Hydrogen Atom Transfer (HAT) Reactivity in Excited-State Molecules

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College of Chemistry and Molecular Engineering, PKU
July 15th 2023

Outline

- **Introduction**
  - Scope and significance
- **Mechanistic aspect of excited-state HAT reactivity**
  - From LMCT states
  - From n/π→π* states
- **Applications: direct C-H functionalization reactions**
  - Oxometal complexes
  - Organic molecules
- **Summary**

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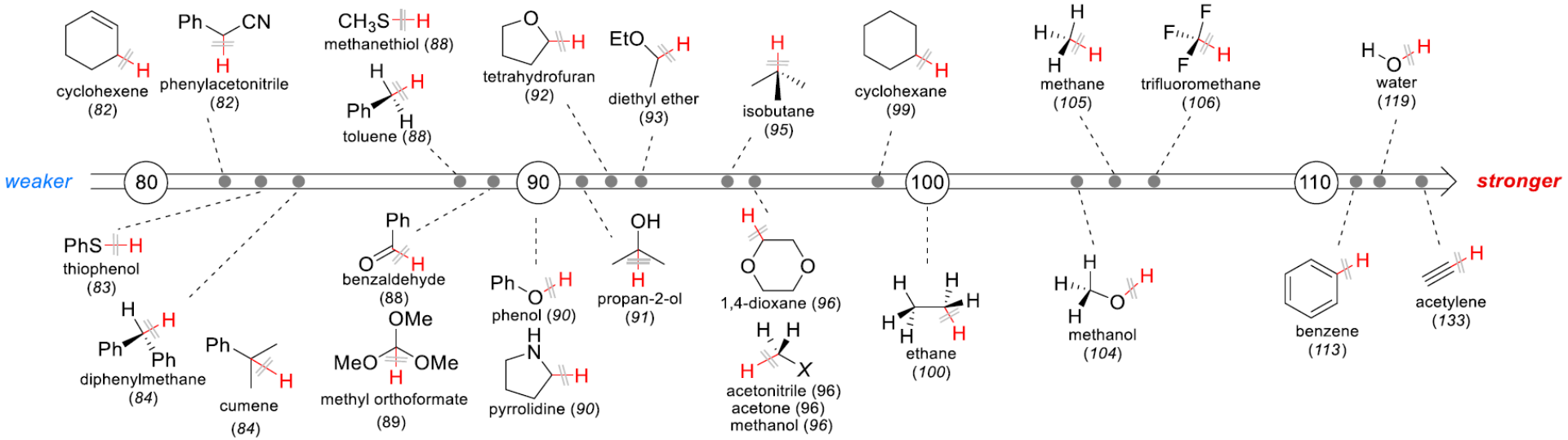
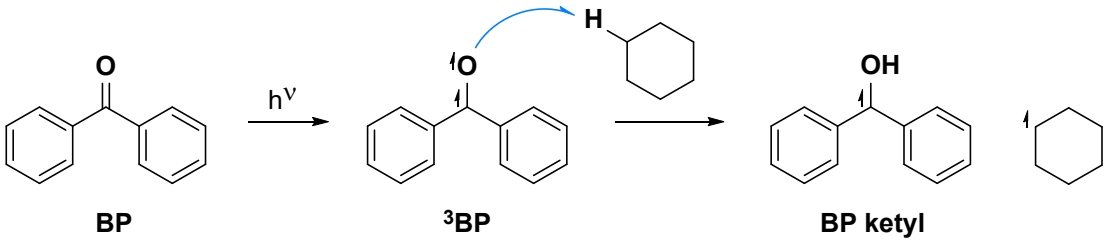
BDEs



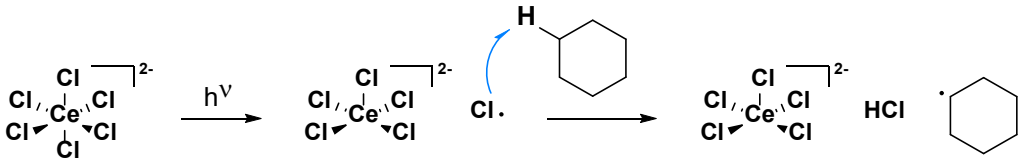
Fagnoni. M. *et al. Chem. Rev.* **2022,** *122*, 1875.

Scope of this report

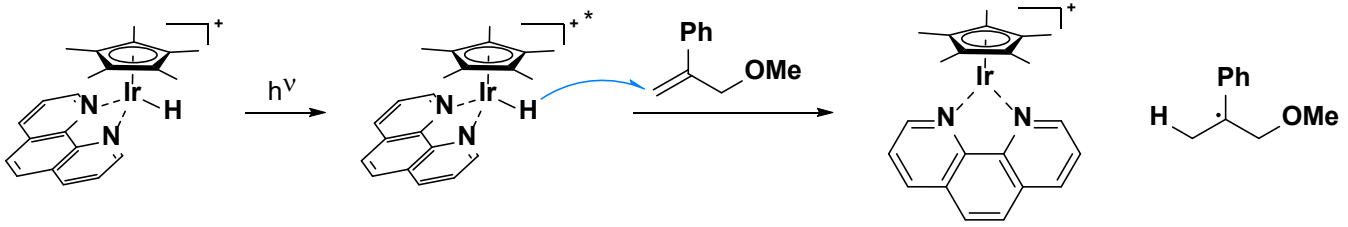
- Included in this report: direct **intermolecular** HAT (*d*-HAT) reactivity in excited state



- Not included in this report:
  - Photoinduced homolysis and subsequent HAT



  - Excited-state MHAT

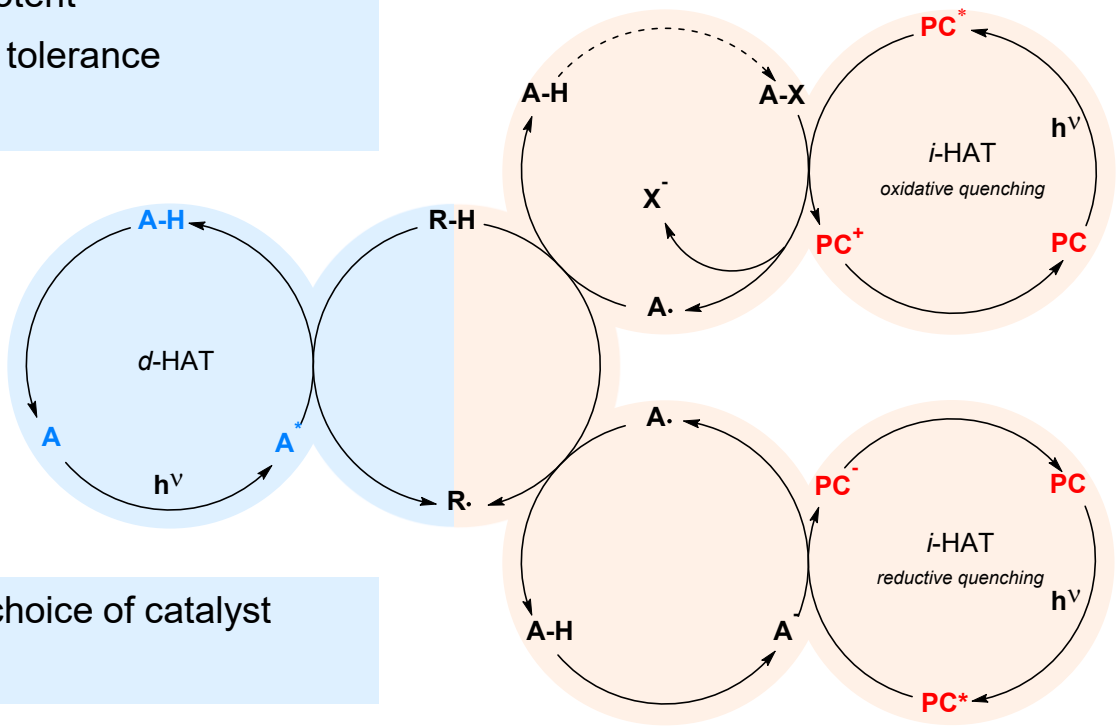


Wenger, O. S. *et al. Chem. Sci.*, **2020**, *11*, 8582.

Photocatalytic *d*-HAT vs. *i*-HAT

+ Clean reaction
+ Less likely side reactions
+ Highly potent
+ High FG tolerance
+ …

- Limited choice of catalyst
- …



+ Highly potent
- Waste production
- Side reactions
- …

+ High tunability
- Energy loss
- FG tolerance
- …

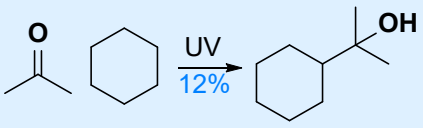
Wu, J. *et al. Chem. Catal.* **2021,** *1,* 523.

A brief timeline

1909, E. Paternò

Photo-reduction of aryl ketones by hydrocarbon

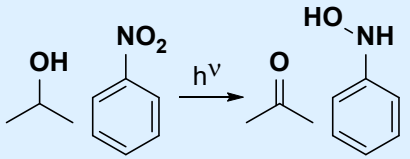
1958, N. C. Yang



1960s

Photo-reduction of aryl ketones by ethers, amines, phenols, thiols, alcohols

1966, A. C. Testa



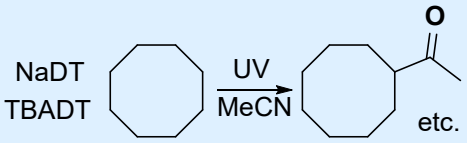
1995, A. Bakac

Quenching experiments of UO_2^{2+} by different hydrocarbons

1995, Hill

DT^{4-} catalyzed alkane functionalization

1988, Hill



1970s

$Ru(bpy)_3^{3+} + e \rightarrow Ru(bpy)_3^{2+*}$

$Ru(bpy)_3^{2+*} + e \rightarrow Ru(bpy)_3^{+}$

2000s

Systematic development of photocatalytic *d*-HAT in aliphatic C-H functionalization

2010s

Prosperous of photocatalytic *i*-HAT in aliphatic C-H functionalization

2018, J. Wu

HAT reactivity in excited neutral eosin Y

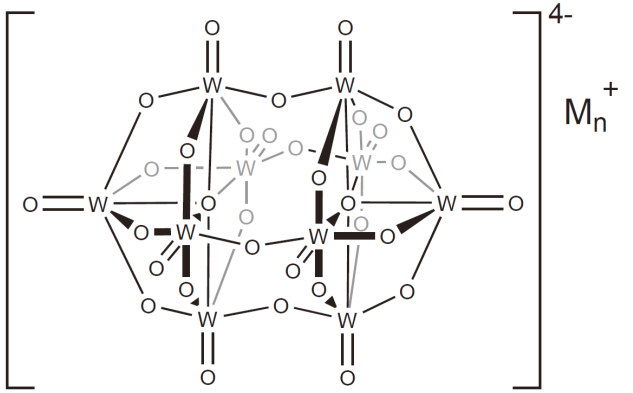
2022, J. Wu

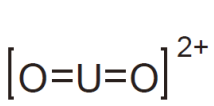
Acid enhanced HAT reactivity of various d-HAT catalysts

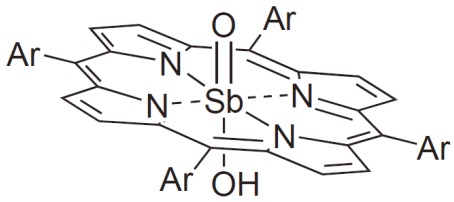
Hill, C. L. *et al. J. Am. Chem. Soc.* **1988,** *110*, 5461.
Yang, N. C. *et al. J. Am. Chem. Soc.* **1958,** *80*, 2913.
Fagnoni, M. *et al. Chem. Rev.* **2022,** *122*, 1875.
Wu, J. *et al. Chem. Catal.* **2021,** *1,* 523.

