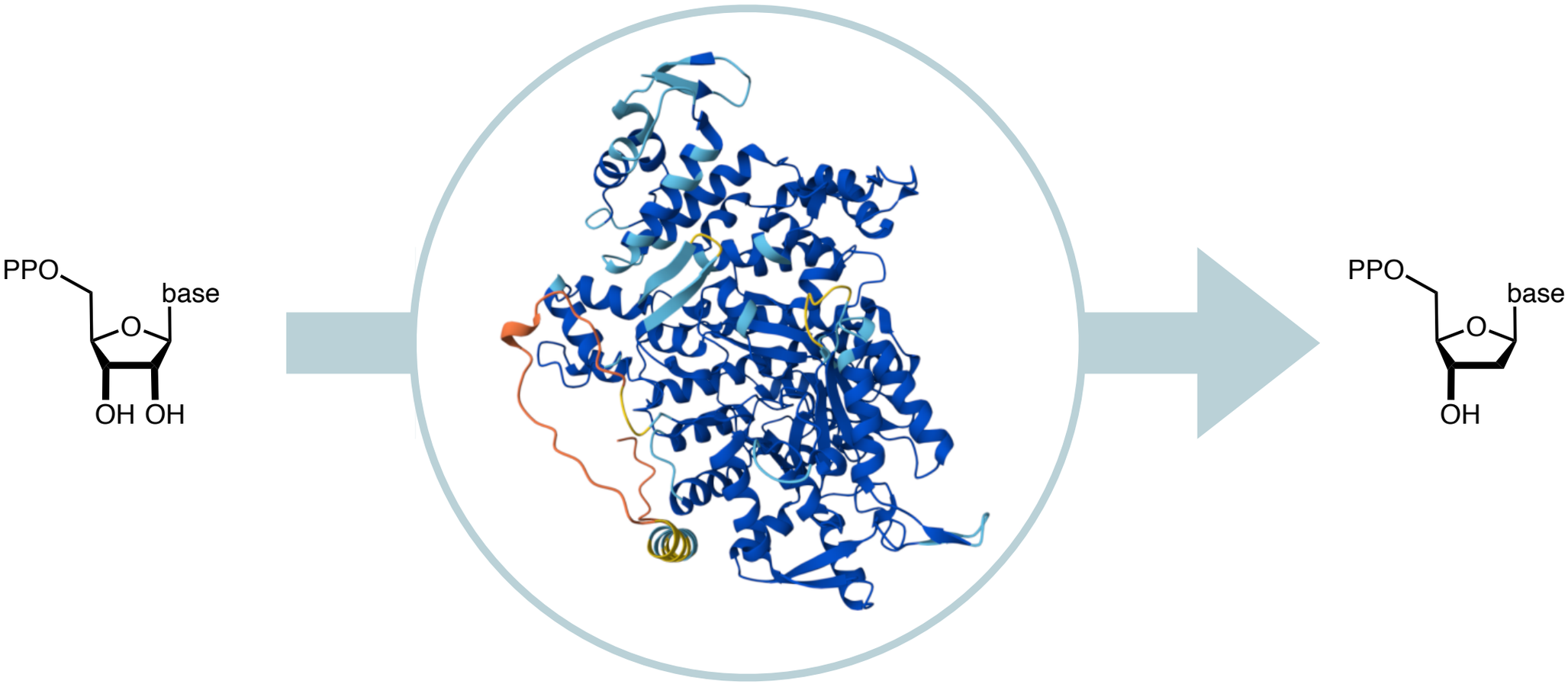
Spin-Center Shift



June 17th, 2025

Will Lyon

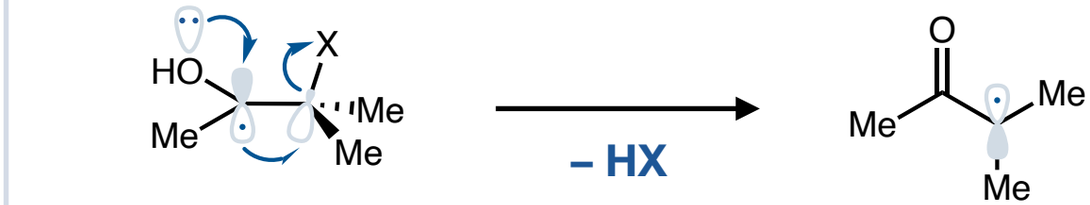
MacMillan Group

Princeton University

What is spin-center shift?

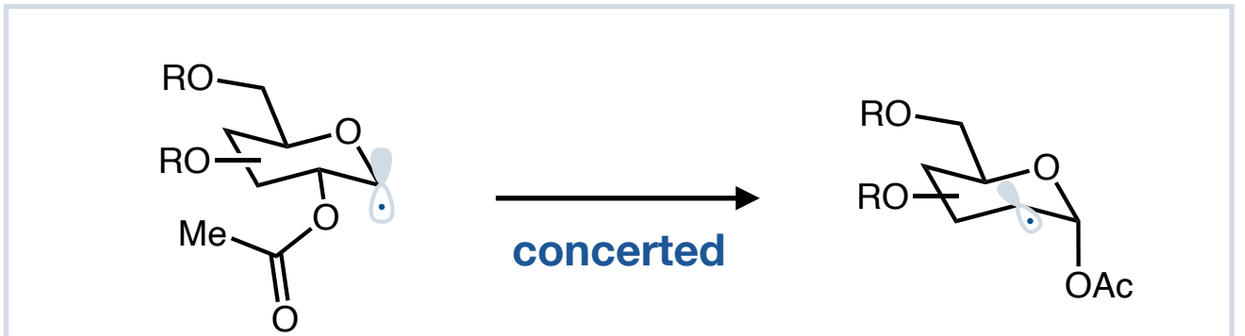
“The 1,2-radical shift accompanied by the elimination of an adjacent leaving group or the corresponding acid”

– Wang, 2022



“Shifting the position of the radical center to another atom in the course of the reaction”

– Ngai, 2021



Zhang, F.-L.; Li, B.; Houk, K. N.; Wang, Y.-F. *JACS Au* **2022**, *2* (5), 1032–1042.

Zhao, G.; Yao, W.; Mauro, J. N.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2021**, *143* (4), 1728–1734.

What is spin-center shift?

“The 1,2-radical shift accompanied by the elimination of an adjacent leaving group or the corresponding acid”

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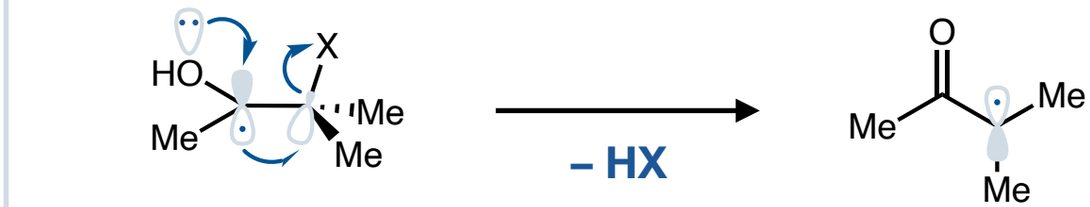

“Shifting the position of the radical center to another atom in the course of the reaction”

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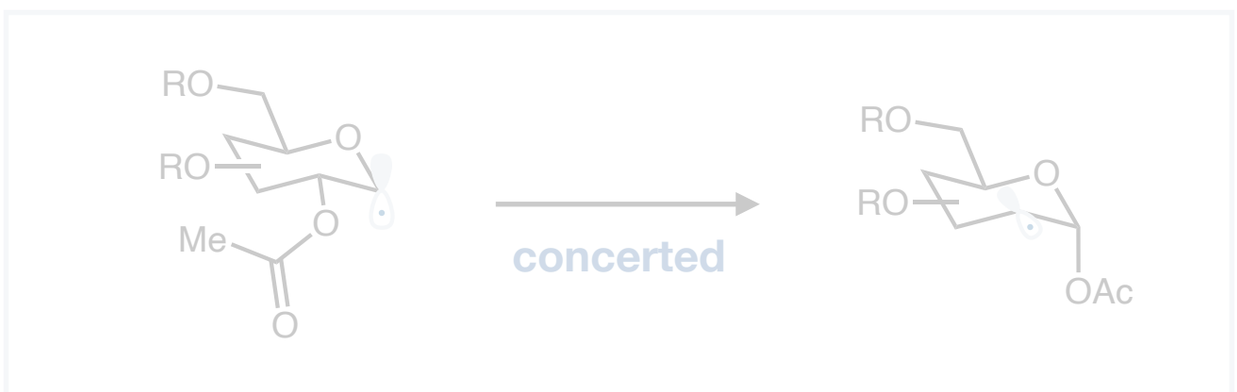
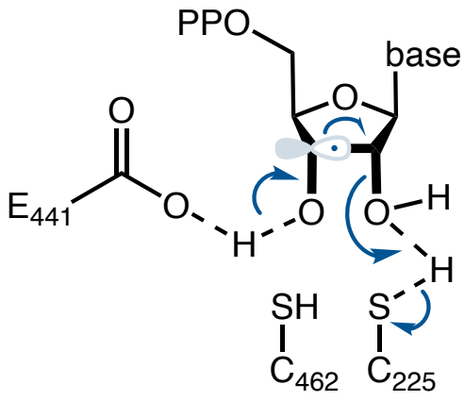


Zhang, F.-L.; Li, B.; Houk, K. N.; Wang, Y.-F. *JACS Au* **2022**, *2* (5), 1032–1042.

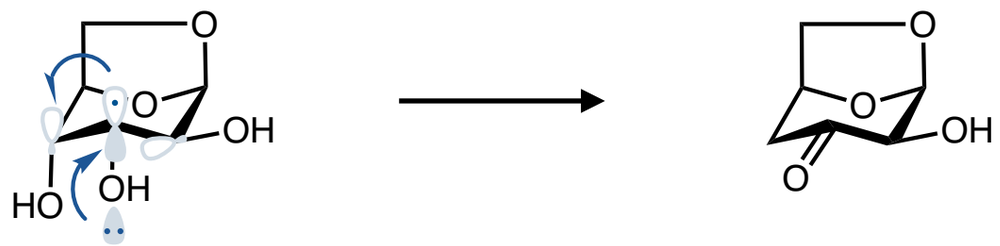
Zhao, G.; Yao, W.; Mauro, J. N.; Ngai, M.-Y. *J. Am. Chem. Soc.* **2021**, *143* (4), 1728–1734.

Outline

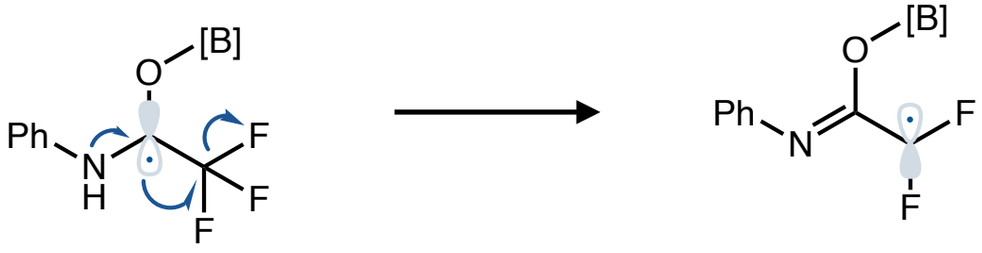
Biochemical and mechanistic background



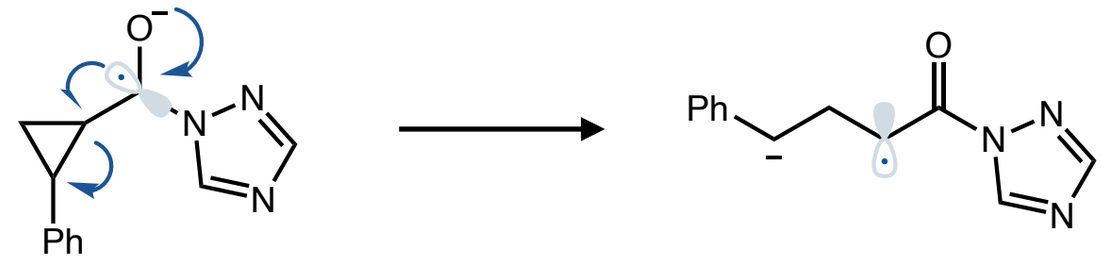
C–O bond activation



C–F bond activation

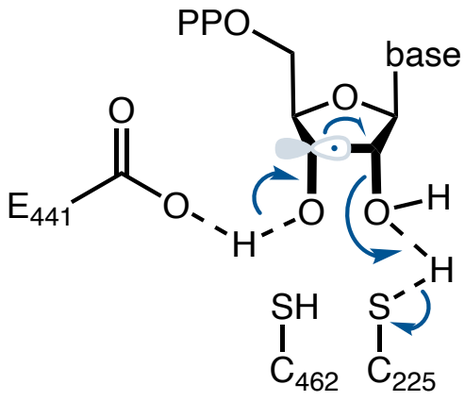


Miscellaneous SCS reactions

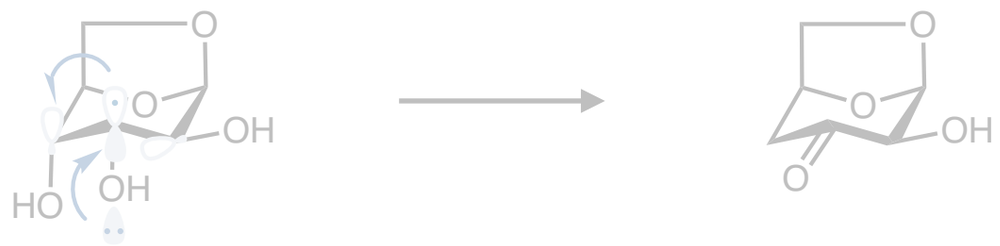


Outline

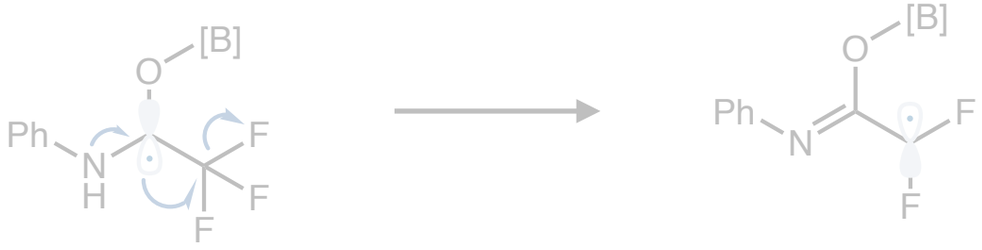
Biochemical and mechanistic background



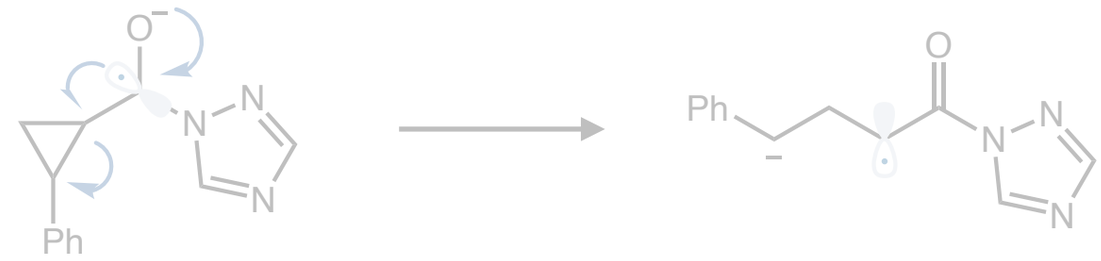
C–O bond activation



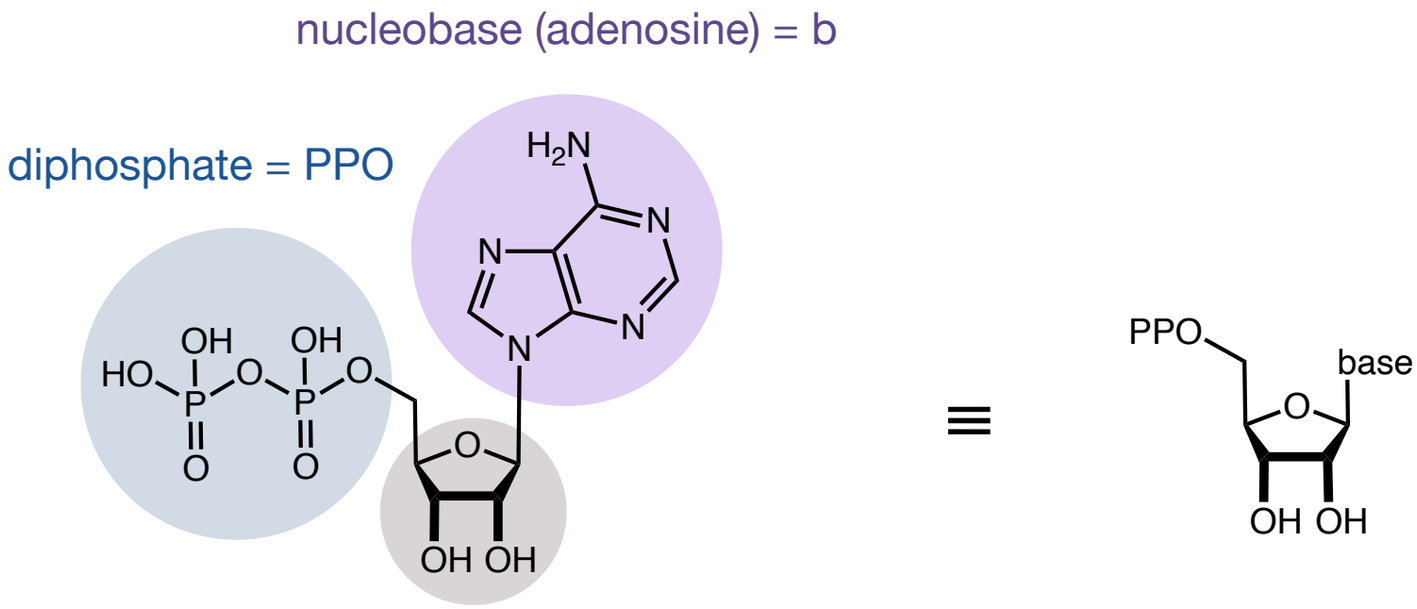
C–F bond activation



Miscellaneous SCS reactions



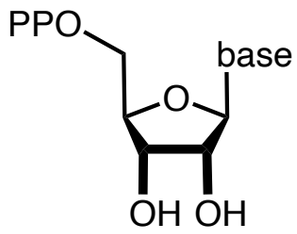
SCS in biological systems: DNA synthesis



***ribo**nucleoside diphosphate*

precursor to DNA

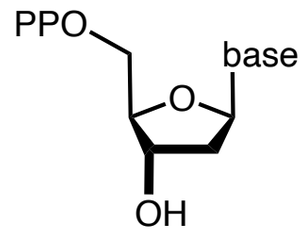
SCS in biological systems: DNA synthesis



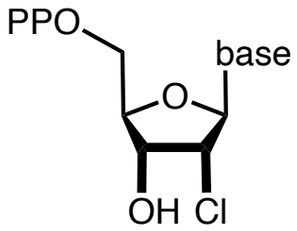
ribonucleoside diphosphate

ribonucleotide reductase

DNA monomer synthesis



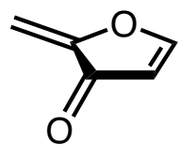
deoxyribonucleoside diphosphate



2-Cl ribonucleoside diphosphate

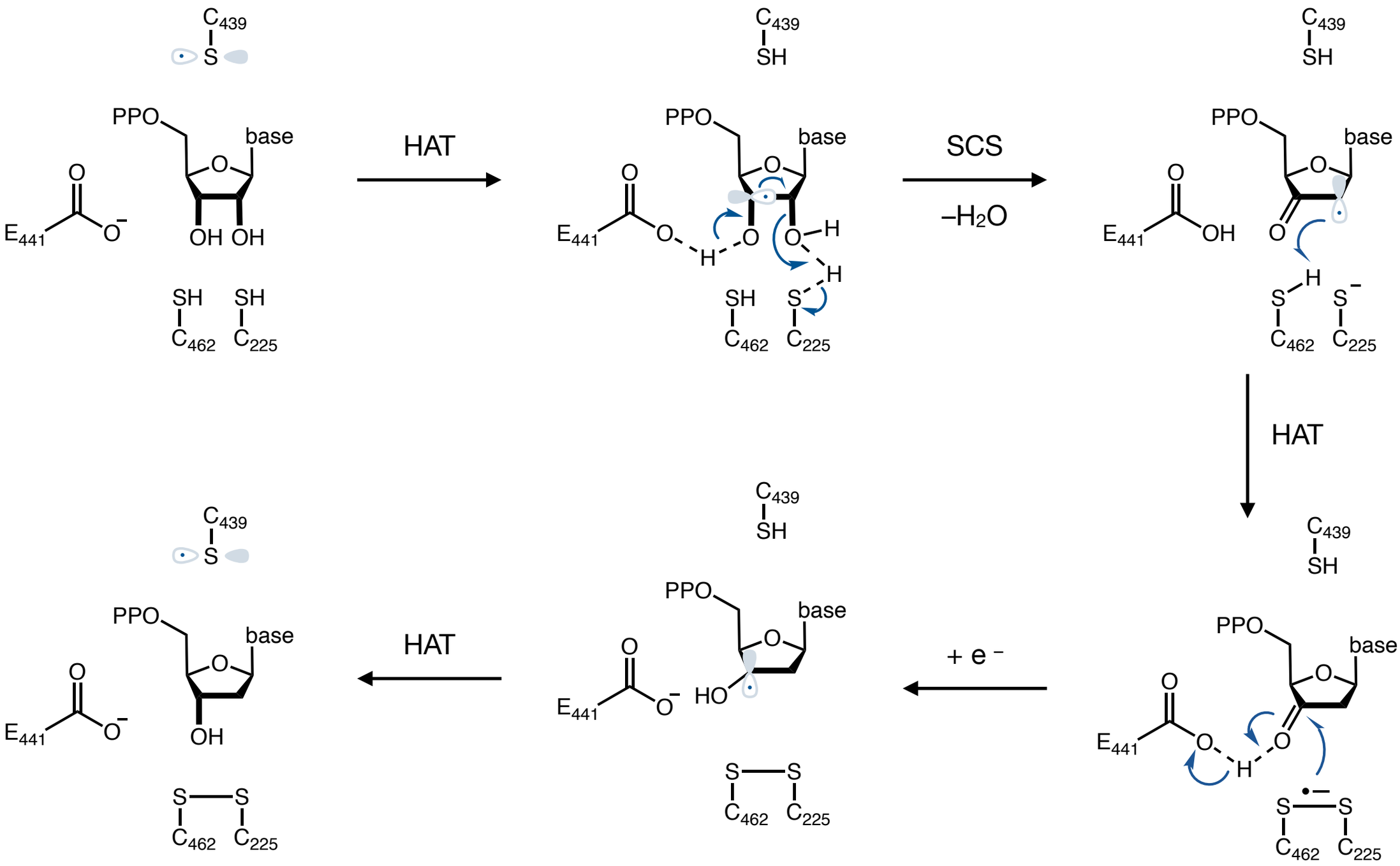
ribonucleotide reductase

Enzyme inactivation



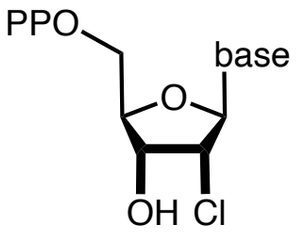
covalent inactivator

SCS in biological systems: DNA synthesis



Himo, F.; Siegbahn, P. E. M. *Chem. Rev.* **2003**, *103* (6), 2421–2456.

