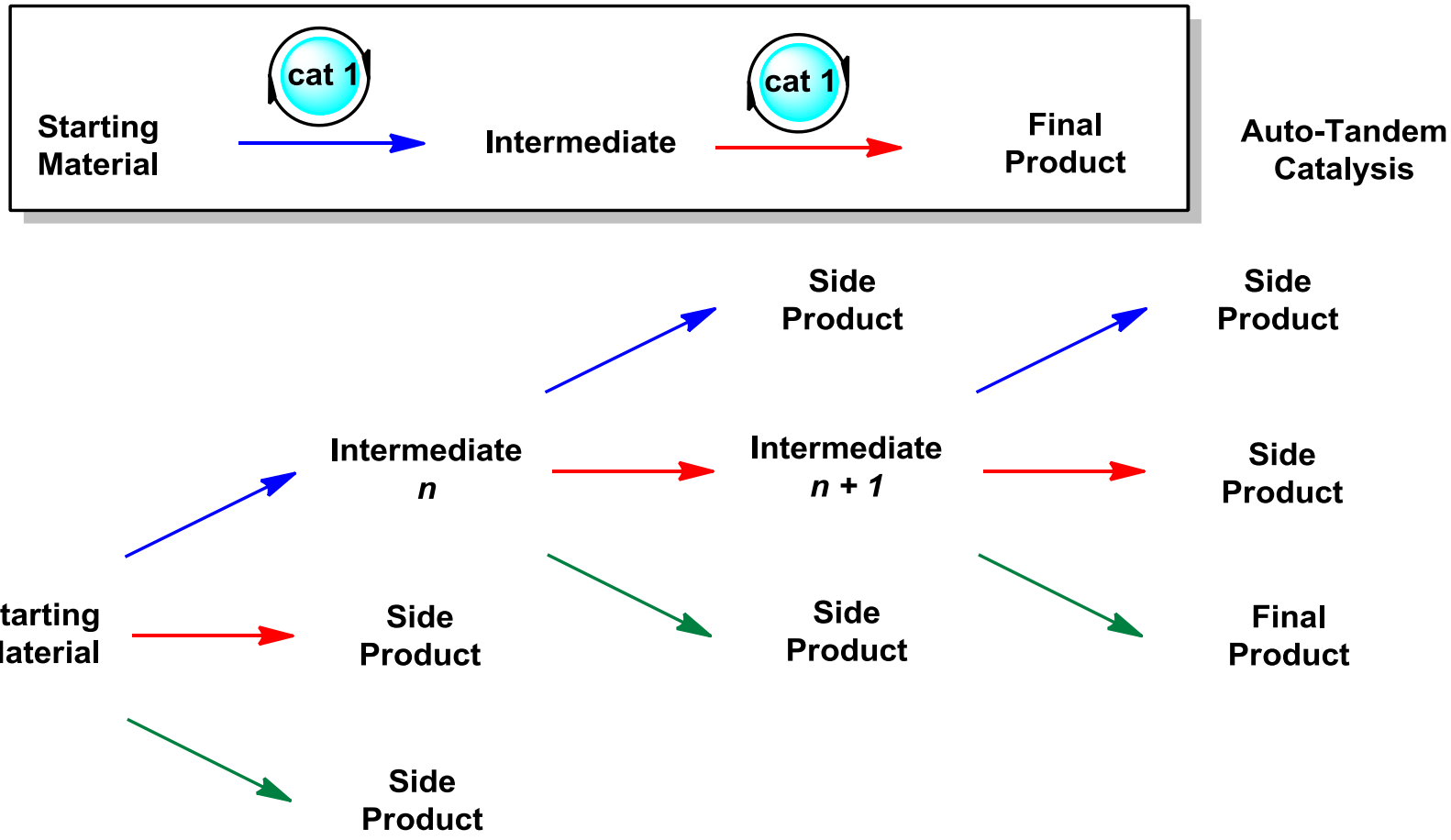
03/02/2014

Temporal separation of catalytic activities allows anti-Markovnikov reductive functionalization of terminal alkynes

