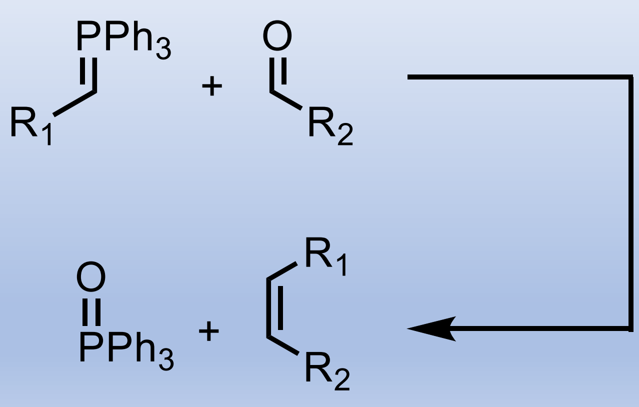
Carbonyl-Olefin Metathesis

Vincent Kassel

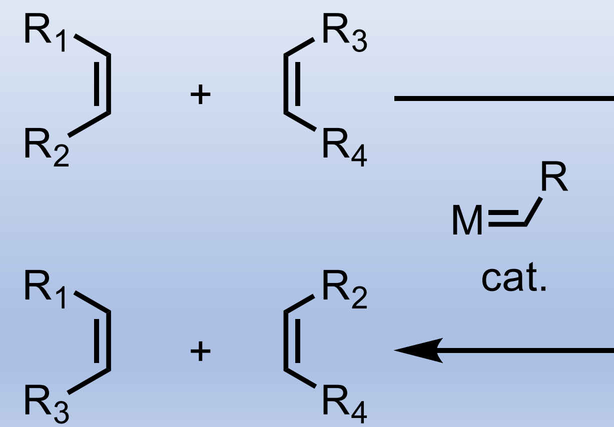
4-20-2021

Double Bond Metathesis in Organic Synthesis

Wittig Olefination:

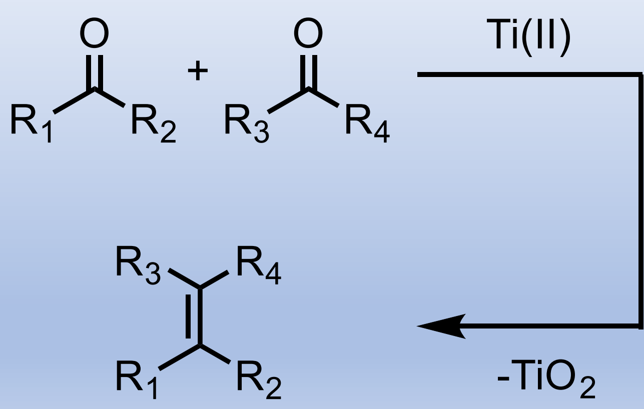


Olefin-Olefin Metathesis:

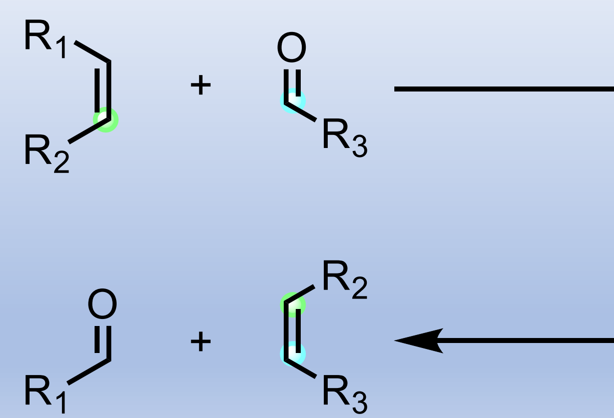


McMurry Coupling:

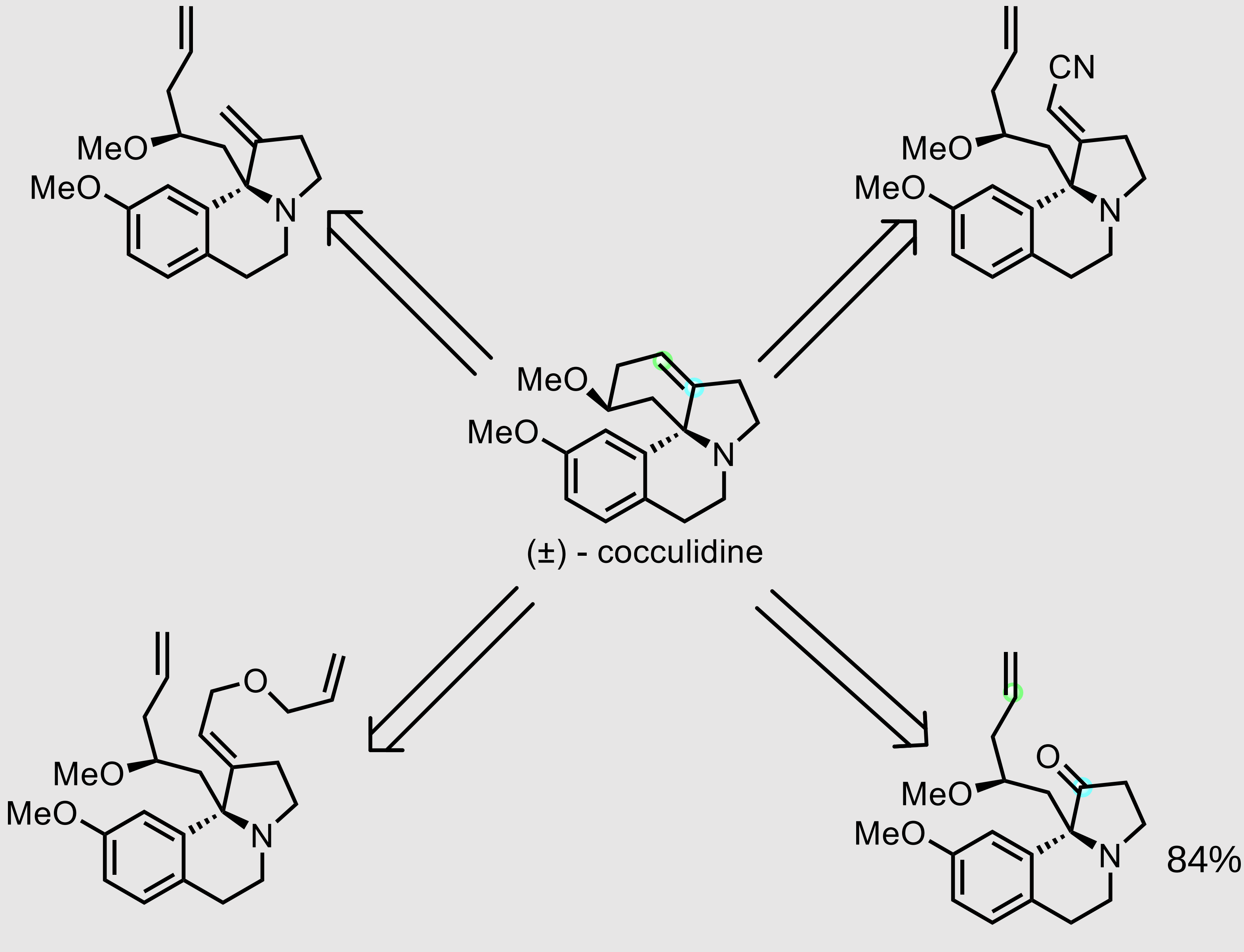
(not formally metathesis)



Carbonyl-Olefin Metathesis:

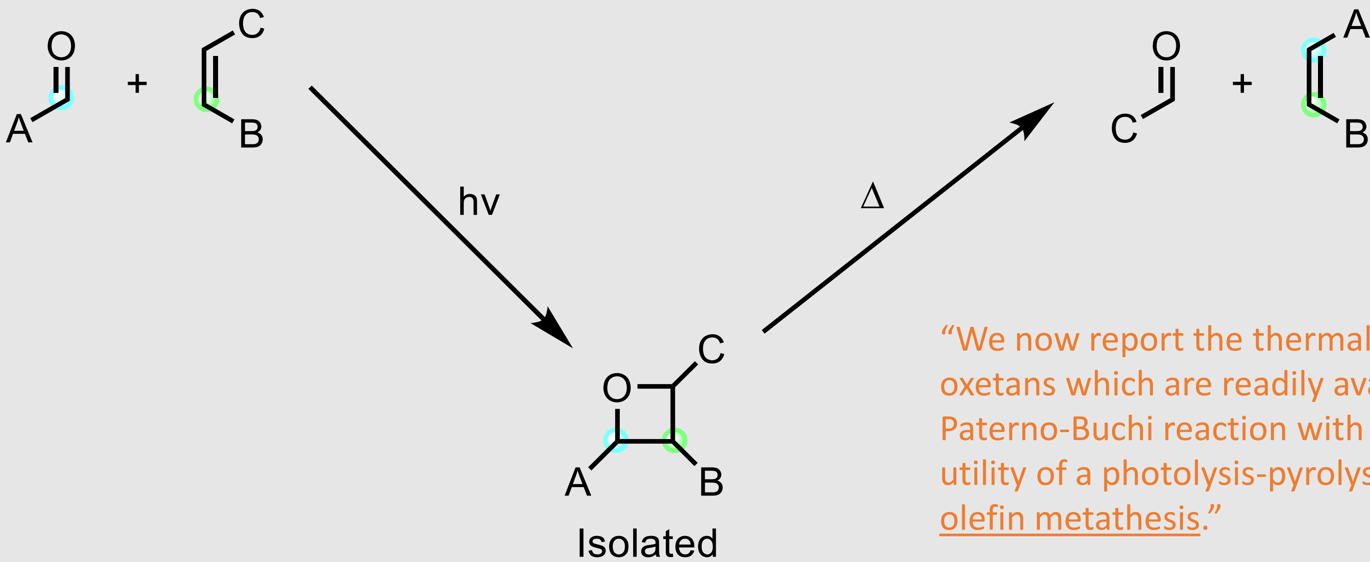


New Disconnections In The Chemist's Toolbox



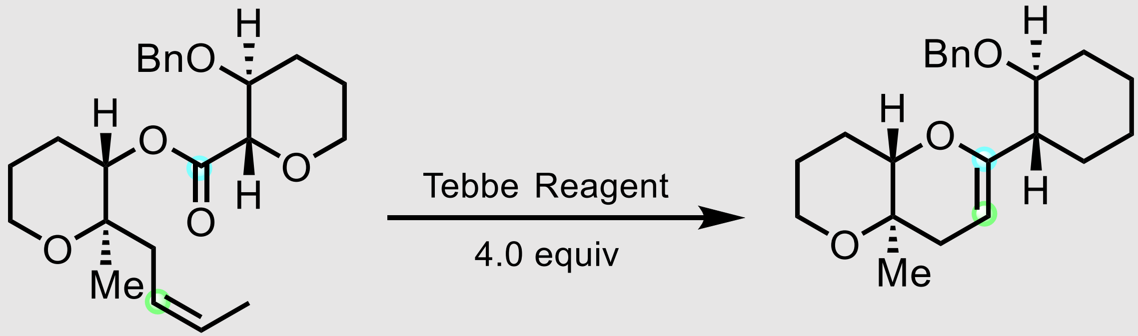
Sarpong, R. et al. *Angew. Chem. Int. Ed.* **2013**, 11129-11133.

"Formal" vs "Actual" Carbonyl-Olefin Metathesis



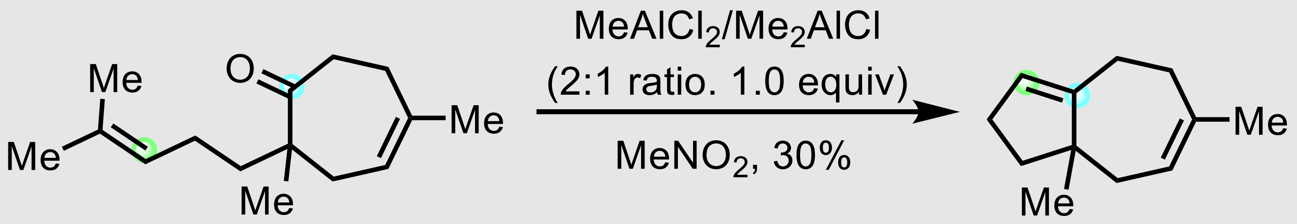
"We now report the thermal transformations of some oxetans which are readily available *via* the photochemical Paterno-Buchi reaction with emphasis on the synthetic utility of a photolysis-pyrolysis sequence involving carbonyl-olefin metathesis."

Jones II, G. et al. *J. Chem. Soc. Chem. Commun.* **1973**, 374–375.



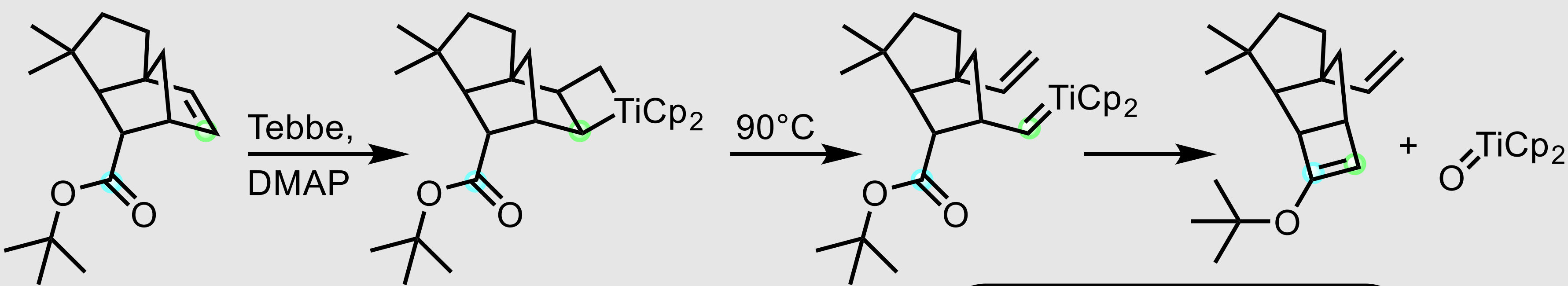
Nicolaou, K.C. et al. *J. Am. Chem. Soc.* **1996**, *118, 10335-10336.*

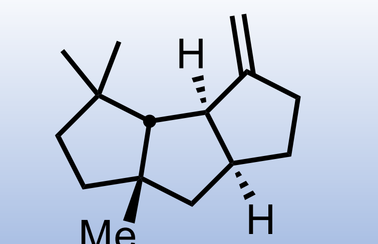
Early Literature Examples



Snider, B.B. et al. *J. Org. Chem.* **1984**, *49*, 3988-3994.

