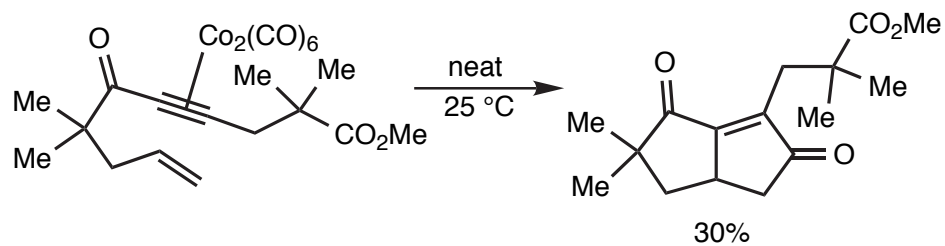
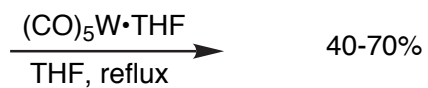
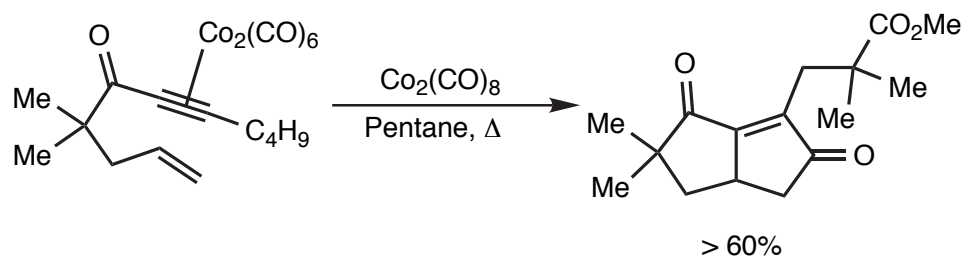


Miscellaneous

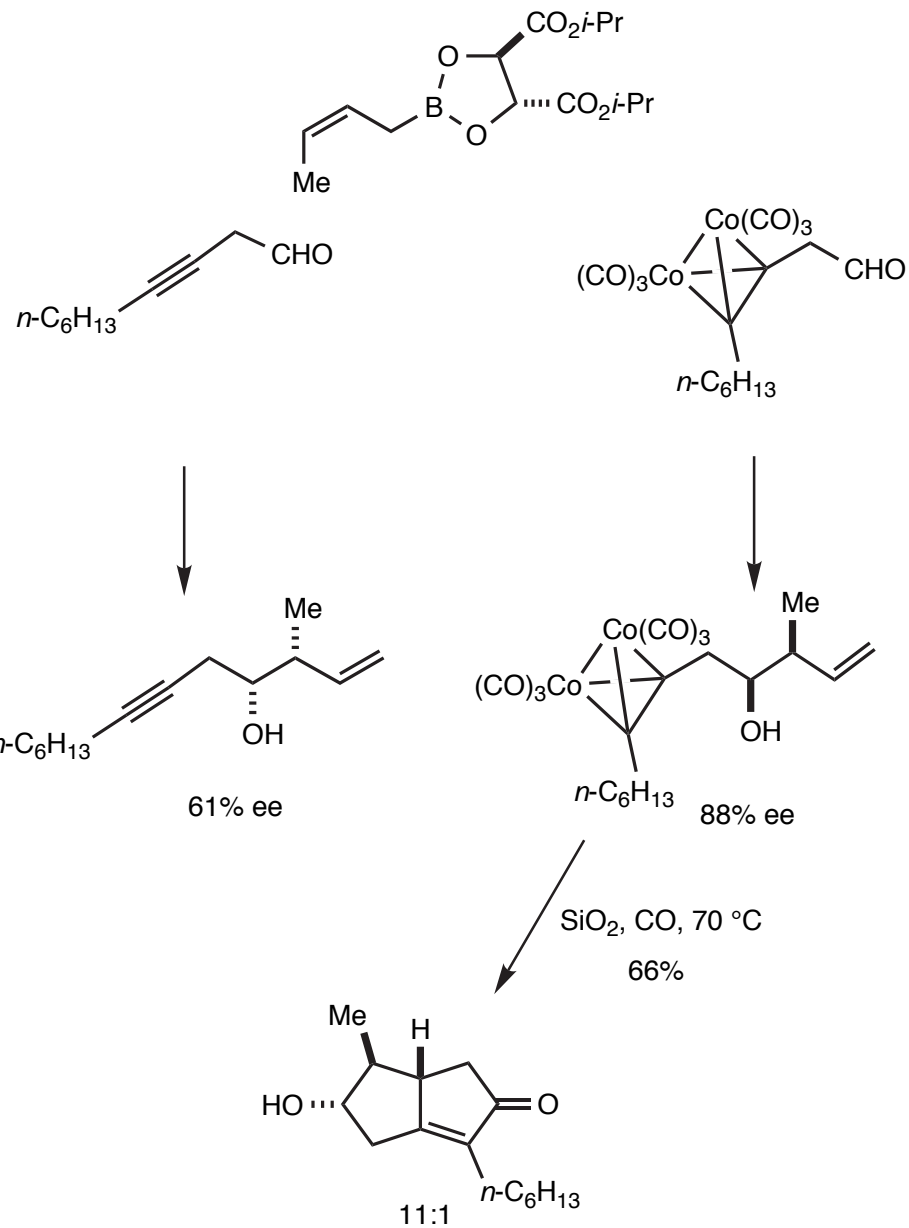


Dinsmore, C. J.; Hoye, T. R. Unpublished results



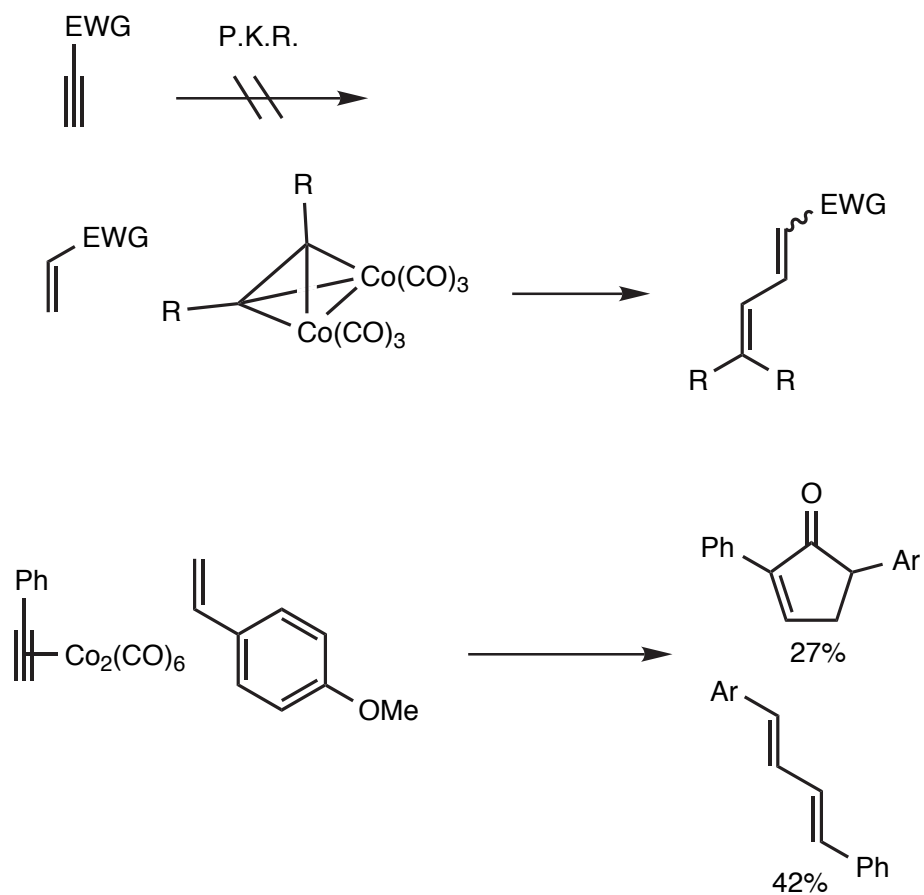
Suriano, J. A.; Hoye, T. R. Unpublished results

