Spin-Center Shift Process in Organic Synthesis

5/22/2026

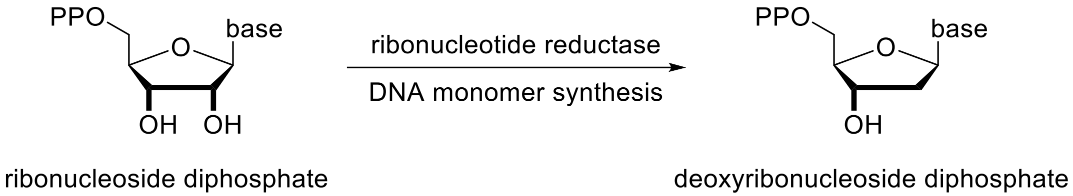
Speaker:	Xuzhou Li (李旭周)
Supervisor:	Prof. Zhang-Jie Shi (施章杰)

Content

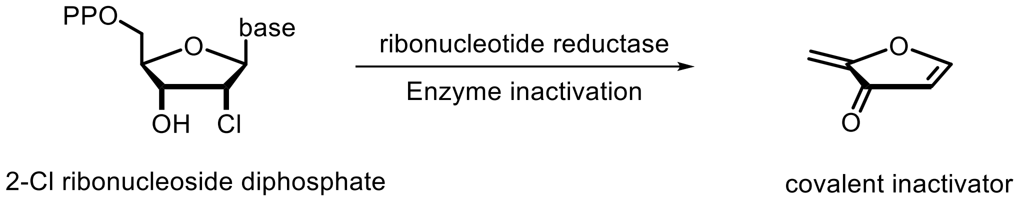
Content

1. Introduction

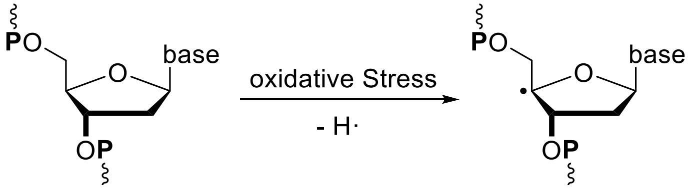
The SCS process in biochemical reactions



Deoxygenation of Ribonucleotides



Inactivation of Ribonucleotide Reductase

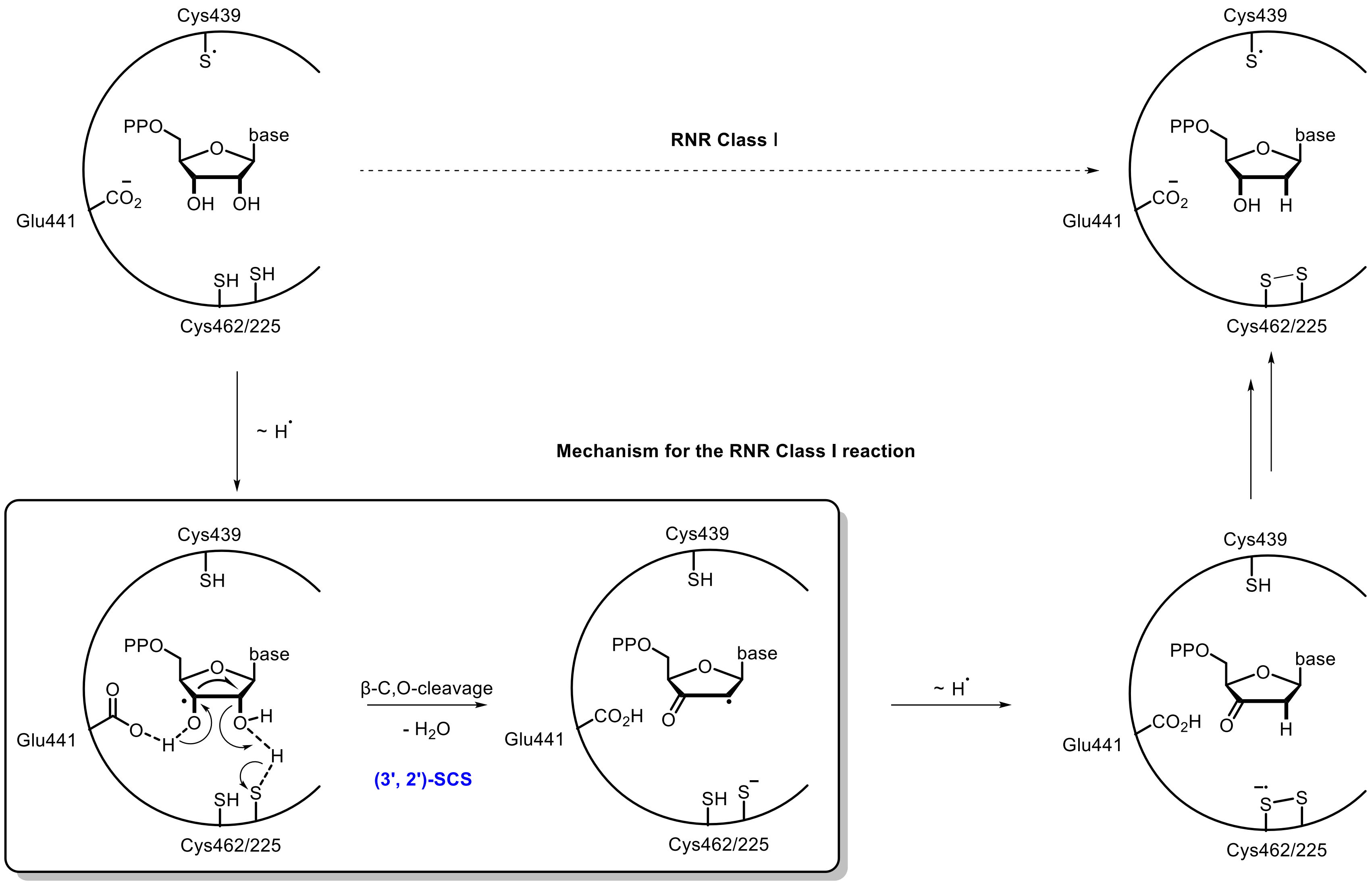


Damage to DNA by Oxidative Stress

1) Ehrenberg, A.; Reichard, P. *J. Biol. Chem.* **1972**, 247, 3485.
2) J. Stubbe, W. van der Donk, *Chem. Biol.* **1995**, 2, 793–801.
3) Behrens, G.; Koltzenburg, G.; Ritter, A.; Schulte-Frohlinde, D. *Int. J. Radiat. Biol.* **1978**, 33(2), 163–171.

1. Introduction

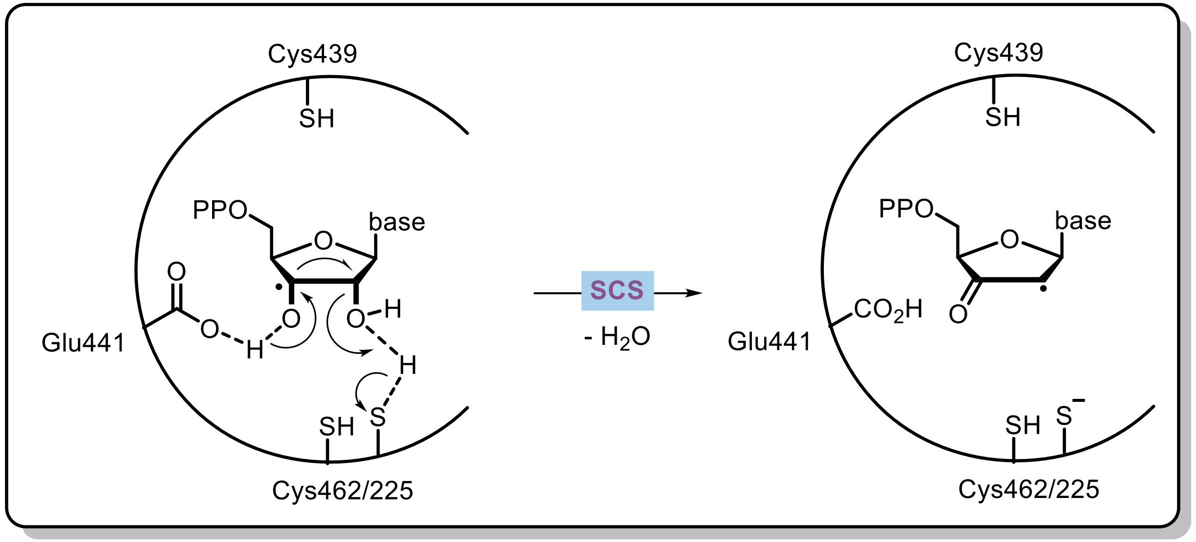
The SCS process in biochemical reactions



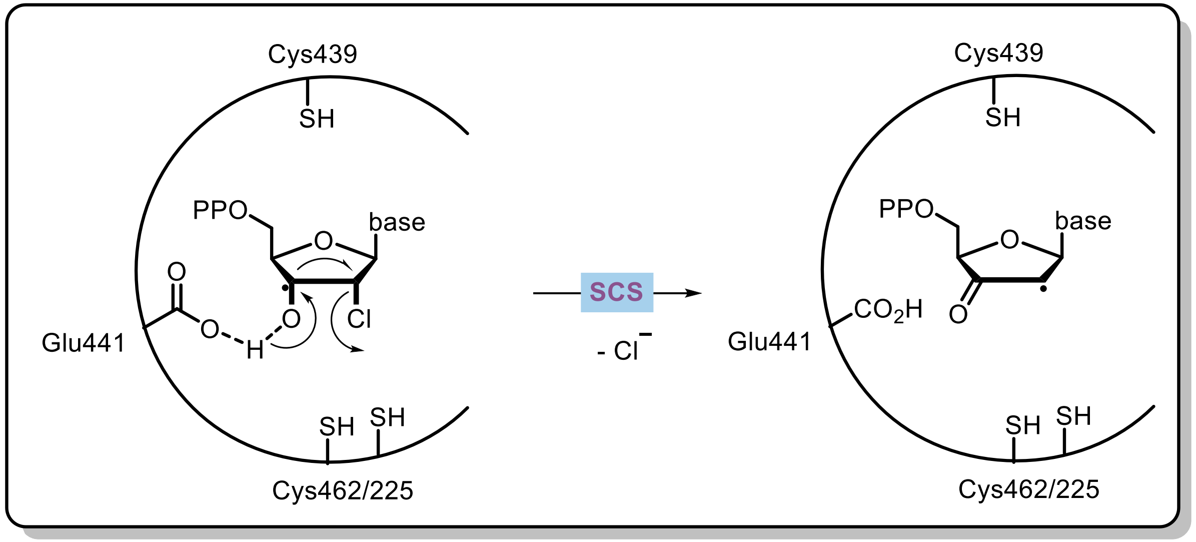
Ehrenberg, A.; Reichard, P. *J. Biol. Chem.* **1972**, 247, 3485.

1. Introduction

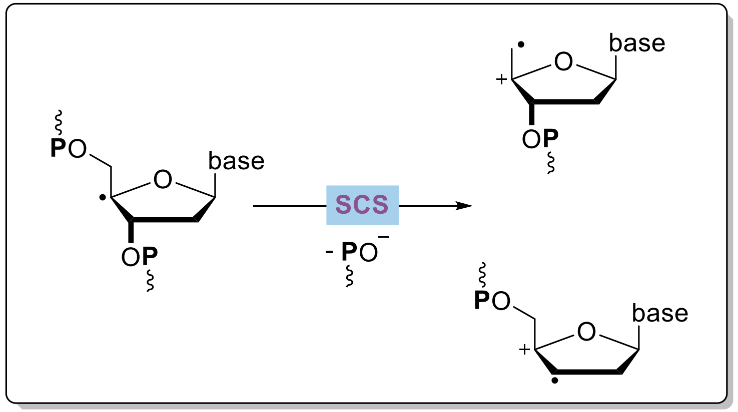
The SCS process in biochemical reactions



Deoxygenation of Ribonucleotides



Inactivation of Ribonucleotide Reductase



Damage to DNA by Oxidative Stress

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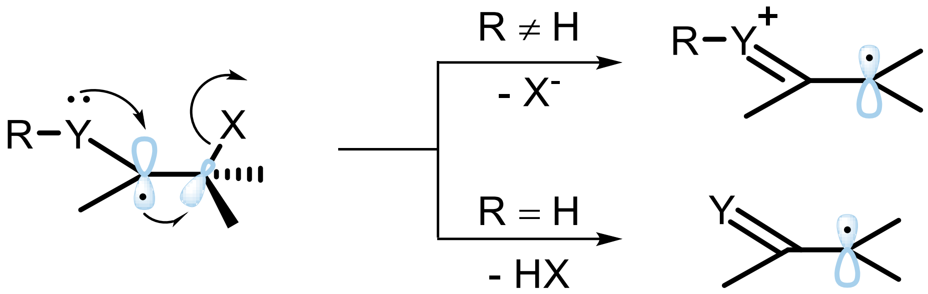
1. Introduction

Concept of SCS process



“The concept of the spin-center shift (SCS), that is, the shift of a radical center as a result of the elimination of an acid or a leaving group, considerably extends the repertoire of radical reactions.”

——Wessig 2007

Wessig, P.; Muehling, O. *Eur. J. Org. Chem.* **2007**, *2007*, 2219–2232.

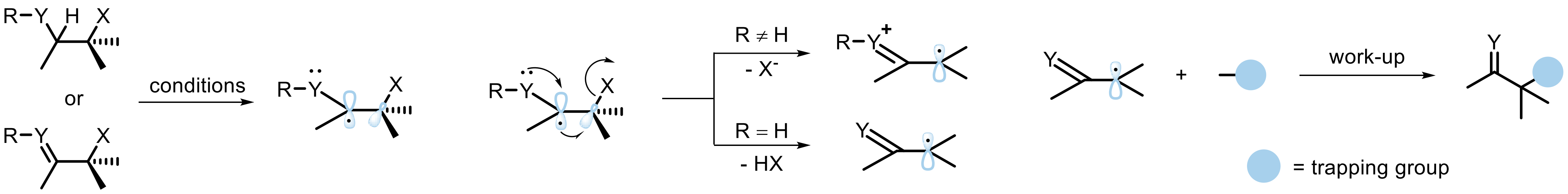
1. Introduction

The Core Process of Spin-Center Shift

(1) The Formation of Free Radicals

(2) Suitable Leaving Group

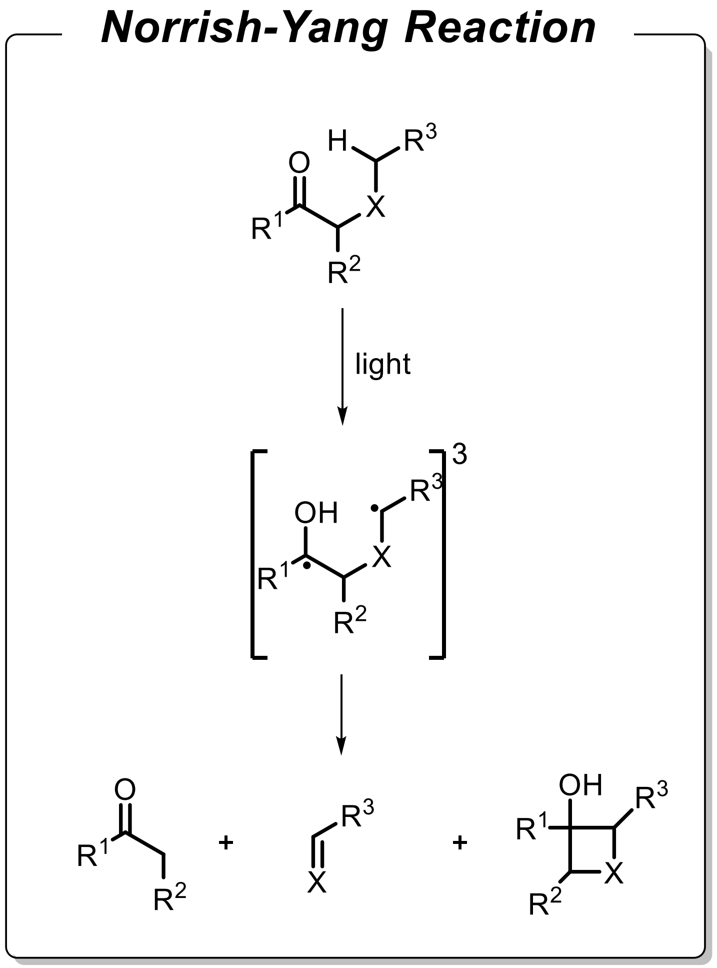
(3) Initiate subsequent reactions



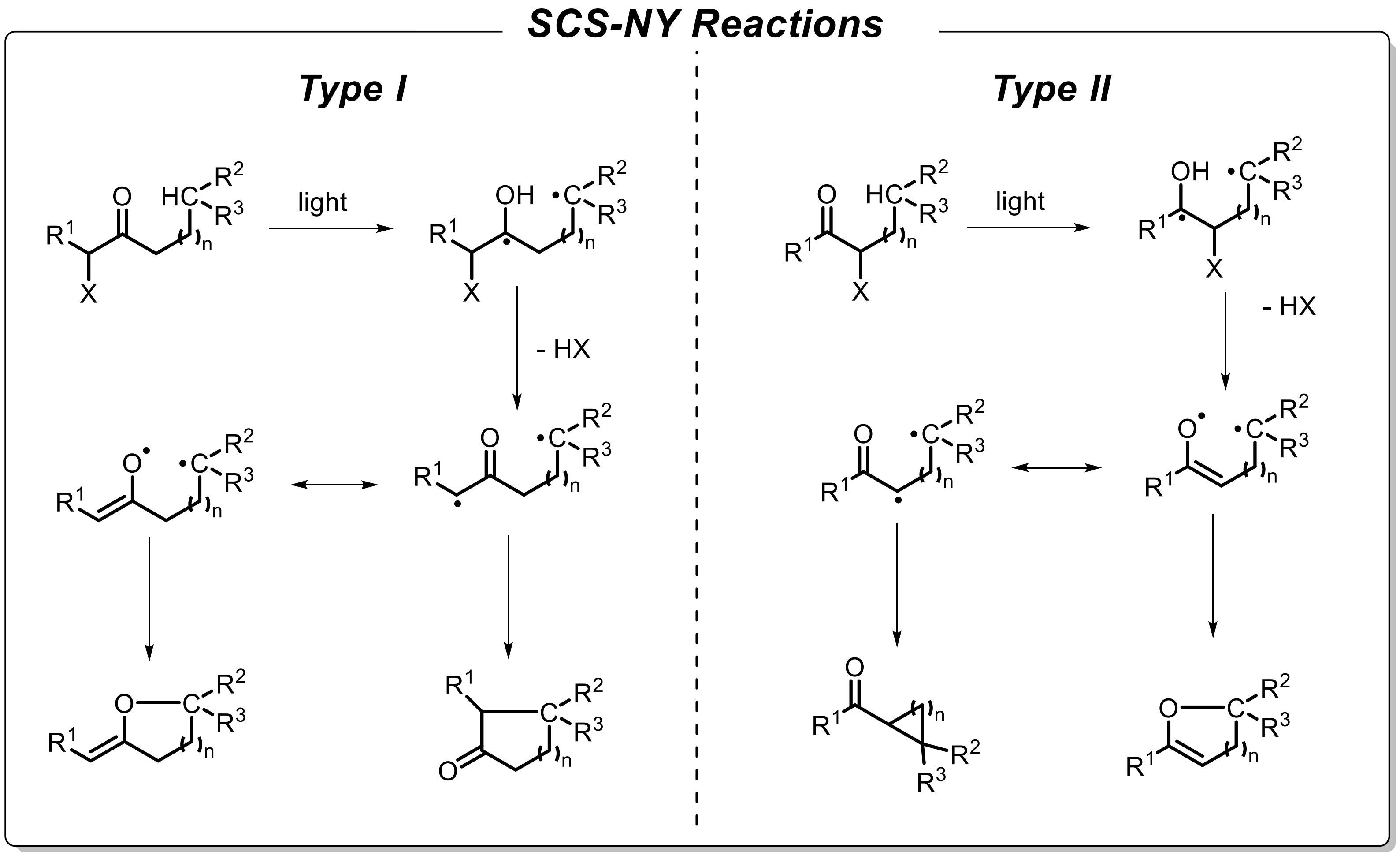
Zhang, F.-L.; Li, B.; Houk, K. N.; Wang, Y.-F. JACS Au **2022**, 2, 1032–1042

1. Introduction

The SCS process in organic chemistry



Norrish-Yang Reaction



SCS-NY Reactions

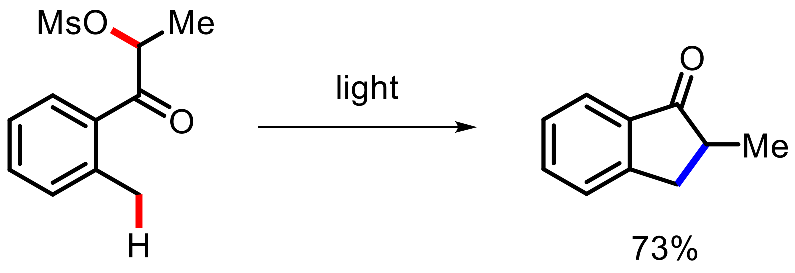
Type I

Type II

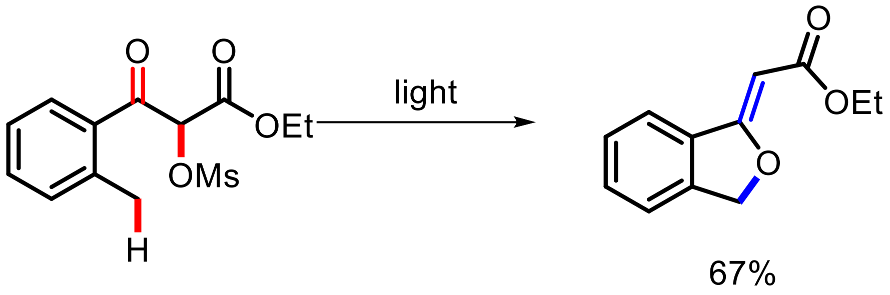
N. C. Yang; Ding-Djung H. Yang. J. Am. Chem. Soc. **1958**, 80, 11, 2913–2914
Wessig, P.; Muehling, O. *Eur. J. Org. Chem.* **2007**, 2219–2232.