"The formation of the unusual metathesis product presumably results from stepwise cycloaddition to give an oxetane which then opens in the other direction and loses acetone"





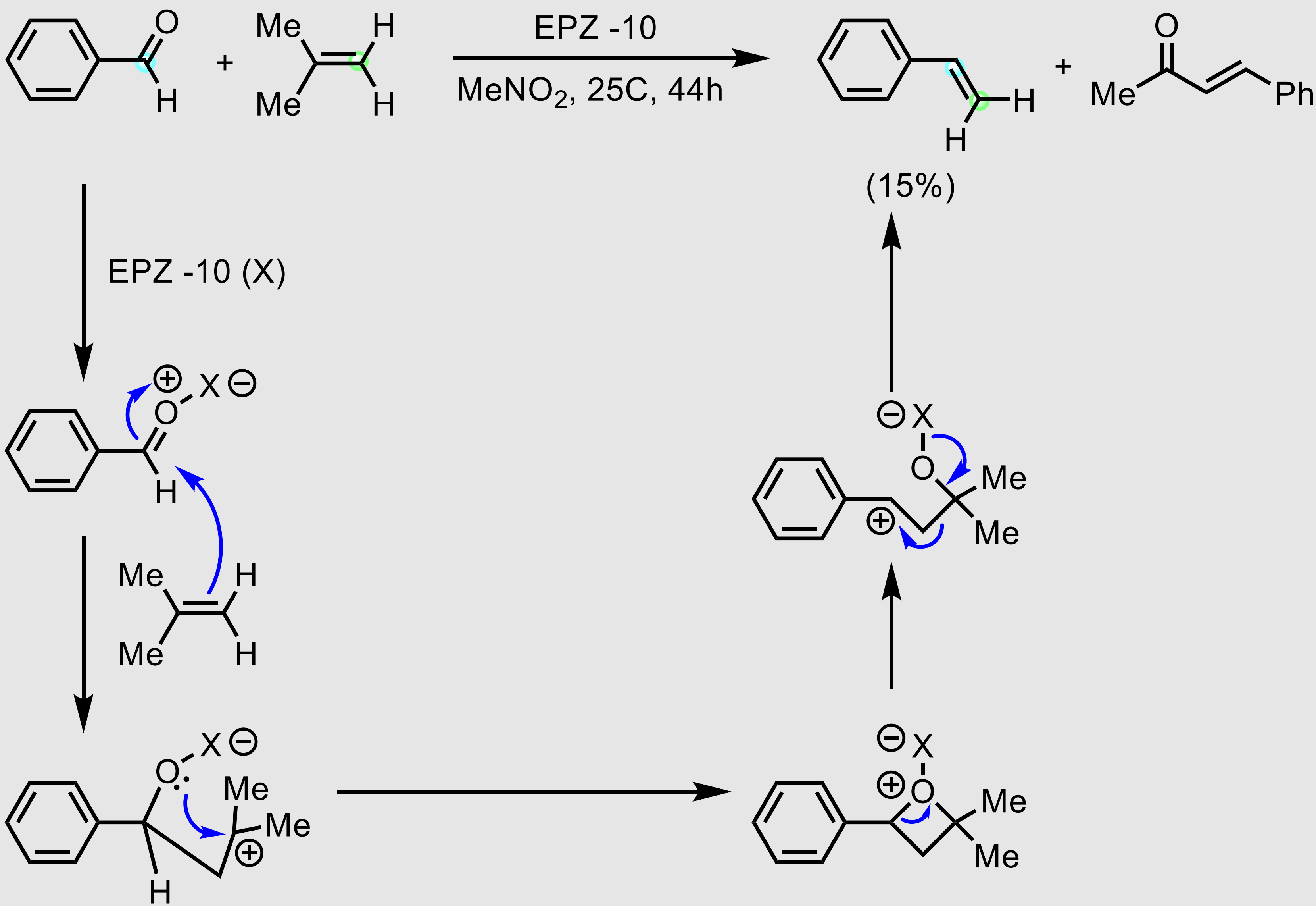
$\Delta^{(9,12)}$ – capnellene

Grubbs R. H. et al. *J. Am. Chem. Soc.* **1986**, *108,* 855-856.

Grubbs R. H. et al. *J. Org. Chem.* **1990**, *55,* 843-862.

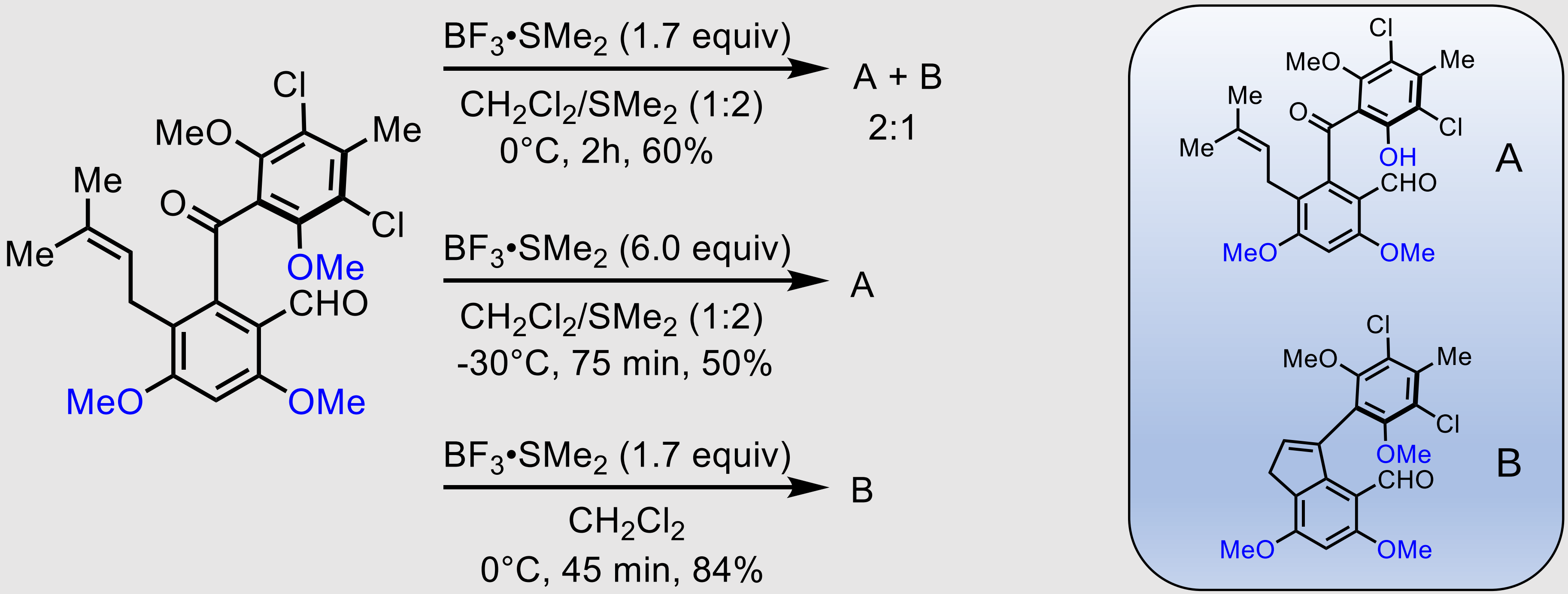
Acid-Catalyzed Olefination of Benzaldehyde

Propose a Mechanism for this Transformation:



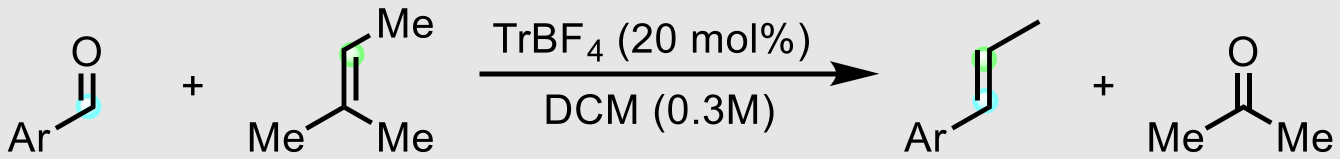
Bickelhaupt, F. et al. *Angew. Chem. Int. Ed.* **1994**, *33,* 1611-1612.

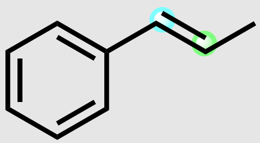
Novel Observation in the Synthesis of Pestalone



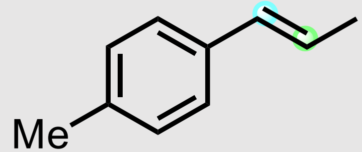
Schmalz, H-G. et al. *Angew. Chem. Int. Ed.* **2010**, *49*, 7588-7591.

Trans-Selective Carbocation-Catalyzed Olefination of Aldehydes

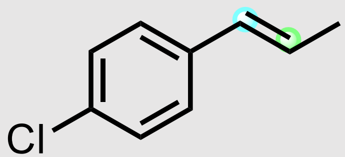




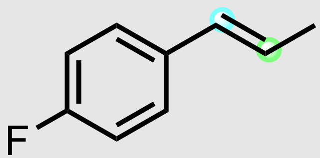
25°C, 30h, 68%



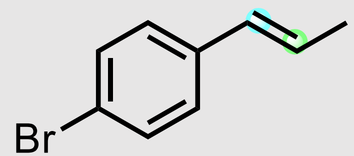
-78°C, 100h, 74%



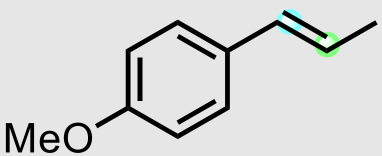
25°C, 30h, 54%



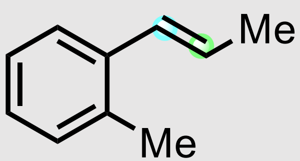
25°C, 30h, 59%



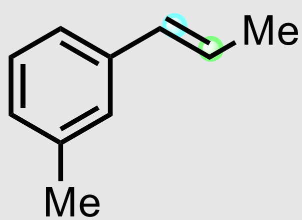
25°C, 30h, 55%



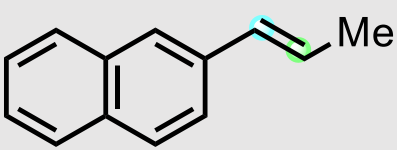
-78°C, 30h, 15%



25°C, 30h, 85%



25°C, 30h, 83%



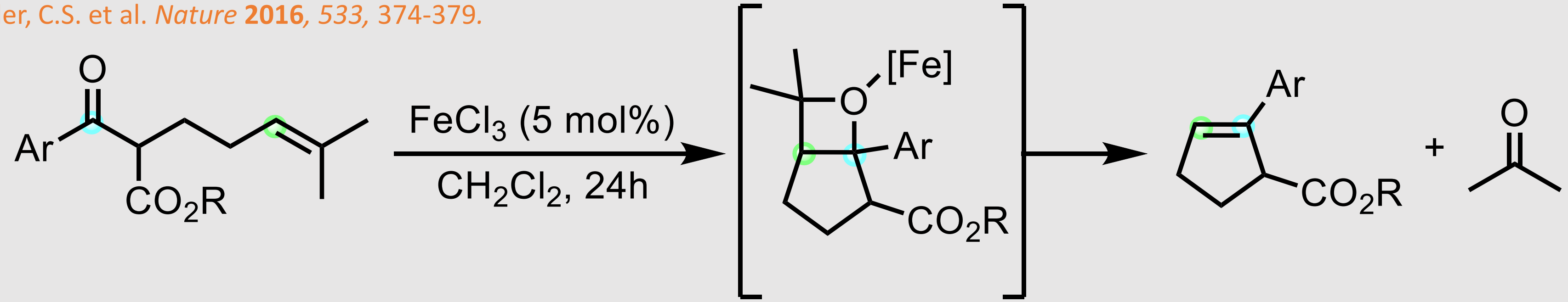
25°C, 30h, 60%

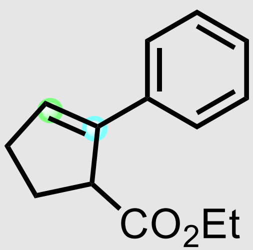
NMR Yields

Franzen, J. et al. *Eur. J. Org. Chem.* **2015**, 1834-1839.

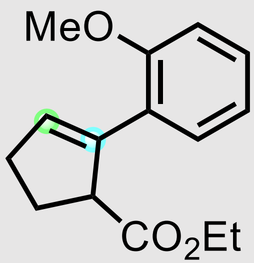
Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)

Shindler, C.S. et al. *Nature* **2016**, *533,* 374-379.