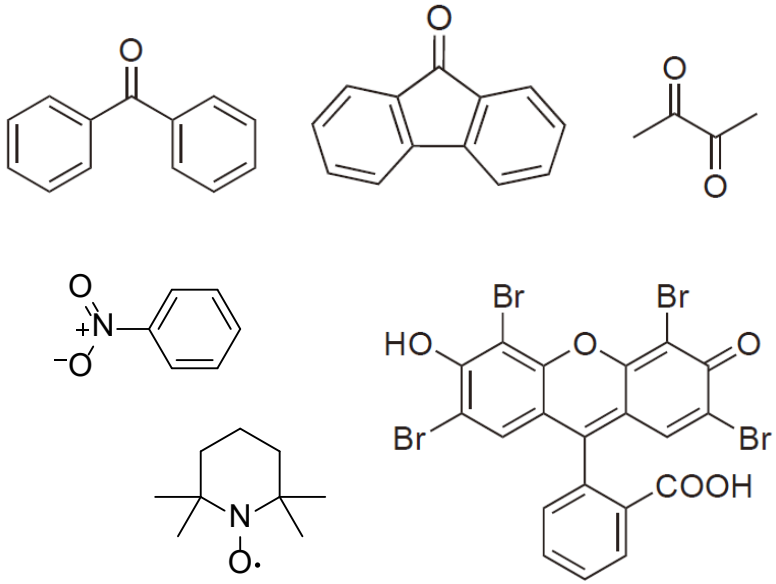
The fundamental principle

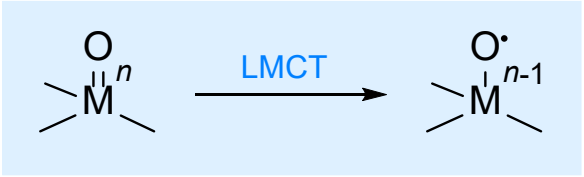
- Generation of transient electrophilic radical
  - LMCT state in Metal-oxo complexes
  - n→π* states in X=O functionality

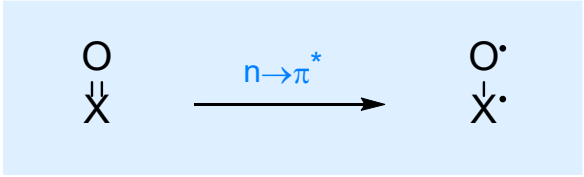












Wu, J. *et al. Chem. Catal.* **2021,** *1,* 523.

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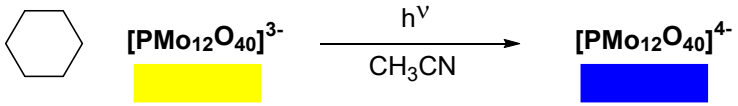
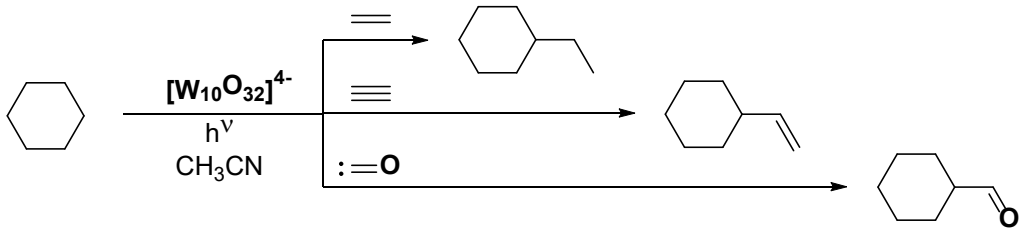
- Acknowledgement

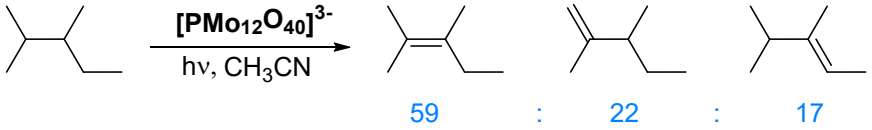
Oxometal complexes

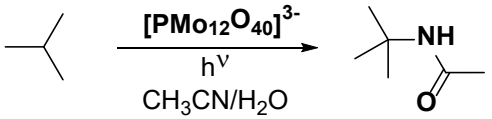
- Polyoxometalates (POMs)

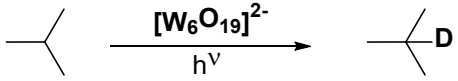


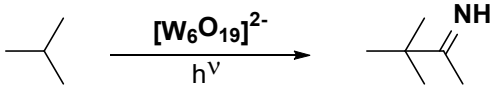
- High reactivity, selectivity with novel reaction modes







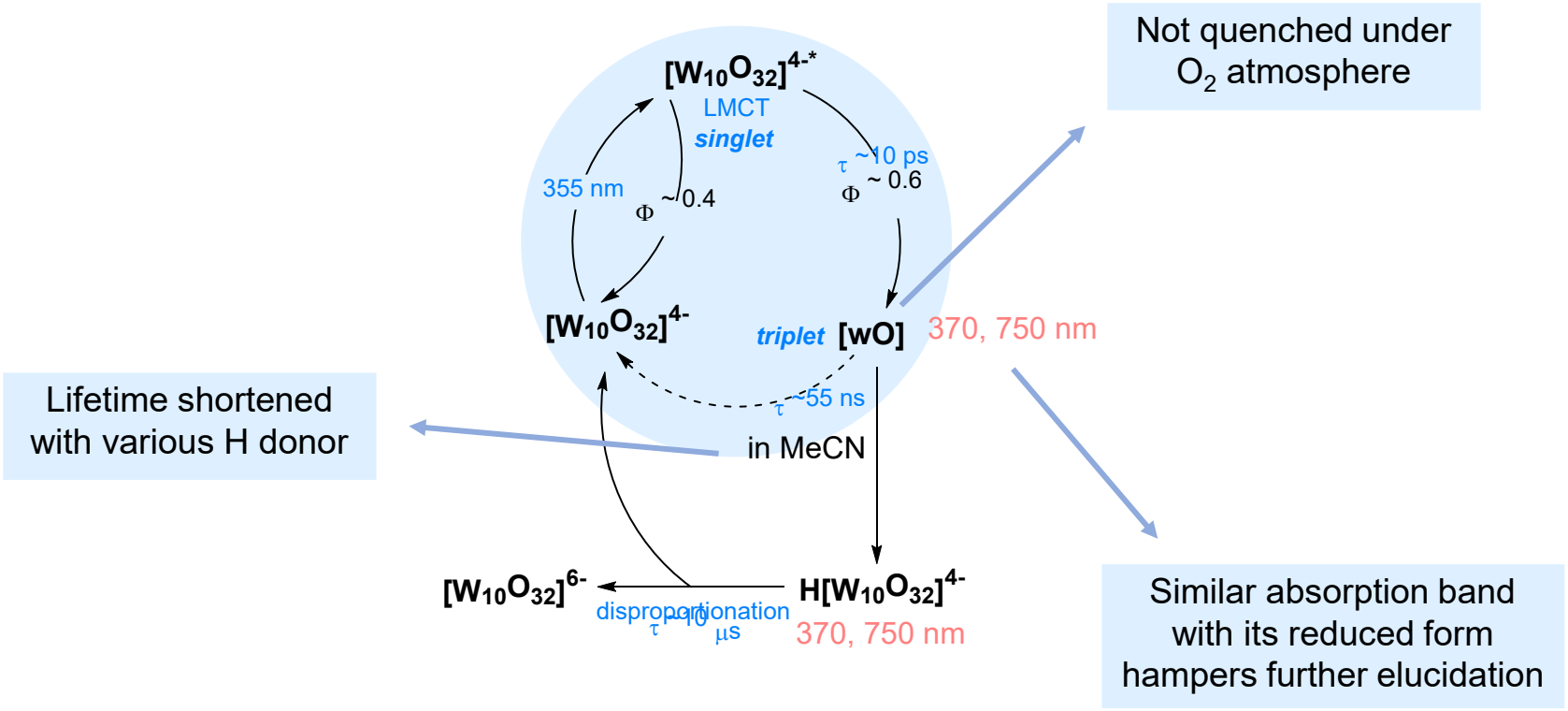




Hill, C. L. *Synlett.* **1995**, *1995*, 127.

Mechanism studies

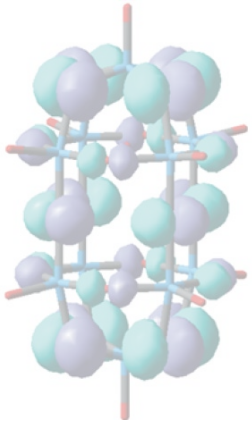
- Extensive kinetic studies revealed the key reactive state of DT^{4-}



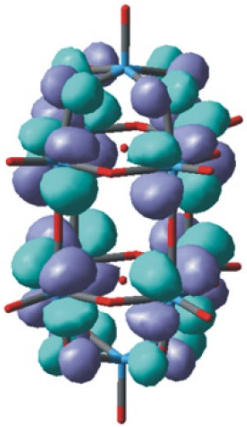
Tanielian, C. *et al. Coord. Chem. Rev.*, **1998**, *178*, 1165.

The mysterious [wO]

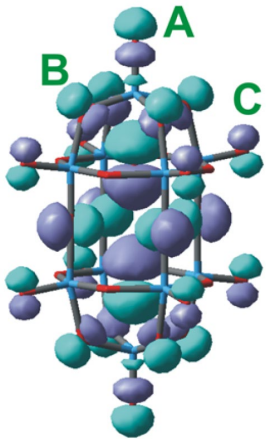
- Theoretical insights



HOMO



LUMO



HOMO-1

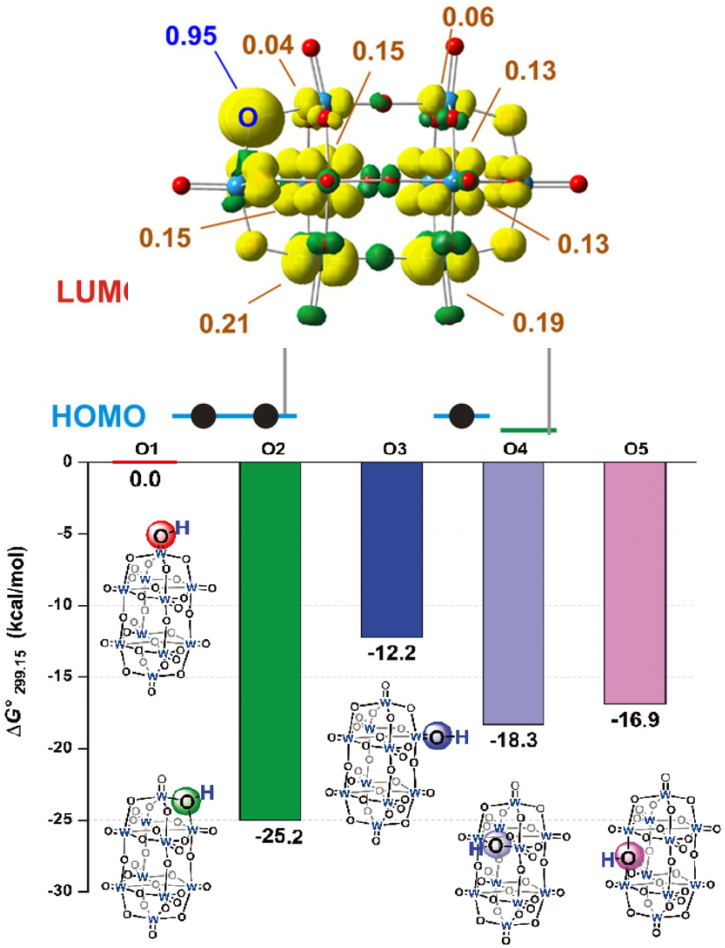
Contribution:

A > B > C

E_{red} (wO/$[W_{10}O_{32}]^{4-}$)

= +2.44 V

- Another version

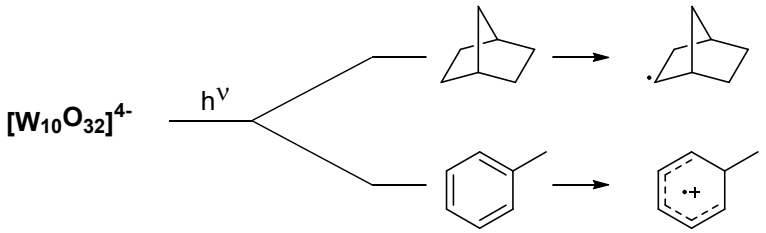


Ravelli, D. *et al. ACS Catal.* **2016**, *6*, 7174.

Su, Z. M. *et al. Inorg. Chem.* **2021**, *60*, 18706.