1. Introduction

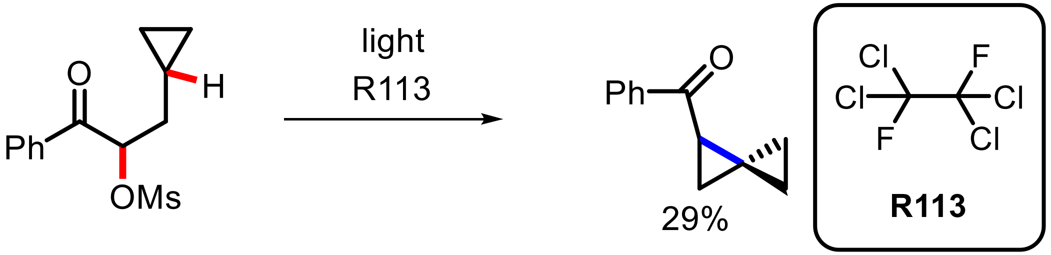
Indanones (SCS-NY Type Ⅰ)



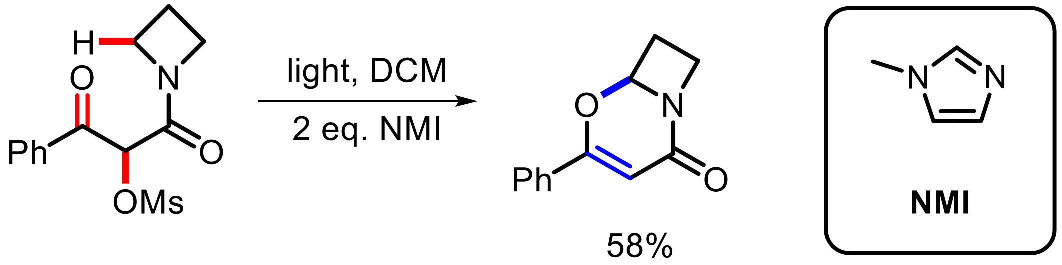
Dihydrobenzofurans (SCS-NY Type Ⅰ)



Cyclopropanes (SCS-NY Type Ⅱ)



Oxazinones (SCS-NY Type Ⅱ)

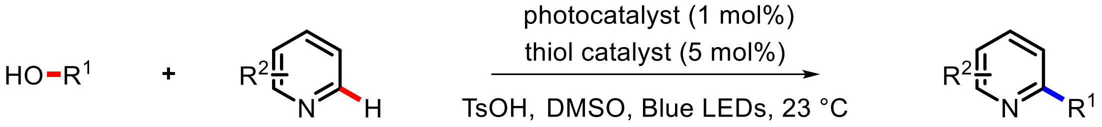


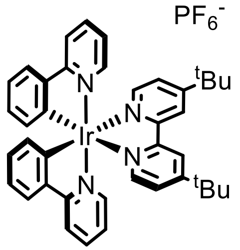
1) Newcomb, M. Kinetics of Radical Reactions: Radical Clocks. In *Radicals in Organic Synthesis*, Vol. 1; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, **2001**; pp 317–336.
2) Wessig, P.; Schwarz, J.; Lindemann, U.; Holthausen, M. C. *Synthesis* **2001**, 1258–1262.
3) Wessig, P.; Glombitza, C.; Müller, G.; Teubner, J. *J. Org. Chem.* **2004**, *69*, 7582–7591.

Content

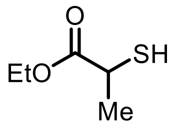
2.1. HAT induced SCS process

Alcohols as alkylating agents in C–H functionalization



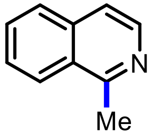


photocatalyst

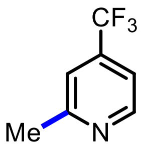


thiol catalyst

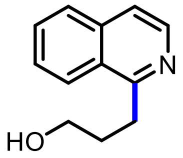
Substrate scope



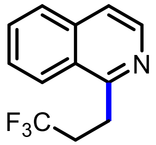
92% yield



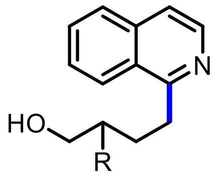
56% yield



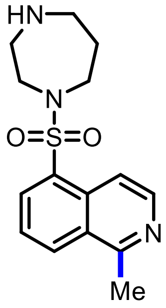
88% yield



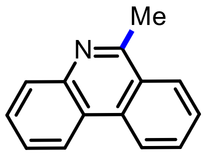
90% yield



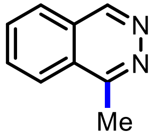
R = H, 90% yield
R = OH, 72% yield



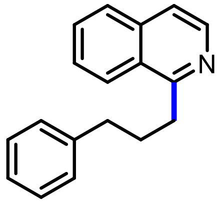
Fasudil derivative
88% yield



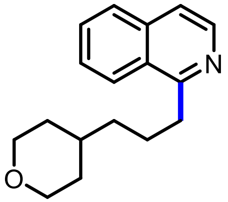
93% yield



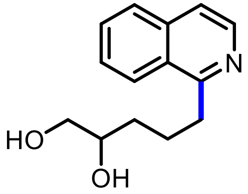
70% yield



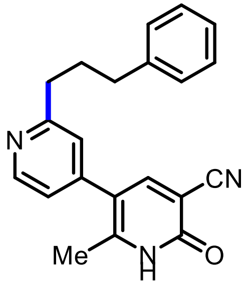
91% yield



90% yield



77% yield

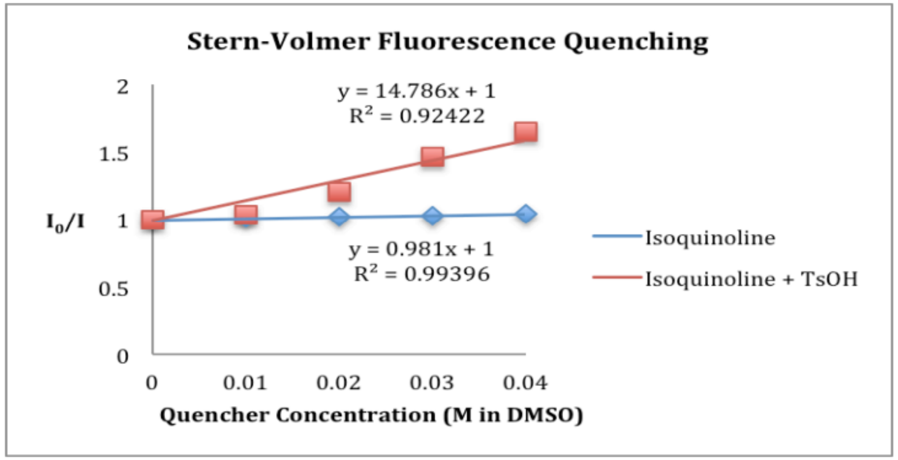


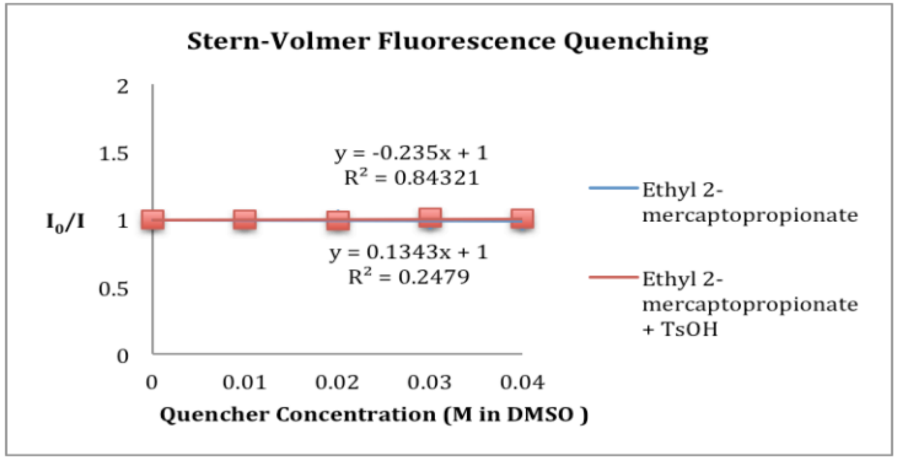
Milrinone derivate
43% yield

Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

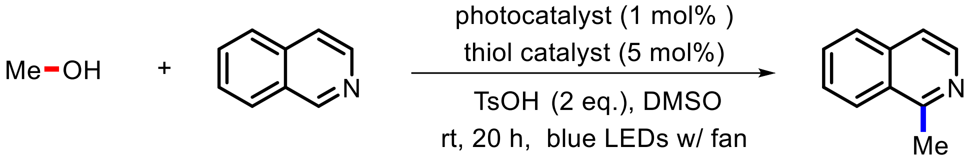
2.1. HAT induced SCS process

Stern-Volmer fluorescence quenching study





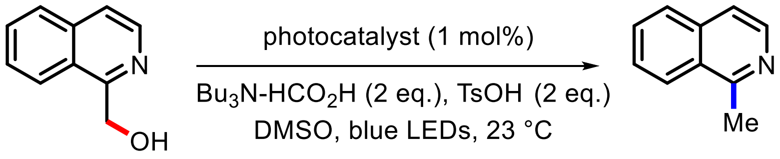
Control experiments



photocatalyst (1 mol%)
thiol catalyst (5 mol%)
TsOH (2 eq.), DMSO
rt, 20 h, blue LEDs w/ fan

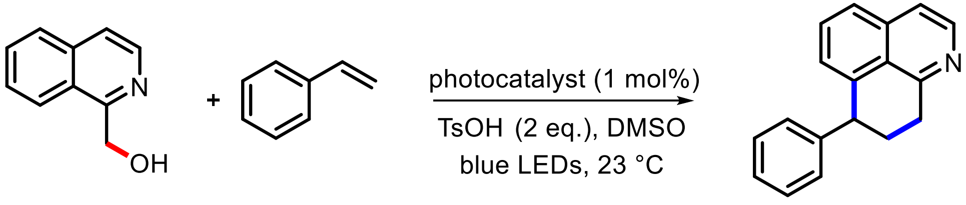
Entry	Control Conditions	Product
1	w/o photocatalyst	0%
2	w/o light	0%
3	w/o acid	0%
4	w/o thiol	3%
5	standard conditions, w/ all	98%

Intermediate exploration



photocatalyst (1 mol%)
$Bu_3N\text{-}HCO_2H$ (2 eq.), TsOH (2 eq.)
DMSO, blue LEDs, 23 °C

60% yield



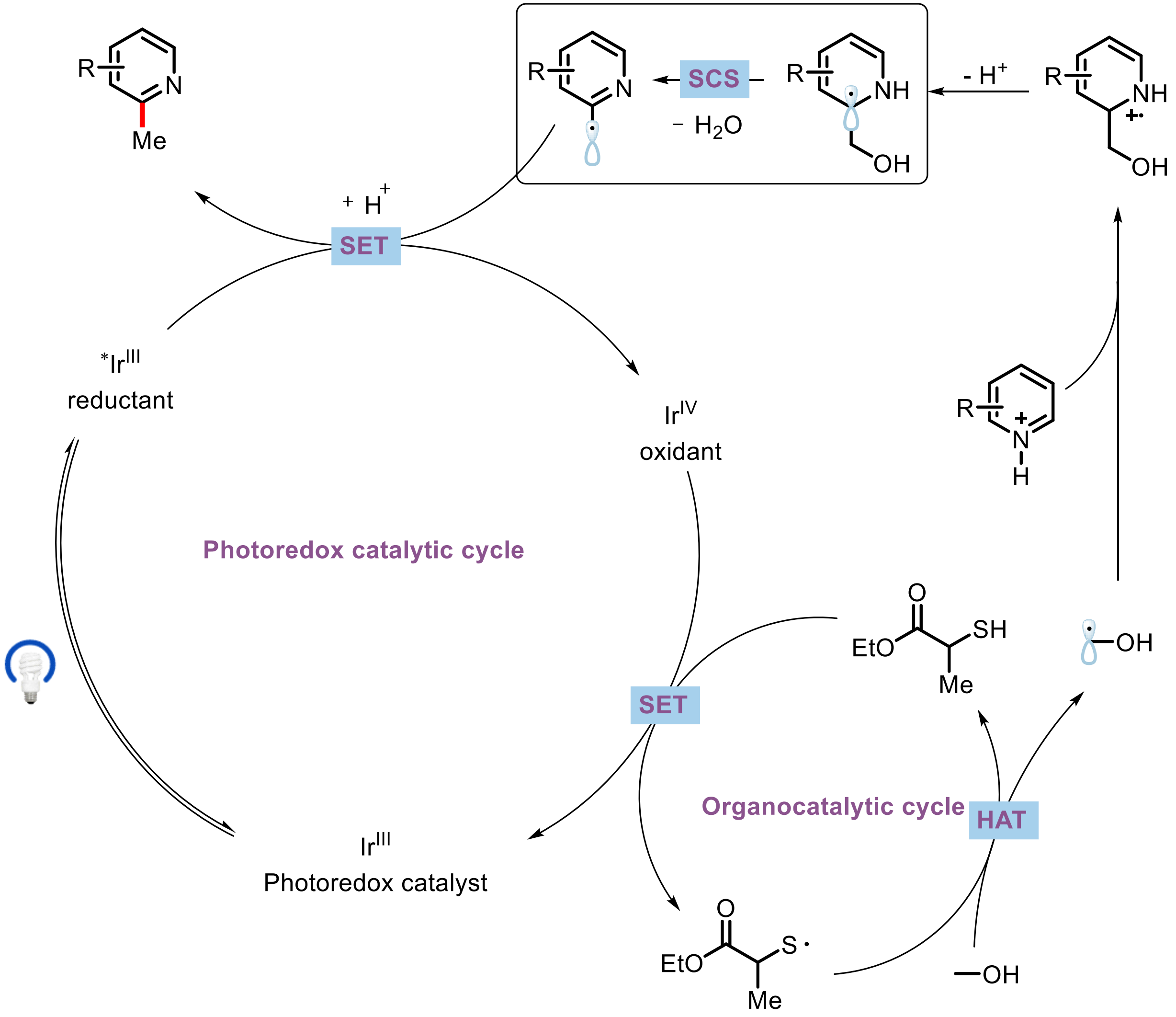
photocatalyst (1 mol%)
TsOH (2 eq.), DMSO
blue LEDs, 23 °C

65% yield

Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

2.1. HAT induced SCS process

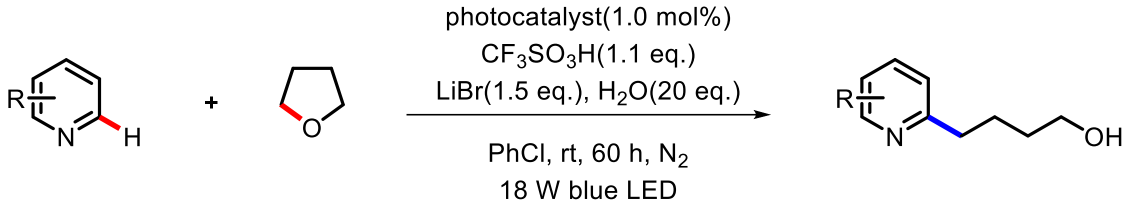
Possible reaction mechanism

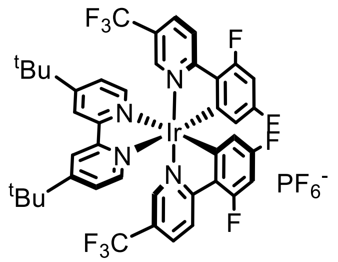


Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

2.1. HAT induced SCS process

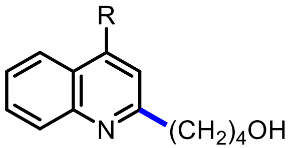
LiBr-Promoted Photoredox Minisci-Type Alkylations of Quinolines with Ethers



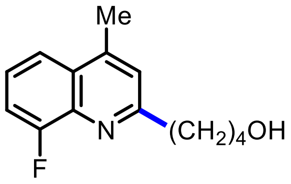


Photocatalyst

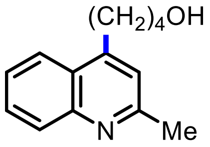
Substrate scope



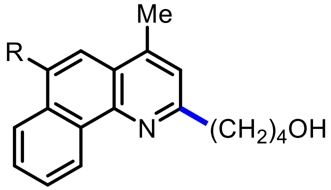
R = Me, 90%
R = Et, 46%



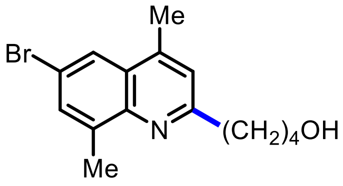
54%



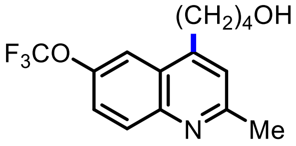
95%



R = Me, 48%
R = Et, 37%

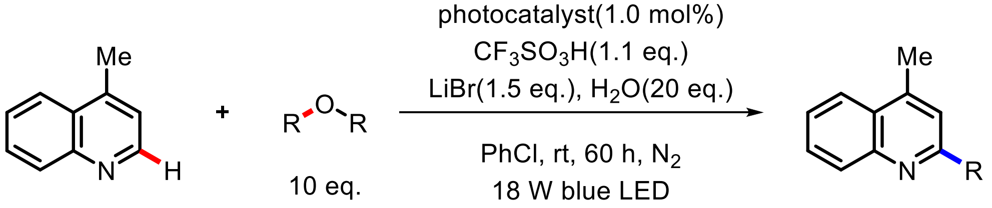


46%

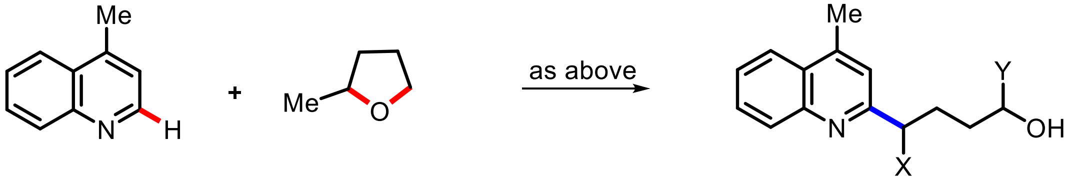


65%

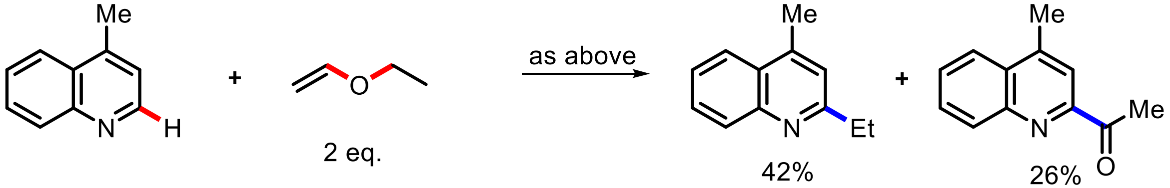
Reaction with other ethers



R = Et 75%
R = Bu 73%



84% (X = H, Y =Me) : (X = Me, Y =H) = 1:1



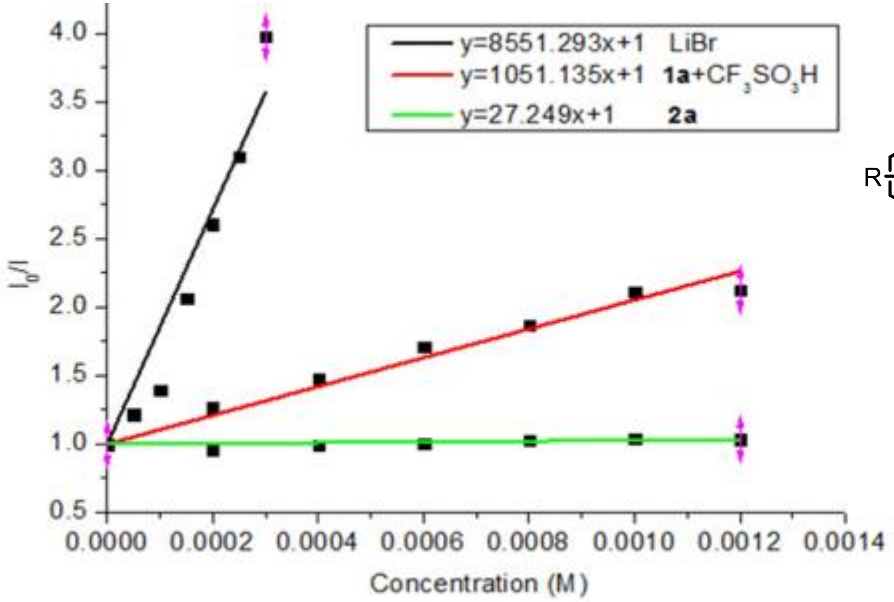
42%

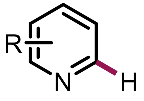
26%

Wang, Z.; Ji, X.; Han, T.; Deng, G.-J.; Huang, H. *Adv. Synth. Catal.* **2019**, *361*, 5643–5647.