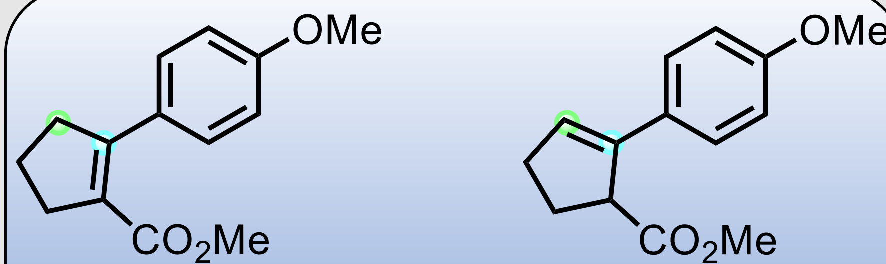




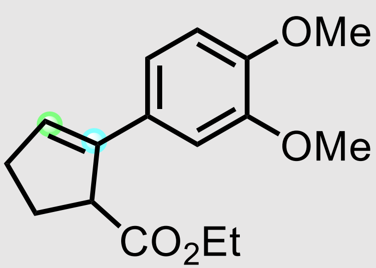
99%



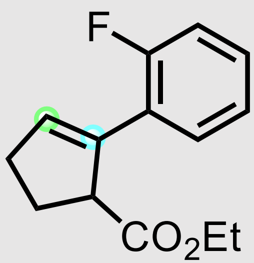
99%



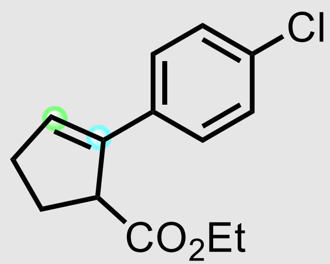
1:2 Mixture, 99%



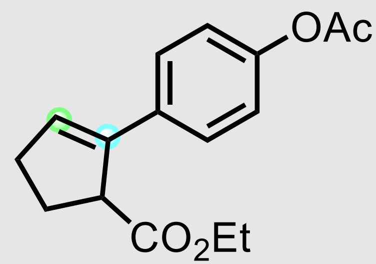
66%



99%



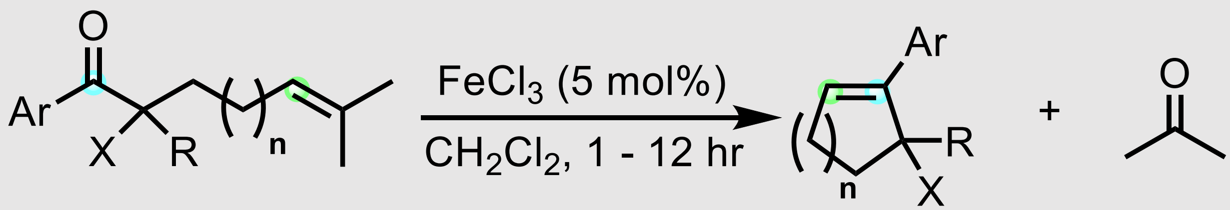
55% r.t.; 99% reflux

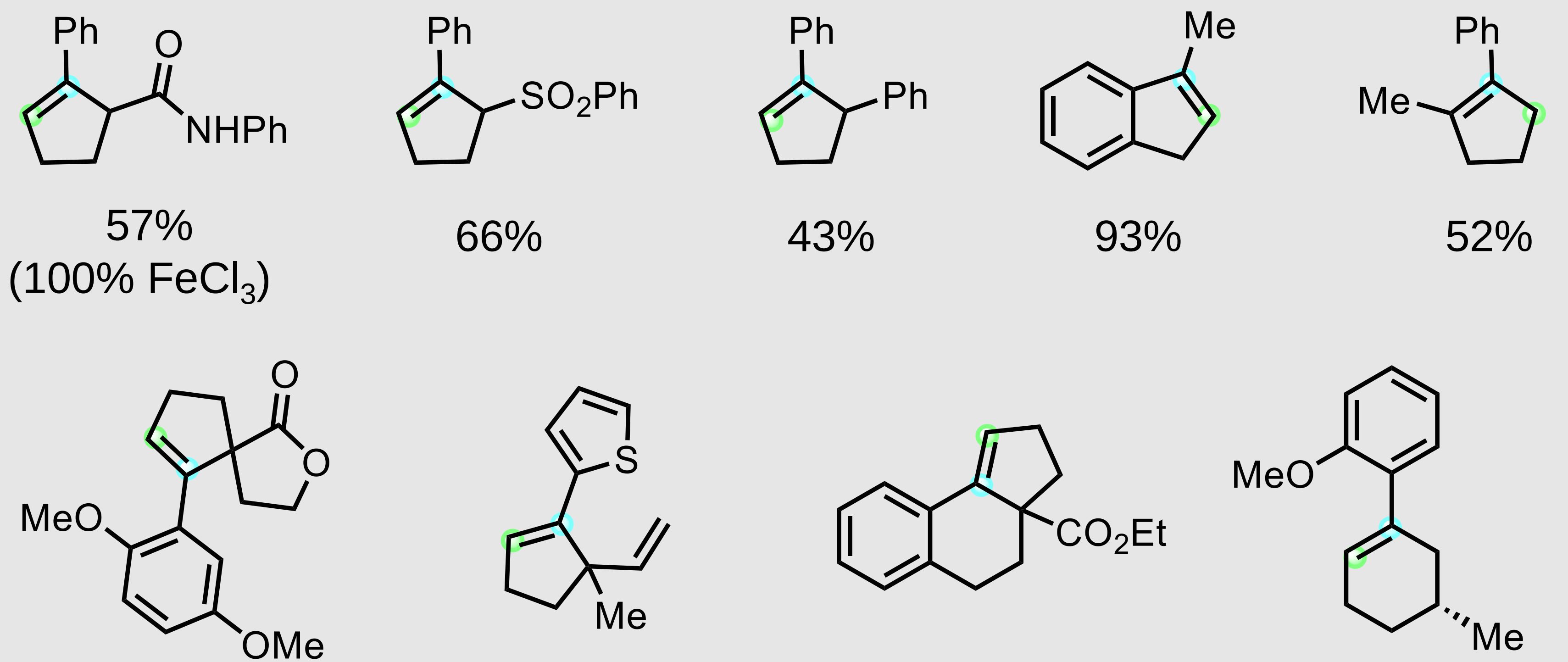


57%

Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)

Shindler, C.S. et al. *Nature* **2016**, *533*, 374-379.



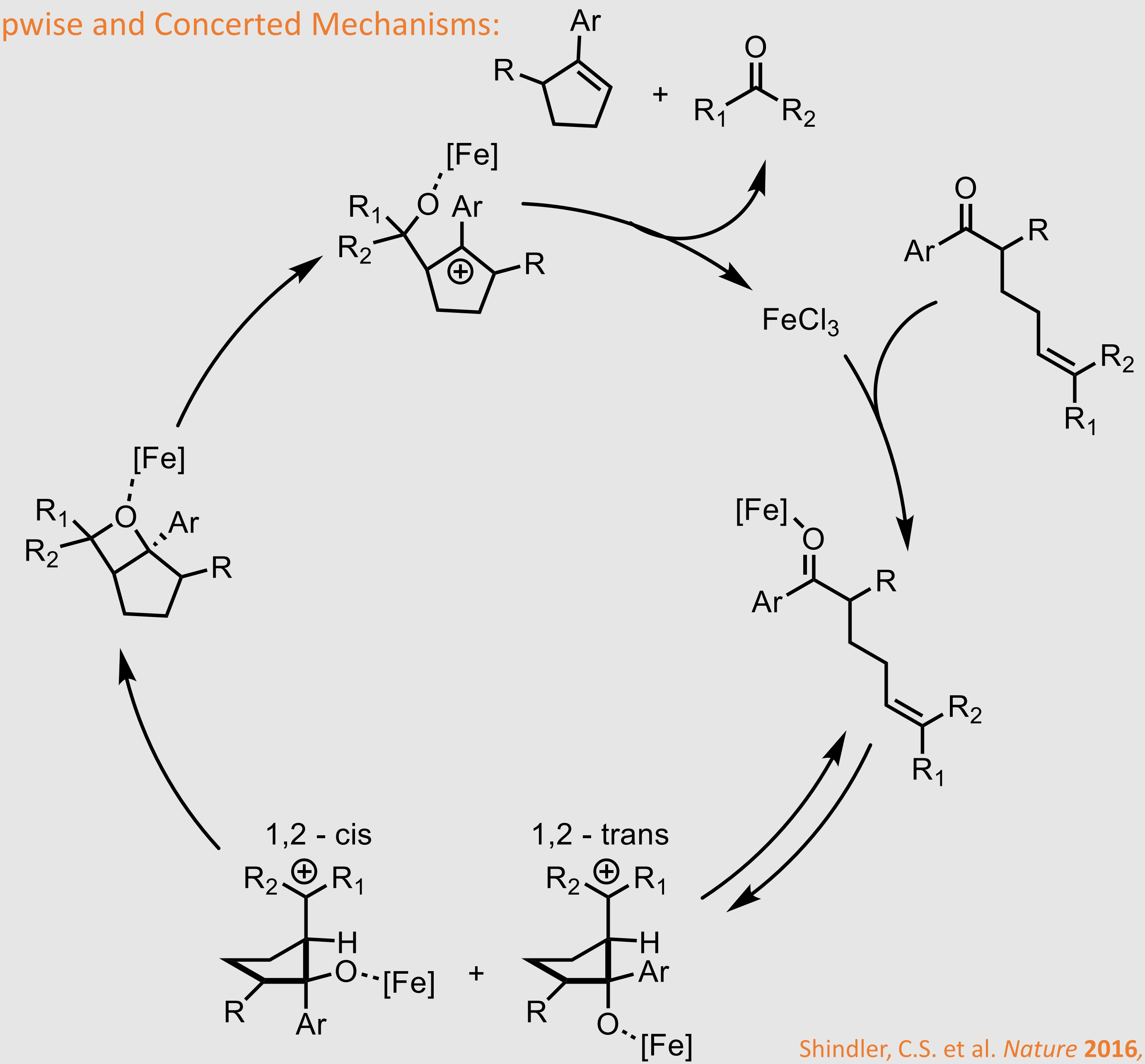


57% (100% $FeCl_3$) | 66% | 43% | 93% | 52%

68% | 76% | 85% | 71%

Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)

Proposed Stepwise and Concerted Mechanisms:



Shindler, C.S. et al. *Nature* **2016**, *533*, 374-379.

Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)

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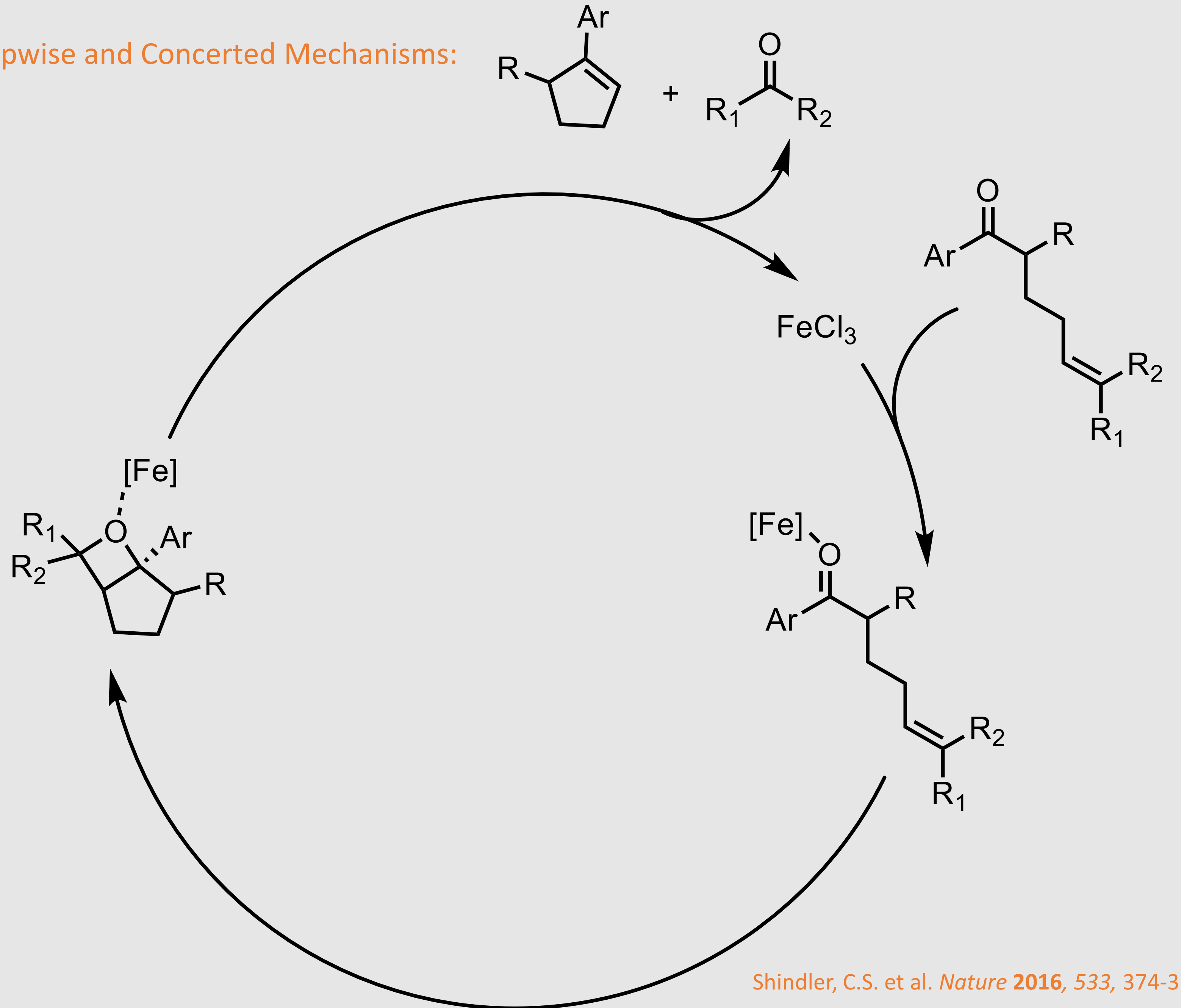
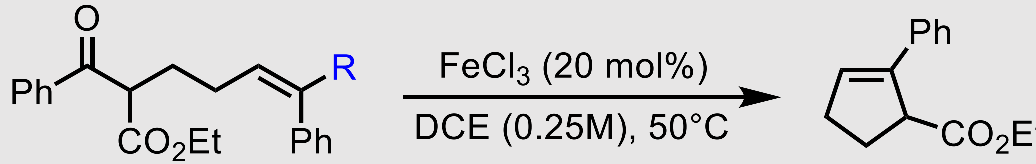


Shindler, C.S. et al. *Nature* **2016**, *533*, 374-379.

Further Mechanistic Investigations

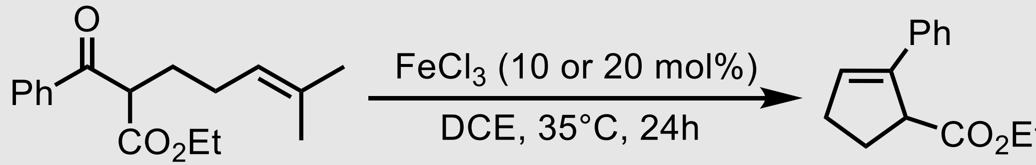
Takeaway Observations:

- Success of metathesis is related to Lewis acidity of metal catalyst, Bronsted acids not operative.
- EPR rules out SET events by iron and suggests binding at carbonyl(s).
- Saturation kinetics observed for iron at 10 and 20 mol% FeCl3 (i.e. turnover-limiting step is impacted by [FeCl3]).
- The reaction displays an inverse β-SKIE (oxetane formation rate-limiting).
- The π-system of the aryl group facilitates delocalization of the HOMO, conserving orbital symmetry.
- Oxetane fragmentation found to depend on pendant olefin identity.