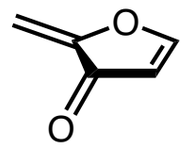
SCS in biological systems: DNA synthesis



2-Cl ribonucleoside diphosphate

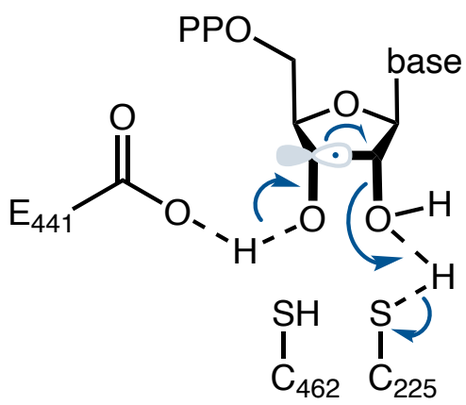
ribonucleotide reductase

Enzyme inactivation

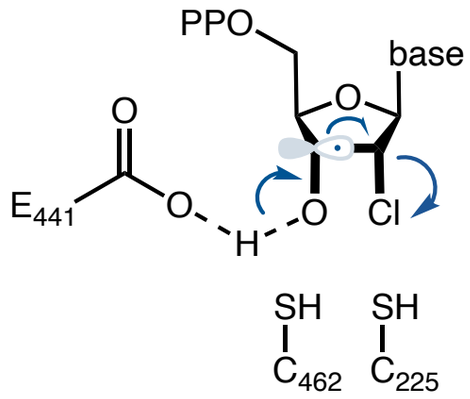


covalent inactivator

Enzyme function directly depends on SCS leaving group



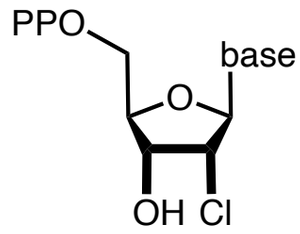
ribonucleoside diphosphate (–H_2O)



2-Cl ribonucleoside diphosphate (– Cl^-)

Robins, M. J. *Nucleosides Nucleotides Nucleic Acids* **2003**, *22*, 519–534.

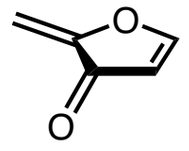
SCS in biological systems: DNA synthesis



2-Cl ribonucleoside diphosphate

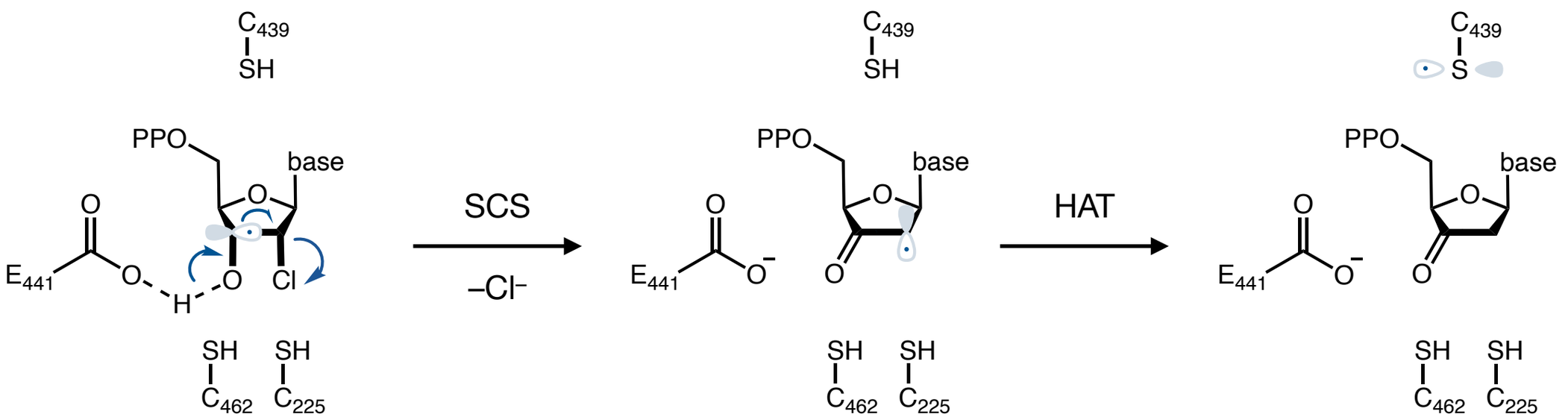
ribonucleotide reductase

Enzyme inactivation



covalent inactivator

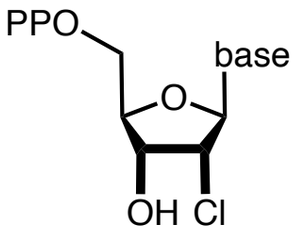
β-elimination (2x)



Radical anion necessary for ketone reduction not generated

Robins, M. J. *Nucleosides Nucleotides Nucleic Acids* **2003**, *22*, 519–534.

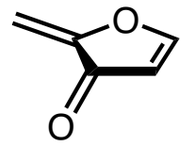
SCS in biological systems: DNA synthesis



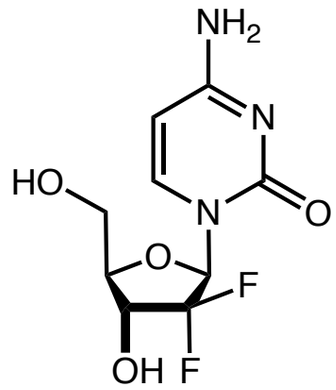
2-Cl ribonucleoside diphosphate

ribonucleotide reductase

Enzyme inactivation



covalent inactivator

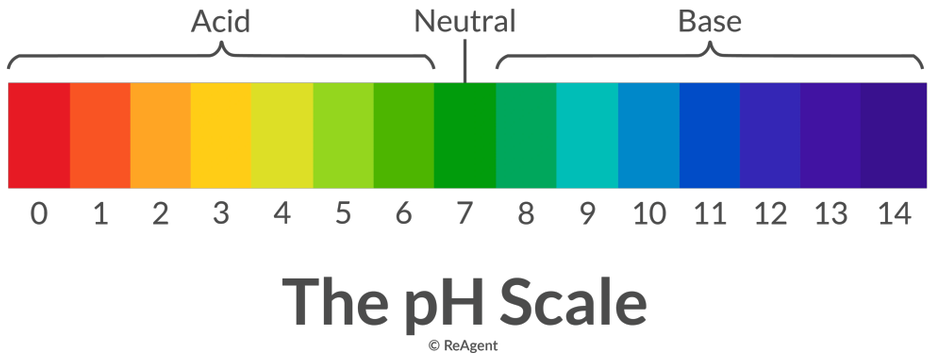


gemcitabine - chemotherapy
2024 sales: $789 million

Robins, M. J. *Nucleosides Nucleotides Nucleic Acids* **2003**, *22*, 519–534.

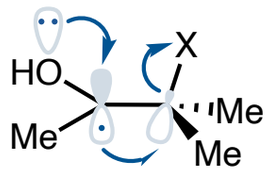
Mechanistic Considerations of SCS Processes

pH dependance

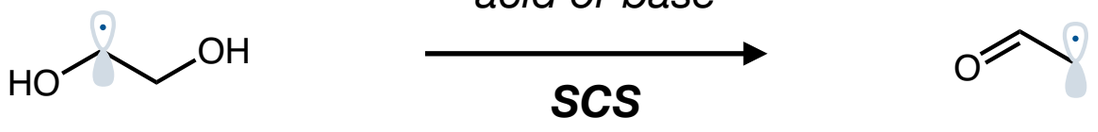


Solvent dependance

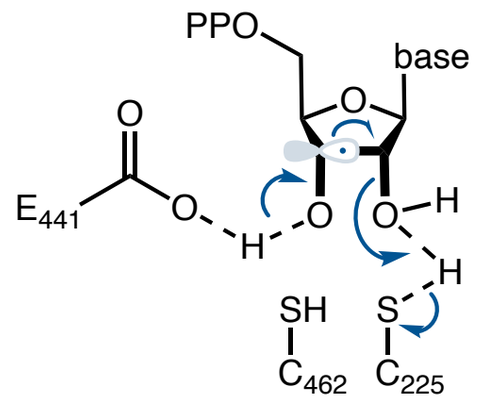
Leaving group ability and mechanism



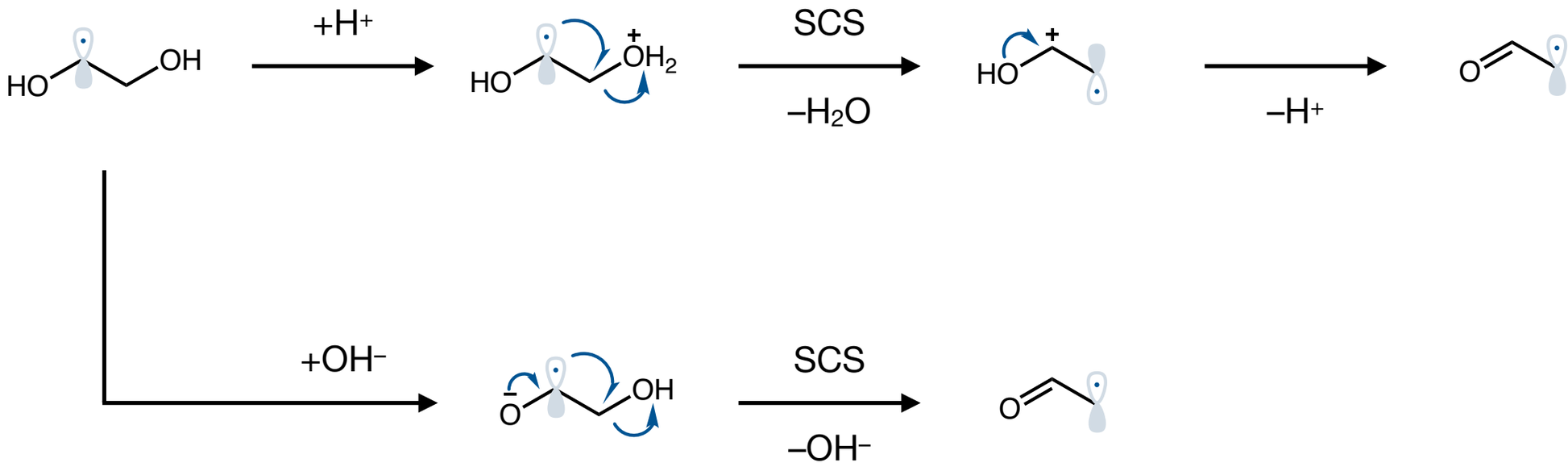
pH dependance



α,β-dihydroxyalkyl radical *formylmethyl radical*



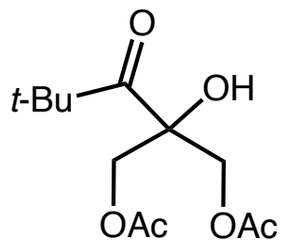
enzymatic SCS activation



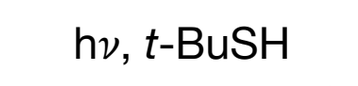
No SCS observed in absence of acid/base

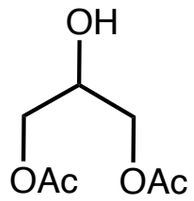
Beckwith, A. L. J.; Crich, D.; Duggan, P. J.; Yao, Q. *Chem. Rev.* **1997**, *97* (8), 3273–3312.

Importance of solvent

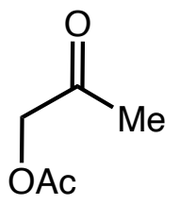


SCS radical precursor

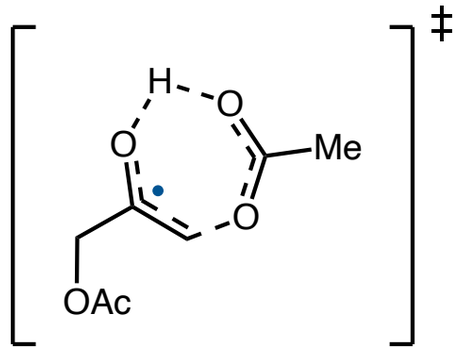




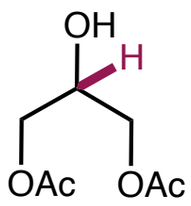
PhMe: 2%
MeOH: 32%

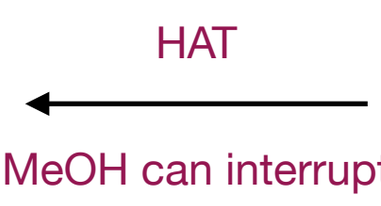


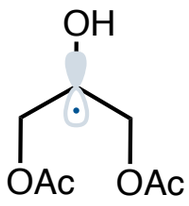
PhMe: 87%
MeOH: 40%

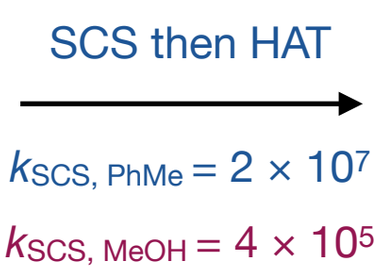


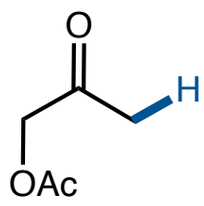
calculated transition state







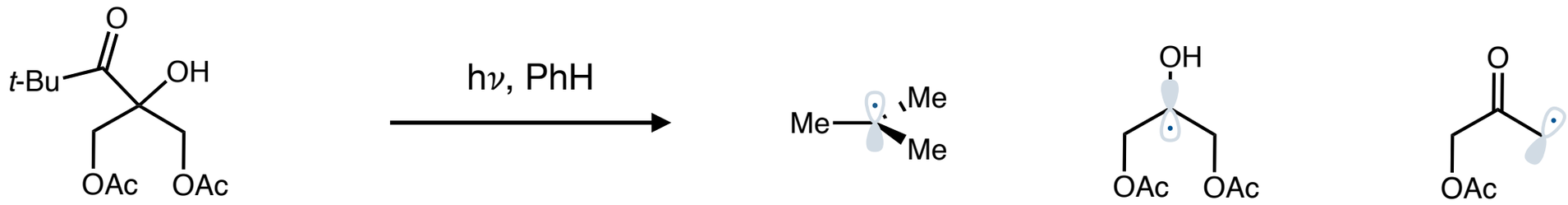




How do non-hydroxyl oxygen nucleophiles perform in SCS?

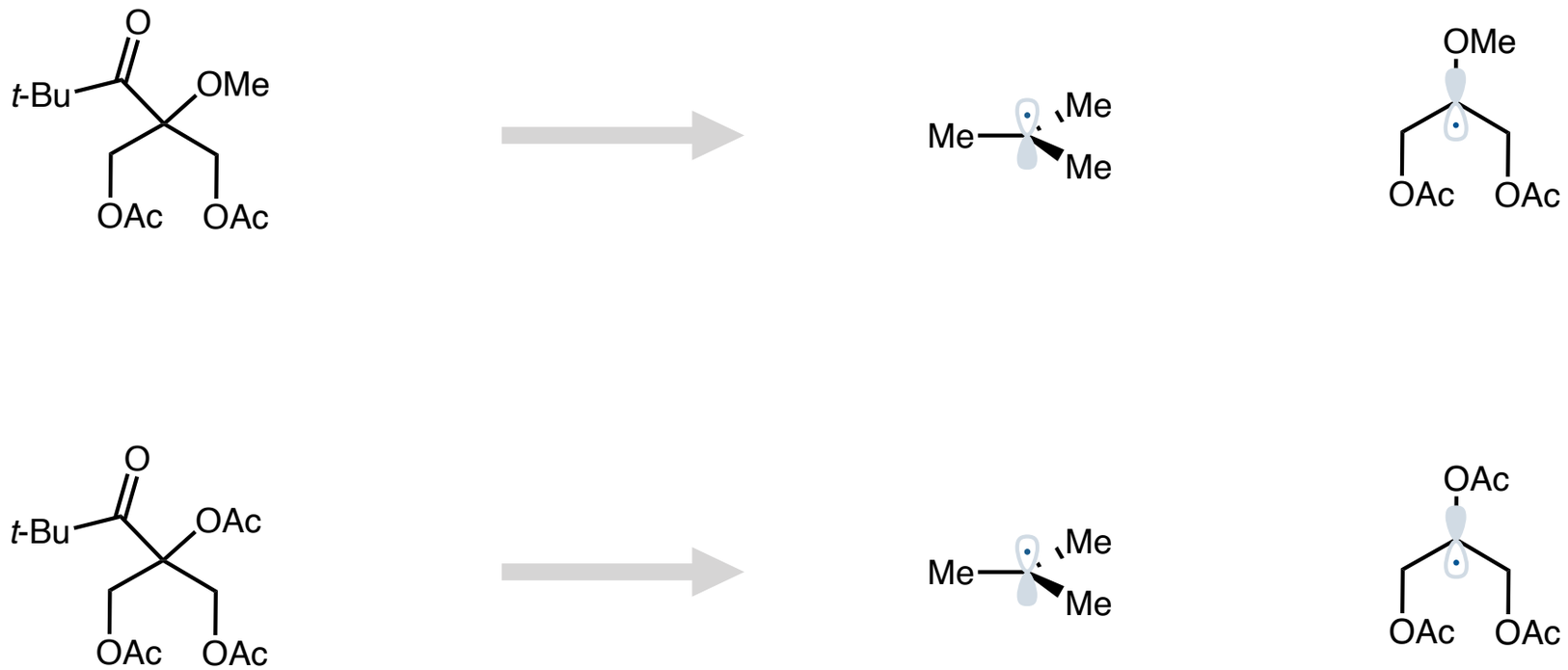
Müller, S. N.; Batra, R.; Senn, M.; Giese, B.; Kisel, M.; Shadyro, O. *J. Am. Chem. Soc.* **1997**, *119* (12), 2795–2803.

