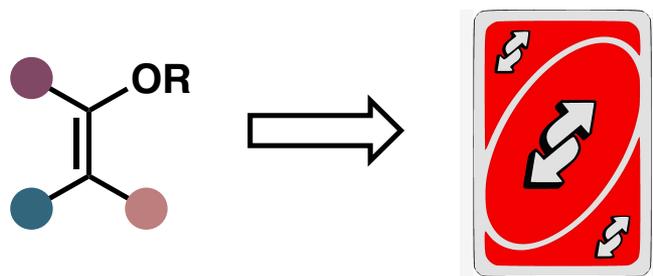
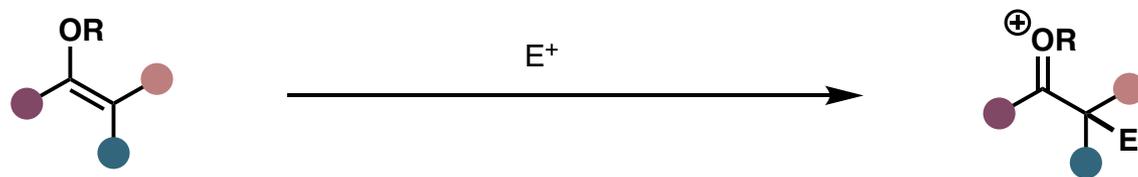


Recent Advances in Enol Ether Umpolung Chemistry

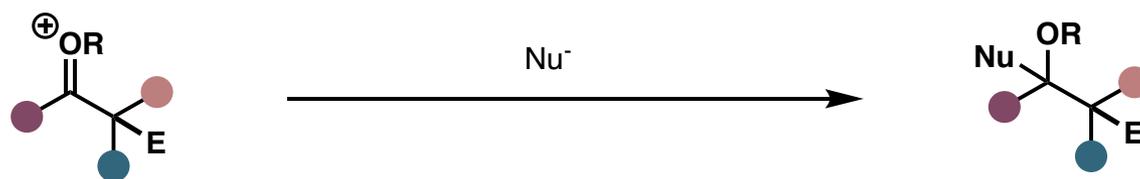
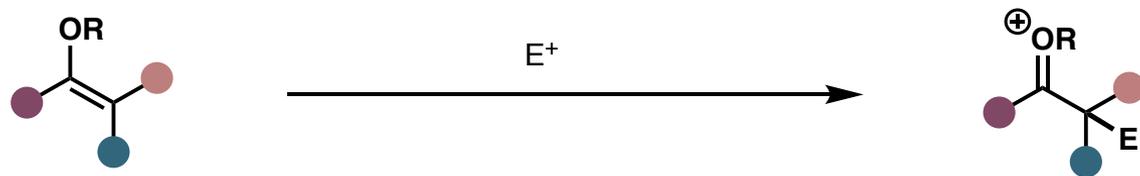