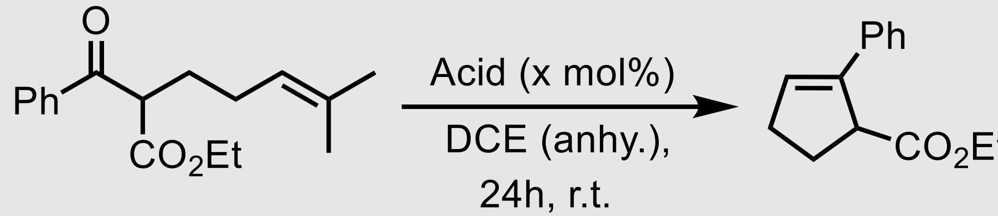


$R=CH_3$
$R=CD_3$

K_H/K_D= 0.65± 0.07
sp^2 to sp^3



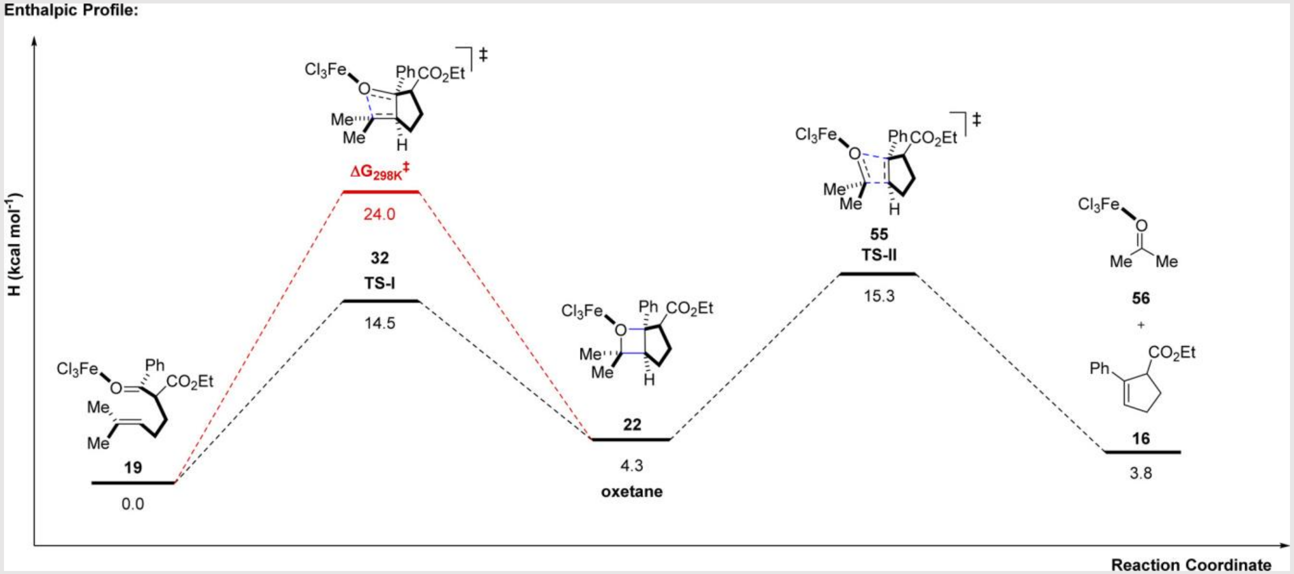
Rate order of $FeCl_3$= 1.1± 0.2

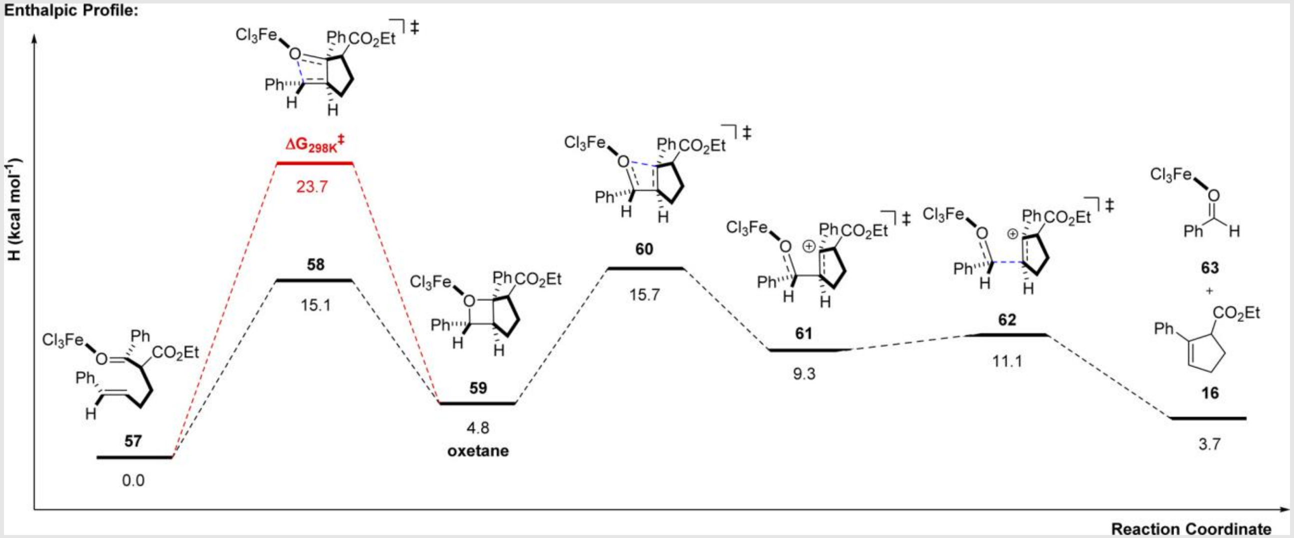


10 mol% $FeCl_3$ (97%)	99%
10 mol% Anhy. $FeCl_3$ (98%)	99%
5 mol% HCl in DCE	0%
100 mol% HCl in DCE	0%

Shindler, C.S. et al. *J. Am. Chem. Soc.* **2017**, *139, 10832*-10842.

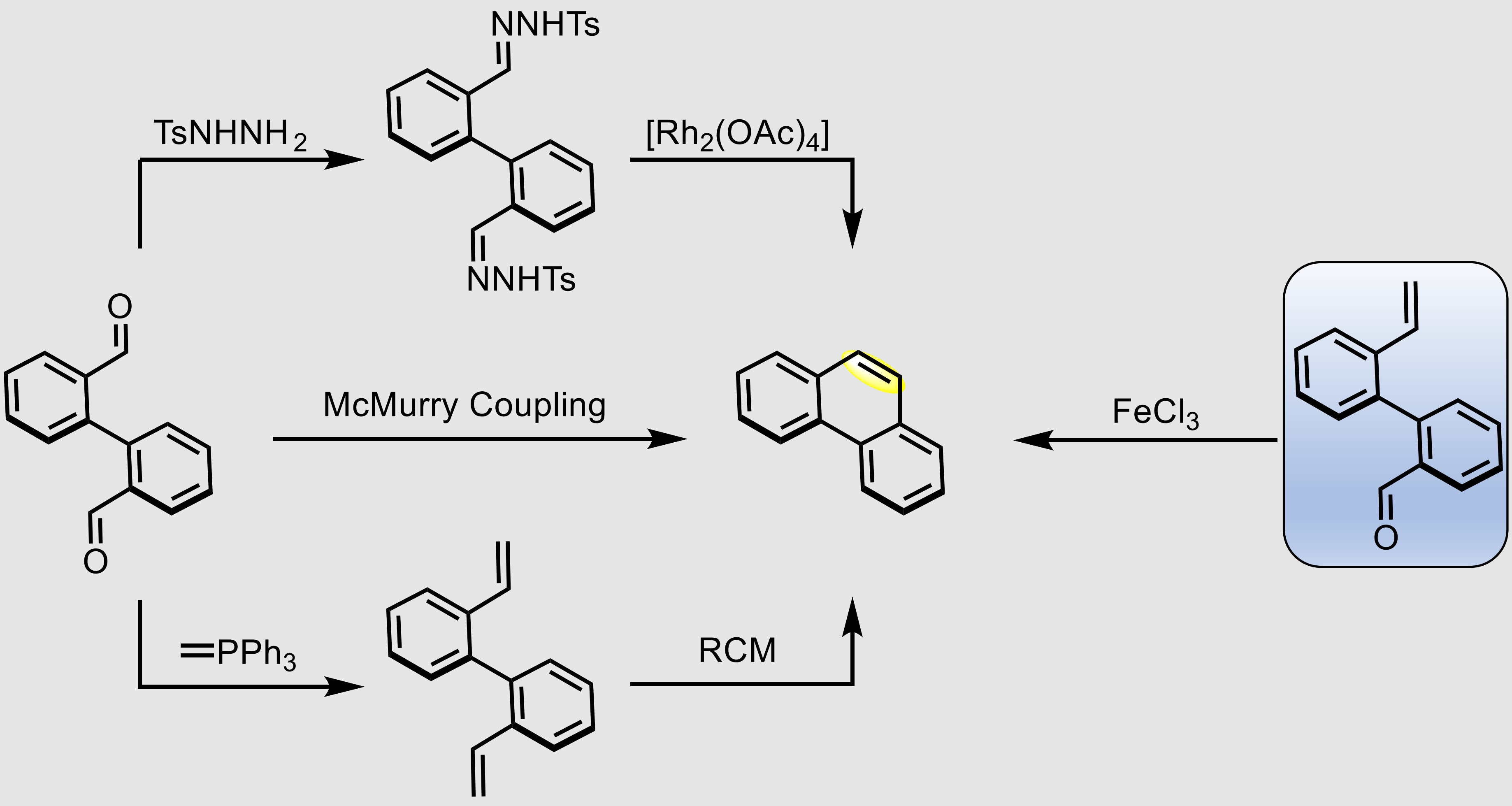
Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)





Shindler, C.S. et al. *J. Am. Chem. Soc.* **2017**, *139, 10832*-10842.

Fe(III)-Mediated Access to Polycyclic Aromatic Compounds

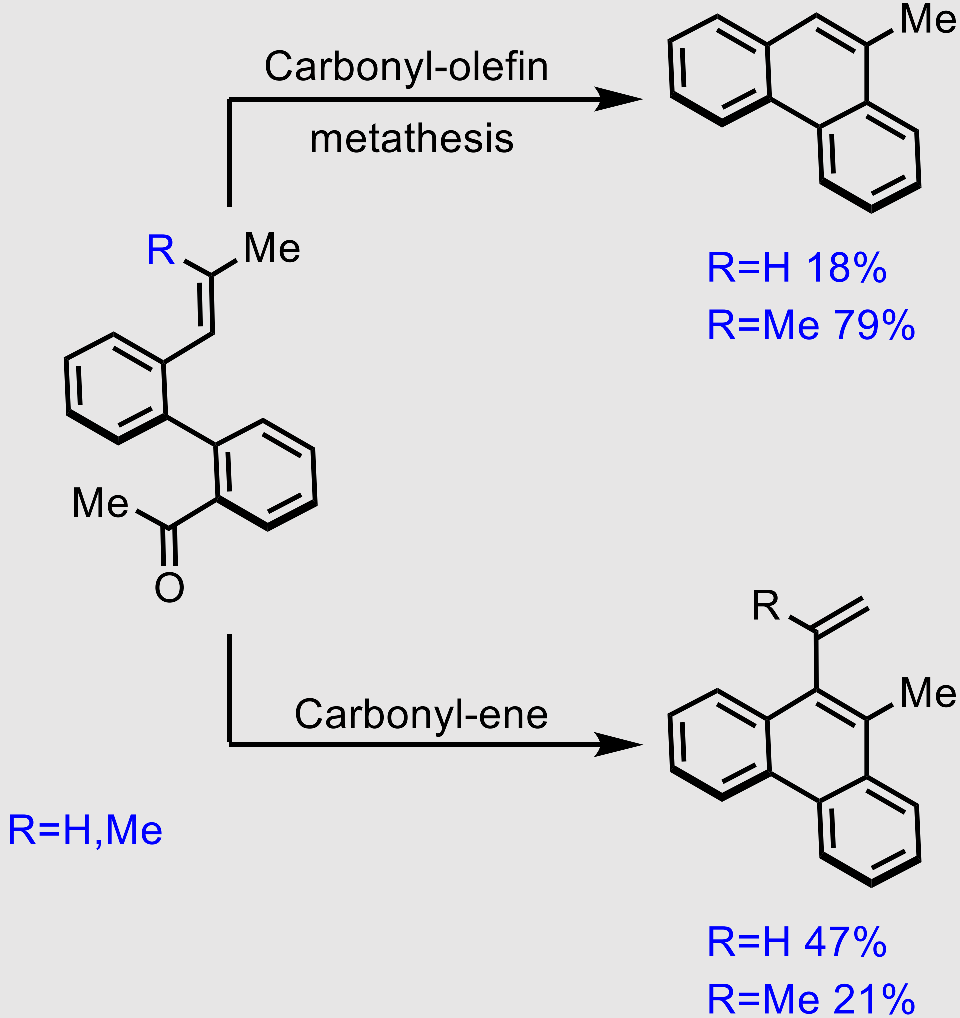


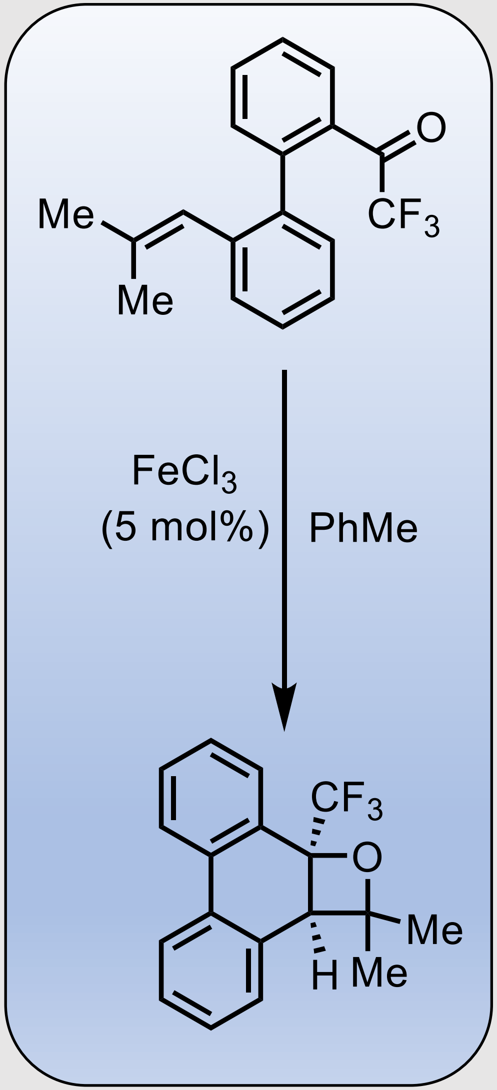
Shindler, C.S. et al. *J. Am. Chem. Soc.* **2017**, *139*, 2960-2963.

Salient Observations

Non-styrenyl olefins compete with carbonyl-ene.

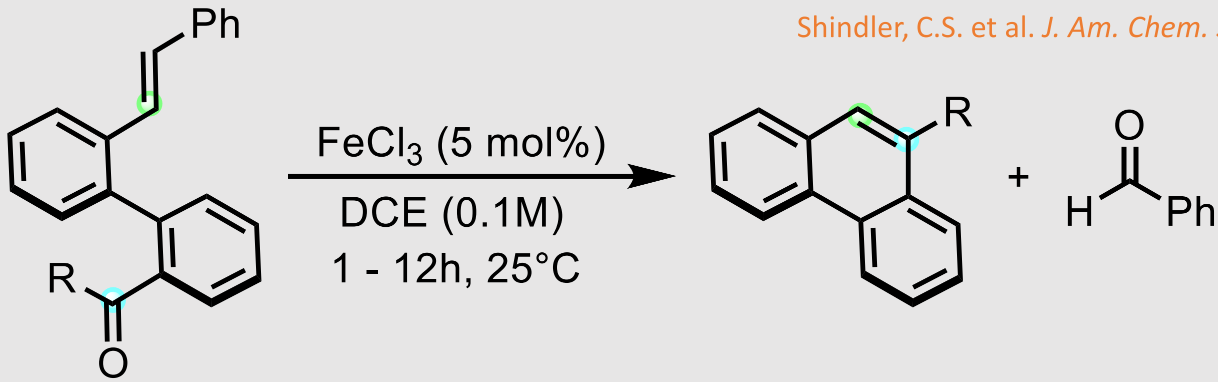
Prenyl previously preferred, aldehydes now work.