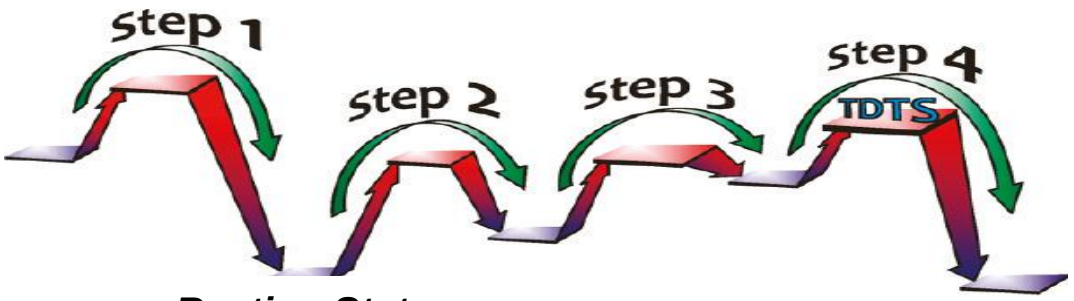
L. Li, S. B. Herzon, *Nature Chemistry*, 2014, *6*, 22

Auto-Tandem Catalysis : Efficiency Increases with Complexity



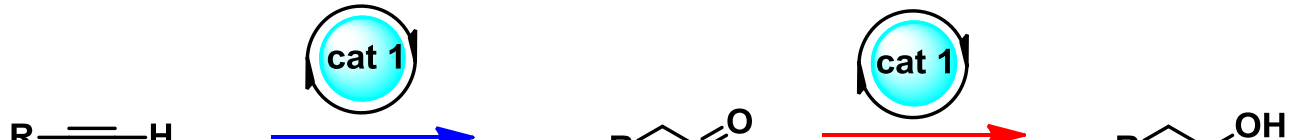
An Alternative Strategy : Temporal Separation