Nicholas A. Falcone
Literature Group Meeting
July 31st, 2020

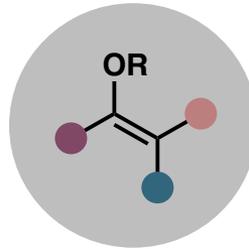
Enol Ethers — Traditional Reactivity



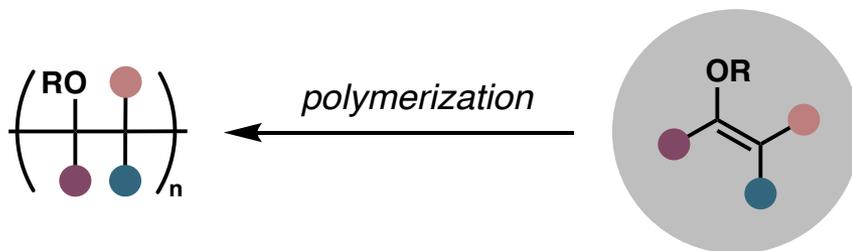
Enol Ethers — Traditional Reactivity



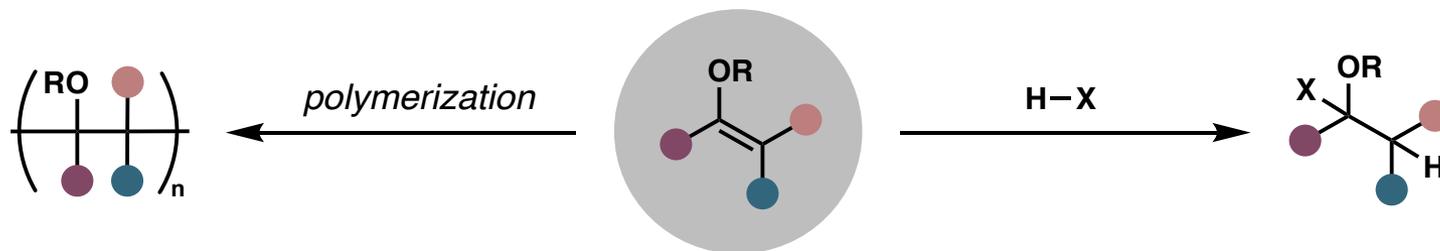
Enol Ethers — Traditional Reactivity



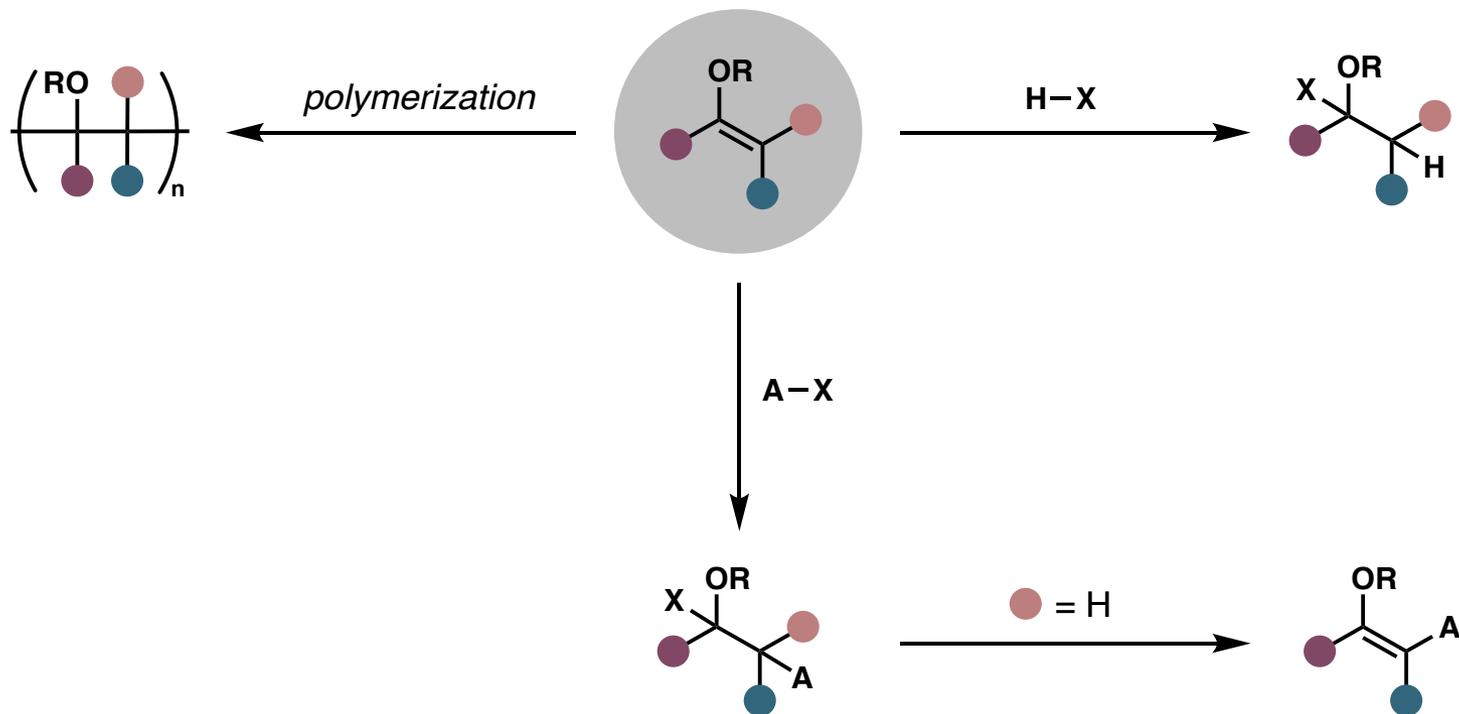
Enol Ethers — Traditional Reactivity



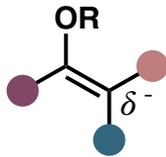
Enol Ethers — Traditional Reactivity



Enol Ethers — Traditional Reactivity

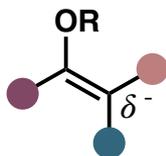


Reversing Enol Ether Polarity

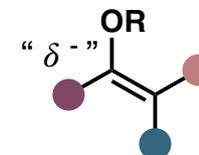


- Nucleophilic at the β -position
- Electrophilic at the α -position
- Closed-shell, polar pathways

Reversing Enol Ether Polarity

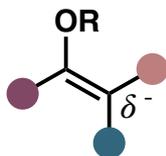


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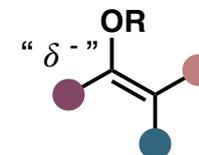


- Nucleophilic at the α -position
- via α -oxy radicals
- Open-shell, radical pathways

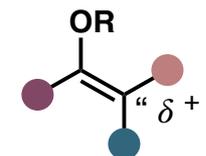
Reversing Enol Ether Polarity



- Nucleophilic at the β -position
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- Closed-shell, polar pathways

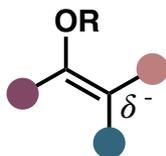


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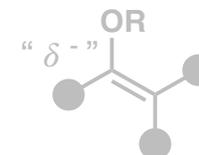


- Electrophilic at the β -position
- via radical cations
- Open-shell, radical pathways

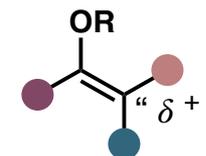
Reversing Enol Ether Polarity



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- Electrophilic at the α -position
- Closed-shell, polar pathways

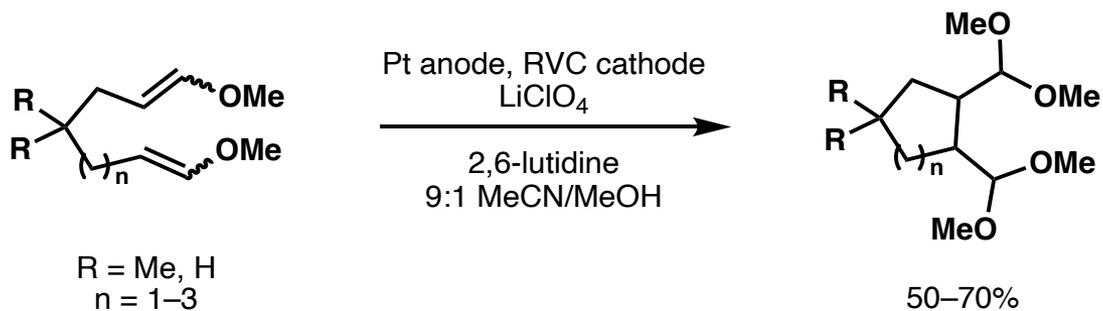
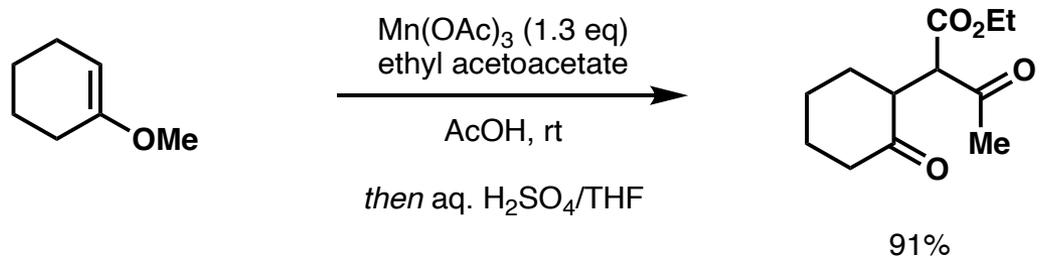


- Nucleophilic at the α -position
- via α -oxy radicals
- Open-shell, radical pathways

