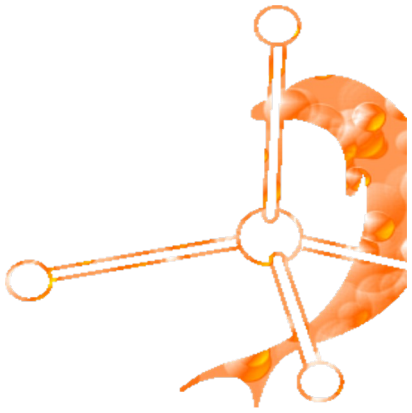
J.M. Hawkins

Pfizer, Groton (USA)



ISCHIA PORTO (NAPOLI), ITALY
HOTEL CONTINENTAL TERME
SEPTEMBER 18-23, 2004

Asymmetric Catalysis in the Pharmaceutical Industry

Angew. Chem. Int. Ed. **2004**, *43*, 3224

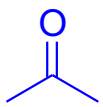
Economics of (Asymmetric) Catalysts

- Consider the total transformation
- Speed to implement & robustness
- Freedom to operate
- Overall costs
- Benefits

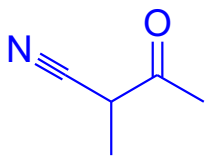
Joel Hawkins
Sept. 20, 2004

Economics of Asymmetric Catalysis

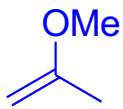
- Consider the total transformation, e.g.
  - how complex is the enolate synthon for an aldol?



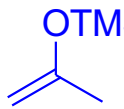
$Ba(OiPr)_2$ / BINOL-Me



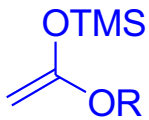
Rh(I) / TRAP



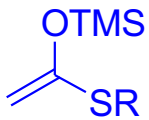
Ti(tridentate-BINOL)$_2$



Sn(II) / diamine
Pd(II) / BINAP



Sn(II) / diamine
Cu(II) / bisheterocycle
B / sulfonamideacid



Sn(II) / diamine
Ti(IV) / BINOL
Cu(II) / bisheterocycle

  - What is the molecular weight of the oxidant and what are the byproducts?

O_2 H_2O_2 TBHP NMO IO_4^- $Fe(CN)_6^{3-}$

  - Asymmetric hydrogenation ideal here: H_2

Economics of Asymmetric Catalysis

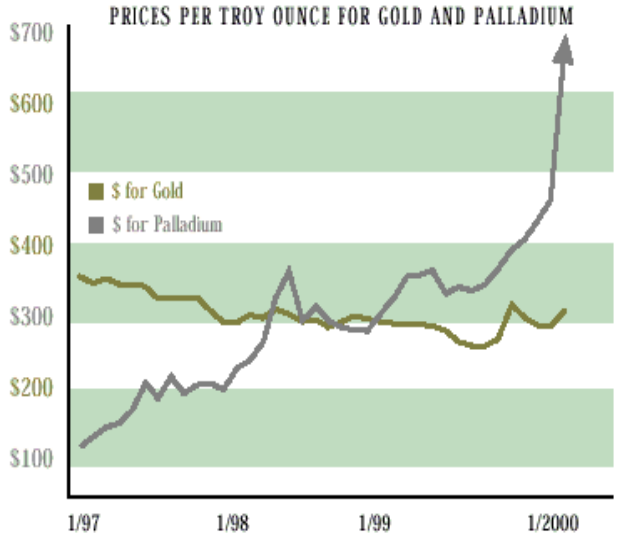
- Speed to implement?
  - the first successful route can gain momentum
    - sourcing raws for routes with proven track records
    - setting impurity profiles
    - setting final form
- Robustness is key
  - translation from lab to scale
  - needs to work every time on scale
  - often at odds with S/C ratio
    - will stalled reactions complete with additional catalyst?

Economics of Asymmetric Catalysis

- Freedom to operate
  - to run internally
  - to outsource to multiple vendors
  - limits to sole sources or royalties tied to % of sales would be major issues
  - FTO a key distinguishing feature between asymmetric catalysts

Costs of Asymmetric Catalysts

- Ligand
  - cheap and available vs. complex multistep
  - not only cost but ease of accessing on large scale quickly without hitches



- Metal
  - cost and availability
  - dependant on geopolitical events?

- Royalties
  - how easily can this cost be established early in the route development process?

Costs of Asymmetric Catalysts

- Ligand
- Metal
- Royalties

- Cost lowered by increased tunover
  - as long as it does not affect robustness
- Throughput directly related to concentration

Benefits of Asymmetric Catalysts

- Increased yield vs. resolution
- Increased *capacity* utilization
- Decreased waste
- Green (if it's accessible)