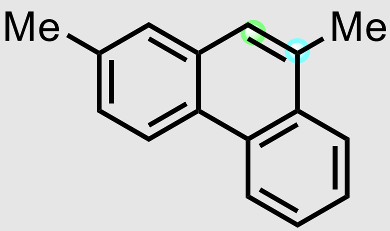


Substrate Examples

Shindler, C.S. et al. *J. Am. Chem. Soc.* **2017**, *139*, 2960-2963.

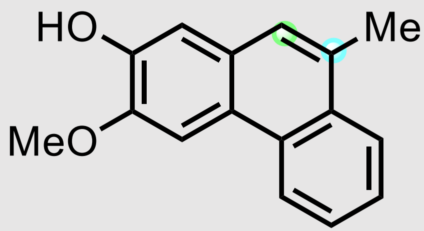


Phenanthrene



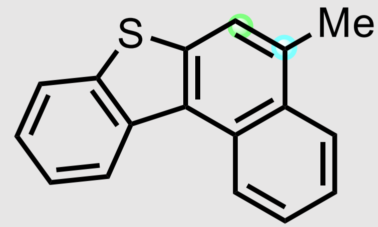
89%

Phenanthrene



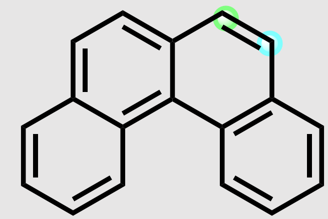
78%

Benzo-
thiophene



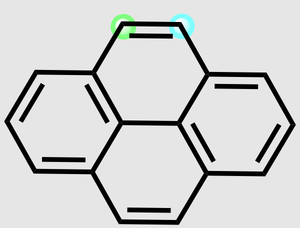
62%*

Benzo-
phenanthrene



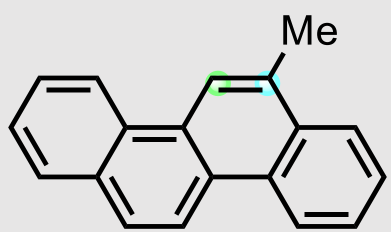
89%

Pyrene



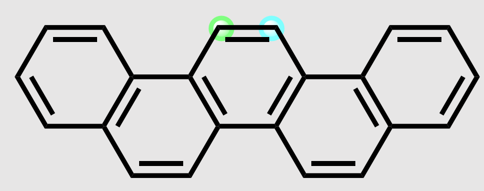
70%

Methyl-
chrysene



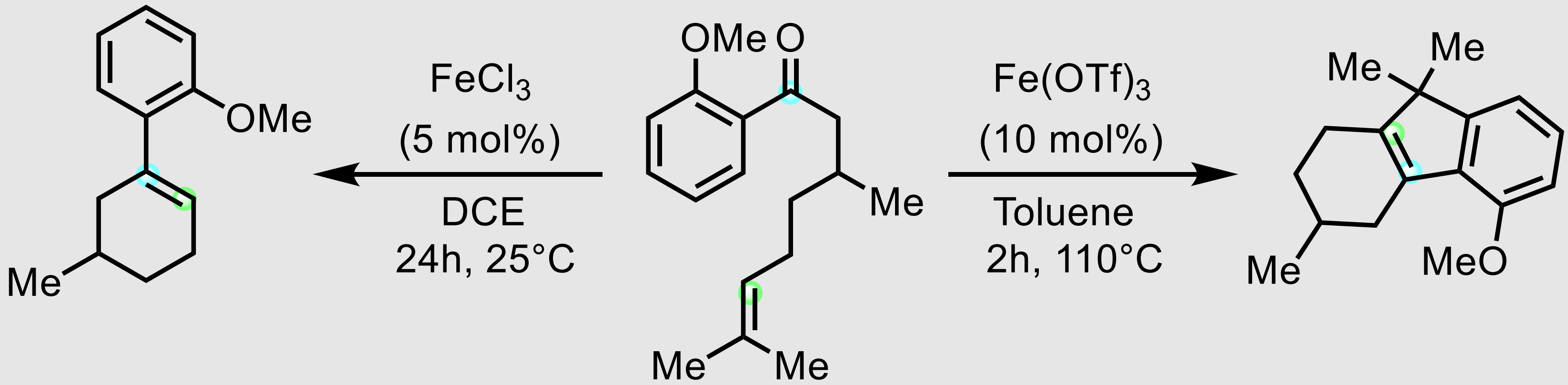
80%

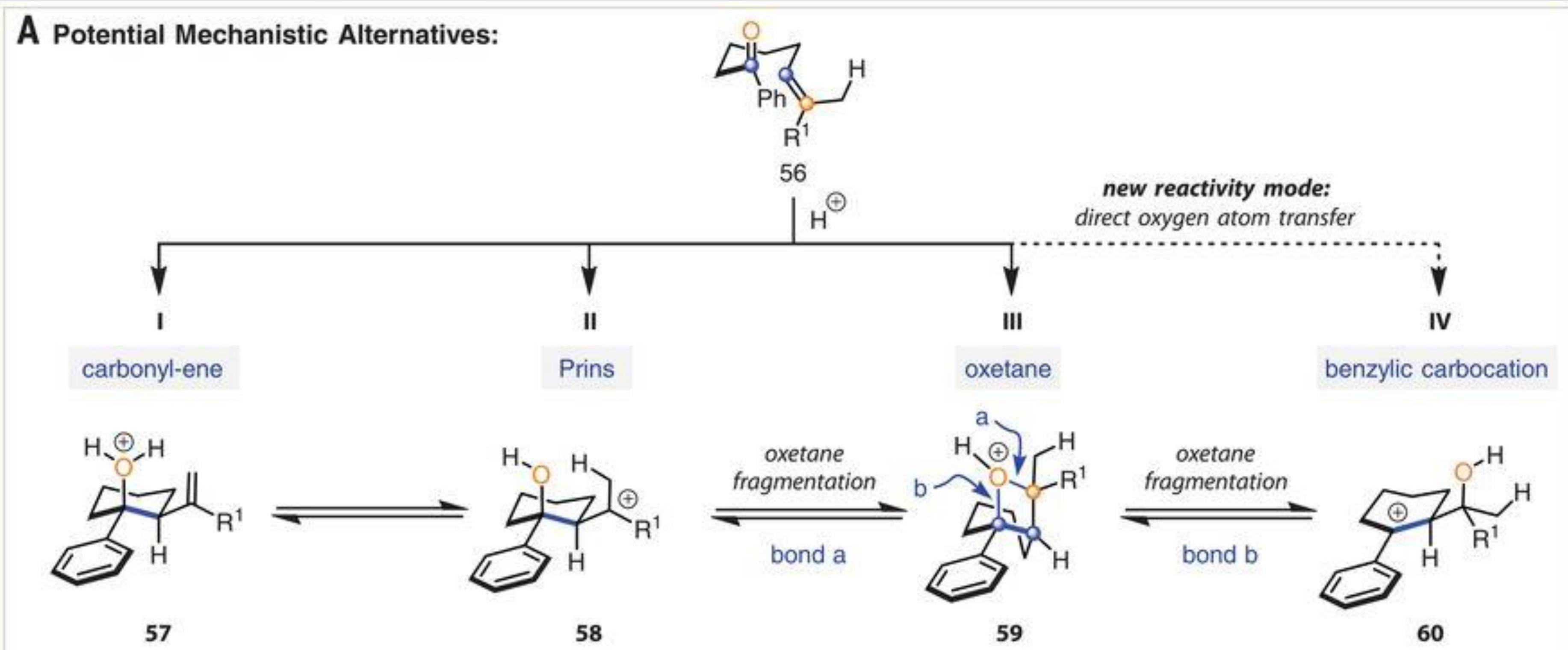
Picene



53%

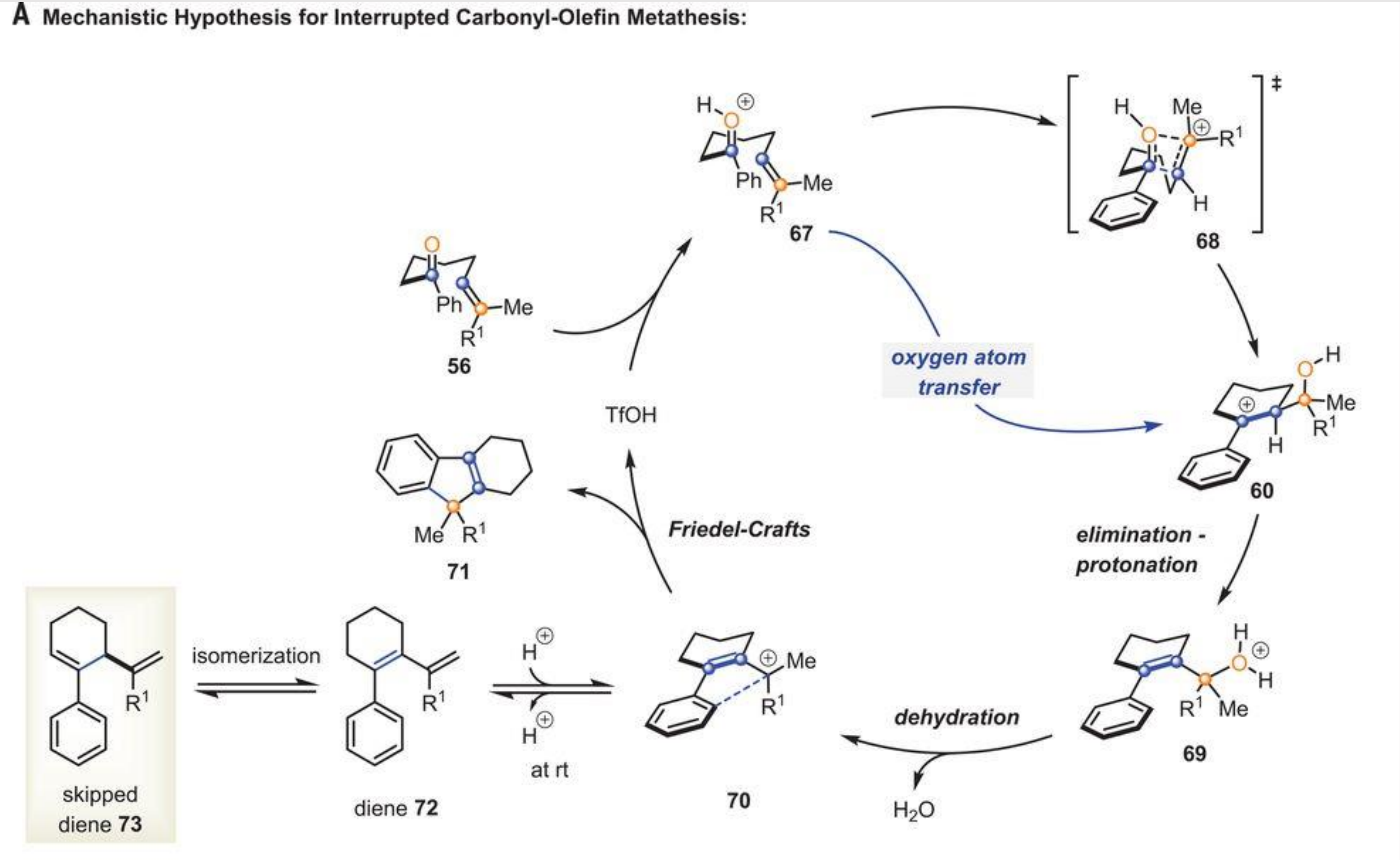
Interrupted Carbonyl-Olefin Metathesis (Tetrahydrofluorenes)



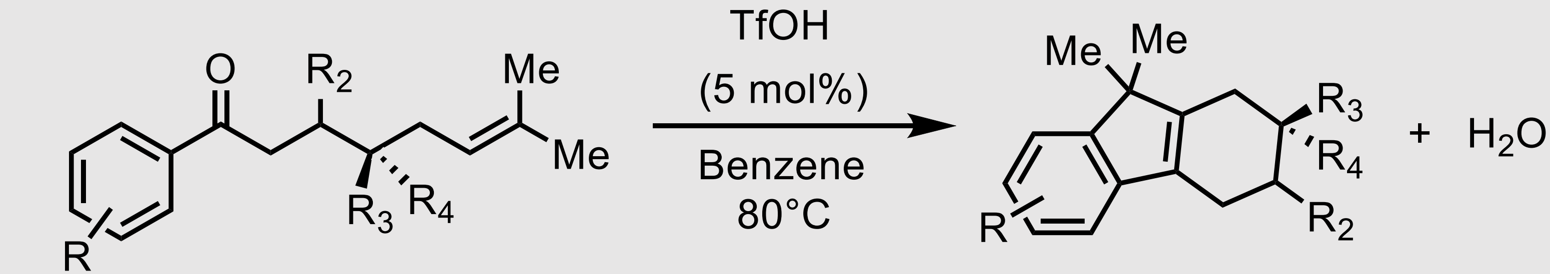


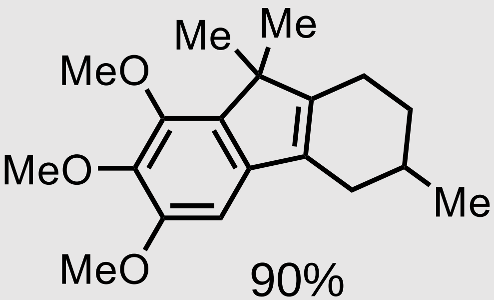
Shindler, C.S. et al. *Science* **2018**, *361,* 1363-1369.