Starting Material → Intermediate *n* → Intermediate *n + 1* → Final Product

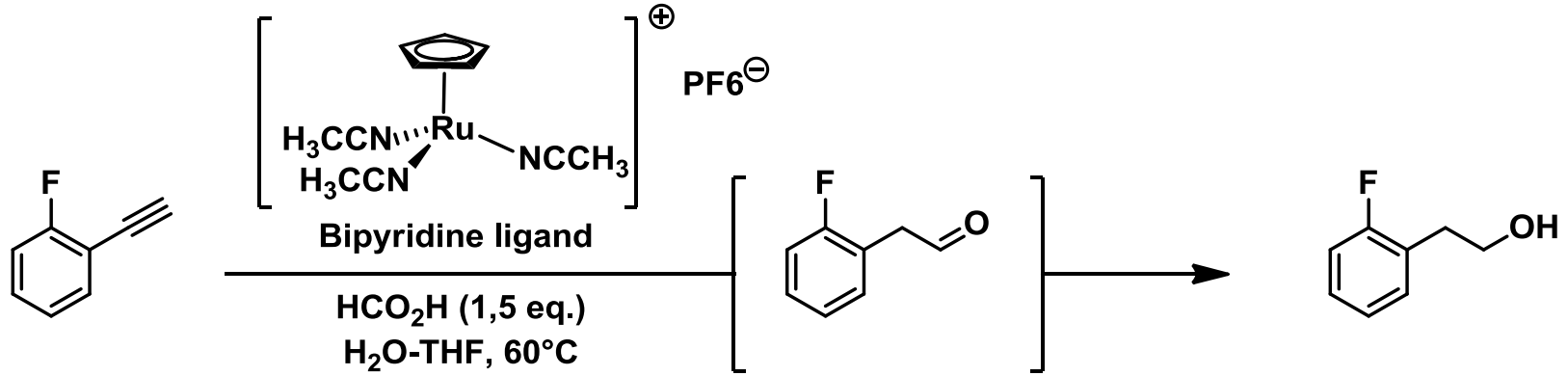


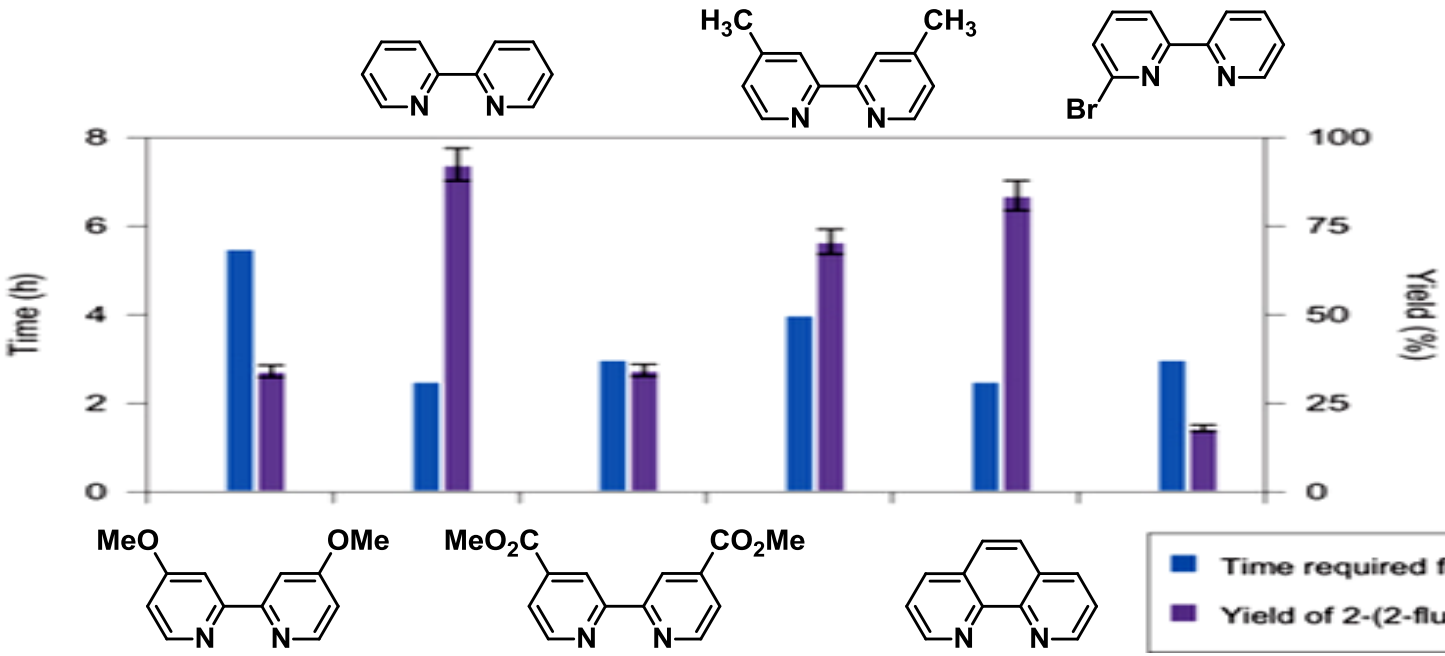
Resting State

[Cat --- substrate]

