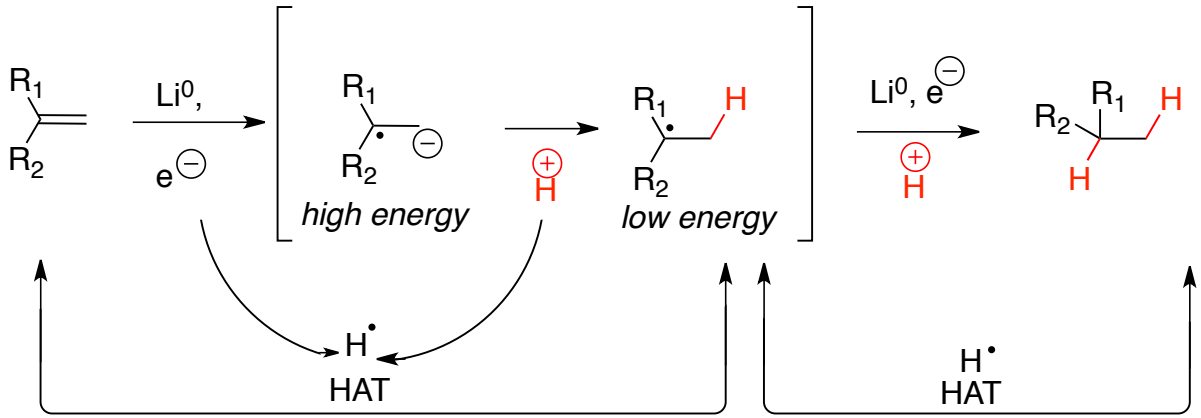
Simple, Chemoselective Hydrogenation with Thermodynamic Stereocontrol

Kotaro Iwasaki, Kanny K. Wan, Alberto Oppedisano, Steven W. M. Crossley and Ryan A. Shenvi

JACS, **2014**, 136, 1300-1303

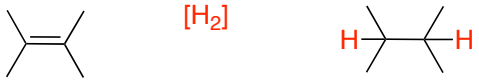


Steph McCabe

Wipf Group Current Literature

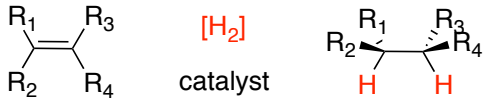
15th February 2014

Quick Overview of Hydrogenation



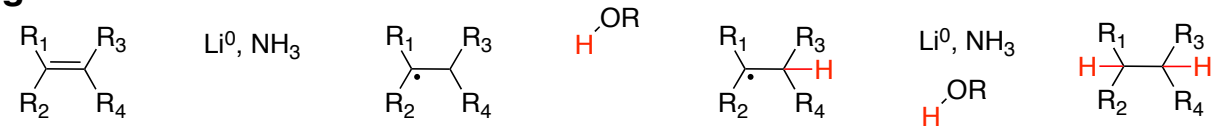
- Formal addition of dihydrogen to alkenes to give alkanes
- Reaction is strongly exothermic (high activation barrier)

Transition Metal Catalysed Hydrogenation (**Homogenous** and **Heterogeneous** forms):



- Overall *syn*-addition with delivery of dihydrogen to the least hindered face of olefin
- Very sensitive to substitution on olefin (mono-> di-> tri-> tetrasubstituted alkenes)
- Good functional group tolerance

Dissolving Metal Reduction:

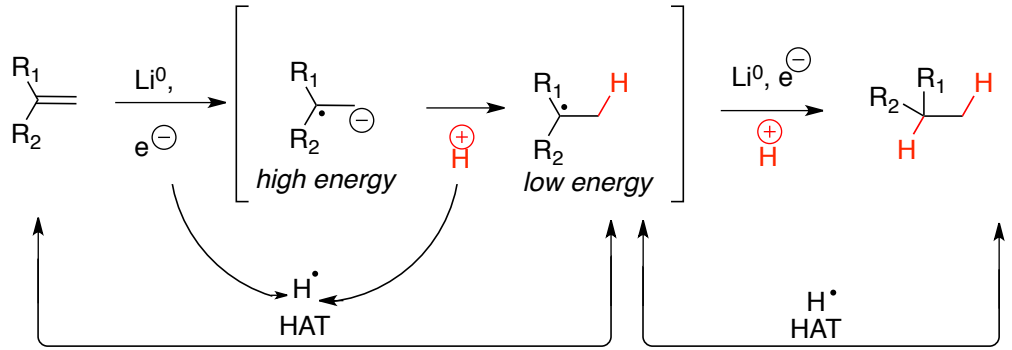


- thermodynamic product favoured
- Conjugated olefins and enones are reduced
- Isolated olefins are generally stable to dissolving metal reductions
- Poor functional group tolerance!

Barton, D. H. R.; Robinson, C. H., *J. Chem. Soc.,* **1954**, 3045; Stork, G.; Darling, S. D.*, J. Am. Chem. Soc.,* **1960**, 82, 1512; Whitesides, G. M.; Ehmann, W. J., *J. Org. Chem.,* **1970**, 35, 3565

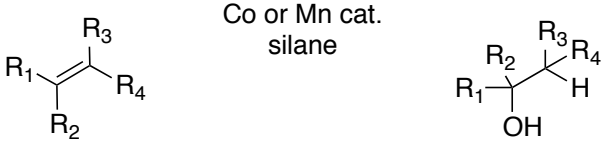
THIS WORK

A LONG STANDGING CHALLENGE is hydrogenation of alkenes to the thermodynamic product when steric constraints of the substrate direct delivery to the less hindered face of the olefin.

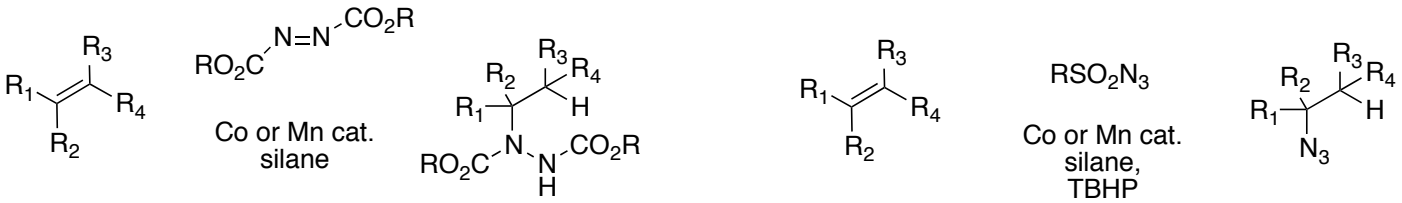


Literature precedent

- ***Mukaiyama***

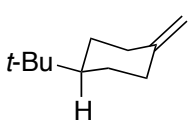


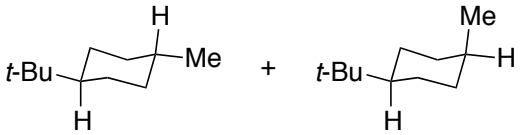
- ***Carreira***



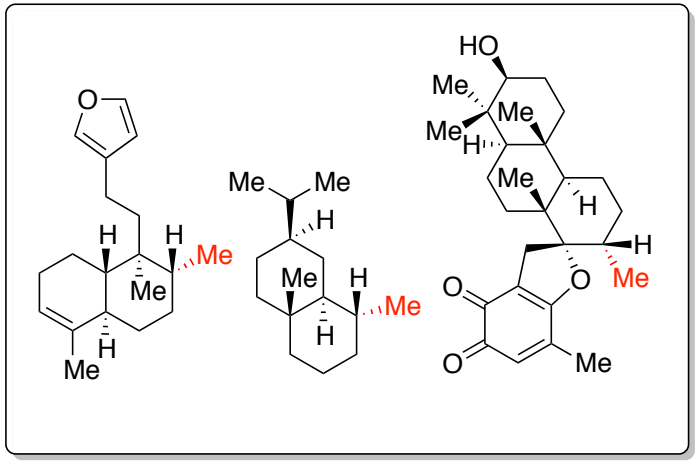
Mukaiyama, T., Yamada, T., *Bull. Chem. Soc. Jpn.*, **1995**, *68*, 17
Waser, J., Gaspar, B., Namnu, H., Carreira, E. M., *JACS*, **2006**, *128*, 11693