Miscellaneous



Roush, W. R.; Park, J. C. *Tetrahedron Lett.* **1991**, *32*, 6285-6288

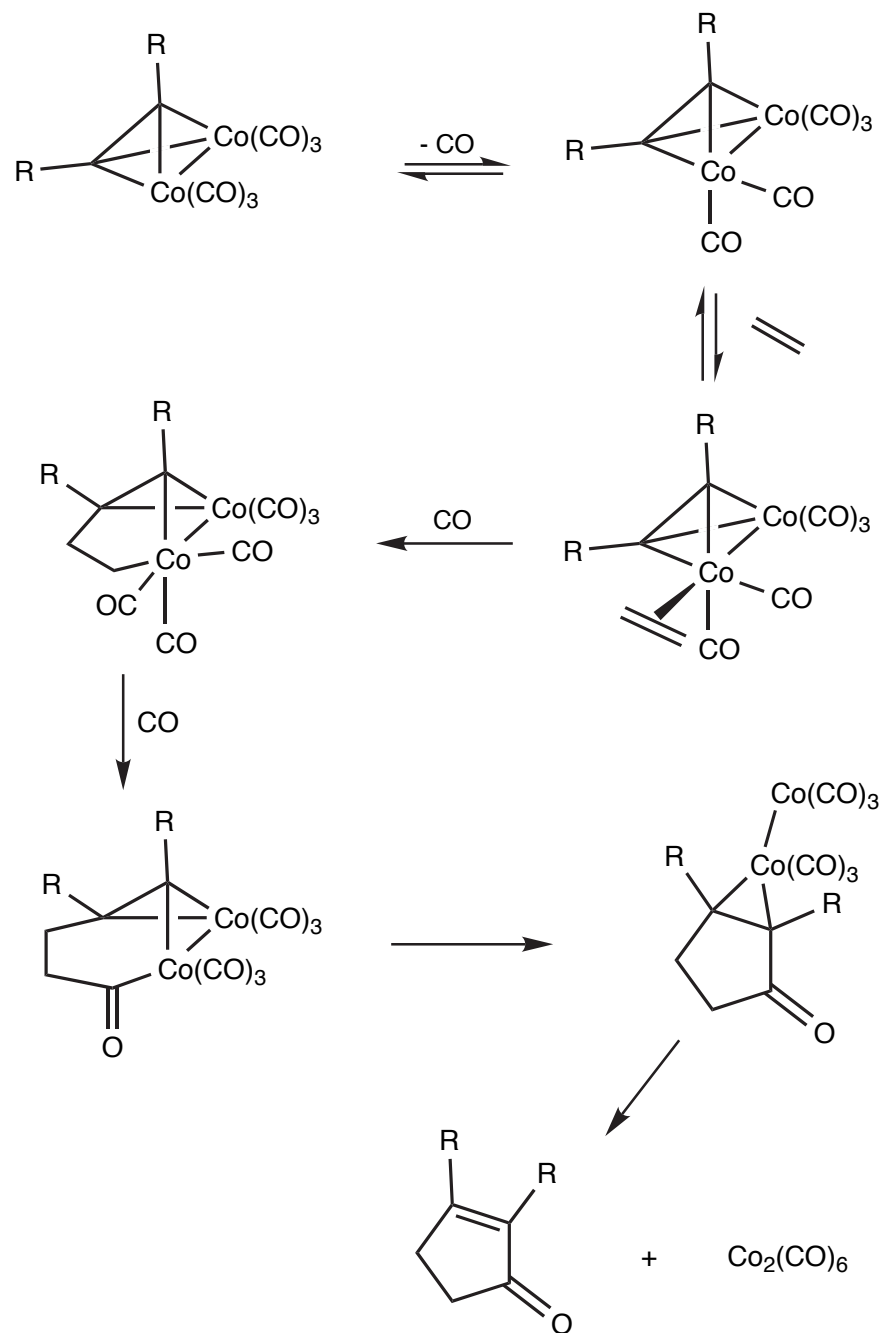
Further Observations:



Most other functionality is well tolerated although allylic and propargylic substituents can be problematic.

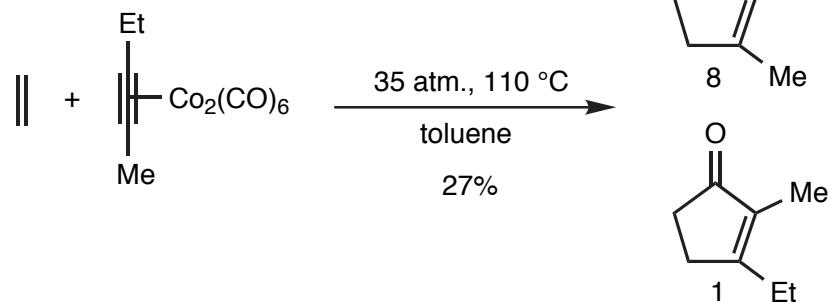
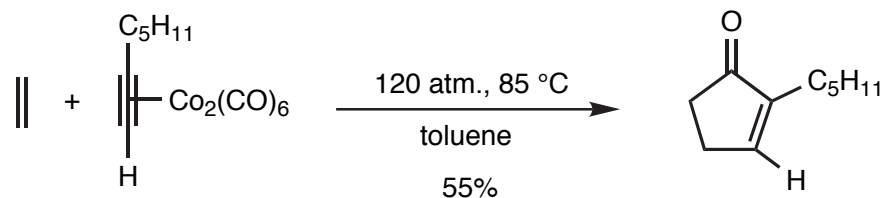
Increased steric hinderance on the alkyne or on the alkene results in lower yields.

Proposed Mechanism:



Intermolecular - Alkyne Regioselectivity

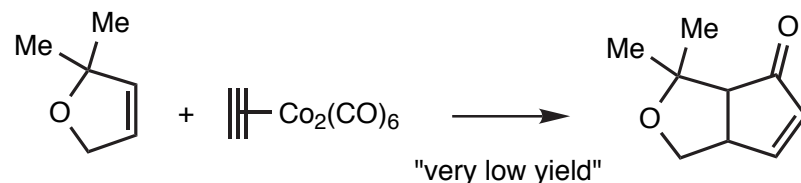
The reaction is consistently regioselective with respect to the alkyne fragment, placing the larger substituent at C-2 of the cyclopentenone



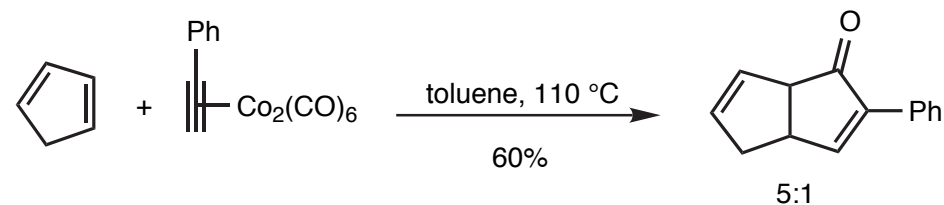
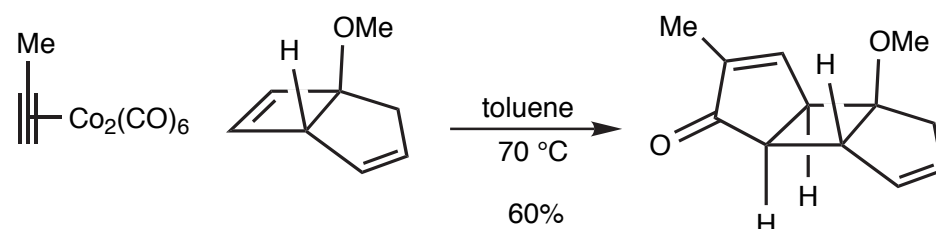
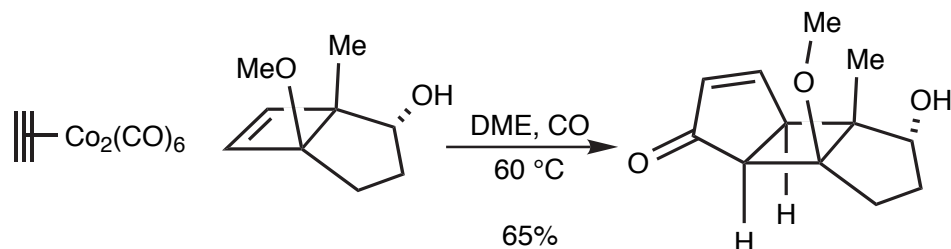
Intermolecular - Alkene Regioselectivity

The reactions of monosubstituted alkenes with monosubstituted alkynes are non-selective

The reactions of 1,2-disubstituted olefins can be regioselective, but predictive ability is limited

