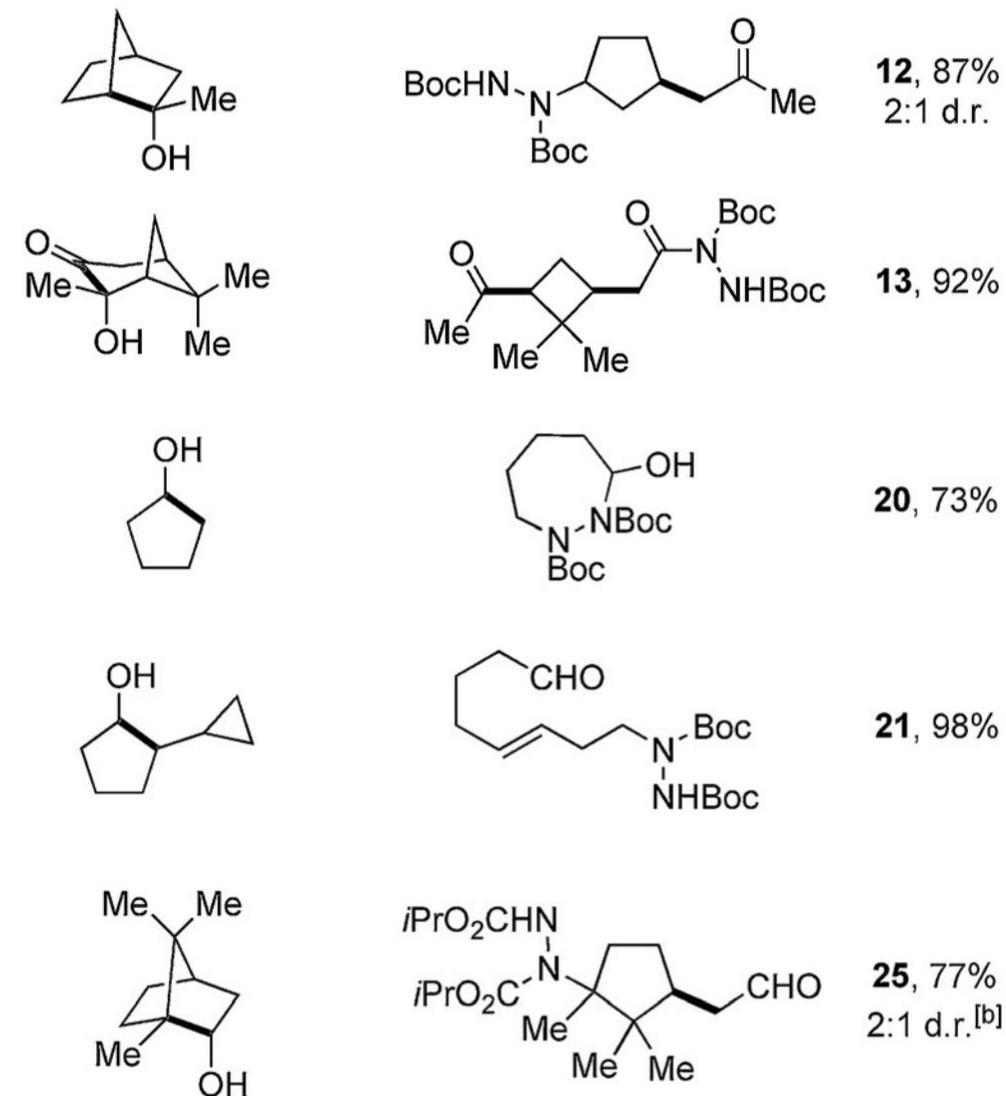
Trahanovsky, W. S. *et al. J. Am. Chem. Soc.* **1969**, *91*, 5068–5072.



Alkoxy Radicals from visible-light-induced photoredox catalysis



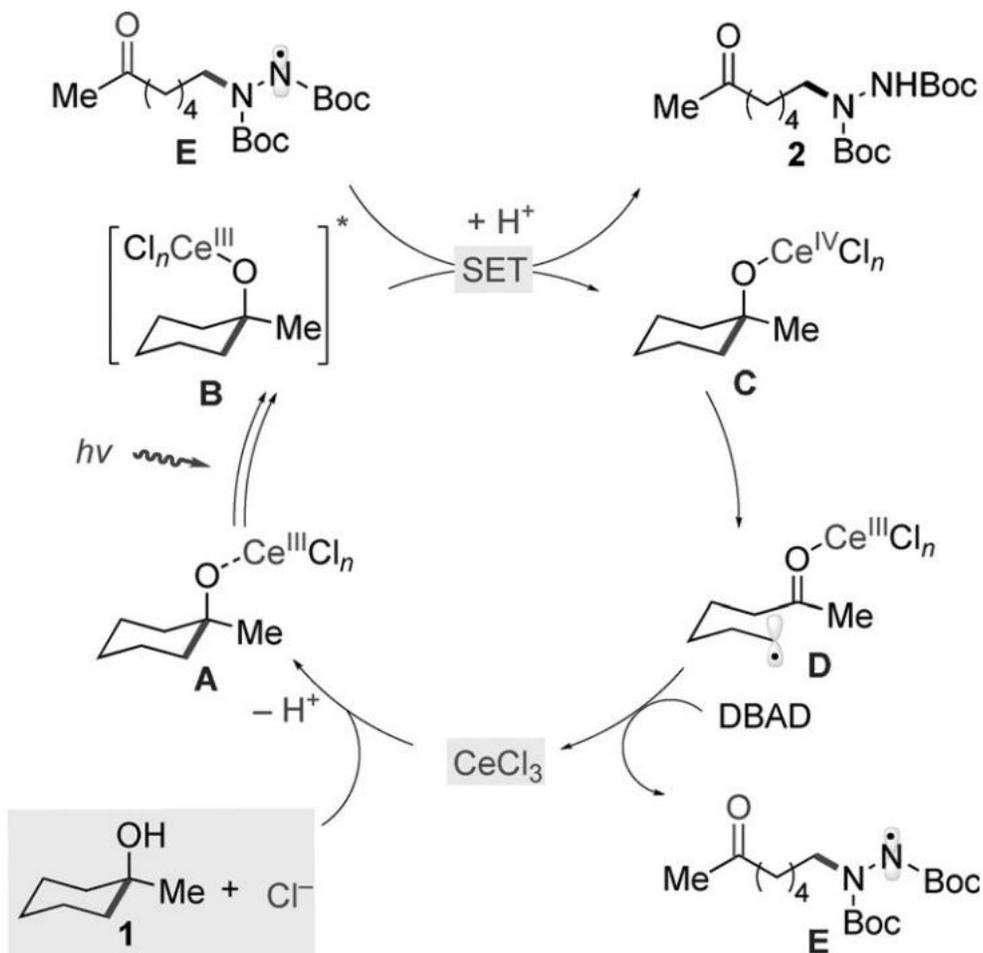
| Entry | Variation from the "standard" conditions | Yield [%] ^[a] |
|-------|--|--------------------------|
| 1 | none | 92 (91) ^[b] |
| 2 | 0.5 mol% CeCl ₃ , 1.2 mol% TBACl | 90 ^[c] |
| 3 | no TBACl | 39 |
| 4 | TBAPF ₆ , instead of TBACl | 25 |
| 5 | TBAOH, instead of TBACl | 0 |
| 6 | TBAOAc, instead of TBACl | 0 |
| 7 | TBAI, instead of TBACl | 0 |
| 8 | CeCl ₃ ·7H ₂ O, 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 |



[a] Reactions were run on 0.4 mmol scale in 0.5 mL acetonitrile for 12 h. Yields were determined by GC analysis of the crude reaction mixtures.

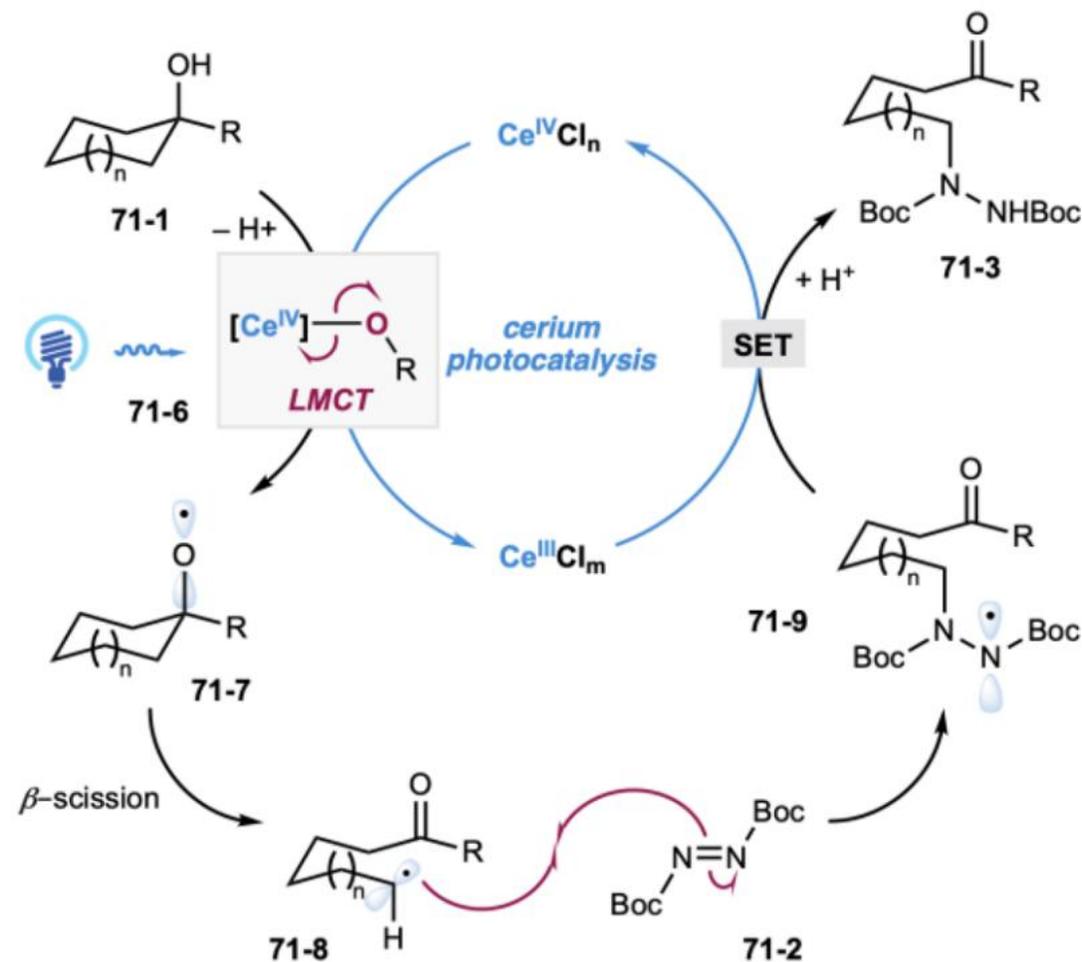
[b] Yield of isolated product is given within parentheses. [c] Irradiation for 24 h.

Alkoxy Radicals from visible-light-induced photoredox catalysis



Angew. Chem. Int. Ed. **2016**, *55*, 15319–15322.

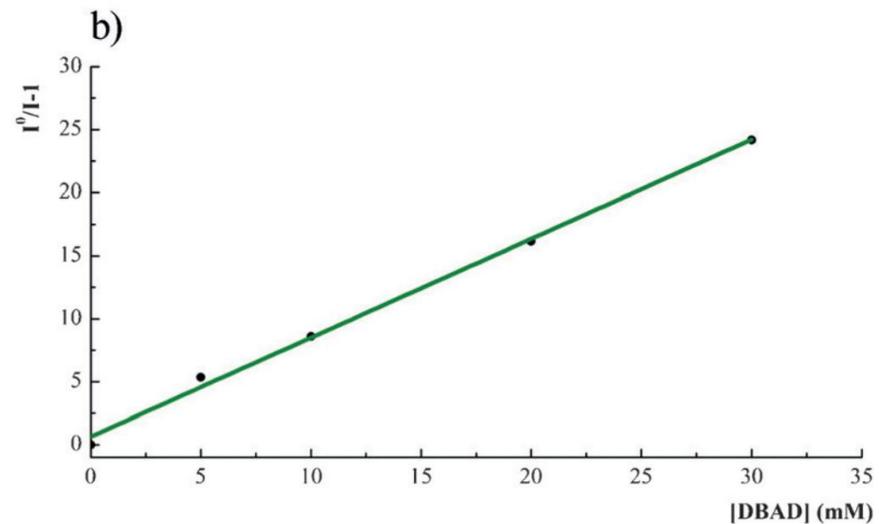
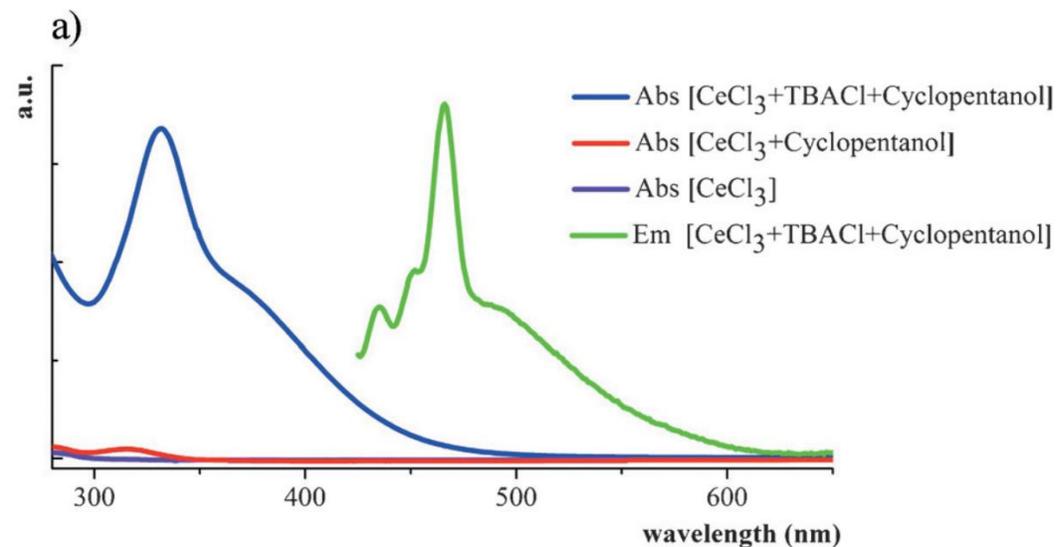
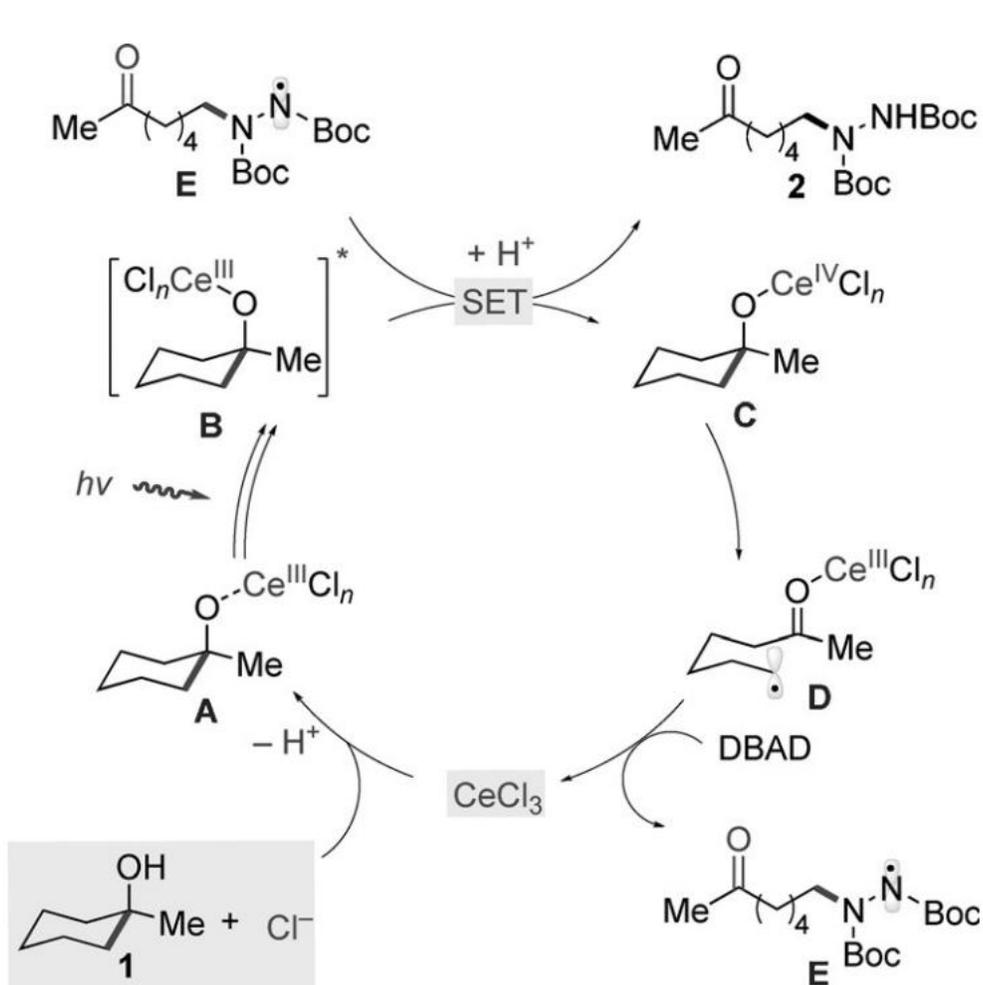
2025/12/31



Chem. Rev. **2022**, *122*, 2429–2486.