DIVERGENT STEREOCONTROL

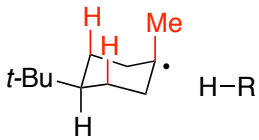


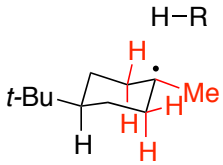


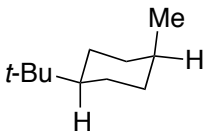
thermodynamic *kinetic*



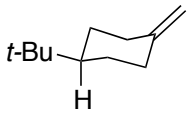
conditions	Yield	**1:2**
Homogenous: 5 mol% $RhCl(PPh_3)_3$, 1 atm H_2, PhH, 18 °C	100	32:68
Heterogeneous: 9 mol% PtO_2, 2 atm H_2, AcOH	100	21:79
Pericyclic: N_2H_4, O_2 EtOH, 55 °C	ND	49: 51
Dissolving metal: Li^0, EDA, 35 °C	ND	95:5
Radical: 10 mol% $Mn(dpm)_3$, 1.0 equiv $PhSiH_3$, 1.5 equiv TBHP, *i*-PrOH, (0.5 M), 22 °C, 1h	86%	84: 16
or: 10 mol% $Co(dpm)_3$, 1.0 equiv $PhSiH_3$, 1.5 equiv TBHP, *i*-PrOH, (0.5 M), 22 °C, 1h	69%	86:14