Proposed Mechanistic Route

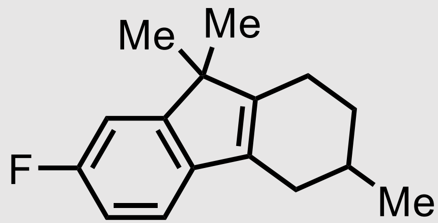


Interrupted Carbonyl-Olefin Metathesis (Tetrahydrofluorenes)

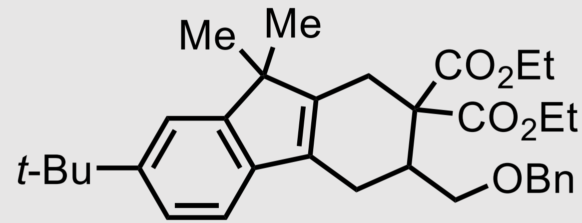




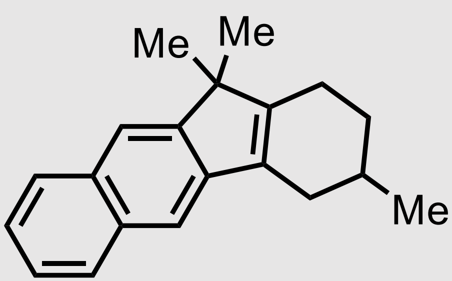
90%



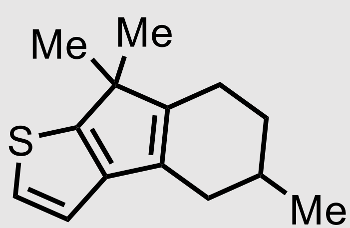
88%



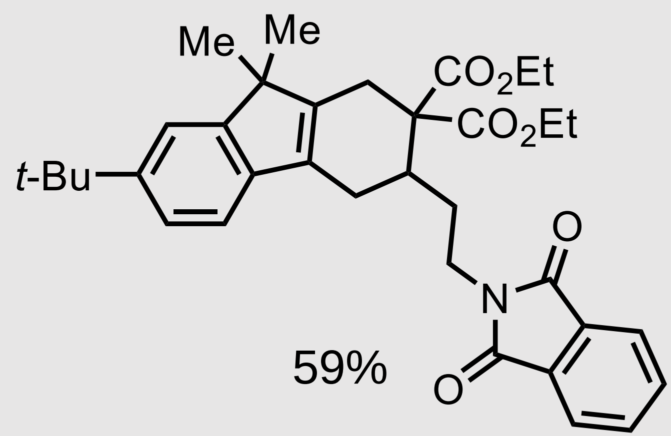
54%



91%



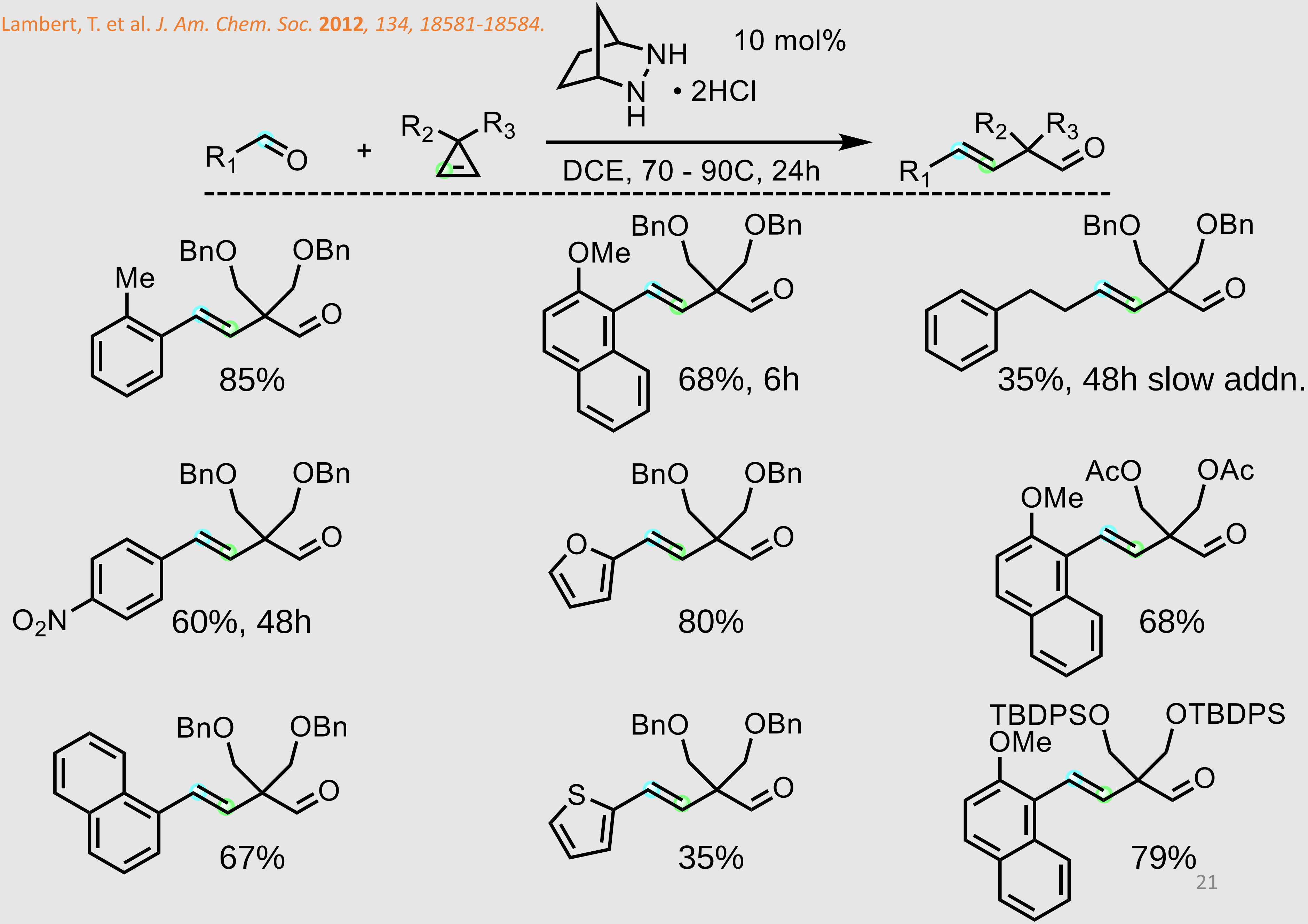
57%



59%

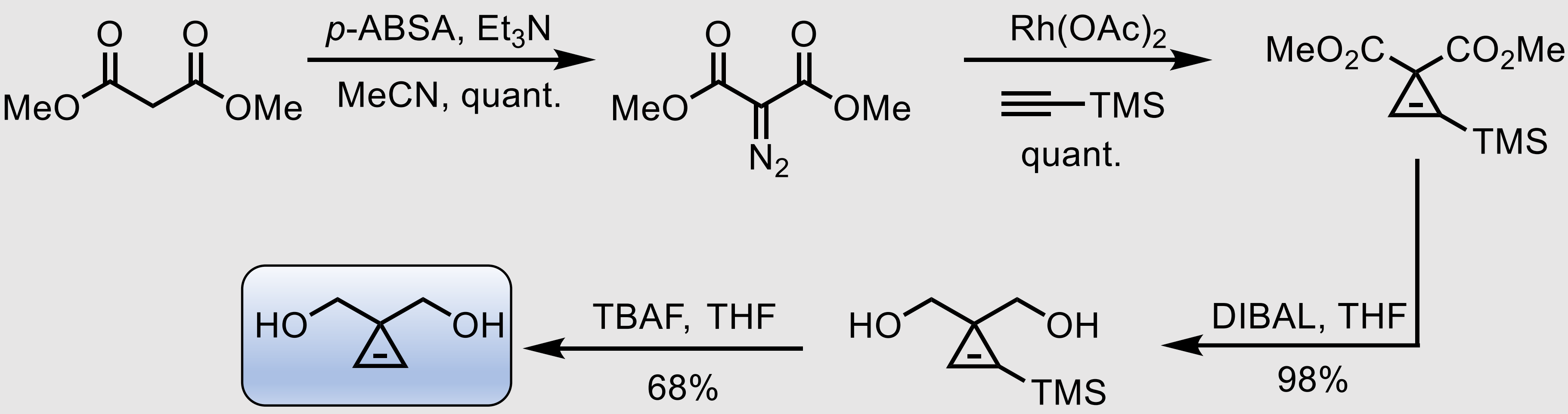
Organocatalytic Carbonyl-Olefin Metathesis

Lambert, T. et al. *J. Am. Chem. Soc.* **2012**, *134, 18581-18584.*

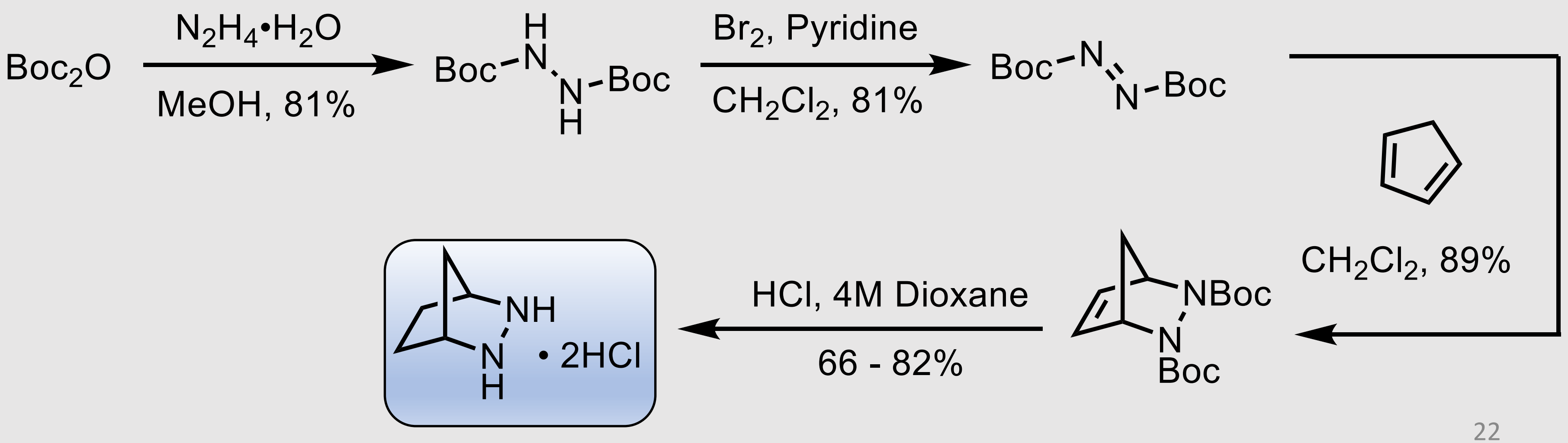


Organocatalytic Carbonyl-Olefin Metathesis

Synthesis of Cyclopropenes (Propose a route):



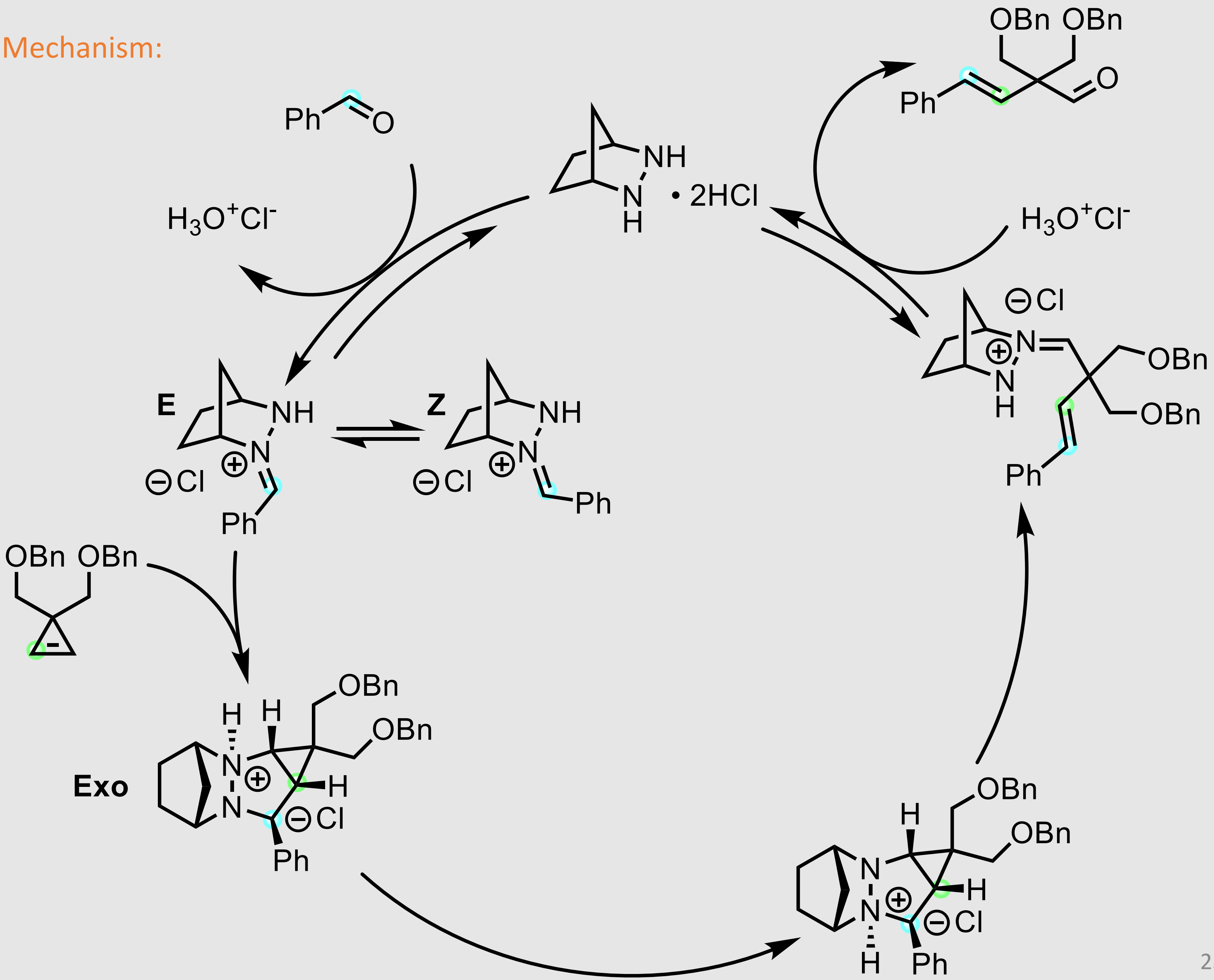
Synthesis of Catalyst (Propose a route):



Lambert, T. et al. *J. Am. Chem. Soc.* **2012**, *134, 18581-18584.*

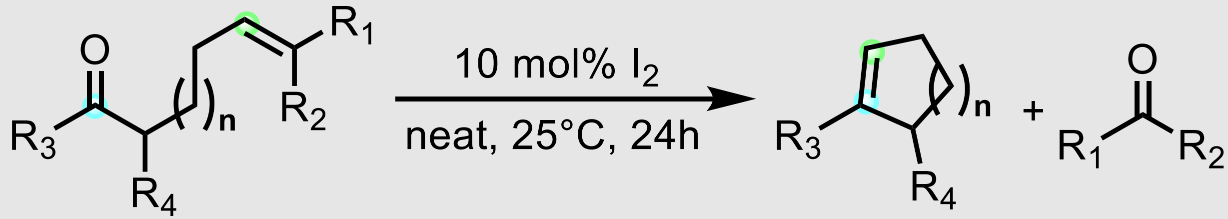
Organocatalytic Carbonyl-Olefin Metathesis

