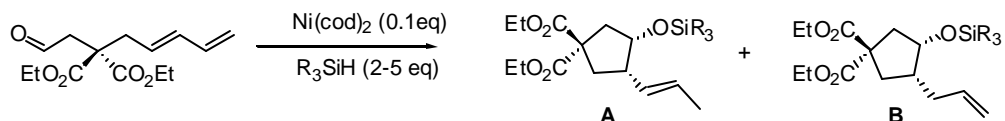


Recently Developed Ni(0) Catalyzed Reactions

1) Recently, Mori et. al reported an asymmetric cyclization of 1,3-dienes to tethered carbonyl groups with moderate enantioselectivity.

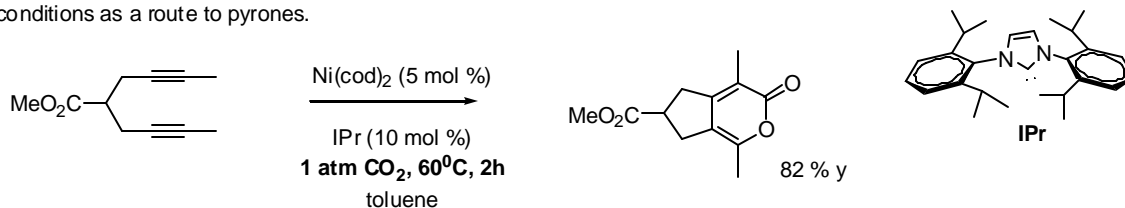
a) Provide mechanism(s) that account for the formation of both products (**A**, **B**) formed in the reaction below:



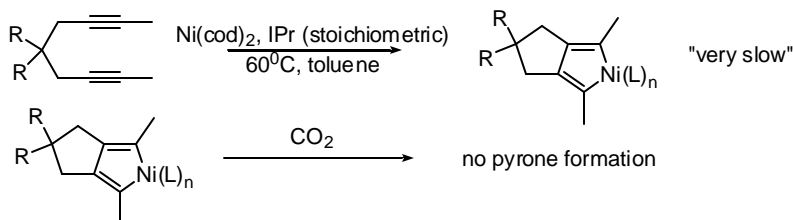
b) Mori provided experimental evidence suggesting that nickel catalyzed double bond isomerization of **A** was not occurring. What simple experiment do you think he ran?

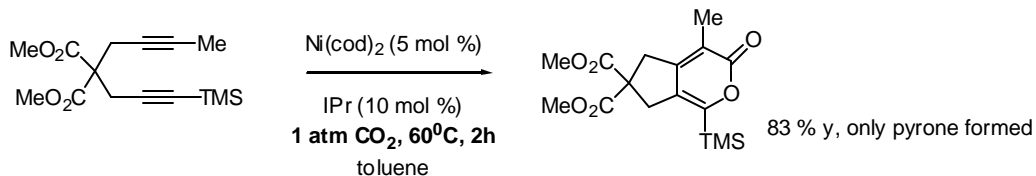
Sato, Y.; Saito, N.; Mori, M. *J. Am. Chem. Soc.* **200**, 122, 2371-2372. Sato, Y.; Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2000**, 122, 1624-1634.

2) Louie et. al have reported a nickel catalyzed formal [2+2+2] cycloaddition of CO₂ and diynes under mild conditions as a route to pyrones.



a) In order to provide mechanistic insight, the authors performed several experiments. Based on the experiments shown below, propose a mechanism for this cycloaddition reaction.



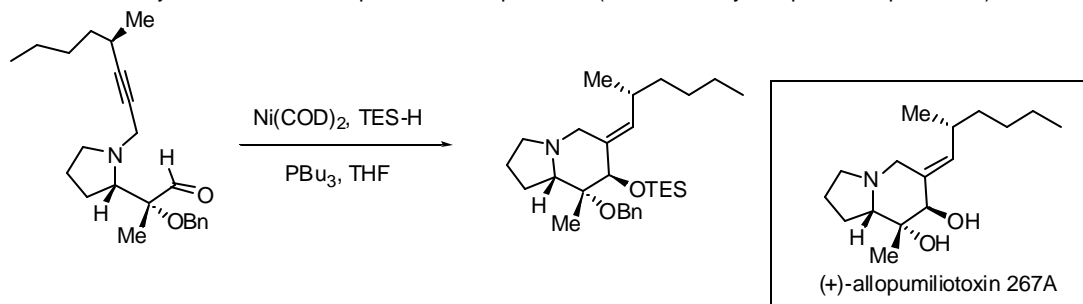


b) The authors make no mention of the use of terminal alkynes, nor provide example of such substrates. Suggest a reason for why terminal alkynes might not work.

c) By the mechanistic evidence provided above, this [2+2+2] reaction is not proceeding by the "classic" mechanism. Provide a reason why the IPr ligand might facilitate this difference in mechanistic pathway.

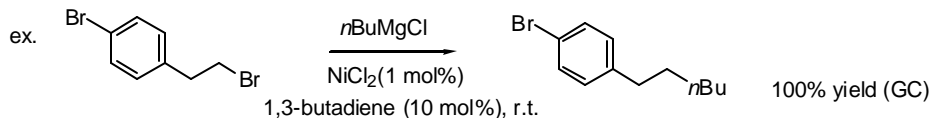
Louie, J.; Gibby, J.E.; Farnworth, M.V.; Tekavec, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188.