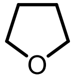
2.1. HAT induced SCS process

Stern-Volmer fluorescence quenching study



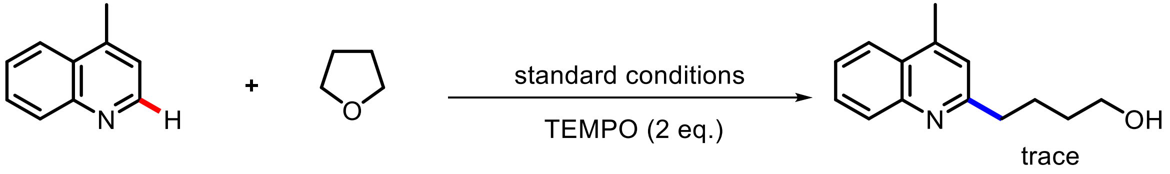


1a

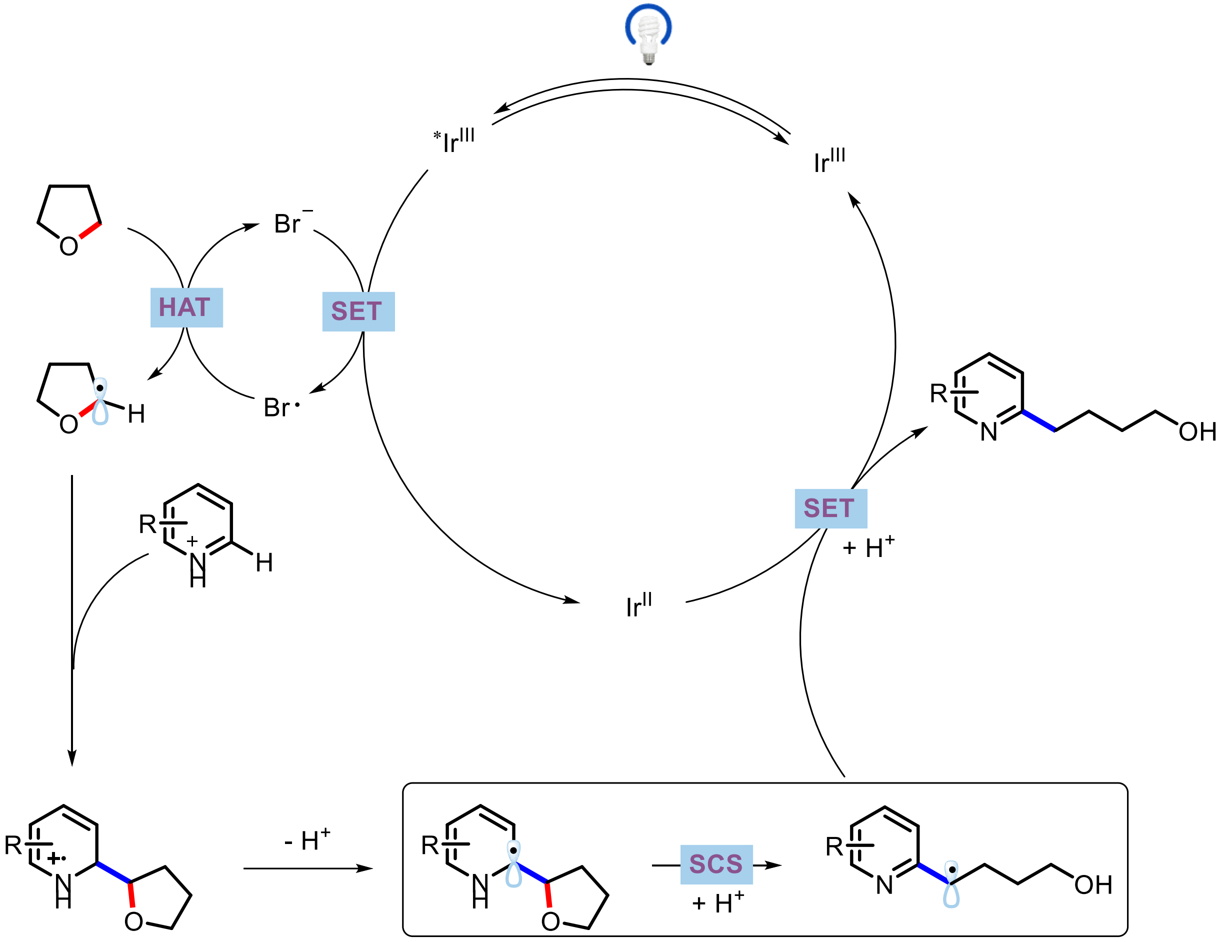


2a

Radical Trapping Experiment



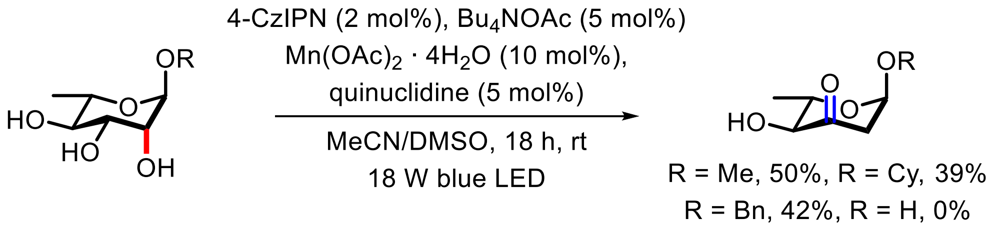
Possible reaction mechanism



Wang, Z.; Ji, X.; Han, T.; Deng, G.-J.; Huang, H. *Adv. Synth. Catal.* **2019**, *361*, 5643–5647.

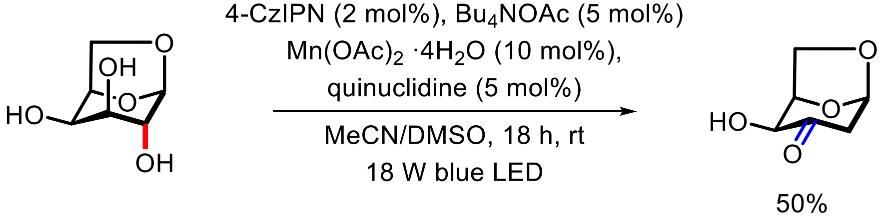
2.1. HAT induced SCS process

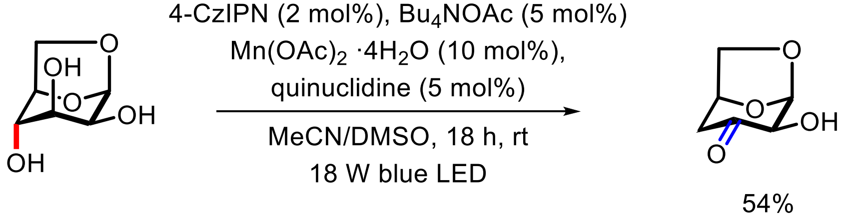
A Unified Strategy to Access 2- and 4-Deoxygenated Sugars



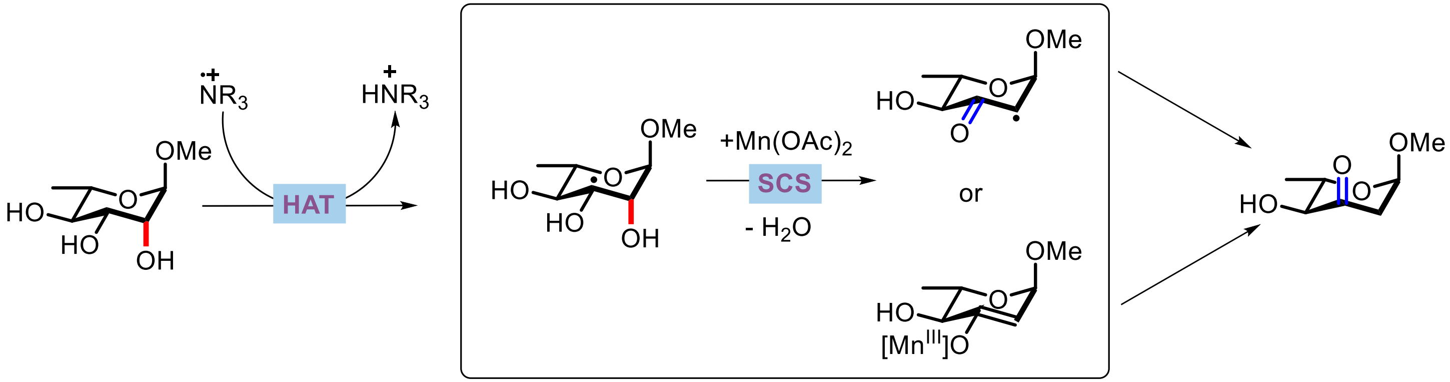
R = Me, 50%, R = Cy, 39%
R = Bn, 42%, R = H, 0%

Examples of regioselectivity





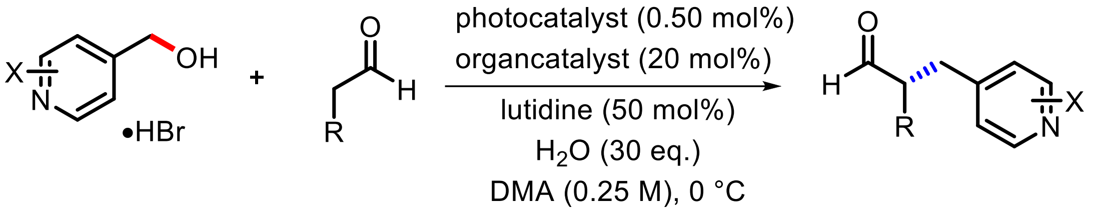
Possible reaction mechanism

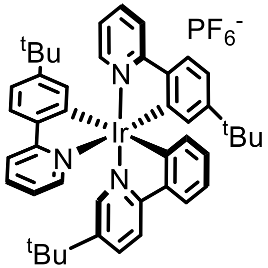


Carder, H. M.; Suh, C. E.; Wendlandt, A. E. *J. Am. Chem. Soc.* **2021**, *143*, 13798–13805.

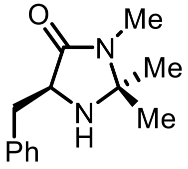
2.2. SET induced SCS process

Direct Enantioselective α-Benzylation of Aldehydes with Alcohols



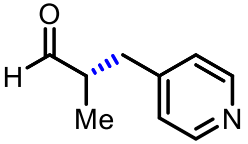


photocatalyst

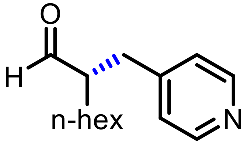


organocatalyst

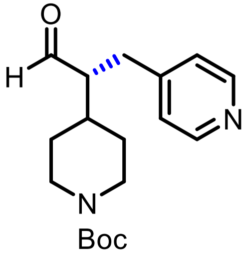
Substrate scope



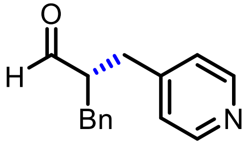
93% yield, 96% ee



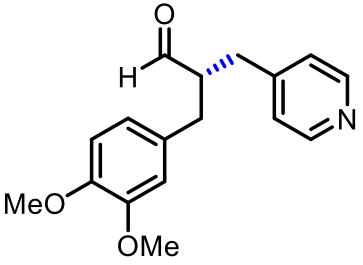
90% yield, 96% ee



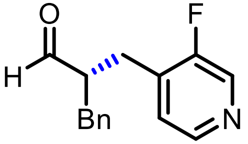
86% yield, 96% ee



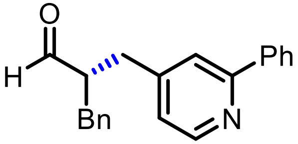
84% yield, 98% ee



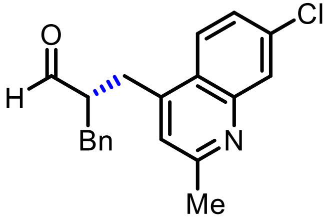
86% yield, 98% ee



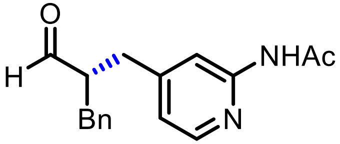
78% yield, 96% ee



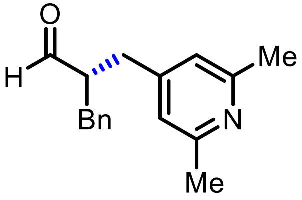
74% yield, 97% ee



76% yield, 99% ee



93% yield, 96% ee

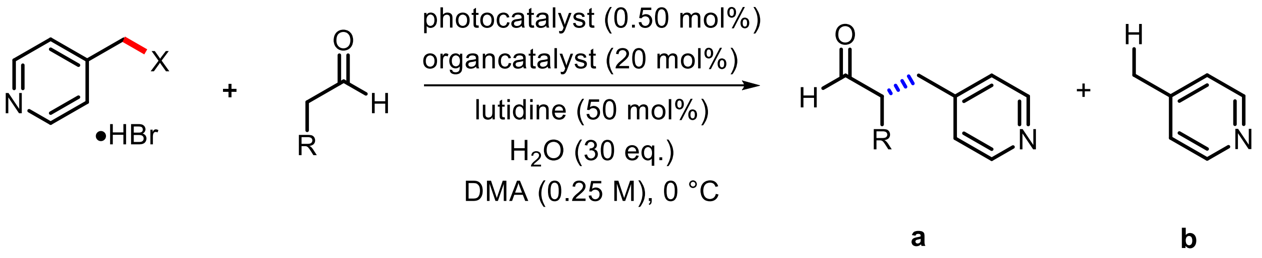


73% yield, 98% ee

Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140*, 3322–3330.

2.2. SET induced SCS process

Leaving group evaluation

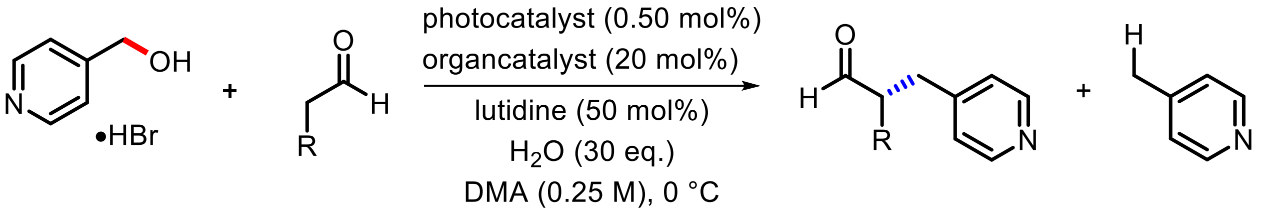


Entry	X	E^{red} (V)	K_{SV} (mM^{-1})	pK_a (XH)	yield (2 h)	yield [time]	a:b
1	OAc	**– 1.19**	0.84	**4.76**	75%	**90% [3 h]**	**18**
2	$NMe_3^+Br^-$	**n.d.**[b]	0.13	**9.80**	67%	**86% [5 h]**	**14**
3	OH	**– 1.29**	1.05	**15.7**	39%	**85% [5 h]**	**7.7**
4	OMe	**– 1.29**	1.15	**15.2**	29%	**71% [24 h]**	**5.1**
5	OTBDPS	**– 1.30**	0.82	**≈13.6**	20%	**61% [48 h]**	**3.1**
6	–	**– 1.30**	1.30	data for pyridine•HBr			

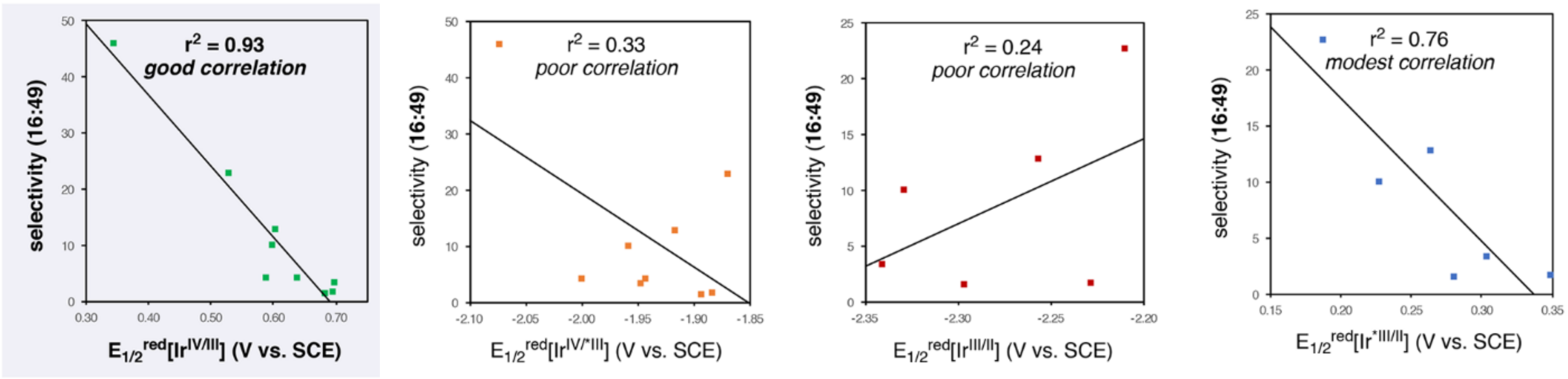
Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140*, 3322–3330.

2.2. SET induced SCS process

Selectivity vs. Photocatalyst electrochemical potentials



a **b**

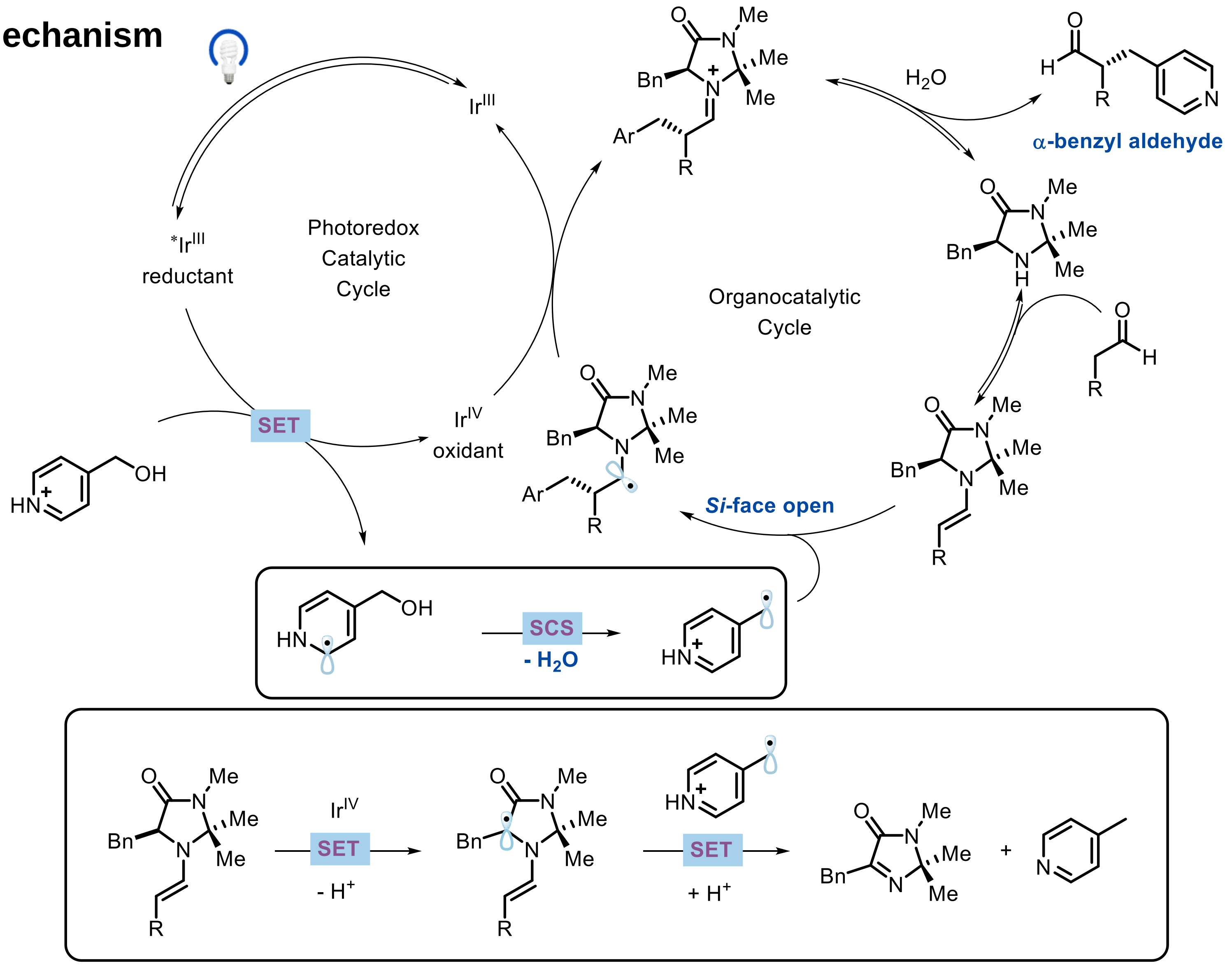


This is a screenshot, where **16** denotes compound **a** and **49** denotes compound **b**.

Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140*, 3322–3330.

2.2. SET induced SCS process

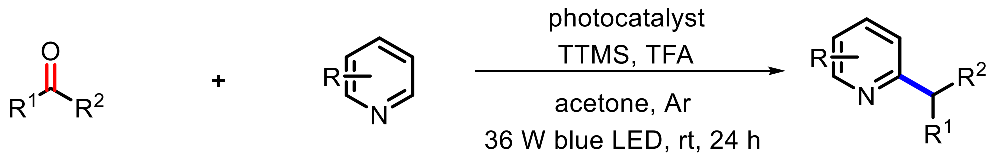
Possible reaction mechanism

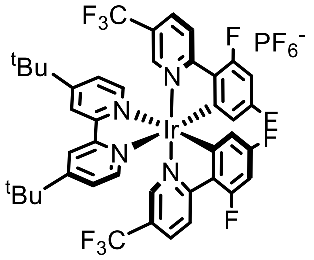


Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140*, 3322–3330.