Features in [wO] HAT process

- Thermodynamics



ΔG_{calc} = -16 kcal mol^{-1}

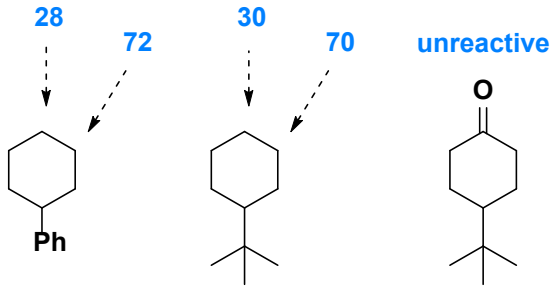
ΔG_{calc} = -23 kcal mol^{-1}

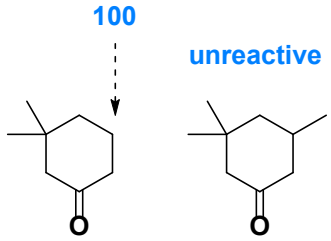
- Kinetics

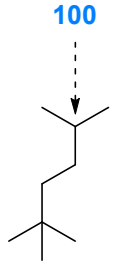
hydrogen acceptor	$k_{R\text{-}H}$ ($M^{-1}\cdot s^{-1}$)
TBADT*	4×10^7
Ph_2CO*	7.2×10^5
xanthone*	8.8×10^5
*t*BuO$^\bullet$	9.6×10^5
BnO$^\bullet$	1.3×10^6
CumO$^\bullet$	$1.1–1.2 \times 10^6$

hydrogen donor	$k_{R\text{-}H}$ ($M^{-1}\cdot s^{-1}$)
CH_3CN	6.5×10^4
$CHCl_3$	2.5×10^6
cyclopentane	2.4×10^7
cyclohexane	4×10^7
cycloheptane	5.6×10^7
$(CH_3)_2CHOH$	1.0×10^8
$PhCH_2OH$	2.8×10^8

- Selectivity



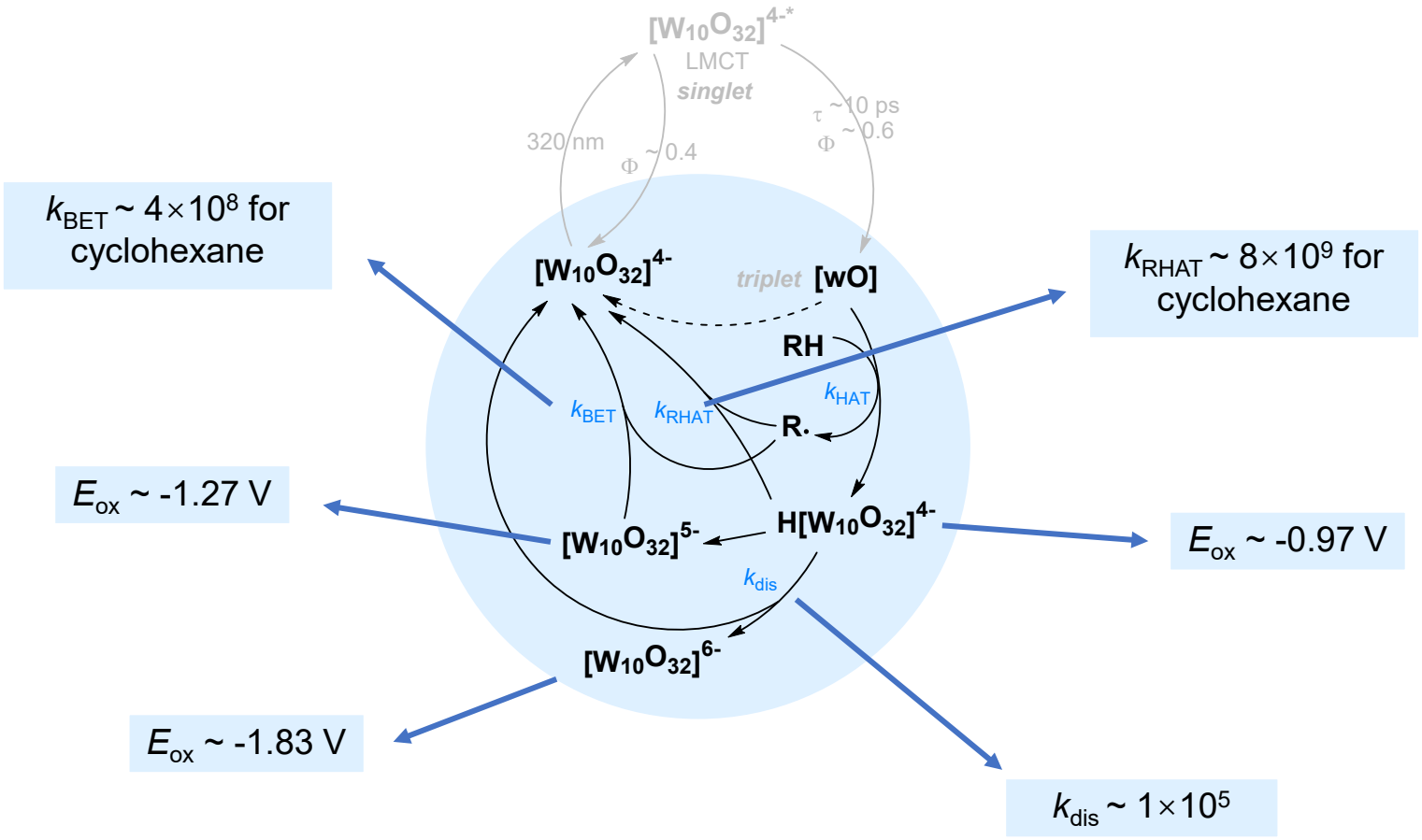




Fagnoni, M. *et al. ACS Catal.* **2018**, *8*, 701.

Closing the cycle

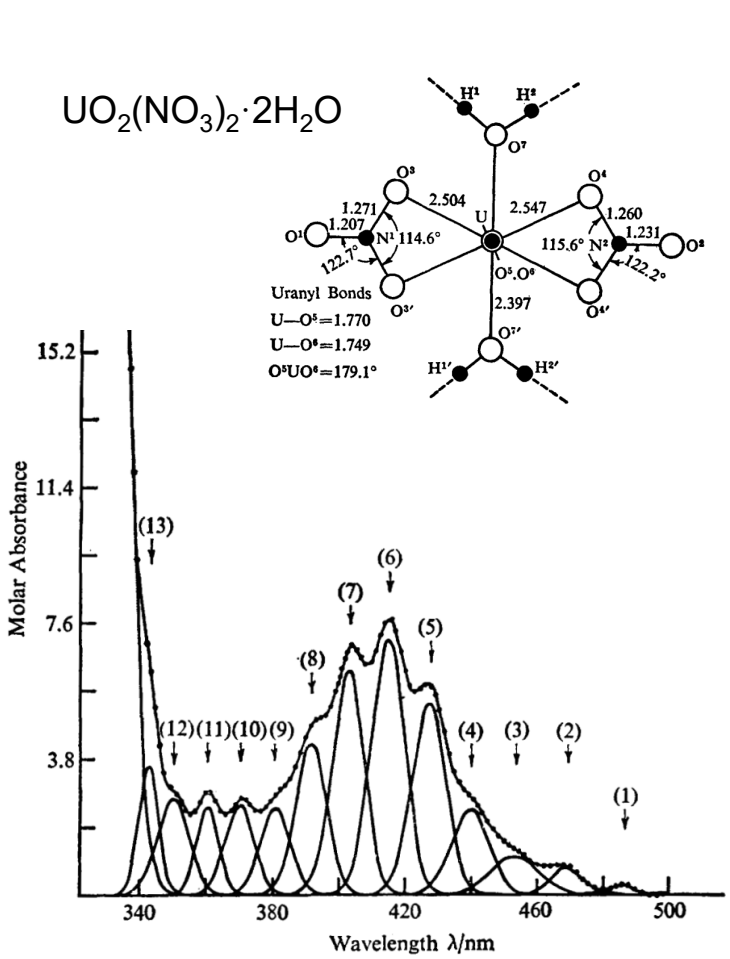
- Three main pathways to close the cycle

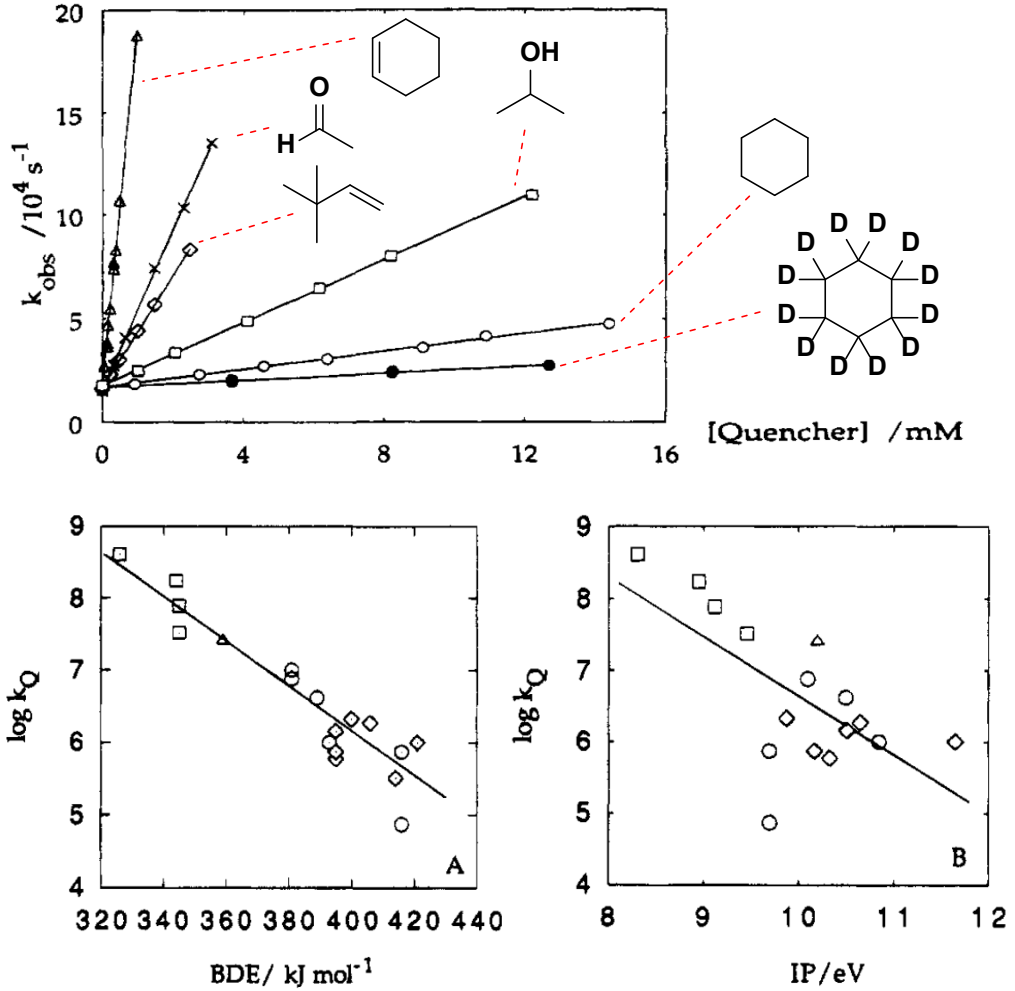


Albini, A. *et al. Chem. Eur. J.* **2006**, *12*, 4153.
Hill, C. L. *et al. J. Am. Chem. Soc.* **1990**, *112*, 6585.

Other oxometal complexes

- U can activate C-H bonds

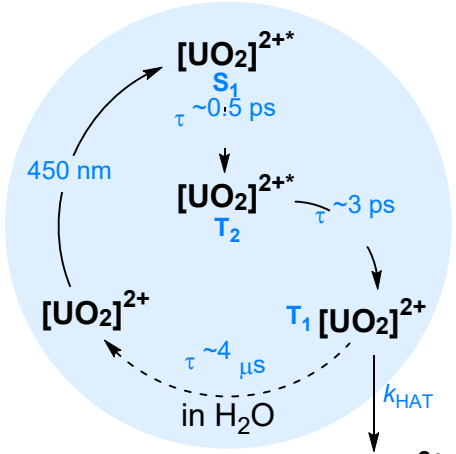




Kemp, T. J. *et al. Chem. Soc. Rev.* **1974**, *3*, 139.
Bakac, A. *et al. Inorg. Chem.* **1995**, *34*, 6034.