Importance of nucleophile



SCS radical precursor

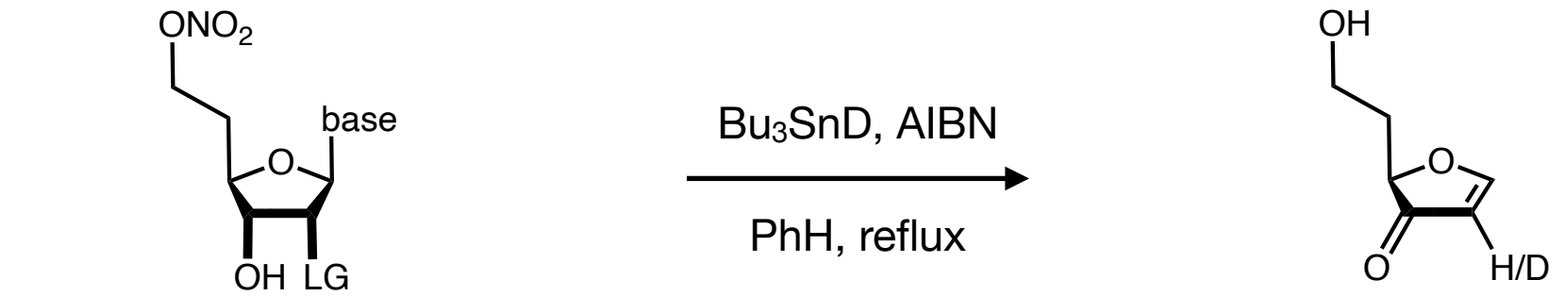
observed alkyl radicals (EPR)



No H-bonding TS possible with OAc or OMe, SCS prohibitively slow

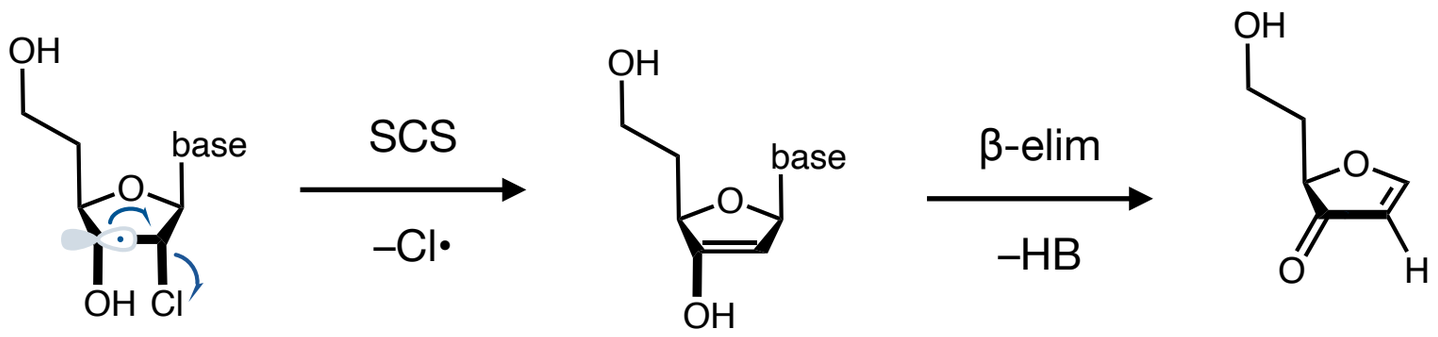
Müller, S. N.; Batra, R.; Senn, M.; Giese, B.; Kisel, M.; Shadyro, O. *J. Am. Chem. Soc.* **1997**, *119* (12), 2795–2803.

Mechanistic implications based on leaving group

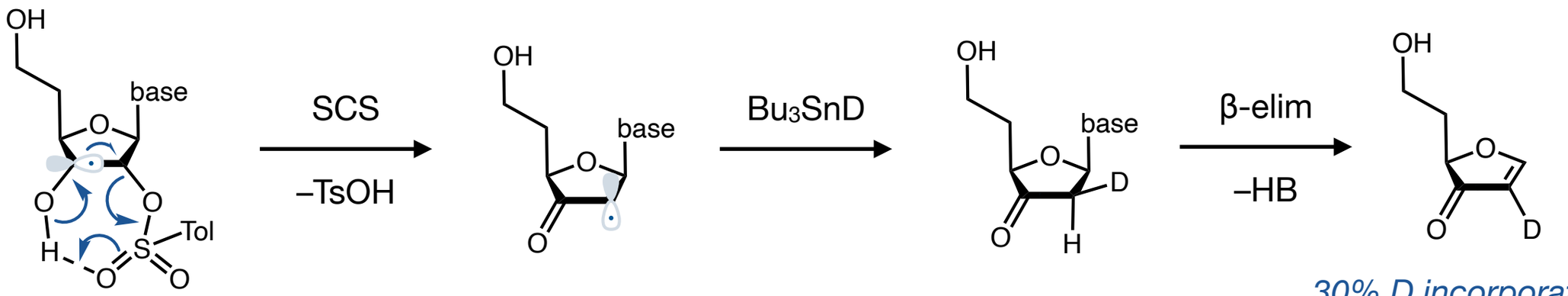


α-hydroxy radical precursor

isotopically labeled product



0% D incorporation

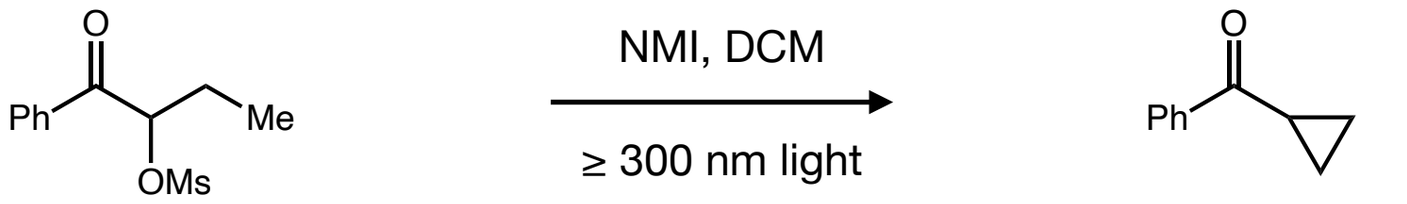


30% D incorporation

Certain radicals can act as leaving groups if cyclic H-bonding TS not possible

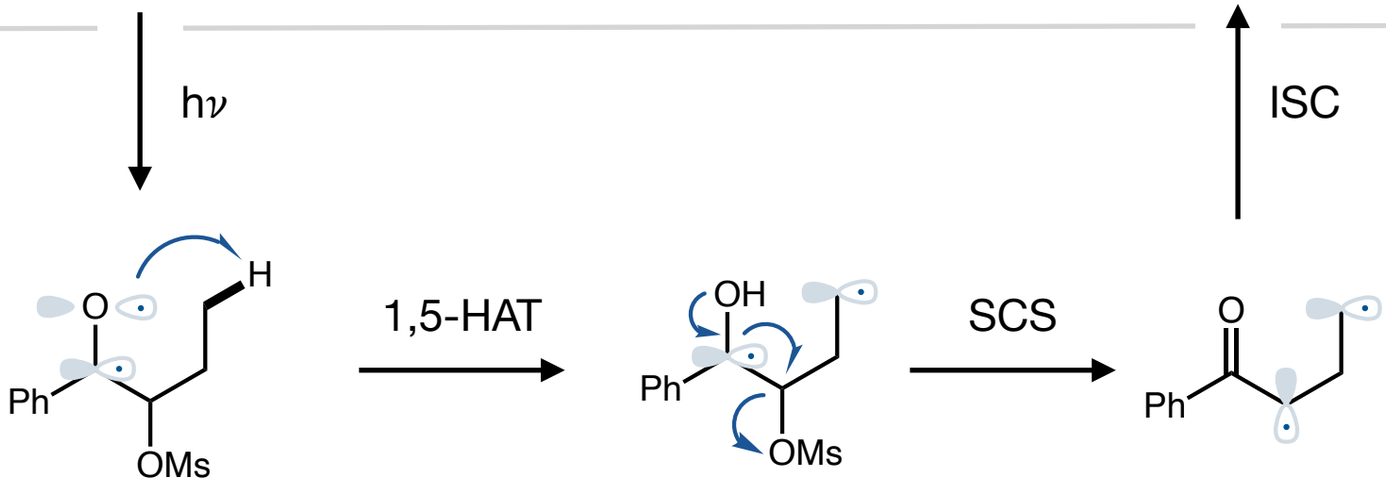
Robins, M. J.; Guo, Z.; Wnuk, S. F. *J. Am. Chem. Soc.* **1997**, *119* (15), 3637–3638.

Cyclopropane synthesis through SCS with diradicals



α-*keto sulfonate*

cyclopropyl ketone (87% yield)

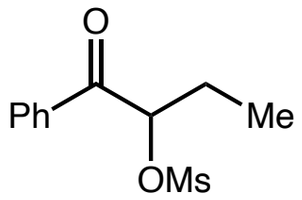


SCS outcompetes Norrish-Yang cyclobutanol synthesis (diradical lifetime ~ 10 ns)

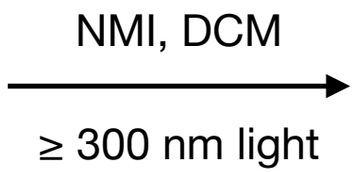
Wessig, P.; Mühling, O. *Angew. Chem. Int. Ed.* **2001**, *40* (6), 1064–1065.

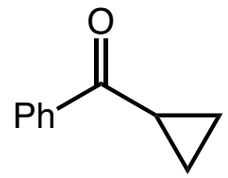
Wessig, P.; Mühling, O. *Helv. Chim. Acta* **2003**, *86* (3), 865–893.

Cyclopropane synthesis through SCS with diradicals



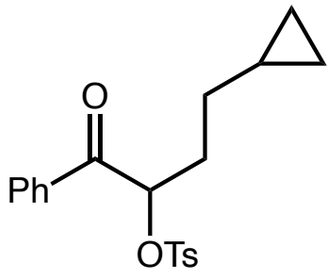
α-*keto sulfonate*

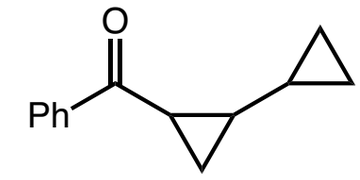




cyclopropyl ketone (87% yield)

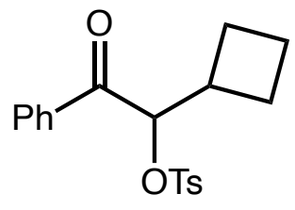
selected scope

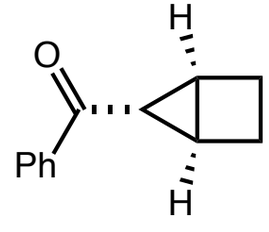


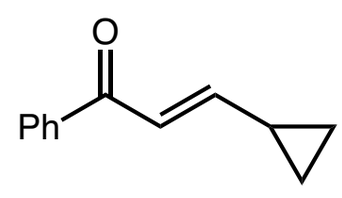


68% yield, no ring opening observed

SCS and ISC faster than 4×10^{7} s^{-1}







61% yield *7% yield*

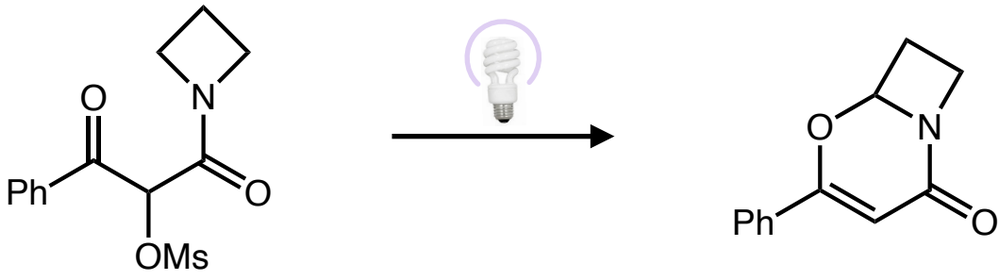
product is stable to irradiation

Wessig, P.; Mühling, O. *Angew. Chem. Int. Ed.* **2001**, *40* (6), 1064–1065.

Wessig, P.; Mühling, O. *Helv. Chim. Acta* **2003**, *86* (3), 865–893.

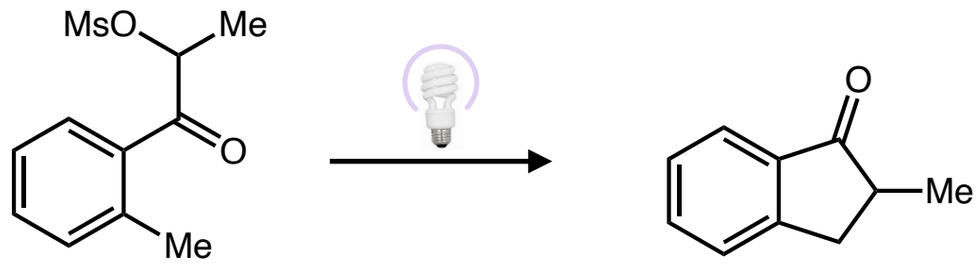
Synthetic Utility: ring synthesis through diradical intermediates

Oxazinones



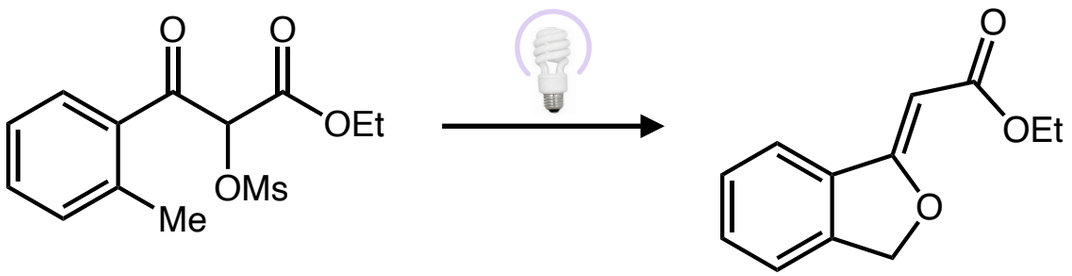
58% yield

Indanones



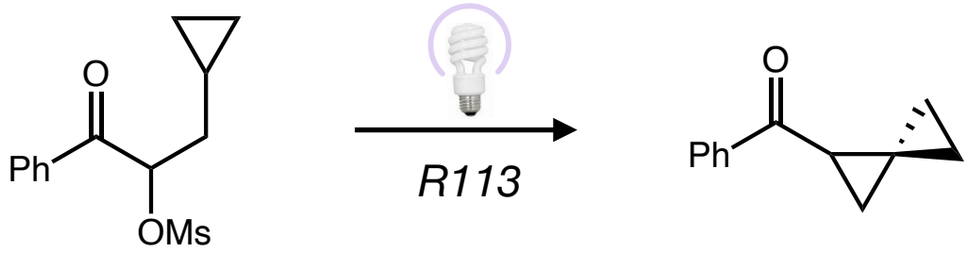
73% yield

Dihydrobenzofurans



67% yield

Spiro[2.2]pentanes

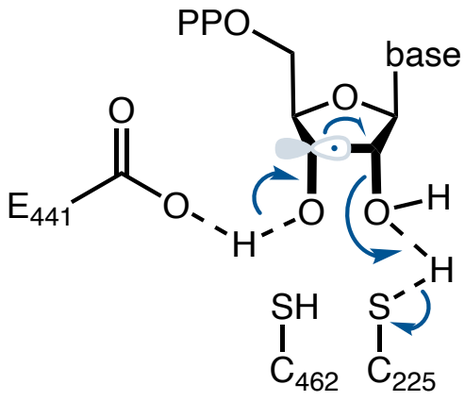


29% yield

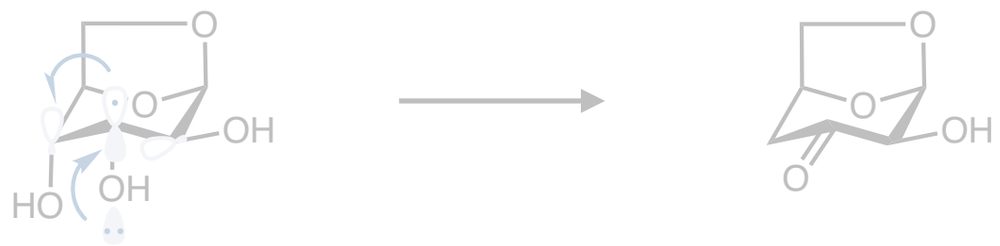
Wessig, P. Spin-Center Shift Reactions. In *CRC Handbook of Organic Photochemistry and Photobiology, Third Edition*. CRC Press, 2019. 201–211.

Outline

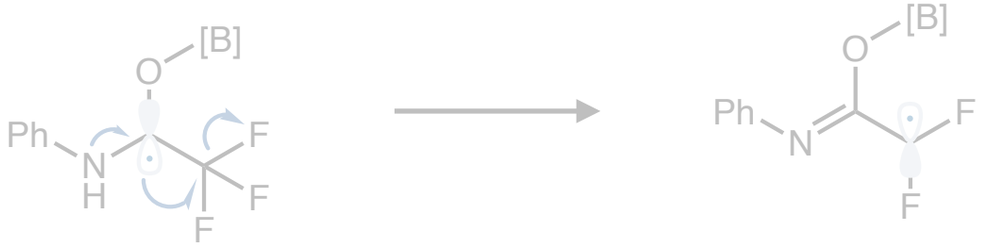
Biochemical and mechanistic background



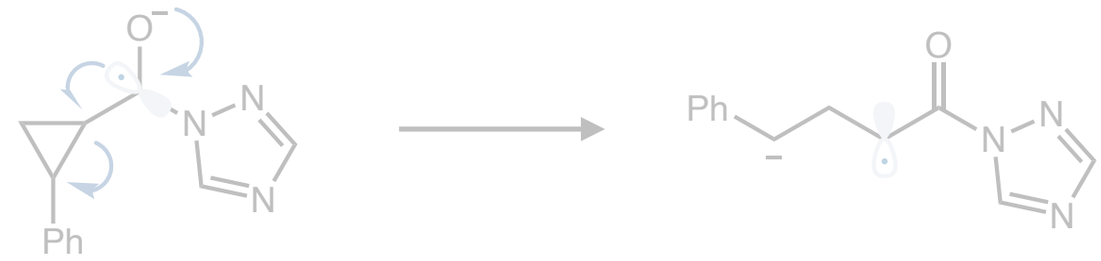
C–O bond activation



C–F bond activation

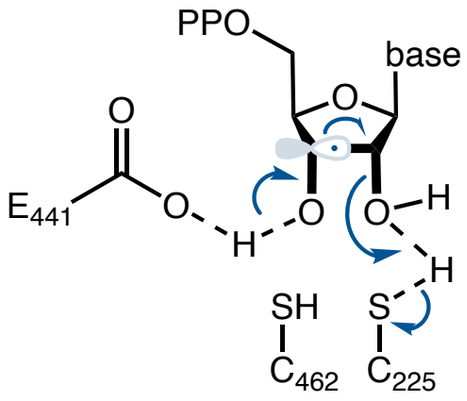


Miscellaneous SCS reactions

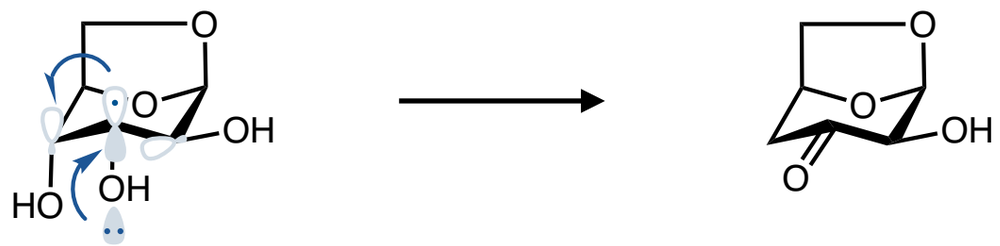


Outline

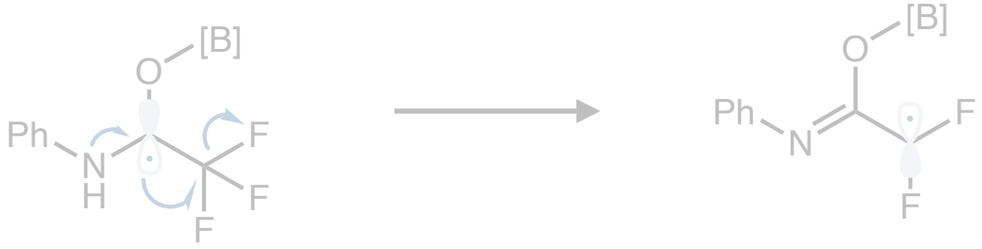
Biochemical and mechanistic background



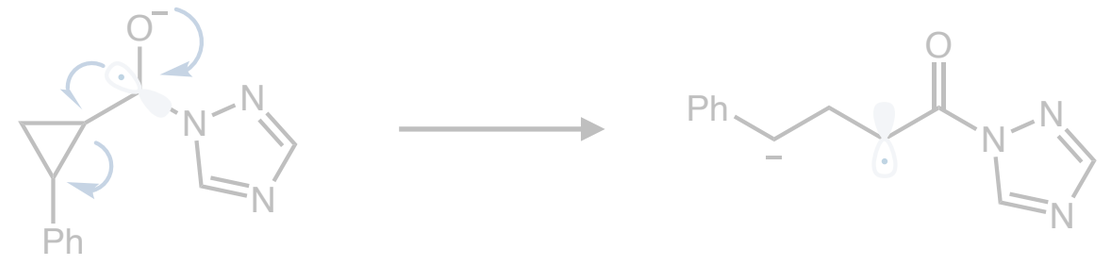
C–O bond activation



C–F bond activation



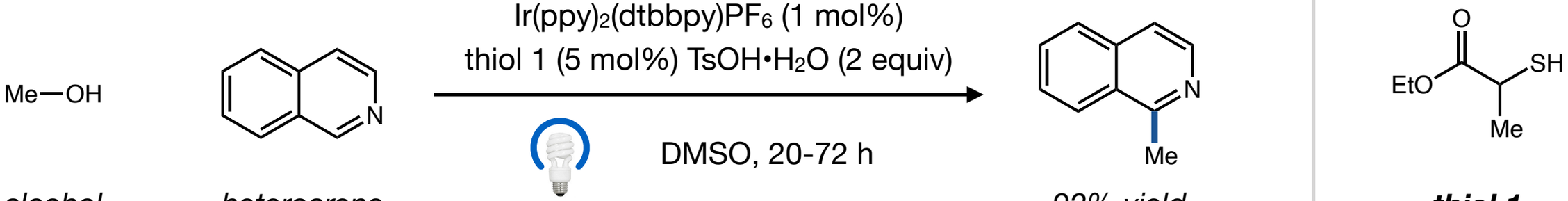
Miscellaneous SCS reactions



SCS is well precedented for unimolecular systems…

What about bimolecular cross-coupling-type reactions?