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Alkoxy Radicals from visible-light-induced photoredox catalysis



Alkoxy Radicals from visible-light-induced photoredox catalysis

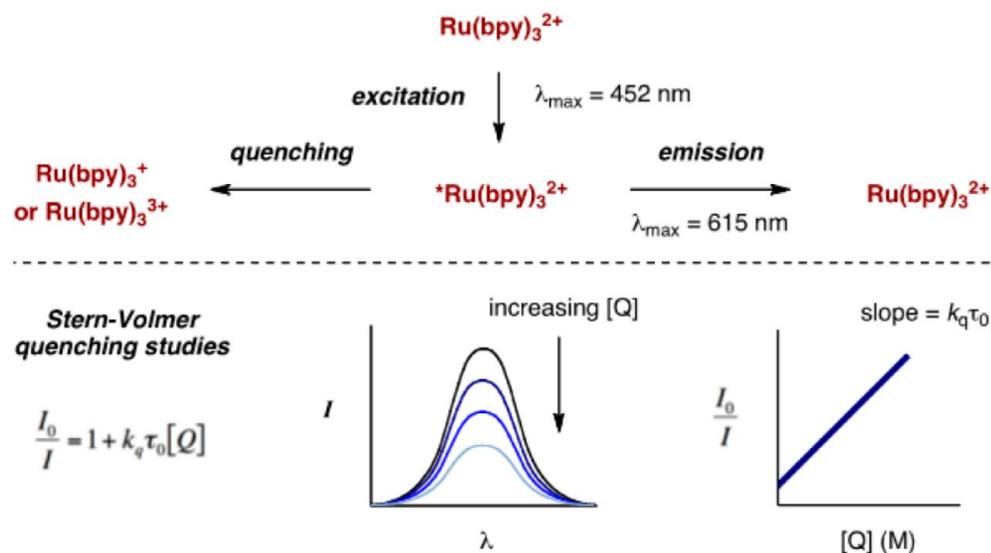
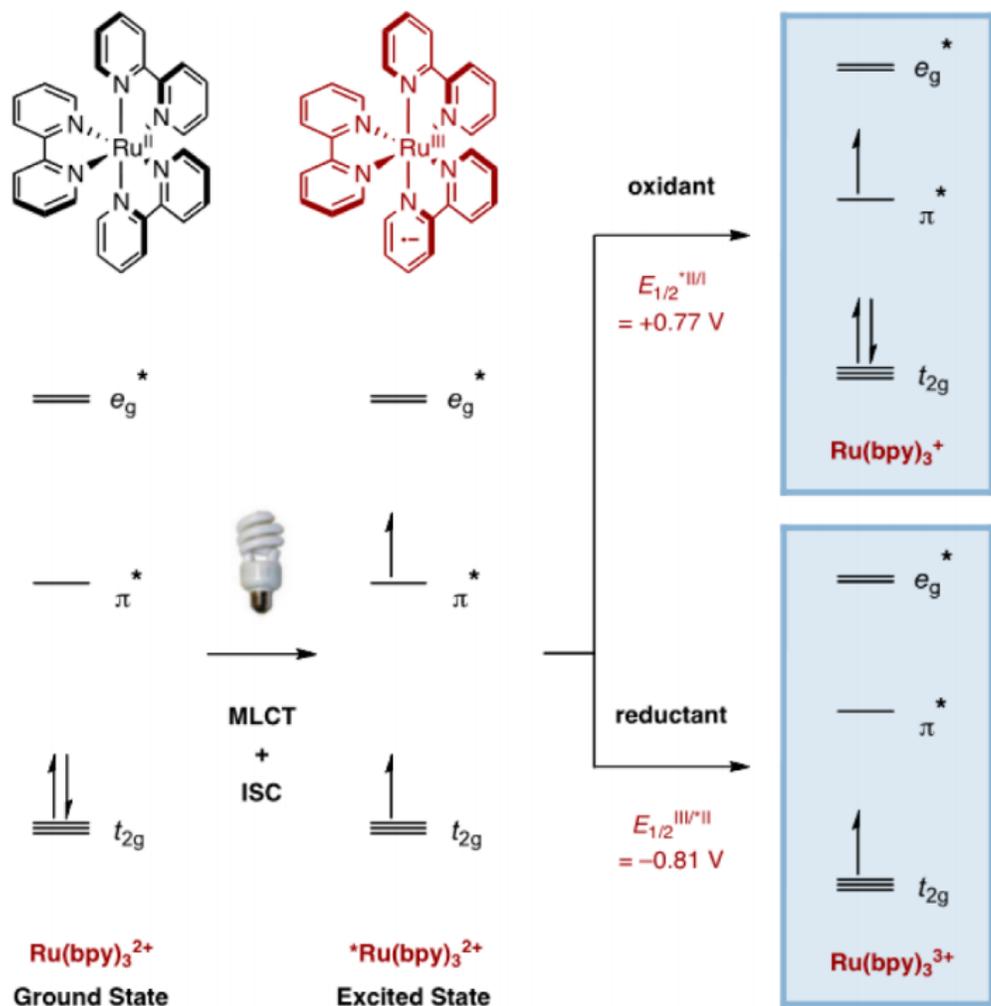
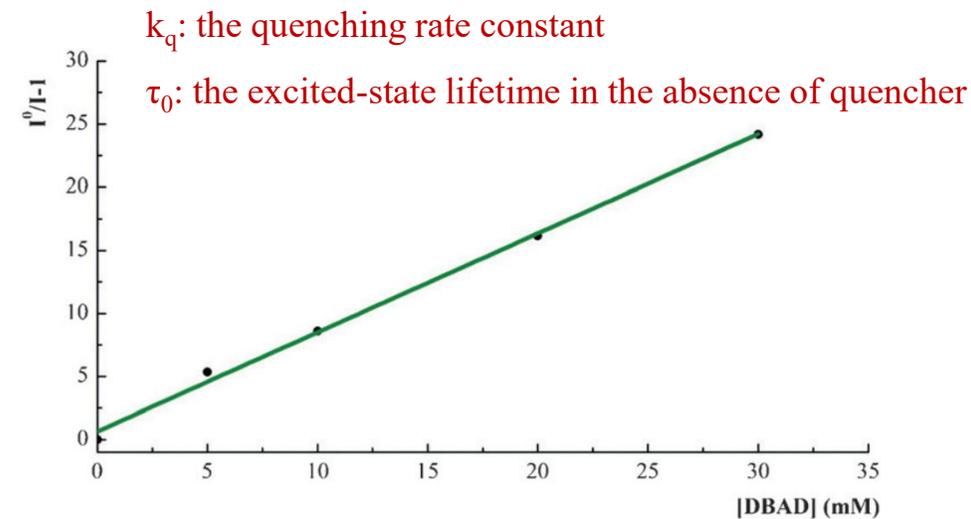
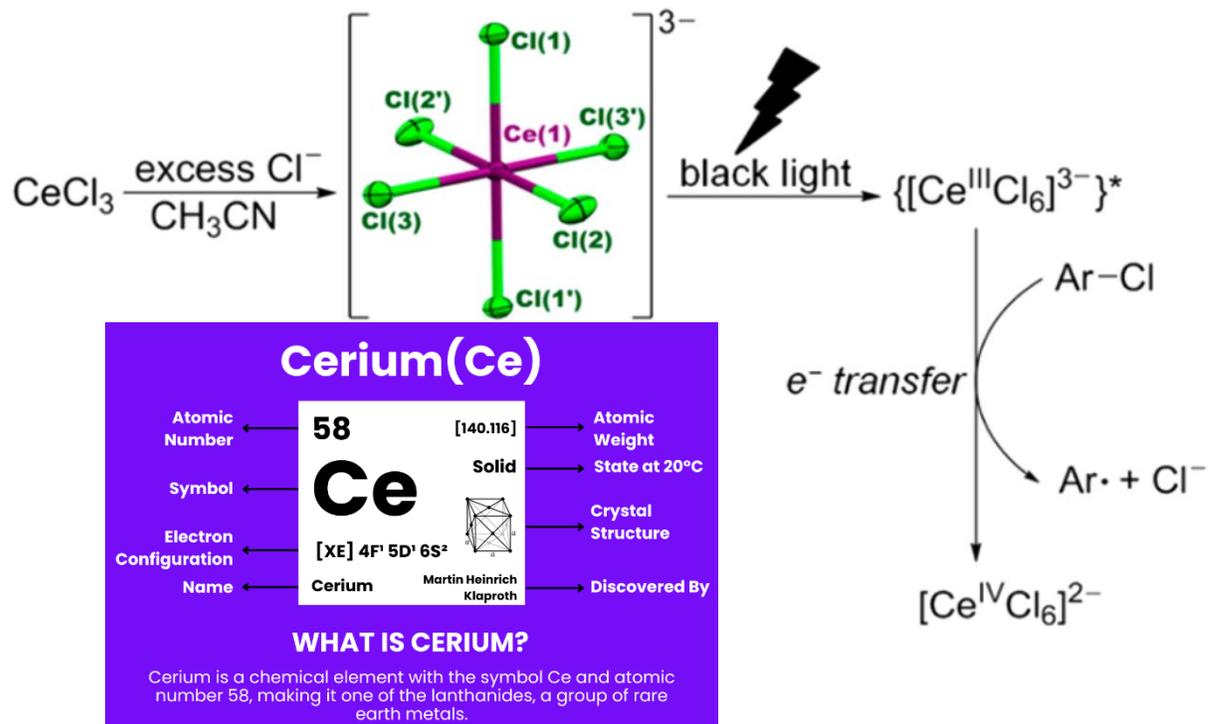


Figure 2. Fluorescence quenching (Stern–Volmer) studies.



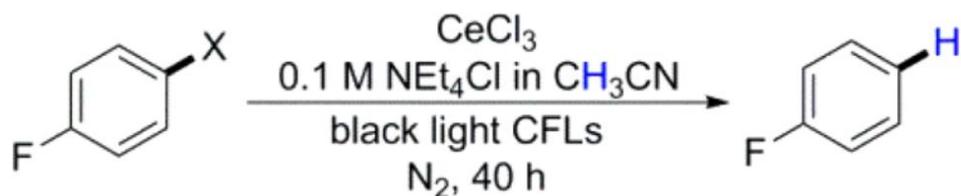
Alkoxy Radicals from visible-light-induced photoredox catalysis

X-ray structure of $[\text{CeCl}_6]^{3-}$

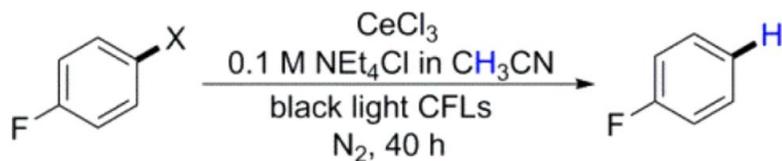


| entry | X | variations from standard conditions ^a | yield ^b (%) |
|-------|----|---|------------------------|
| 1 | Cl | none | 67(69 ^c) |
| 2 | Cl | 72 h instead of 40 h | 77(81 ^c) |
| 3 | Cl | 104 h instead of 40 h | 84 |
| 4 | Cl | no CeCl ₃ | <i>d</i> |
| 5 | Cl | LaCl ₃ instead of CeCl ₃ | <i>d</i> |
| 6 | Cl | [NEt ₄] ₃ [CeCl ₆] | 65 |
| 7 | Cl | Ce(OTf) ₃ instead of CeCl ₃ | 70 |
| 8 | Cl | no NEt ₄ Cl | <i>d</i> |
| 9 | Cl | CeCl ₃ ·7H ₂ O instead of CeCl ₃ | 52 |
| 10 | Cl | NEt ₄ Cl·H ₂ O instead of NEt ₄ Cl | 45 |
| 11 | Cl | CeCl ₃ ·7H ₂ O instead of CeCl ₃ , NEt ₄ Cl·H ₂ O instead of NEt ₄ Cl | 36 |
| 12 | Cl | in the dark instead of UVA light | <i>d</i> |
| 13 | Cl | visible light CFL instead of black light | 10 |
| 14 | F | none | <i>d</i> |
| 15 | Br | none | 87 ^c |
| 16 | I | none | >95 ^c |
| 17 | Br | CeBr ₃ and NEt ₄ Br | 12 |

^aStandard conditions: 0.2 mmol of substrate, 0.2 mmol of CeCl₃, 30 mL CH₃CN solution of 0.1 M NEt₄Cl irradiated by two 23 W black light compact fluorescent lamps, 40 h. ^bYield determined by ¹⁹F NMR integrated using *p*-fluorotoluene as internal standard. ^cReaction conducted in quartz glass bombs. ^dNo reaction.

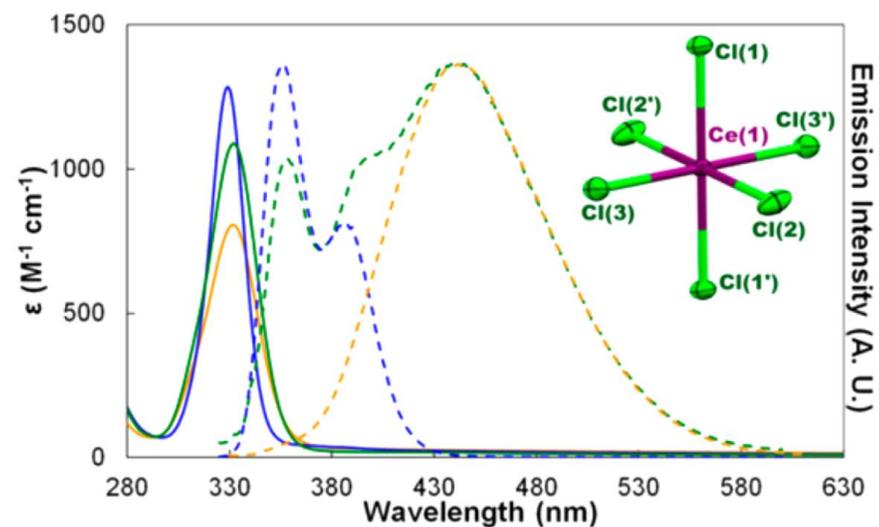


Alkoxy Radicals from visible-light-induced photoredox catalysis

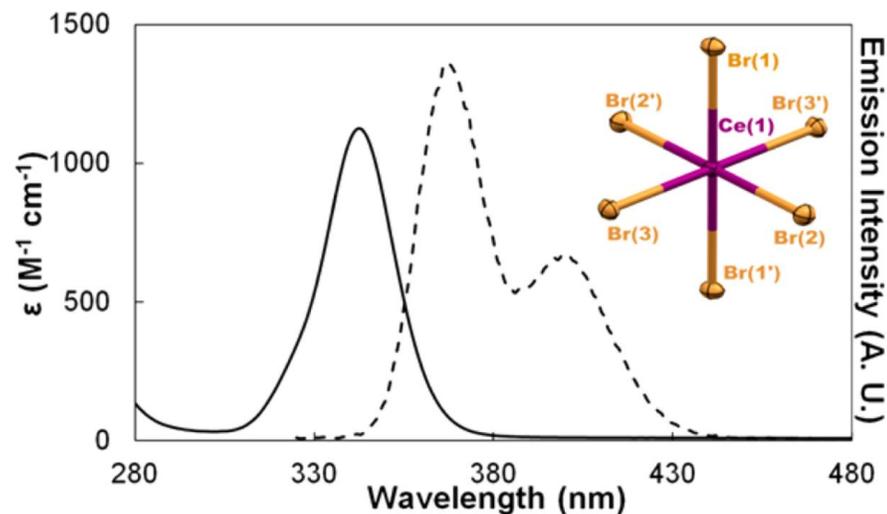


| entry | X | variations from standard conditions ^a | yield ^b (%) |
|-------|----|--|------------------------|
| 1 | Cl | none | 67(69 ^c) |
| 2 | Cl | 72 h instead of 40 h | 77(81 ^c) |
| 3 | Cl | 104 h instead of 40 h | 84 |
| 4 | Cl | no CeCl_3 | <i>d</i> |
| 5 | Cl | LaCl_3 instead of CeCl_3 | <i>d</i> |
| 6 | Cl | $[\text{NEt}_4]_3[\text{CeCl}_6]$ | 65 |
| 7 | Cl | $\text{Ce}(\text{OTf})_3$ instead of CeCl_3 | 70 |
| 8 | Cl | no NEt_4Cl | <i>d</i> |
| 9 | Cl | $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ instead of CeCl_3 | 52 |
| 10 | Cl | $\text{NEt}_4\text{Cl} \cdot \text{H}_2\text{O}$ instead of NEt_4Cl | 45 |
| 11 | Cl | $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ instead of CeCl_3 , $\text{NEt}_4\text{Cl} \cdot \text{H}_2\text{O}$ instead of NEt_4Cl | 36 |
| 12 | Cl | in the dark instead of UVA light | <i>d</i> |
| 13 | Cl | visible light CFL instead of black light | 10 |
| 14 | F | none | <i>d</i> |
| 15 | Br | none | 87 ^c |
| 16 | I | none | >95 ^c |
| 17 | Br | CeBr_3 and NEt_4Br | 12 |

^aStandard conditions: 0.2 mmol of substrate, 0.2 mmol of CeCl_3 , 30 mL CH_3CN solution of 0.1 M NEt_4Cl irradiated by two 23 W black light compact fluorescent lamps, 40 h. ^bYield determined by ^{19}F NMR

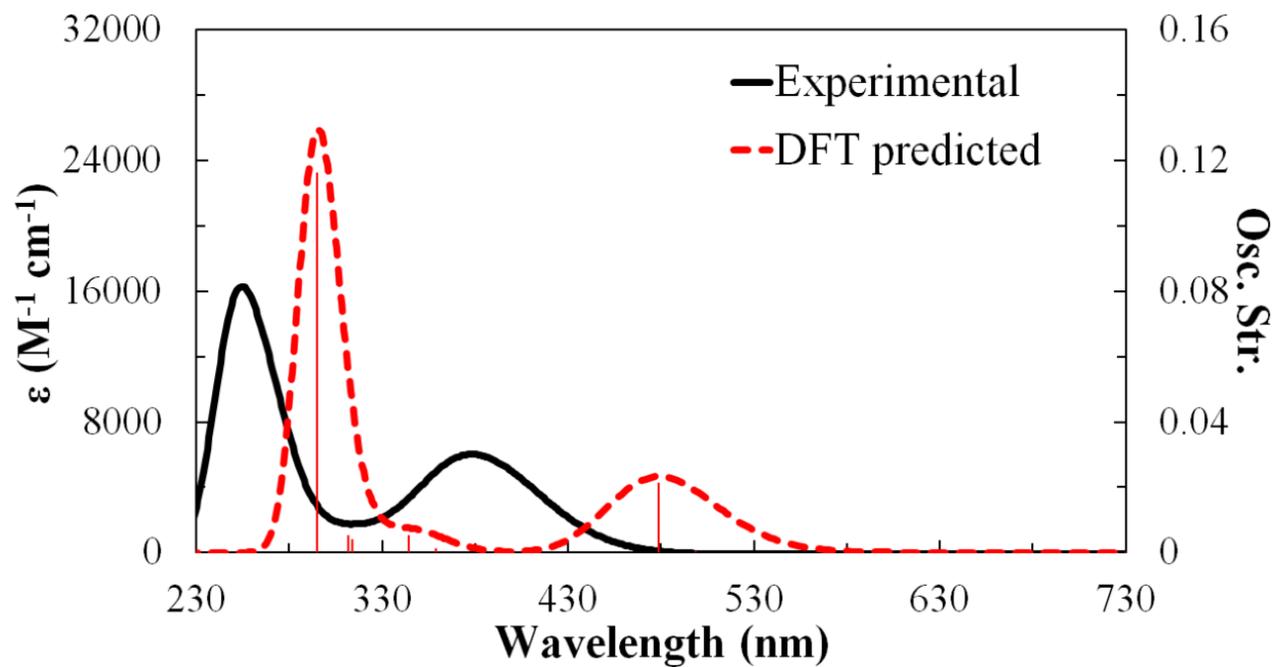


Absorption (solid lines) and emission (dashed lines) spectra for an acetonitrile solution of $[\text{Ce}^{\text{III}}\text{Cl}_6]^{3-}$.