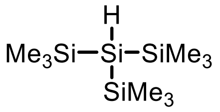
2.2. SET induced SCS process

Photoredox Alkylations of Heteroarene with Ketones or Aldehydes





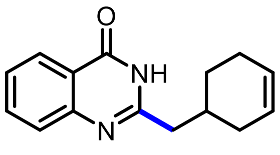
Photocatalyst



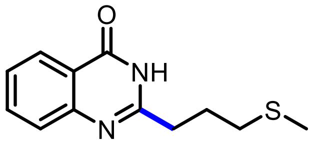
$\mathrm{Me_3Si{-}\overset{H}{\underset{SiMe_3}{Si}}{-}SiMe_3}$

TTMS

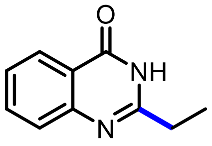
Substrate scope



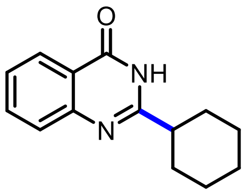
58%



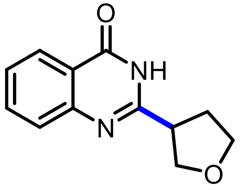
41%



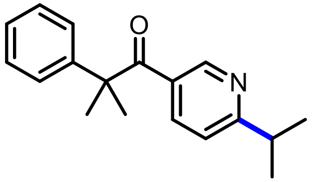
50%



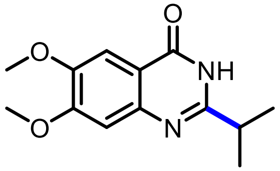
90%



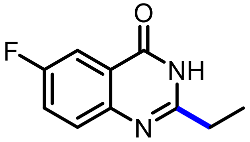
63%



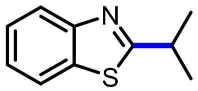
Metyrapone, 35%



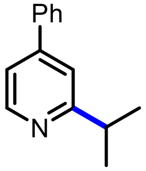
90%



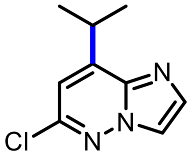
63%



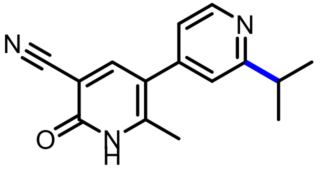
51%



56%



57%

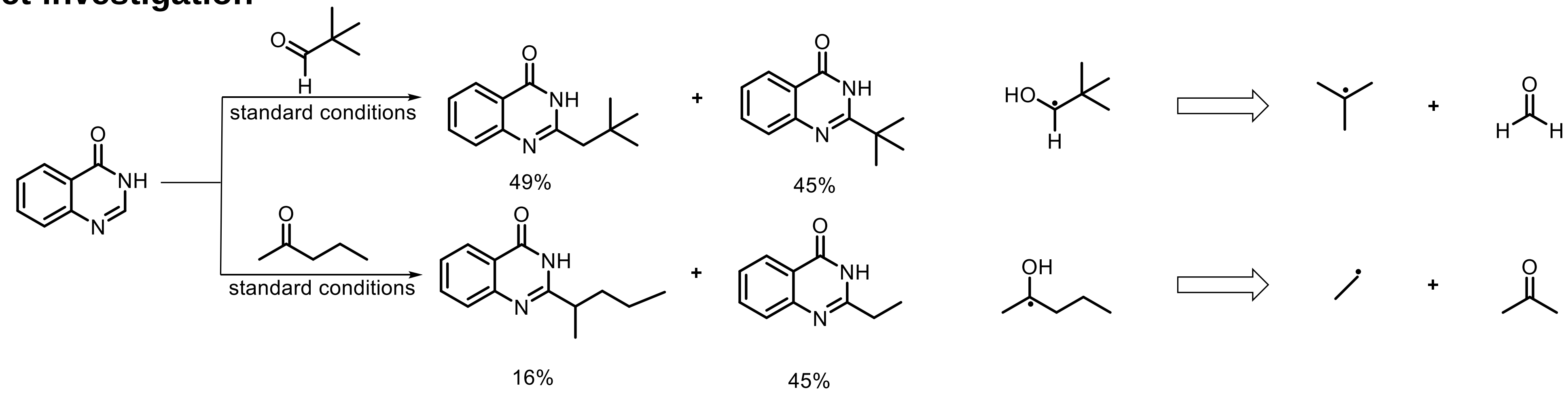


Milrinone, 41%

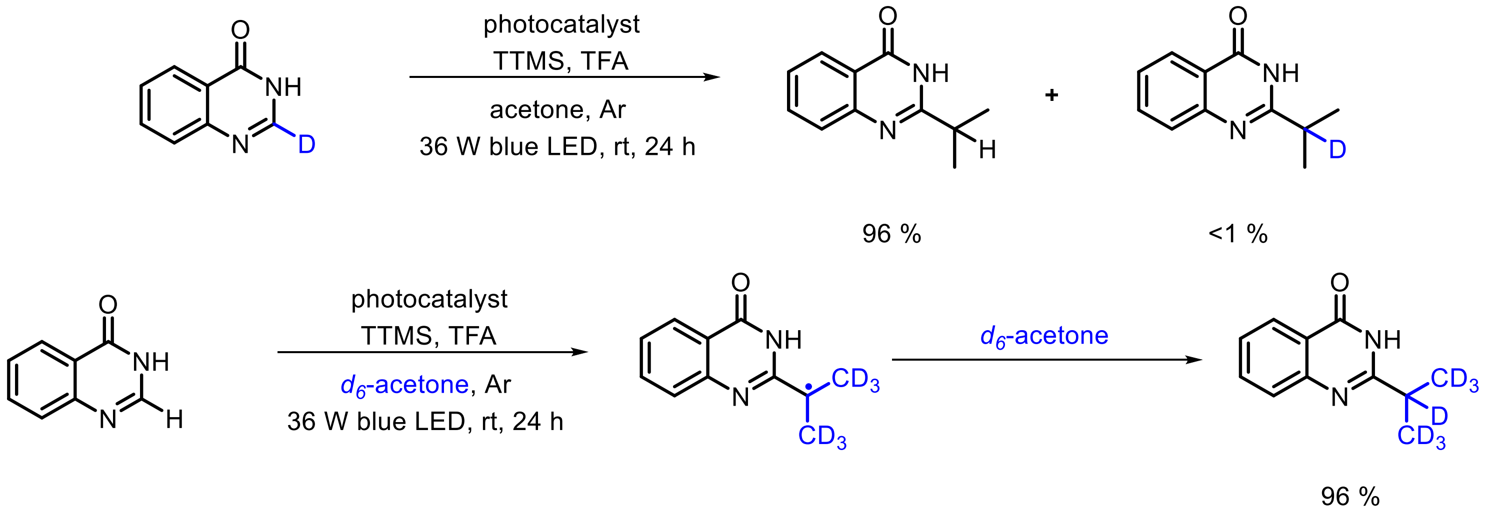
Dong, J.; Wang, Z.; Wang, X.; Song, H.; Liu, Y.; Wang, Q. *Sci. Adv.* **2019**, *5*, eaax9955.

2.2. SET induced SCS process

Byproduct investigation



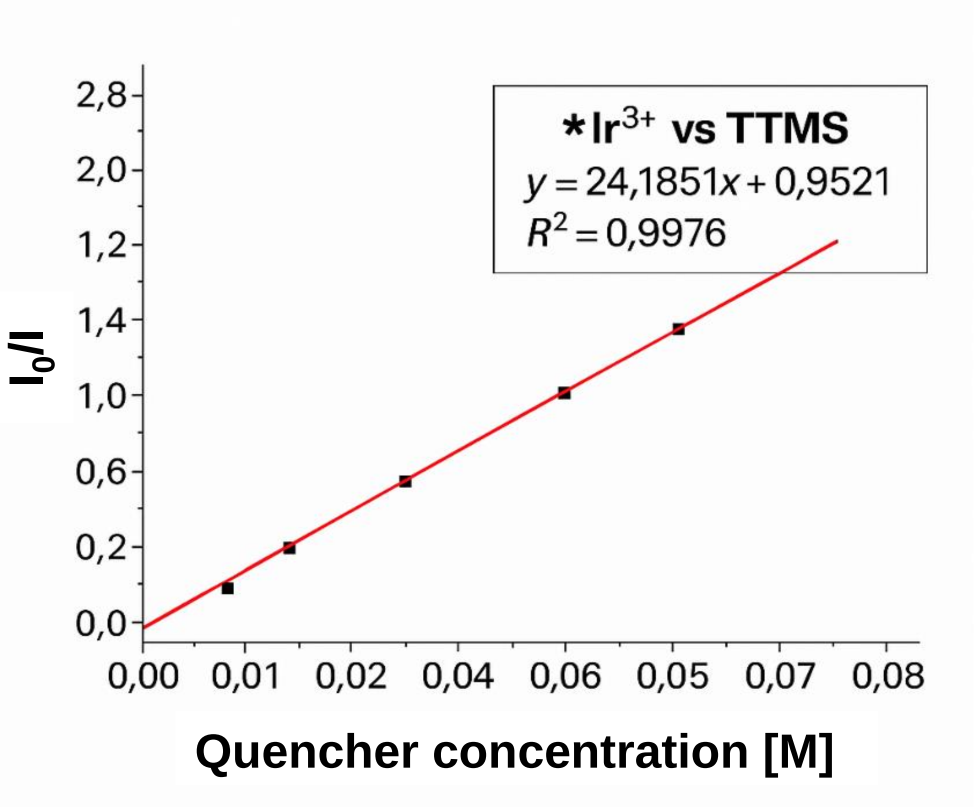
Deuterium-labeling studies



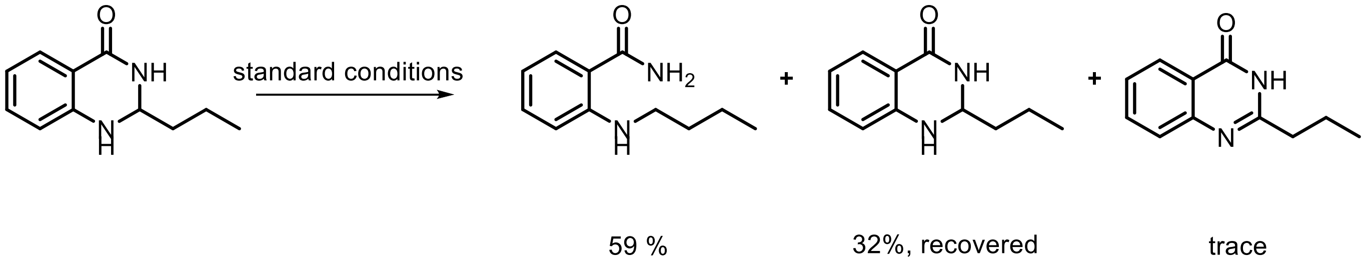
Dong, J.; Wang, Z.; Wang, X.; Song, H.; Liu, Y.; Wang, Q. *Sci. Adv.* **2019**, *5*, eaax9955.

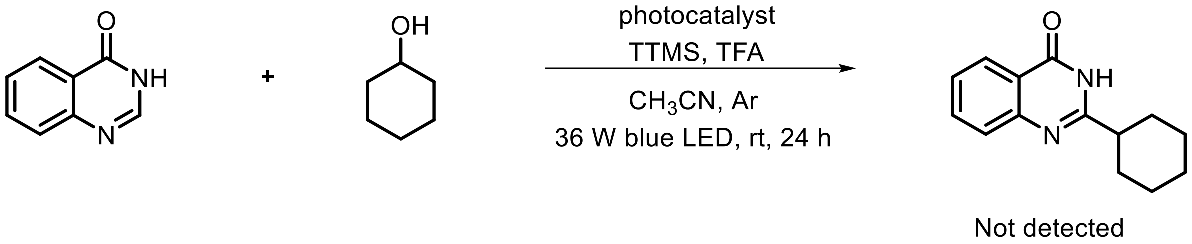
2.2. SET induced SCS process

Stern-Volmer fluorescence quenching study



Intermediate exploration

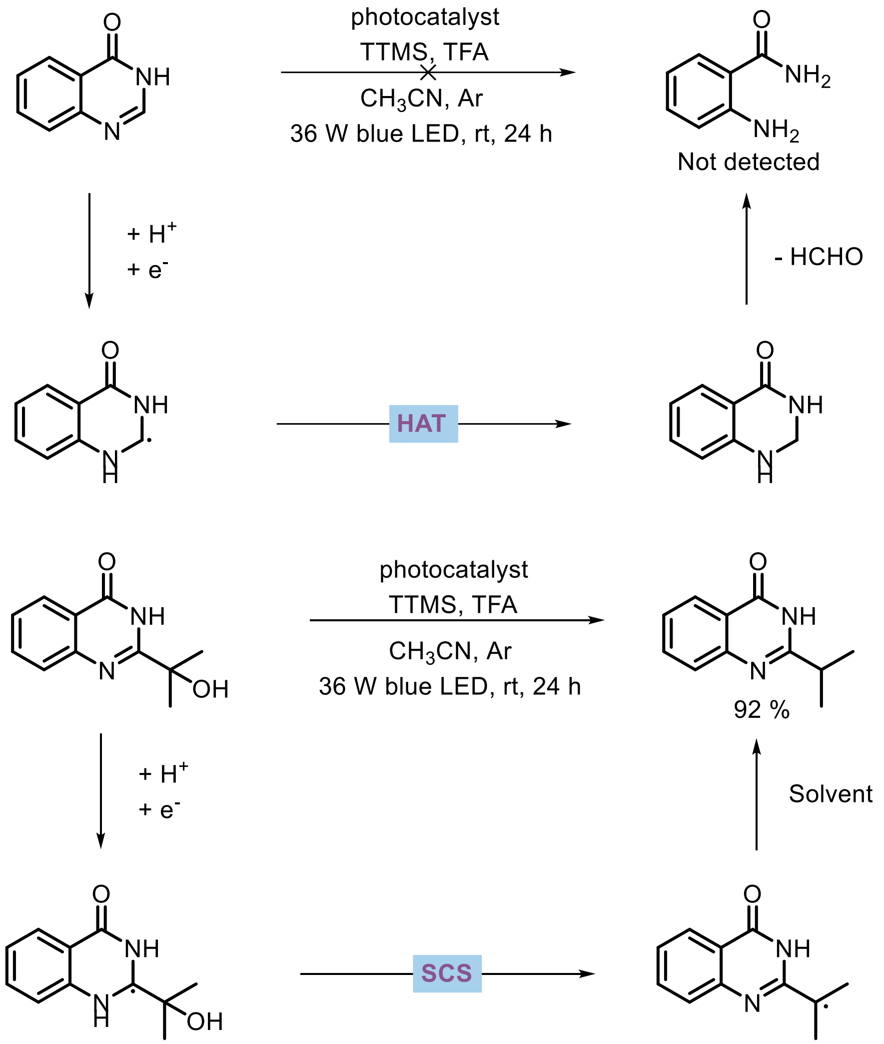




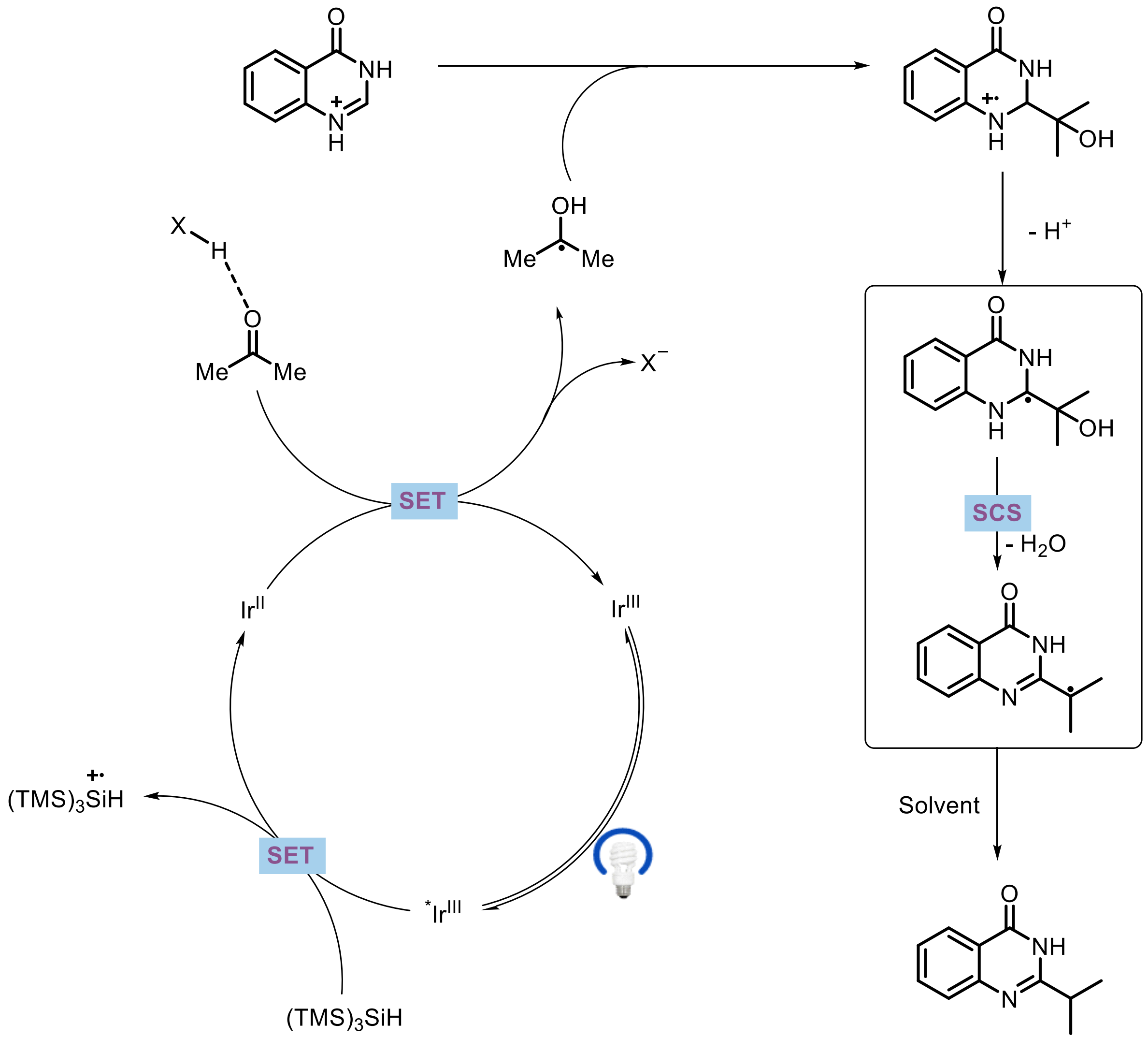
Dong, J.; Wang, Z.; Wang, X.; Song, H.; Liu, Y.; Wang, Q. *Sci. Adv.* **2019**, *5*, eaax9955.

2.2. SET induced SCS process

Intermediate exploration



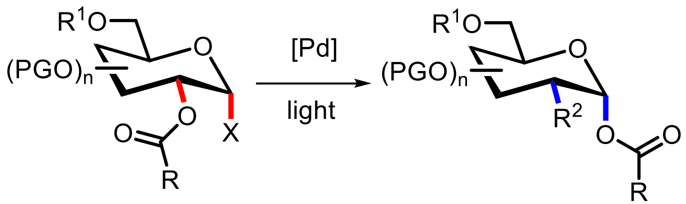
Possible reaction mechanism



Dong, J.; Wang, Z.; Wang, X.; Song, H.; Liu, Y.; Wang, Q. *Sci. Adv.* **2019**, *5*, eaax9955.

2.2. SET induced SCS process

Excited-State Palladium-Catalyzed 1,2-Spin-Center Shift



X = Br / I

R^2 = H

Pd(PPh$_3$)$_4$ (5.0 mol%)
DIPEA (2.0 eq.)
^{i}PrOAc (0.05 M)
24 W Blue LED, rt, 20 h

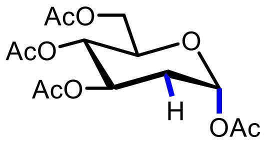
R^2 = D

Pd(PPh$_3$)$_4$ (5.0 mol%)
Cs$_2$CO$_3$(2.0 eq.)
d$_8$-THF (0.05 M)
24 W Blue LED, rt, 20 h

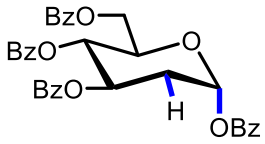
X = R^2 = I

Pd(PPh$_3$)$_4$ (5.0 mol%)
Cs$_2$CO$_3$(25 mol%)
^{t}BuOH (0.10 M)
24 W Blue LED, rt, 20 h

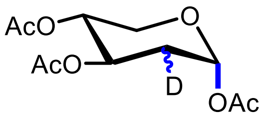
Substrate scope



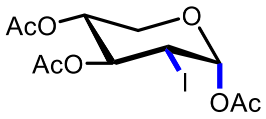
94%, (> 20:1)



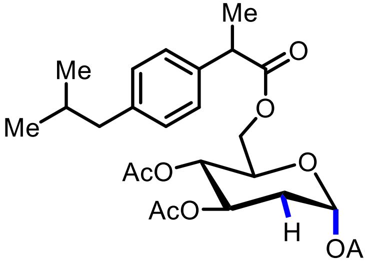
95%, (> 20:1)



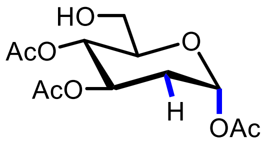
88%, (10:1)
82%D



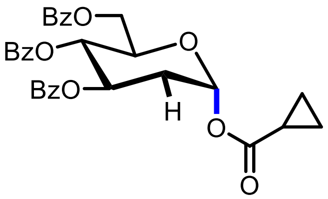
78%, (1.2:1)



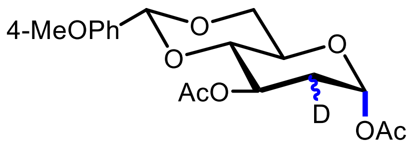
84%, (> 20:1)
Ibuprofen derivative



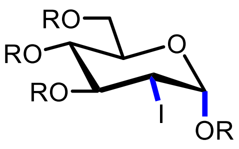
72%, (> 20:1)



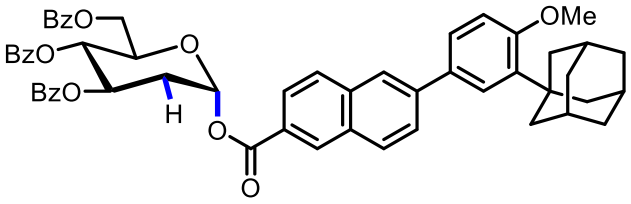
83%, (> 20:1)



95%, (8.5:1)
75%D



R = PhC(O), 78%, (> 10:1)

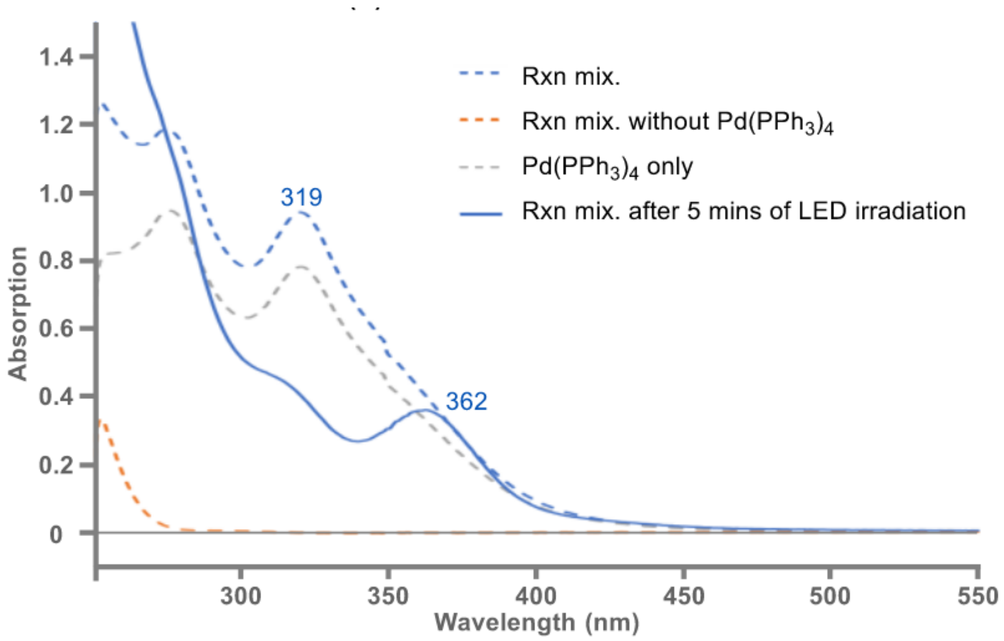


64%, (> 20:1)
Adapalene derivative

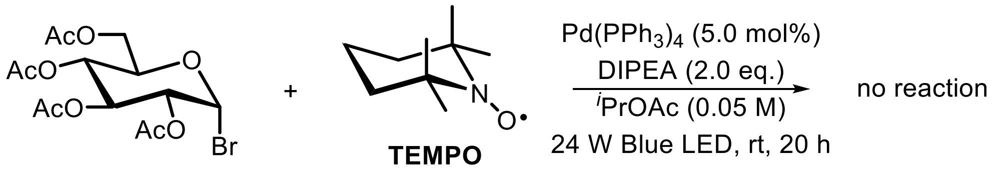
Zhao, G.; Yao, W.; Mauro, J. N.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2021**, *143*, 1728–1734.