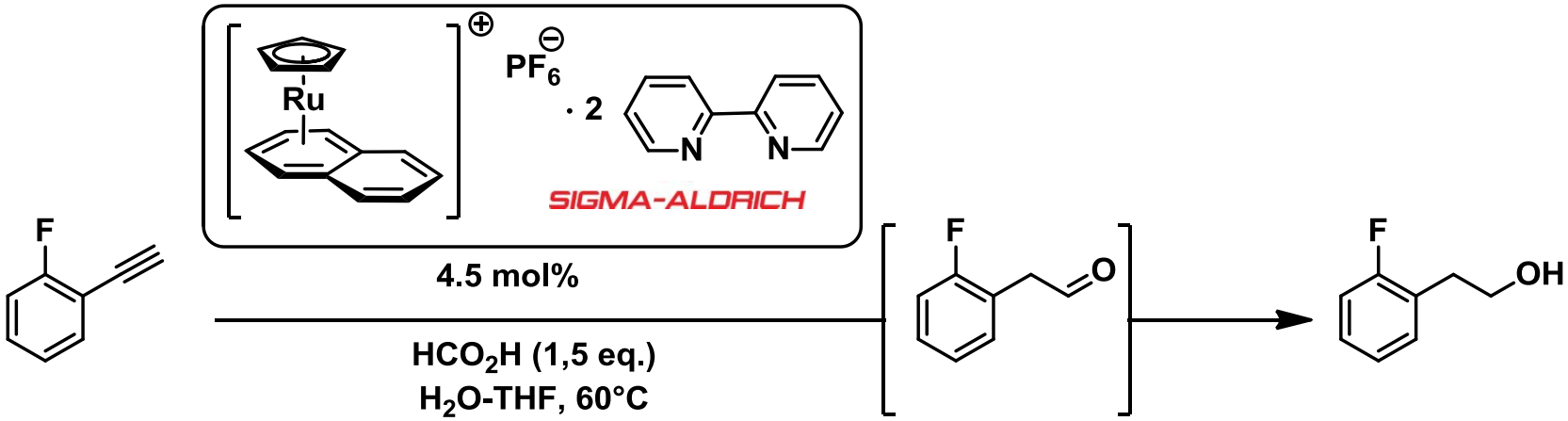


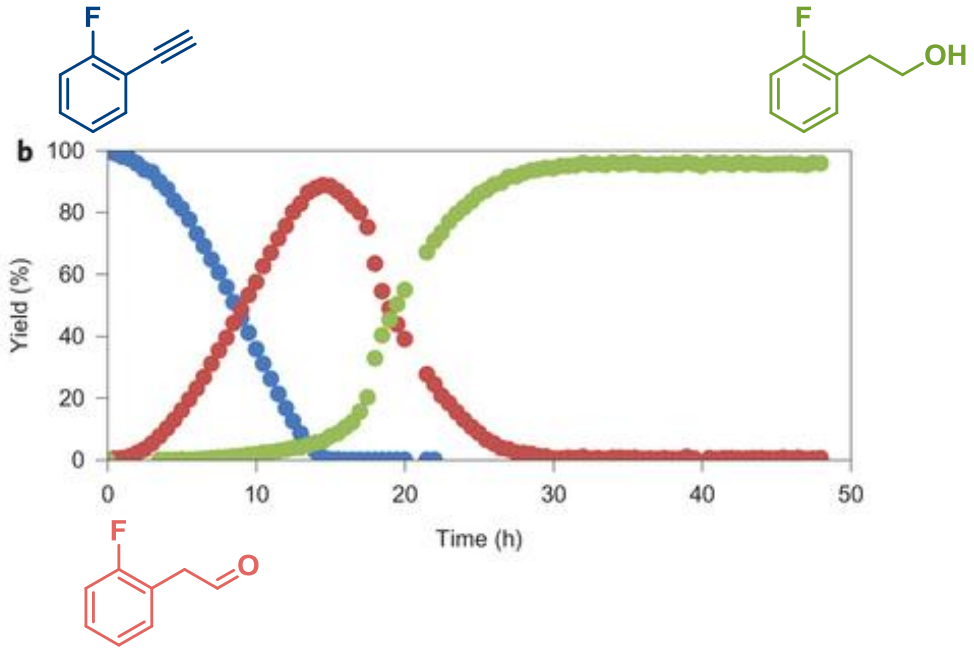
Preliminary Studies



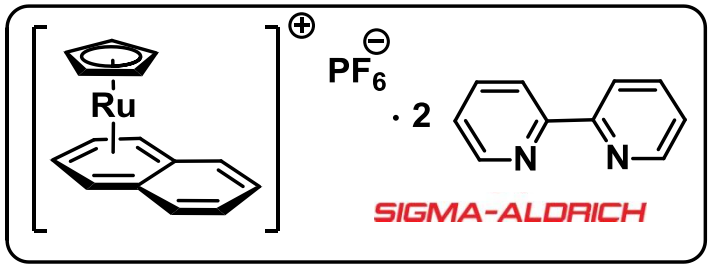


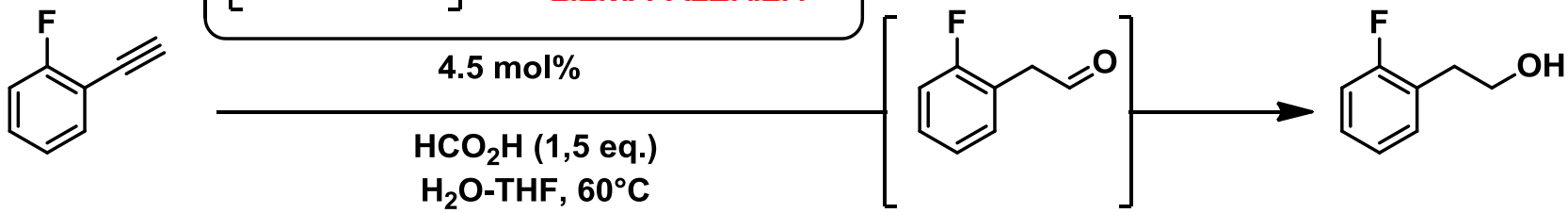
Temporal Separation Probe



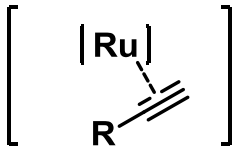


Temporal Separation Probe

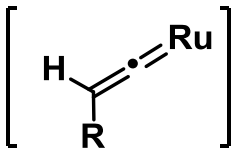


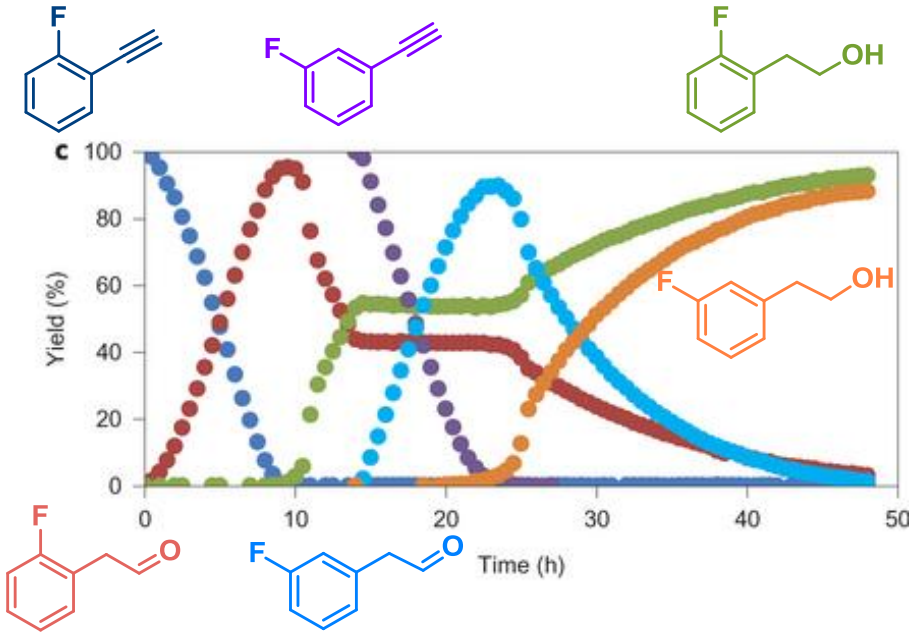


Possible Resting-States

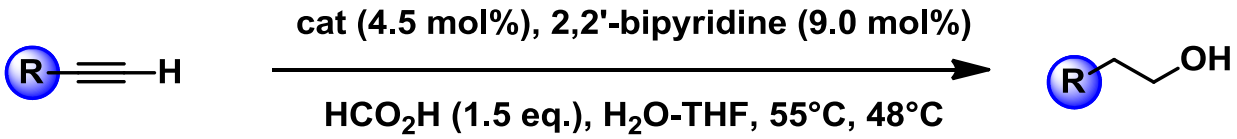


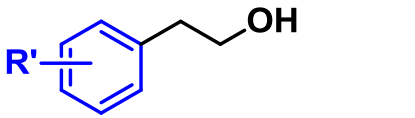
or





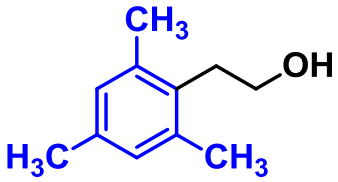
Scope of the Reaction