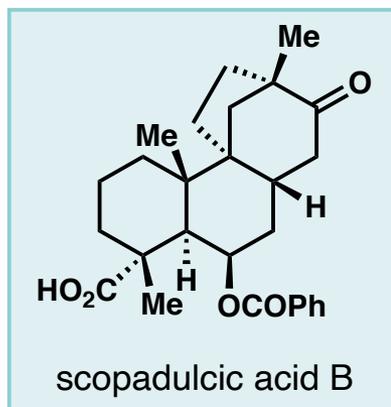
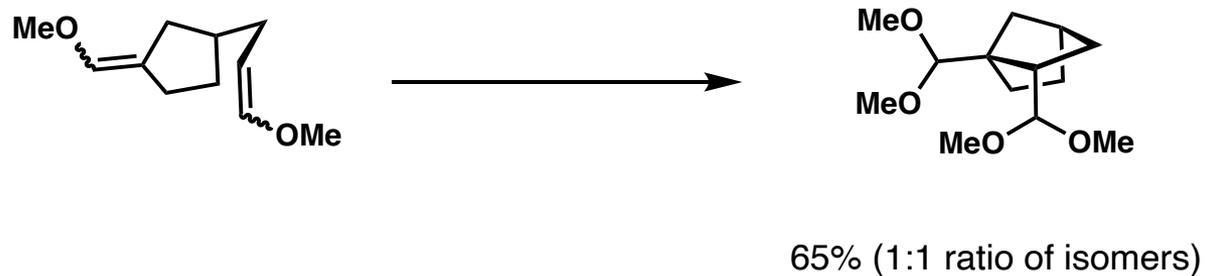
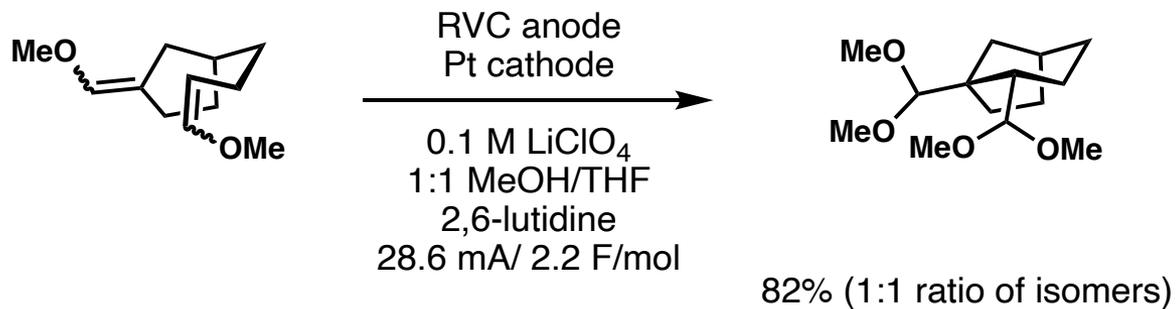


- Electrophilic at the β -position
- via radical cations
- Open-shell, radical pathways

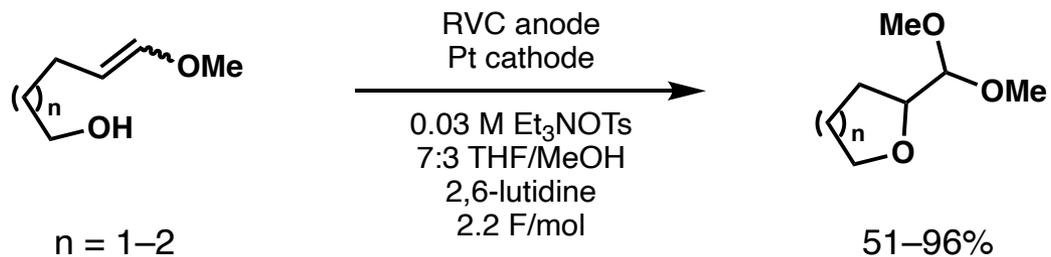
Early Examples of Enol Ether Polarity Reversal



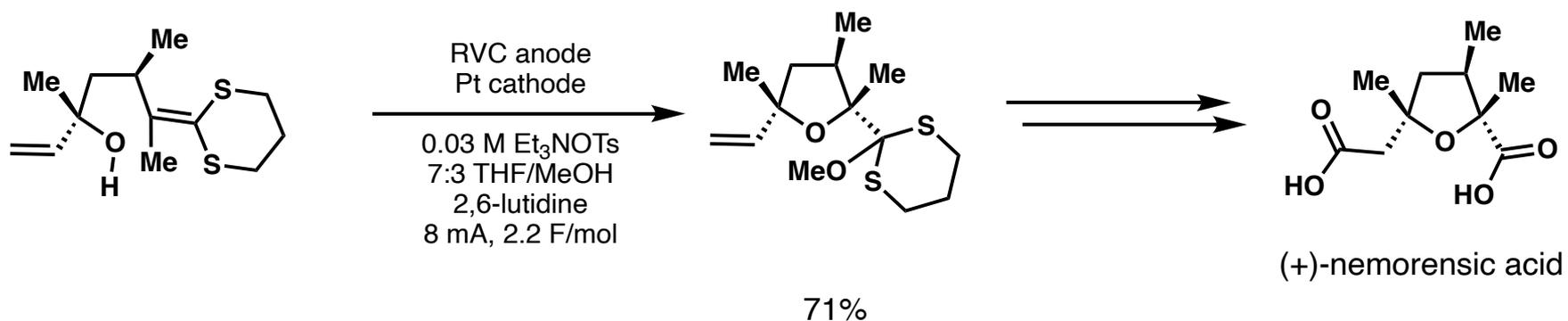
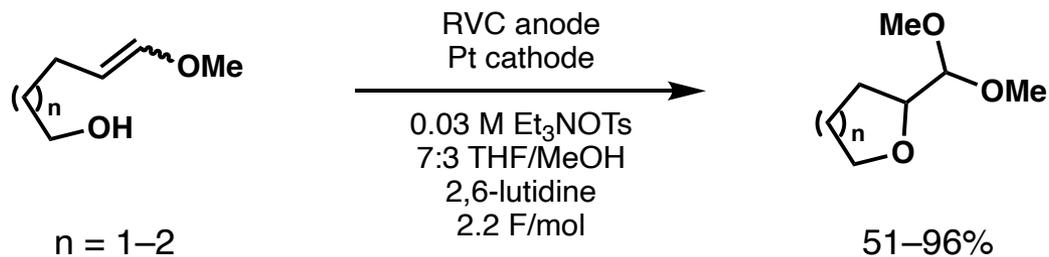
Natural Product-Inspired Cyclizations