2.2. SET induced SCS process

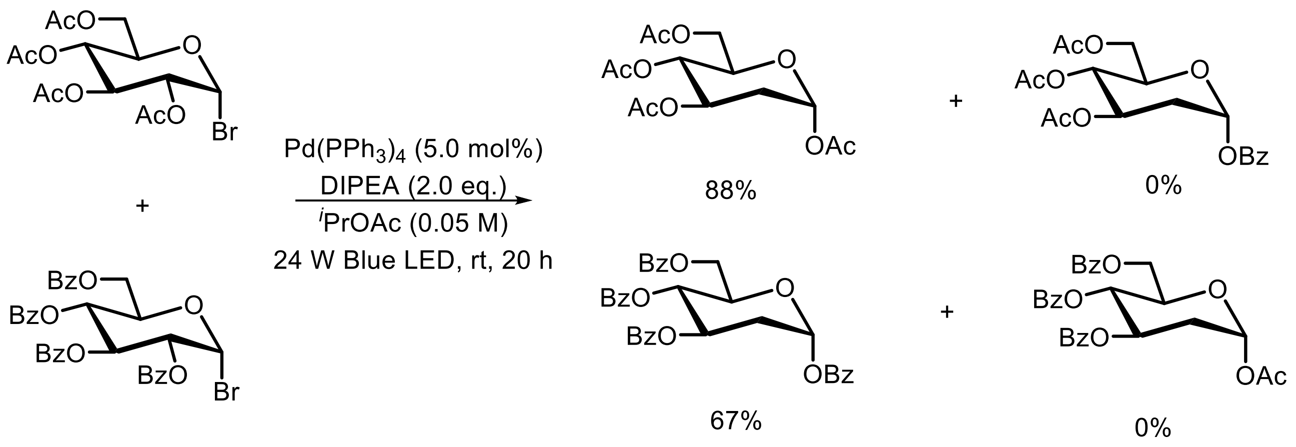
UV-vis measurement



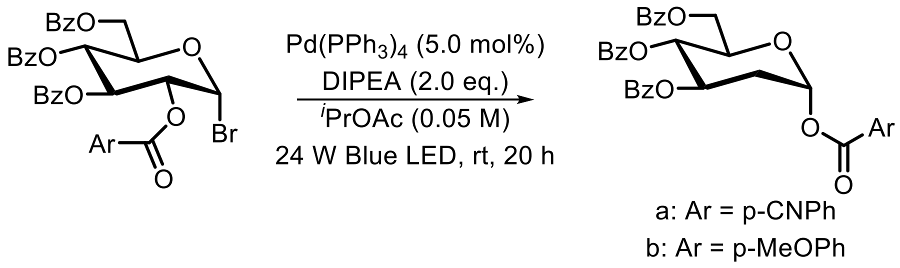
Radical trapping experiment



Cross-over experiments



Reaction rate measurement

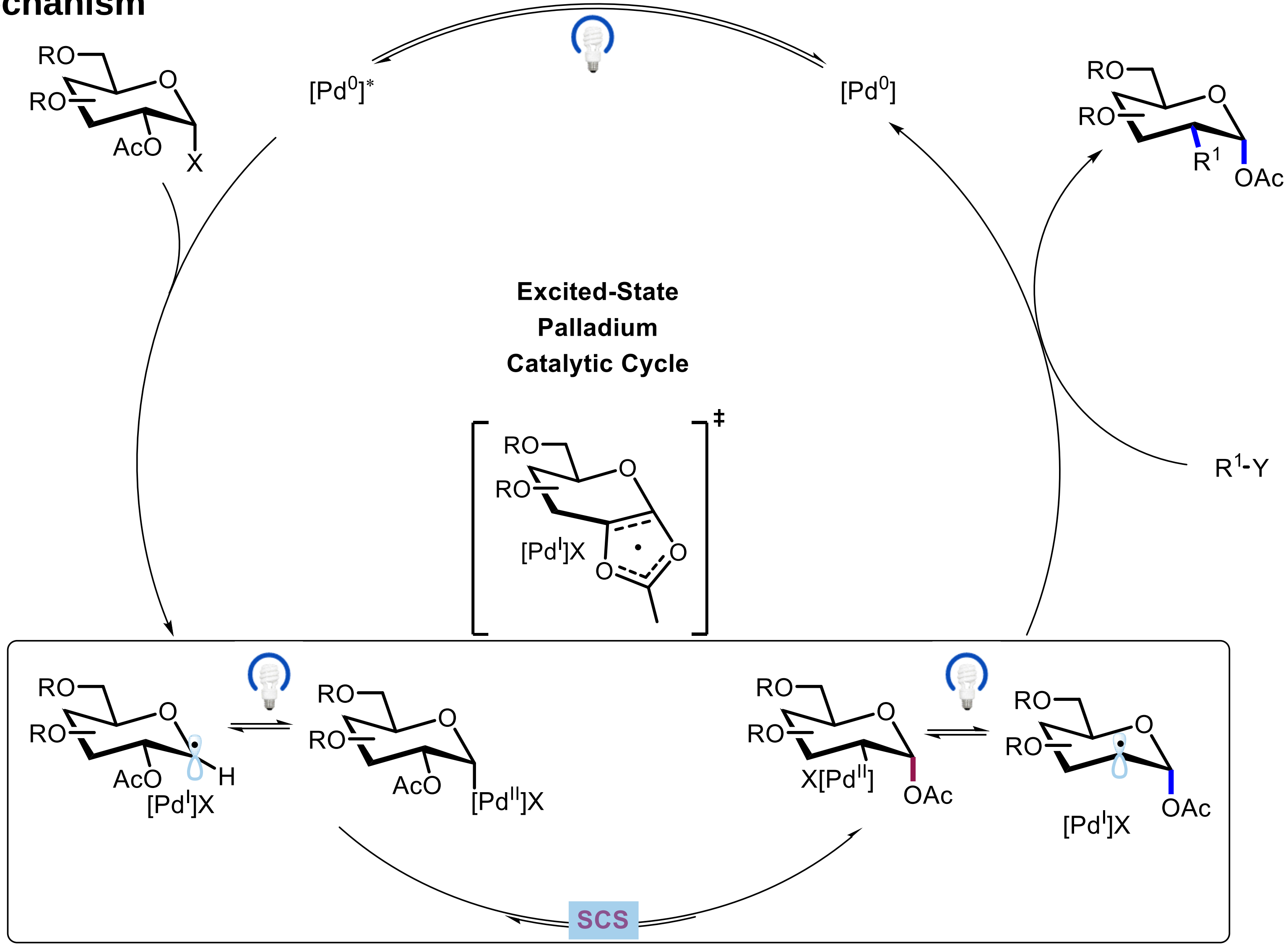


Time (h)	Yield (%)	
	a	b
0.5	7	8
1.0	11	12
2.0	23	24
4.0	33	34
8.0	45	48

Zhao, G.; Yao, W.; Mauro, J. N.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2021**, *143*, 1728–1734.

2.2. SET induced SCS process

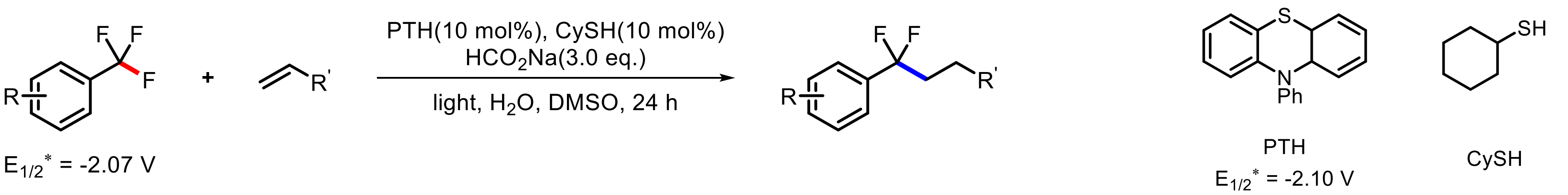
Possible reaction mechanism



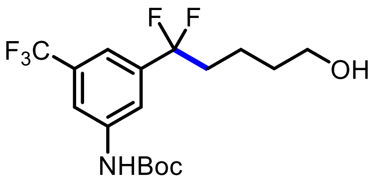
Zhao, G.; Yao, W.; Mauro, J. N.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2021**, *143*, 1728–1734.

2.2. SET induced SCS process

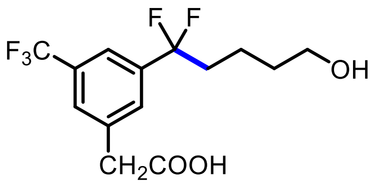
Catalytic Defluoroalkylation of Trifluoromethylaromatics



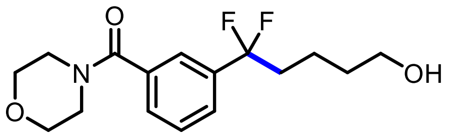
Substrate scope



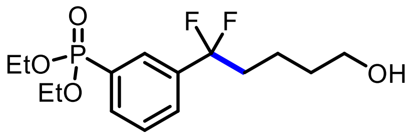
89 %



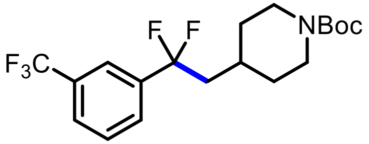
73 %



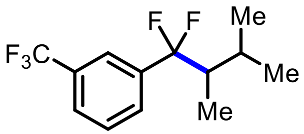
81 %



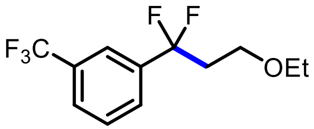
56 %



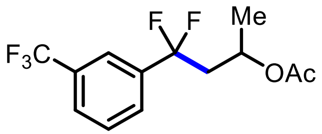
81 %



78 %



86 %

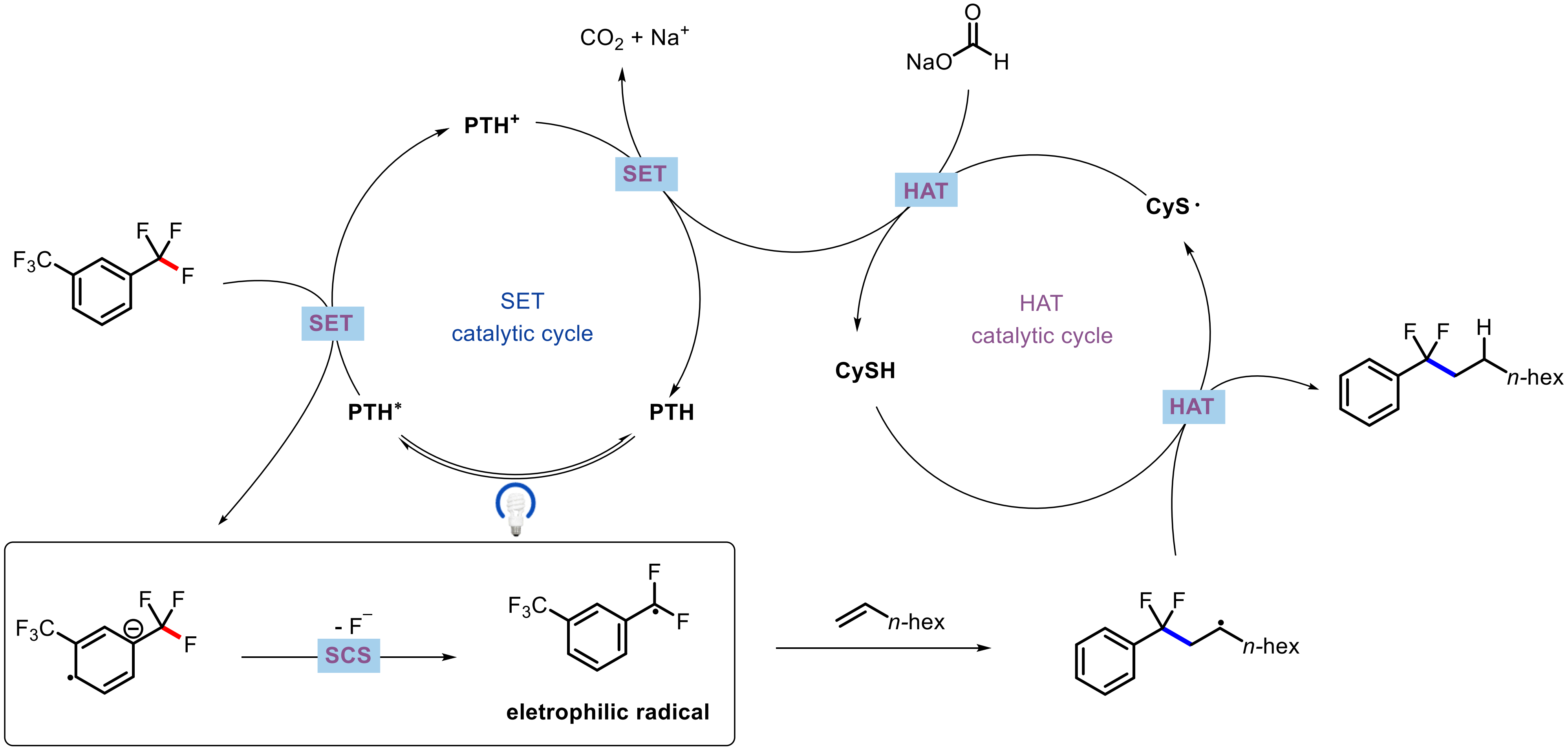


86 %

Wang, H.; Jui, N. T. *J. Am. Chem. Soc.* **2018**, *140*, 163–166.

2.2. SET induced SCS process

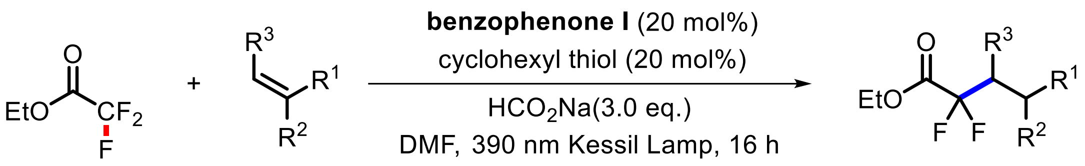
Possible reaction mechanism

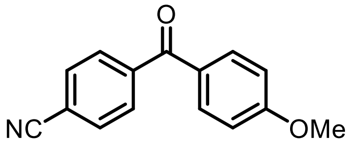


Wang, H.; Jui, N. T. *J. Am. Chem. Soc.* **2018**, *140*, 163–166.

2.2. SET induced SCS process

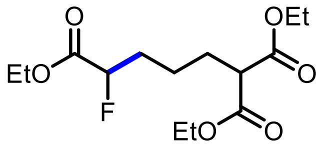
Photochemical C−F Activation with Sodium Formate



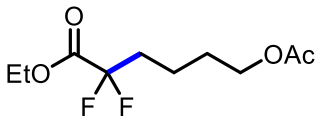


benzophenone I

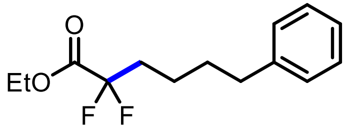
Substrate scope



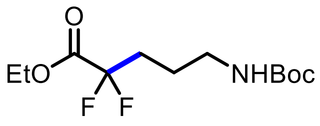
98 %



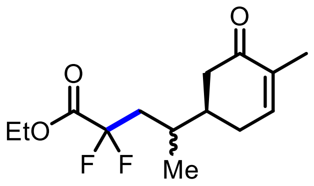
98 %



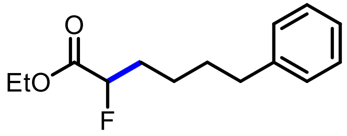
80 %



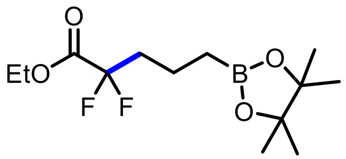
80 %



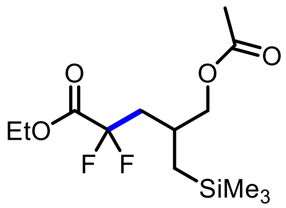
53%, dr = 1:1
from (-)-carvone



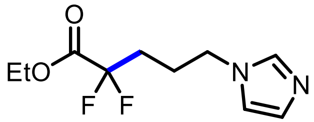
85 %



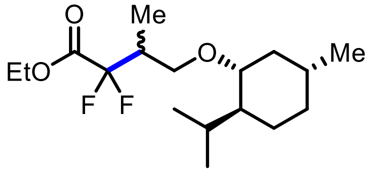
92 %



44 %



62 %

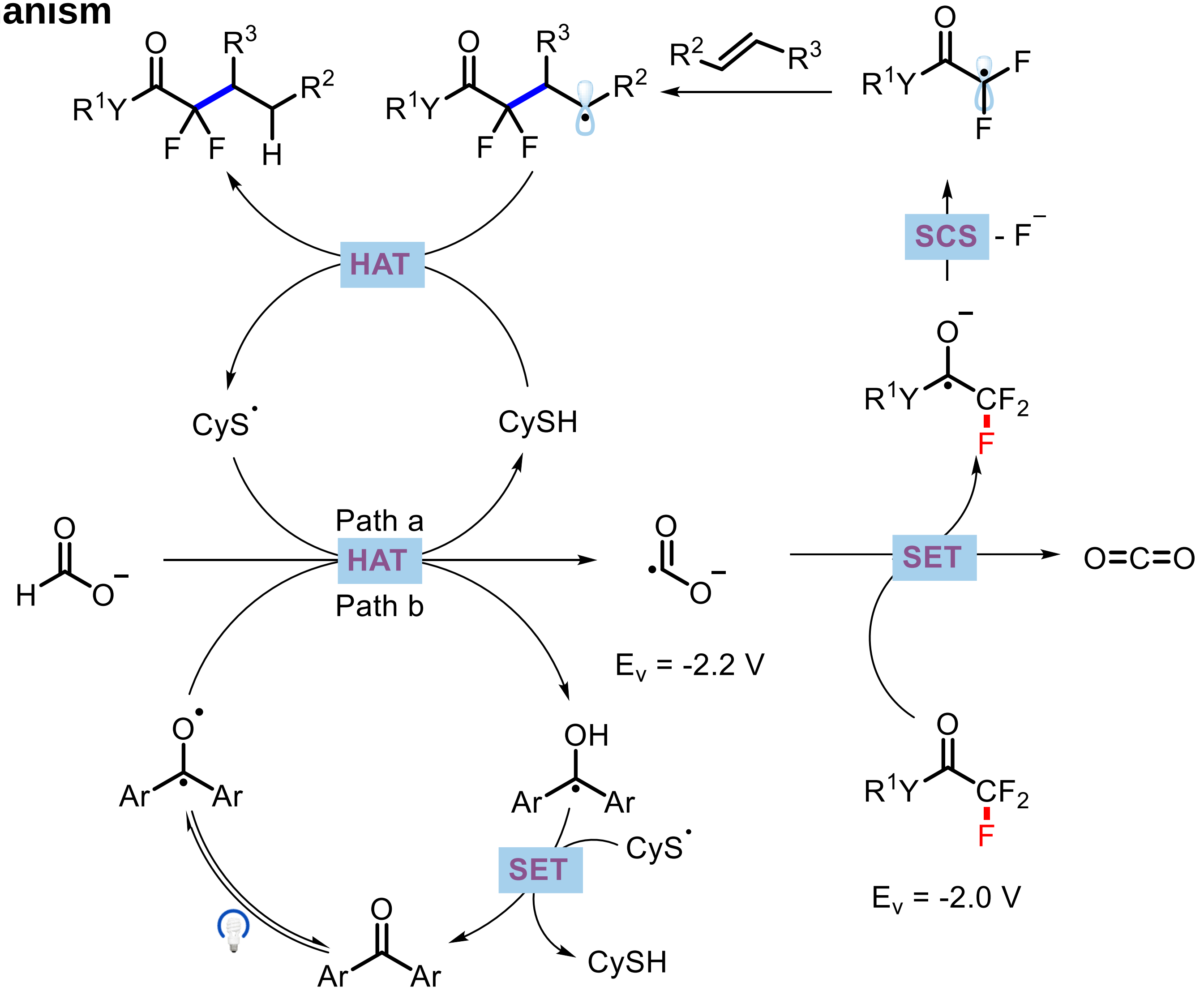


92%, dr = 1:1
from (-)-menthol

Campbell, M. W.; Polites, V. C.; Patel, S.; Lipson, J. E.; Majhi, J.; Molander, G. A. *J. Am. Chem. Soc.* **2021**, *143*, 19648–19654.