R' = *m*-F, *o*-CH_3, *m*-CH_3, *m*-Cl
H, *p*-OCH_3, *p*-F, *p*-CH_3

85-97%



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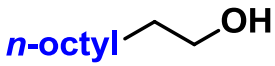
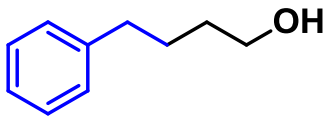
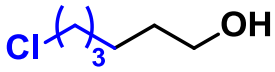


95%



88%



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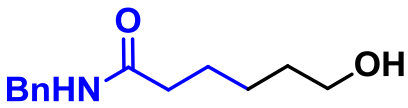
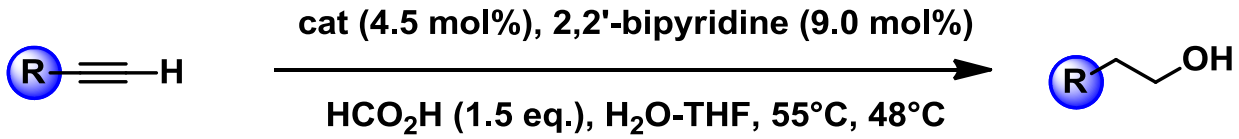
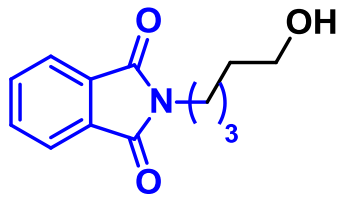


90%

Scope of the Reaction





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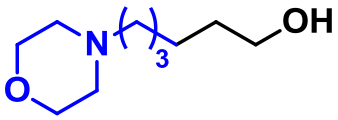

