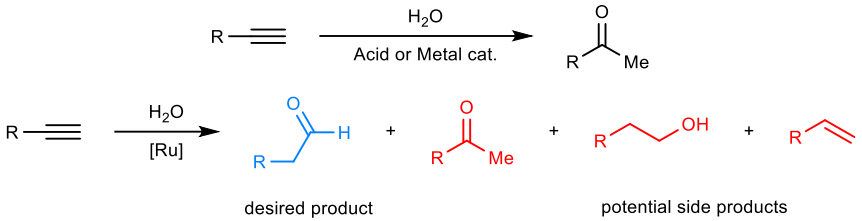
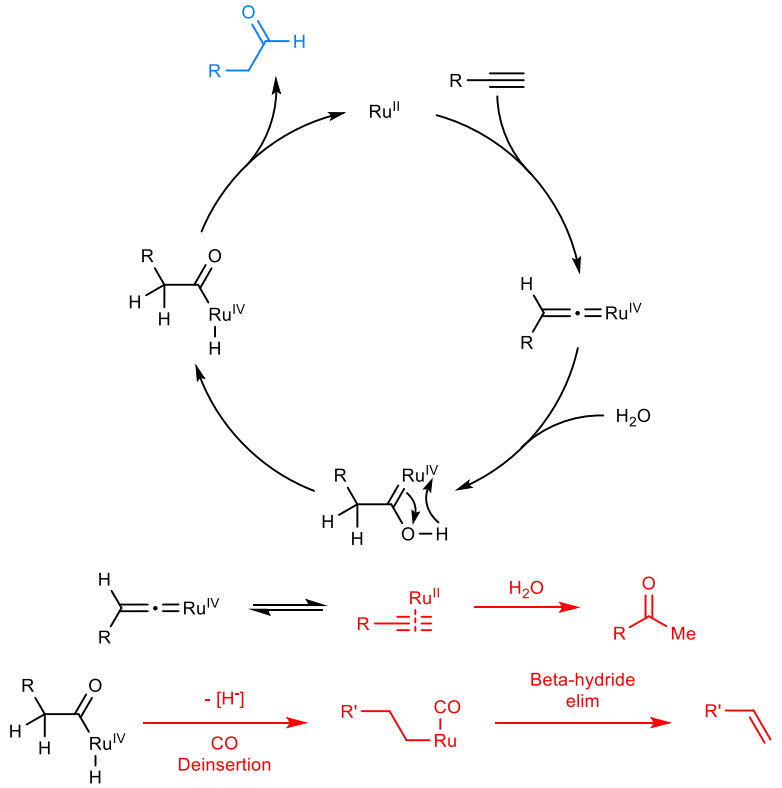
Ru-Cat. Anti-Markovnikov Alkyne Hydration

Background

Markovnikov vs. Anti-Markovnikov hydration

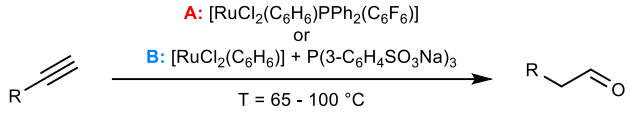




J. Org. Chem. 2015, 80, 17, 8604–8618 https://doi.org/10.1021/acs.joc.5b01220

Angew. Chem. Int. Ed.2014,53, 7892 –7895 https://doi.org/10.1002/anie.201404320

Initial Discovery – Wakatsuki (1998)



Cat. A:

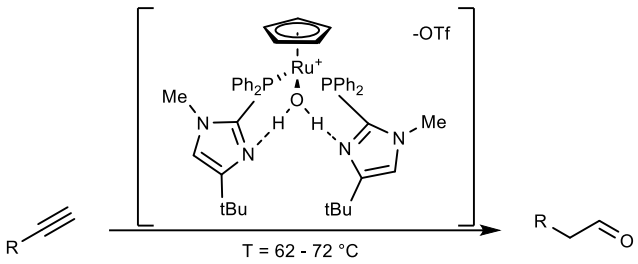
R = C_4H_9 -- 71%
R = $C_{10}H_{21}$ -- 50%
R = $(CH_2)_2OCH_2Ph$ -- 62%
R = Ph -- 0.7% (GC)
R = $(CH_2)_3Cl$ -- 60%