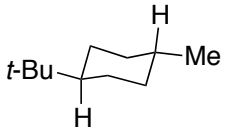






minor

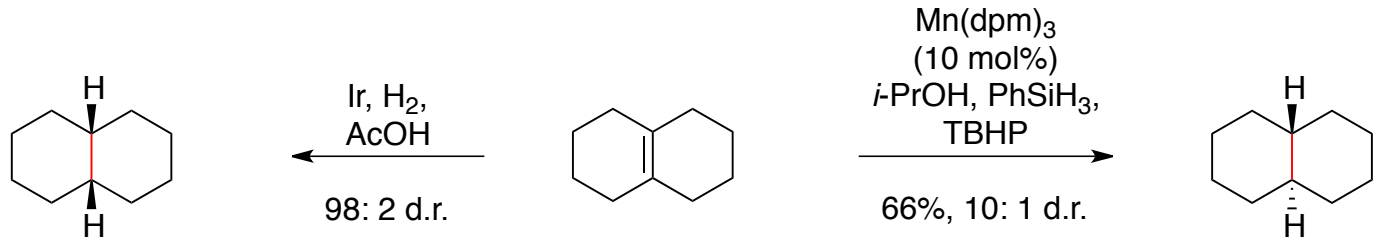


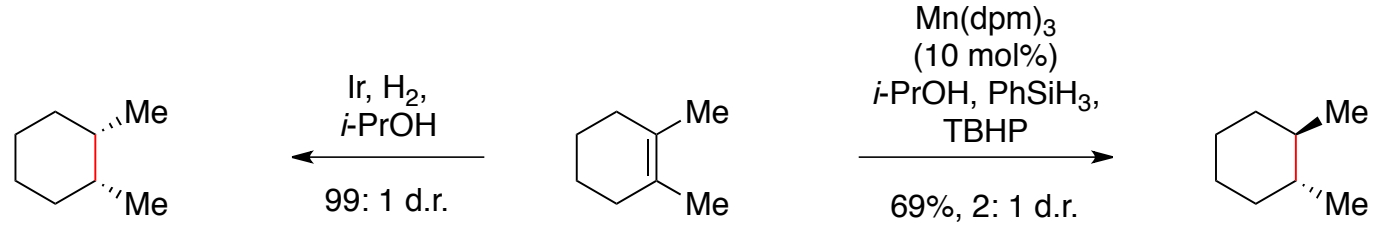


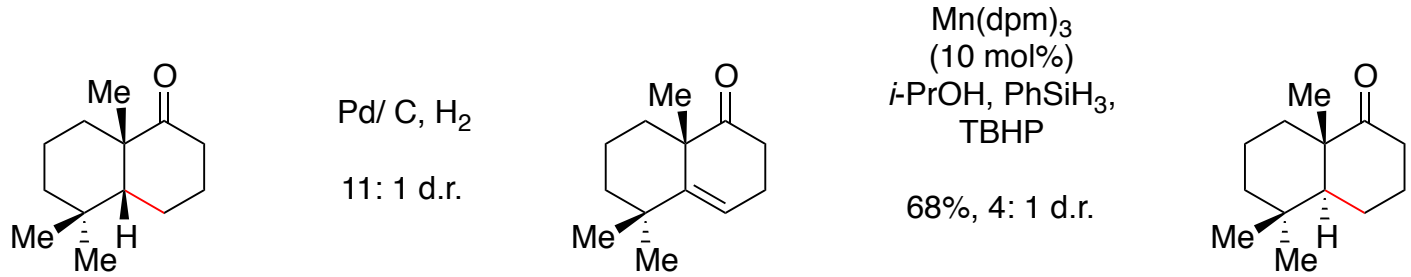
major

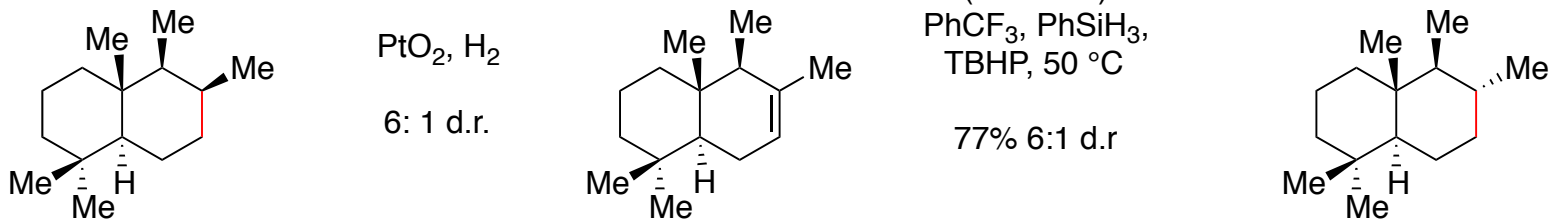
Damm, W., Giese, B., Hartung, J., Hasskerl, T., Houk, K. N., Huter, O., Zipse, H., *JACS*, **1992**, *114*, 4067

DIVERGENT STEREOCONTROL – polycyclic systems are also hydrogenated to the thermodynamic product