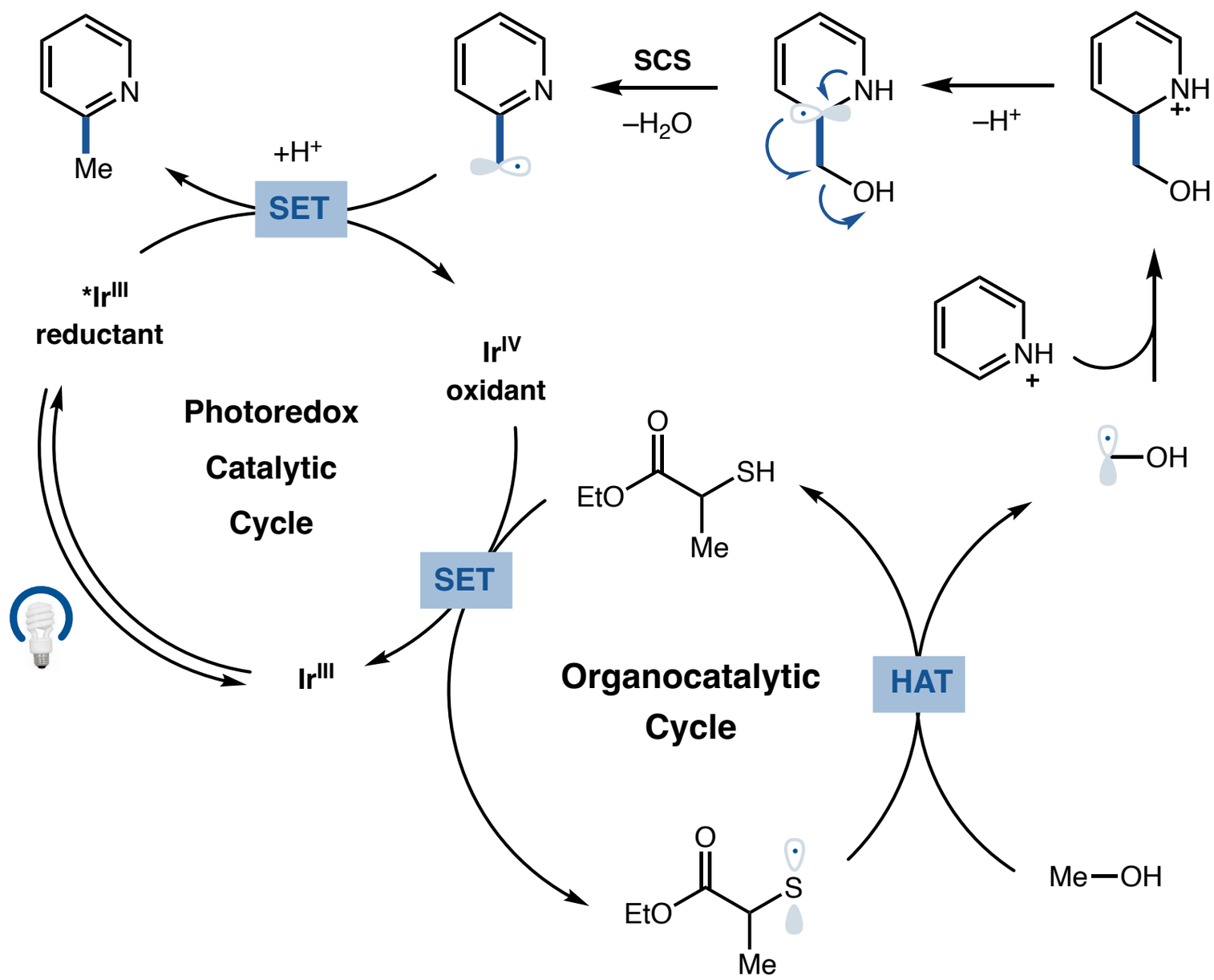
Deoxygenative alkylation of heteroarenes



alcohol *heteroarene* *92% yield* ***thiol 1***

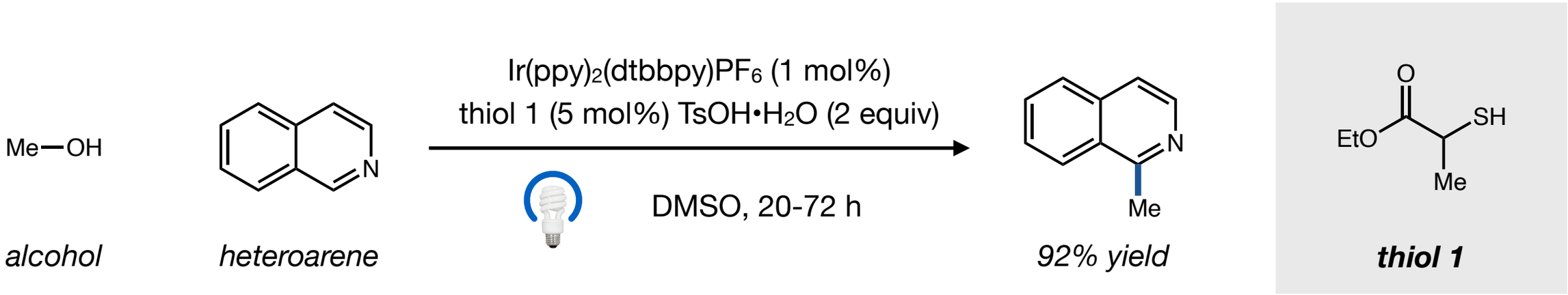
Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

Deoxygenative alkylation of heteroarenes



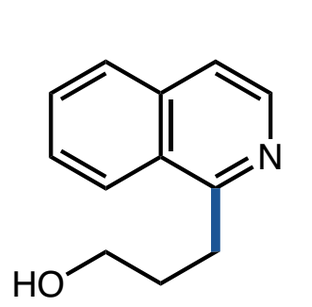
Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

Deoxygenative alkylation of heteroarenes

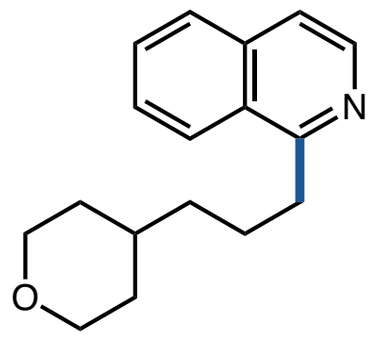


alcohol *heteroarene* *92% yield* ***thiol 1***

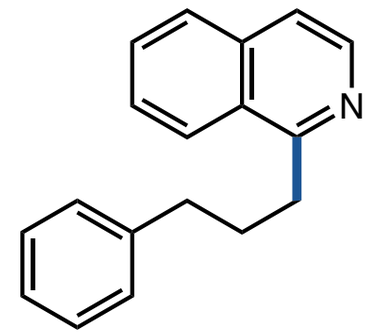
selected scope



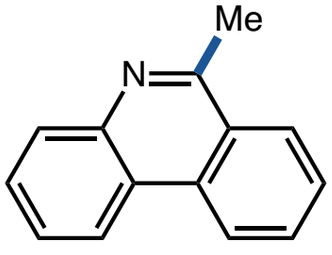
88% yield



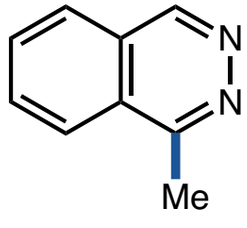
90% yield



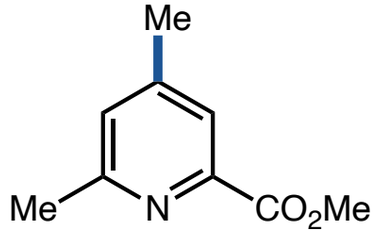
91% yield



93% yield



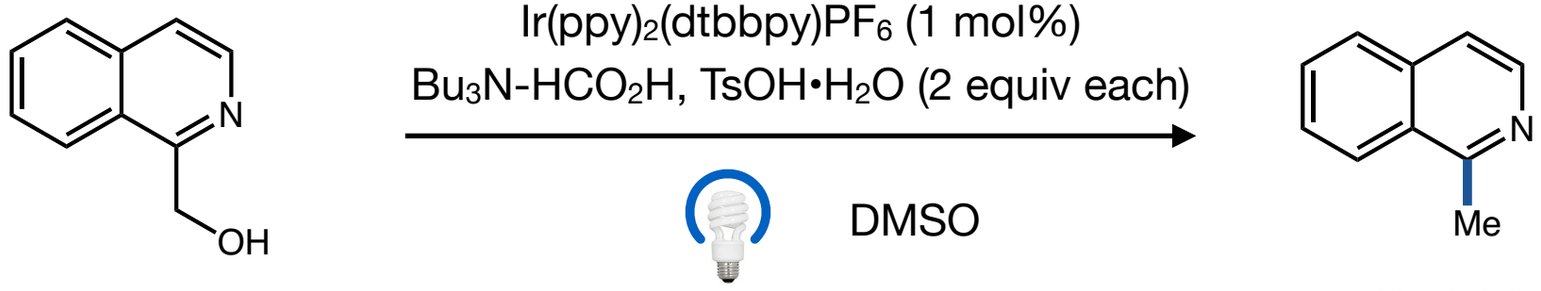
70% yield



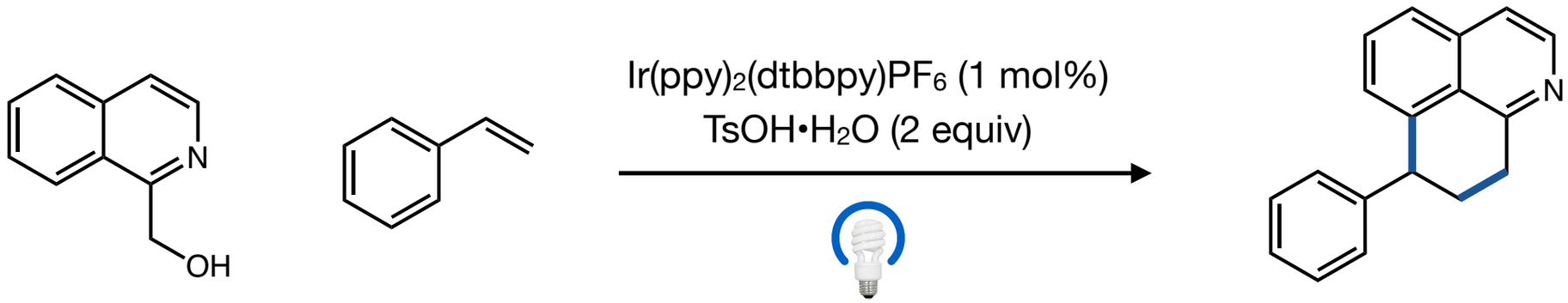
81% yield

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

Deoxygenative alkylation of heteroarenes

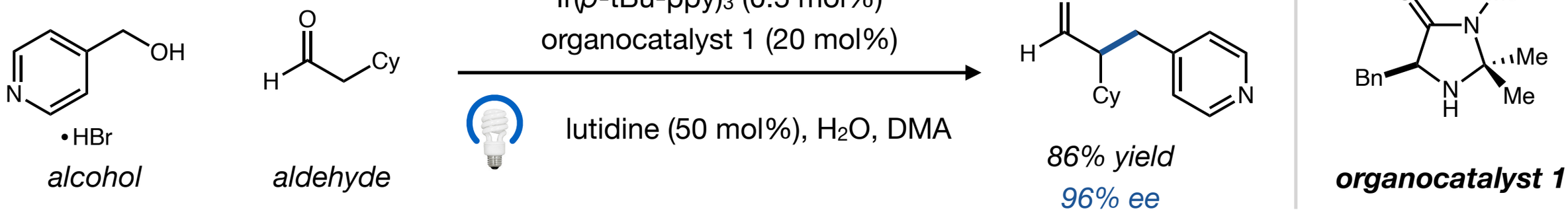


Saturated ring synthesis



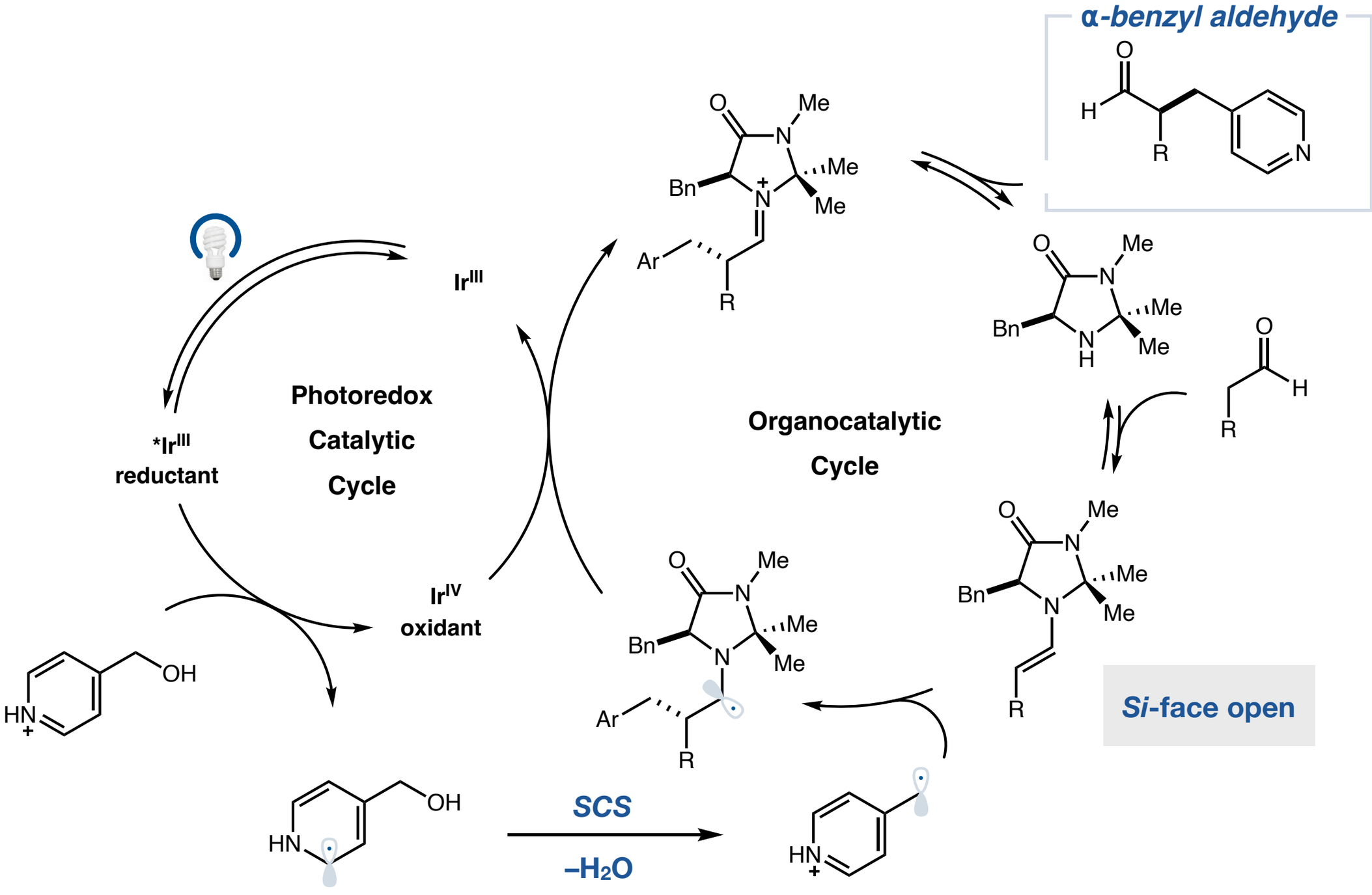
Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87–90.

Enantioselective α-benzylation of aldehydes



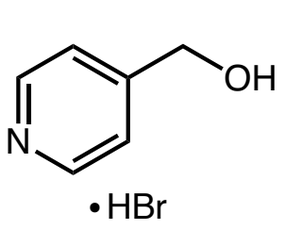
Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140* (9), 3322–3330.

Enantioselective α-benzylation of aldehydes

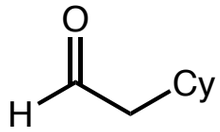


Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140* (9), 3322–3330.