Absorption (black solid lines) and emission (black dashed lines) spectra for an acetonitrile solution of $[\text{Ce}^{\text{III}}\text{Br}_6]^{3-}$.

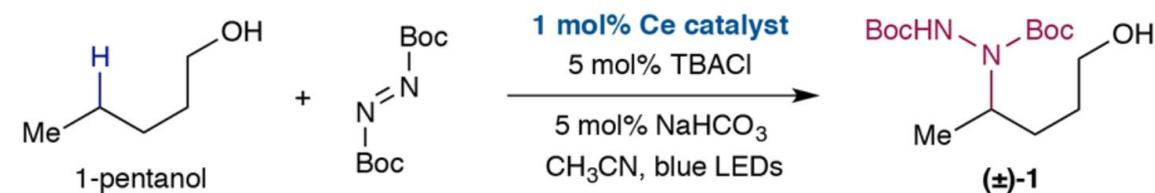
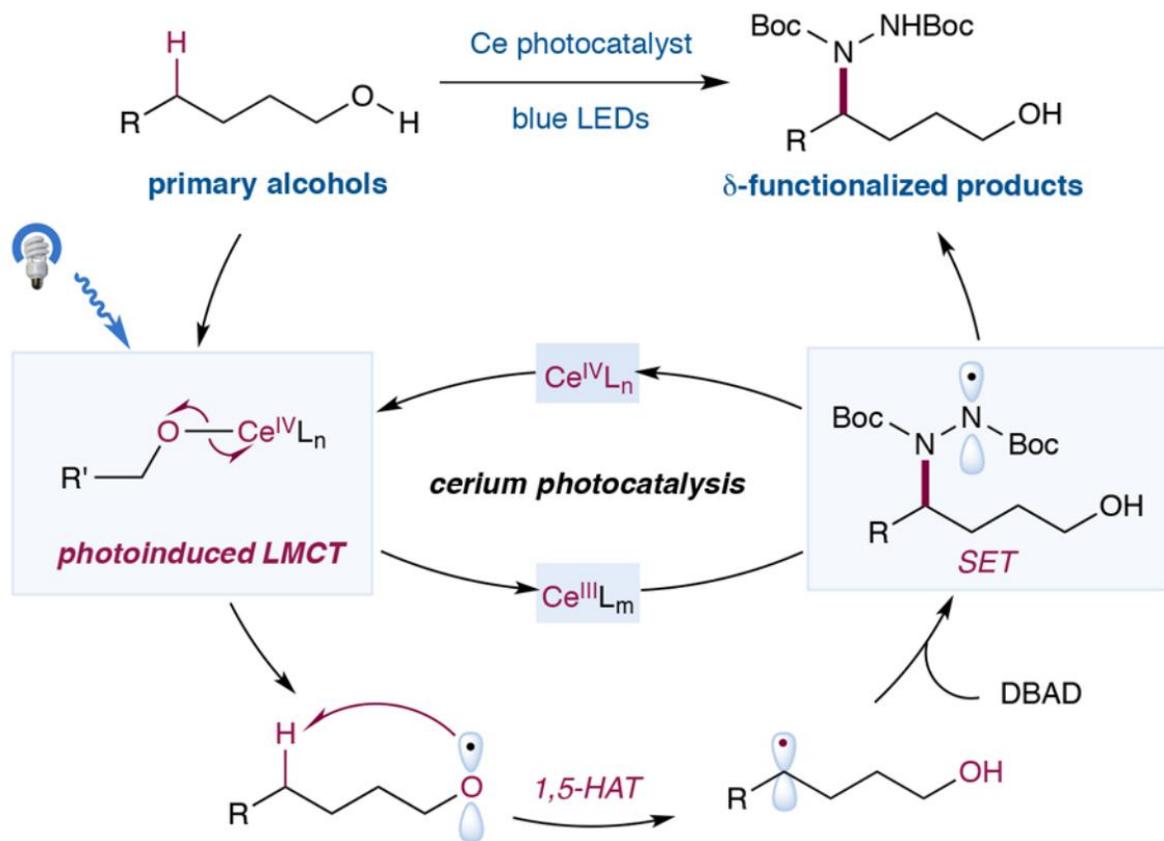
Alkoxy Radicals from visible-light-induced photoredox catalysis



Experimental electronic absorption spectra of $[NEt_4]_2[Ce^{IV}Cl_6]$ in MeCN (black solid line) and DFT predicted absorption spectra of $[Ce^{IV}Cl_6]^{2-}$ in the gas phase (red dashed lines).

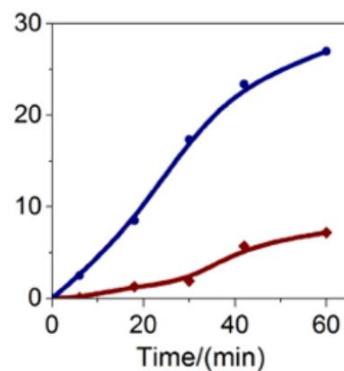
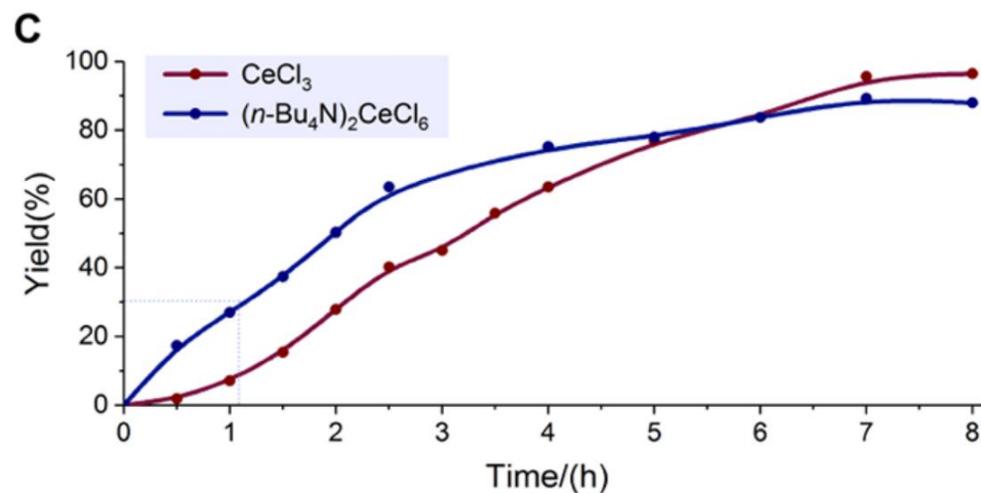
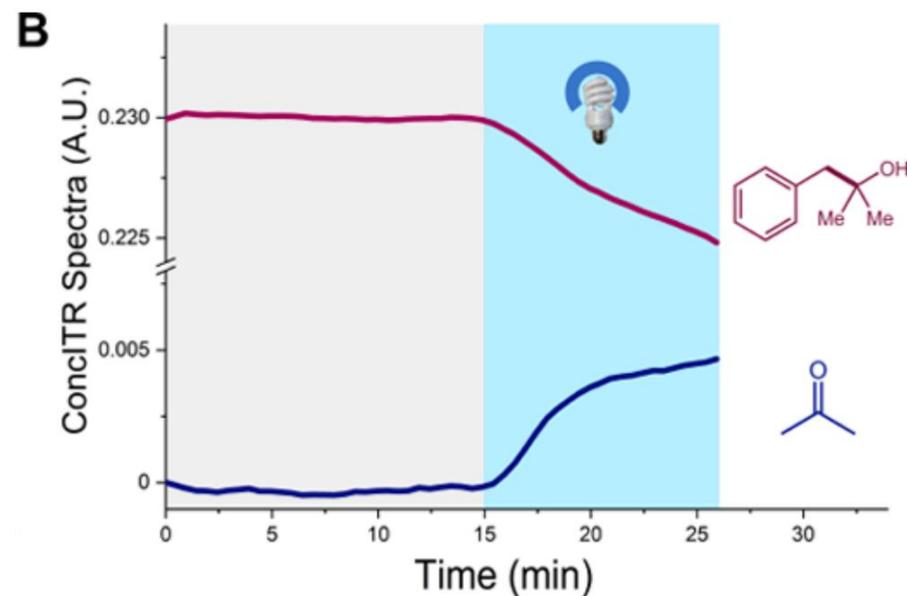
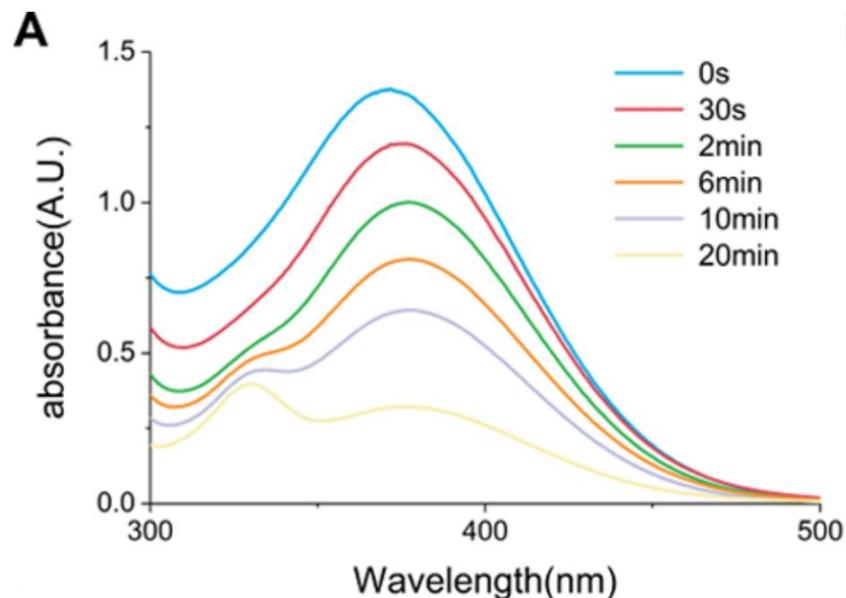
transitions are assigned to **LMCT transitions (Ligand to Metal Charge Transfer)** from **ligand** to **Ce^{IV} 4f-orbitals**: the transition at **478 nm** originates from **ligand t_{1g} set of orbitals**; the transition at **344 nm** originates from **ligand t_{2g} set**; the transition at **295 nm** originates from **e_g and a_{1g} sets**.

Alkoxy Radicals from visible-light-induced photoredox catalysis



| Entry | Catalyst | Light | Yield (%) ^a |
|----------------|--|------------|------------------------|
| 1 | Ce(OTf) ₄ | blue LEDs | 43 |
| 2 | (<i>n</i> -Bu ₄ N) ₂ [CeCl ₆] | blue LEDs | 89 |
| 3 | - | blue LEDs | 0 |
| 4 | (<i>n</i> -Bu ₄ N) ₂ [CeCl ₆] (10%) | OFF (60°C) | 0 |
| 5 ^b | CeCl ₃ | blue LEDs | 92 |

Alkoxy Radicals from visible-light-induced photoredox catalysis

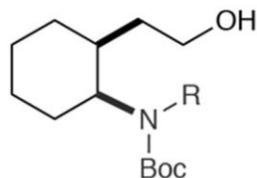
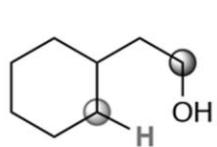


A. UV-vis spectral changes a solution of $\text{Ce}^{\text{IV}}(\text{OC}_5\text{H}_{11})\text{Cl}_n$ complex in CH_3CN under blue light (0–20 min).

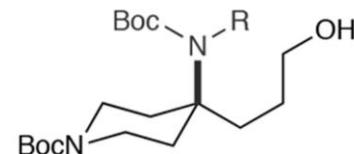
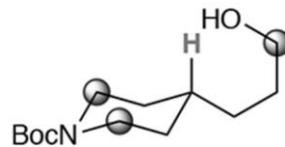
B. IR experiments with a solution of $(n\text{-Bu}_4\text{N})_2\text{CeCl}_6$ and 2-methyl-1-phenyl-2-propanol in the dark (0–15 min) and with blue-light irradiation (15–25 min).

C. Reaction profiles for the $\delta\text{-C-H}$ amination of 1-pentanol catalyzed by $(n\text{-Bu}_4\text{N})_2\text{CeCl}_6$ and CeCl_3 .

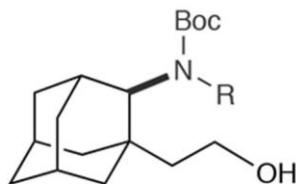
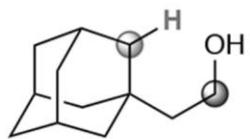
Alkoxy Radicals from visible-light-induced photoredox catalysis



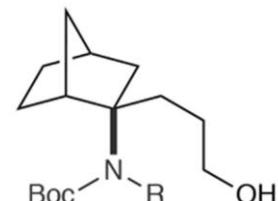
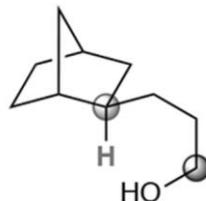
(±)-**5** 81% yield
1.2 : 1 d.r.



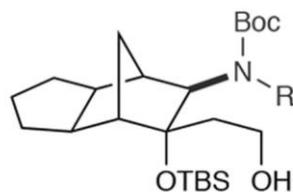
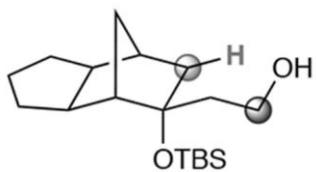
(±)-**15** 87% yield^b



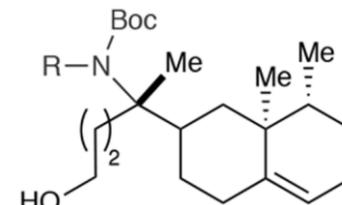
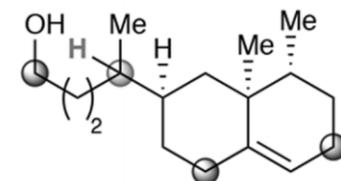
(±)-**6** 67% yield^b



(±)-**16** 81% yield
1.2 : 1 d.r.



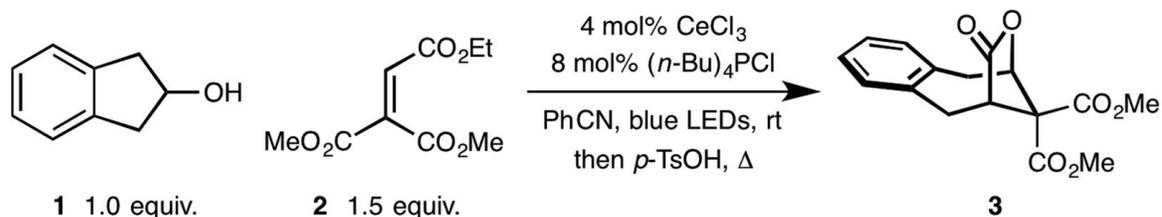
7 44% yield^b
2 : 1 d.r.



17 76% yield
1.2 : 1 d.r.

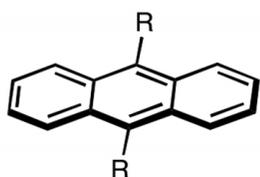
General reaction conditions:
DBAD (0.4 mmol), alcohol
substrate (1.2 mmol), CeCl₃ (0.004
mmol), TBACl (0.02 mmol),
CH₃CN (4 mL), 90 W blue LEDs.