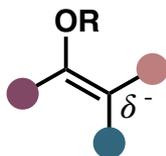
Natural Product-Inspired Cyclizations



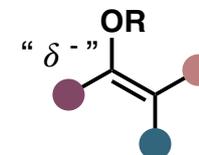
Natural Product-Inspired Cyclizations



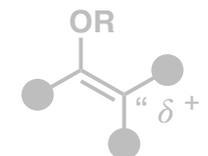
Reversing Enol Ether Polarity



- Nucleophilic at the β -position
- Electrophilic at the α -position
- Closed-shell, polar pathways

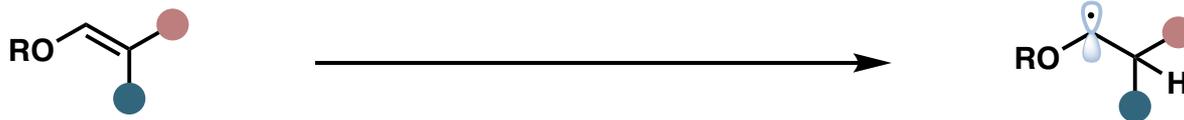


- Nucleophilic at the α -position
- via α -oxy radicals
- Open-shell, radical pathways



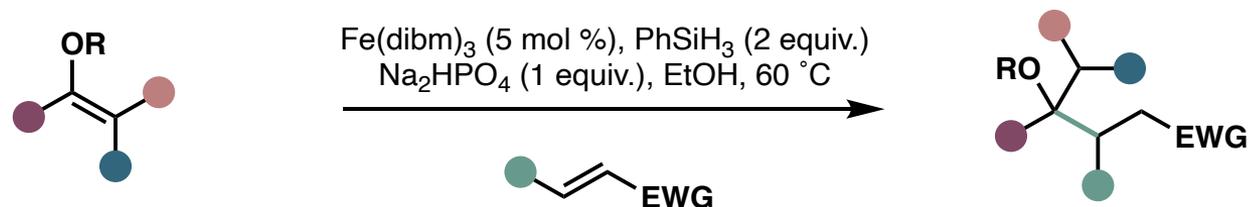
- Electrophilic at the β -position
- via radical cations
- Open-shell, radical pathways

Polarity Reversal via α -Oxy Radicals

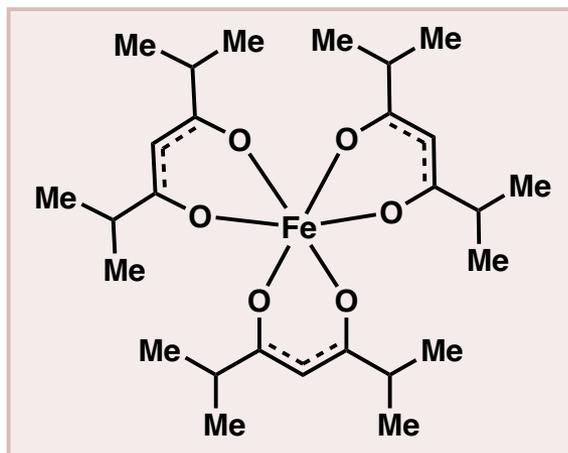
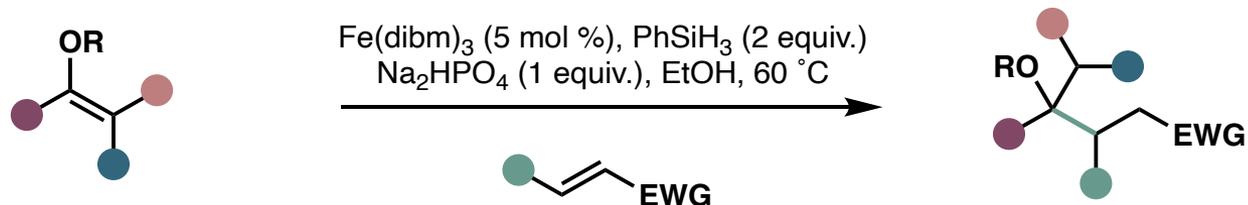


- Nucleophilic radical
- HAT/SET pathways
- New modes of reactivity

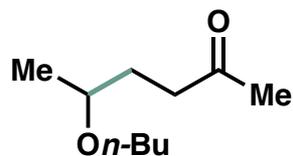
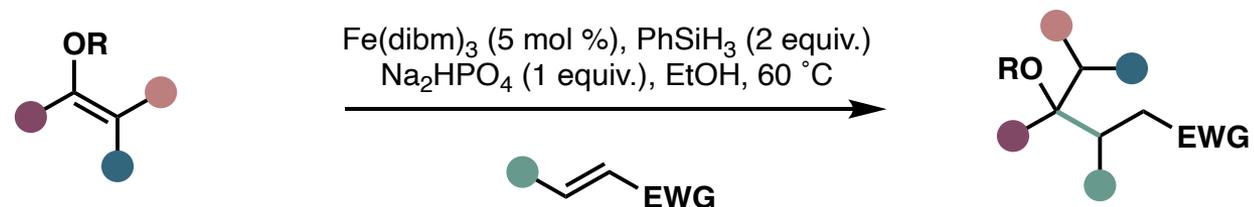
Polarity Reversal via α -Oxy Radicals



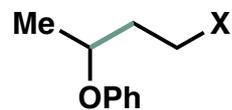
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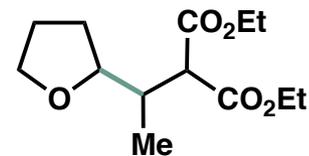
Polarity Reversal via α -Oxy Radicals



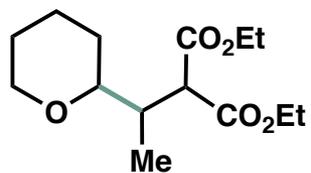
51%



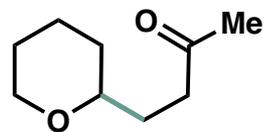
59% (X = CN)
58% (X = CO₂Me)
31% (X = C(O)Me)



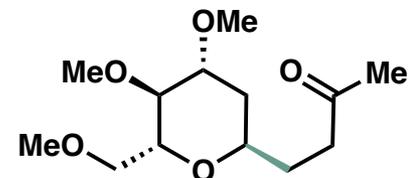
54%



76%



43%



64%, >99:1 d.r.