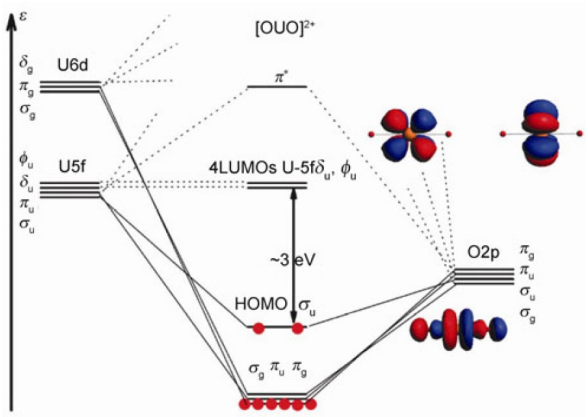
Uranyl ion

- Kinetics

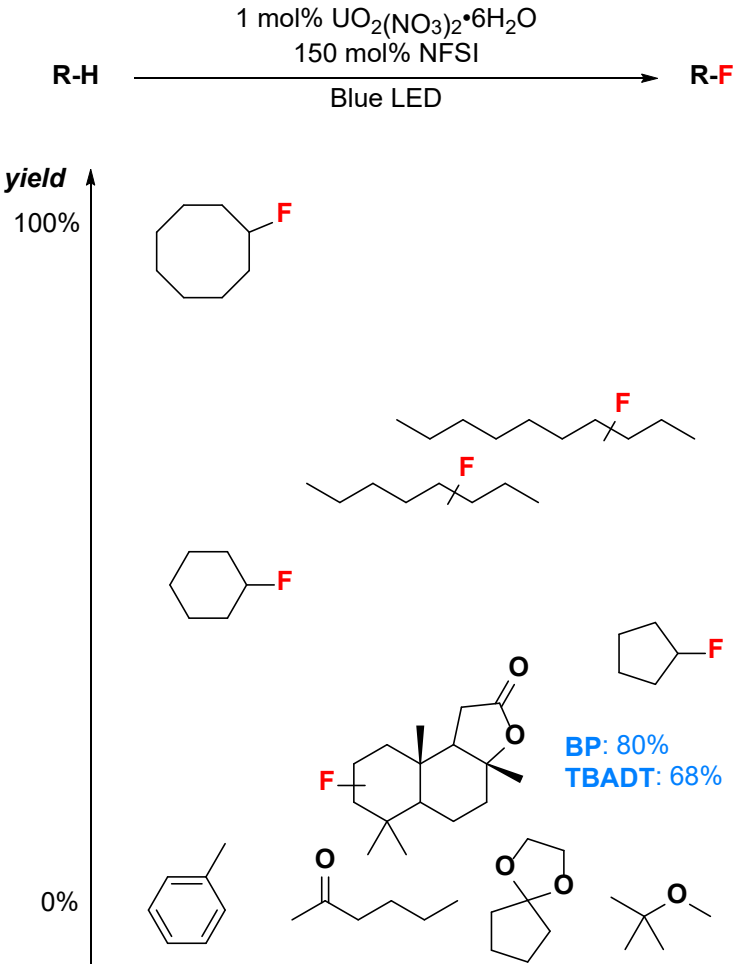


E_{red} = +2.38 V

E_{ox} ~ +0.1 V



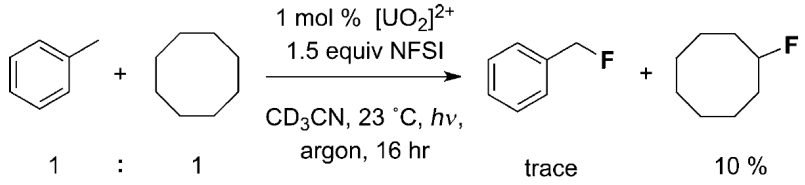
- Unique selectivity

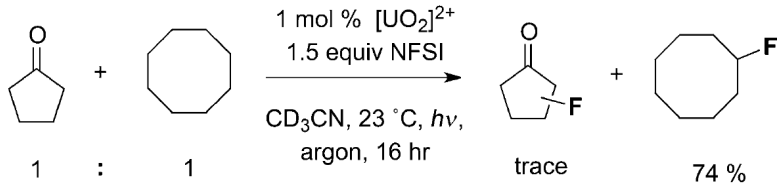


Sorensen, E. J. *et al. Angew. Chem. Int. Ed.* **2016**, *55*, 8923 and references therein.

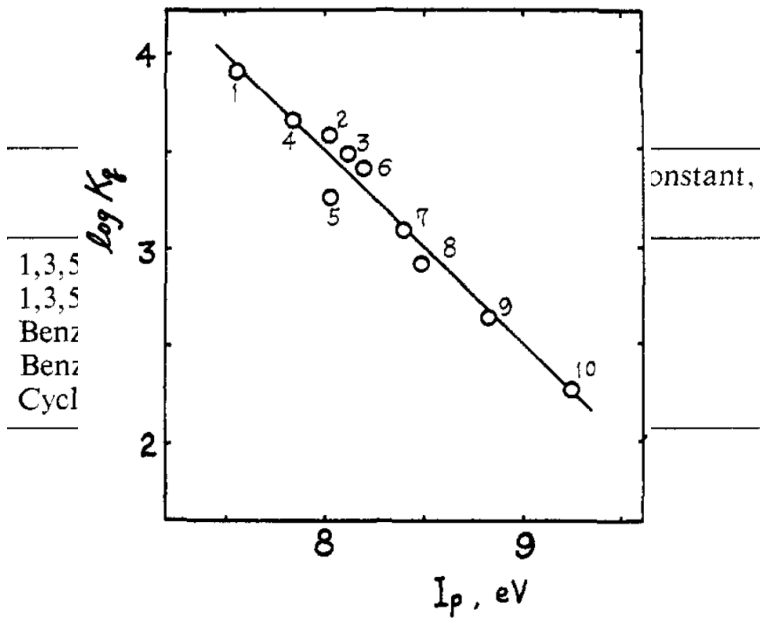
Pathway of deactivation

- Inhibition experiment

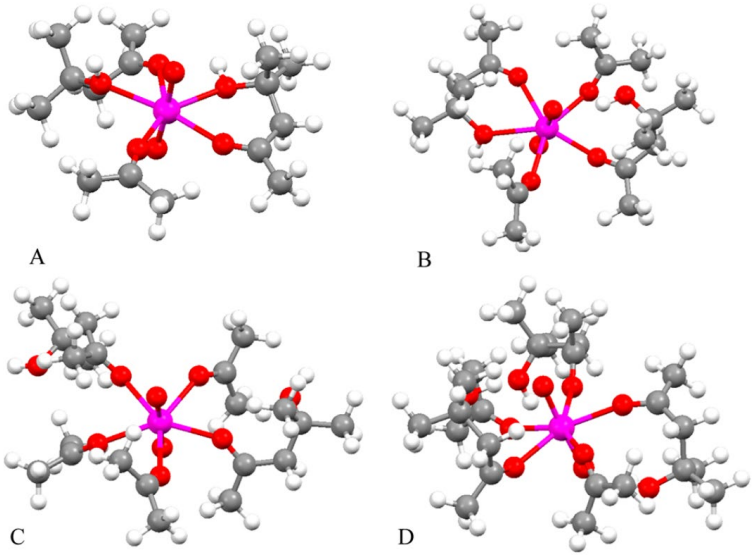




- Quenching through exciplex formation



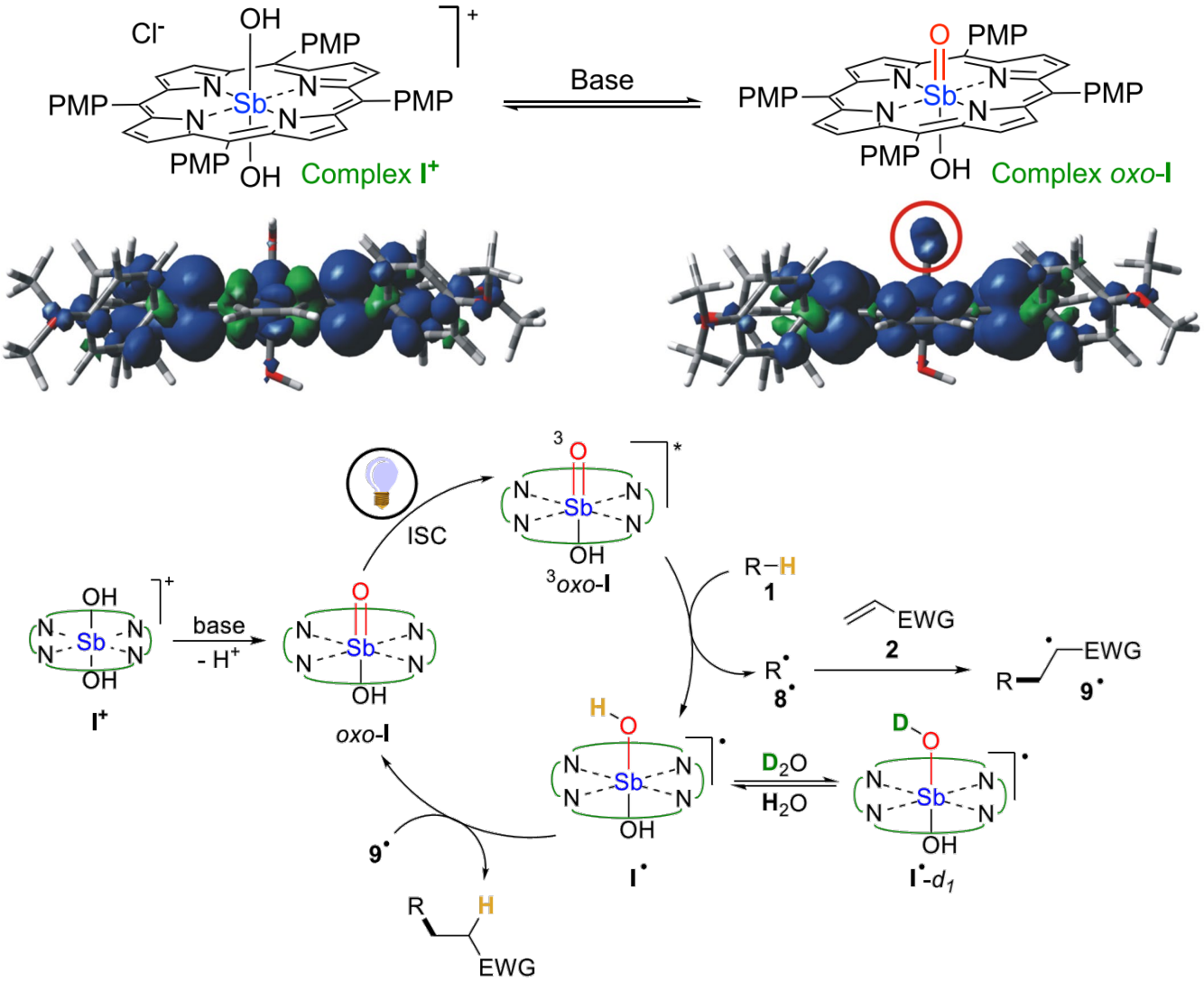
- Quenching through weak coordination?



Matsushima, R. *J. Am. Chem. Soc.* **1972**, *94*, 6010.

Sorensen, E. J. *et al. Angew. Chem. Int. Ed.* **2016**, *55*, 8923 and references therein.

Oxoantimony-porphyrins complex



Ravelli, D. *et al. ACS Catal.* **2020**, *10*, 9057.

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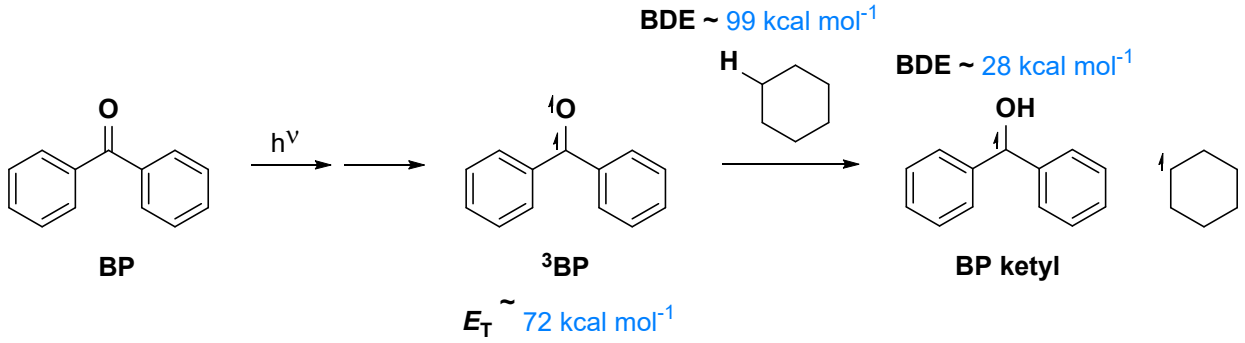
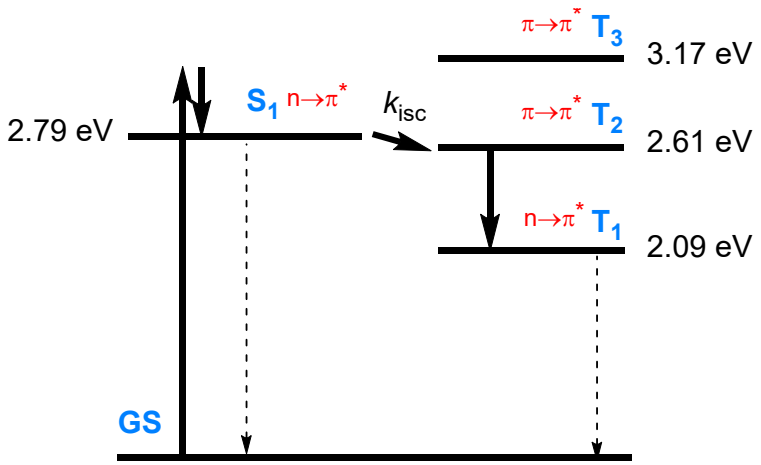
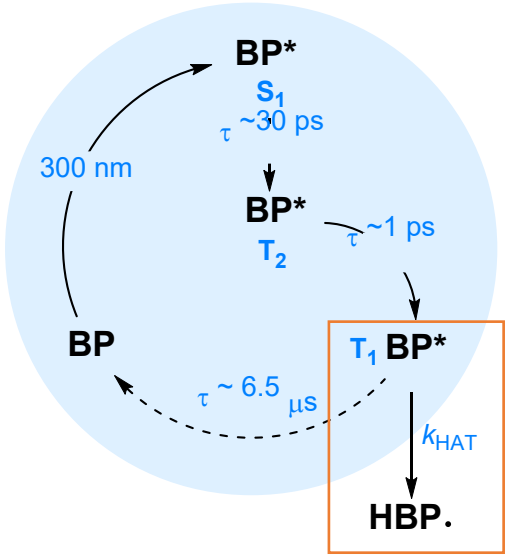
Photochemistry of carbonyl compounds

- Excited kinetics of benzophenone





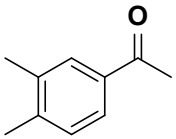
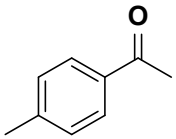
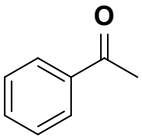
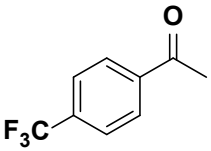


- Structure-HAT reactivity relationship?