2.2. SET induced SCS process

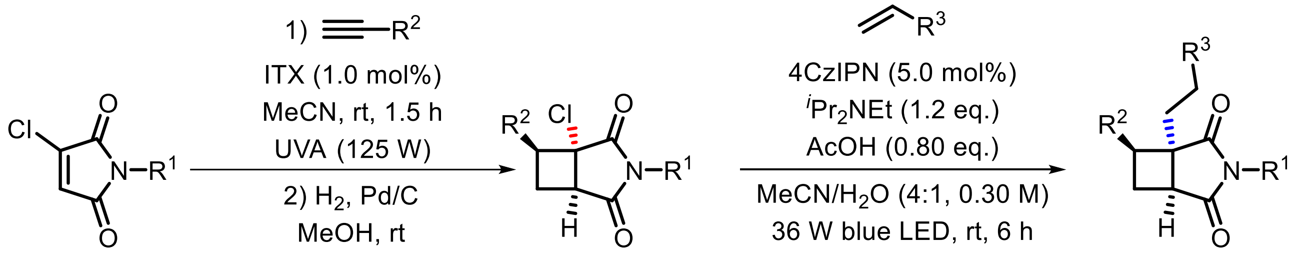
Possible reaction mechanism



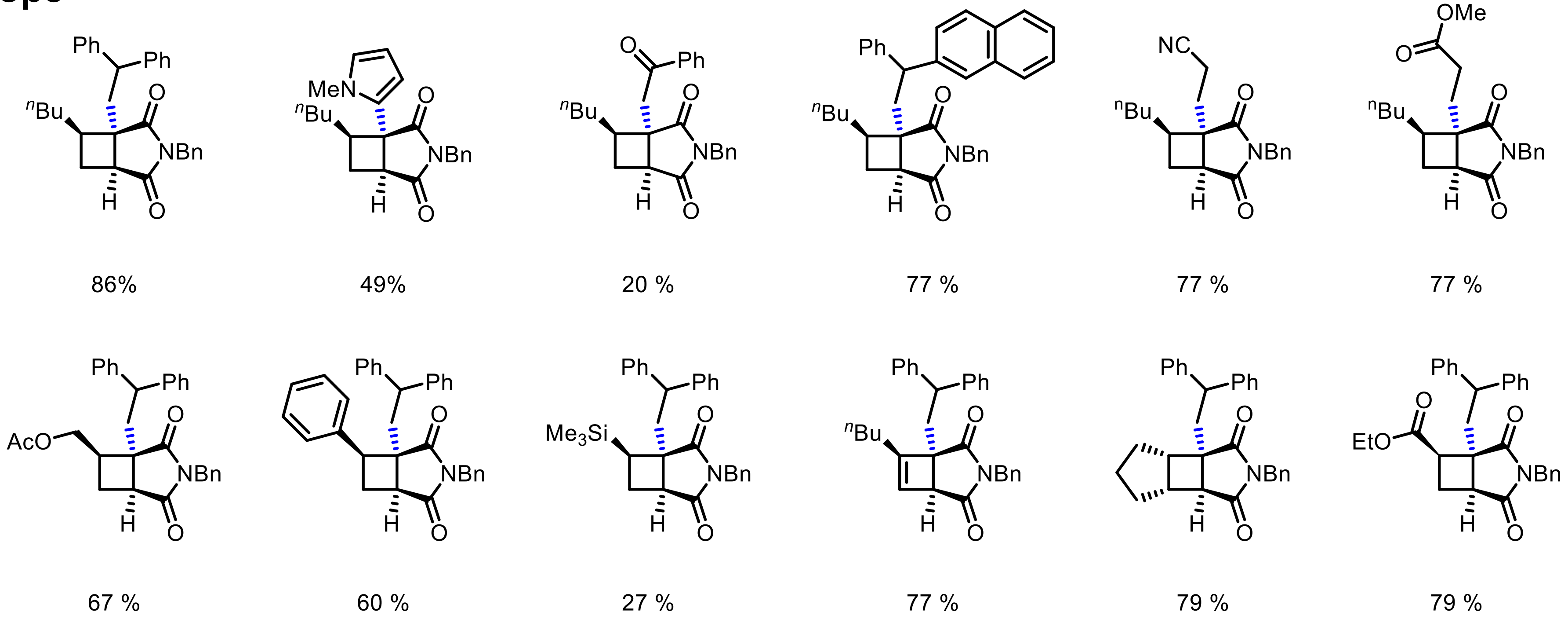
Campbell, M. W.; Polites, V. C.; Patel, S.; Lipson, J. E.; Majhi, J.; Molander, G. A. *J. Am. Chem. Soc.* **2021**, *143*, 19648–19654.

2.2. SET induced SCS process

Sequential Photocatalytic Reactions for the Synthesis of Cyclobutane Scaffolds



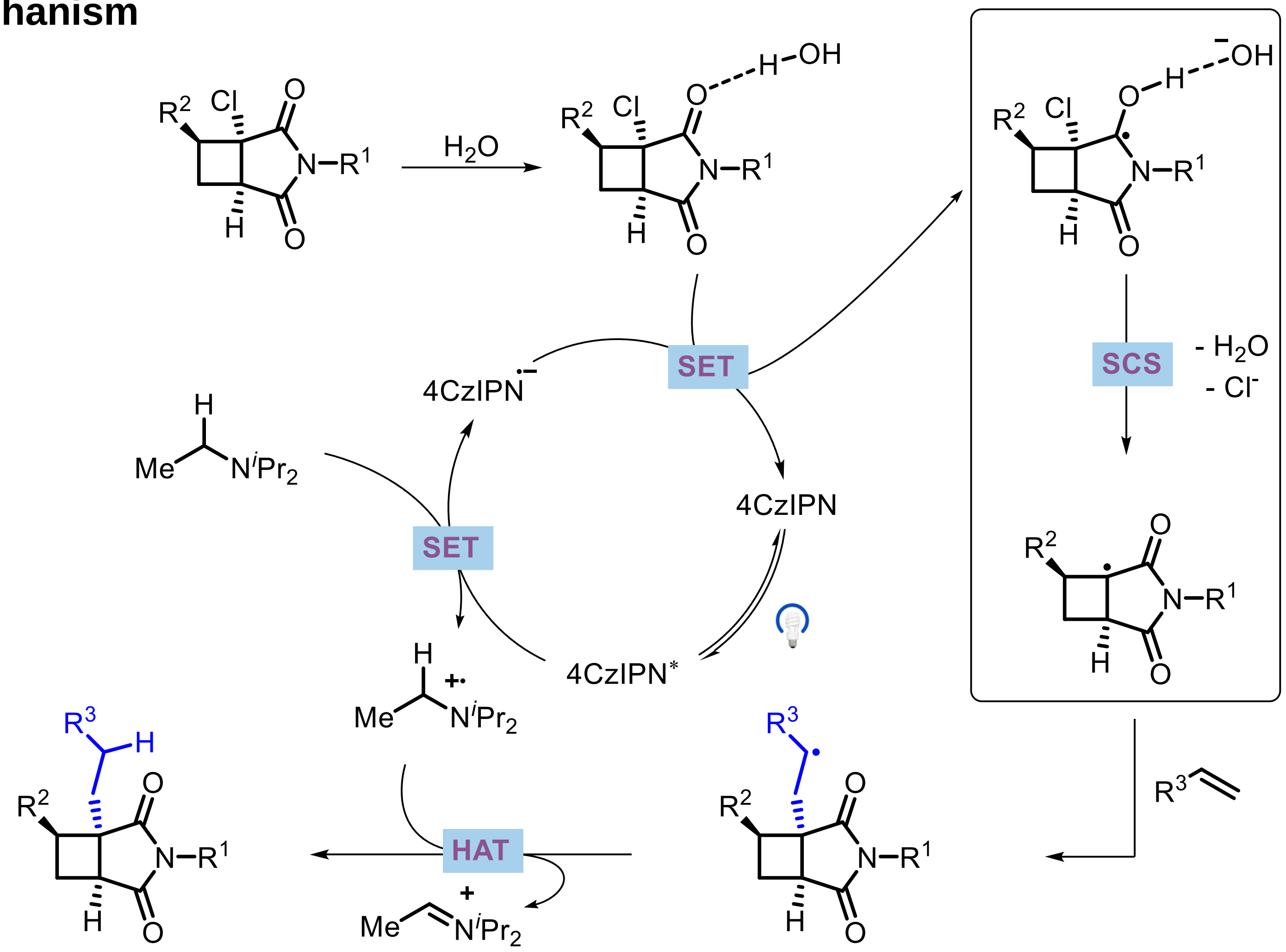
Substrate scope



Deeprose, M. J.; Lowe, M.; Noble, A.; Booker-Milburn, K. I.; Aggarwal, V. K. *Org. Lett.* **2022**, *24*, 137–141.

2.2. SET induced SCS process

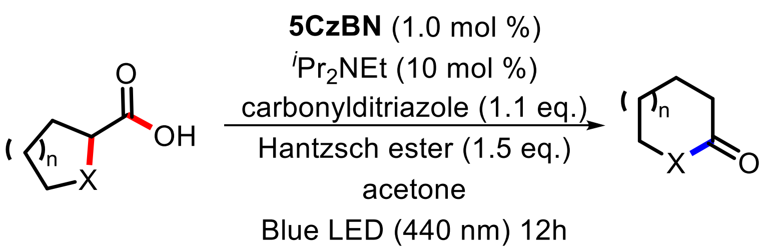
Possible reaction mechanism



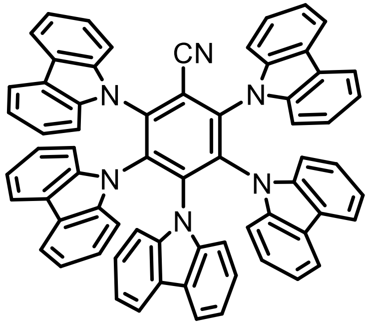
Deeprose, M. J.; Lowe, M.; Noble, A.; Booker-Milburn, K. I.; Aggarwal, V. K. *Org. Lett.* **2022**, *24*, 137–141.

2.2. SET induced SCS process

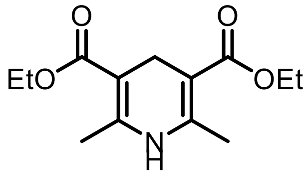
Carbonylative Ring Expansion of Cyclic Carboxylic Acids



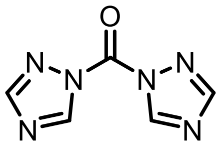
5CzBN (1.0 mol %)
$^{i}Pr_2NEt$ (10 mol %)
carbonylditriazole (1.1 eq.)
Hantzsch ester (1.5 eq.)
acetone
Blue LED (440 nm) 12h



5CzBN

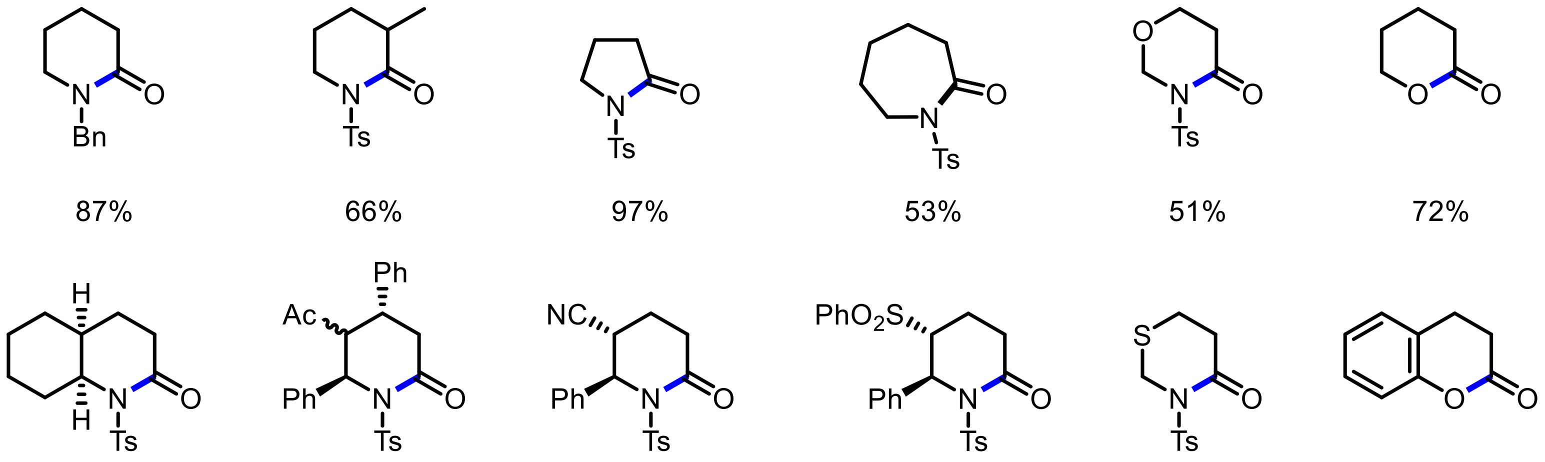


Hantzsch ester



carbonylditriazole

Substrate scope



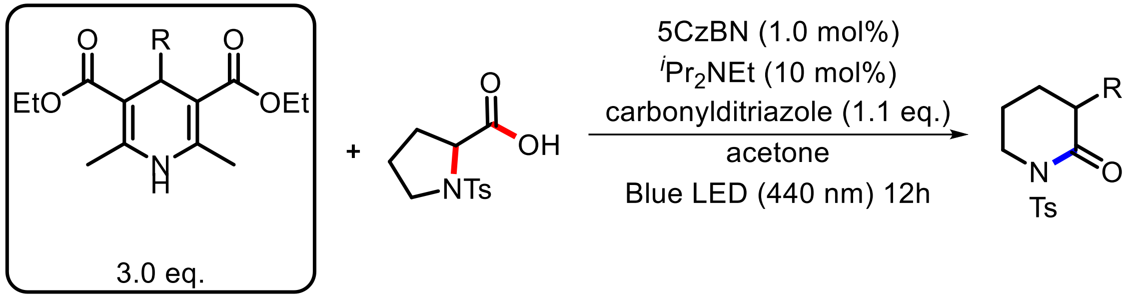
87% 66% 97% 53% 51% 72%

73% 74%, dr 1.1:1 62% 95% 61% 90%

Hiroki Shimono, Mayu Kusakabe, Kazunori Nagao, et al. Carbonylative Ring Expansion of Cyclic Carboxylic Acids through Spin-Center Shift. ChemRxiv. 26 May 2025.
DOI: https://doi.org/10.26434/chemrxiv-2025-0856k

2.2. SET induced SCS process

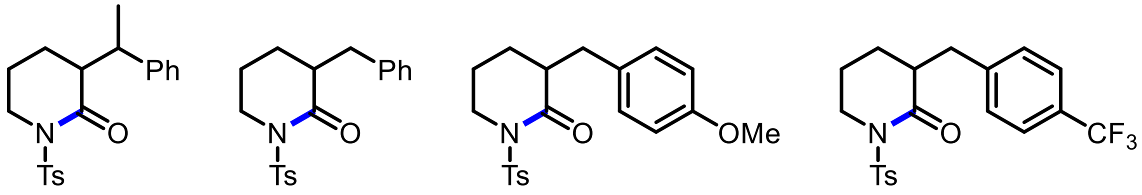
Reactions with alkyl radical precursors



3.0 eq.

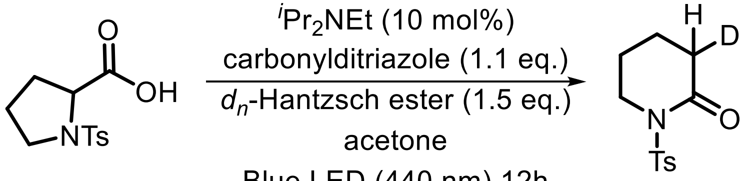
5CzBN (1.0 mol%)
$^{i}Pr_2NEt$ (10 mol%)
carbonylditriazole (1.1 eq.)
acetone
Blue LED (440 nm) 12h

Substrate scope

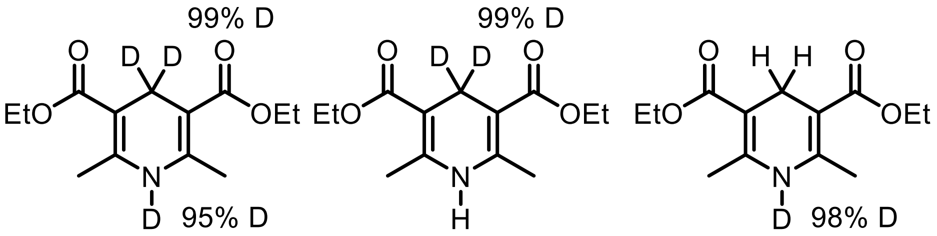


27%
28%
13%
22%

Deuterium labelling experiments



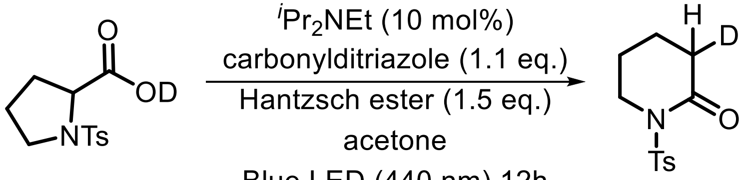
5CzBN (1.0 mol%)
$^{i}Pr_2NEt$ (10 mol%)
carbonylditriazole (1.1 eq.)
d_n-Hantzsch ester (1.5 eq.)
acetone
Blue LED (440 nm) 12h



d_3-Hantzsch ester
86% yield, 77% D

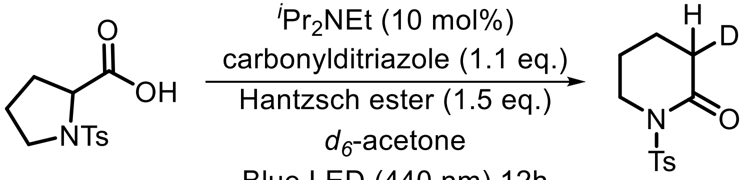
d_2-Hantzsch ester
83% yield, 72% D

d_1-Hantzsch ester
88% yield, 6% D



5CzBN (1.0 mol%)
$^{i}Pr_2NEt$ (10 mol%)
carbonylditriazole (1.1 eq.)
Hantzsch ester (1.5 eq.)
acetone
Blue LED (440 nm) 12h

92% yield,
3% D



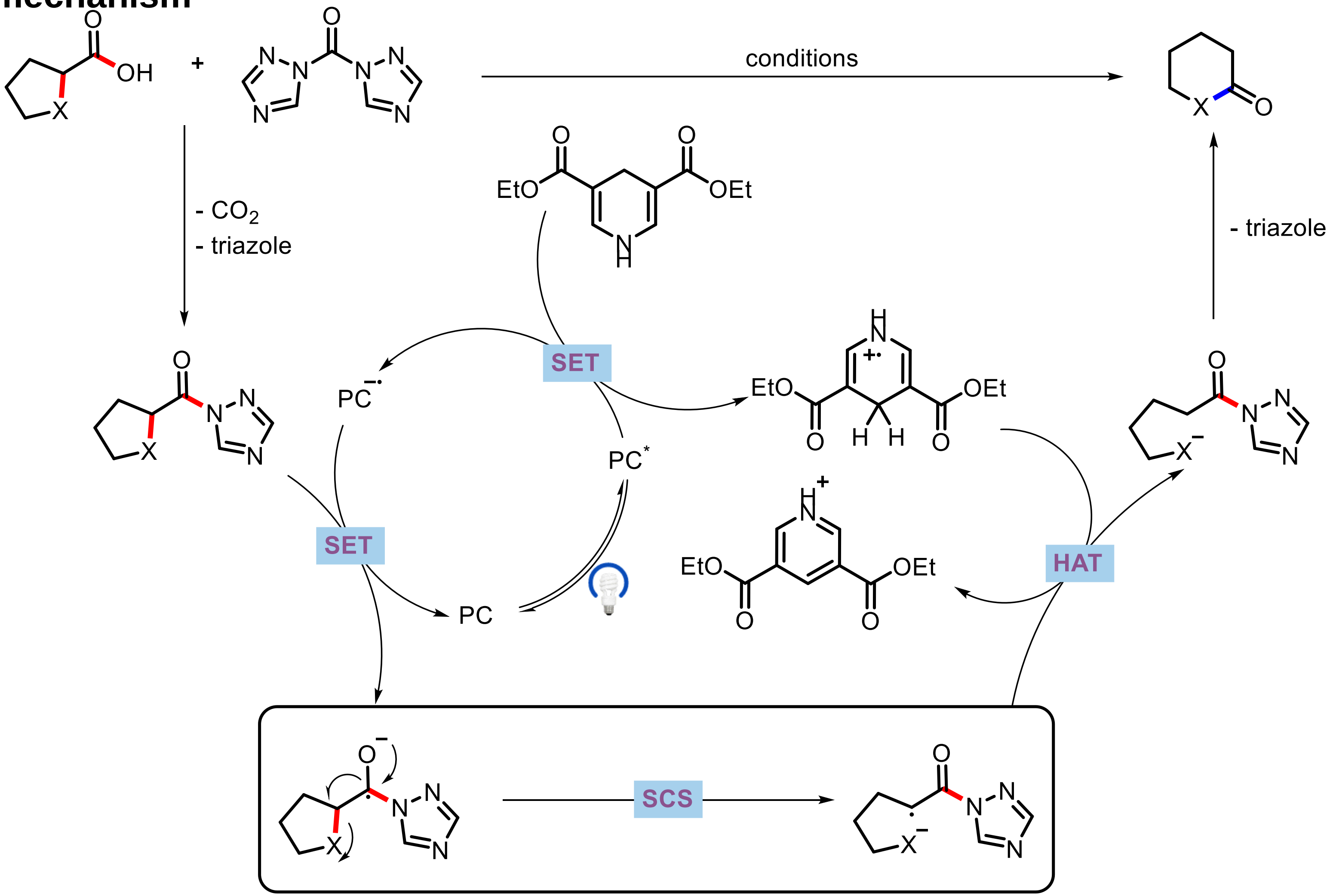
5CzBN (1.0 mol%)
$^{i}Pr_2NEt$ (10 mol%)
carbonylditriazole (1.1 eq.)
Hantzsch ester (1.5 eq.)
d_6-acetone
Blue LED (440 nm) 12h