Polarity Reversal via α -Oxy Radicals

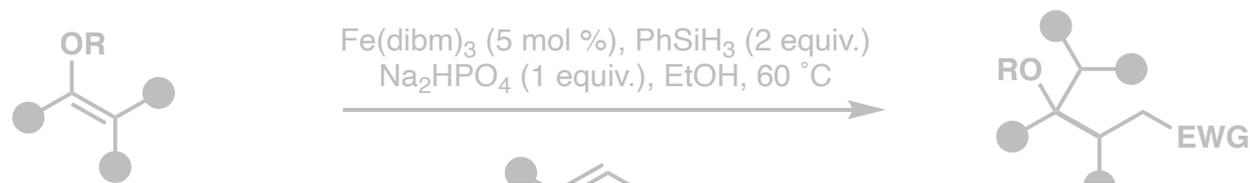
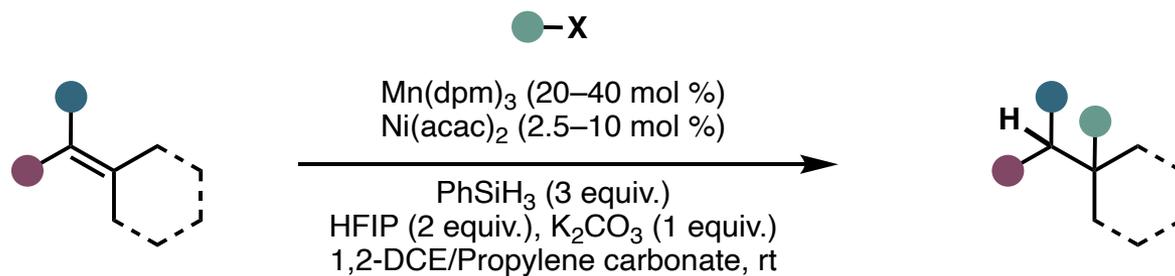


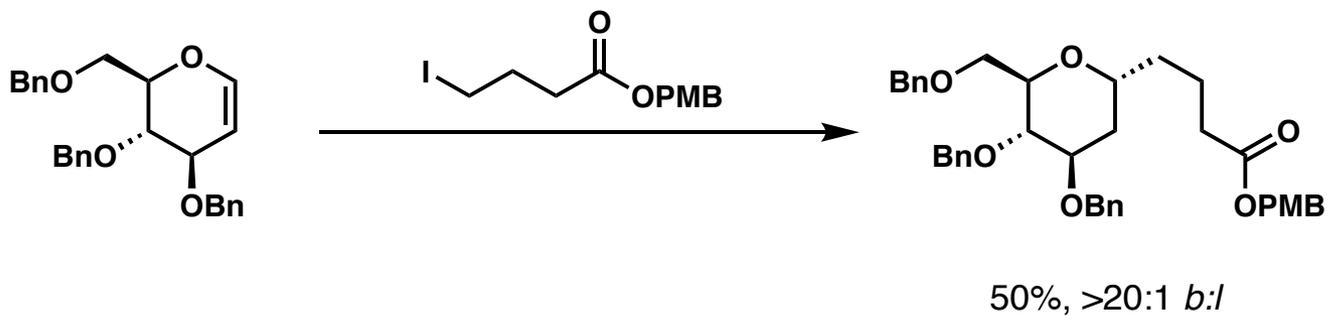
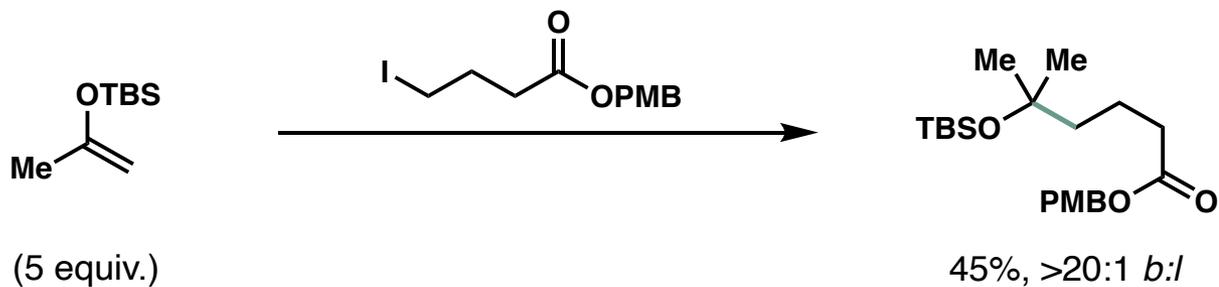
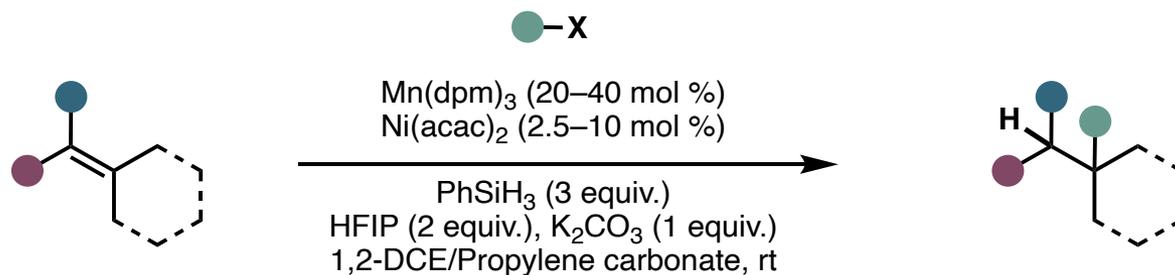
Figure S23. Reaction mixtures using solvents A–E prior to heating at 60 °C.