Kaji, H. *et al. J. Phys. Chem. A* **2021**, *125*, 9000.

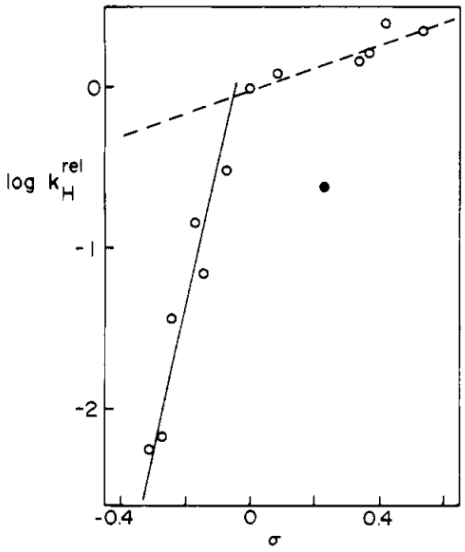
Electronic configuration

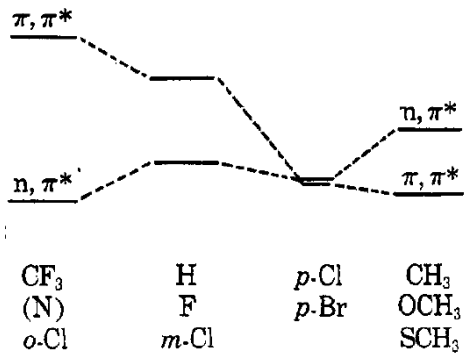
- Substituents effect

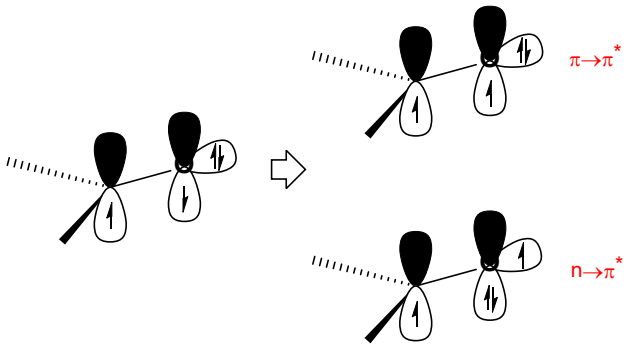





k_{HAT} with ^{i}PrOH	**8.4×10^{3}** s^{-1}	**3.9×10^{4}** s^{-1}	**4.3×10^{5}** s^{-1}	**2.76×10^{6}** s^{-1}
$\Delta E_{(n\text{-}\pi^*)\text{-}(\pi\text{-}\pi^*)}$	**+0.21** eV	**+0.16** eV	**-0.11** eV	**-0.14** eV

- HAT reactivity is closely related with the relative energies of n-π* and π-π* transitions







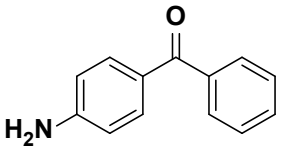
10^5 vs. 10^9 (toward Bu_3SnH)

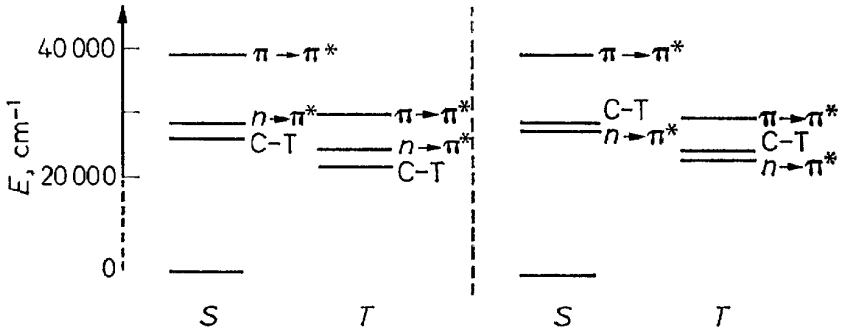
Yang, N. C. *et al. J. Am. Chem. Soc.* **1968**, *90*, 5899.

Wagner, P. J. *et al. J. Am. Chem. Soc.* **1973**, *95*, 5604.

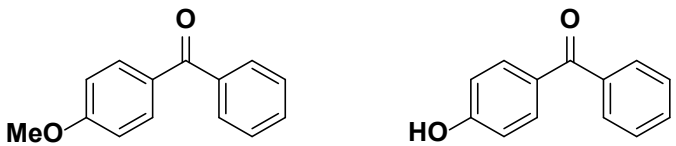
Electronic configuration

- A CT state with no HAT reactivity might involves given a strong electron donating group

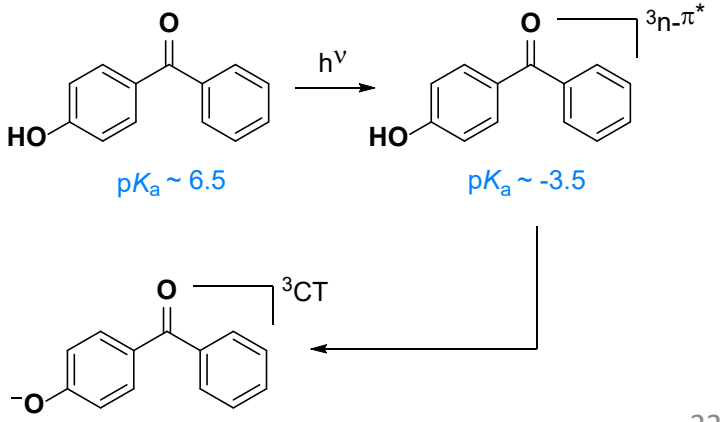




- An interesting fact:



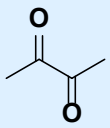
(Irradiation in ^{i}PrOH)

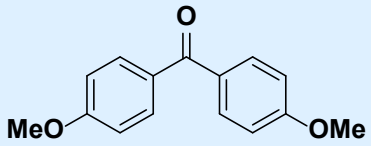


Suppan, P. *et al. Pure Appl. Chem*. **1964**, *9*, 499.

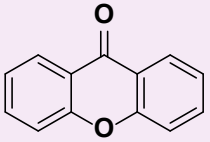
Aryl ketone photocatalysts

Weak abstractor

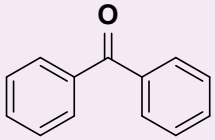


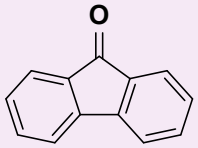


Sensitive to solvent polarity and temperature (ranging from 10^4 to 10^8)

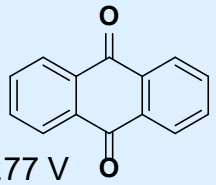


E^*_{red} = 1.76 V

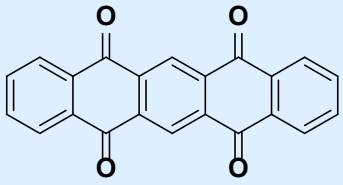




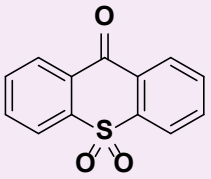
E^*_{red} = 0.97 V



E^*_{red} = 1.77 V



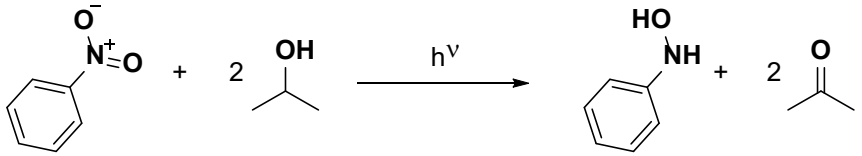
Very reactive



Scaiano, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 7747.

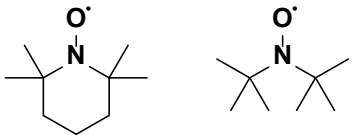
Nitroxides

- Nitro compounds

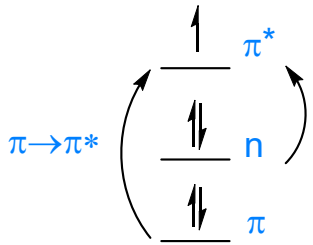


Fast radiationless decay

- Nitroxide radicals

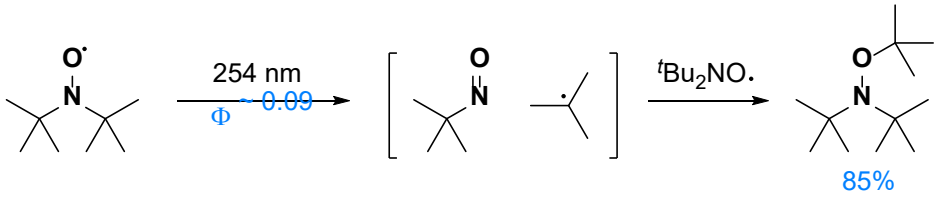


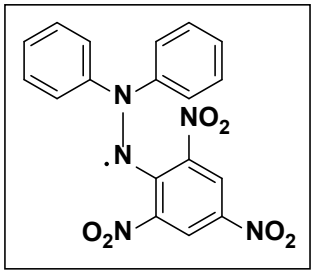
Maximum at ~ 237 nm



Maximum at ~ 465 nm

- reactivities



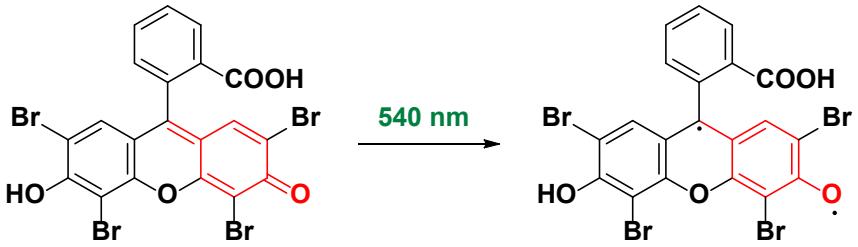


Testa, A. C. *J. Am. Chem. Soc.* **1967**, *89*, 6917.

Koch, T. H. *et al. Tetrahedron Lett.* **1977**, *18*, 3015 and references therein.

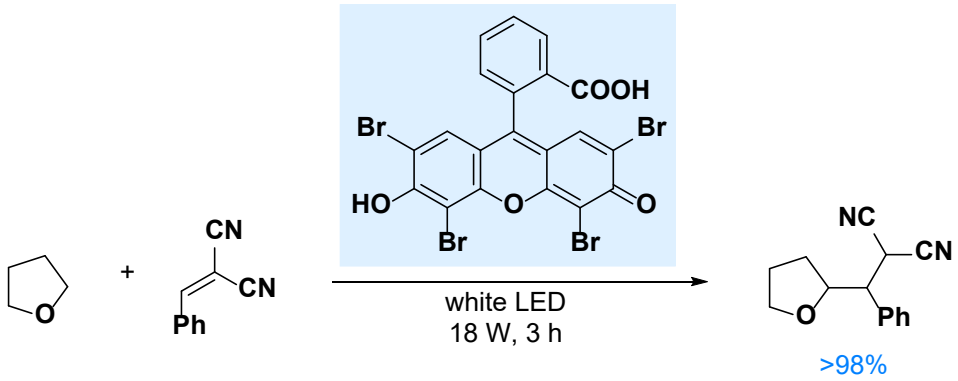
Neutral eosin Y

- A new *d*-HAT photocatalyst in green light region



Eosin Y

+ readily available
+ metal-free
+ long wavelength absorption
+ TADF molecule
+ inhibited dimerization

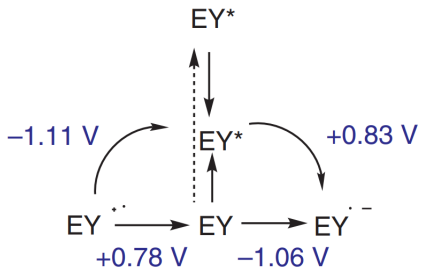


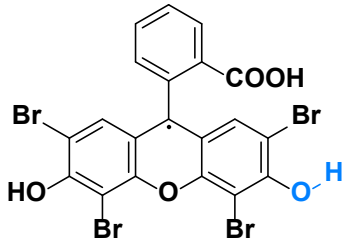
Catalyst	Solvent	Time	Yield (%)
Fluorescein	THF	24h	<10
Rose bengal	THF	24h	38
Eosin Y (neutral)	THF	3h	>98
Eosin B (neutral)	THF	24h	25
Rhodamine B	THF	24h	<10
Na_2Eosin Y	THF	3h	12

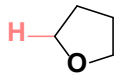
Wu, J. *et al. Angew. Chem. Int. Ed.* **2018**, *57*, 8514.