85% yield,
0% D

Hiroki Shimono, Mayu Kusakabe, Kazunori Nagao, et al. Carbonylative Ring Expansion of Cyclic Carboxylic Acids through Spin-Center Shift. ChemRxiv. 26 May 2025.
DOI: https://doi.org/10.26434/chemrxiv-2025-0856k

2.2. SET induced SCS process

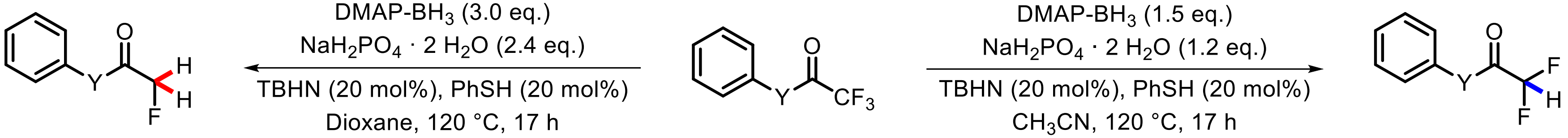
Possible reaction mechanism



Hiroki Shimono, Mayu Kusakabe, Kazunori Nagao, et al. Carbonylative Ring Expansion of Cyclic Carboxylic Acids through Spin-Center Shift. ChemRxiv. 26 May 2025.
DOI: https://doi.org/10.26434/chemrxiv-2025-0856k

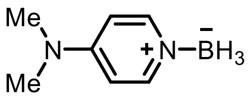
2.3. Radical addition induced SCS process

Sequential Hydrogenolysis of C–F Bonds

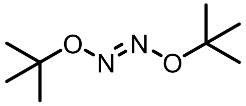


DMAP-BH_3 (3.0 eq.)
$NaH_2PO_4 \cdot 2\ H_2O$ (2.4 eq.)
TBHN (20 mol%), PhSH (20 mol%)
Dioxane, 120 °C, 17 h

DMAP-BH_3 (1.5 eq.)
$NaH_2PO_4 \cdot 2\ H_2O$ (1.2 eq.)
TBHN (20 mol%), PhSH (20 mol%)
CH_3CN, 120 °C, 17 h

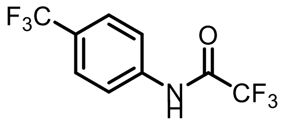


DMAP-BH_3

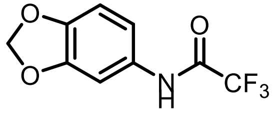


TBHN

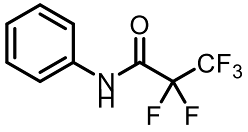
Substrate scope



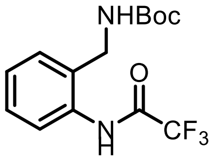
58 % CF_2H, 73% CFH_2



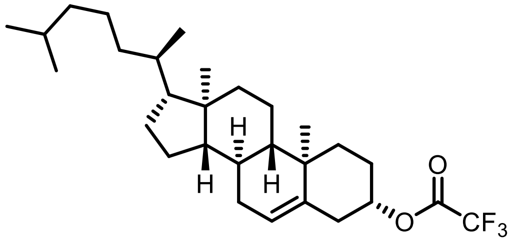
76 % CF_2H, 84% CFH_2



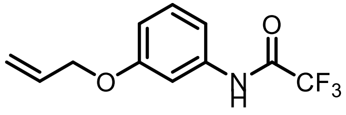
92 % $CFHCF_3$, 94% CH_2CF_3



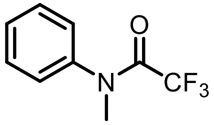
65 % CF_2H, 80% CFH_2



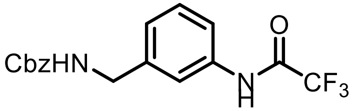
56 % CF_2H, trace CFH_2



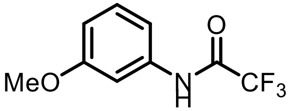
34 % CF_2H, 50% CFH_2



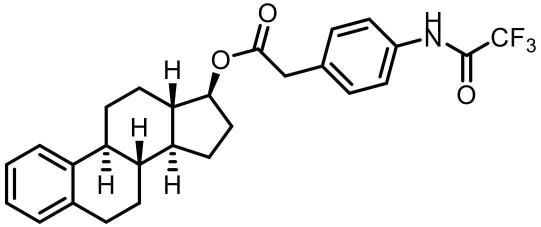
41 % CF_2H, 51% CFH_2



70 % CF_2H, 90% CFH_2



44 % CF_2H, trace CFH_2

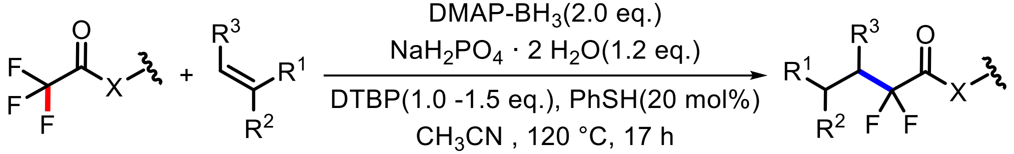


65 % CF_2H, 76% CFH_2

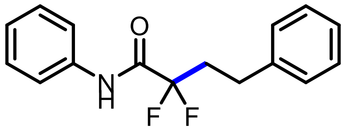
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

2.3. Radical addition induced SCS process

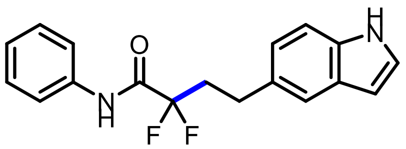
Sequential Hydrogenolysis of C–F Bonds



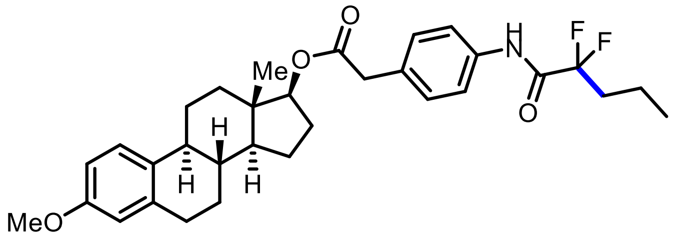
Substrate scope



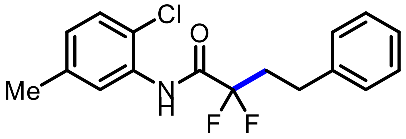
75%
(gram-scale, 59%)



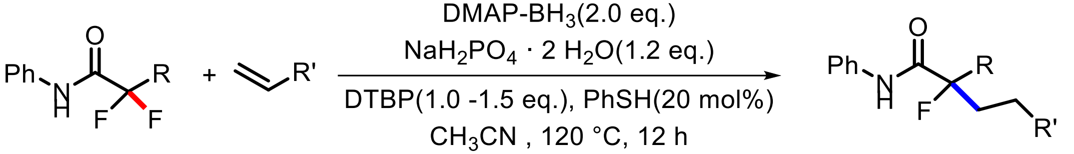
83%



65%

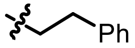


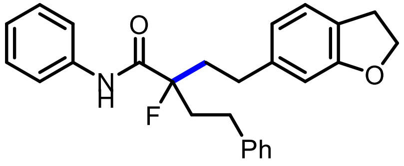
70%



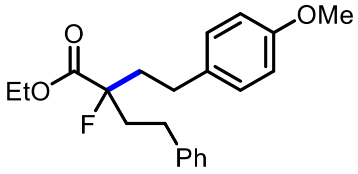
Substrate scope

R =

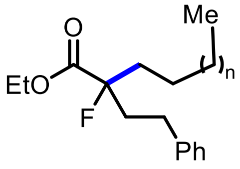




42%

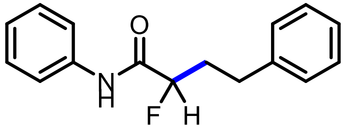


60%

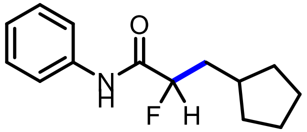


30%

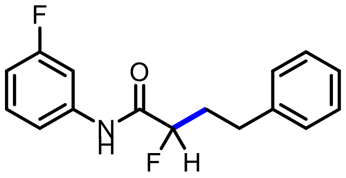
R = H



70%
(gram-scale, 77%)



64%

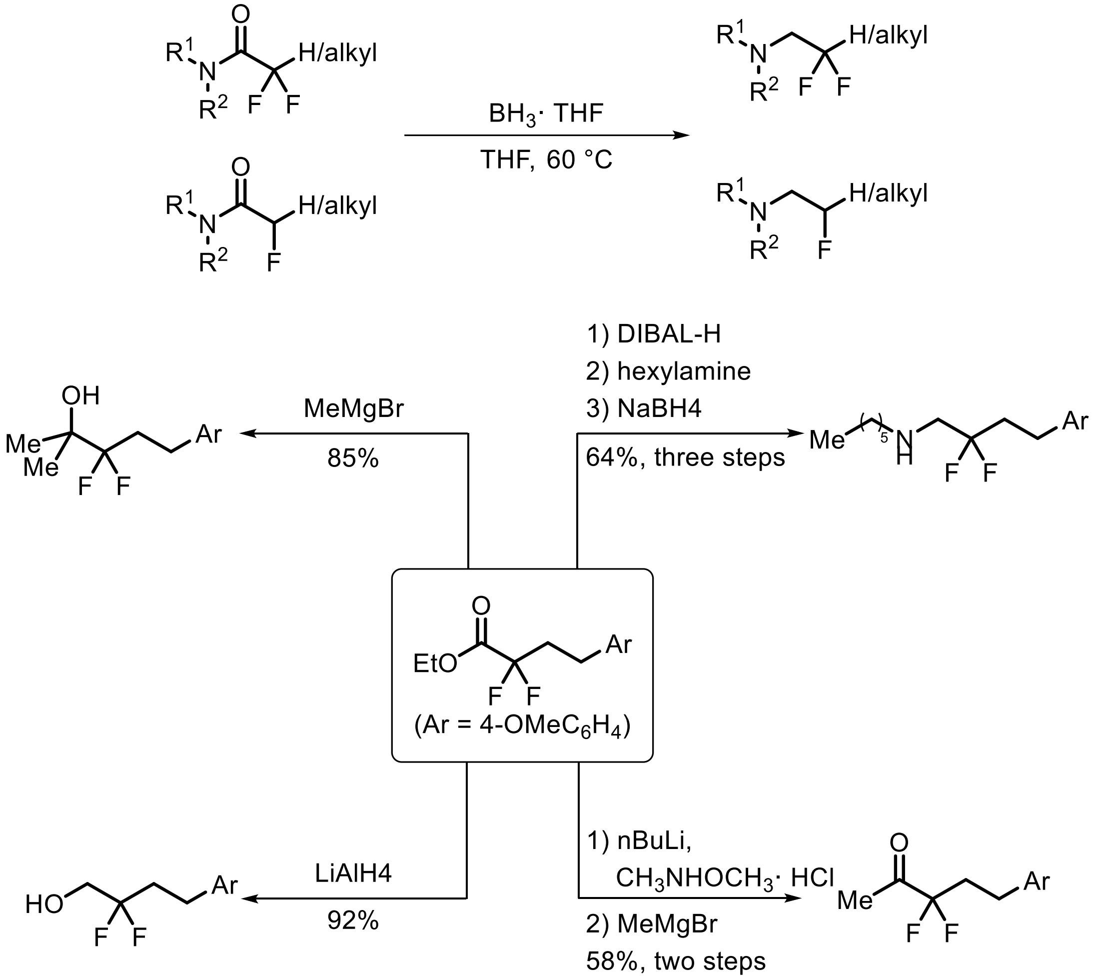


68%

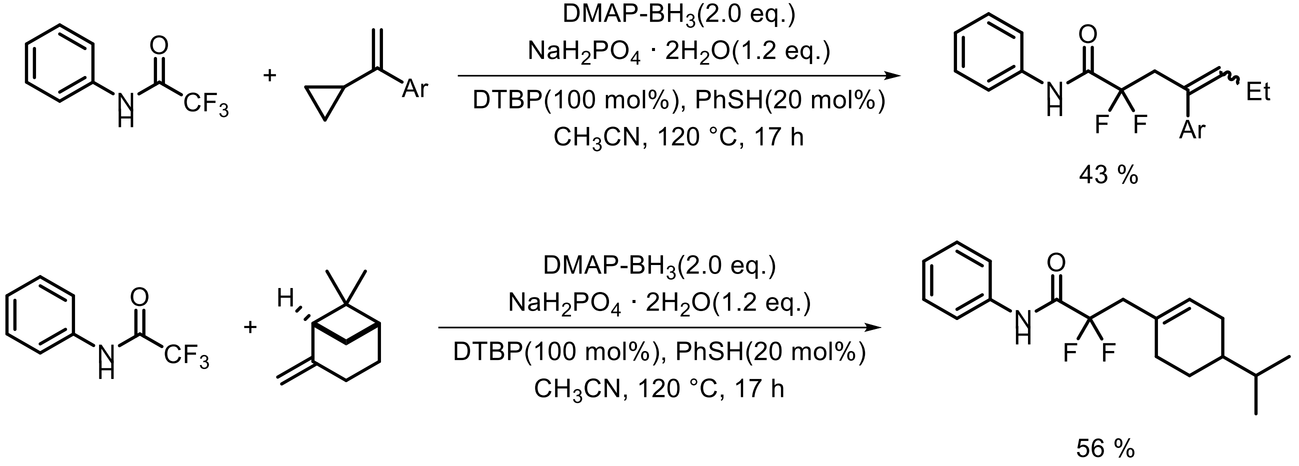
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

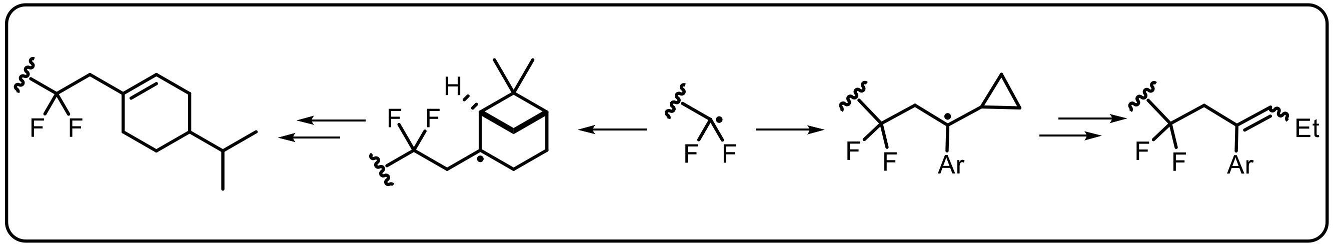
2.3. Radical addition induced SCS process

Synthetic applications



Radical clock experiments

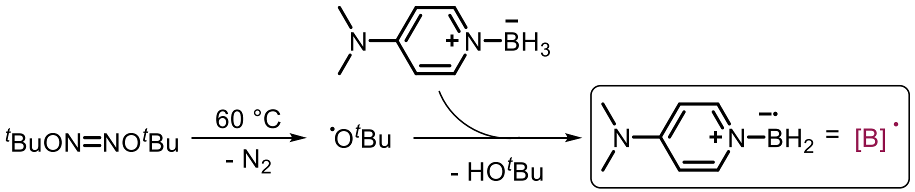


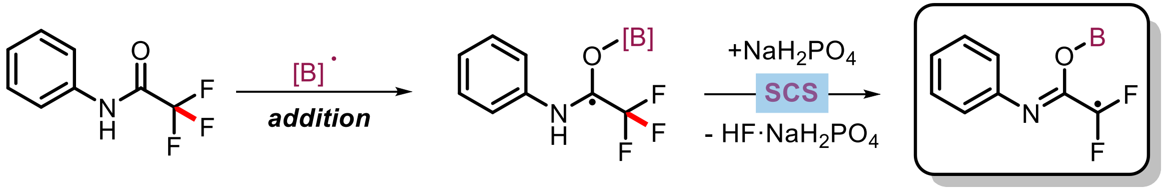


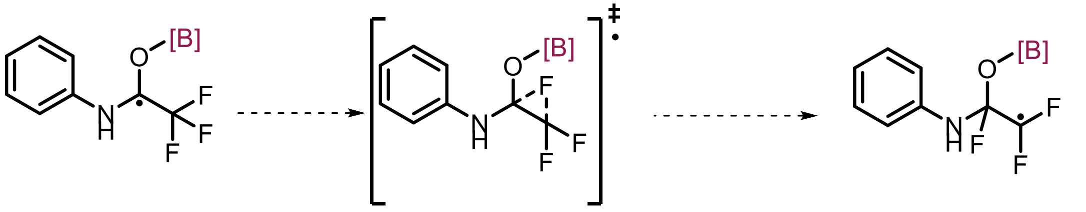
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

2.3. Radical addition induced SCS process

Possible pathways for C–F bond cleavage



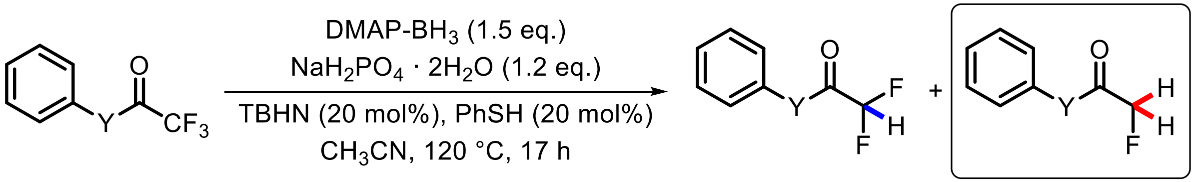




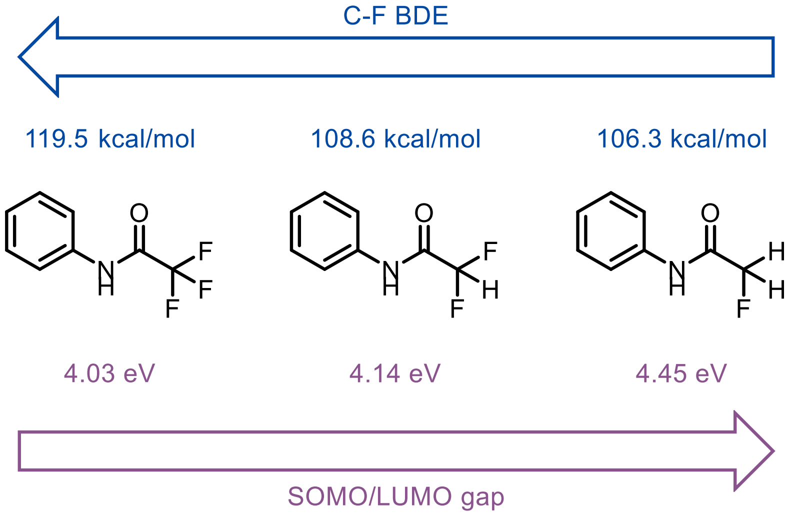
(ΔG‡ = 23.9 kcal/mol)

(ΔG = 12.1 kcal/mol)

Trend in the addition of DMAP-BH$_2$· to the substrates



why not yield?



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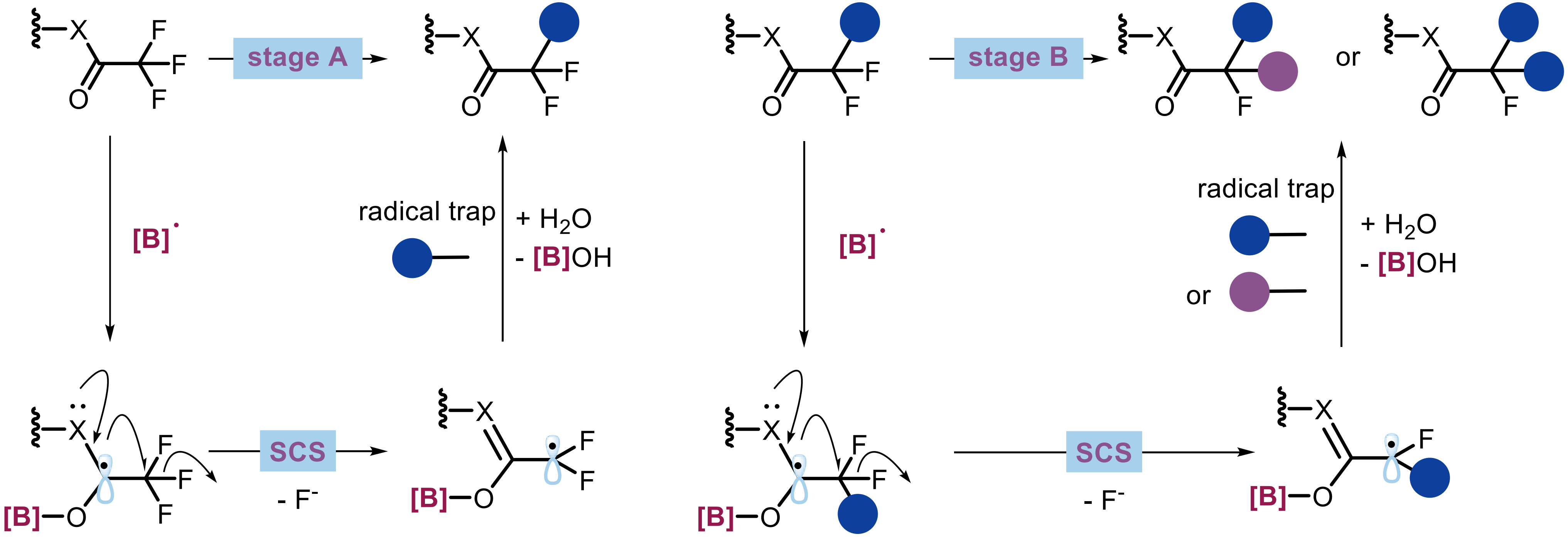
2.3. Radical addition induced SCS process

Possible reaction mechanism



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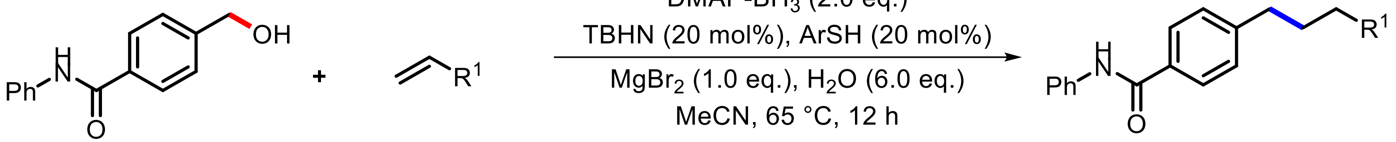
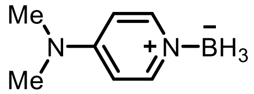
2.3. Radical addition induced SCS process