3) Montgomery, et. al recently reported a synthesis of (+)-Allopumiliotoxin utilizing a tethered alkyne/aldehyde cyclization which highlights this methodology in the context of complex synthesis. Provide a mechanism for this reaction and account for the diastereoselectivity at the silylated carbinol center and the olefin geometry. Hint: this reaction proceeds similarly to the reaction that produces **B** in problem 1 (established by competition experiments).



Tang, X-Q.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 6098.

4) A nickel catalyzed cross-coupling of Grignard reagents with alkyl halides and tosylates was recently reported.

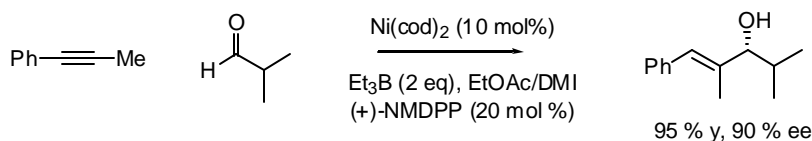


a) Propose a probable mechanism for this reaction.

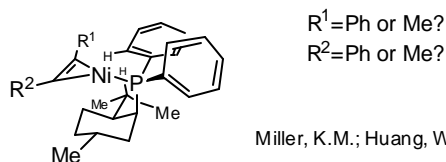
b) What would happen if the alkyl bromide and grignard were treated without any catalysts?

Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222.

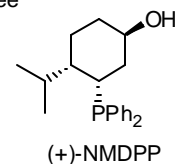
5) Jamison et. al have recently reported a series of papers on the intermolecular version of Mongomery's "ynal" cyclizations including an enantioselective reductive coupling of alkynes to aldehydes. The enantiodetermining step in this reaction is the migratory insertion of the nickel-alkyne complex across the carbon-oxygen double bond.



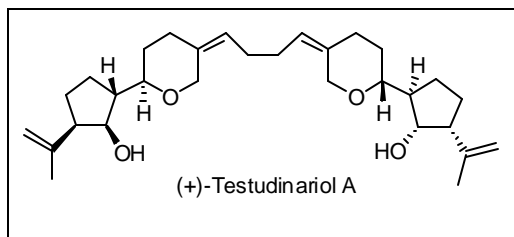
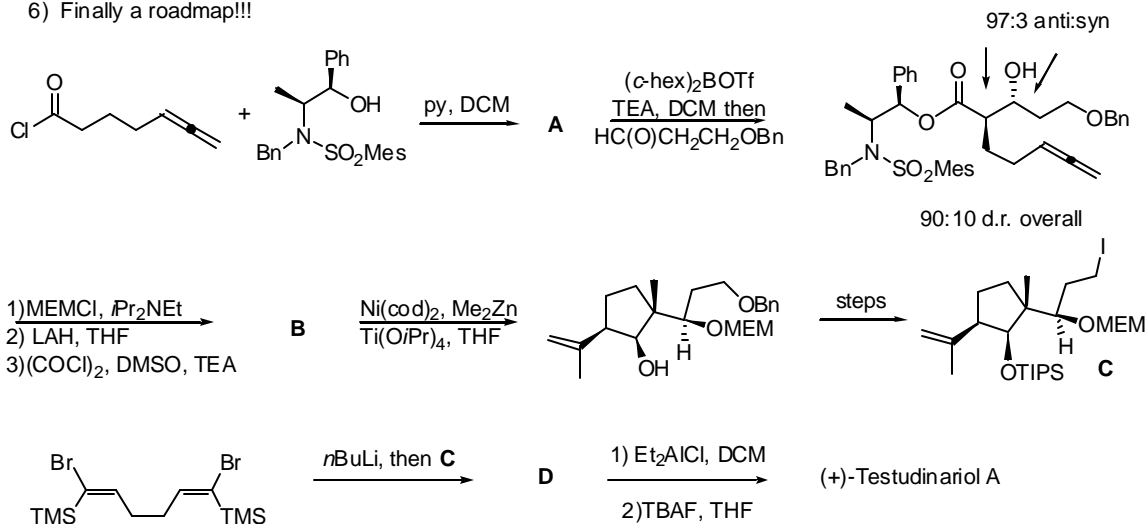
Examine the below nickel-(+)-NMDPP-alkyne complex and rationalize where the aldehyde coordinates to the nickel atom and where the phenyl group and methyl group should be placed in order to explain the absolute stereochemistry of the allylic alcohol product. Remember that this reaction is not only highly enantioselective but very regioselective (why?).



Miller, K.M.; Huang, W-S.; Jamison, T.F. *J. Am. Chem. Soc.* **2003**, 125, 3442.



6) Finally a roadmap!!!



Diastereoselectivity for reaction of **A**?

Mechanism/diastereoselectivity for nickel catalyzed reaction?

Mechanism for the final two steps?

Amarasinghe, K. K. D.; Montgomery, J. *J. Am. Chem. Soc.* **2002**, 124, 9366.