Enantioselective α-benzylation of aldehydes



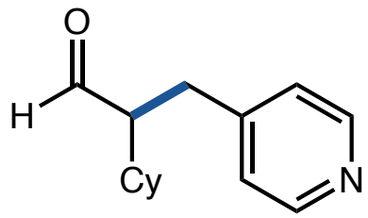
alcohol



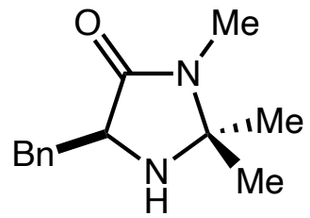
aldehyde

$Ir(p\text{-}tBu\text{-}ppy)_3$ (0.5 mol%)
organocatalyst 1 (20 mol%)

lutidine (50 mol%), H_2O, DMA

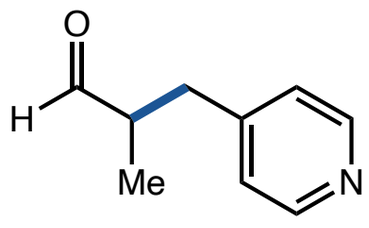


86% yield
96% ee

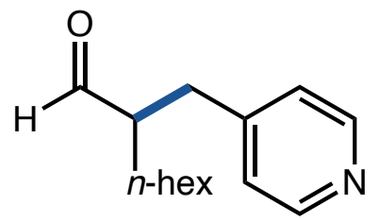


organocatalyst 1

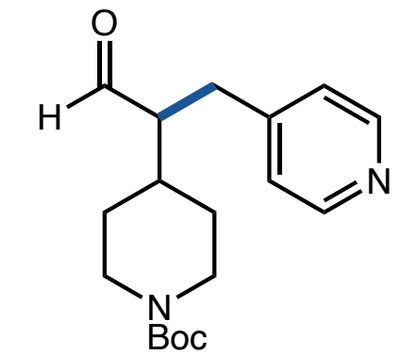
selected scope



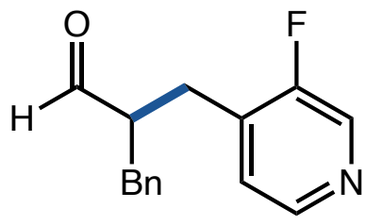
93% yield, 96% ee



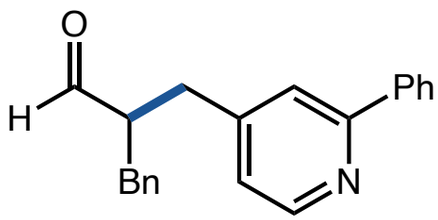
90% yield, 96% ee



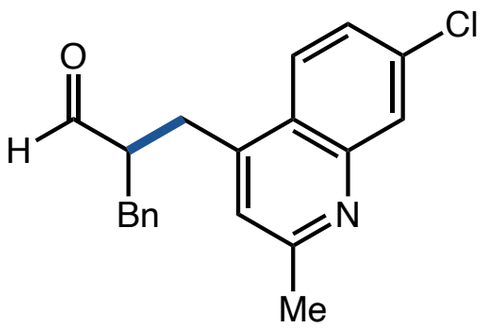
86% yield, 96% ee



78% yield, 96% ee



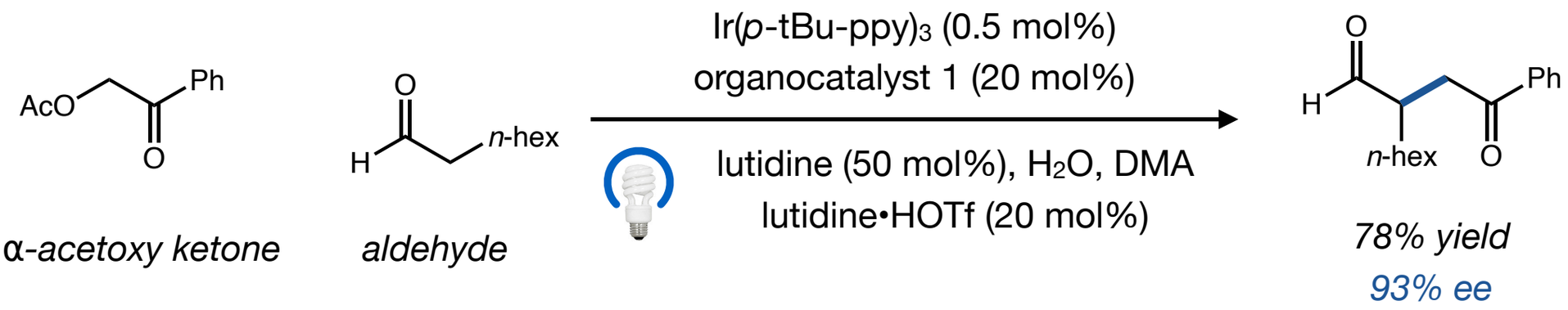
74% yield, 97% ee

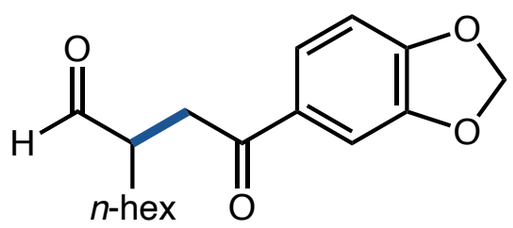


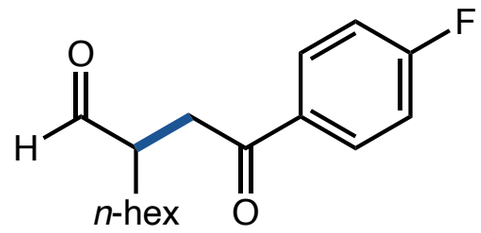
76% yield, 99% ee

Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140* (9), 3322–3330.

Enantioselective α-benzylation of aldehydes

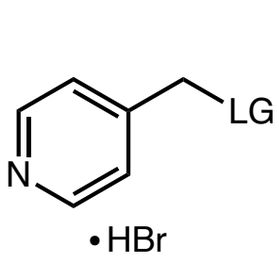




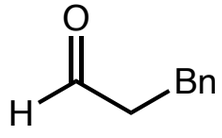


Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140* (9), 3322–3330.

Enantioselective α-benzylation of aldehydes



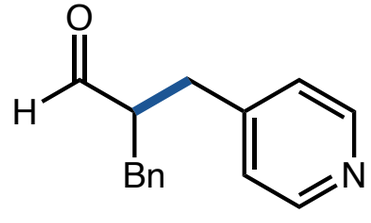
heteroaryl electrophile



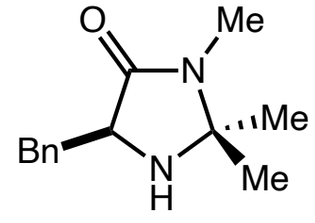
aldehyde

$Ir(p\text{-}tBu\text{-}ppy)_3$ (0.5 mol%)
organocatalyst 1 (20 mol%)

lutidine (50 mol%), H_2O, DMA

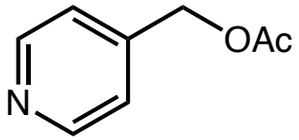


97% ee for each LG

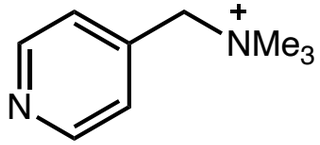


organocatalyst 1

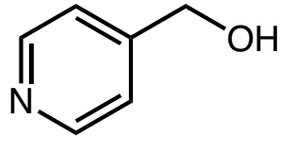
alternative leaving groups



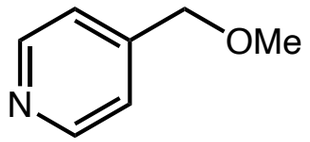
90% yield



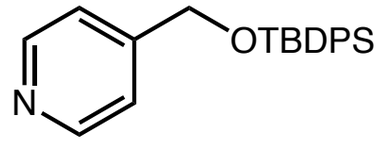
86% yield



85% yield



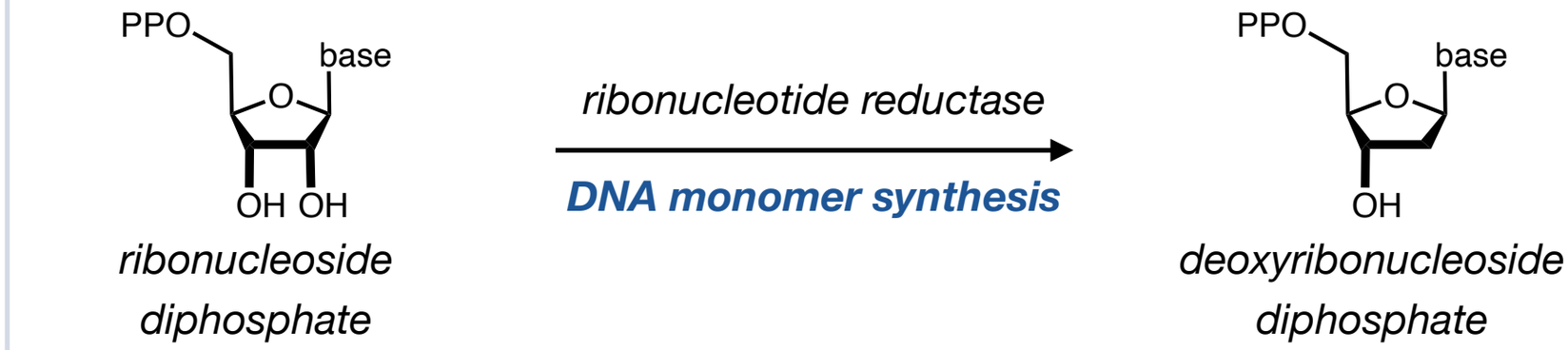
71% yield



61% yield

Variety of LGs are competent for transformation - ee is not affected

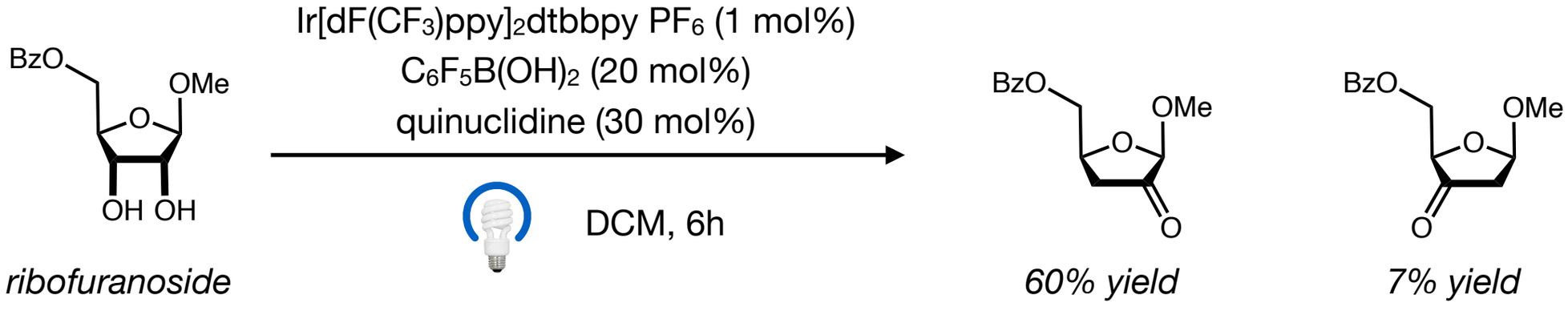
Nacsa, E. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2018**, *140* (9), 3322–3330.



SCS is heavily utilized in biological systems…

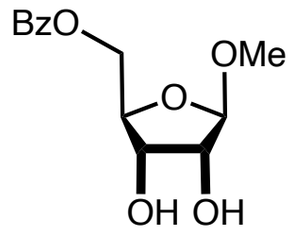
What about synthetic methods on bio-relevant molecules?

Deoxygenation of furanosides by photoredox catalysis



Dimakos, V.; Gorelik, D.; Su, H. Y.; Garrett, G. E.; Hughes, G.; Shibayama, H.; Taylor, M. S. *Chem. Sci.* **2020**, *11* (6), 1531–1537.

Deoxygenation of furanosides by photoredox catalysis

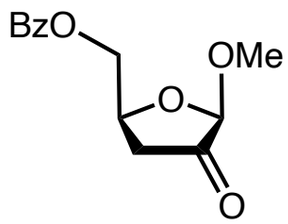


ribofuranoside

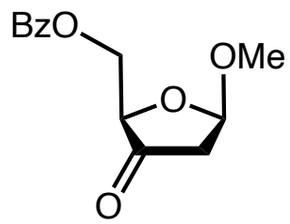
$Ir[dF(CF_3)ppy]_2dtbbpy\ PF_6$ (1 mol%)
$C_6F_5B(OH)_2$ (20 mol%)
quinuclidine (30 mol%)

DCM, 6h

9 examples >60% yield

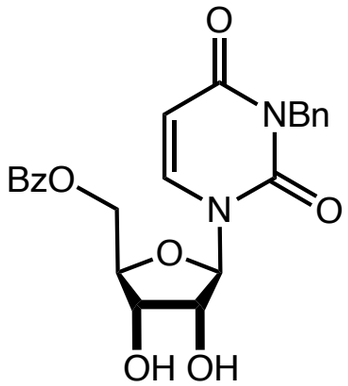


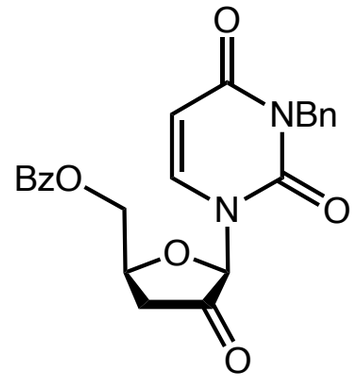
60% yield



7% yield

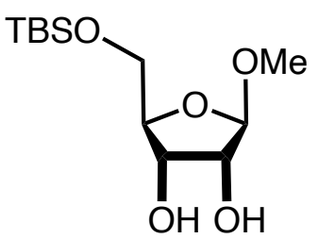
limitations

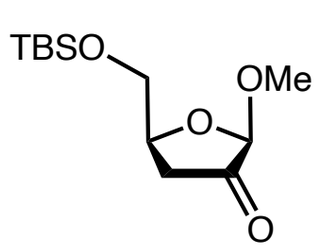


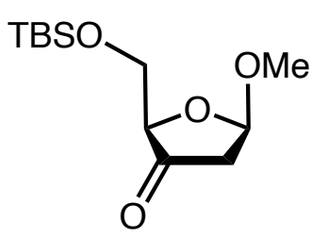


27% yield, >20:1 selectivity

elimination of uracil





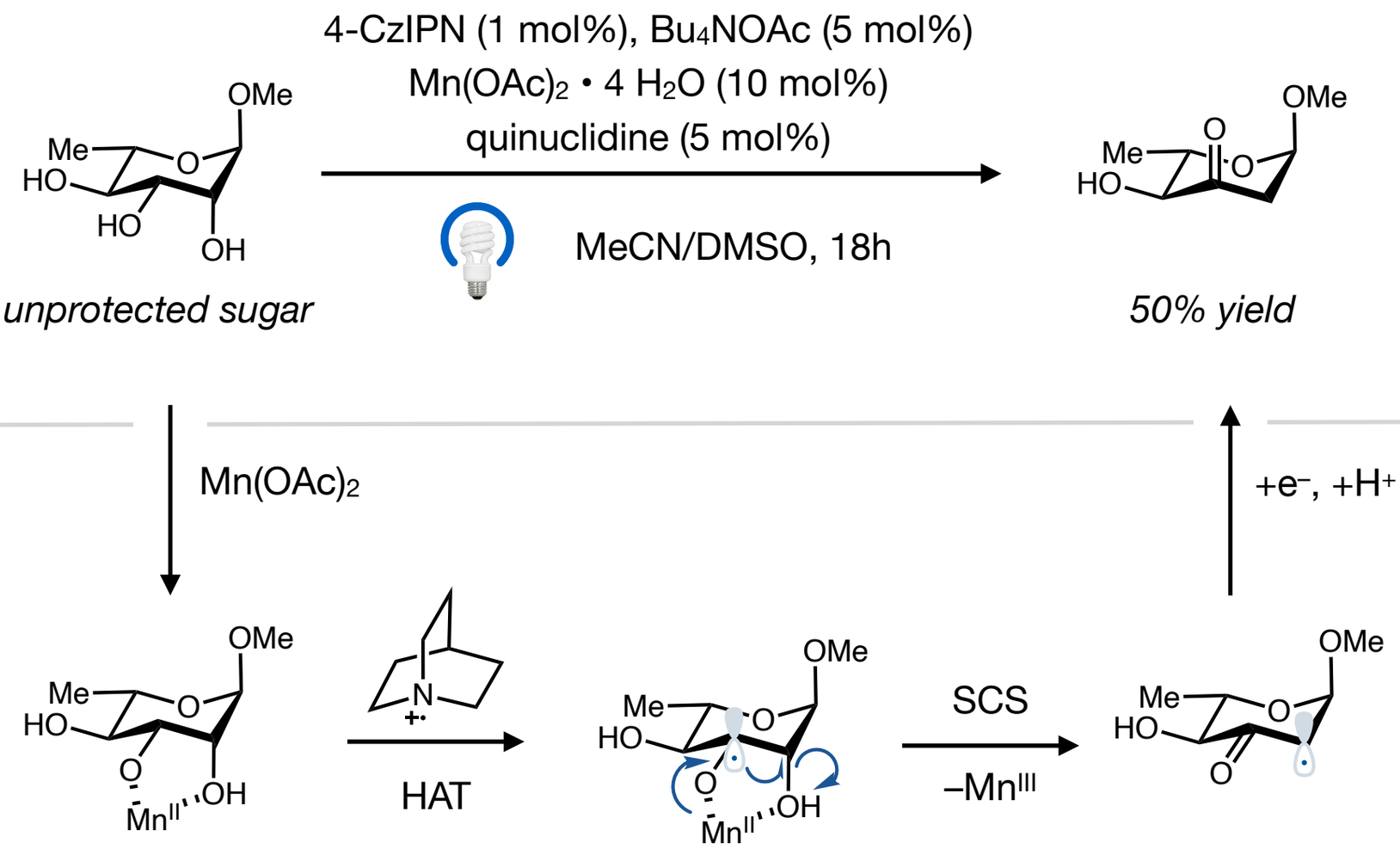


28% yield, 2:1 selectivity

inductively withdrawing PG required

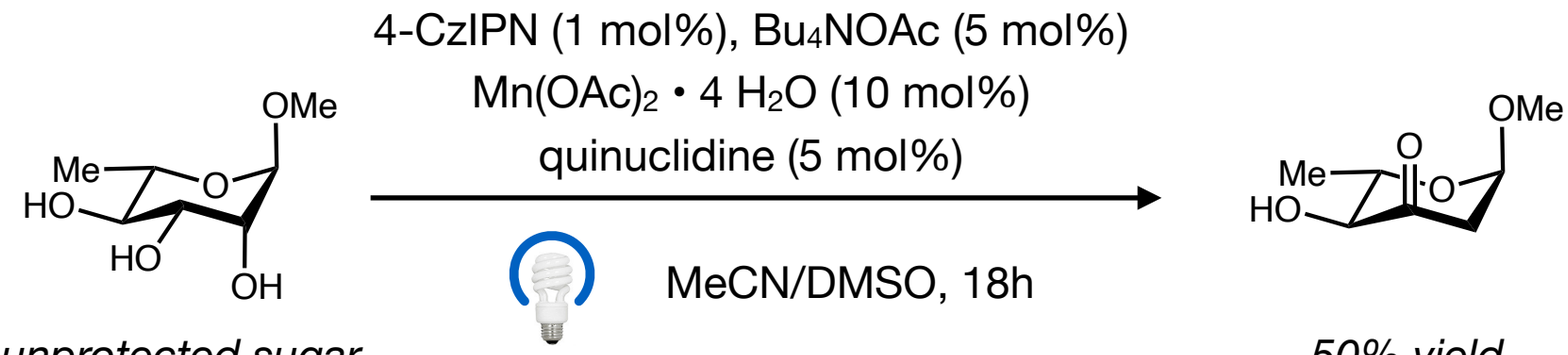
Dimakos, V.; Gorelik, D.; Su, H. Y.; Garrett, G. E.; Hughes, G.; Shibayama, H.; Taylor, M. S. *Chem. Sci.* **2020**, *11* (6), 1531–1537.

Deoxygenation of unprotected sugars by photoredox catalysis

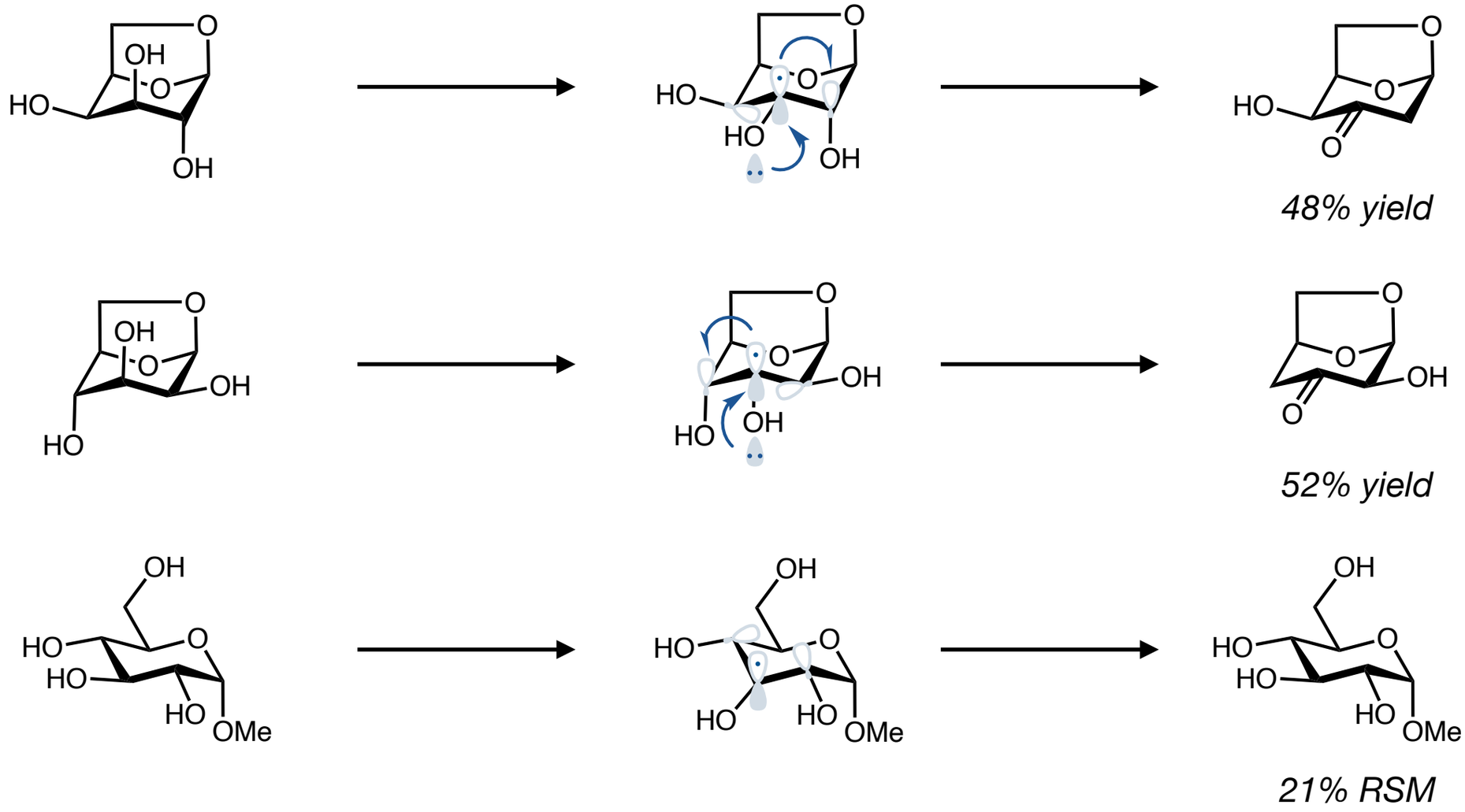


Carder, H. M.; Suh, C. E.; Wendlandt, A. E. *J. Am. Chem. Soc.* **2021**, *143* (34), 13798–13805.