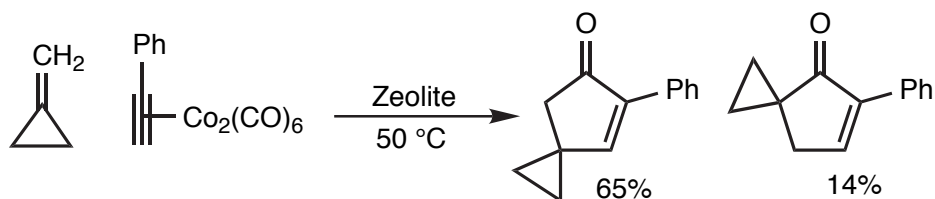


Billington, D. C. *Tetrahedron Lett.* **1983**, 24, 2905

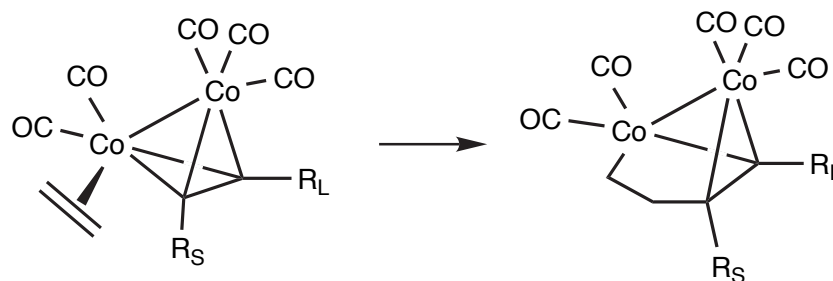


Intermolecular - Alkene Regioselectivity

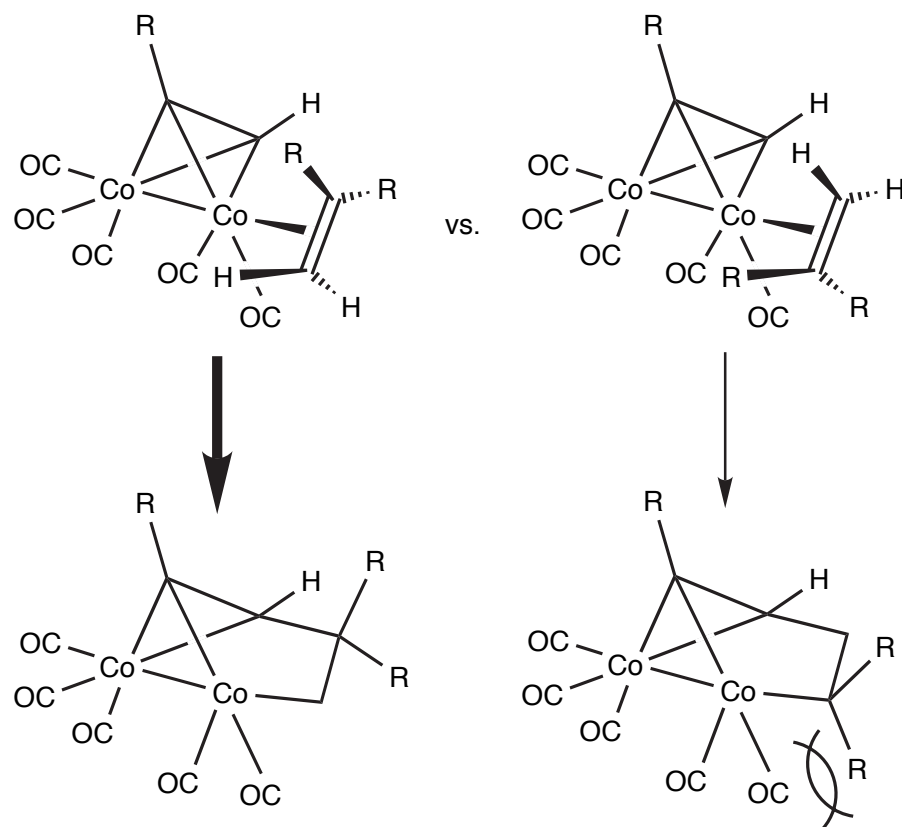
The reactions of 1,1-disubstituted and trisubstituted alkenes are regioselective with the bulkier end of the olefin incorporated at C-4 of the cyclopentenone



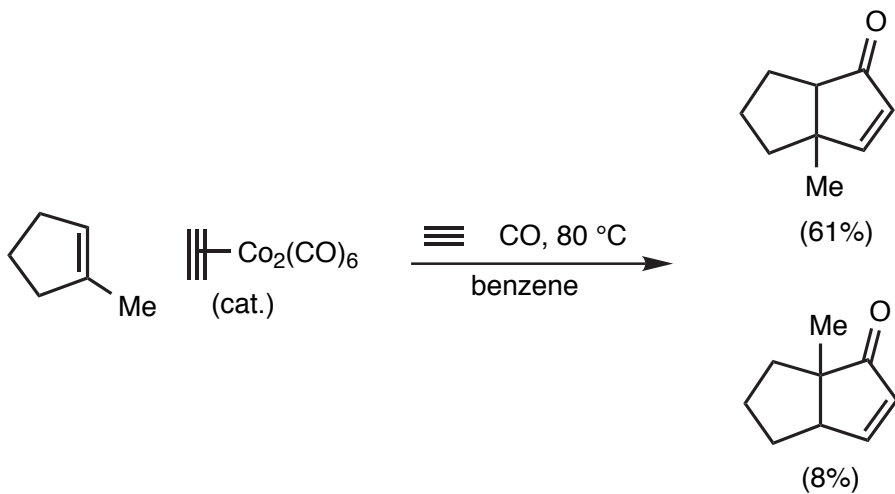
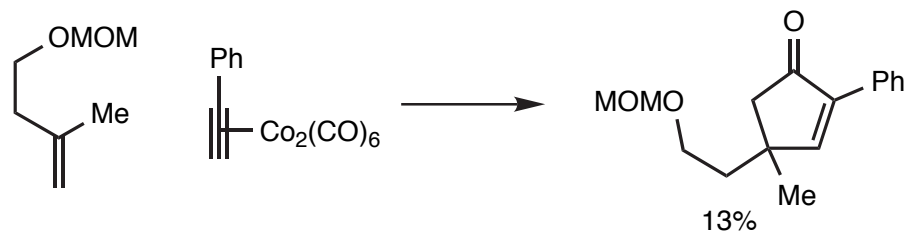
Rationale for alkyne regioselectivity:



Rationale for 1,1-disubstituted and trisubstituted alkene regiochemistry:

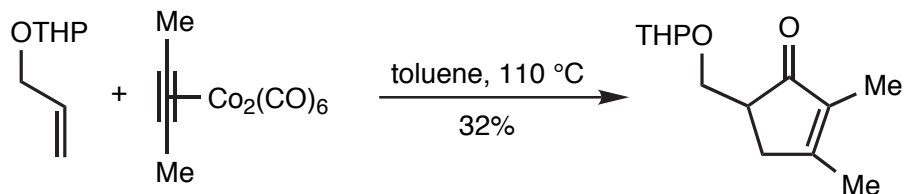


Krafft, M. E. *et al.* *J. Am. Chem. Soc.* **1991**, 113, 1693-1703

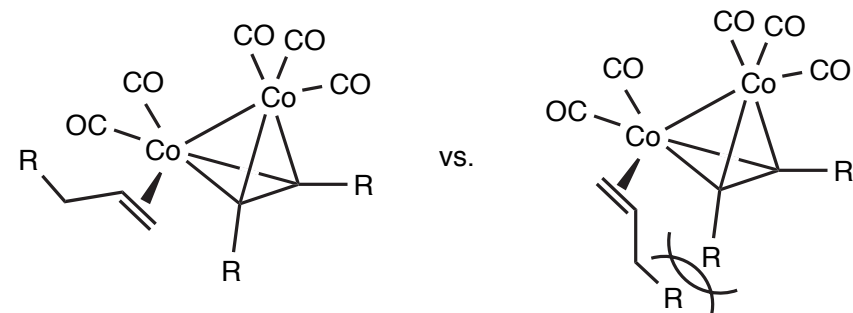
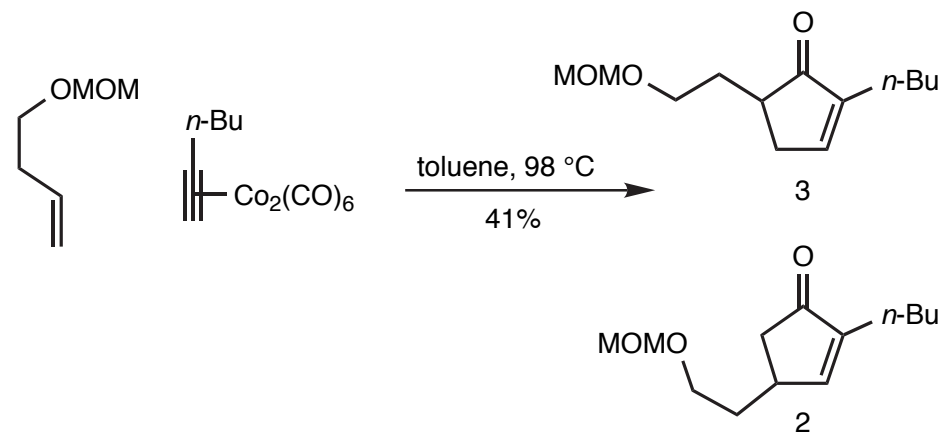
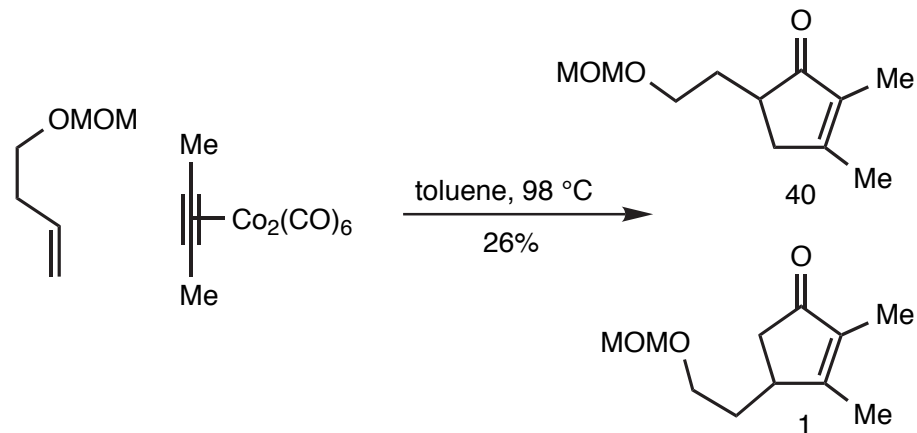
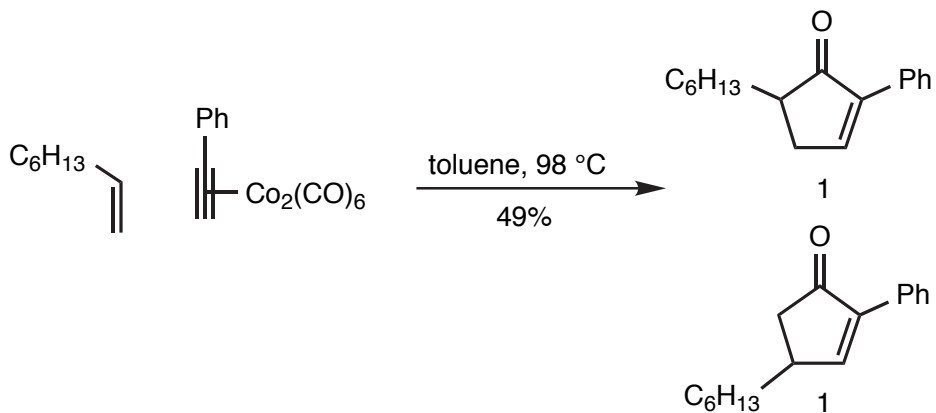
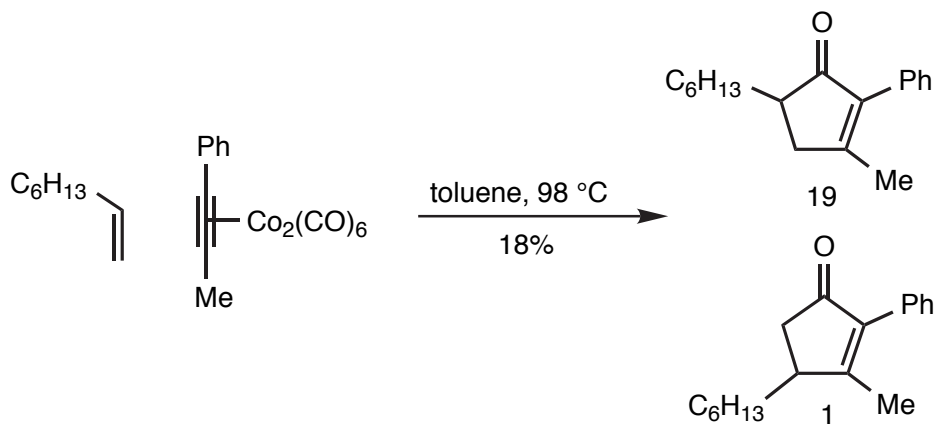


Intermolecular - Internal Alkynes:

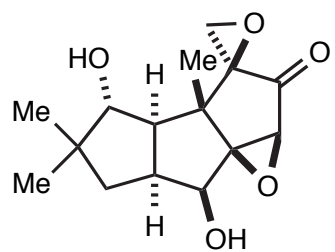
The use of internal acetylenes results in dramatic increases in alkene regiocontrol and diminished yields.



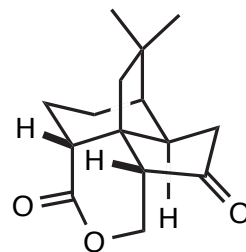
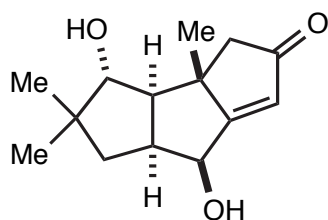
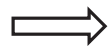
Billington, D. C.; Pauson, P. L. *Organometallics*, **1982**, 1, 1560



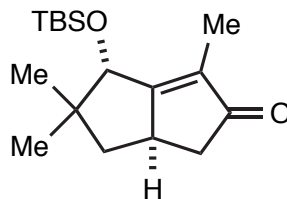
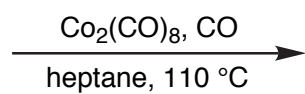
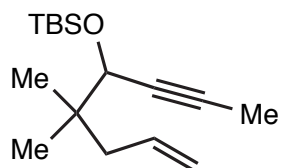
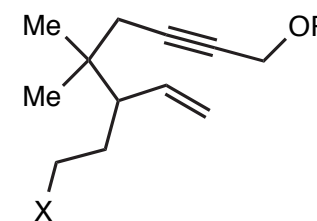
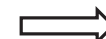
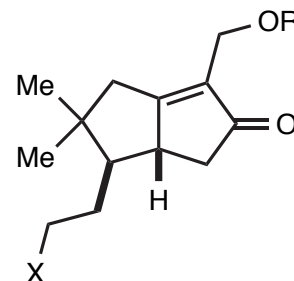
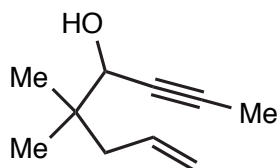
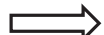
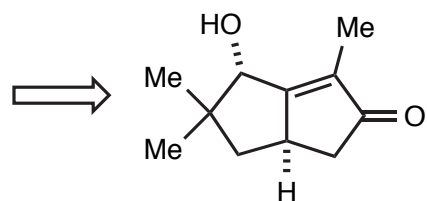
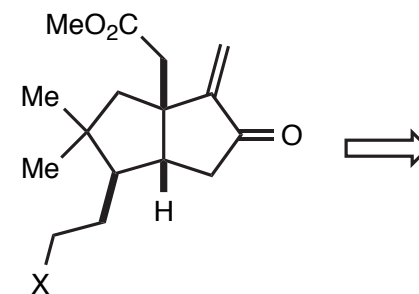
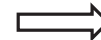
Krafft, M. E. *Tetrahedron Lett.* **1988**, 29, 999-1002



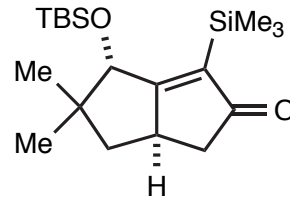
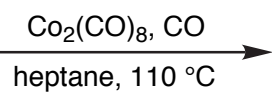
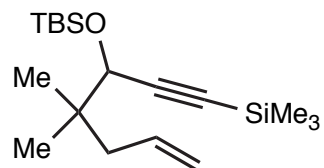
Coriolin



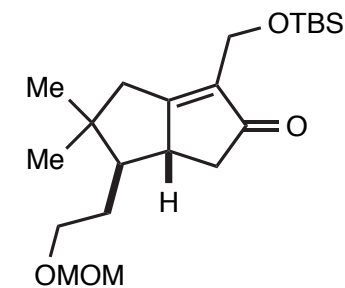
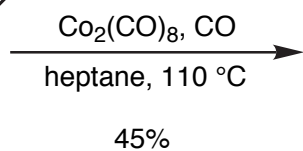
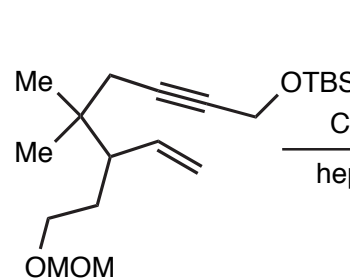
Quadrone