Remote Spin-Center Shift for C-O bond

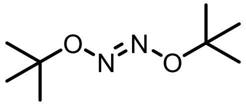


DMAP-BH_3 (2.0 eq.)
TBHN (20 mol%), ArSH (20 mol%)
$MgBr_2$ (1.0 eq.), H_2O (6.0 eq.)
MeCN, 65 °C, 12 h

Condition A

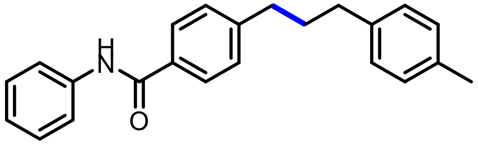


DMAP-BH_3



TBHN

Substrate scope



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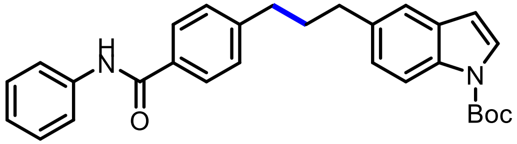

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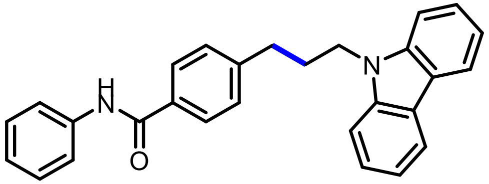

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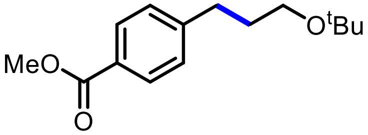

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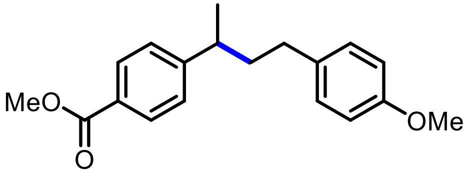

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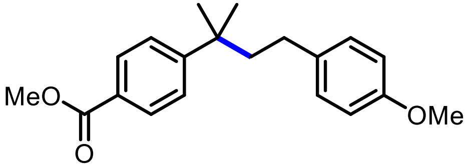

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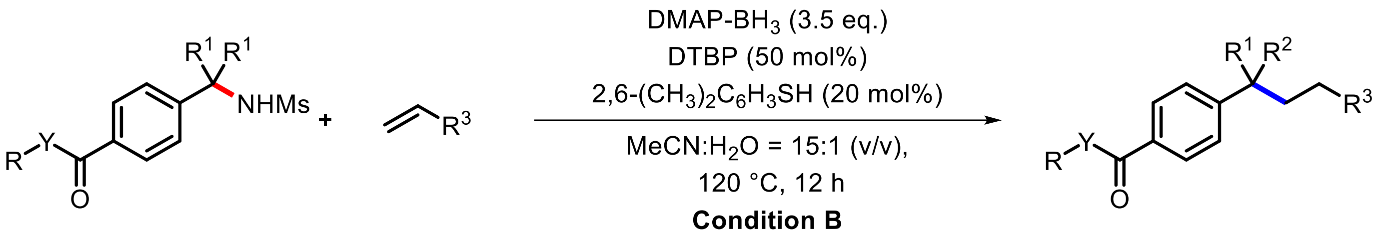
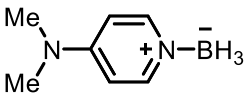
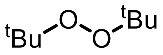
2.3. Radical addition induced SCS process

Remote Spin-Center Shift for C-N bond



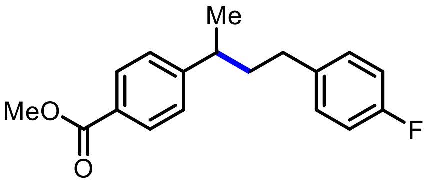


DMAP-BH_3



DTBP

Substrate scope



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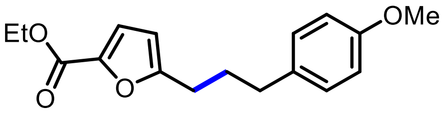

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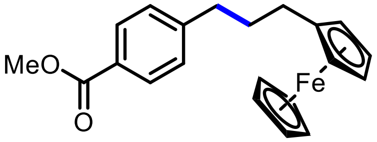

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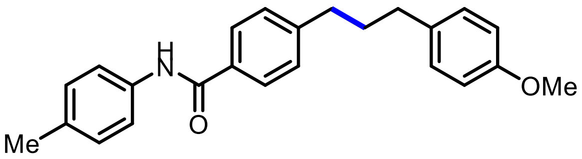

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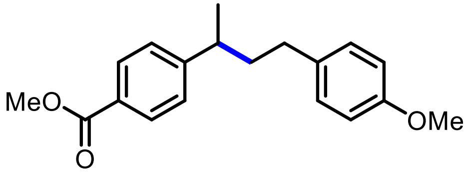

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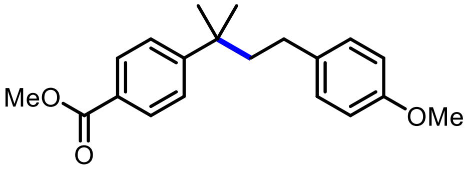

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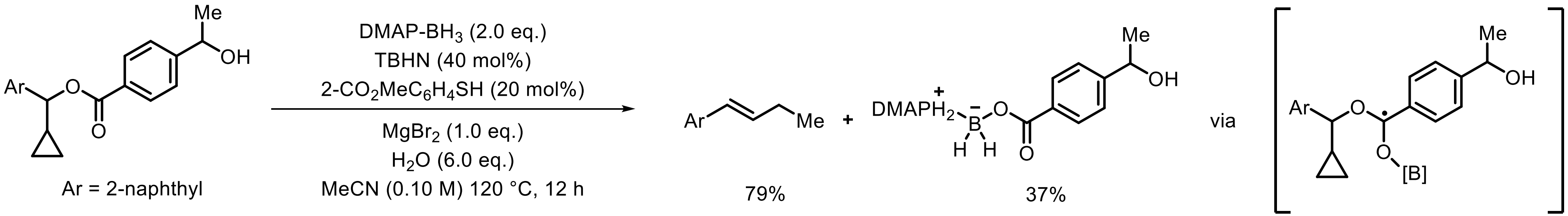
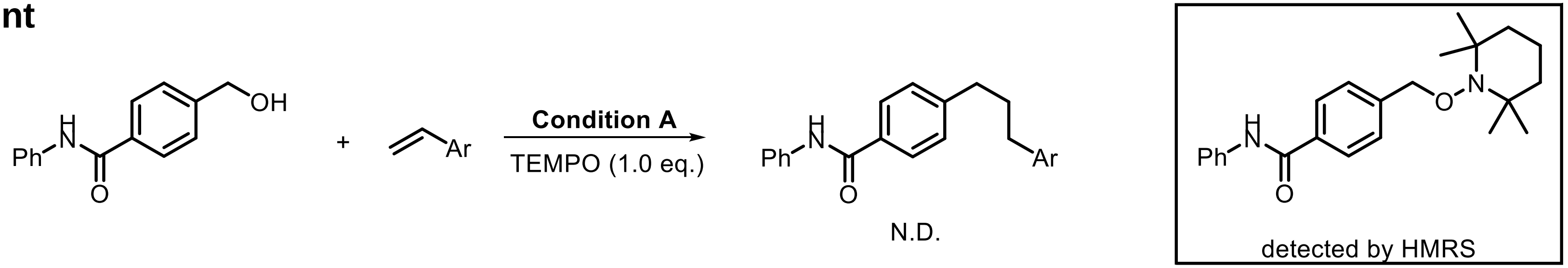
2.3. Radical addition induced SCS process

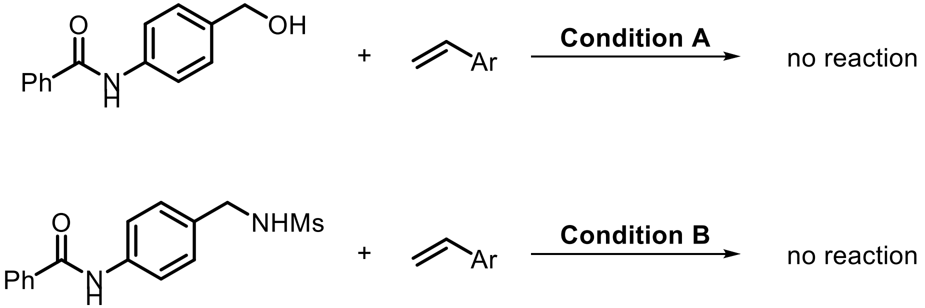
Radical clock experiment



Radical trapping experiment



The necessity of benzyl radical generation



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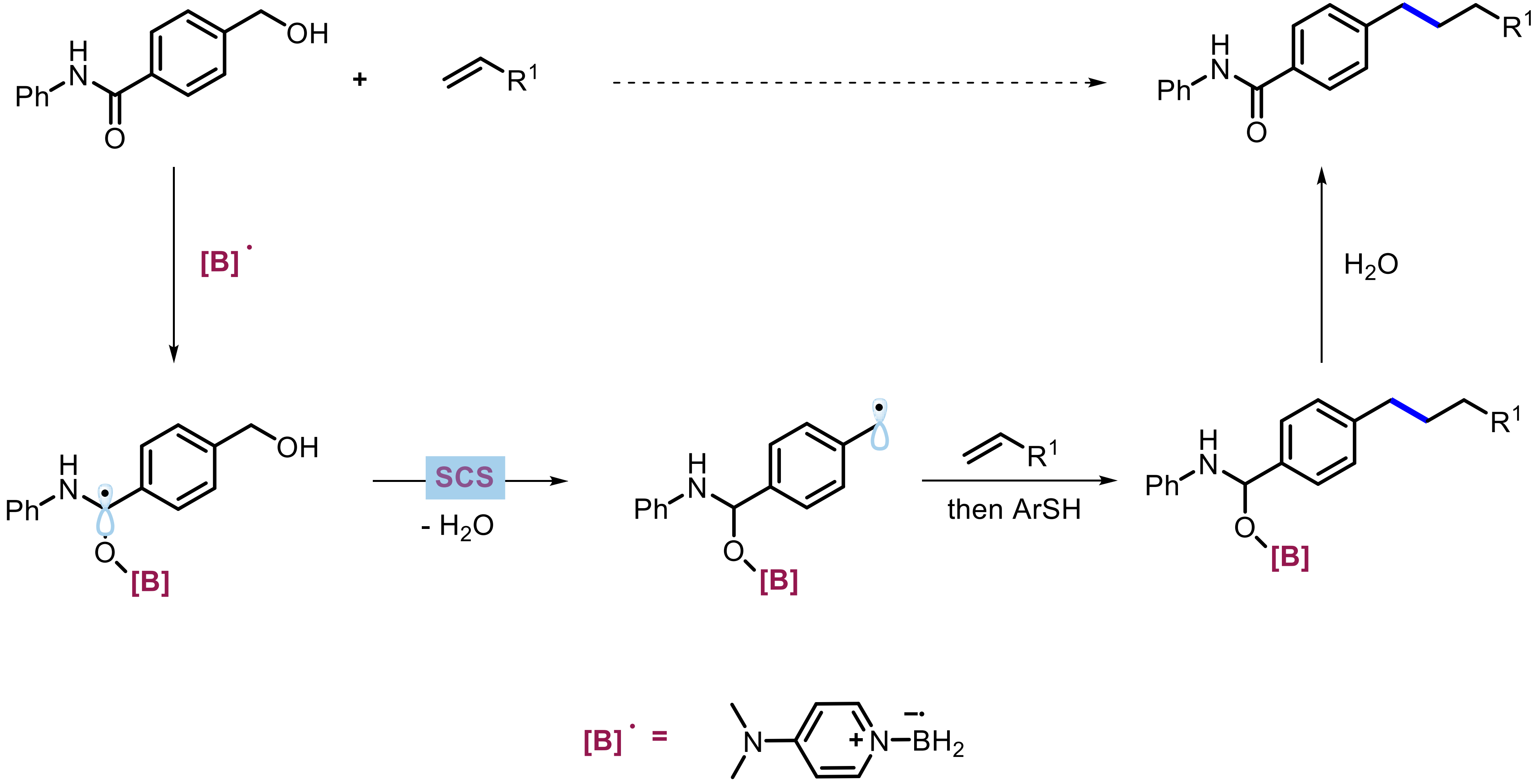
2.3. Radical addition induced SCS process

Possible reaction mechanism



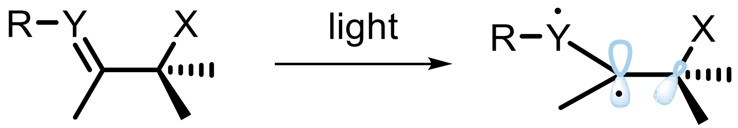
Hui, L.; Phang, Y. L.; Ye, C.; Lai, J.; Zhang, F.; Fu, Y.; Wang, Y. *Angew. Chem., Int. Ed.* **2025**, *64*, e202506771.

Content

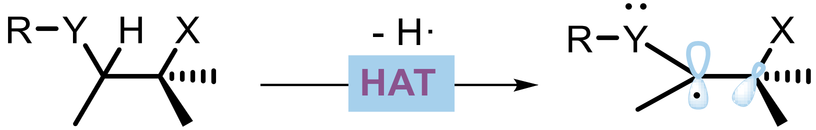
3. Summary and Outlook

Four Methods for Generating Free Radicals

Direct Photoexcitation



HAT



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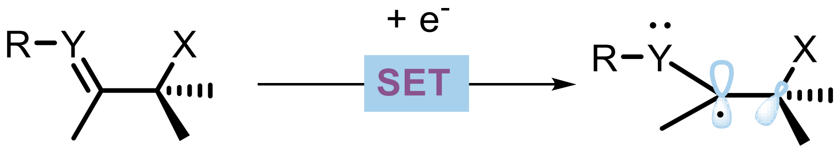

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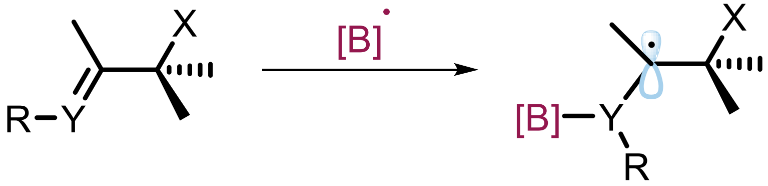
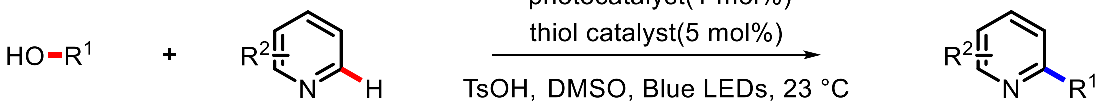


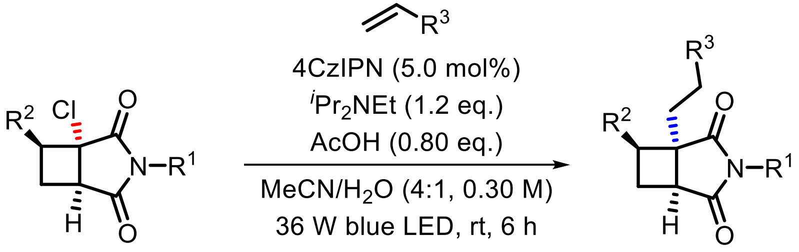
3. Summary and Outlook

Four Types of Carbon-Heteroatom Bond Activation

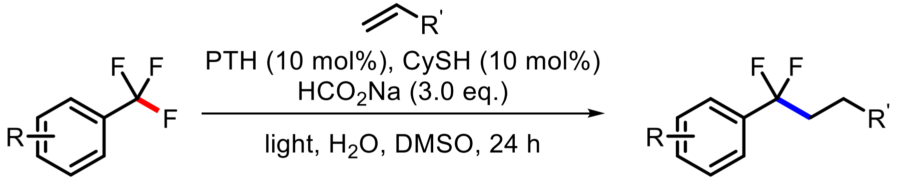
C–O Bond Activation



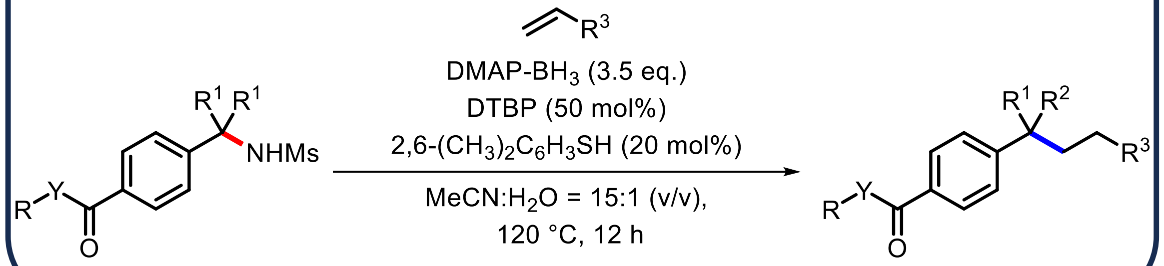
C-Cl Bond Activation



C-F Bond Activation



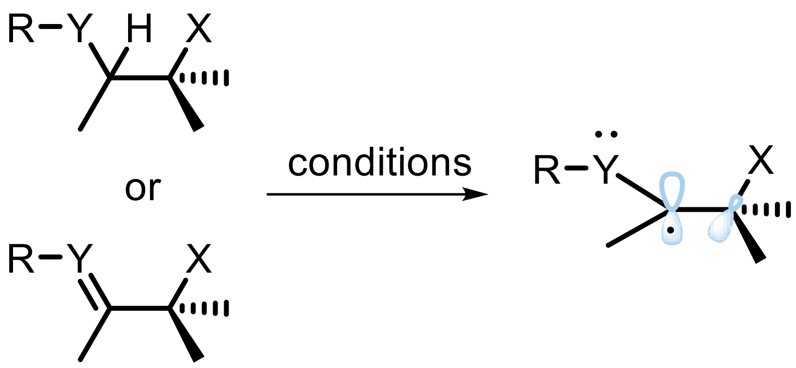
C-N Bond Activation



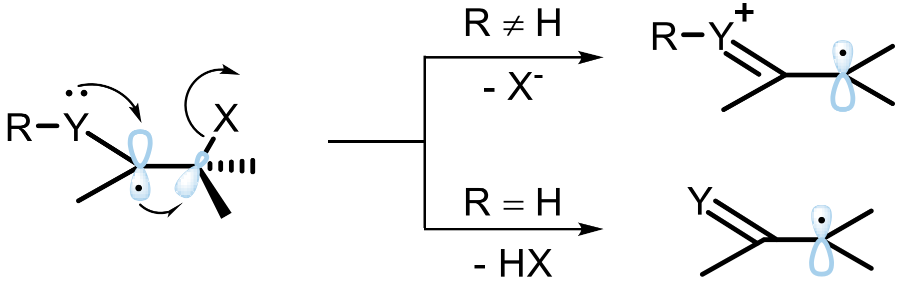
1) Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.
2) Deeprose, M. J.; Lowe, M.; Noble, A.; Booker-Milburn, K. I.; Aggarwal, V. K. *Org. Lett.* **2022**, *24*, 137–141.
3) Wang, H.; Jui, N. T. *J. Am. Chem. Soc.* **2018**, *140*, 163–166.
4) Hui, L.; Phang, Y. L.; Ye, C.; Lai, J.; Zhang, F.; Fu, Y.; Wang, Y. *Angew. Chem., Int. Ed.* **2025**, *64*, e202506771.

3. Summary and Outlook

Other Methods for Generating Free Radical

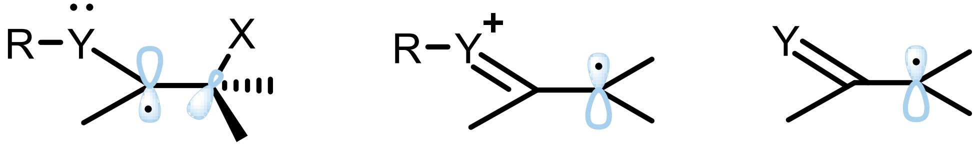


Other Functional Group for Leaving

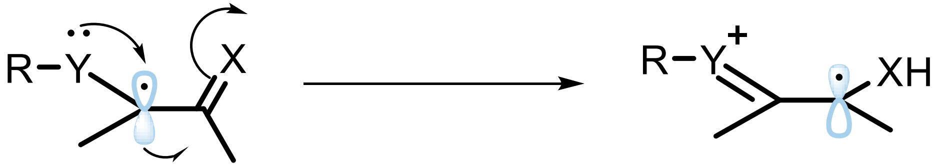


X = S, C, H.......

Characterization and Separation of Intermediates



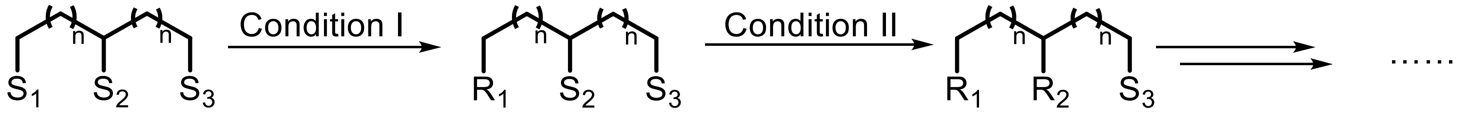
Extended SCS process



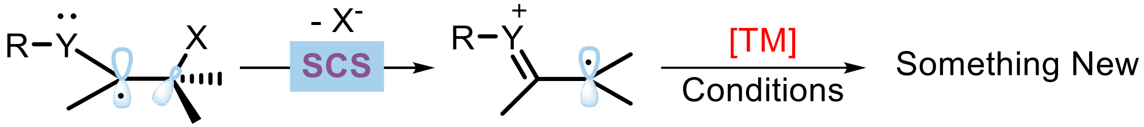
3. Summary and Outlook

Other Possible New Reactions

The Sequential Functionalization of Different Carbon−Heteroatom Bonds



The Merger of Transition Metal Catalysis with SCS Processes



Thanks