Alkoxy Radicals from visible-light-induced photoredox catalysis

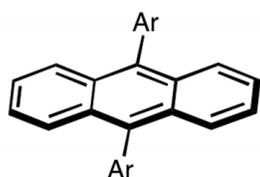


| Entry | Additives | Light | Yield (%) ^a |
|-------|-------------------|-----------|------------------------|
| 1 | none | blue LEDs | 8 |
| 2 | 2 mol% anthracene | blue LEDs | 19 |
| 3 | 2 mol% DBA | blue LEDs | 32 |
| 4 | 2 mol% DMA | blue LEDs | 56 |
| 5 | 2 mol% DCA | blue LEDs | 10 |

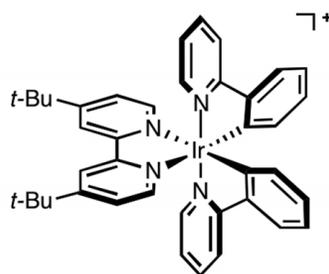
| | | | |
|-----------------|---|-----------|----|
| 6 | 2 mol% DPA | blue LEDs | 82 |
| 7 | 2 mol% 4 | blue LEDs | 78 |
| 8 | 2 mol% 5 | blue LEDs | 42 |
| 9 | 2 mol% Ir(ppy) ₂ (dtbbpy)PF ₆ | blue LEDs | 48 |
| 10 ^b | 2 mol% DPA | blue LEDs | 71 |
| 11 ^c | 2 mol% DPA | blue LEDs | 2 |
| 12 ^d | 2 mol% DPA | blue LEDs | 0 |
| 13 ^d | 2 mol% Ir(ppy) ₂ (dtbbpy)PF ₆ | blue LEDs | 0 |
| 14 | 2 mol% DPA | dark | 0 |



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



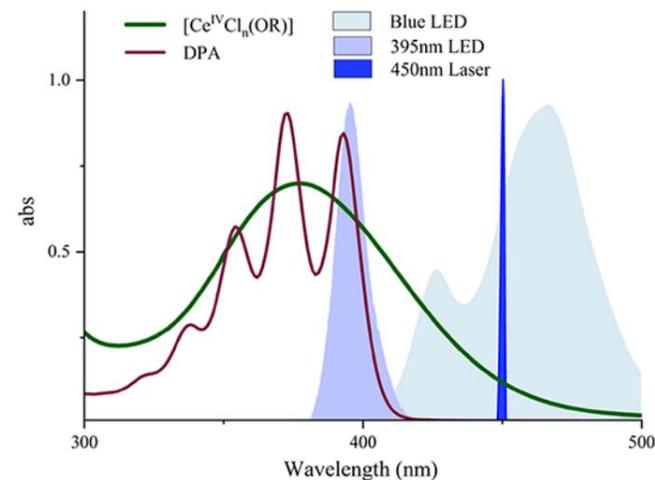
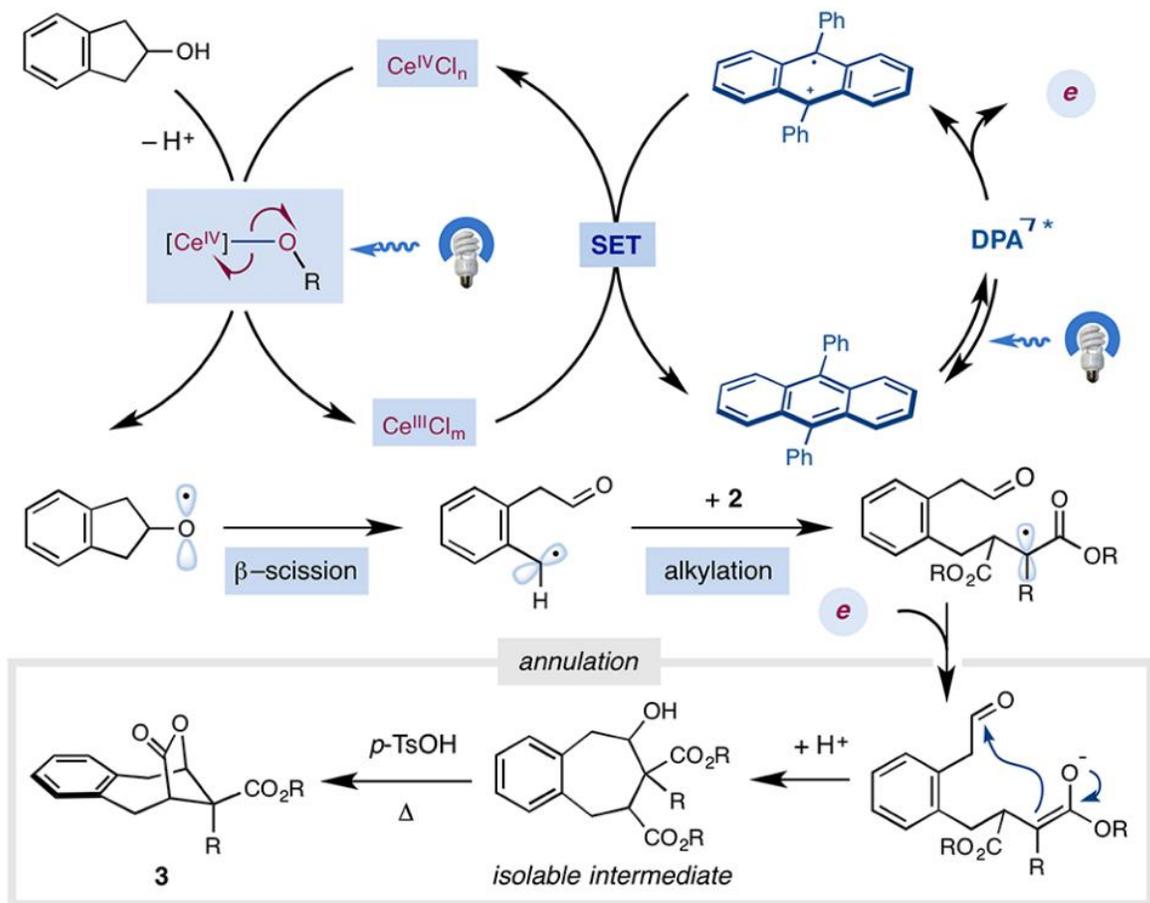
Ar = Ph, **DPA**
 Ar = 2,4-di-F-C₆H₃, **4**
 Ar = 3,4-di-OMe-C₆H₃, **5**



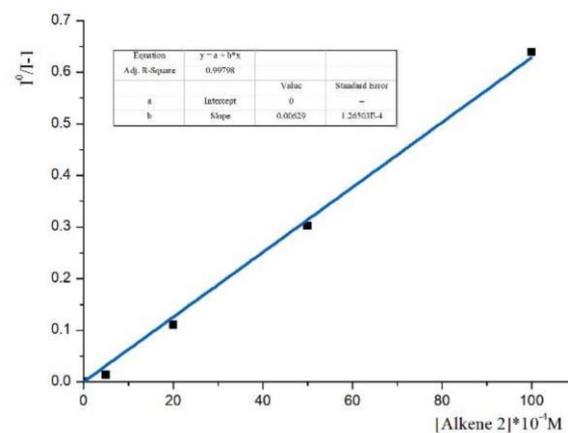
Ir(ppy)₂(dtbbpy)PF₆

^aYields were determined by GC analysis of the crude reaction mixtures. ^bReaction was run with CeCl₃·7H₂O. ^cReaction was run in the absence of (n-Bu)₄PCl. ^dReactions were run in the absence of CeCl₃.

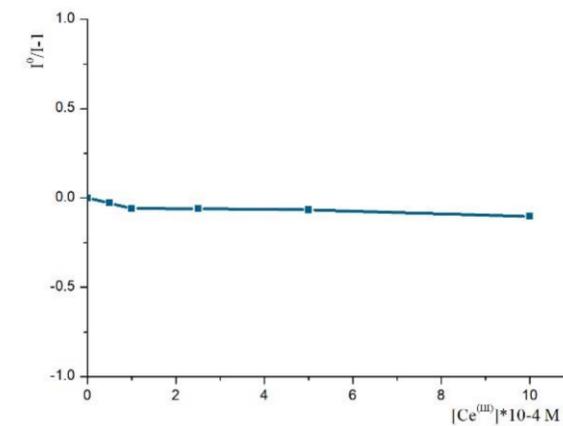
Alkoxy Radicals from visible-light-induced photoredox catalysis



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

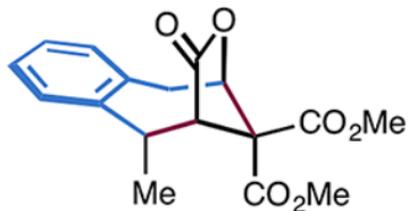
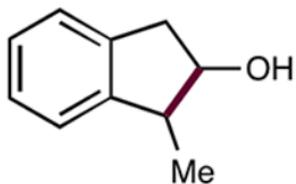


Stern-Volmer quenching studies of **DPA** by **alkene**

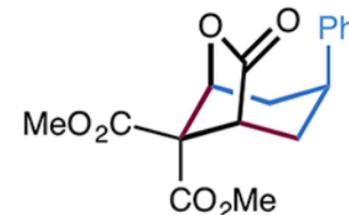
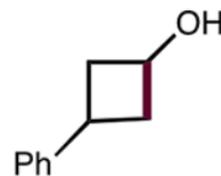


Stern-Volmer quenching studies of **DPA** by $\text{Ce}^{\text{III}}\text{Cl}_n(\text{OC}_5\text{H}_9)$

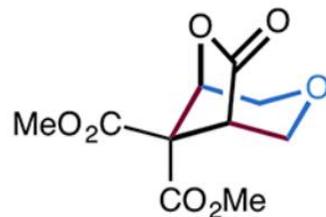
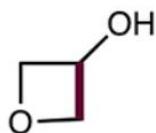
Alkoxy Radicals from visible-light-induced photoredox catalysis



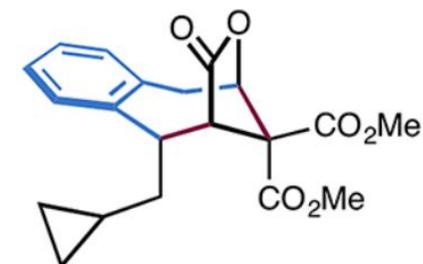
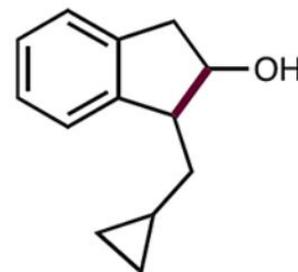
6 12 h, 69% yield
1.4 : 1 d.r.



17 15 h, 82% yield
2.5 : 1 d.r.



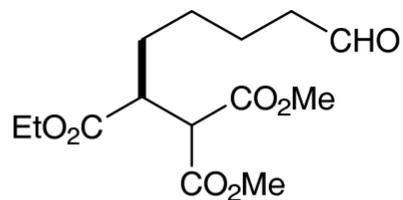
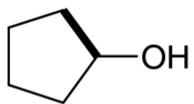
16 36 h, 61% yield



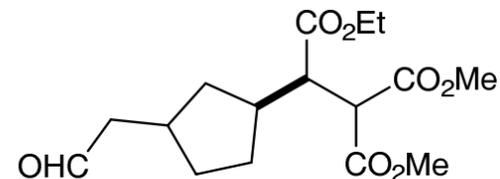
8 24 h, 77% yield
1.5 : 1 d.r.

General reaction conditions: alcohol substrate (0.2 mmol), alkene substrate (0.3 mmol), CeCl_3 (0.008 mmol), DPA (0.004 mmol), tetrabutylphosphonium chloride (0.016 mmol), benzonitrile (0.5 mL), 90W blue LEDs.

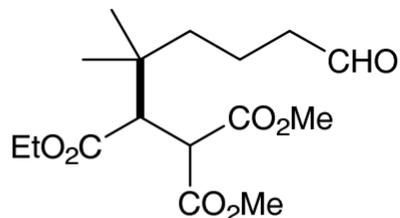
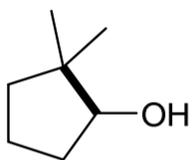
Alkoxy Radicals from visible-light-induced photoredox catalysis



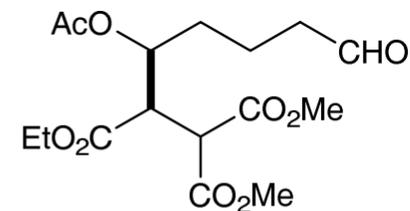
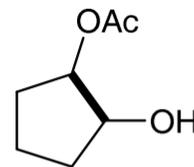
S10 70% yield



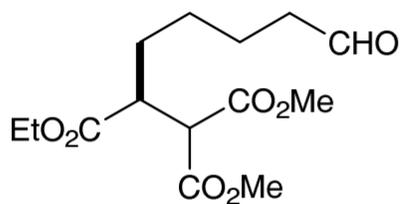
S15 85% yield
1:1 d.r.



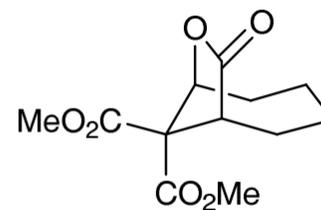
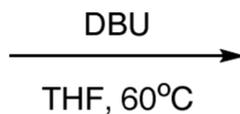
S11 66% yield



S13 54% yield
1:1 d.r.

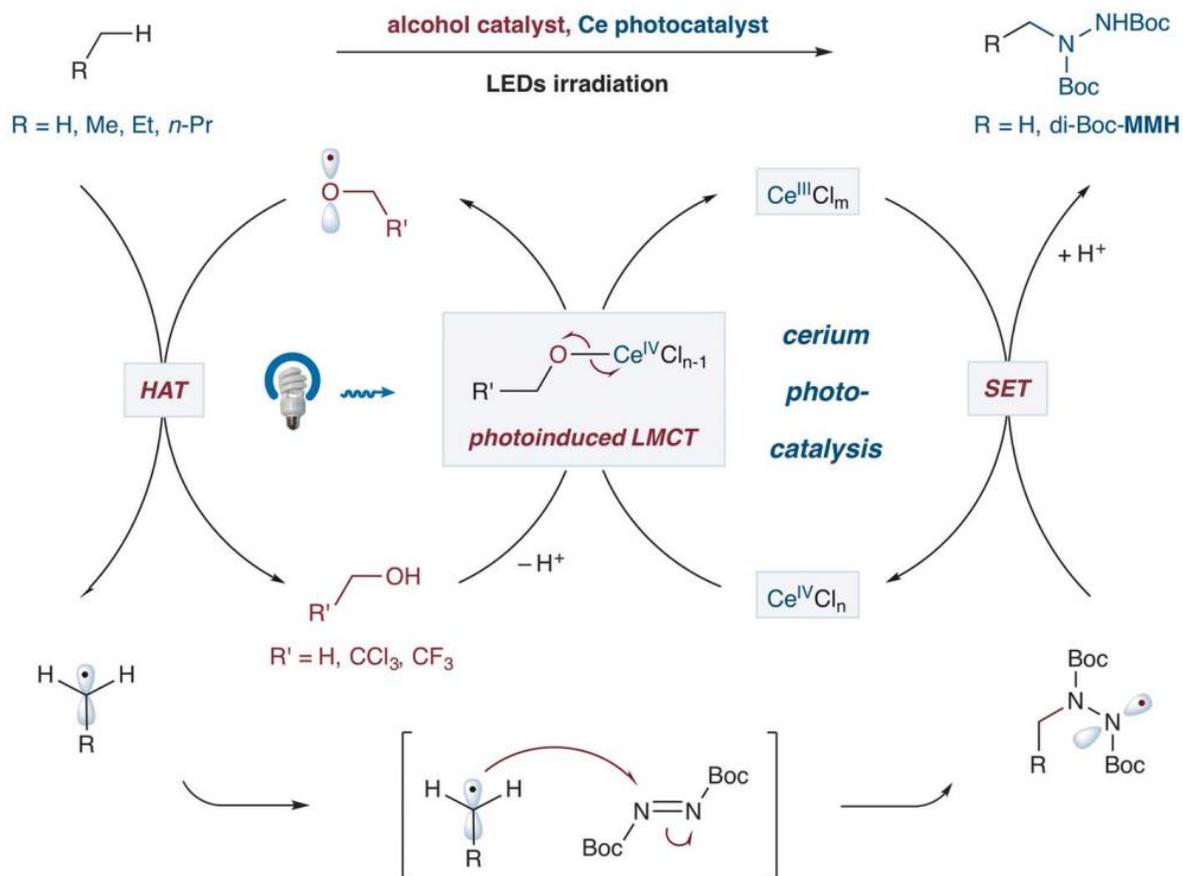


S10

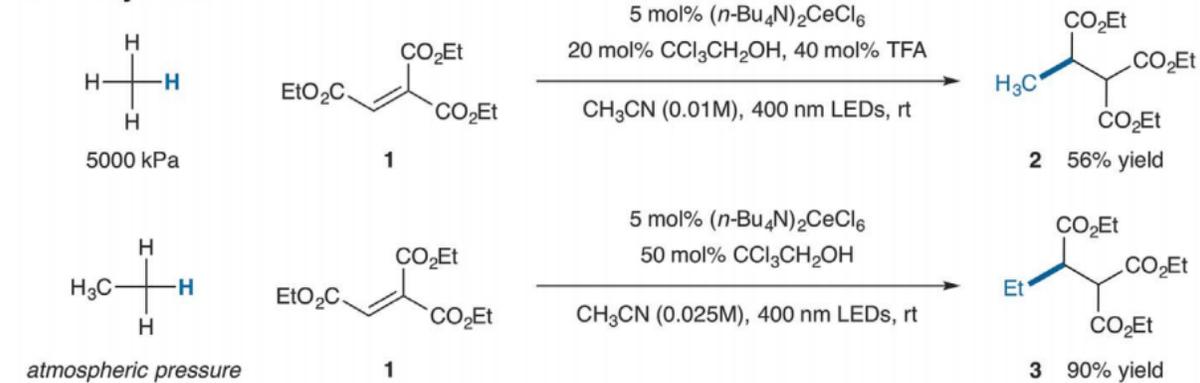


S16 54% yield

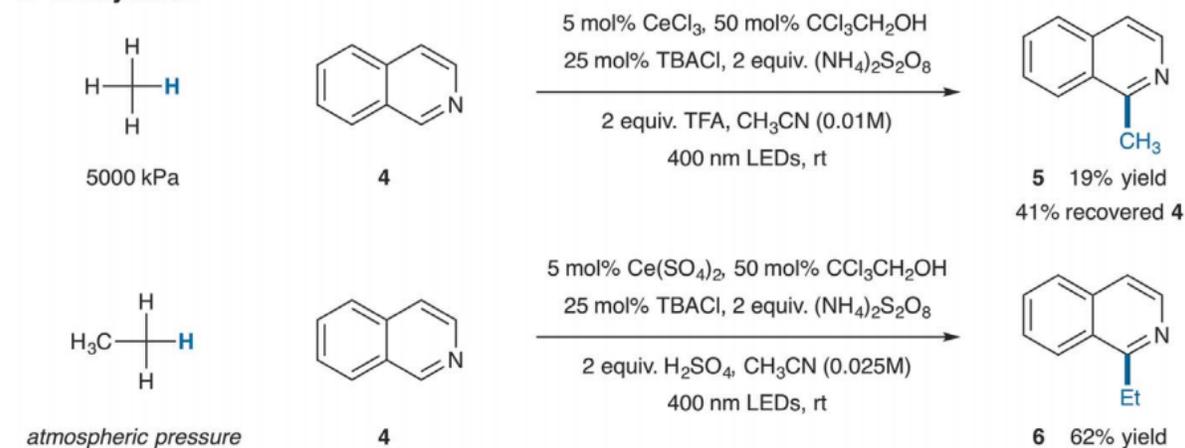
Alkoxy Radicals from visible-light-induced photoredox catalysis



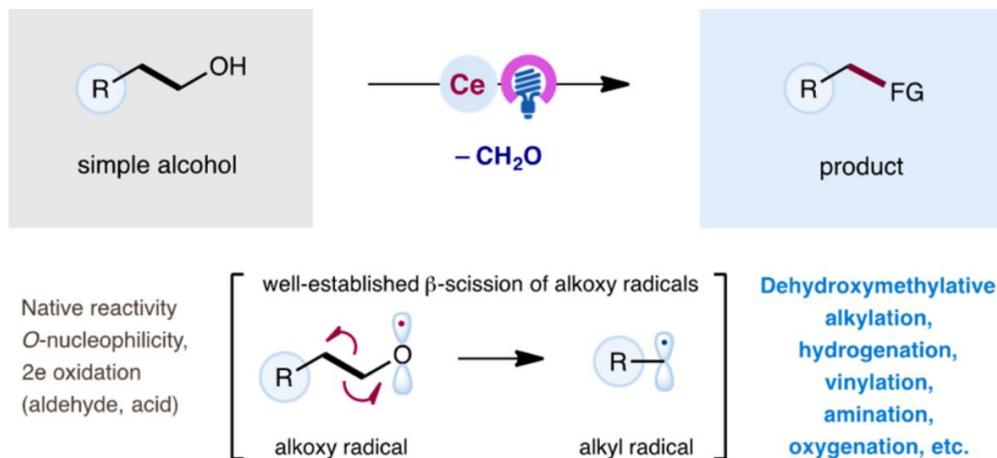
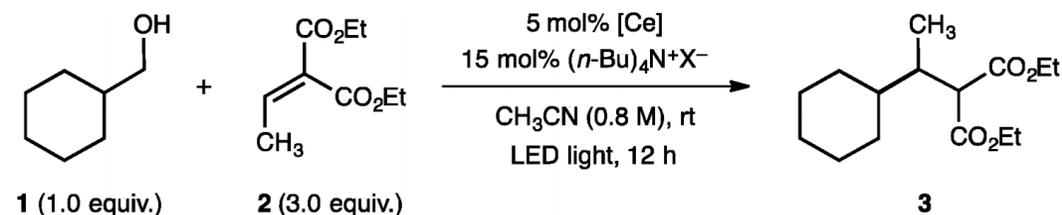
C-H Alkylation