3:1,
50% isolated yield



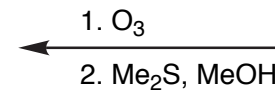
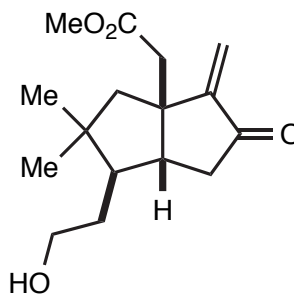
26:1,
79% isolated yield



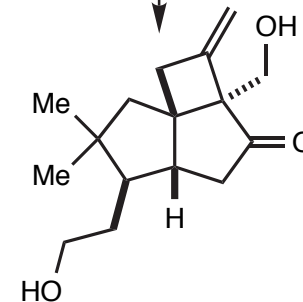
45%

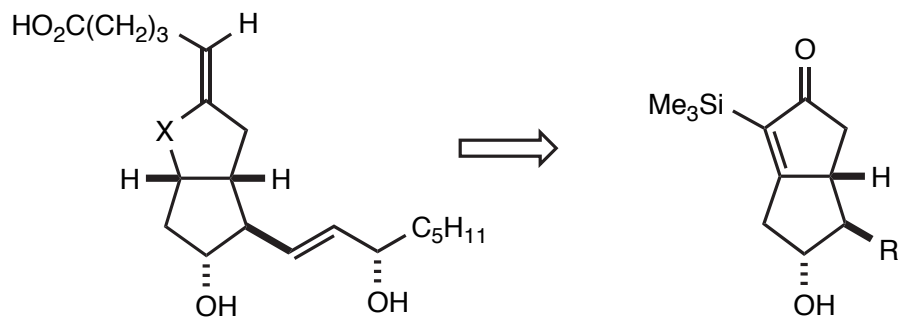
1. allene, $h\nu$
2. $\text{H}_2\text{SO}_4/\text{HBF}_4$

81%

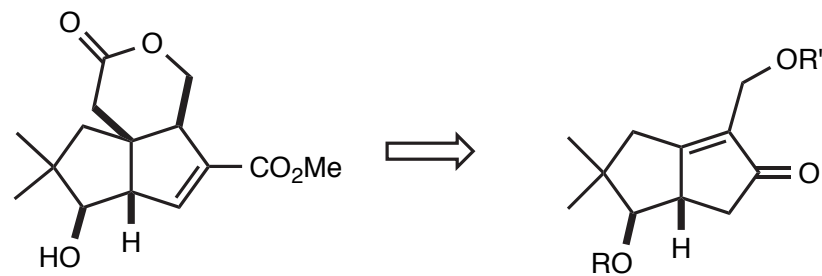
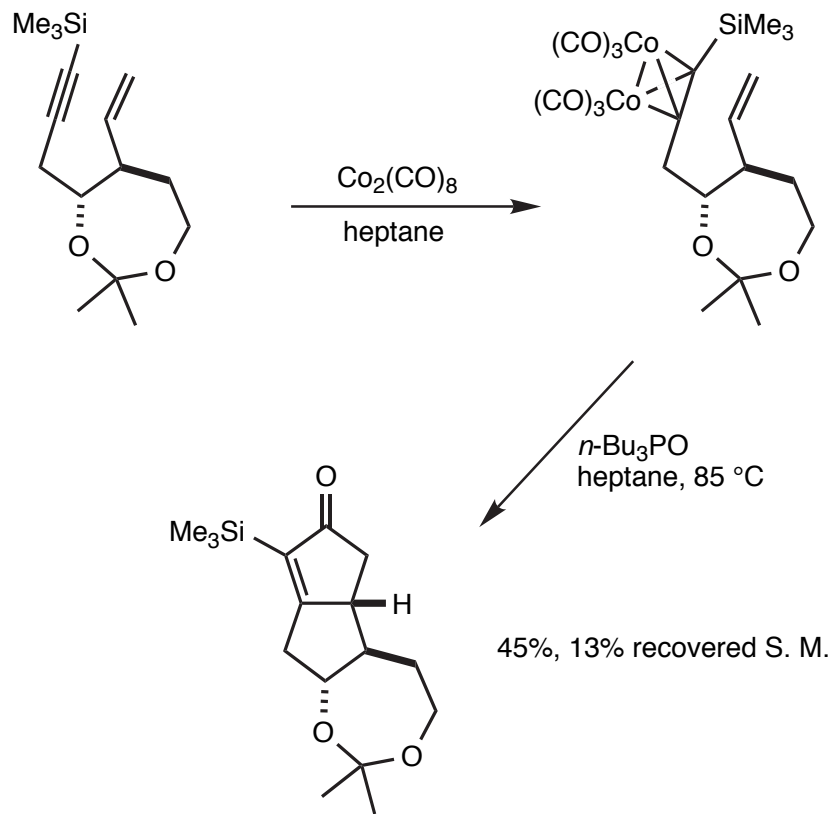