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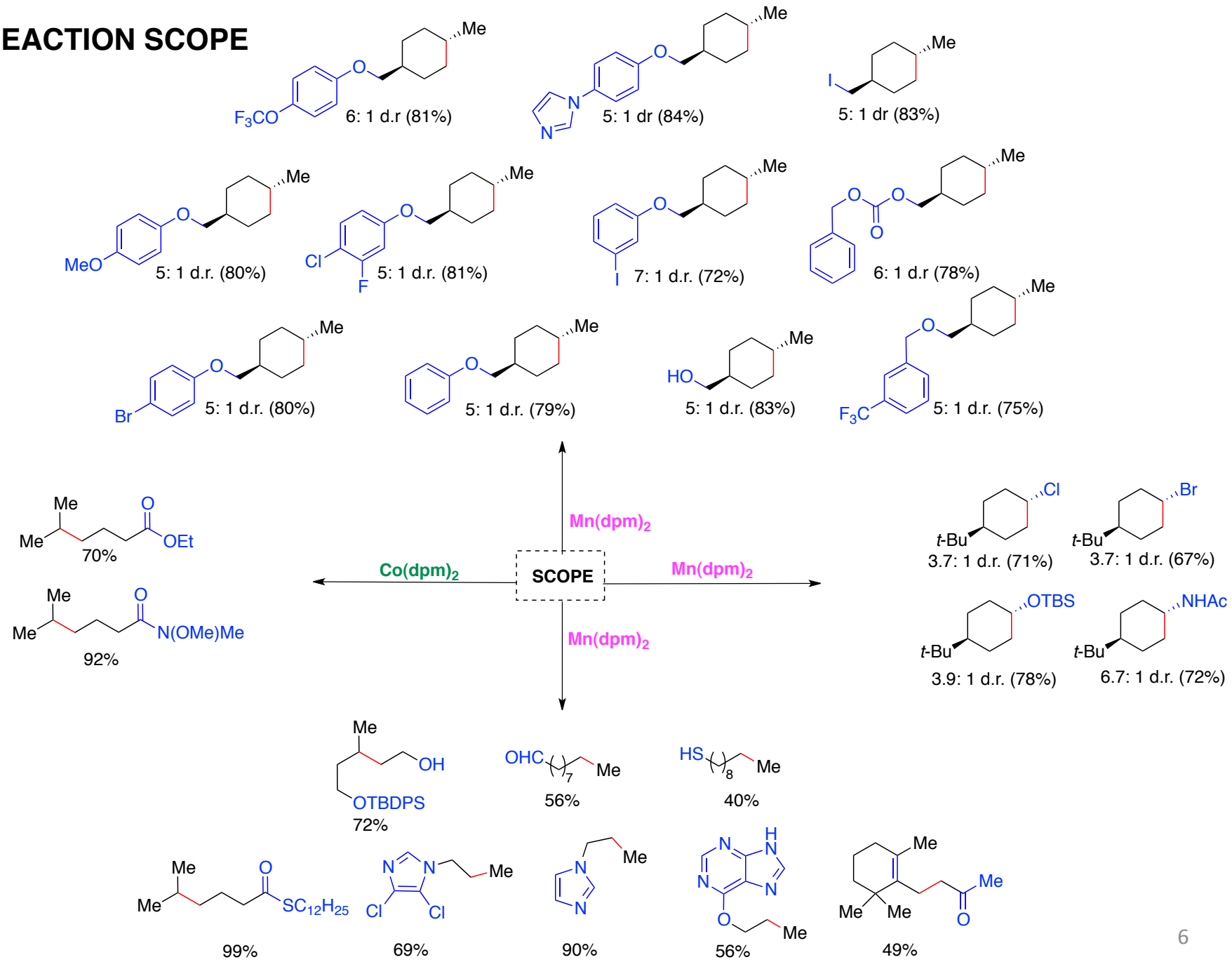
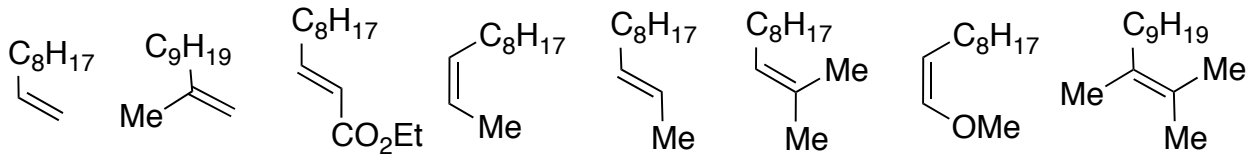
REACTION SCOPE



CONCLUSIONS AND COMMENTS

- Orthogonal stereoselectivity to transition metal based hydrogenation
  - Broad scope (reduction of halogenated alkenes)

decreasing rate of consumption



- Mechanism (in the works)?
- Asymmetric Variant (in the works)?