Deoxygenation of unprotected sugars by photoredox catalysis



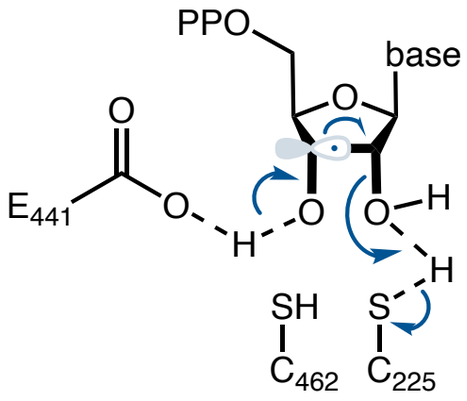
stereoelectronic effects



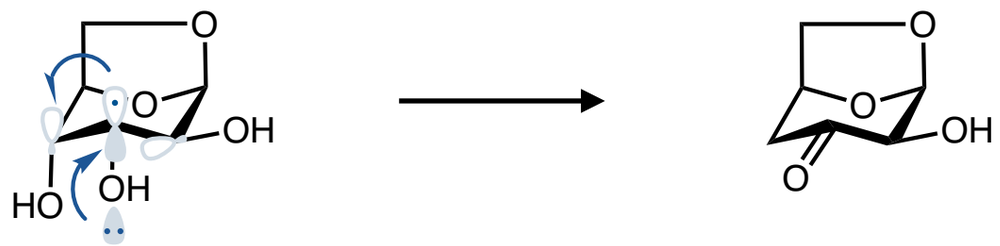
Carder, H. M.; Suh, C. E.; Wendlandt, A. E. *J. Am. Chem. Soc.* **2021**, *143* (34), 13798–13805.

Outline

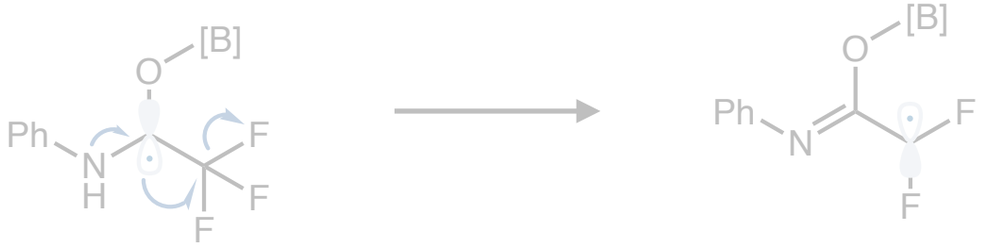
Biochemical and mechanistic background



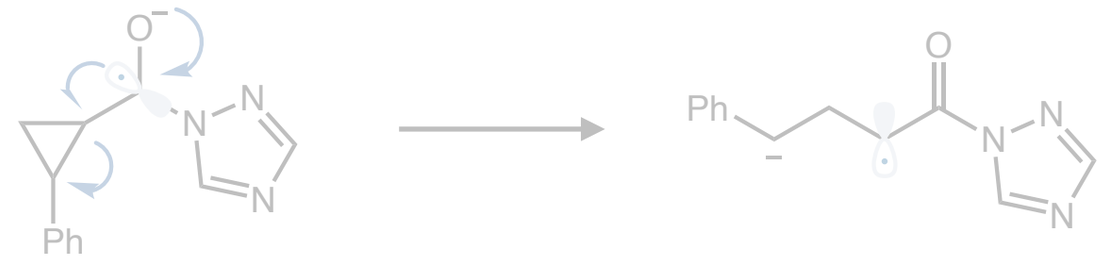
C–O bond activation



C–F bond activation

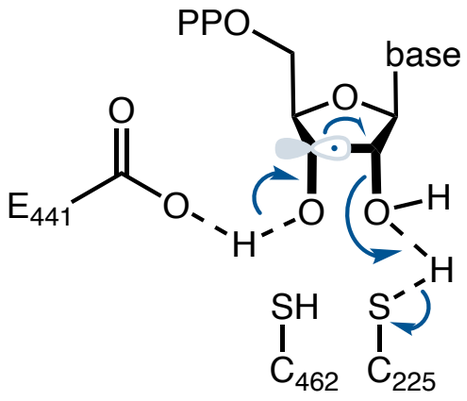


Miscellaneous SCS reactions

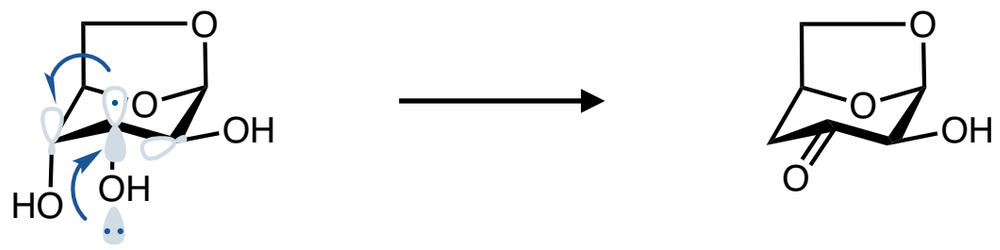


Outline

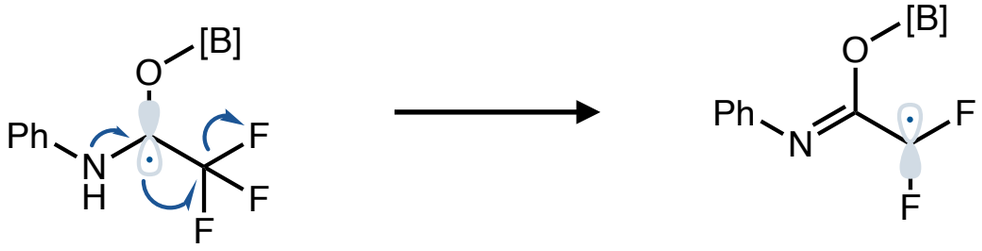
Biochemical and mechanistic background



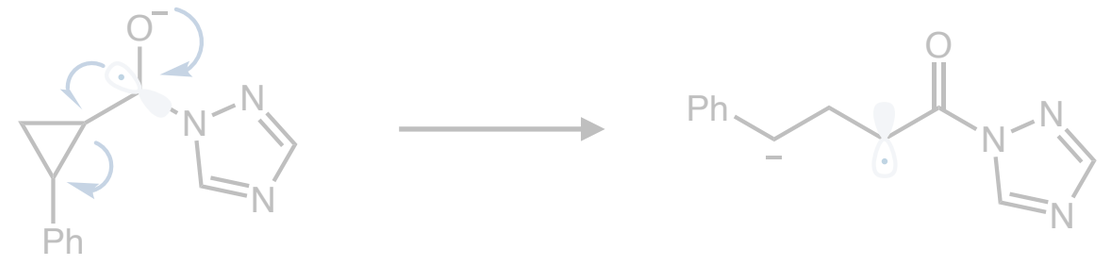
C–O bond activation



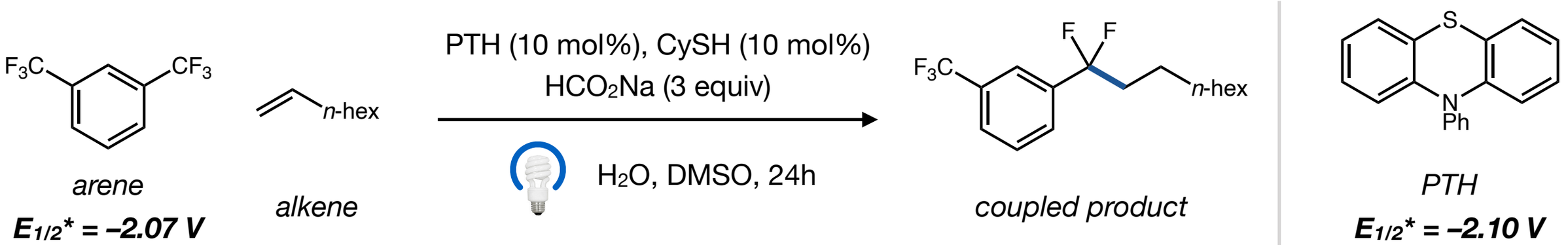
C–F bond activation



Miscellaneous SCS reactions



Defluorination of electron-deficient trifluoromethylarenes



arene

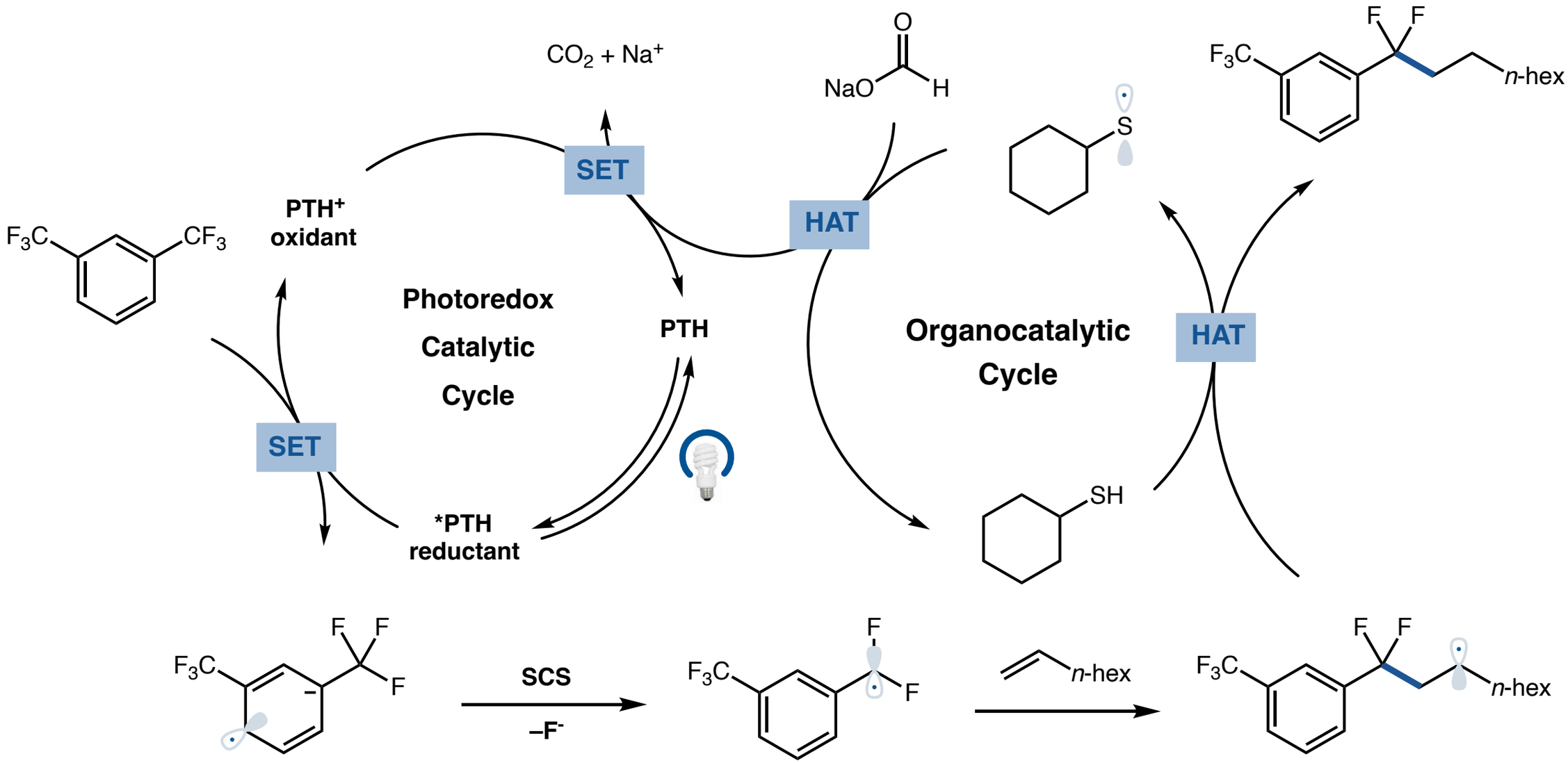
$E_{1/2}^{*} = -2.07$ V

alkene

coupled product

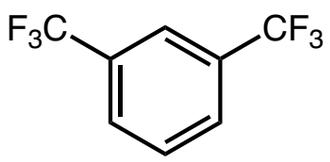
PTH

$E_{1/2}^{*} = -2.10$ V



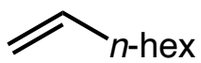
Wang, H.; Jui, N. T. *J. Am. Chem. Soc.* **2018**, *140* (1), 163–166.

Defluorination of electron-deficient trifluoromethylarenes



arene

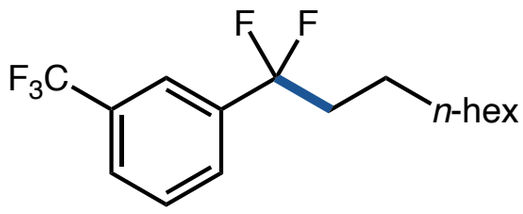
***E*$_{1/2}$* = –2.07 V**



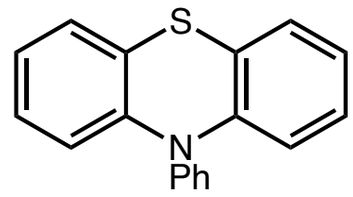
alkene

PTH (10 mol%), CySH (10 mol%)
HCO_2Na (3 equiv)

H_2O, DMSO, 24h



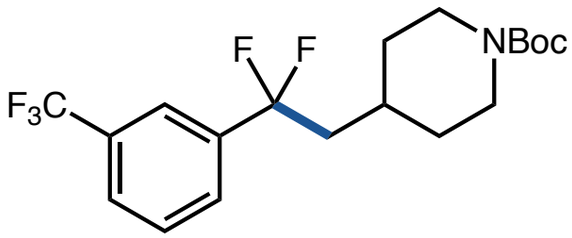
coupled product



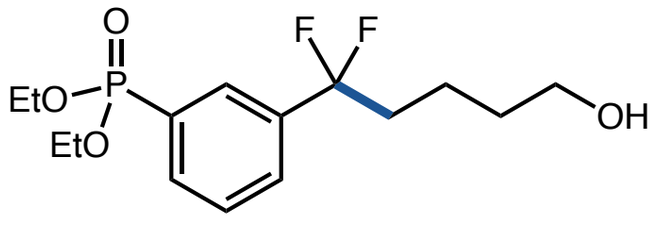
PTH

***E*$_{1/2}$* = –2.10 V**

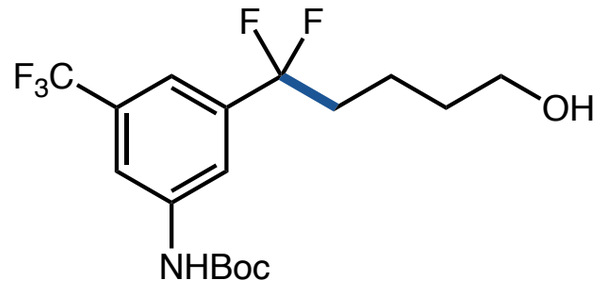
selected scope



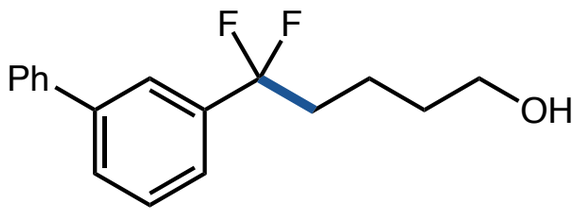
81% yield



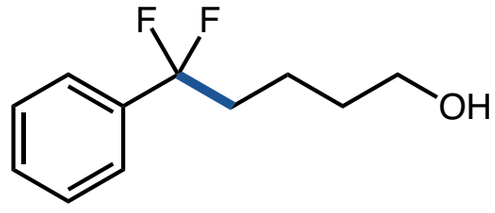
56% yield



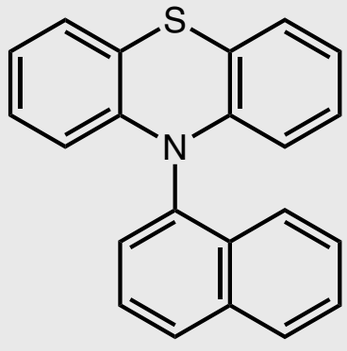
89% yield



60% yield - with N-(1-Np)PTH



11% yield - with N-(1-Np)PTH

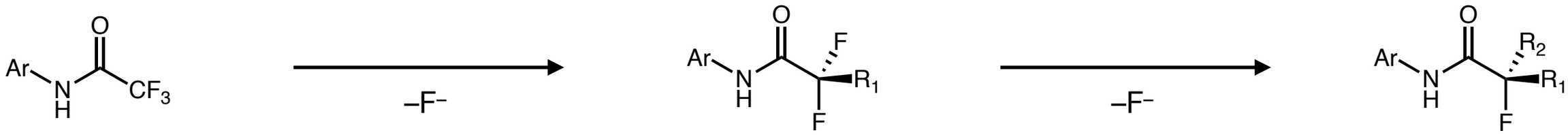


N-(1-Np)PTH

***E*$_{1/2}$* = –2.23 V**

Wang, H.; Jui, N. T. *J. Am. Chem. Soc.* **2018**, *140* (1), 163–166.

Sequential defluorination of trifluoroacetamides and acetates

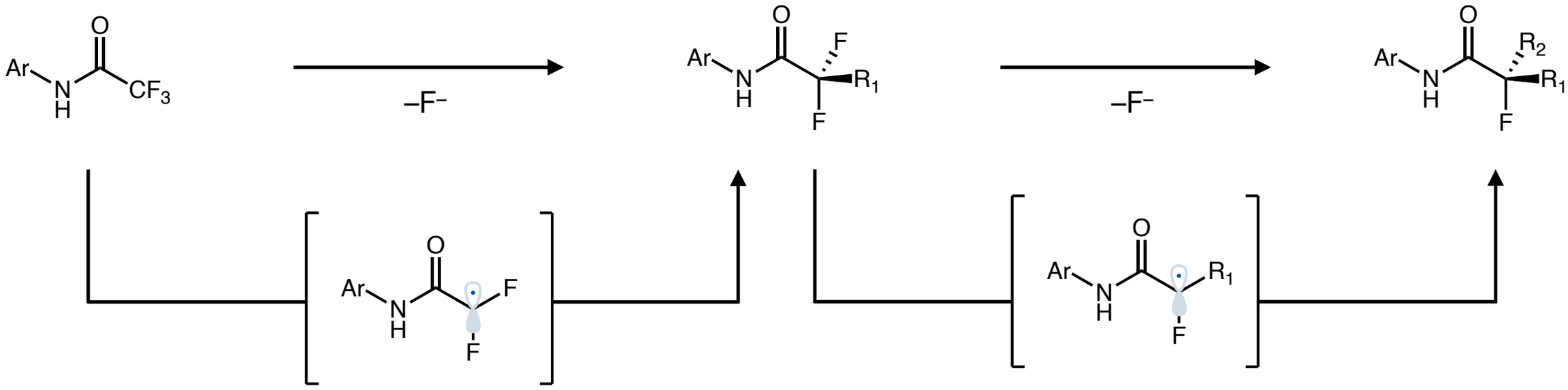


trifluoroacetamide

readily accessible

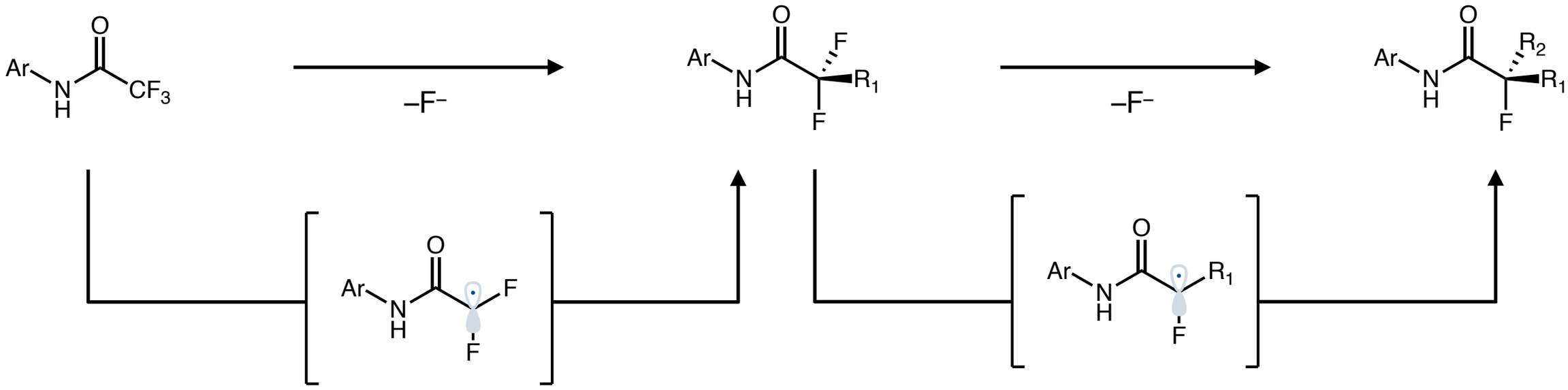
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

Sequential defluorination of trifluoroacetamides and acetates



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.