C-H Arylation

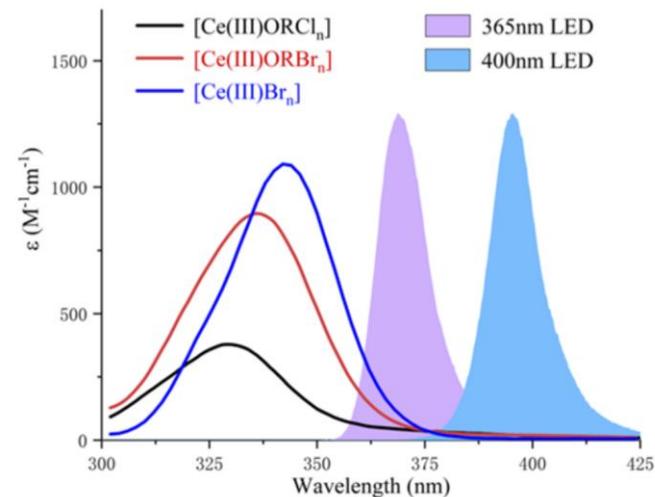
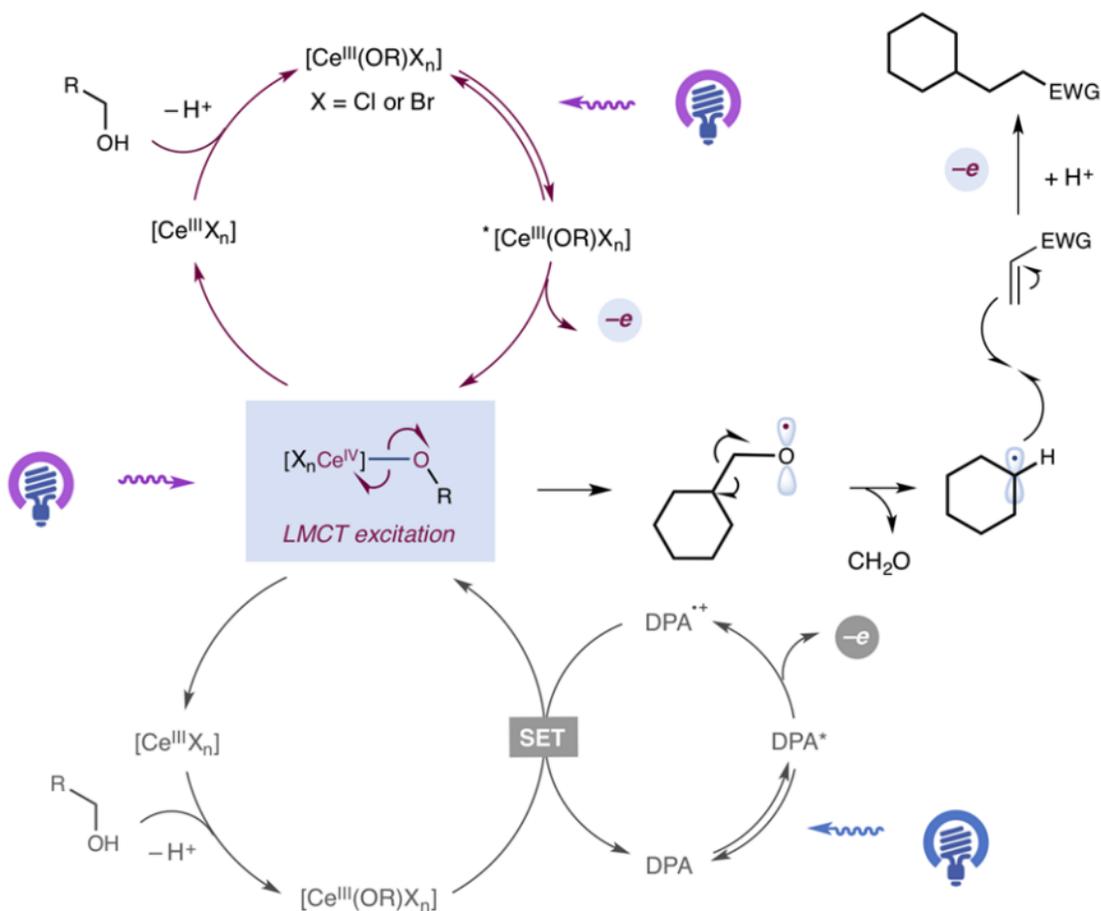


Alkoxy Radicals from visible-light-induced photoredox catalysis

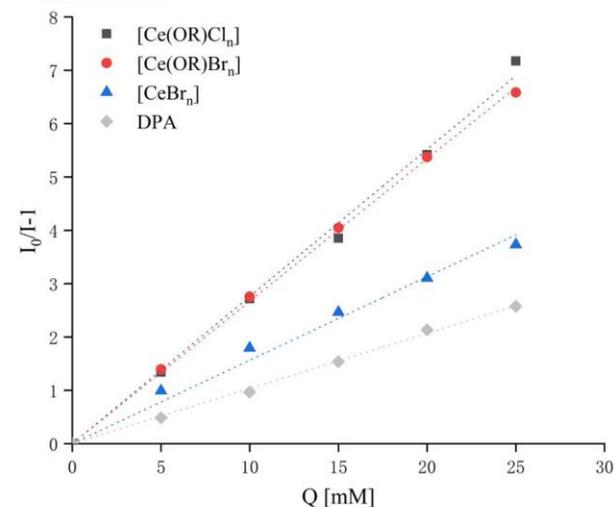


| entry | catalysts | light | yield (%) ^a | O-addition (%) ^a |
|-------|--|--------|------------------------|-----------------------------|
| 1 | CeCl ₃ , (<i>n</i> -Bu) ₄ NCl | 400 nm | 2 | 6 |
| 2 | CeCl ₃ , (<i>n</i> -Bu) ₄ NCl | 365 nm | 39 | 10 |
| 3 | CeCl ₃ , (<i>n</i> -Bu) ₄ NBr | 400 nm | 15 | 12 |
| 4 | CeCl ₃ , (<i>n</i> -Bu) ₄ NBr | 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 % (<i>n</i> -Bu) ₄ NBr | 365 nm | 79 | trace |
| 8 | (<i>n</i> -Bu) ₄ NBr | 365 nm | 0 | 0 |
| 9 | CeBr ₃ , (<i>n</i> -Bu) ₄ NBr | dark | 0 | 27 |
| 10 | entry 1, 2 mol % DPA | 400 nm | 51 | trace |
| 11 | entry 1, 5 mol % DPA | 400 nm | 81 | trace |

Alkoxy Radicals from visible-light-induced photoredox catalysis

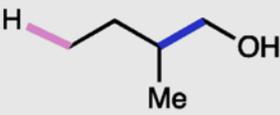
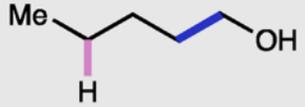
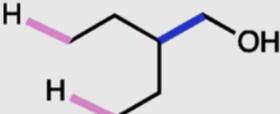
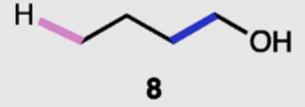
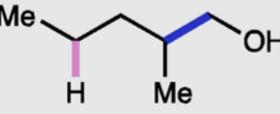
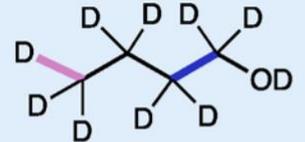


UV-vis absorption spectra of in situ formed $[Ce^{III}Br_n]$, $[Ce^{III}ORCl_n]$, and $[Ce^{III}ORBr_n]$. ROH cyclohexanemethanol.

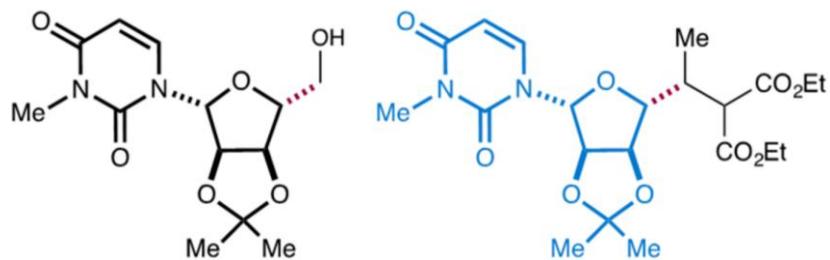


Stern-Volmer quenching studies of $[Ce^{III}]$, DPA by alkene

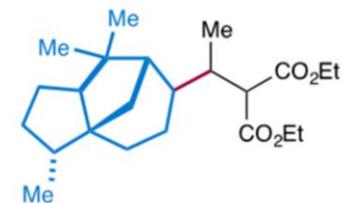
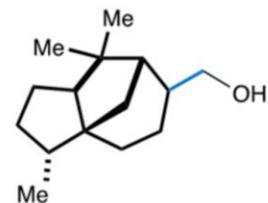
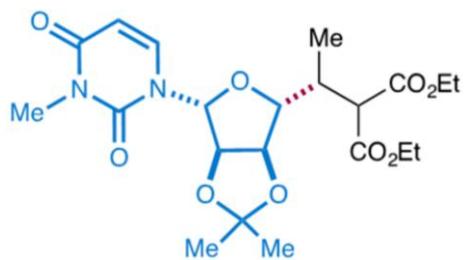
Alkoxy Radicals from visible-light-induced photoredox catalysis

| Alcohols | Conditions | Dehydroxylation Vs. HAT | | |
|---|-------------------|-------------------------|--|---|
|  <p>4 primary vs. secondary</p> | entry 4, table 1 | 88% : 0% (> 20:1 ratio) |  <p>7 secondary vs. primary</p> | entry 2, table 1 7% : 25% (1:3.6 ratio) |
| | entry 11, table 1 | 72% : 0% (> 20:1 ratio) | | entry 4, table 1 20% : 17% (1.2:1 ratio) |
|  <p>5 primary vs. secondary</p> | entry 4, table 1 | 90% : 0% (> 20:1 ratio) |  <p>8 primary vs. primary</p> | entry 2, table 1 11% : 6% (1.8:1 ratio) |
| | entry 11, table 1 | 62% : 0% (> 20:1 ratio) | | entry 4, table 1 30% : 6% (5:1 ratio) |
|  <p>6 secondary vs. secondary</p> | entry 4, table 1 | 89% : 0% (> 20:1 ratio) |  <p>9 primary vs. primary</p> | entry 2, table 1 15% : 0% (> 20:1 ratio) |
| | entry 11, table 1 | 79% : 0% (> 20:1 ratio) | | entry 4, table 1 52% : 0% (> 20:1 ratio) |

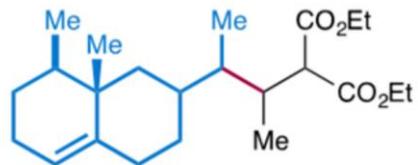
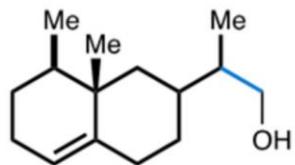
Alkoxy Radicals from visible-light-induced photoredox catalysis



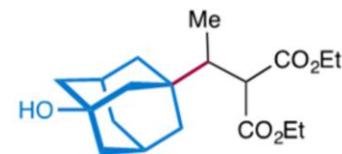
34 75% yield
1.6:1.3:1 d.r.^a



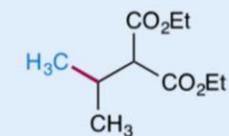
32 87% yield, 2:1 d.r.



33 67% yield, 1.2:1 d.r.

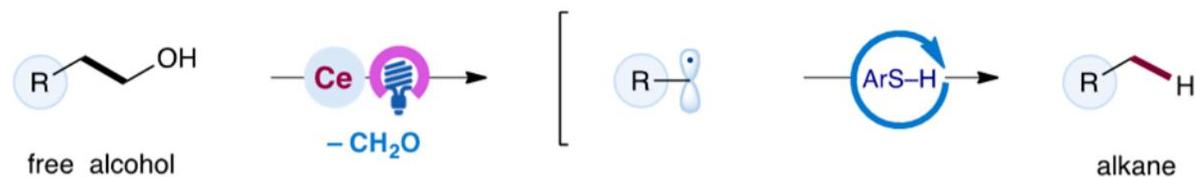


29 89% yield



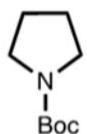
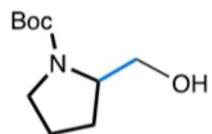
36 from EtOH, 15% yield
from *i*-PrOH, 30% yield
from *t*-BuOH, 65% yield

Alkoxy Radicals from visible-light-induced photoredox catalysis

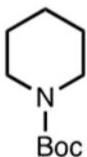
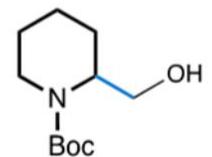


starting materials

products ^a



53 75% yield



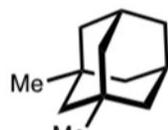
55 96% yield



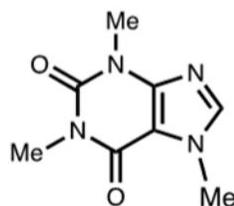
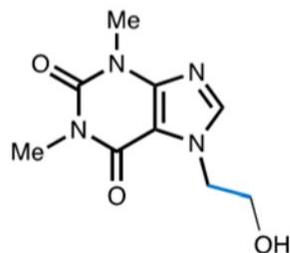
57 95% yield

starting materials

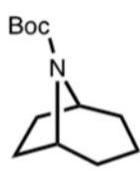
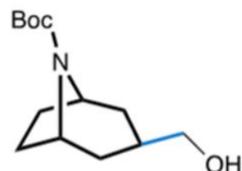
products ^a



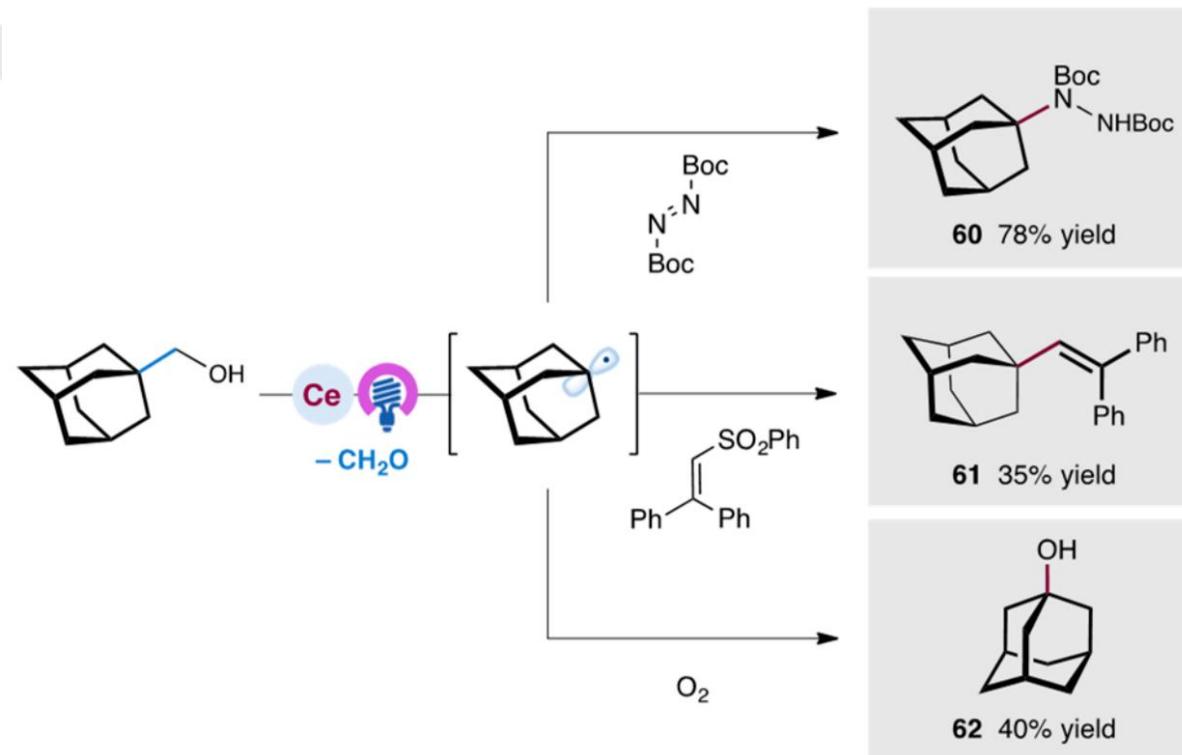
54 69% yield



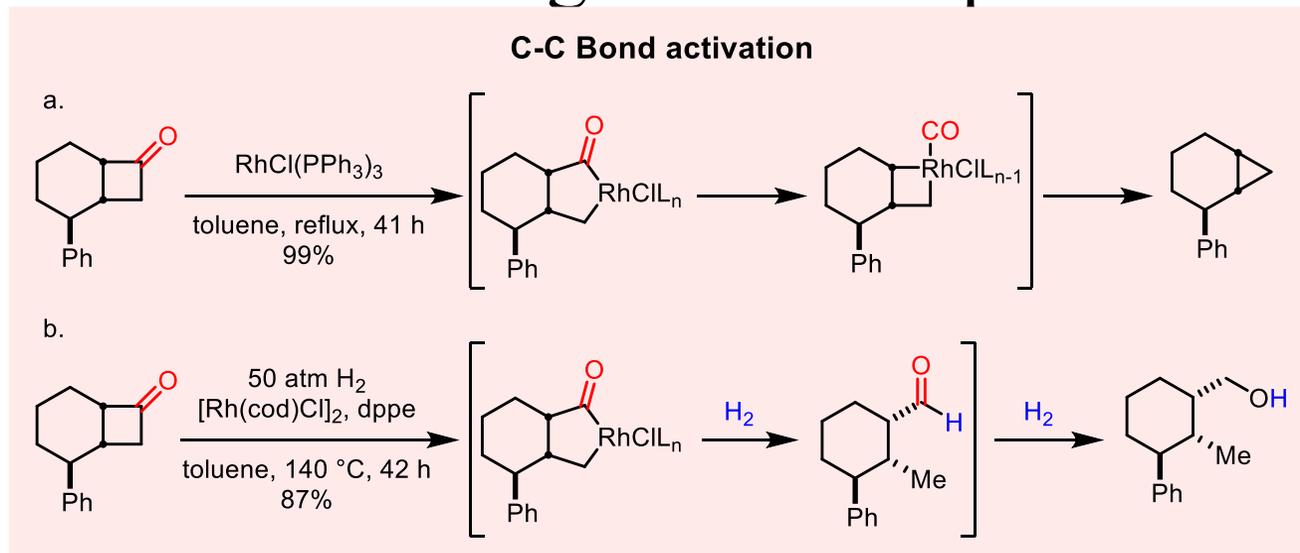
56 63% yield



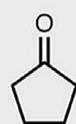
58 70% yield



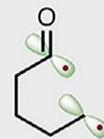
Alkoxy Radicals from visible-light-induced photoredox catalysis