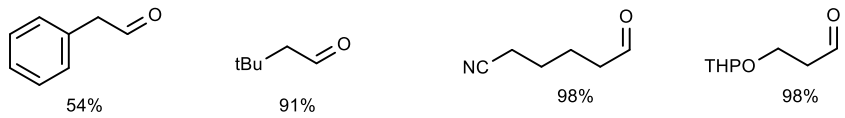
Cat. B:

R = C_6H_{13} -- 41%
R = Bn -- 2.2%

- Requires the use of electron poor phosphine ligands to promote ruthenium vinylidene formation
- Still necessitates elevated reaction temperature for good conversion
- Poor regioselectivity for aryl or benzyl substituted alkynes
  - Major side product is the methyl ketone from Markovnikov hydration

P,N-Ligands – Grotjahn (2001)





- Cationic ruthenium allows for lower reaction temperatures.
- More sterically hindered alkynes also tolerated!

Org. Lett., 3, 5, 2001 10.1021/ol0003937 *Angew. Chem. Int. Ed.* 2001, 40

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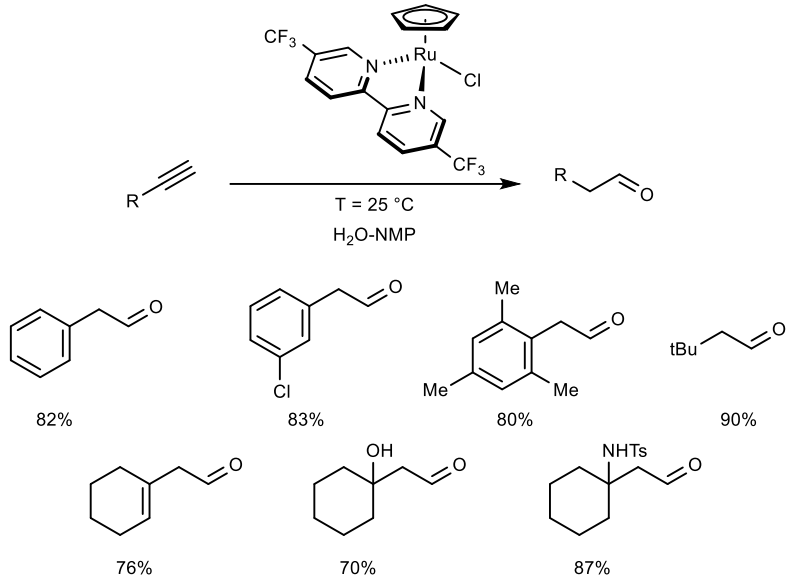
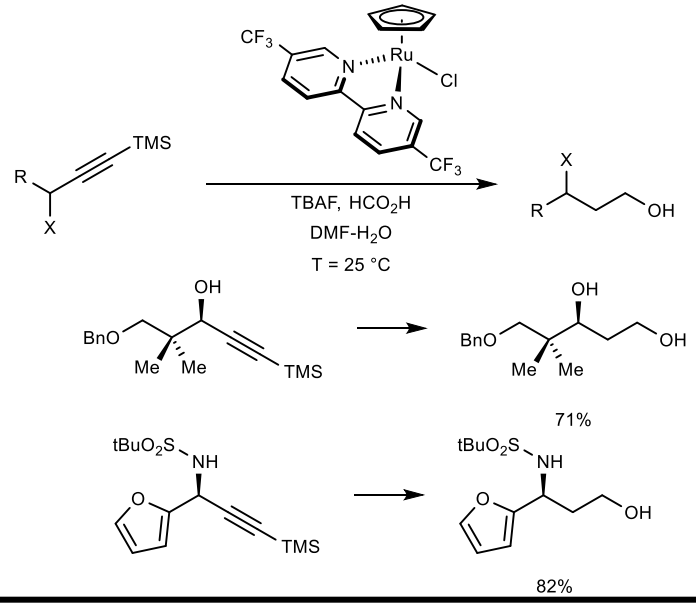
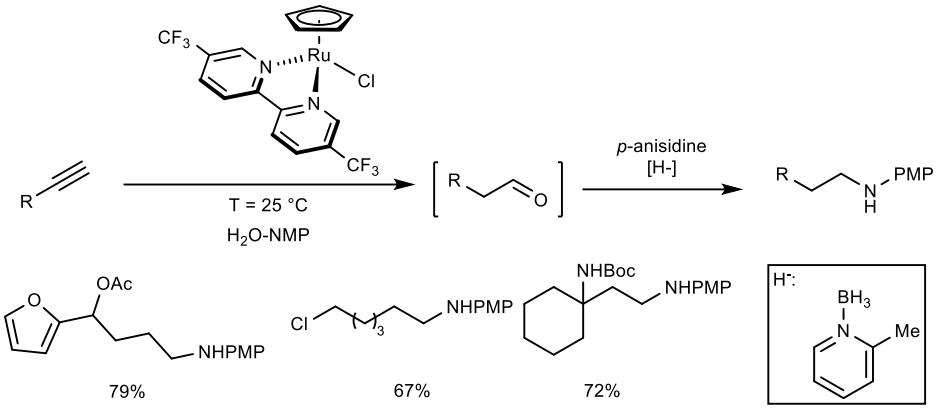
N,N-Ligands – Herzon (2014)