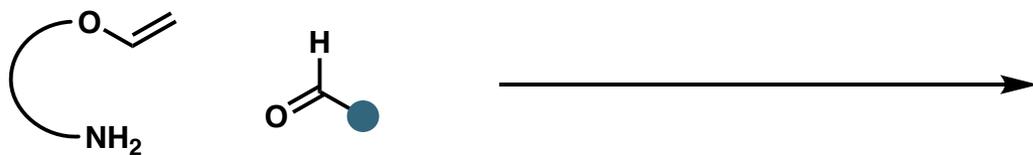
MHAT-Based Hydroalkylation of Olefins



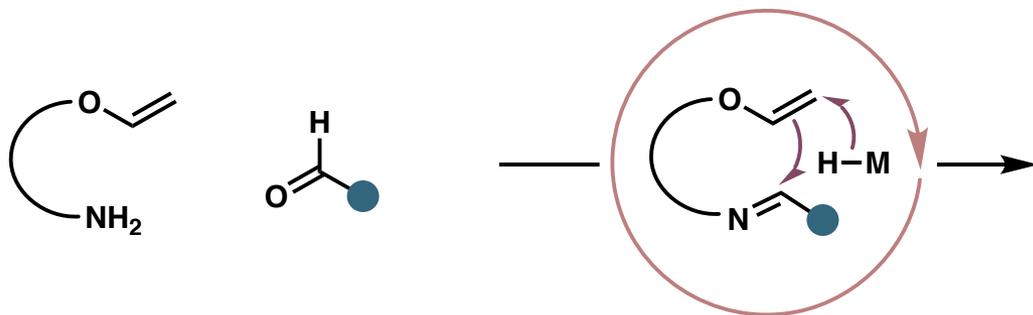
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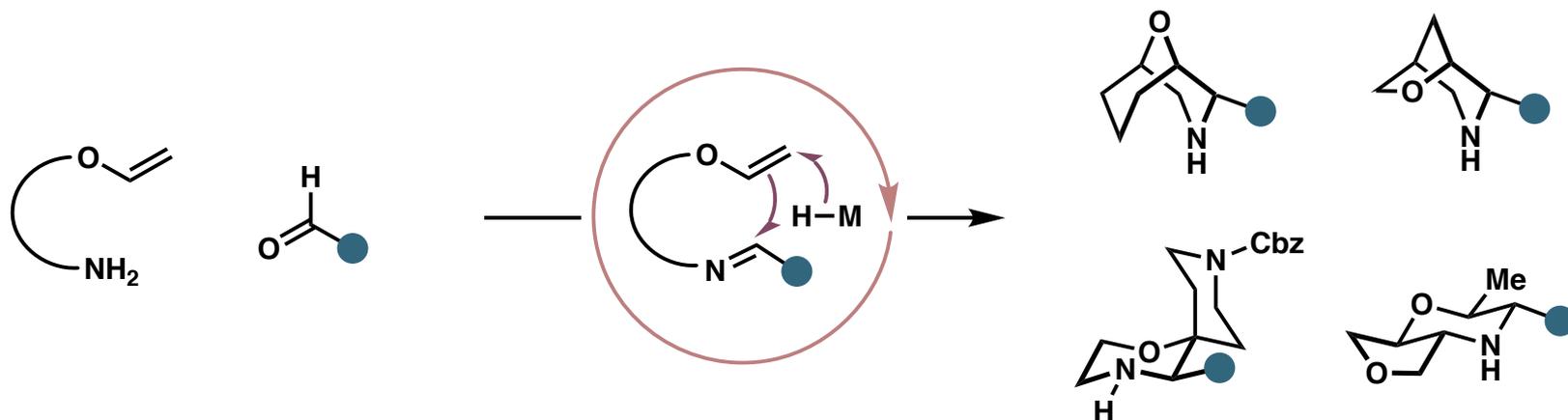
Olefin Amine (OLA) Reagents for Heterocycle Synthesis



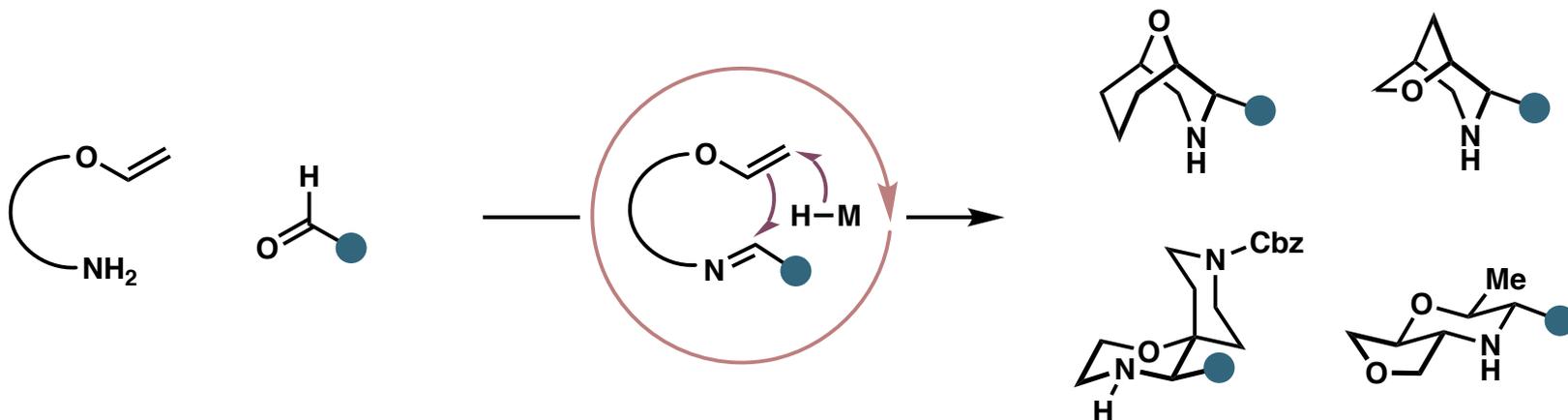
Olefin Amine (OLA) Reagents for Heterocycle Synthesis



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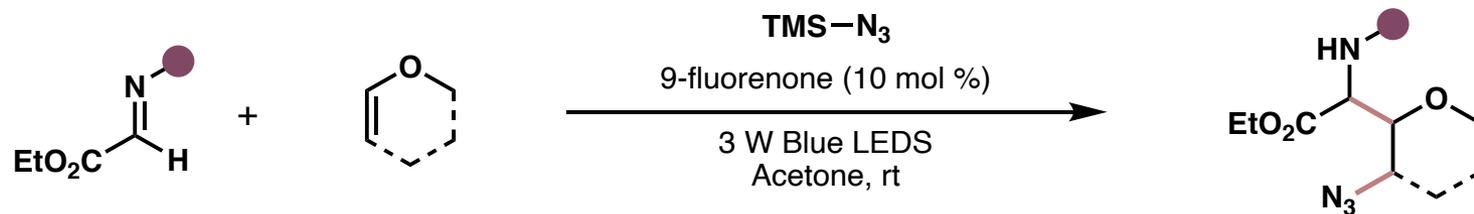


Conditions

- 1) 4Å MS, CH₂Cl₂, rt, 12 h
- 2) 5 mol % Mn(dpm)₃ PhSiH₃ (4–6 equiv.)
Air, *i*-PrOH, 60–85 °C, 24 h