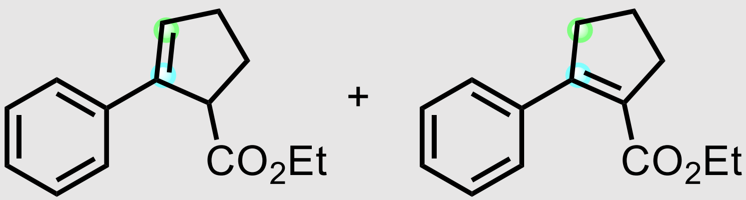
Posited Mechanism:



Lambert, T. et al. *J. Am. Chem. Soc.* **2012**, *134, 18581-18584.*

Iodine-Catalyzed Carbonyl-Olefin Metathesis





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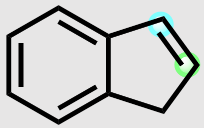

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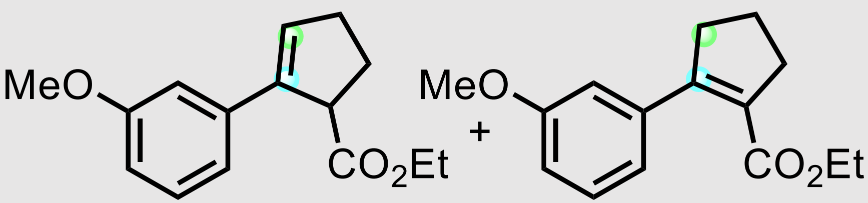
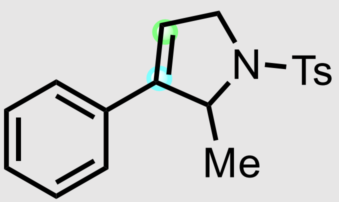


83%; 4:1



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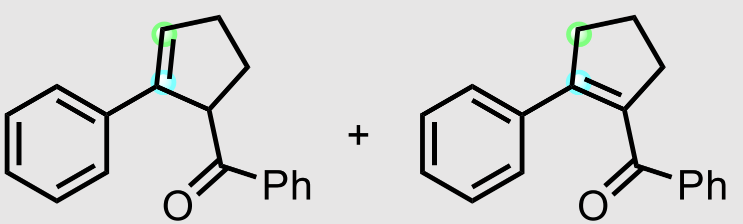
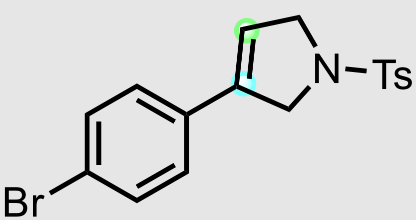


60%; 1:3

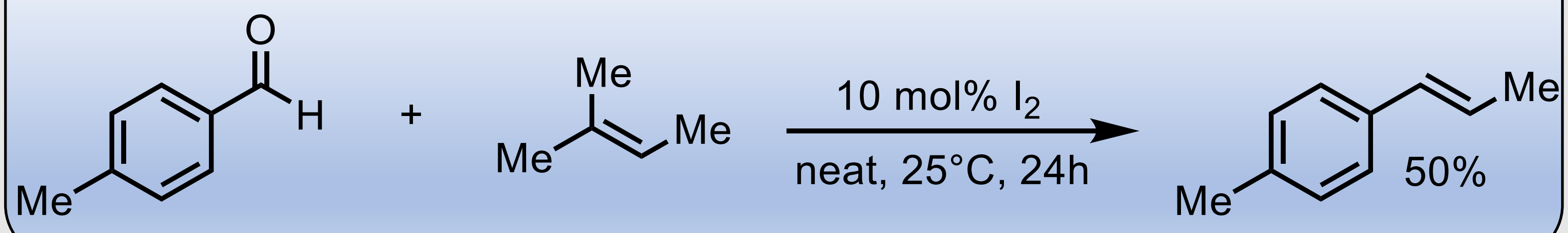


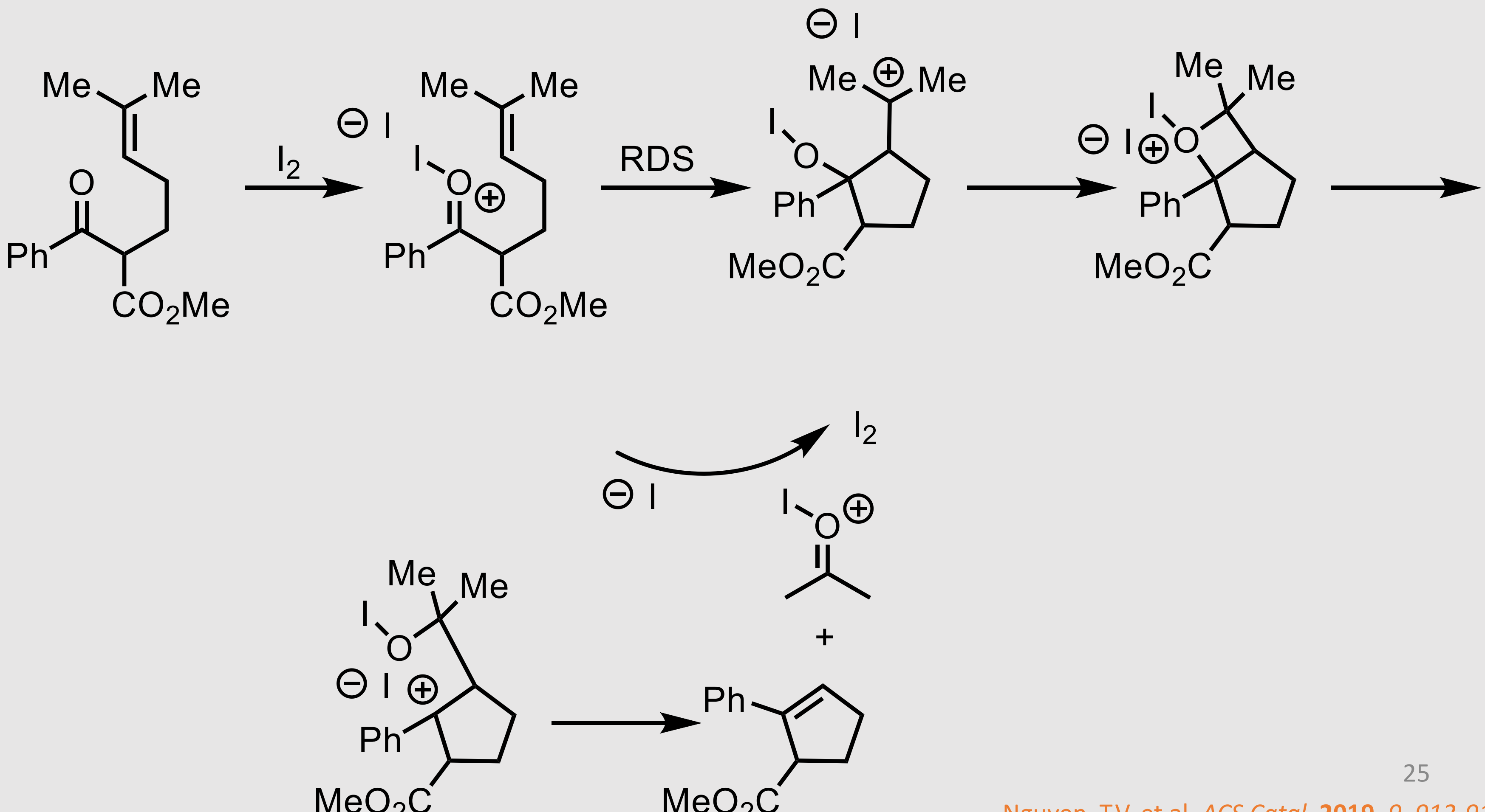
78%

Nguyen, T.V. et al. *ACS Catal.* **2019**, *9, 912-919.*

Iodine-Catalyzed Carbonyl-Olefin Metathesis

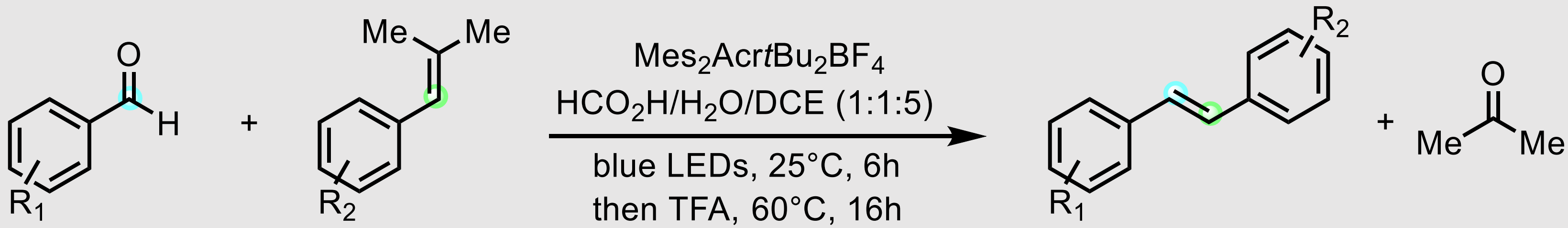
Cross-Metathesis Example:

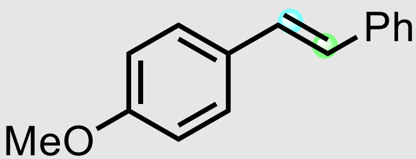




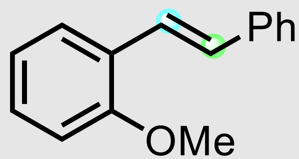
Nguyen, T.V. et al. *ACS Catal.* **2019**, *9, 912-919.*

Photoredox Carbonyl-Olefin Metathesis

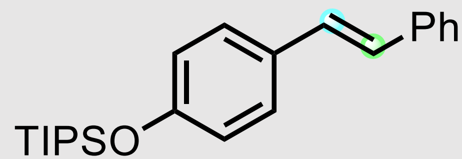




70%; 8:1 E:Z



86%; 10:1 E:Z



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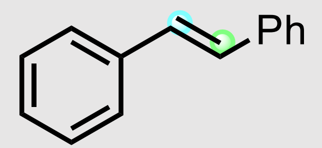
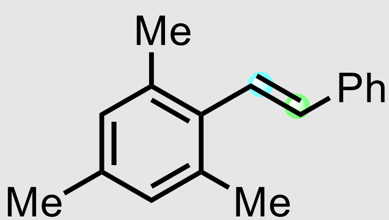


41%; >20:1 E:Z



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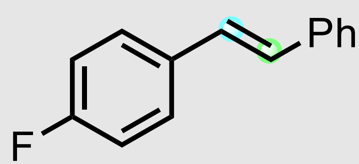

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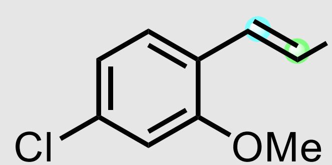
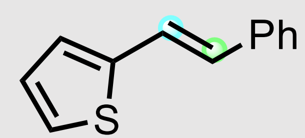
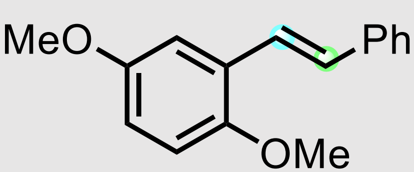


71%; >20:1 E:Z



34%; 5:1 E:Z



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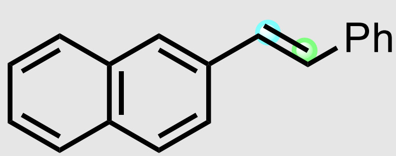
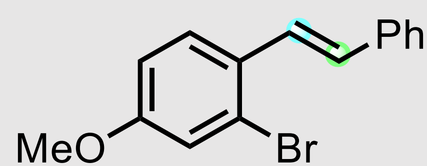
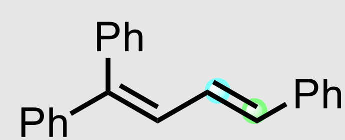