Photochemistry: Norrish type I reaction, α -cleavage of excited ketones

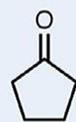


high-energy UV light

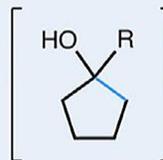


- biradical intermediate
- radical recombination
- harsh conditions

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

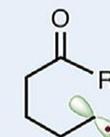


Lewis acid
catalysis



nucleophilic additions

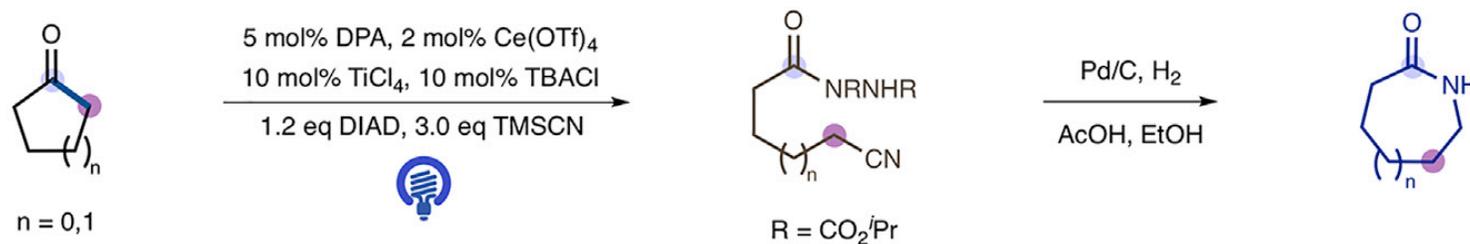
LMCT catalysis



radical cross couplings

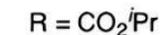
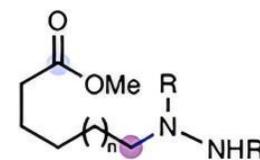
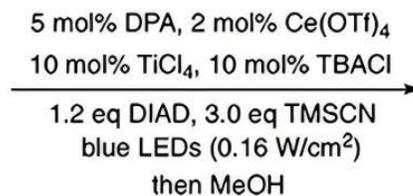
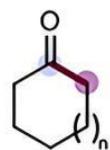
■ sequential polar- and radical-mediated functionalization

Alkoxy Radicals from visible-light-induced photoredox catalysis



| cylic ketone | product cleaved | product lactam | cylic ketone | product cleaved | product lactam | cylic ketone | product cleaved | product lactam |
|---------------------|---------------------|----------------|---------------------|---------------------|----------------|-----------------------------------|------------------------------------|----------------|
| | | | | | | | | |
| 2a 72% yield | 2b 72% yield | | 7a 75% yield | 7b 71% yield | | 12a 65% yield 10:1 d.r. | 12b 65% yield 1.5:1 d.r. | |
| | | | | | | | | |
| 3a 93% yield | 3b 93% yield | | 8a 70% yield | 8b 70% yield | | 13a 69% yield | 13b 69% yield | |

Alkoxy Radicals from visible-light-induced photoredox catalysis



cyclic ketone

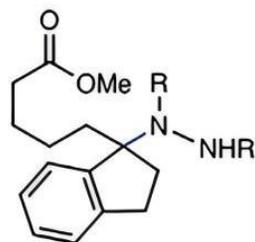
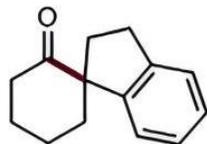
product

cyclic ketone

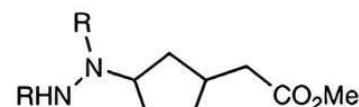
product

cyclic ketone

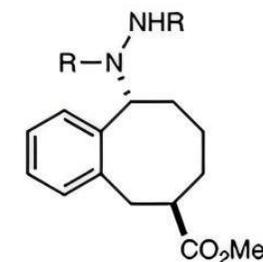
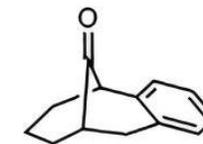
product



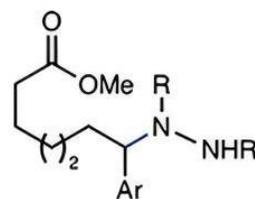
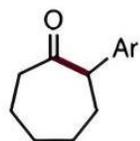
28 62% yield



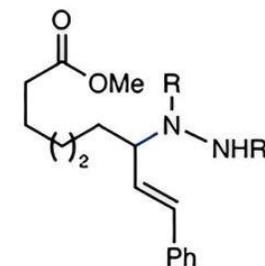
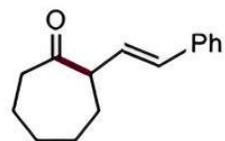
29 53% yield
d.r. 1:1



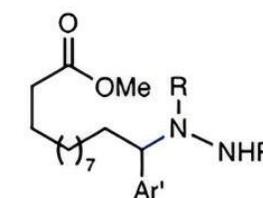
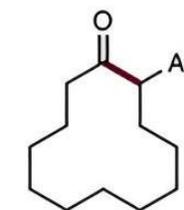
30 44% yield
d.r. 3:1



31 53% yield

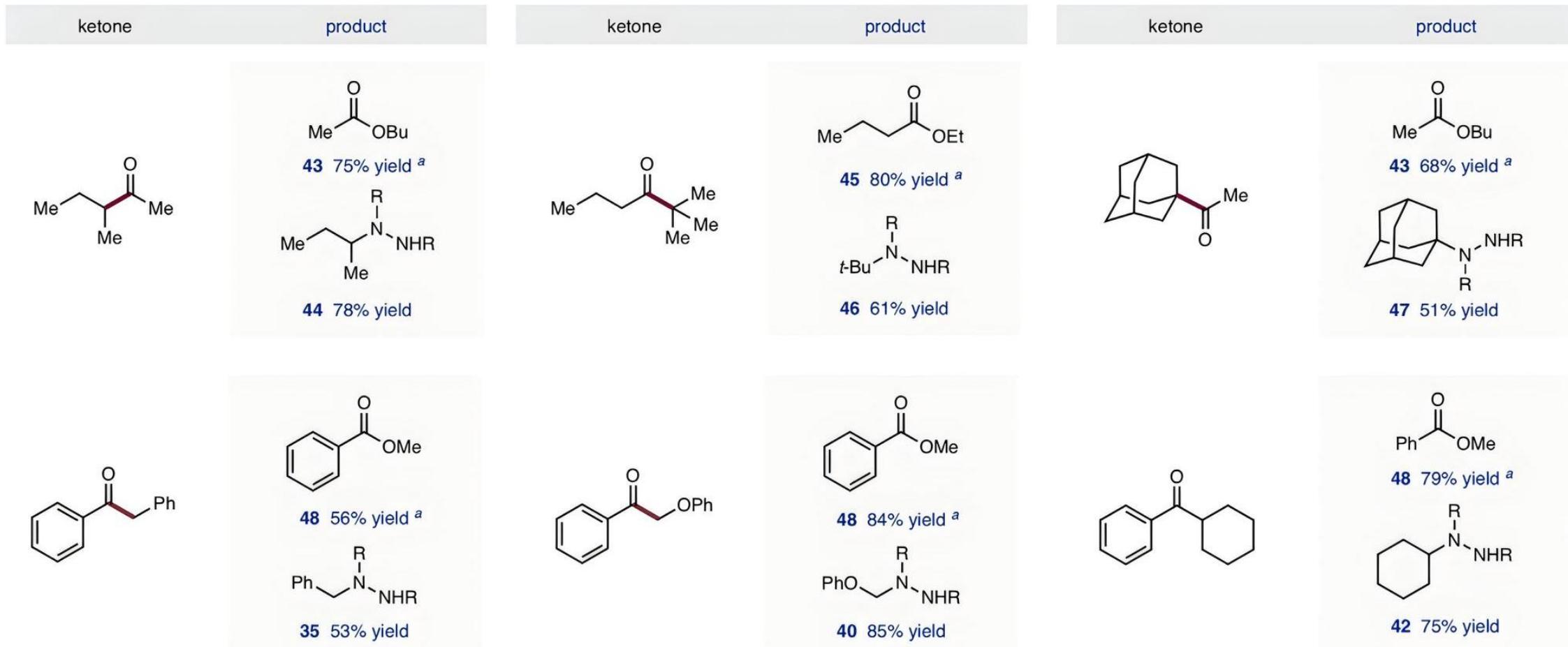
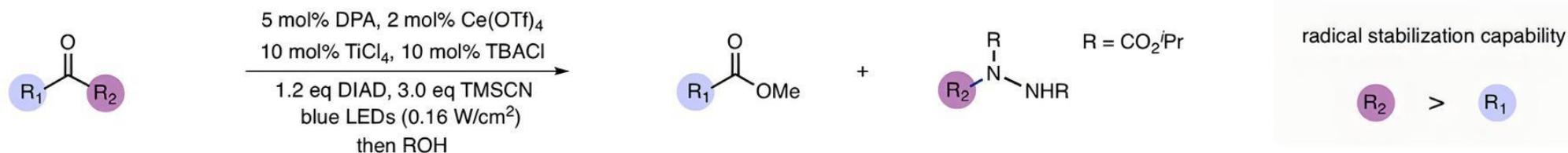


32 52% yield
r.r. 7:1

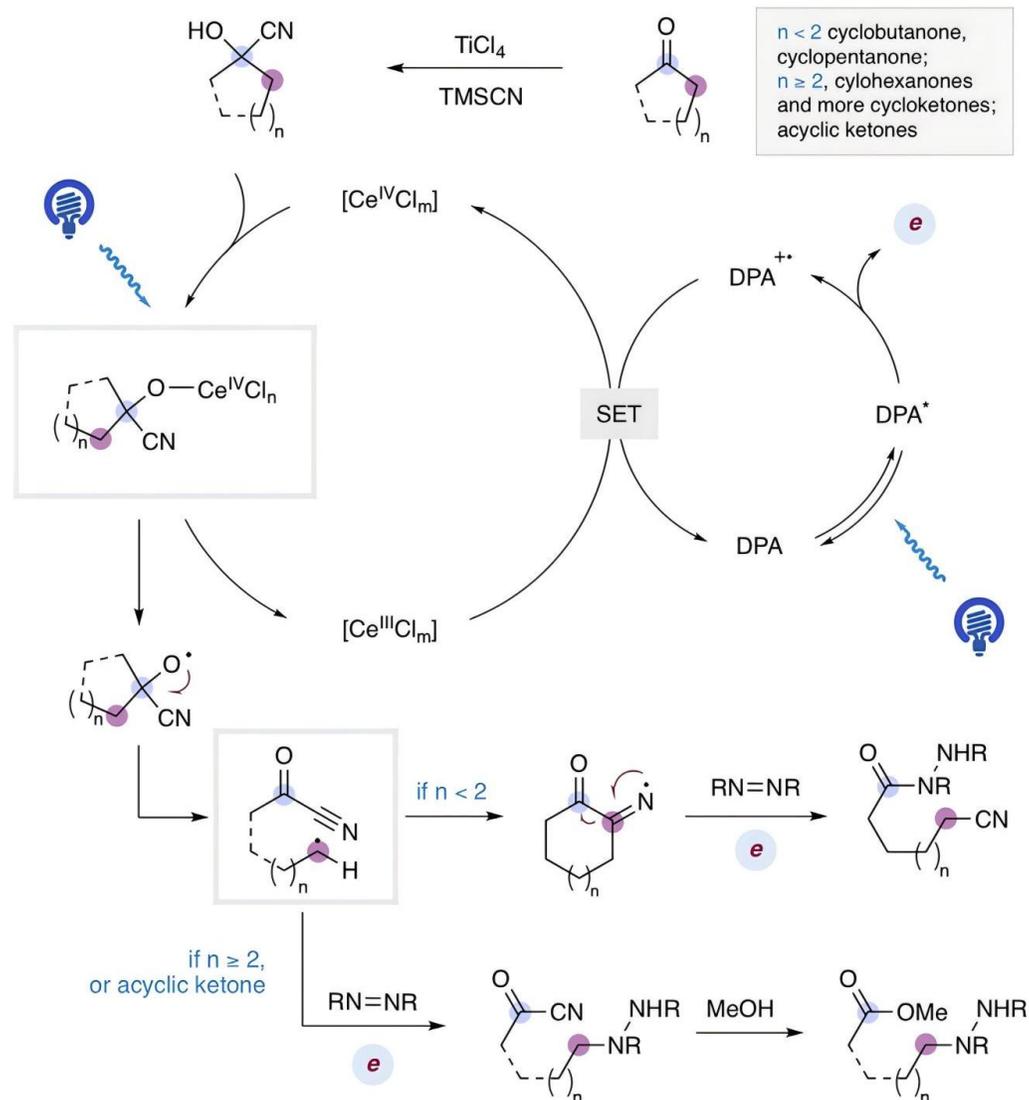


33 40% yield

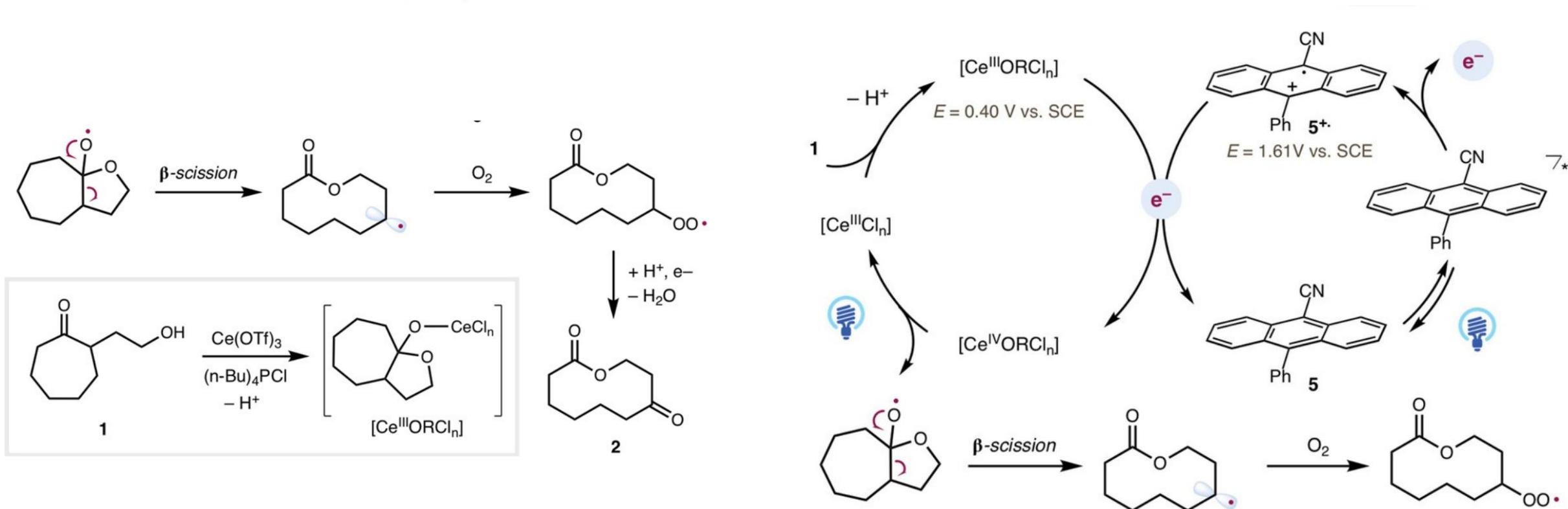
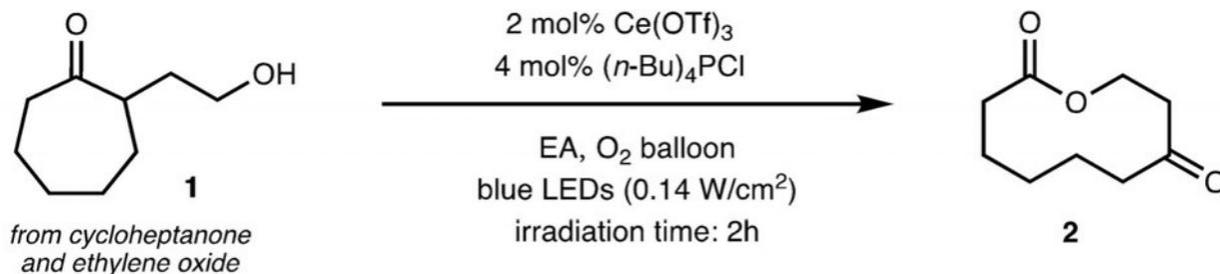
Alkoxy Radicals from visible-light-induced photoredox catalysis