Mechanism study

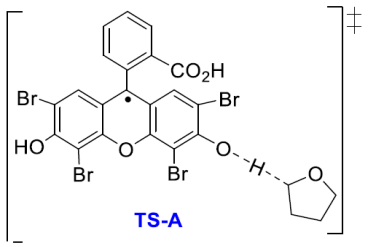
- Direct reverse HAT is unfavored in this case

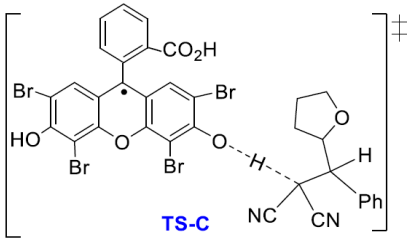


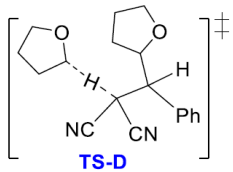


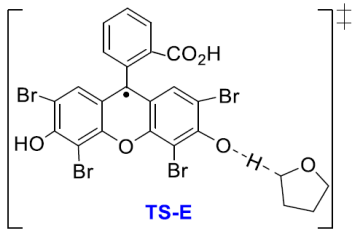
BDE = 92 kcal mol^{-1} 

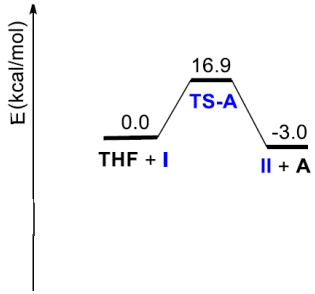
BDE_{calc} = 92 kcal mol^{-1}

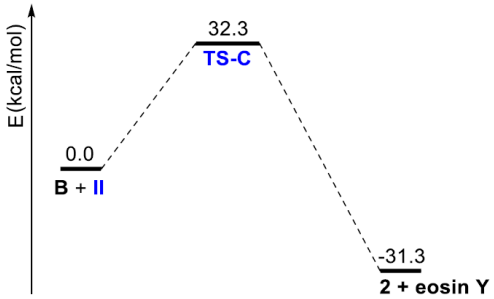


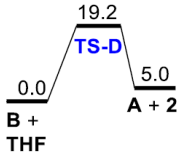


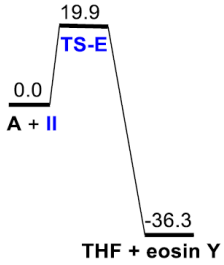








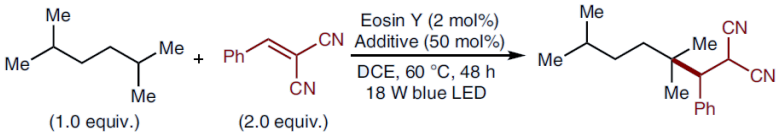




Wu, J. *et al. Angew. Chem. Int. Ed.* **2018**, *57*, 8514.

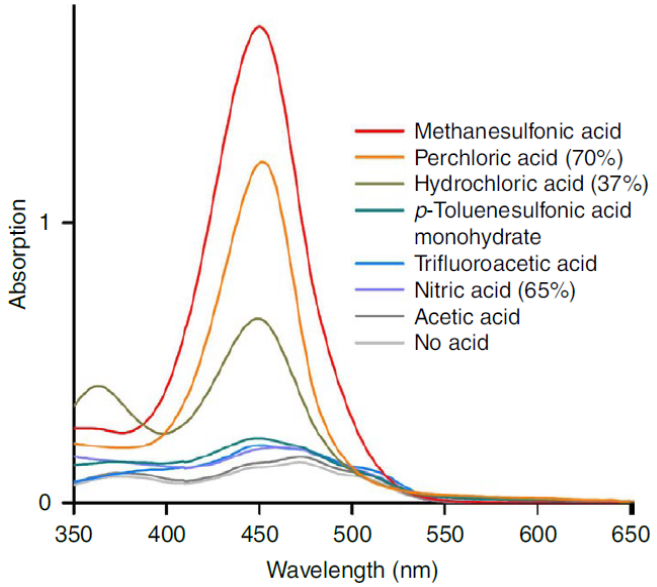
Enhancing HAT reactivity with acid

- Activation of unactivated C-H bond

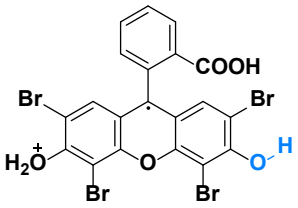


Entry	Additive	Additive type	Yield (%)
1	None	—	26
2	$BF_3{\cdot}Et_2O$	Lewis acid	14
3	$Yb(OTf)_3$	Lewis acid	15
4	$Cu(OTf)_2$	Lewis acid	0
5	CF_3COOH	Brønsted acid	39
6	CH_3SO_3H	Brønsted acid	81
7	$pTSA{\cdot}H_2O$	Brønsted acid	47
8	$HClO_4$	Brønsted acid	69

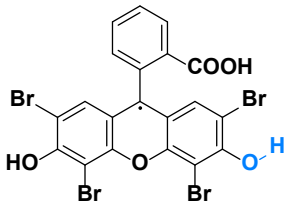
- Enhanced absorption



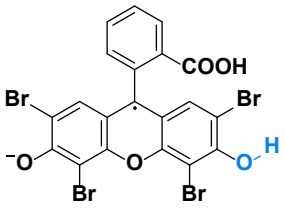
- Raised BDE



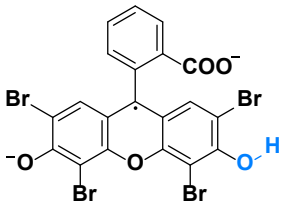
93.8 kcal mol_{-1}



92.0 kcal mol_{-1}



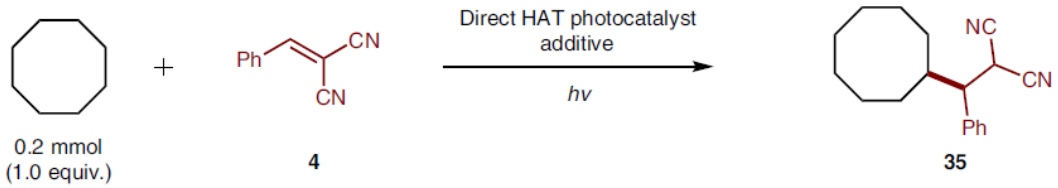
83.8 kcal mol_{-1}



86.9 kcal mol_{-1}

Wu, J. *et al. Nat. Synth.* **2022**, *1*, 794.

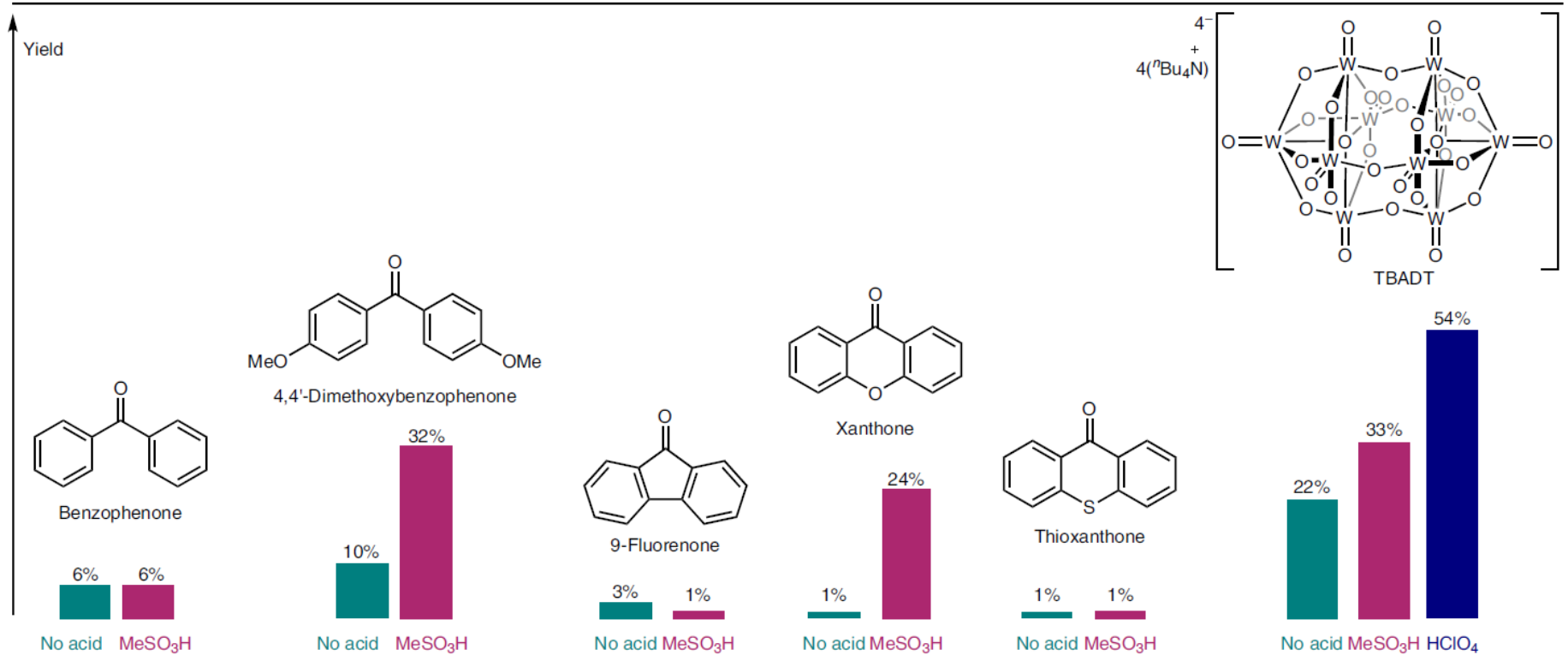
Enhancing HAT reactivity with acid



0.2 mmol
(1.0 equiv.)

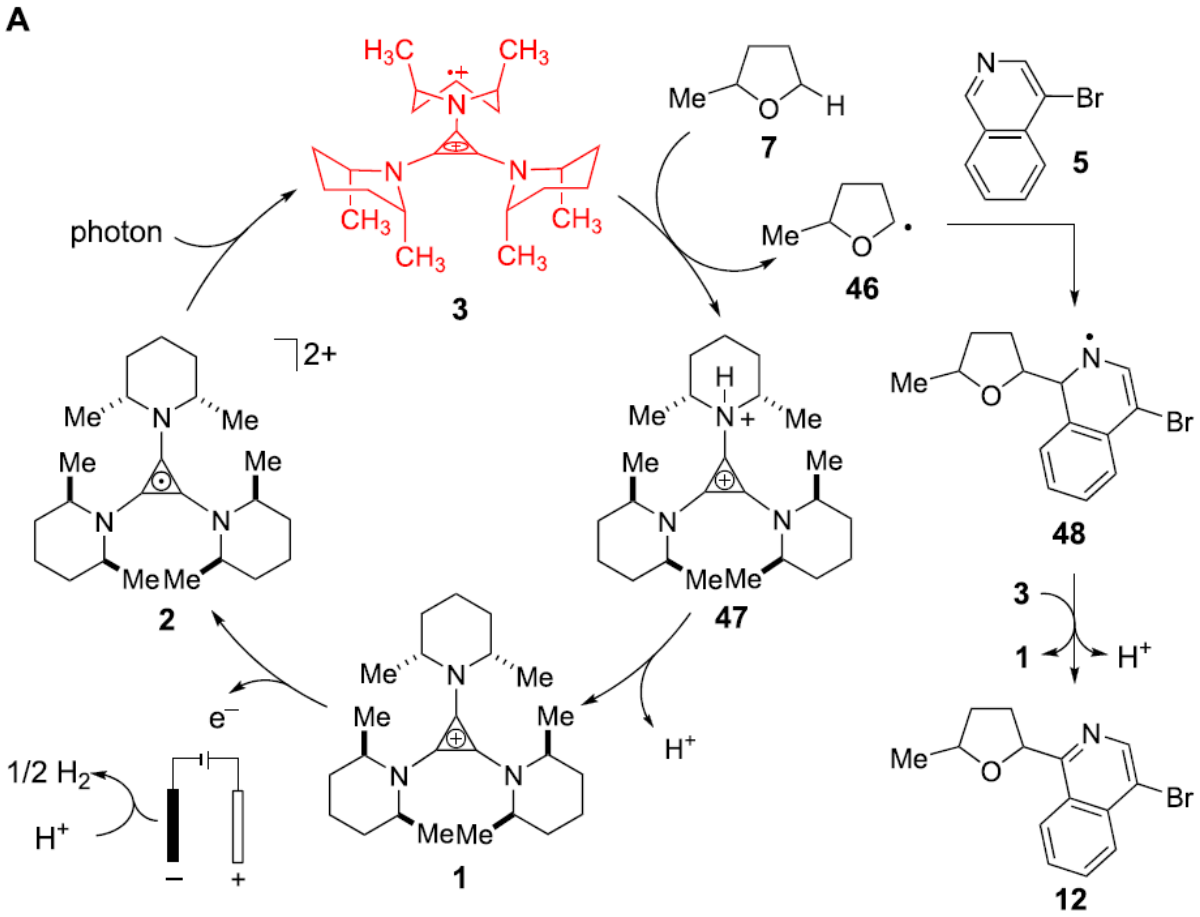
4

35



Wu, J. *et al. Nat. Synth.* **2022**, *1*, 794.