90%

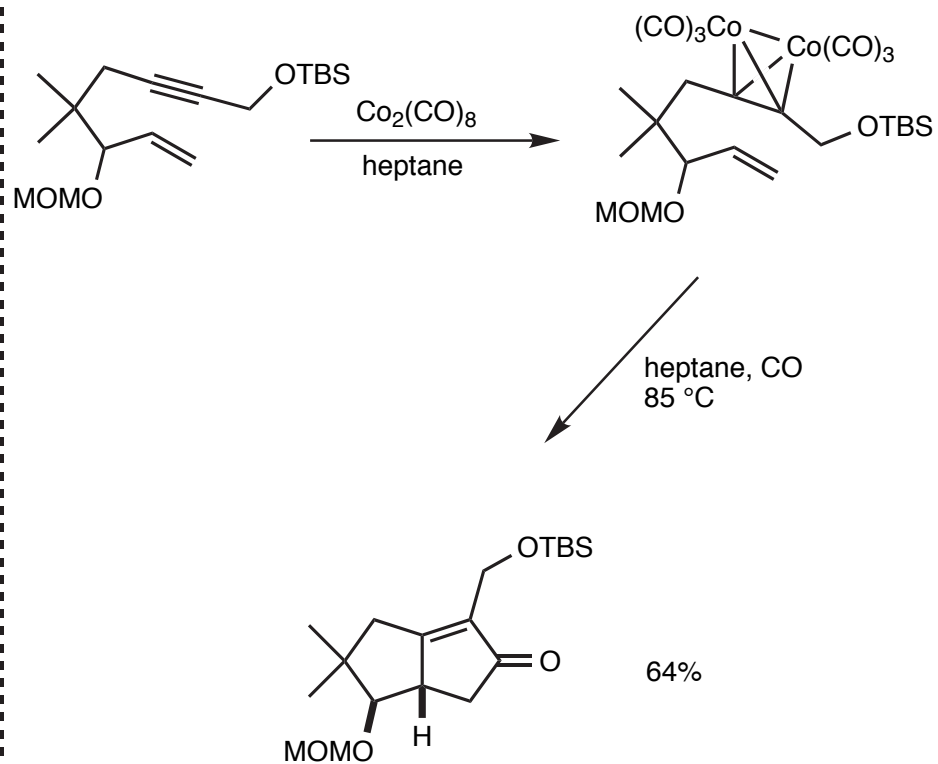




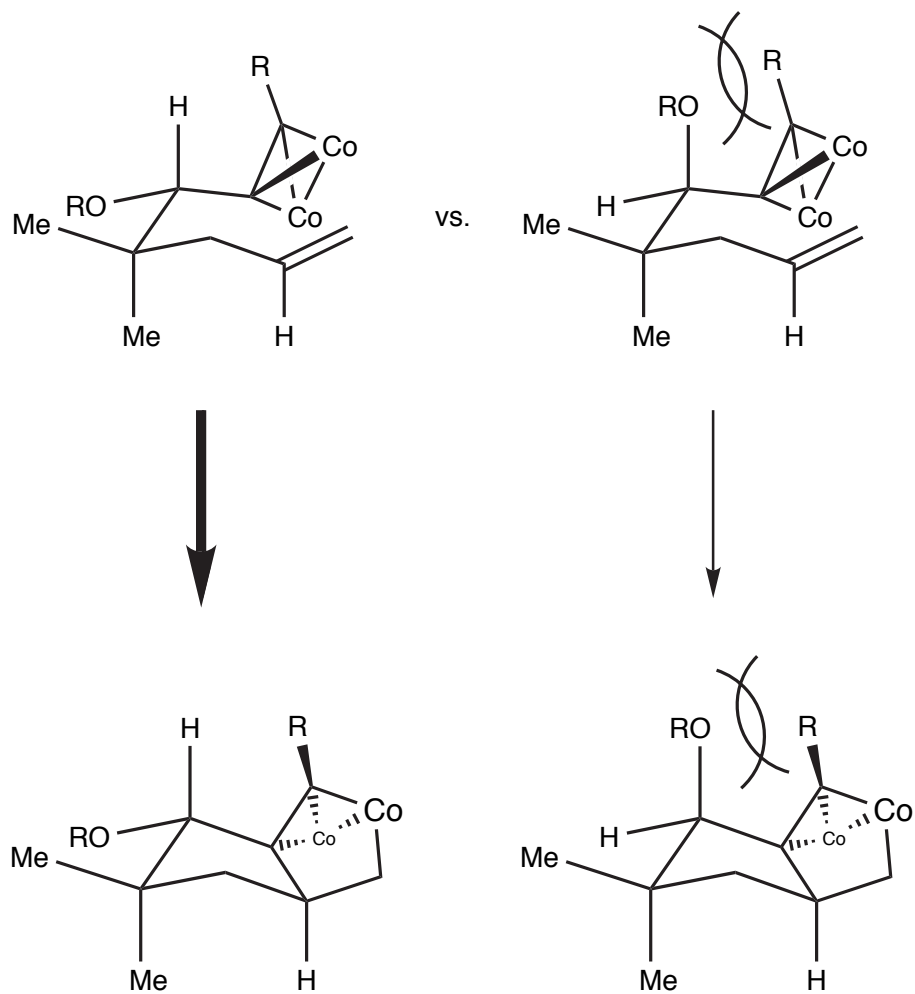
X = O, Prostacyclin (PGI₂)
X = CH₂, Carbacyclin



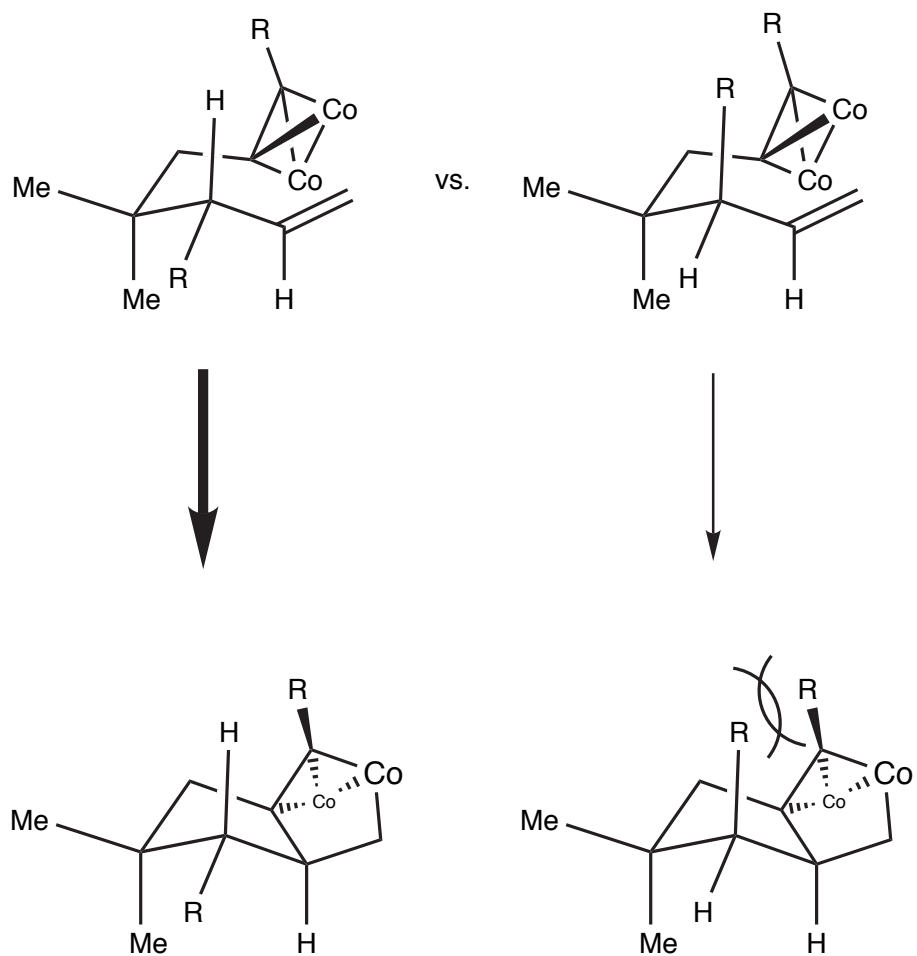
Methyl Deoxynor-
pentalenolactone H



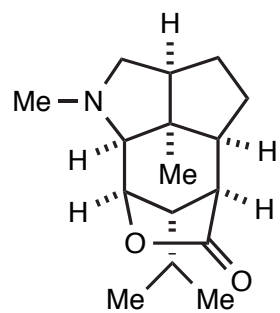
Magnus' Explanation for Selectivity - Propargylic:



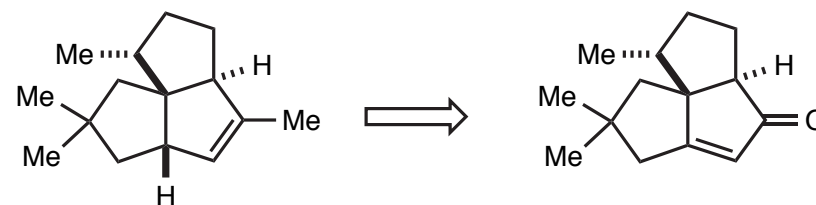
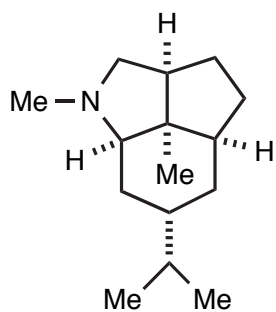
Magnus' Explanation for Selectivity - Allylic:



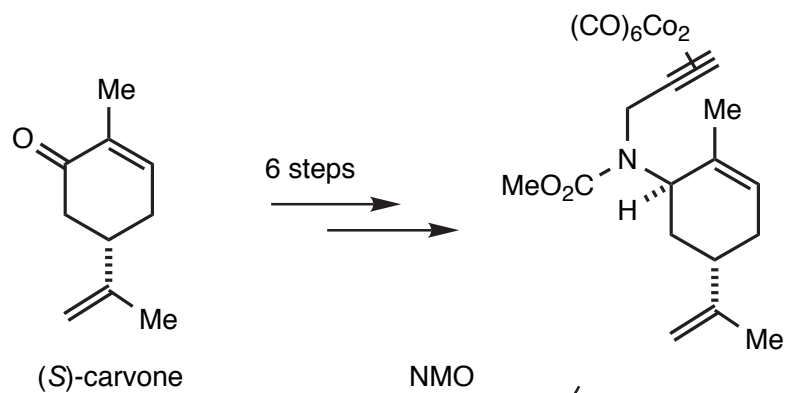
Other Notable Intramolecular Examples:



Dendrobine

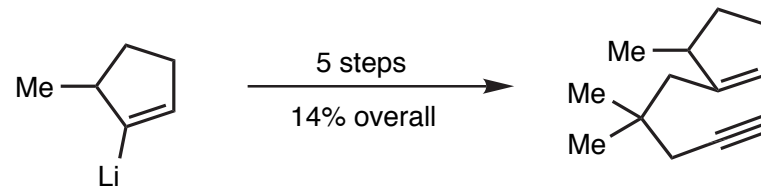
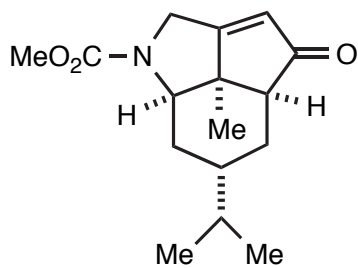


Pentalenene

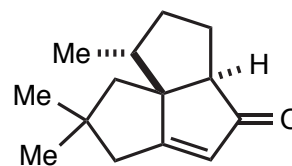


NMO
CH₂Cl₂
0 °C-R.T.