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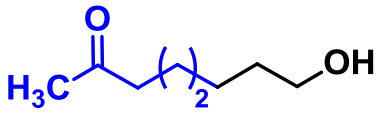

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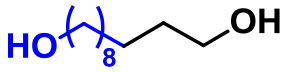

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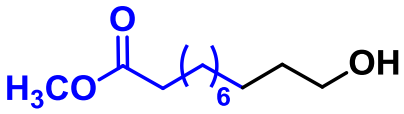

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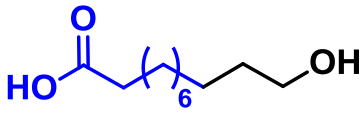

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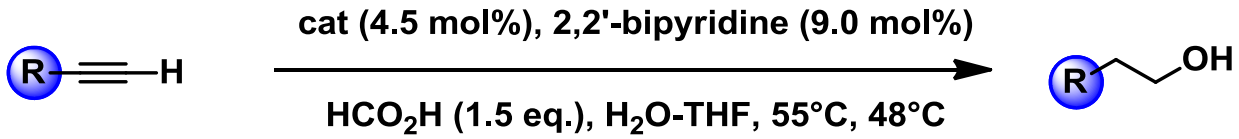
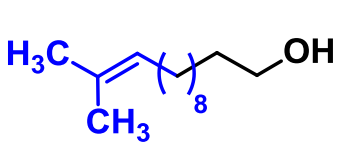
Scope of the Reaction