Sequential defluorination of trifluoroacetamides and acetates

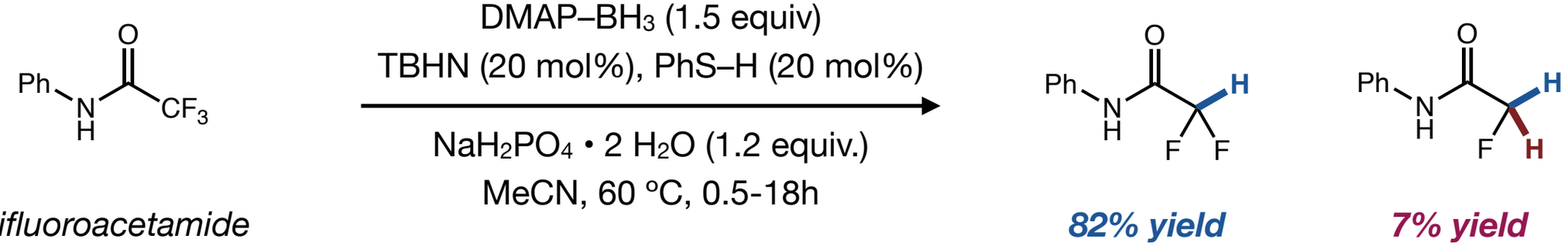


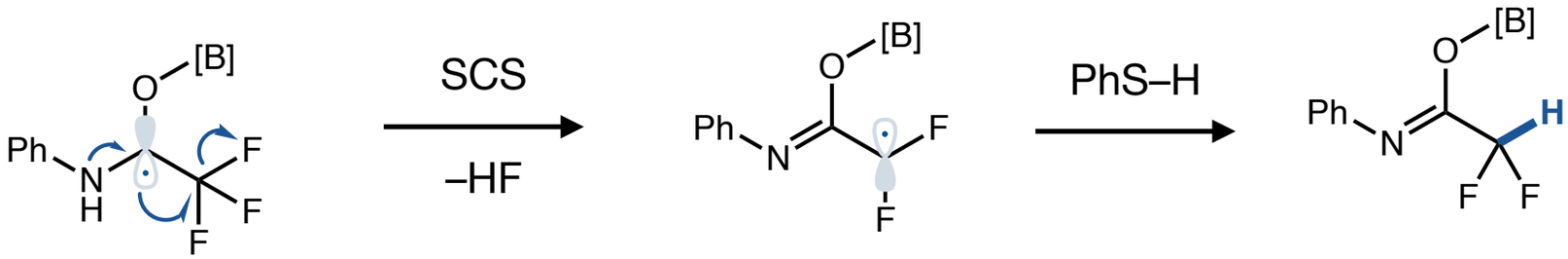
How can a selective and modular defluorination process be achieved?

How can overdefluorination be avoided?

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.

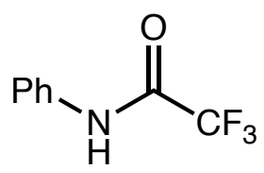
Sequential defluorination of trifluoroacetamides and acetates





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.

Sequential defluorination of trifluoroacetamides and acetates



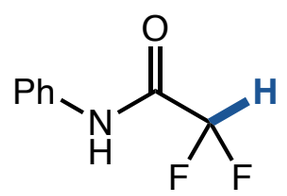
trifluoroacetamide

DMAP–BH_3 (**3.0 equiv**)

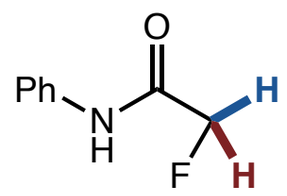
TBHN (20 mol%), PhS–H (20 mol%)

$NaH_2PO_4 \cdot 12\ H_2O$ (2.4 equiv.)

Dioxane, 60 °C, 0.5-18h



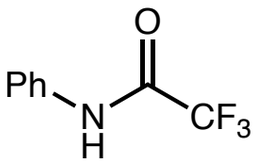
0% yield



85% yield

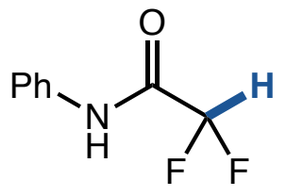
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

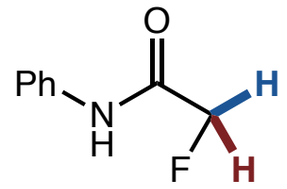
Sequential defluorination of trifluoroacetamides and acetates



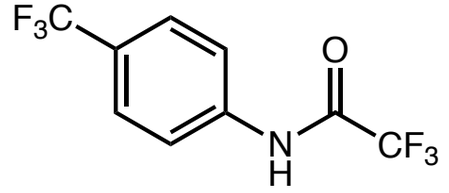
trifluoroacetamide

$DMAP–BH_3$ (1.5 or 3.0 equiv)
TBHN (20 mol%), PhS–H (20 mol%)
$NaH_2PO_4 \cdot x\ H_2O$ (1.2 or 2.4 equiv.)
MeCN or Dioxane, 60 °C, 0.5-18h

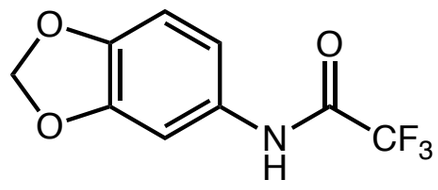




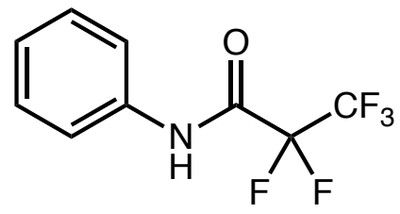
selected scope



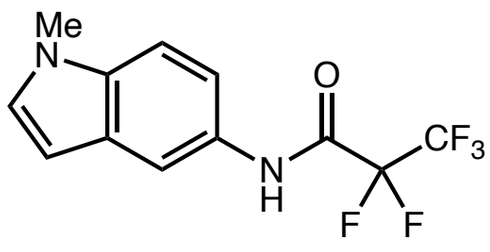
58% CF_2H, 73% CFH_2



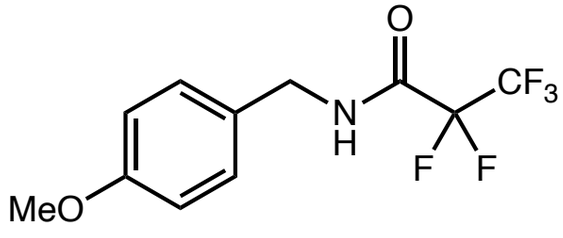
76% CF_2H, 84% CFH_2



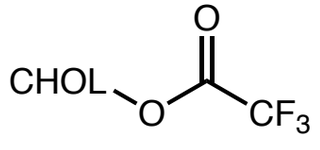
92% CF_2H, 94% CFH_2



84% CF_2H, 55% CFH_2



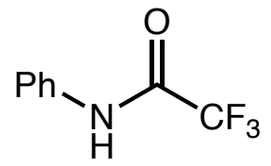
44% CF_2H, trace CFH_2

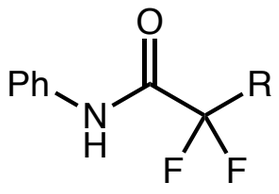


56% CF_2H, trace CFH_2

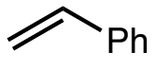
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

Sequential defluorination of trifluoroacetamides and acetates





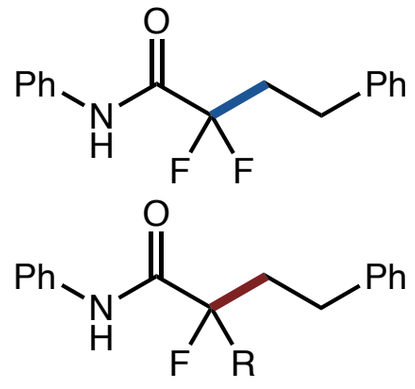
***tri*- or**
***di*fluoroacetamide**



alkene

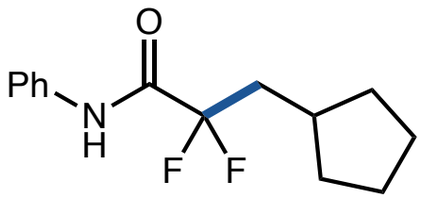
DMAP–BH_3 **(2 or 3-4 equiv)**
DTBP (**1-1.5 equiv**), PhS–H (20 mol%)

$NaH_2PO_4 \cdot 2\ H_2O$ **(1.2 or 3-4 equiv.)**
MeCN, 120 °C

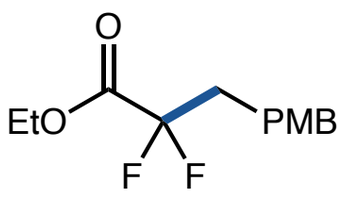


alkylated products

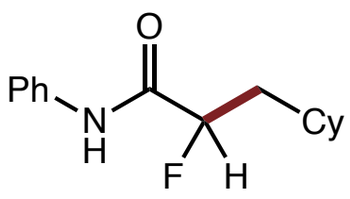
selected scope



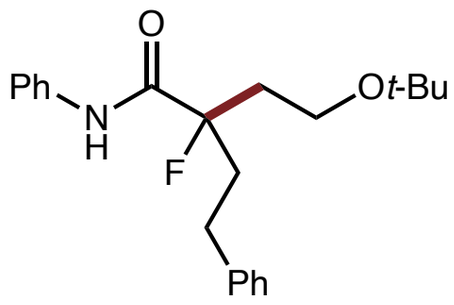
51% yield



48% yield



61% yield



46% yield

What enables the selective and sequential defluorination process?

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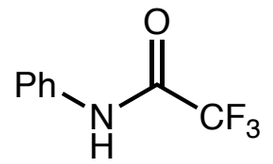
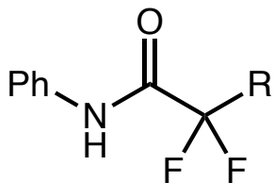
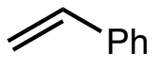




***tri*- or *di*fluoroacetamide**



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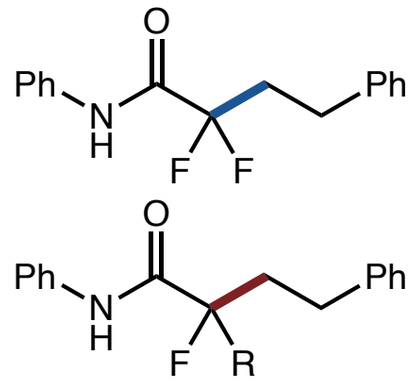
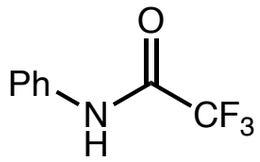
MeCN, 120 °C



alkylated products

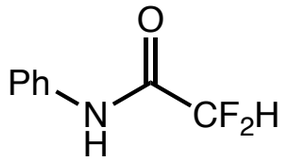
C–F BDE (ease of SCS)

119.5 kcal/mol



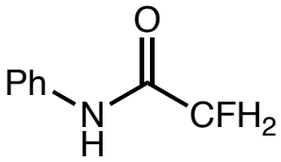
4.03 eV

108.6 kcal/mol



4.14 eV

106.3 kcal/mol



4.45 eV

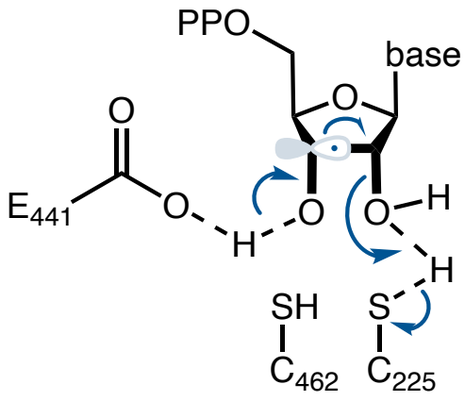
SOMO/LUMO gap (ease of DMAP–BH_2• addition)

Inductive withdrawal by F atoms lowers the carbonyl LUMO

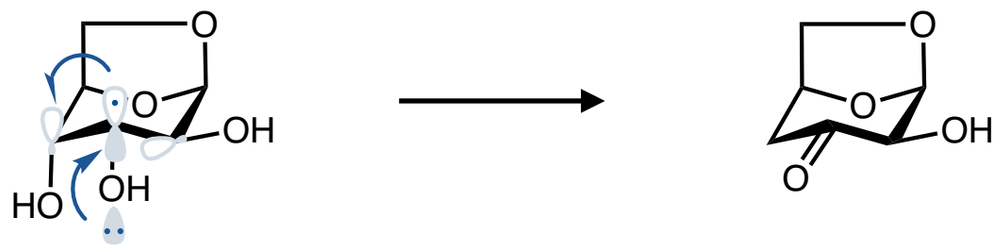
Yu, Y.-J.; Zhang, F.-L.; Peng, T.-Y.; Wang, C.-L.; Cheng, J.; Chen, C.; Houk, K. N.; Wang, Y.-F. *Science* **2021**, *371*, 1232–1240.

Outline

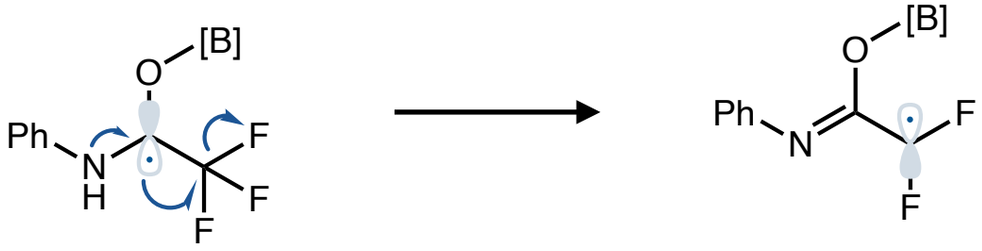
Biochemical and mechanistic background



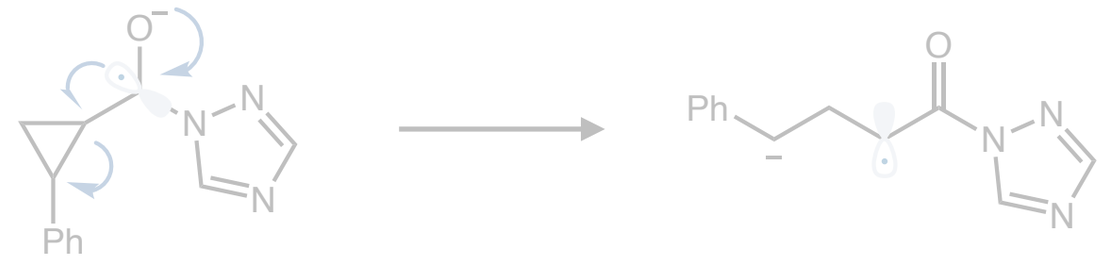
C–O bond activation



C–F bond activation

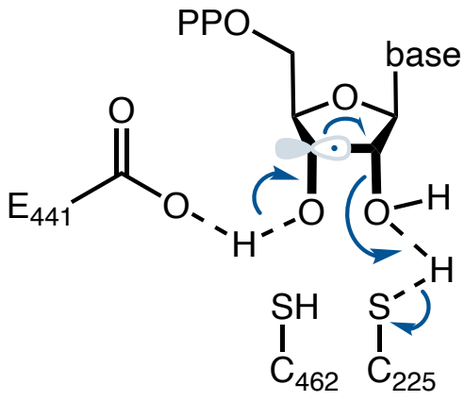


Miscellaneous SCS reactions

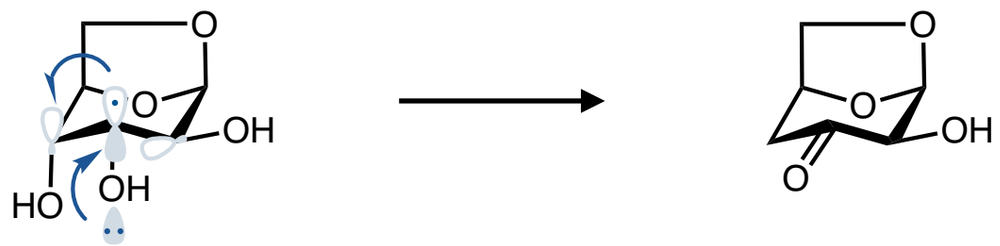


Outline

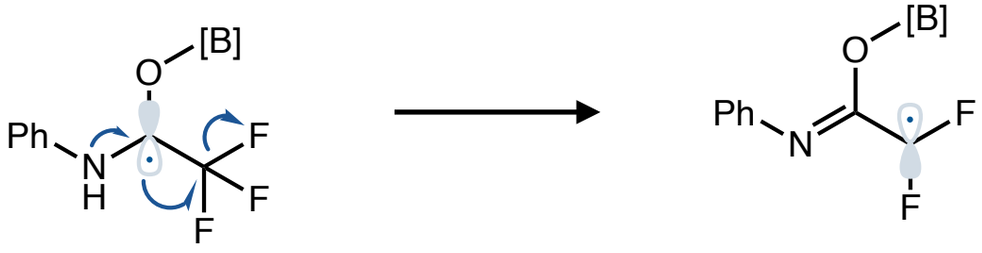
Biochemical and mechanistic background



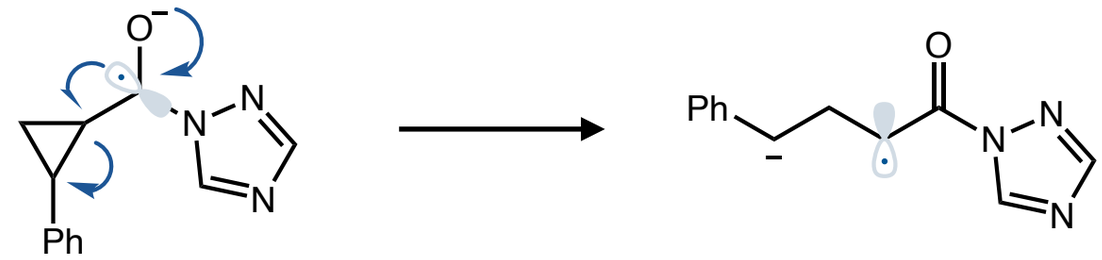
C–O bond activation



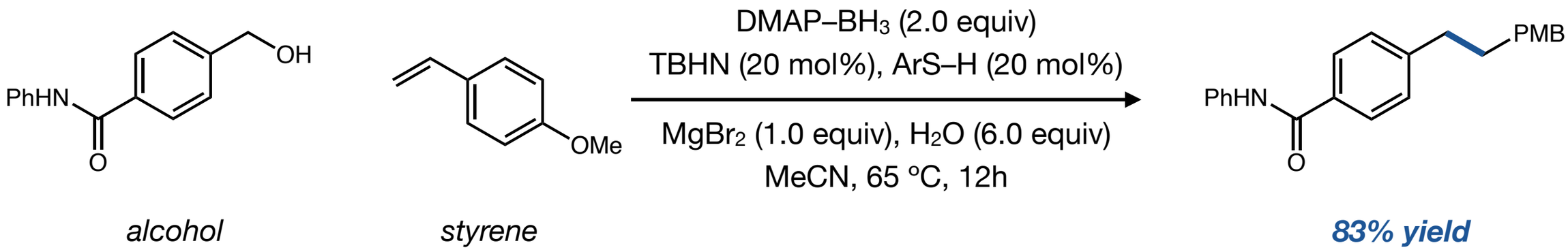
C–F bond activation

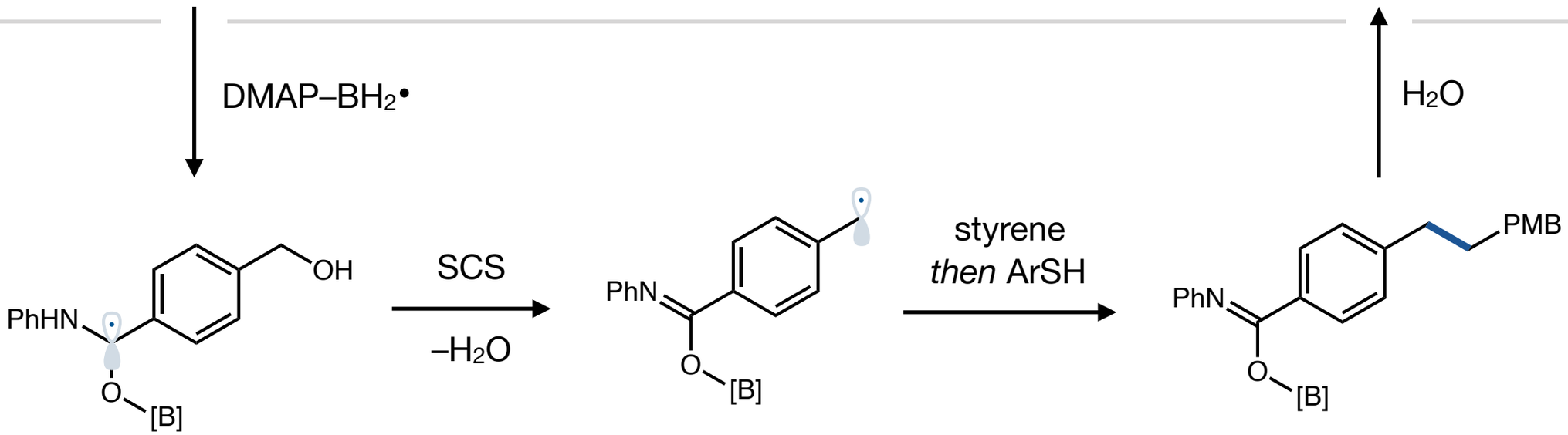


Miscellaneous SCS reactions



Remote SCS enabled benzylic deoxygenation and deamination





Hui, L.; Phang, Y. L.; Ye, C.; Lai, J.; Zhang, F.; Fu, Y.; Wang, Y. *Angew. Chem. Int. Ed.* **2025**, *64* (24), e202506771.