Trisaminocyclopropenium (TAC)



Lambert, T. H. *et al. J. Am. Chem. Soc.* **2020**, *142*, 1698.

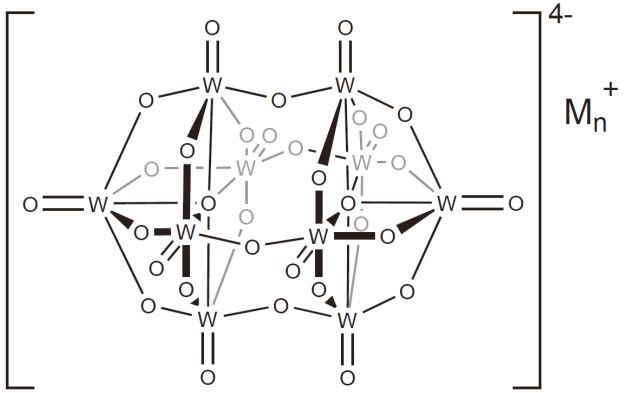
Outline

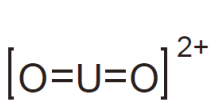
- Introduction
  - Scope and significance
- Mechanistic aspect of excited-state HAT reactivity
  - From LMCT states
  - From n/π→π* states
- **Applications: direct C-H functionalization reactions**
  - Oxometal complexes
  - Organic molecules
- Summary

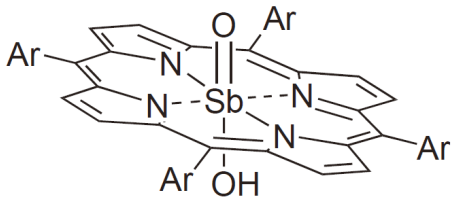
The fundamental principle

- **What's the intrinsic difference?**

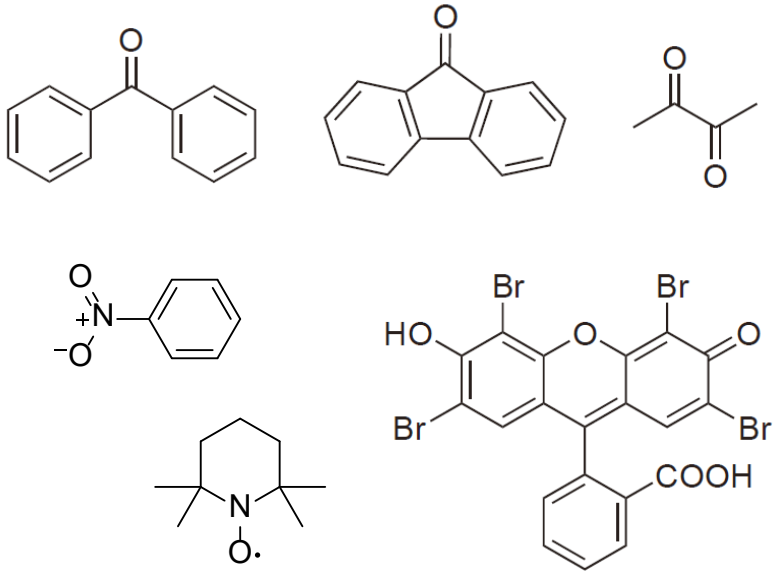
- LMCT state in Metal-oxo complexes

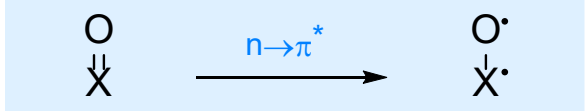






- n→π* states in X=O functionality

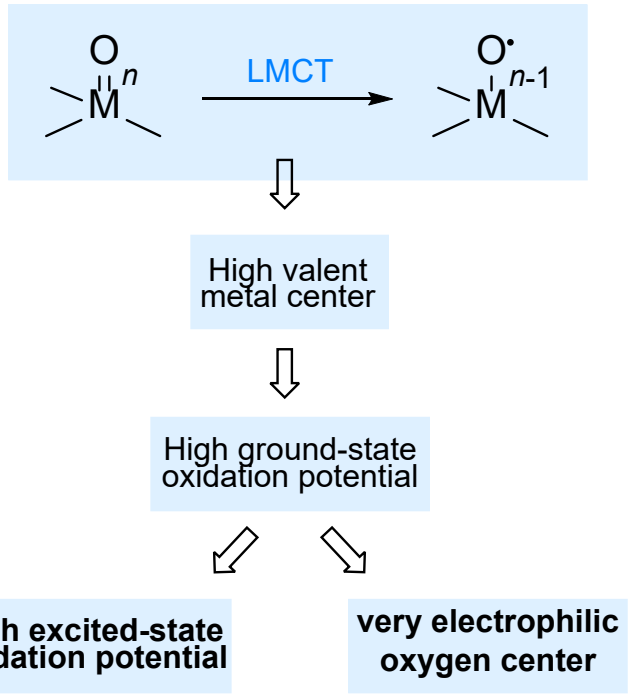




Wu, J. *et al. Chem. Catal.* **2021,** *1,* 523.