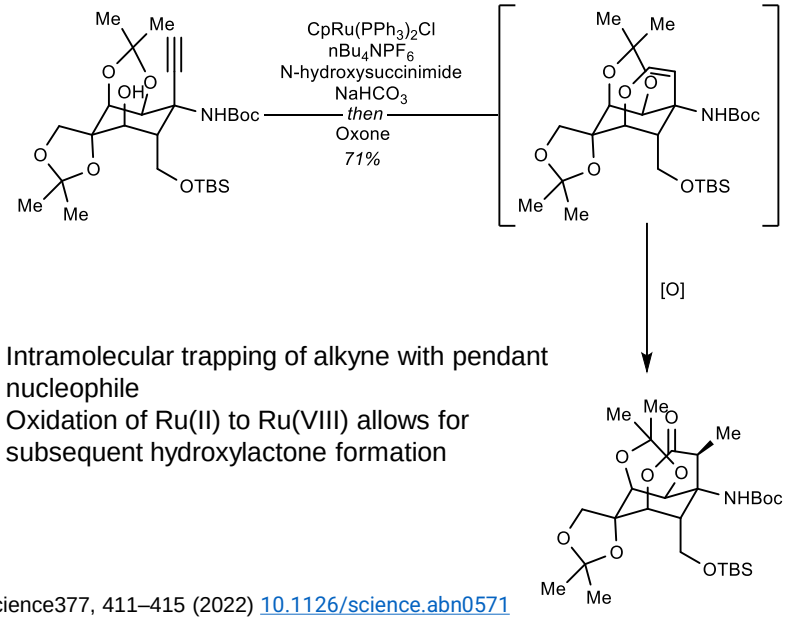






- N,N-ligands allow for even lower reaction temperatures
- Subsequent reduction of aldehyde yields alcohols or amines
- Subsequent oxidation yields acids (not shown here)

Synthetic Utility



- Intramolecular trapping of alkyne with pendant nucleophile
- Oxidation of Ru(II) to Ru(VIII) allows for subsequent hydroxylactone formation

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