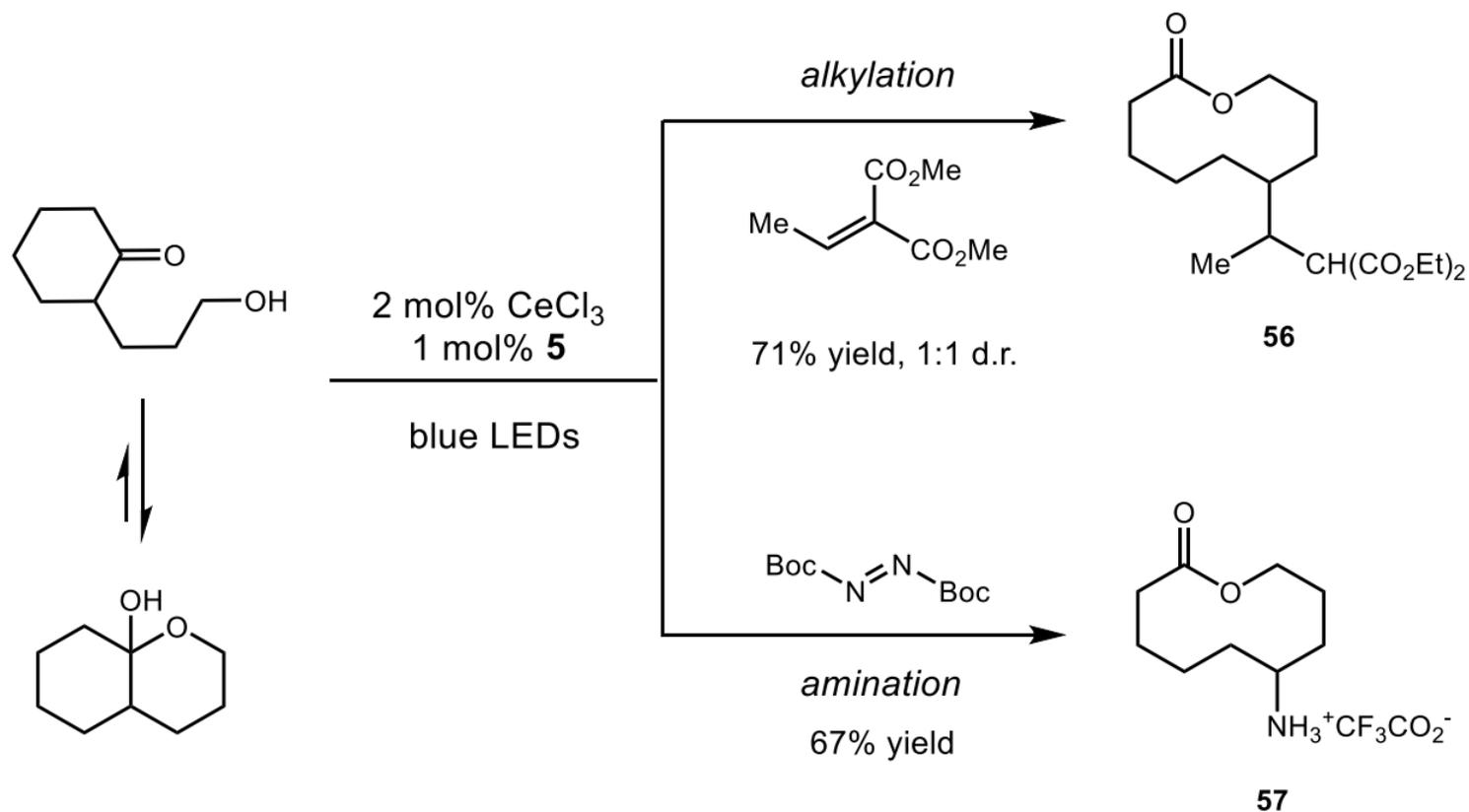
Alkoxy Radicals from visible-light-induced photoredox catalysis



Alkoxy Radicals from visible-light-induced photoredox catalysis



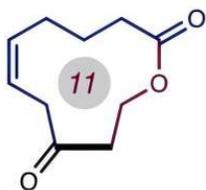
Alkoxy Radicals from visible-light-induced photoredox catalysis



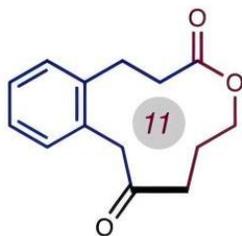
C-C bond formations, and amination using appropriate radical trapping reagents.

Alkoxy Radicals from visible-light-induced photoredox catalysis

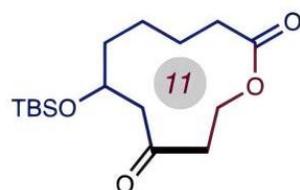
11- or higher membered lactone



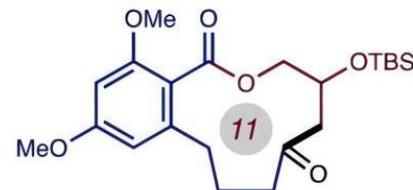
45 61% yield



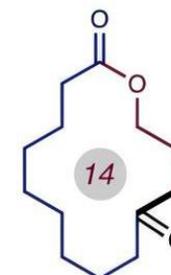
46 65% yield^a



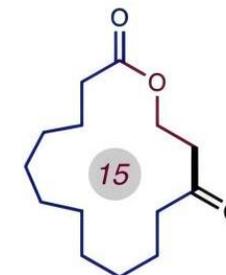
47 64% yield



48 70% yield^a

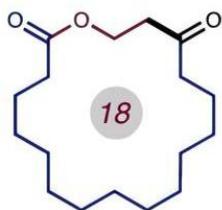


49 60% yield

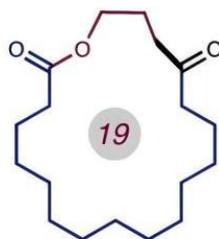


50 65% yield

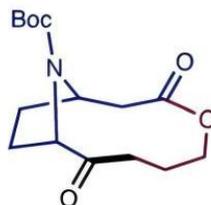
ring expansion of complex cyclic ketones



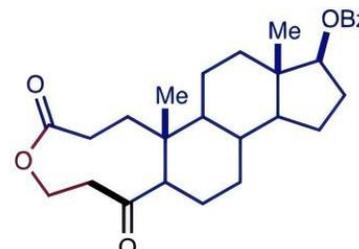
51 72% yield



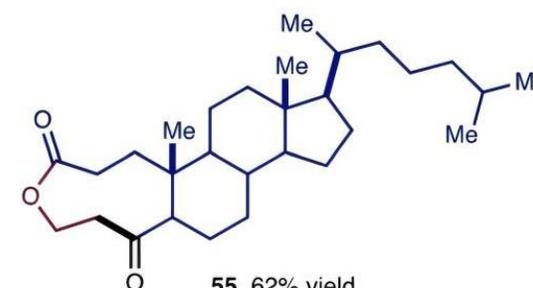
52 61% yield



53 50% yield^a

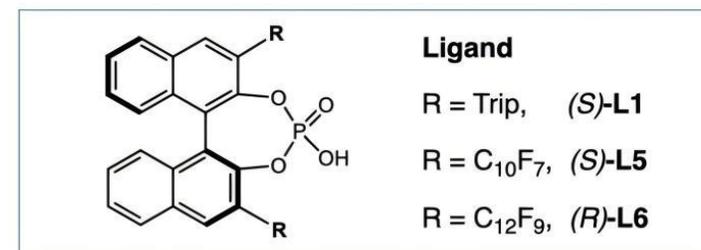
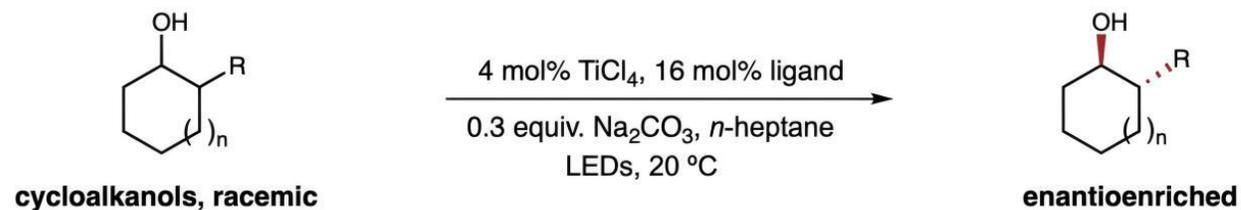


54 73% yield



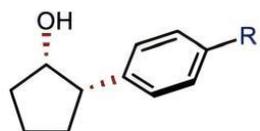
55 62% yield

Alkoxy Radicals from visible-light-induced photoredox catalysis

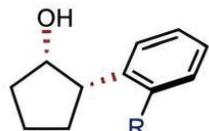


substrates with tertiary stereogenic centers

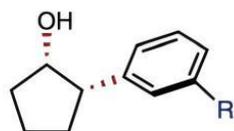
cyclopentanol*



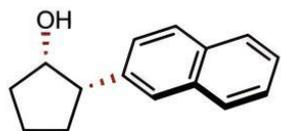
(+)-2 OMe 93%, 14:1 d.r., 98:2 er
(+)-3 SMe 91%, 9:1 d.r., 96:4 er
(+)-4 OCF₃ 95%, 4:1 d.r., 95:5 er
(+)-5 Cl 90%, 6:1 d.r., 97:3 er
(+)-6 F 96%, 6.4:1 d.r., 96:4 er



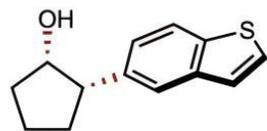
(+)-7 Me 95%, 3.2:1 d.r., 94:6 er
(+)-8 OMe 95%, 6.4:1 d.r., 92:8 er



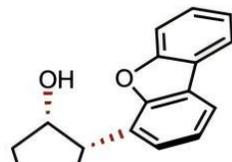
(+)-9 SMe 90%, 9:1 d.r., 98:2 er
(+)-10 F 94%, 6.5:1 d.r., 98:2 er



(+)-11
 94%, 6.5:1 d.r., 93:7 er

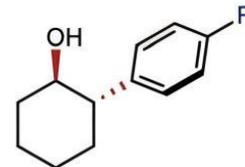


(+)-12
 93%, 9:1 d.r., 95:5 er

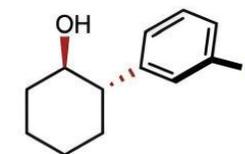


(+)-13
 93%, 13:1 d.r., 96:4 er

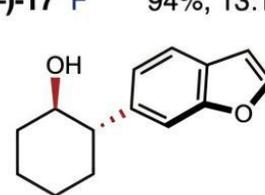
cyclohexanol†



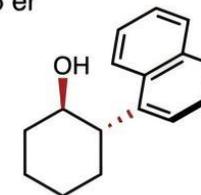
(-)-14 H 96%, 13:1 d.r., 96:4 er
(-)-15 OMe 94%, 4:1 d.r., 92:8 er
(-)-16 Cl 93%, 12:1 d.r., 94:6 er
(-)-17 F 94%, 13:1 d.r., 94:6 er



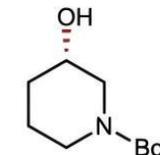
(-)-18 SMe 93%, 20:1 d.r., 93:7 er
(-)-19 Cl 91%, 20:1 d.r., 92:8 er
(-)-20 CF₃ 95%, 20:1 d.r., 91:9 er



(-)-21
 91%, 9:1 d.r., 96:4 er



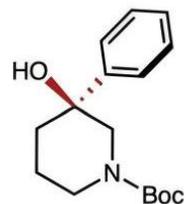
(-)-22
 97%, 9:1 d.r., 99:1 er



(+)-23 †¶
 94%, 91:9 er

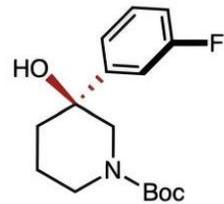
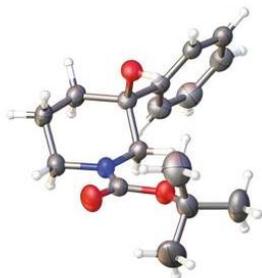
Alkoxy Radicals from visible-light-induced photoredox catalysis

substrates with fully-substituted carbons [§]



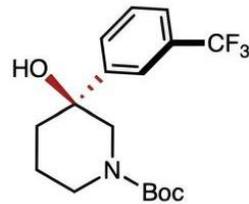
(+)-24

94%, 98:2 er



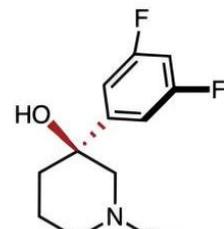
(+)-25

92%, 97:3 er



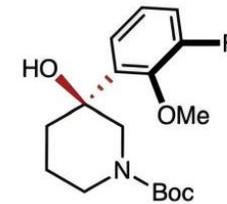
(+)-26

90%, 96:4 er



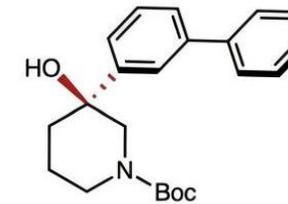
(+)-27

93%, 96:4 er



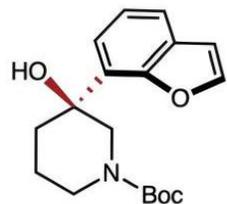
(+)-28

95%, 94:6 er



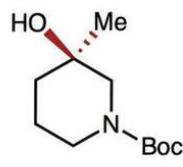
(+)-29

95%, 98:2 er



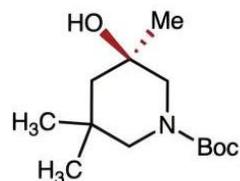
(+)-30

90%, 98:2 er



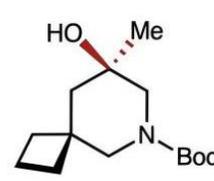
(+)-31

91%, 98:2 er



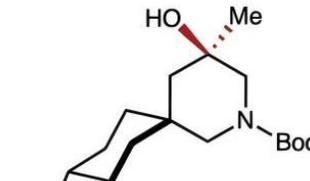
(-)-32

94%, 95:5 er



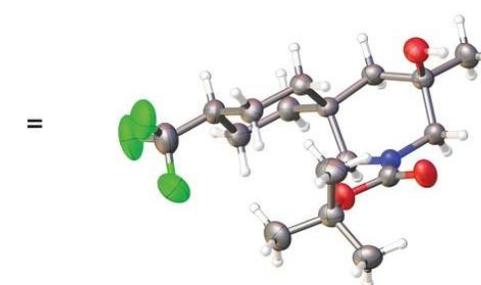
(+)-33

90%, 93:7 er

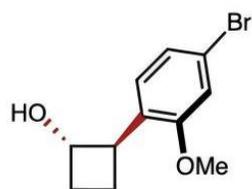


(-)-34

96%, 97:3 er

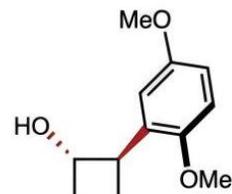


substrates with strained ring systems



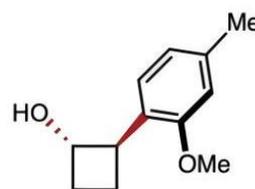
(-)-35 †

81%, 8.9:1 d.r., 93:7 er



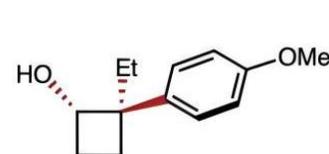
(-)-36 †

84%, 3.8:1 d.r., 92:8 er



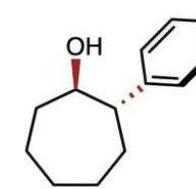
(-)-37 †

91%, 3.3:1 d.r., 91:9 er



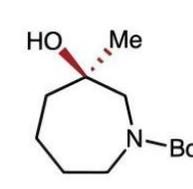
(+)-38 †#

82%, 3:1 d.r., 90:10 er



(+)-39 †

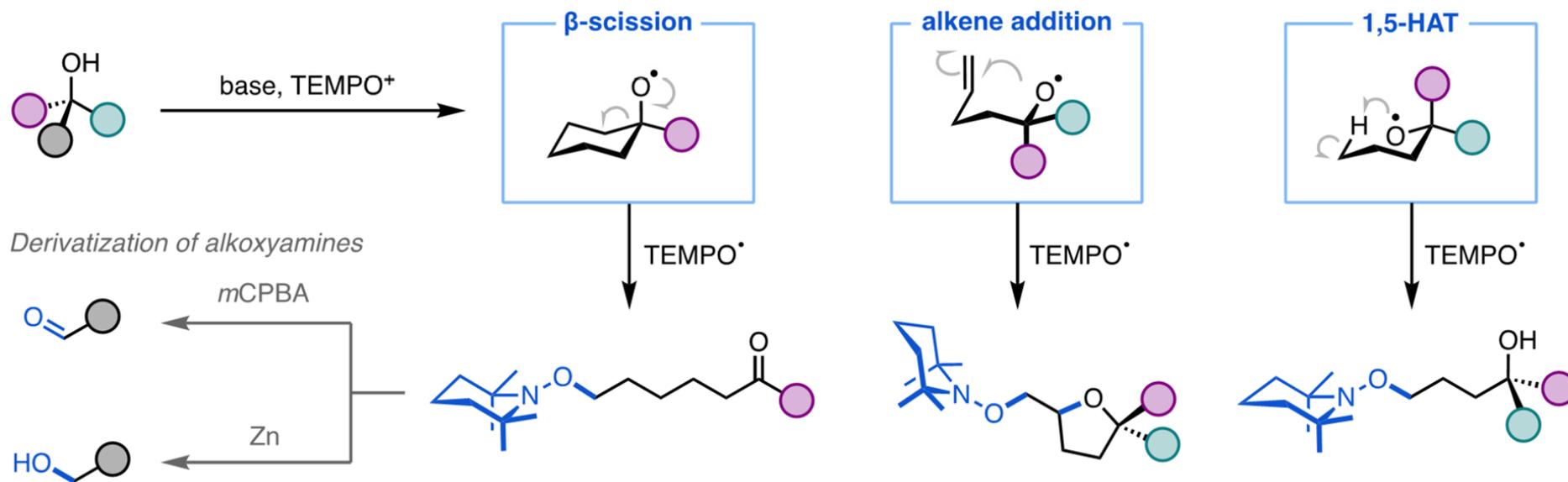
85%, 10:1 d.r., 90:10 er



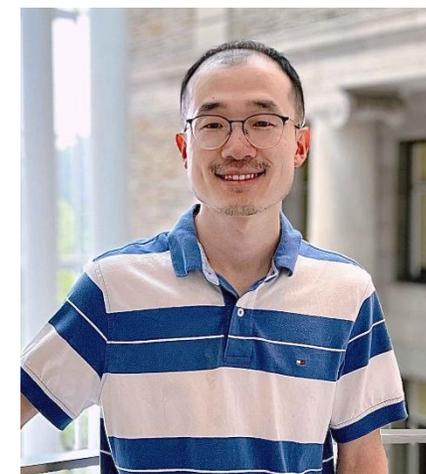
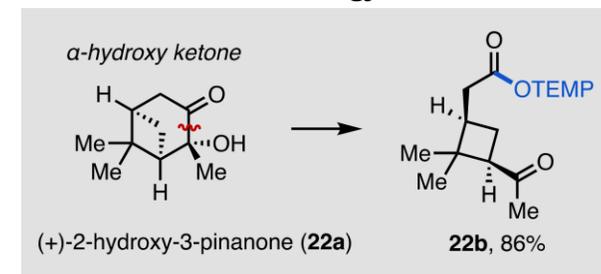
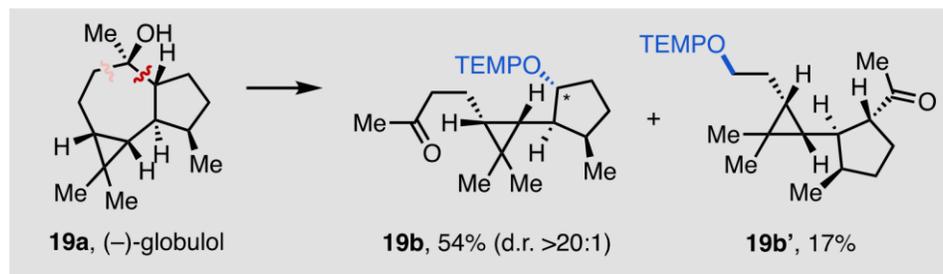
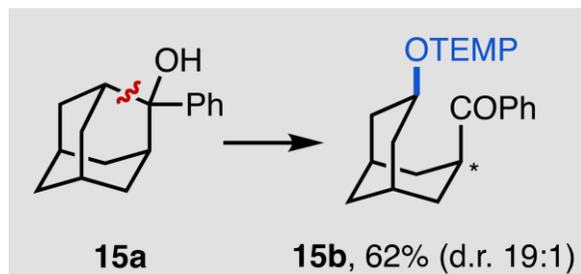
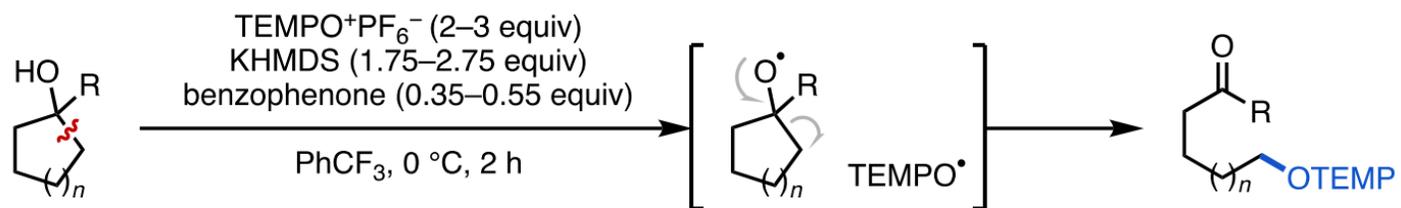
(-)-40 §#