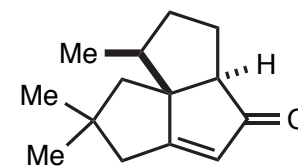
89%



Co₂(CO)₈
heptane, 110 °C

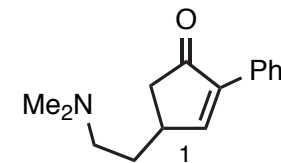
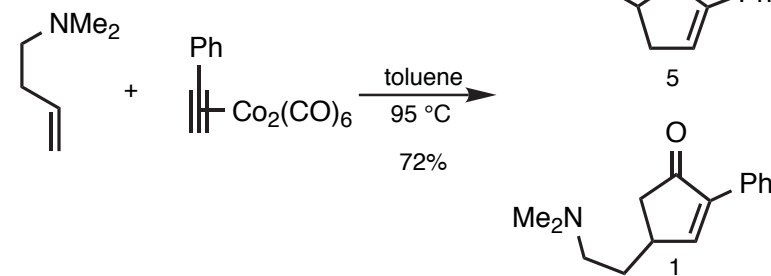
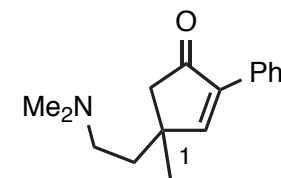
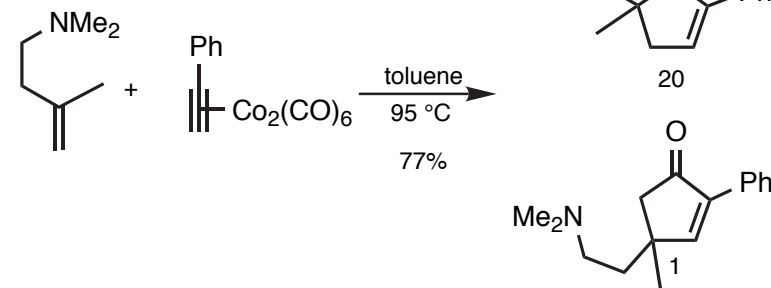
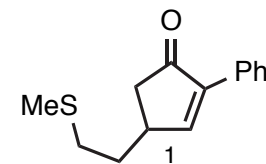
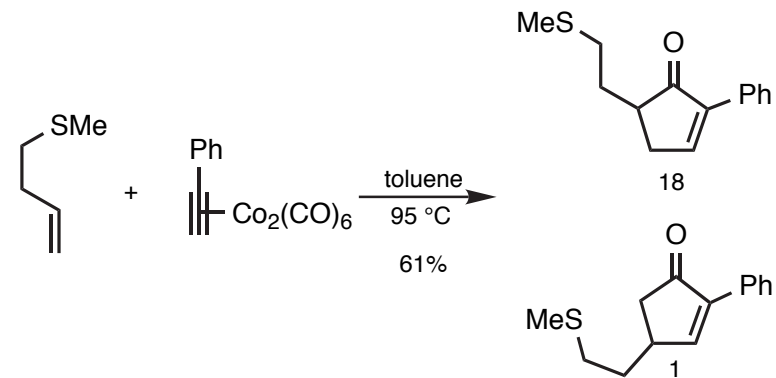
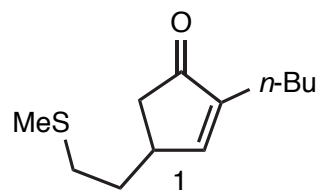
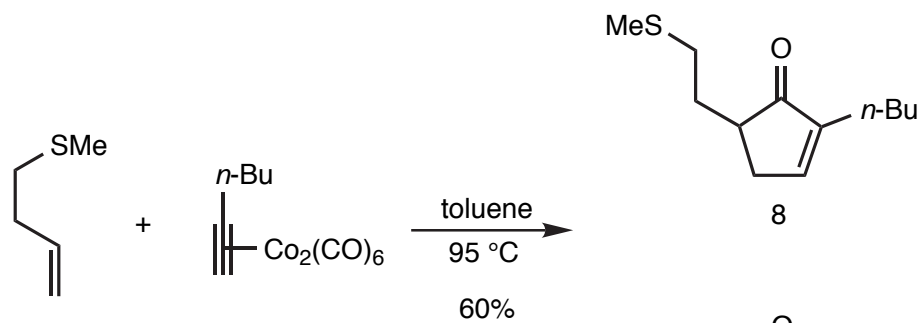
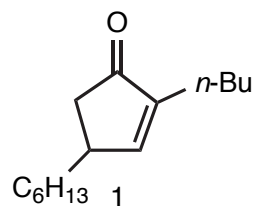
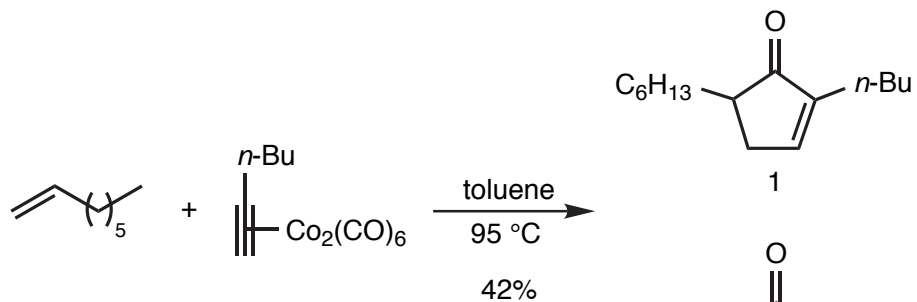


45%



6%

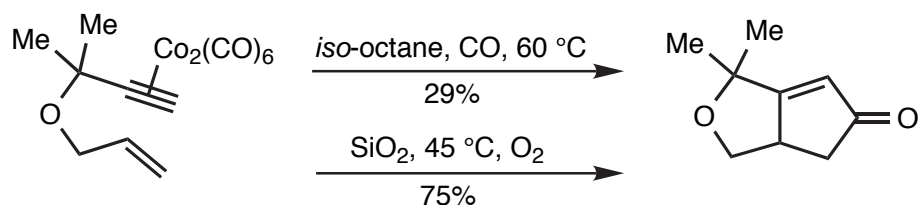
The Directed Pauson-Khand Reaction:



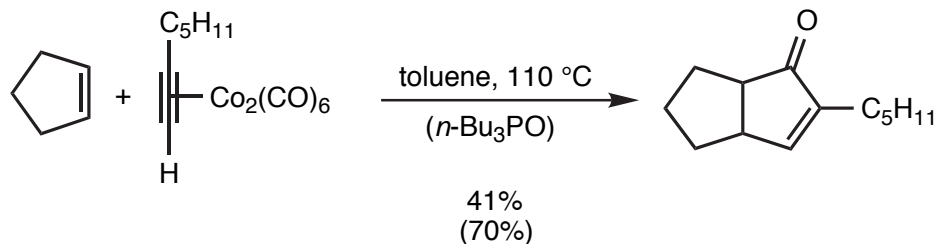
Improvements in Reaction Efficiency

1. **Ultrasound.** Sonication of the reaction mixture can lead to faster rates at lower temperatures.

2. **Solid supports.** Pre-adsorption of the cobalt complex onto one of several solid supports - silica, alumina, Zeolite NaX - can result in dramatic improvements in yields.



3. **Phosphine oxides.** Addition of phosphine oxides to the reaction mixture can result in higher yields.

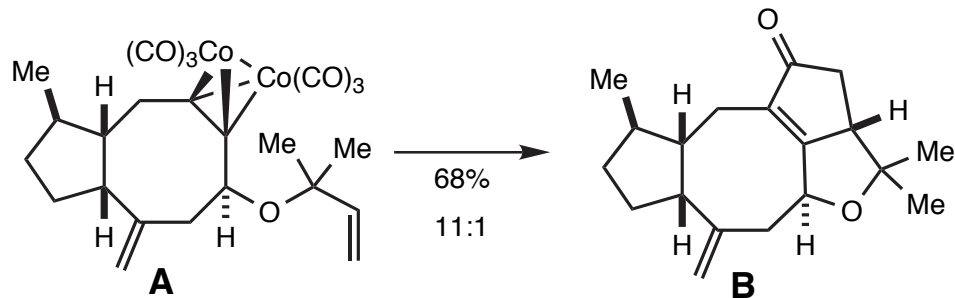
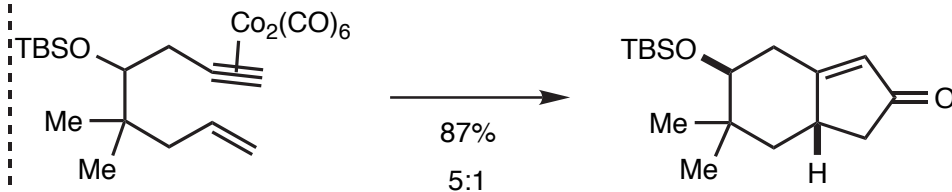
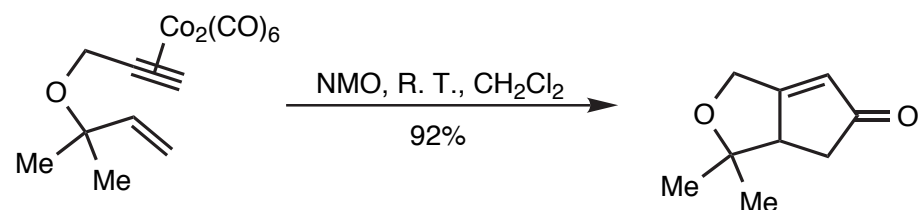