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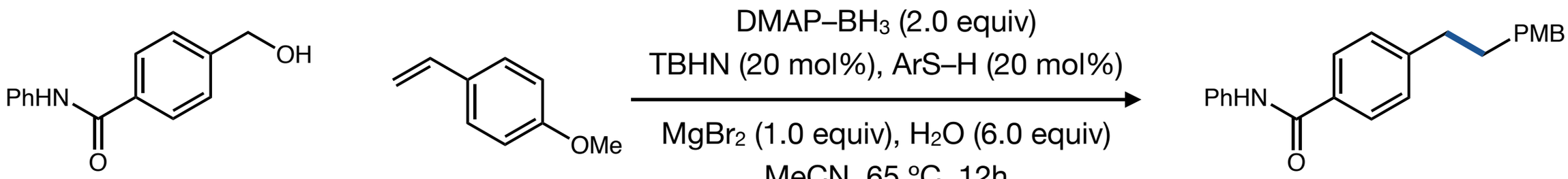
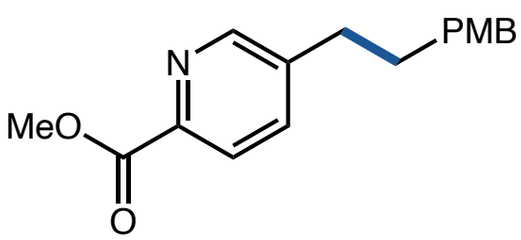


alcohol *styrene* ***83% yield***

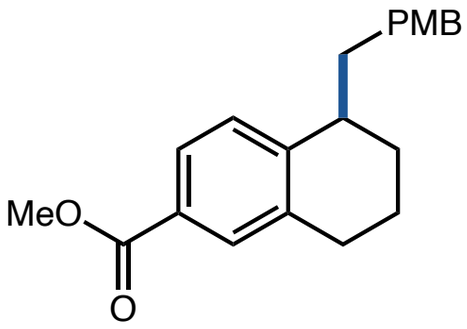
selected scope

pyridine



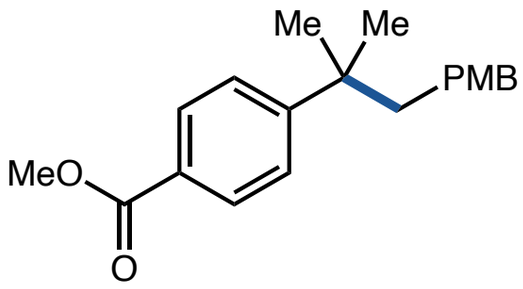
37% yield

secondary



33% yield

tertiary



43% yield

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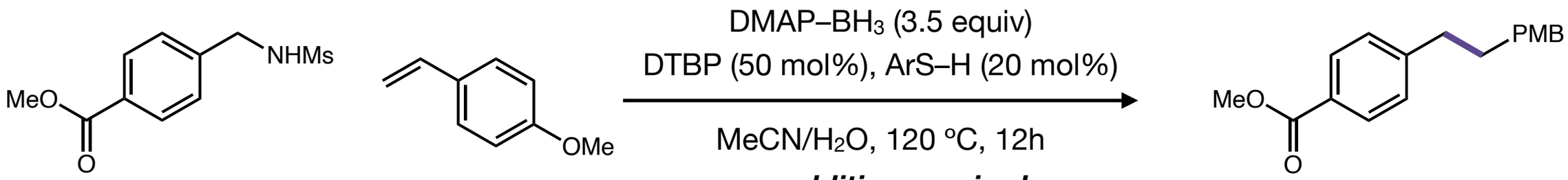
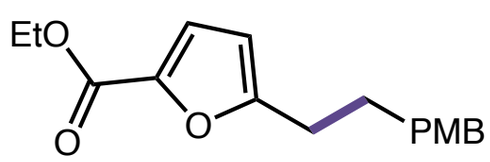


sulfonamide *styrene* ***74% yield***

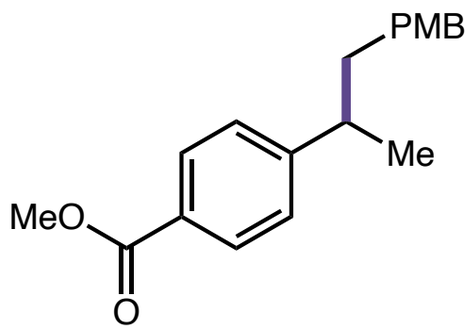
selected scope

furan



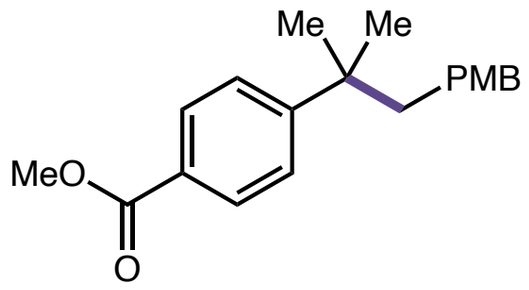
60% yield

secondary



69% yield

tertiary



36% yield

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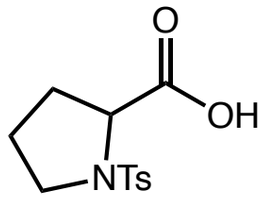
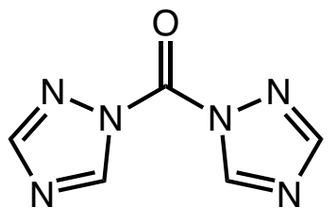
SCS-enabled ring expansion of cyclic carboxylic acids



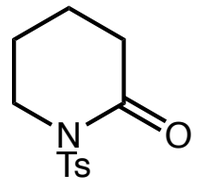
carboxylic acid



carbonylditriazole

5CzBN (1 mol%), *i*Pr_2NEt (10 mol%)

Hantzsch ester (1.5 equiv)
acetone, 3 Å MS, 12h

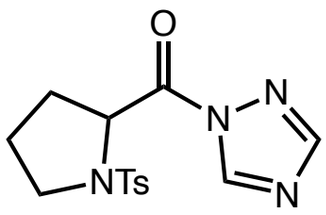


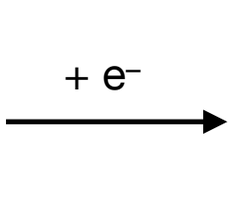
ring expanded product

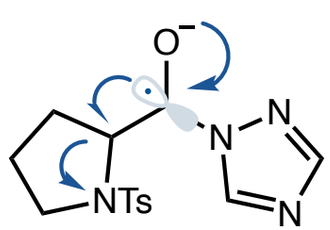
83% yield

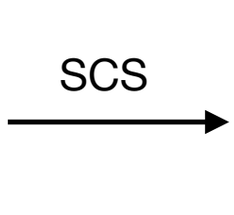
– triazole

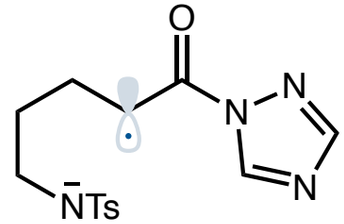
– triazole

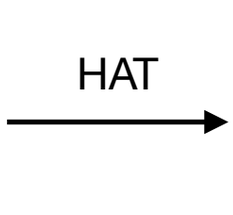


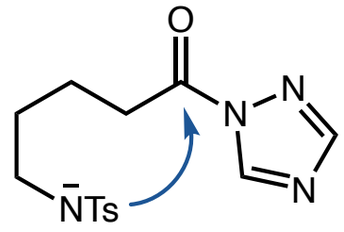






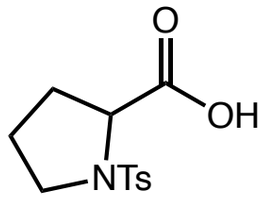




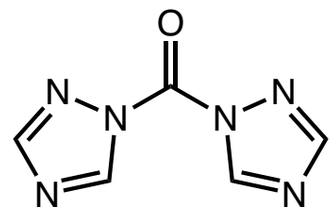


Shimono, H.; Kusakabe, M.; Nagao, K.; Ohmiya, H. *ChemRxiv* **2025**, doi.org/10.26434/chemrxiv-2025-0856k.

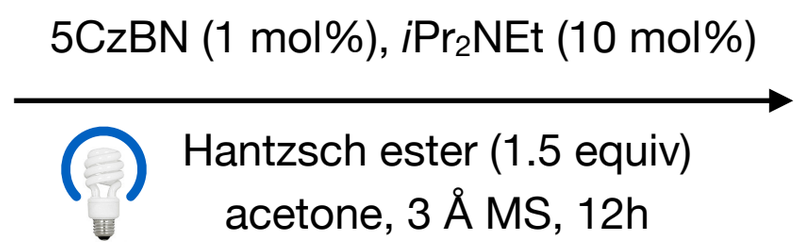
SCS-enabled ring expansion of cyclic carboxylic acids

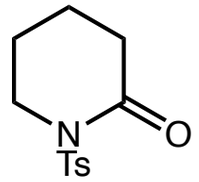


carboxylic acid



carbonylditriazole

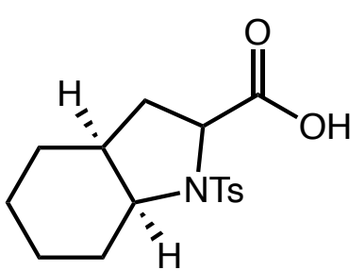


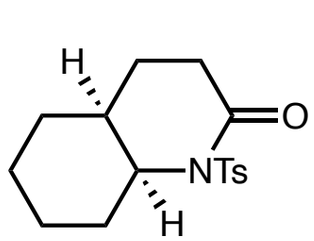


ring expanded product

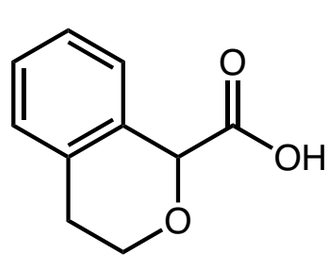
83% yield

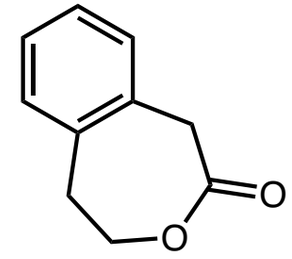
heteroatom leaving groups



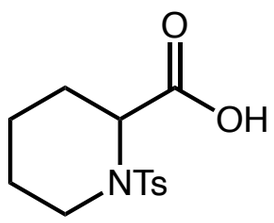


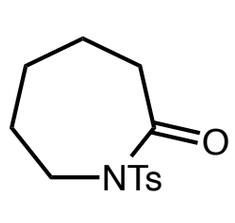
73% yield



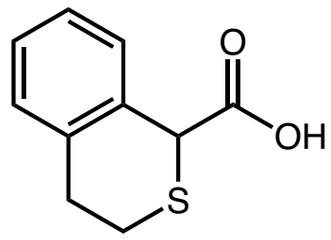


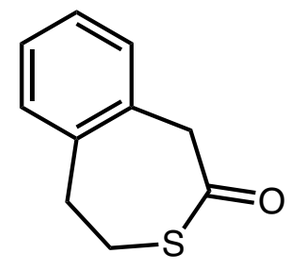
79% yield





53% yield

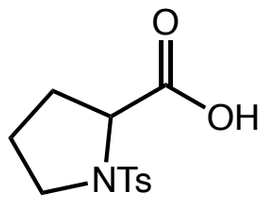




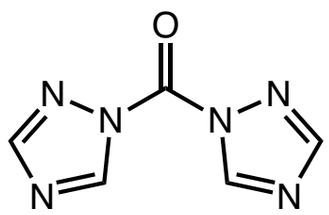
76% yield

Shimono, H.; Kusakabe, M.; Nagao, K.; Ohmiya, H. *ChemRxiv* **2025**, doi.org/10.26434/chemrxiv-2025-0856k.

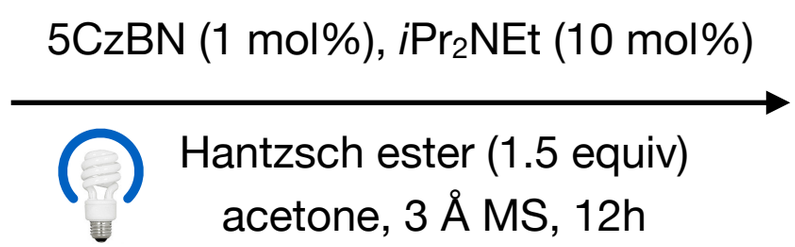
SCS-enabled ring expansion of cyclic carboxylic acids

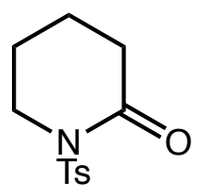


carboxylic acid



carbonylditriazole

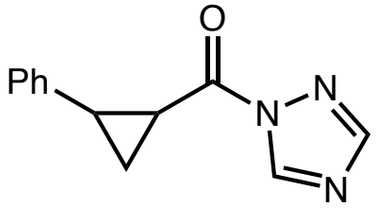


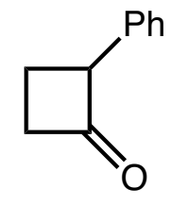


ring expanded product

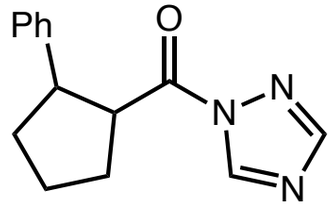
83% yield

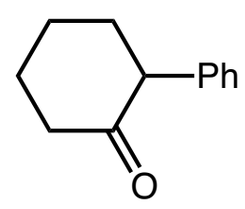
carbon leaving groups



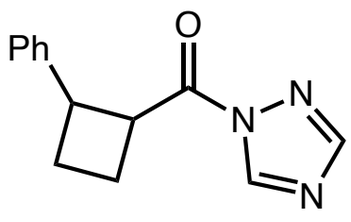


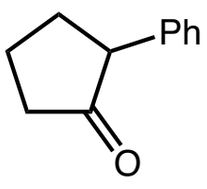
55% yield



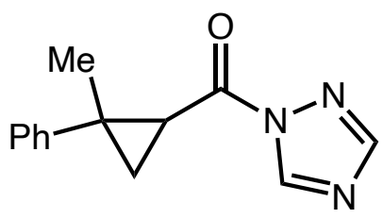


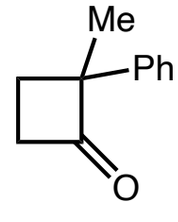
0% yield





53% yield



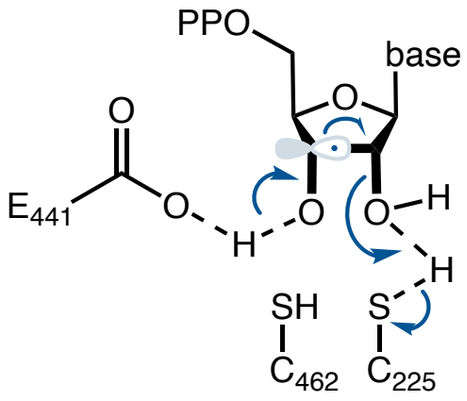


76% yield

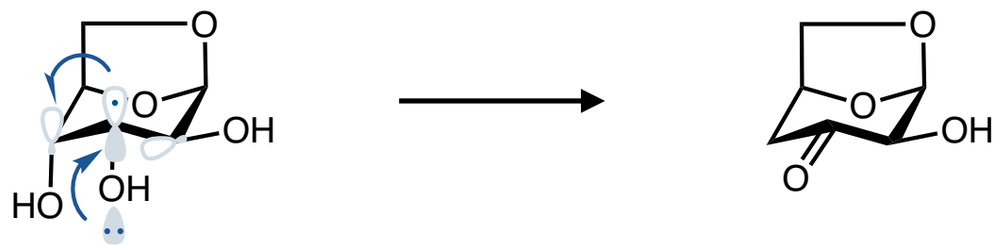
Shimono, H.; Kusakabe, M.; Nagao, K.; Ohmiya, H. *ChemRxiv* **2025**, doi.org/10.26434/chemrxiv-2025-0856k.

Outline

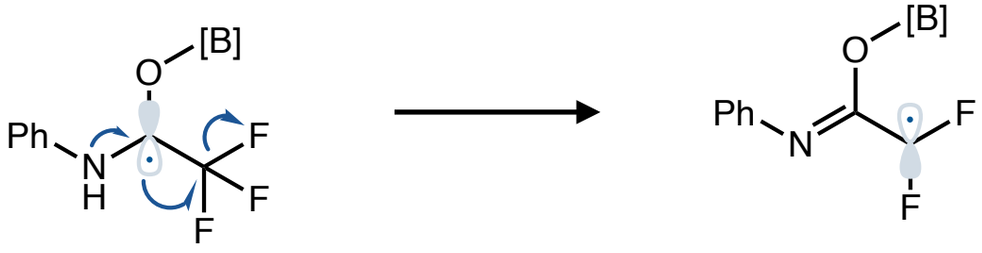
Biochemical and mechanistic background



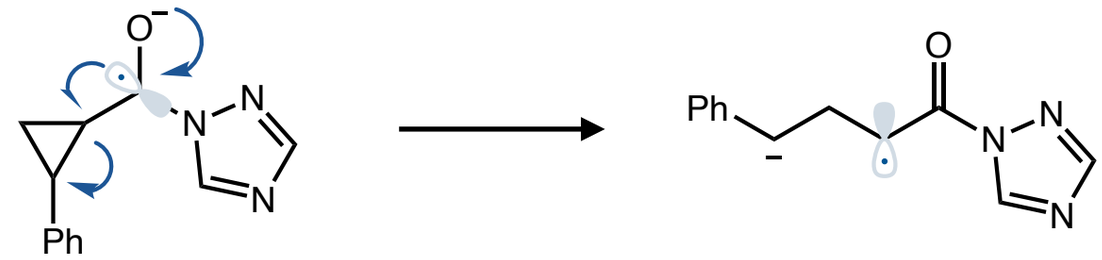
C–O bond activation



C–F bond activation



Miscellaneous SCS reactions



Questions?