80%, 91:9 er

Alkoxy Radicals via other methods



- Free alcohol functionalization
- Three reaction modes
- Operationally simple and scalable
- Redox derivatization of alkoxyamines



Lin Song (林松)

Cornell University

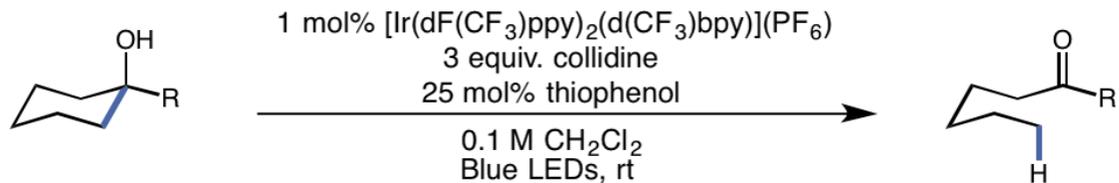
2004–2008

Peking University, B.S.

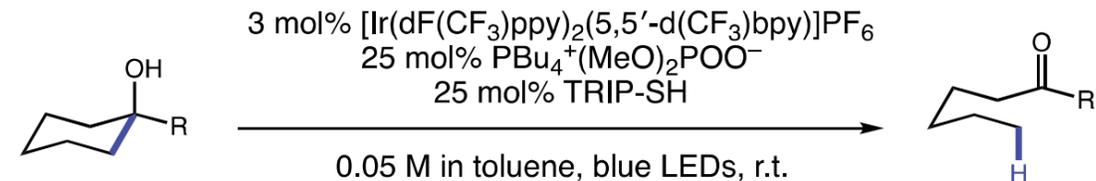
Research Advisor:

Zhangjie Shi

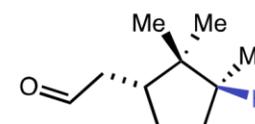
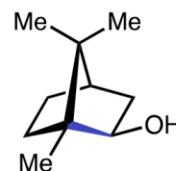
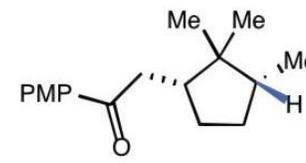
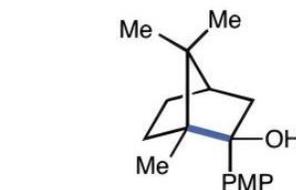
Alkoxy Radicals via other methods



J. Am. Chem. Soc. **2016**, *138*, 10794–10797.

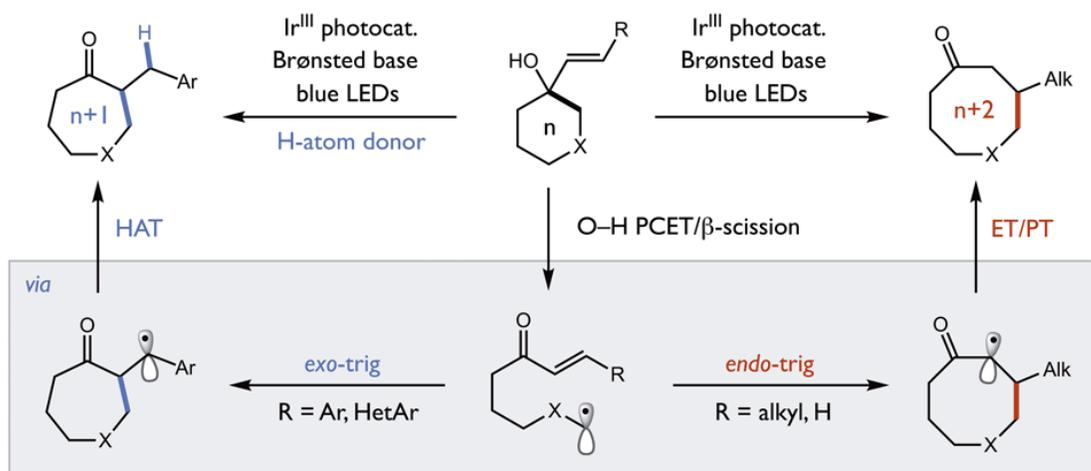


J. Am. Chem. Soc. **2019**, *141*, 1457–1462.

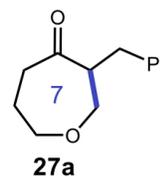
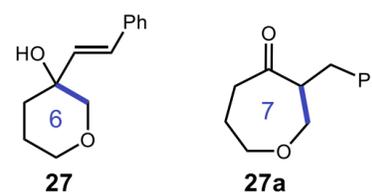


Robert Knowles

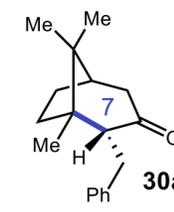
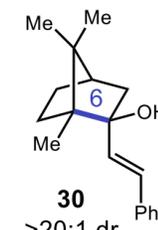
Princeton University



J. Am. Chem. Soc. **2019**, *141*, 8752–8757.



67%^j

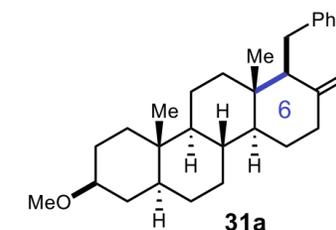
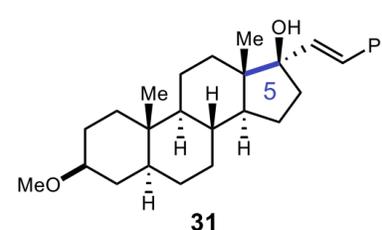


77%^{h,j}
>20:1 dr

Starting material

Product

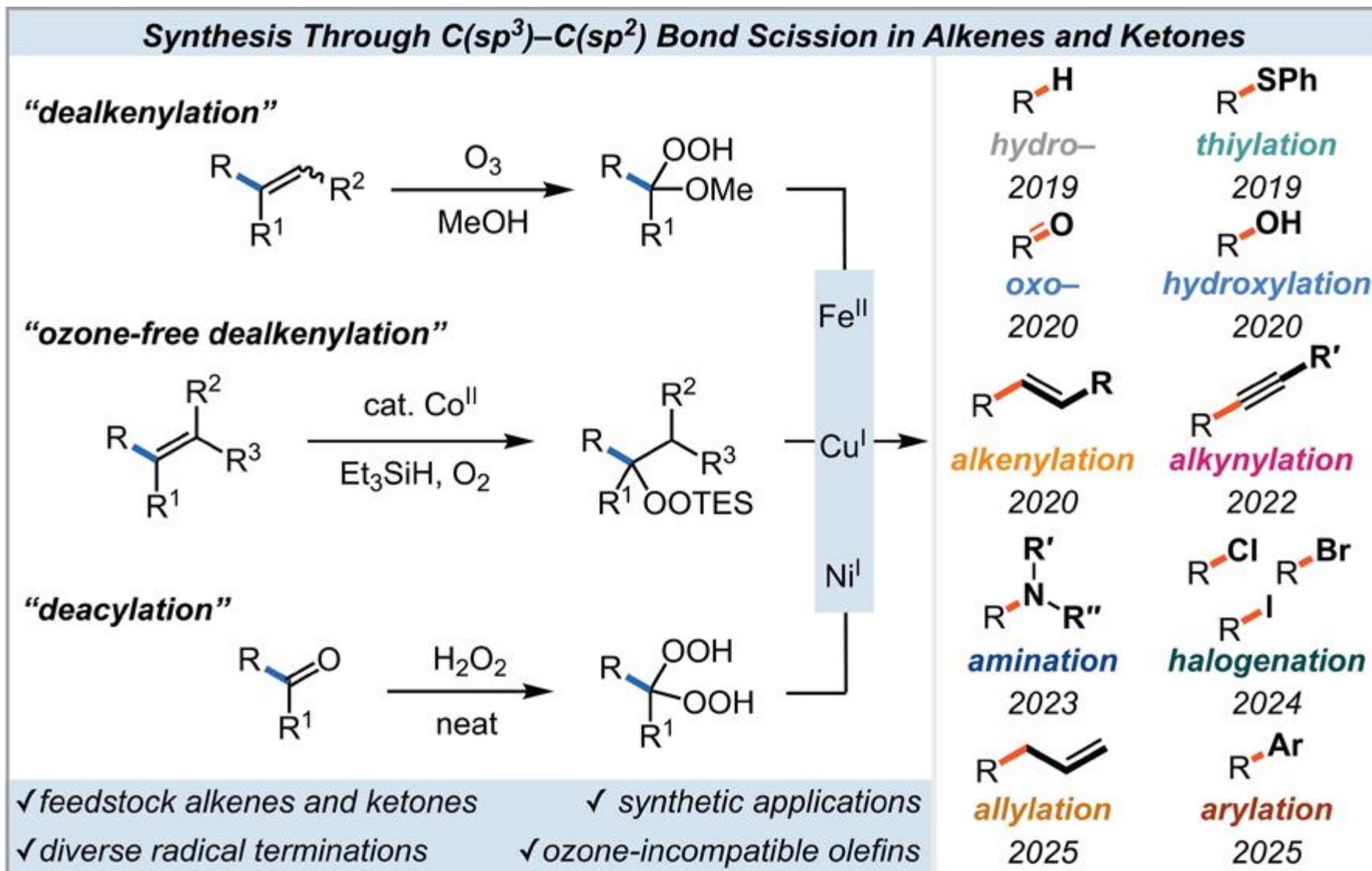
Yield



61%^{ij}
>20:1 dr

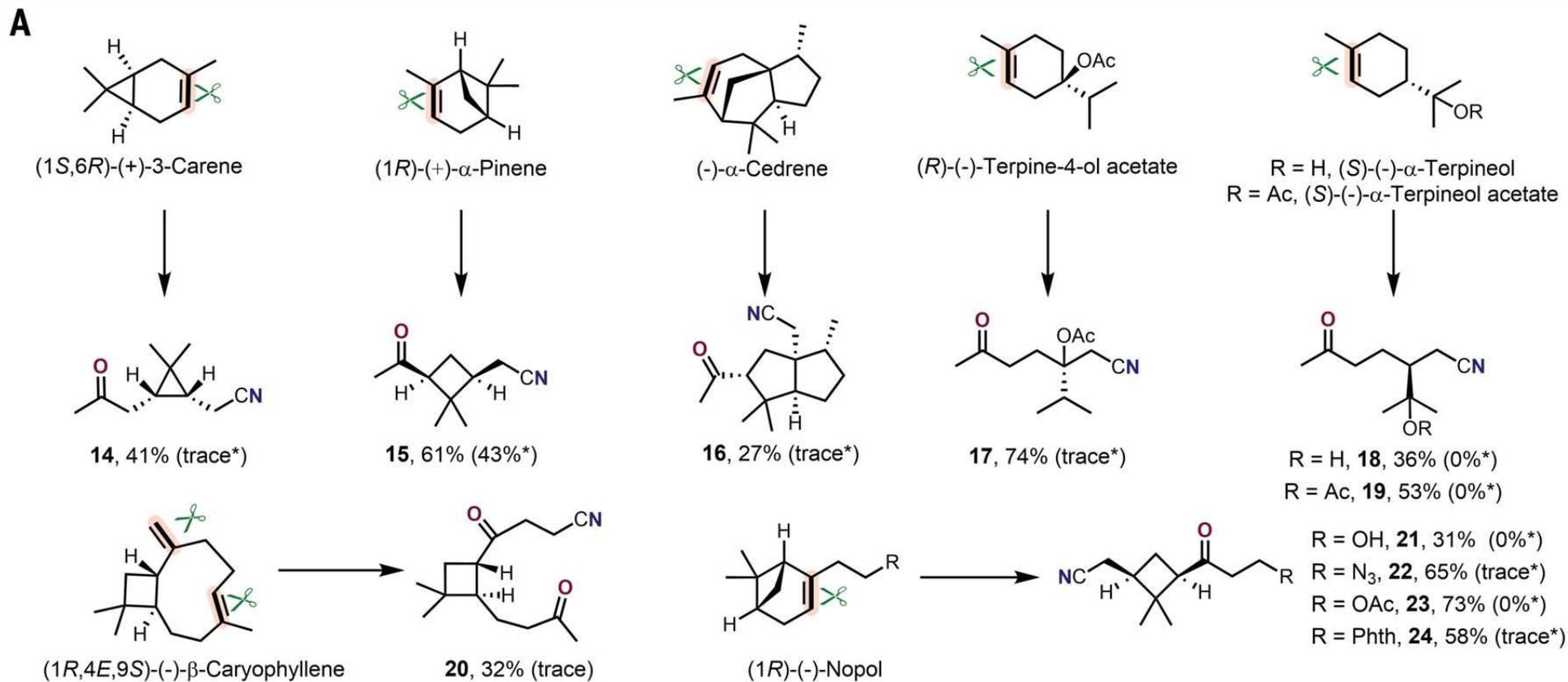
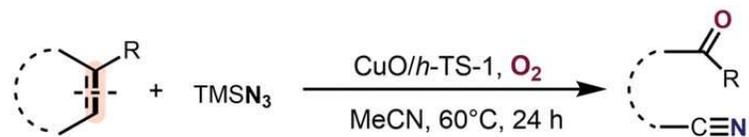
- 01 Strategies for Inert C–C bond Cleavages
- 02 C-C Bond Cleavage via Alkoxy Radical
- 03 C-C Bond Cleavage via Hidden Alkoxy Radical**

C-C Bond Cleavage via Hidden Alkoxy Radical



Ohyun Kwon
UCLA

C-C Bond Cleavage via Hidden Alkoxy Radical

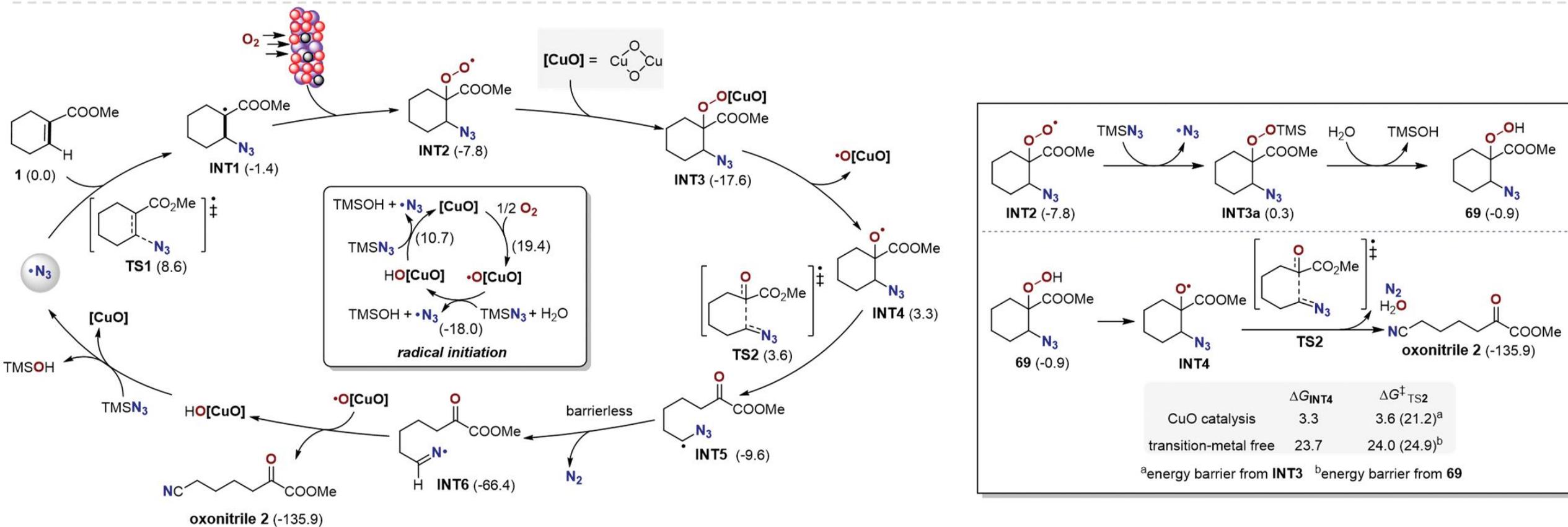


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Peking University

Science **2025**, 387, 1083–1090.

C-C Bond Cleavage via Hidden Alkoxy Radical



Science 2025, 387, 1083–1090.