The fundamental difference

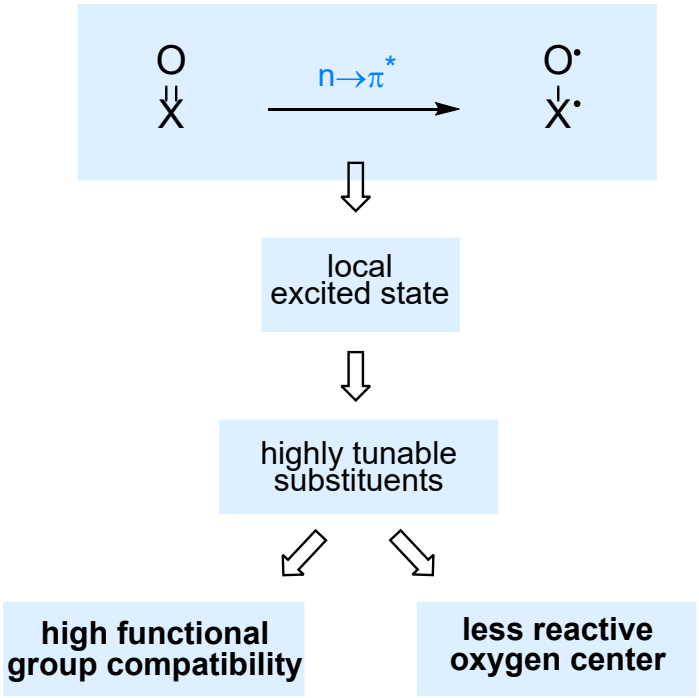
- LMCT state in Metal-oxo complexes



E^*_{red} ca. **2~2.5** V

BDE ca. **100~110** kcal mol^{-1}

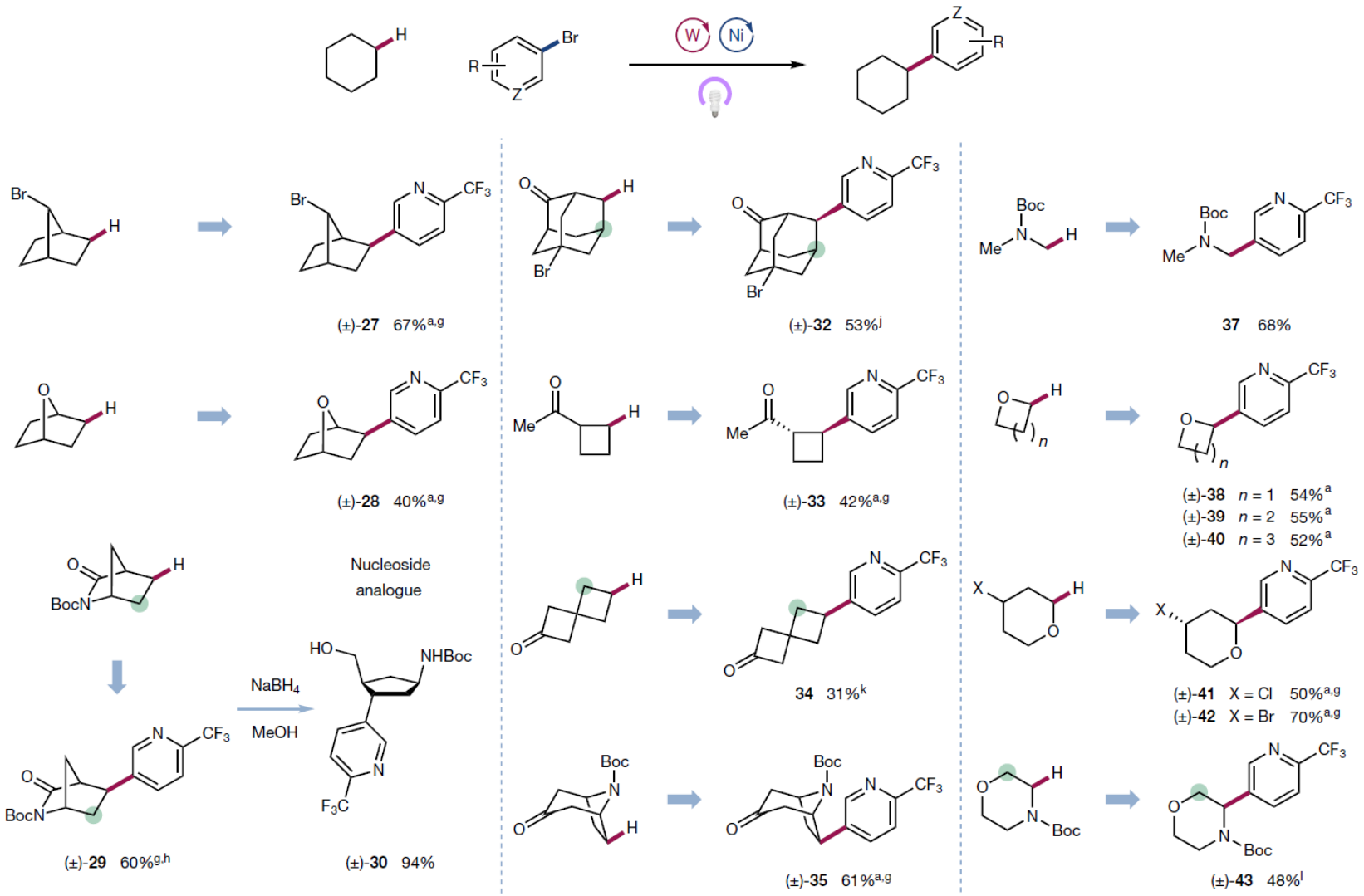
- n→π* states in X=O functionality



E^*_{red} ca. **0.8~2** V

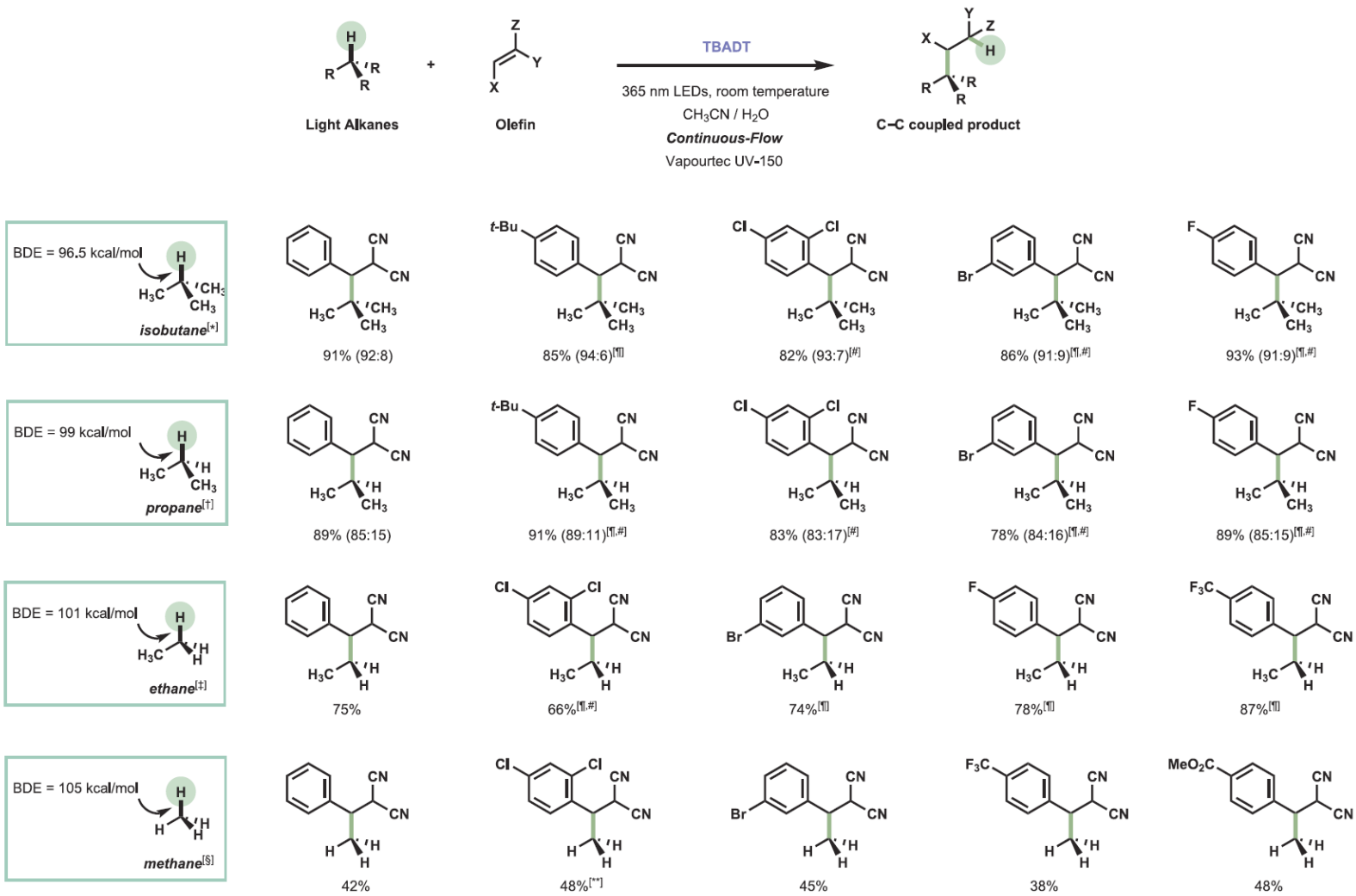
BDE ca. **90~105** kcal mol^{-1}

Light hydrocarbon functionalization



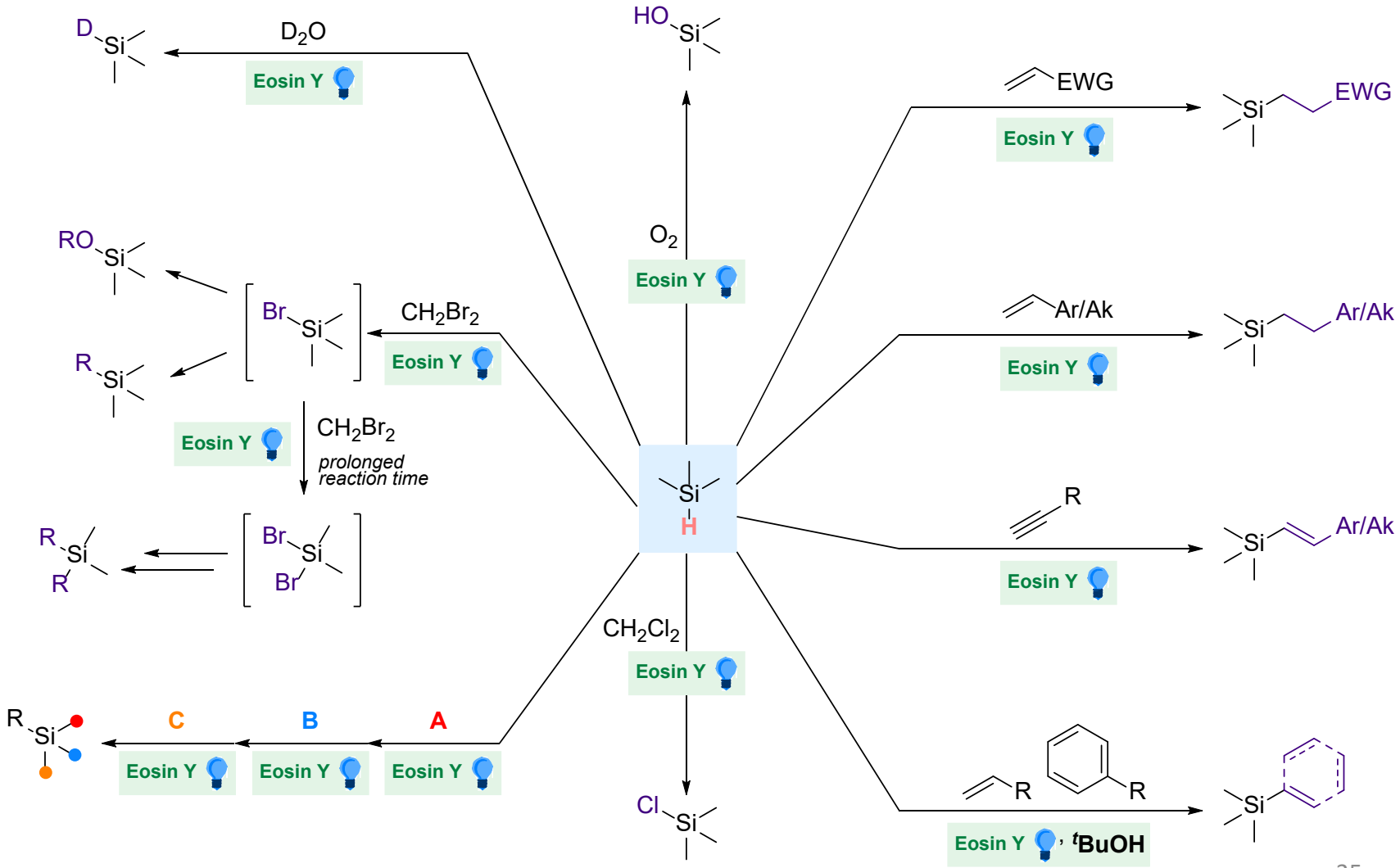
Macmillan, D. W. C. *et al. Nature* **2018**, *560*, 70.

Light hydrocarbon functionalization



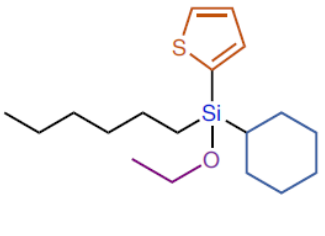
Noël, T. *et al. Science* **2020**, *369*, 92.

Modular functionalization of silane



Wu, J. *et al. Nat. Chem.* **2023,** *15*, 666.

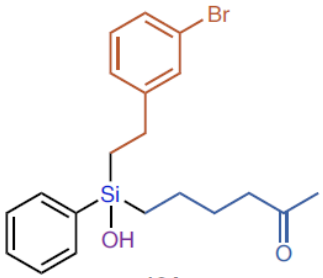
Modular functionalization of silane



133

G → C → E

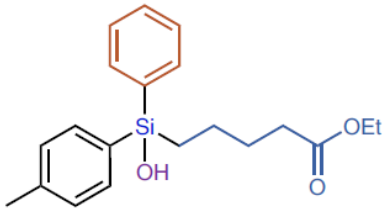
i) 90% yield
ii) 54% yield
iii) 82% yield



134

H → H → O

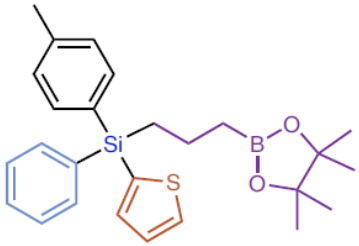
i) 87% yield
ii) 74% yield
iii) 68% yield



135

H → C → O

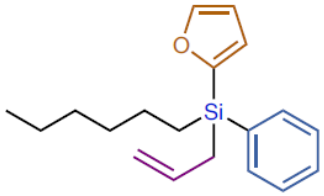
i 82% yield
ii) 64% yield
iii) 63% yield



137

C → C → H

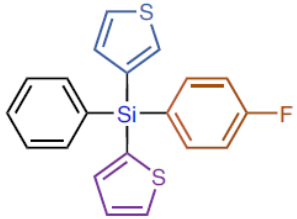
i) 43% yield
ii) 54% yield
iii) 71% yield



138

C → G → G

i) 54% yield
ii) 86% yield
iii) 90% yield



139

G → G → C

i) 95% yield
ii) 88% yield
iii) 36% yield

Wu, J. *et al. Nat. Chem.* **2023,** *15*, 666.

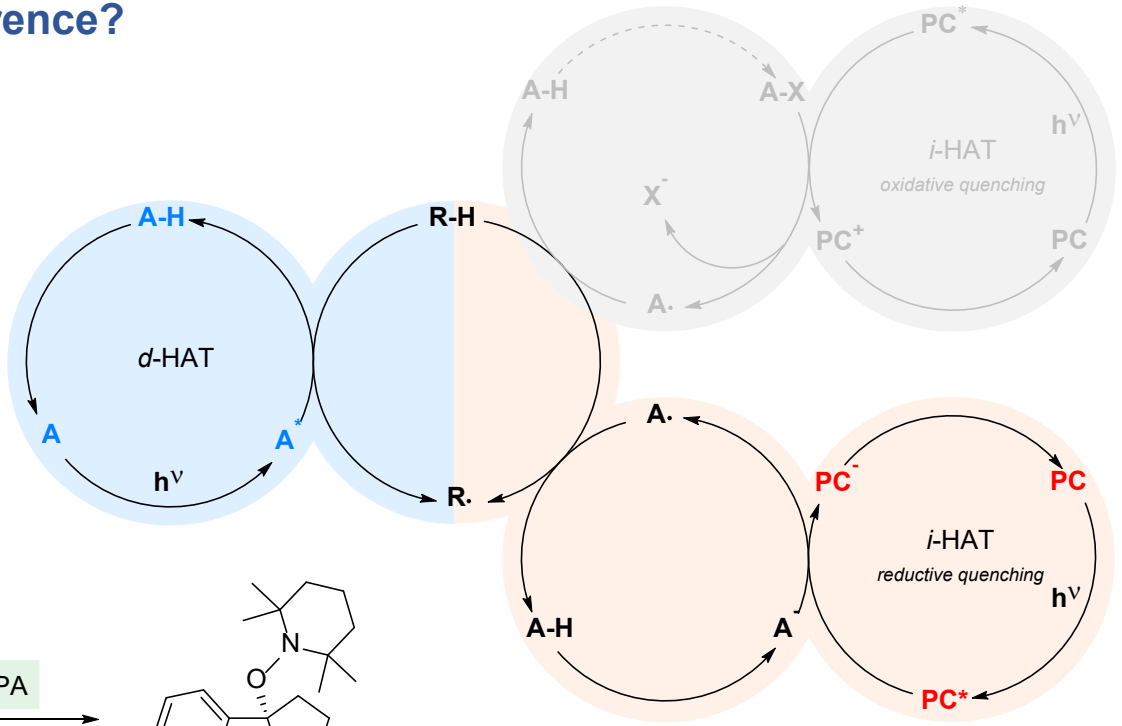
Outline

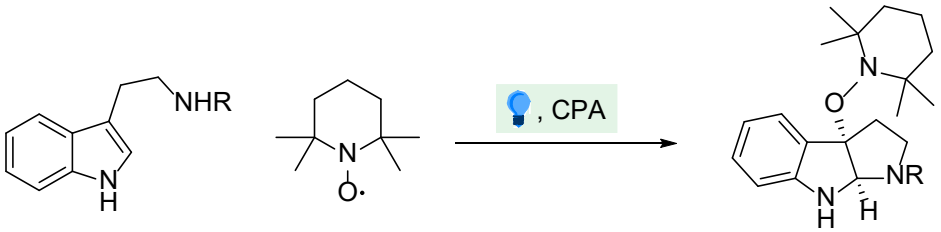
- Introduction
  - Scope and significance
- Mechanistic aspect of excited-state HAT reactivity
  - From LMCT states
  - From n/π→π* states
- Applications: direct C-H functionalization reactions
  - Oxometal complexes
  - Organic molecules
- **Summary**

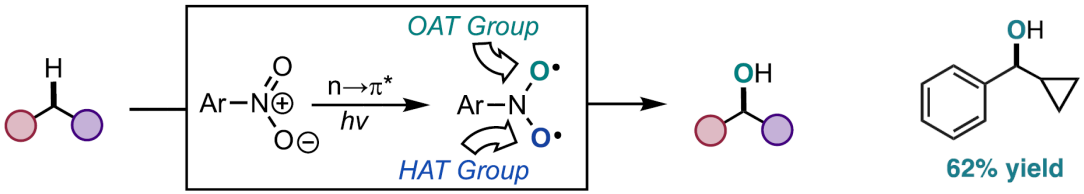
Summary

- **What's the intrinsic difference?**

- **SET vs. HAT**
- **Inter/intramolecular spin separation**
- **post-HAT reactivity**







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