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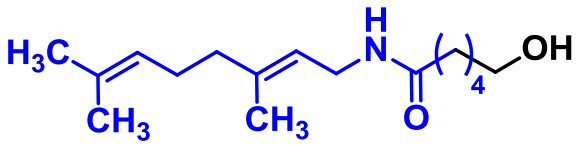

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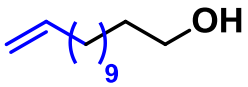

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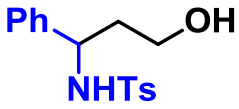

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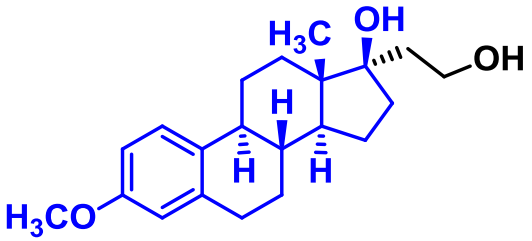
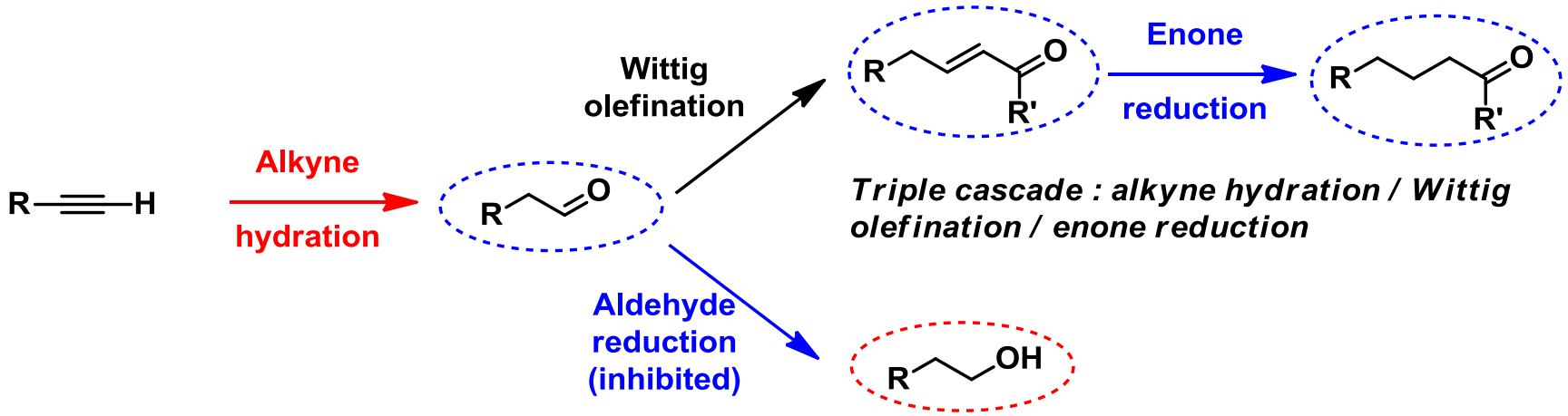
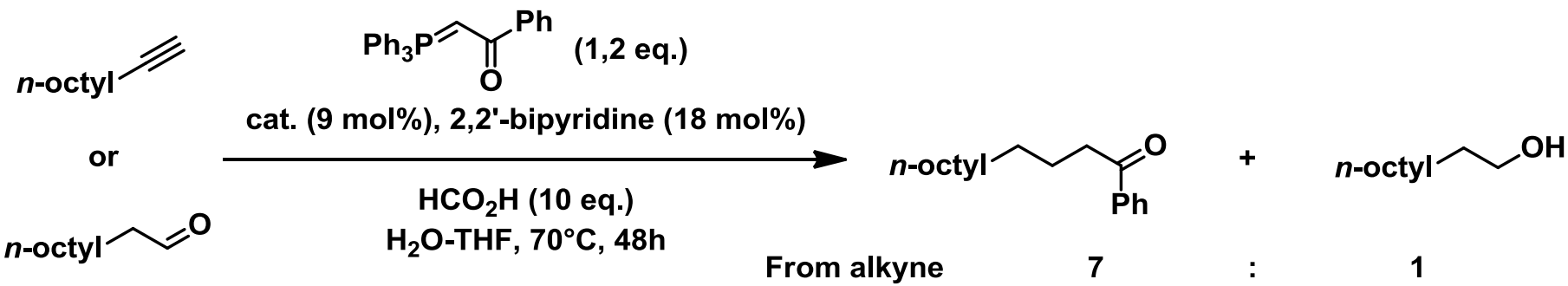