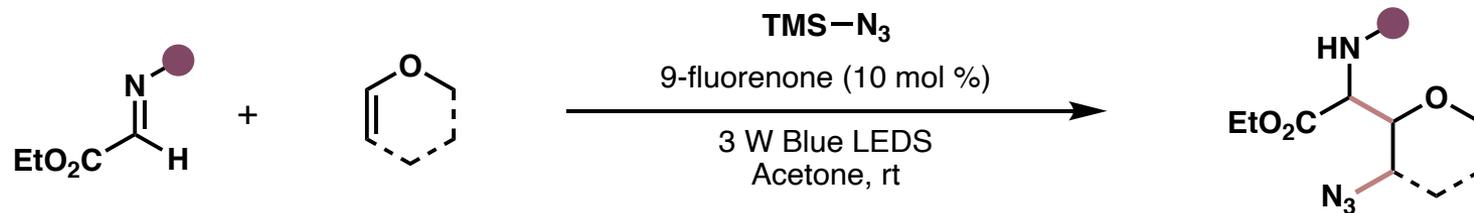
- Aryl/heteroaryl aldehydes
- 2–4 atom tether

Polarity-Reversed Addition Using Visible Light



Gong, Y. *et al.* *Org. Lett.* **2019**, *21*, 8464.

Polarity-Reversed Addition Using Visible Light

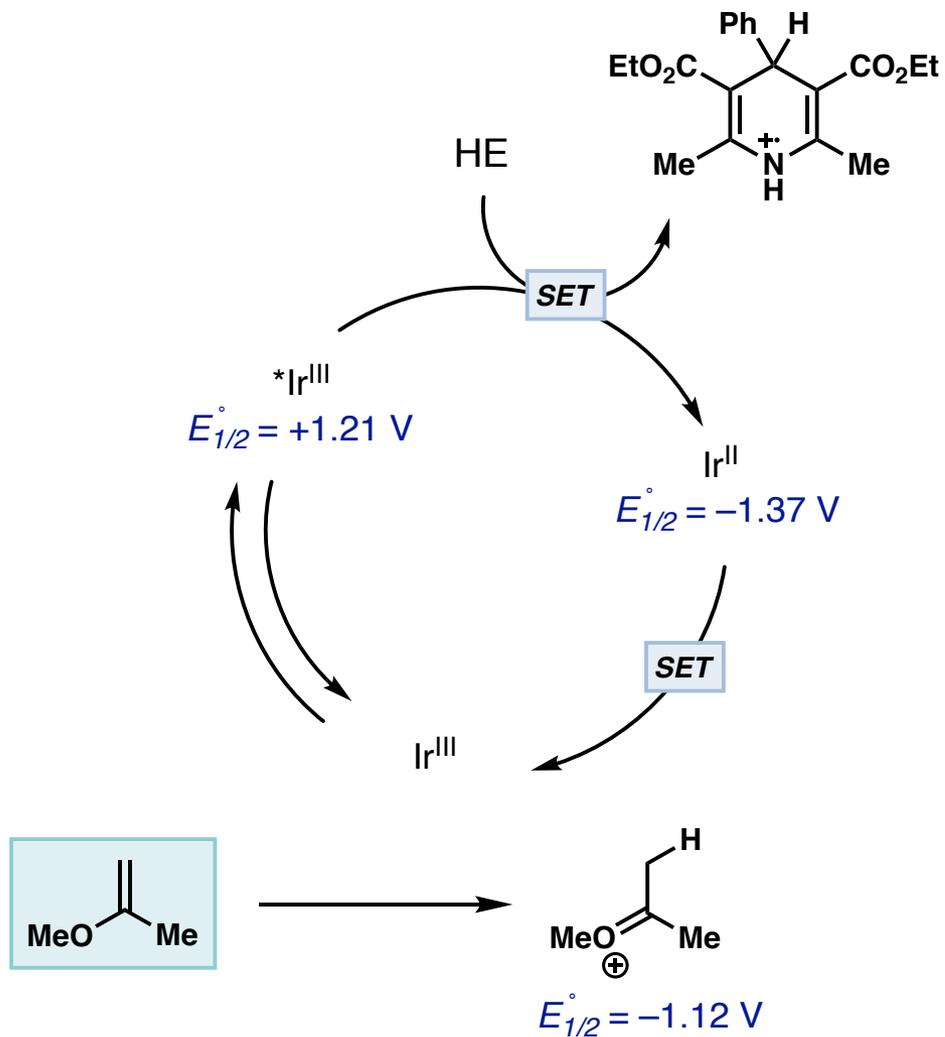


Gong, Y. *et al. Org. Lett.* **2019**, *21*, 8464.