1. and 3. Billington, D. C.; Helps, I. M.; Pauson, P. L.; Thomson, W.; Willison, D. *J. Organometal. Chem.* **1988**, 354, 233-242

2. Simonian, S. O.; Smit W. A. *et al. Tetrahedron Lett.* **1986**, 27, 1245
 Smit, W. A. *et al. Tetrahedron Lett.* **1989**, 30, 4021

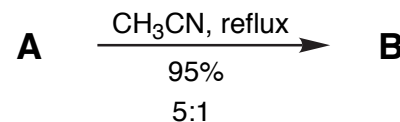
Improvements in Reaction Efficiency

4. **Amine Oxides.** The use of amine oxides in intramolecular Pauson-Khand reactions has been shown to consistently give higher yields at lower reaction temperatures.



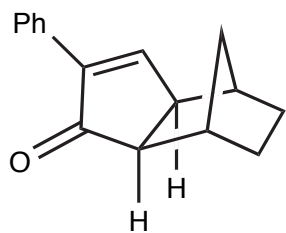
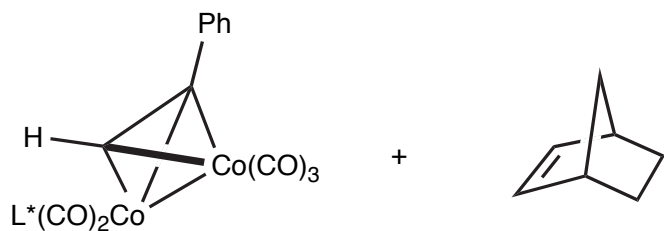
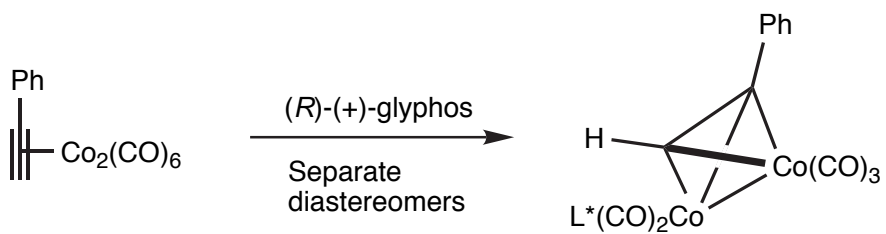
Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, 31, 5289-5292

5. **Acetonitrile.** The use of acetonitrile as solvent can lead to increased reaction efficiency at reduced temperatures.



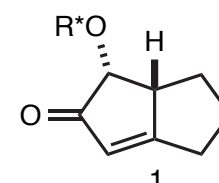
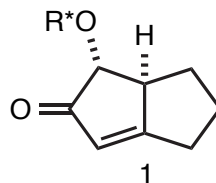
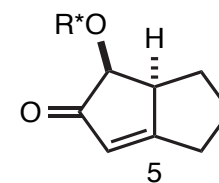
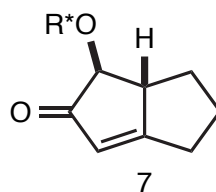
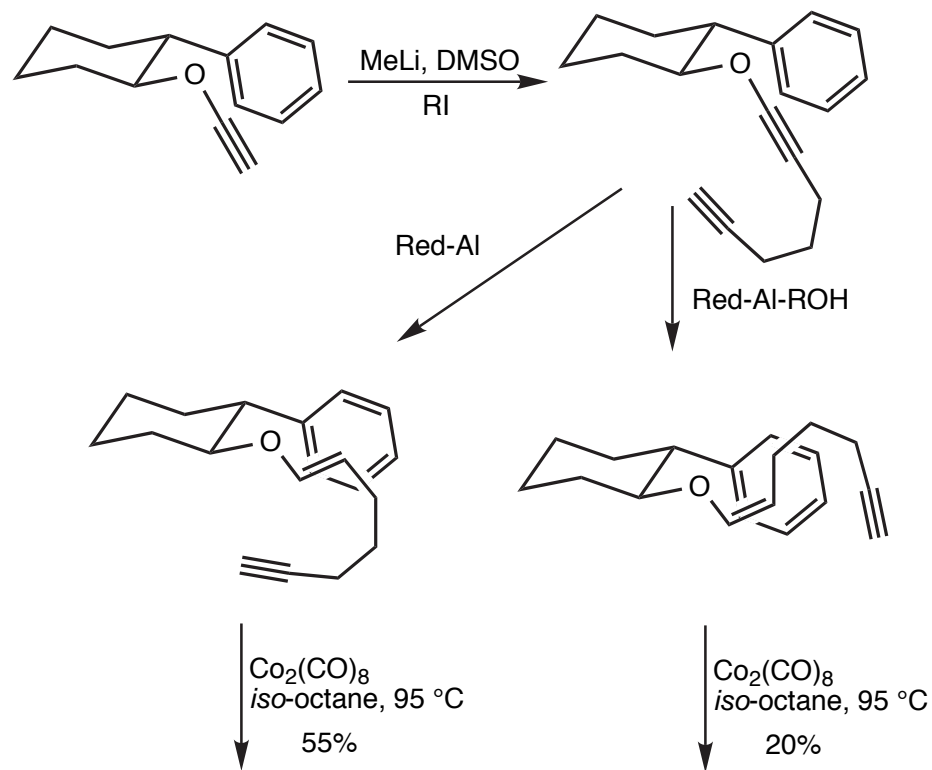
Shambayati, S. Personal communication

Enantioselective Pauson-Khand Reaction

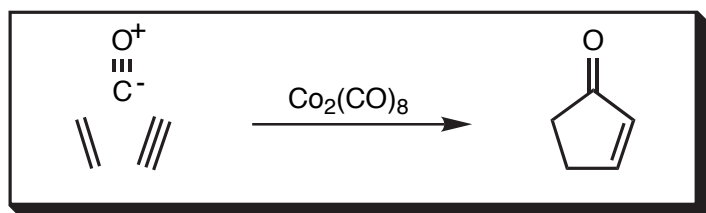


31%
100% ee

Chiral Auxiliary Controlled Pauson-Khand Reaction



The Pauson-Khand Reaction

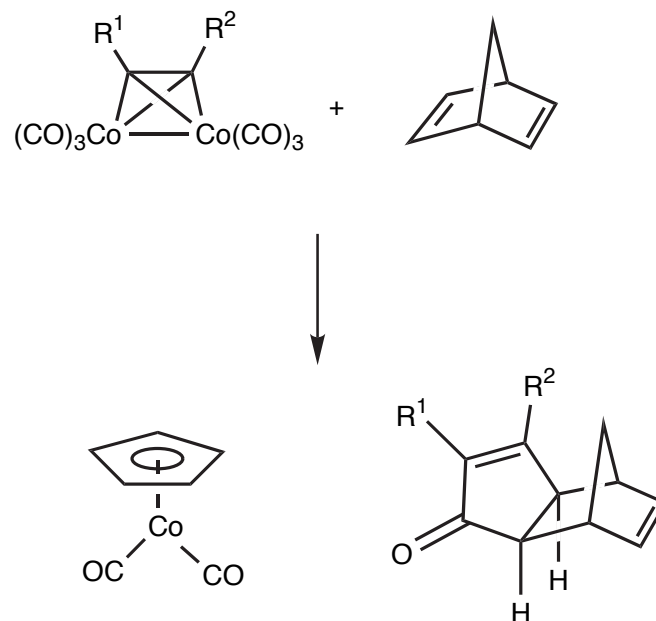


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Review: Schore, N. E. *Org. Reactions*, **1991**, 40, 1-90

Discovery:



Initial Observations:

1. The reaction works best with strained alkenes
2. The reaction is stereospecific, giving only *exo* products
3. The reaction is regioselective with respect to an unsymmetrical alkyne, placing the large substituent at C-2 of the cyclopentenone
4. The reaction can be run *catalytic* in cobalt (< 10 turnovers)

Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 977