72%

Toward a Triple Cascade

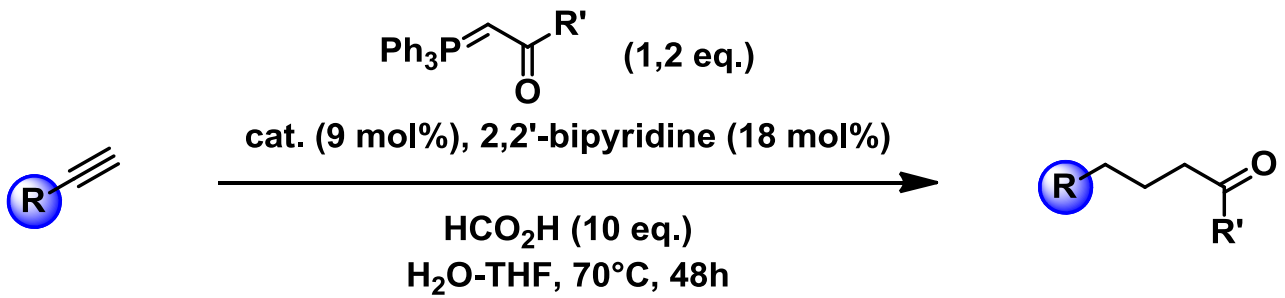


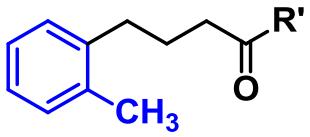
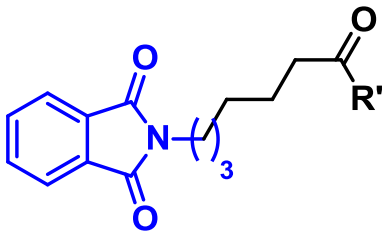
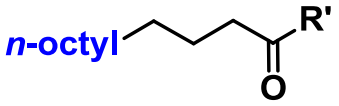
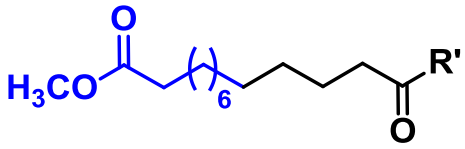
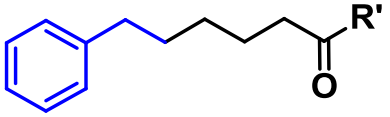
Triple cascade : alkyne hydration / Wittig olefination / enone reduction



From alkyne	7	:	1
From aldehyde	2	:	1

Scope of the Reaction



	R' = Ph	R' = CH_3		R' = Ph	R' = CH_3
	75%	71%		81%	76%
	72%	70%		72%	76%
	75%	70%			

Conclusion

- ***The first recognition and investigation of temporal separation in tandem catalysis***
- ***A strategy which cannot be used in all catalytic systems***
- ***Novel candidate reactions need to be developed***
- ***A further understanding of the reaction mechanism must be provided notably with the highlighting of the resting state structure***