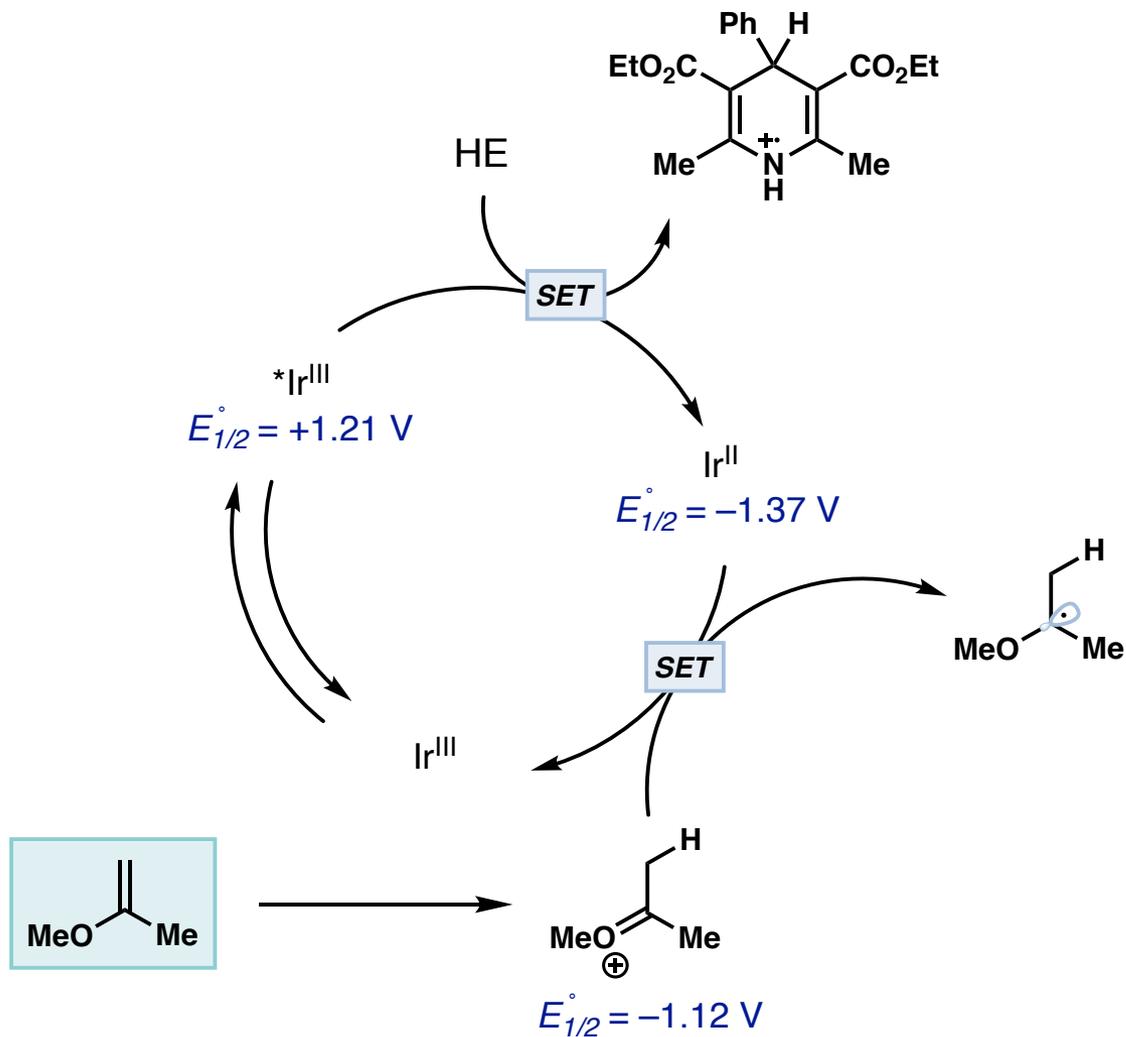


- 1,1-disubstituted alkenes
- Mostly Giese-type additions
- Alkyl and benzyl enol ethers

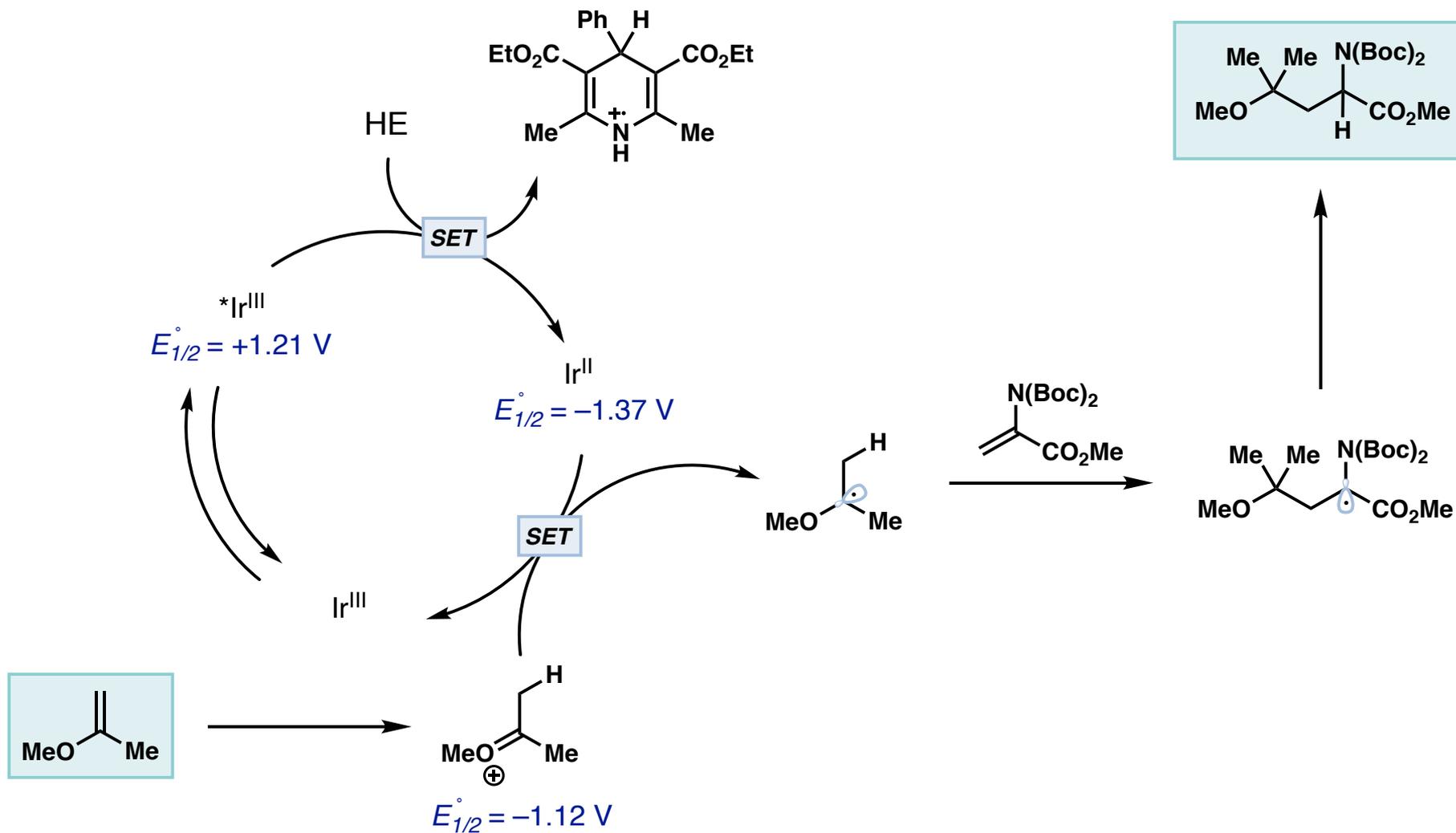
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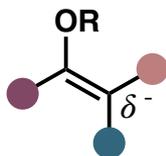
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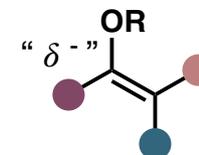
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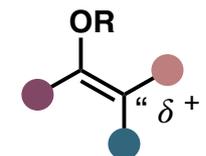
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- Electrophilic at the β -position
- via radical cations
- Open-shell, radical pathways