61%; >20:1 E:Z



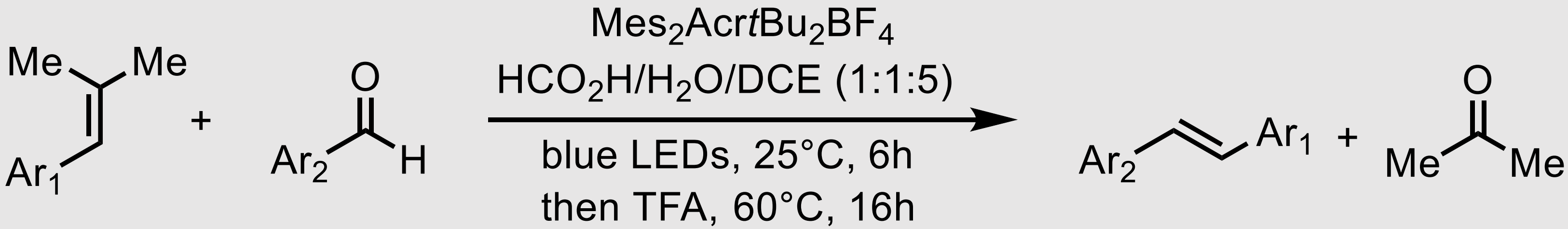
67%; >12:1 E:Z



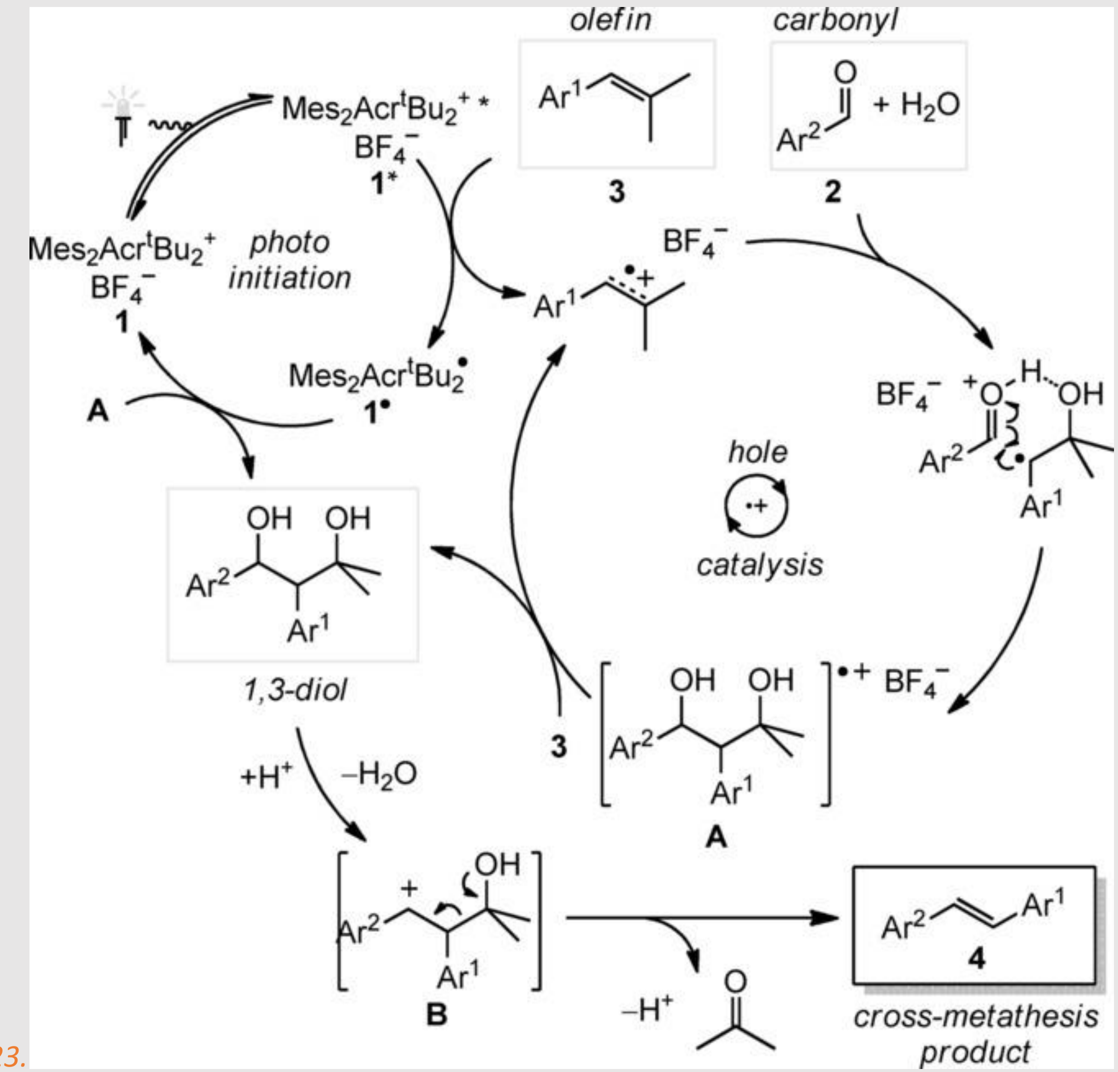
63%; 20:1 E:Z

Glorius, F. et al. *Angew. Chem. Int. Ed.* **2018**, *57, 16219-16223.*

Photoredox Carbonyl-Olefin Metathesis

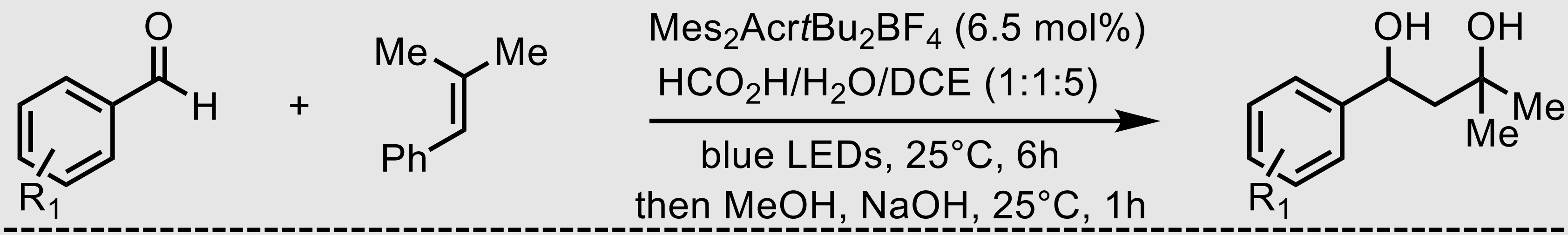


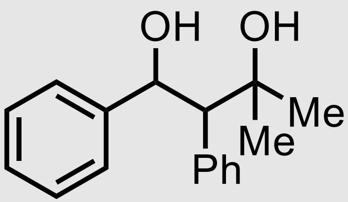
Propose a catalytic cycle.
Hints: This is proposed to operate via hole catalysis. Also, an oxetane is not the putative intermediate.



Glorius, F. et al. *Angew. Chem. Int. Ed.* **2018**, *57, 16219-16223.*

Photoredox Carbonyl-Olefin Metathesis





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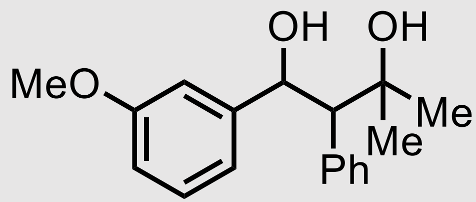

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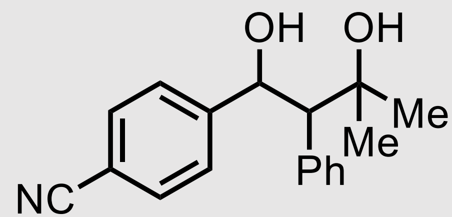

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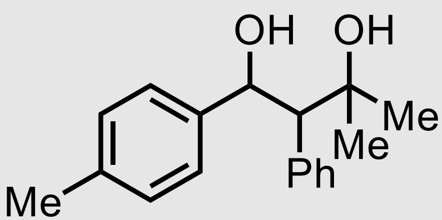

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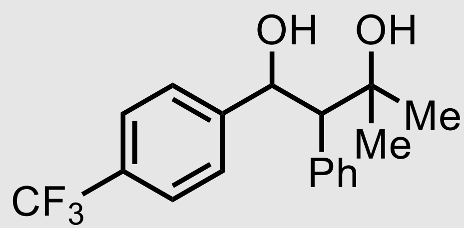

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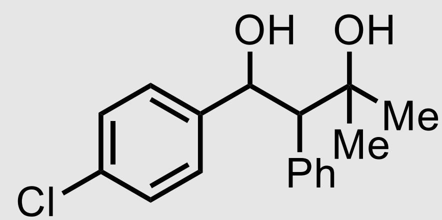
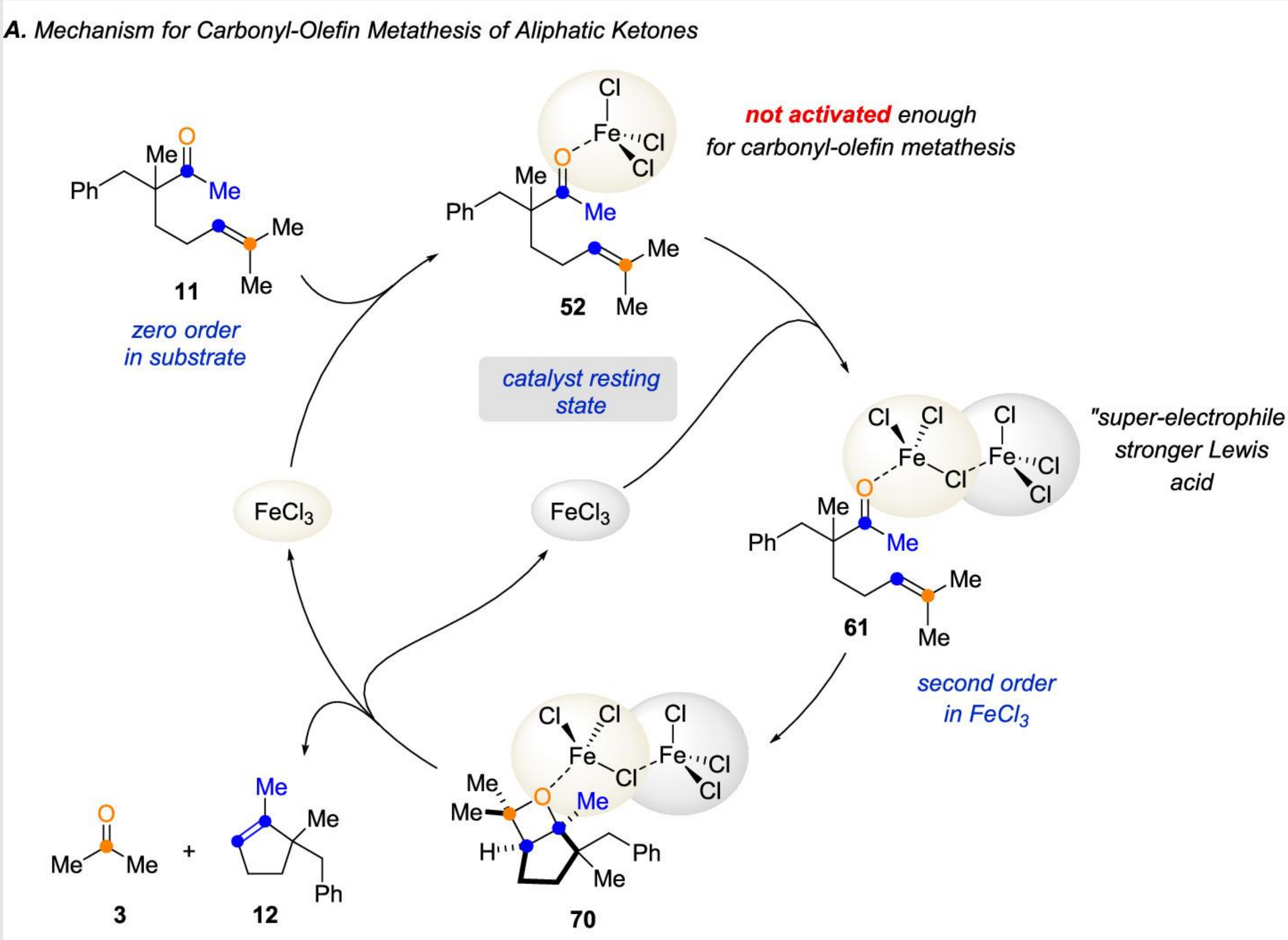


59%

Glorius, F. et al. *Angew. Chem. Int. Ed.* **2018**, *57, 16219-16223.*

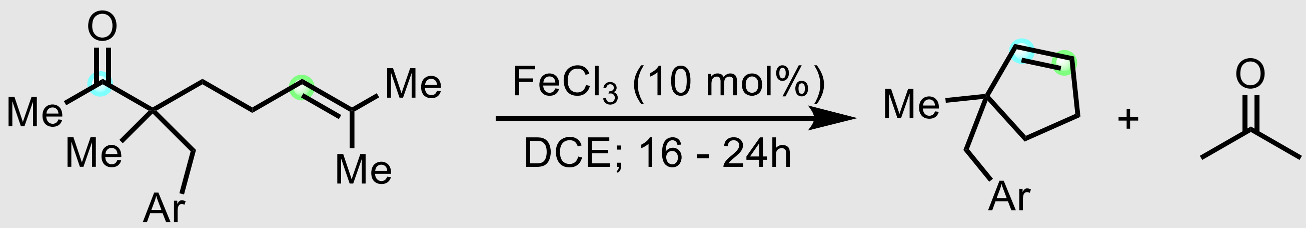
Carbonyl-Olefin Metathesis of Aliphatic Ketones

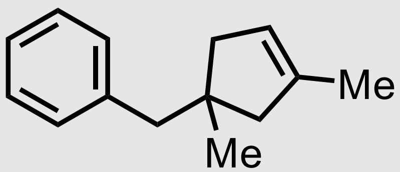


Schindler, C.S. Sigman, M.S. et al. *J. Am. Chem. Soc.* **2019**, *141, 1690-1700.*

Fe(III)-Mediated Carbonyl-Olefin Metathesis (Schindler)

Schindler, C.S. Sigman, M.S. et al. *J. Am. Chem. Soc.* **2019**, *141, 1690-1700.*





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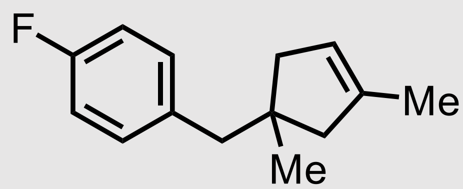

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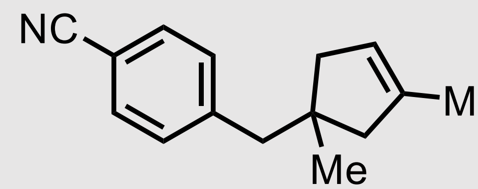

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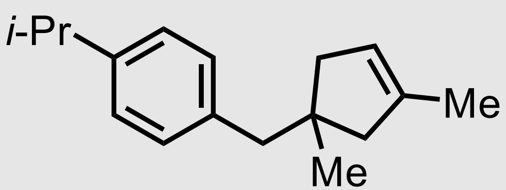

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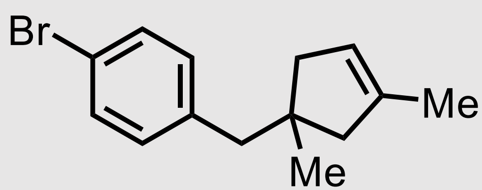

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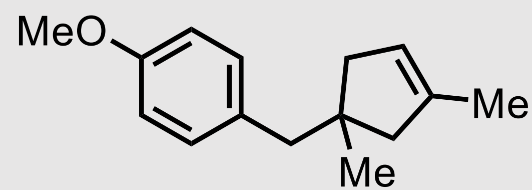

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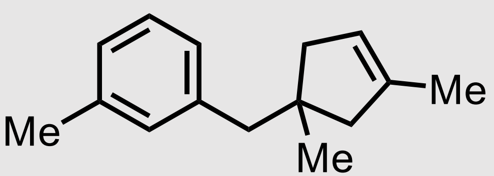

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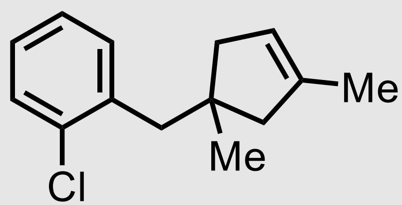

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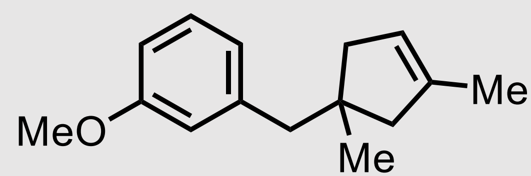
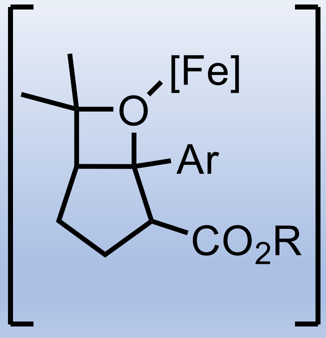


64%

Conclusions



Future Directions:

- **Imine-carbonyl metathesis via azetidines?**
- **Ways to turnover metal-oxo by-products?**
- **Mechanistic paradigms outside of oxetanes.**
- **More methods involving photoredox processes.**
- **What about McMurry!? (Although not actually metathesis)**