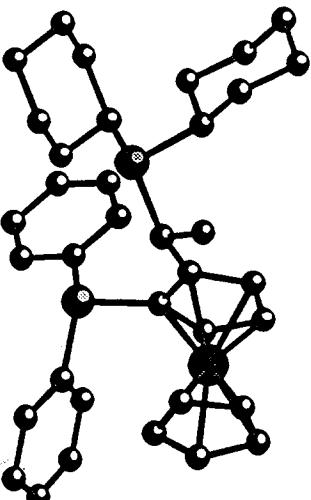
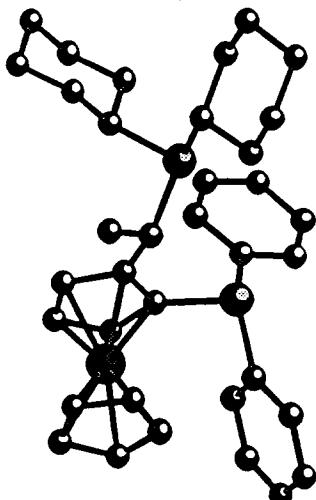


Why Ferrocenyl Ligands in Asymmetric Catalysis

A. Togni, ETH



- A Ligand Construction Kit
Synthesis and Properties
- Rh-Catalyzed Hydrogenation
and Hydroboration
- Pd-Catalyzed Hydrosilylation
of Olefins
- Ir-Catalyzed Hydroamination
of Olefins
- Synthesis and Applications
of Dendritic Derivatives

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Dr. Marie C. Soares
Dr. Pascal Steffanut
Dr. Ivo Steiner
Stefan Zürcher

Prof. P.S. Pregosin
Renzo Salzmann
Gerald Trabesinger

} 2D NMR-studies

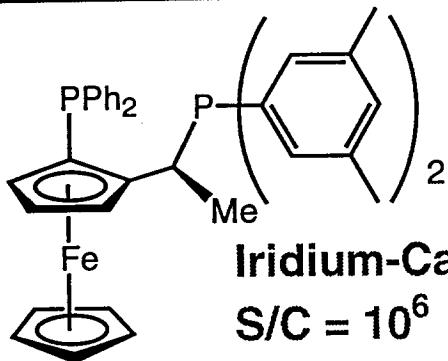
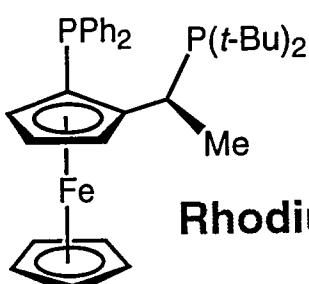
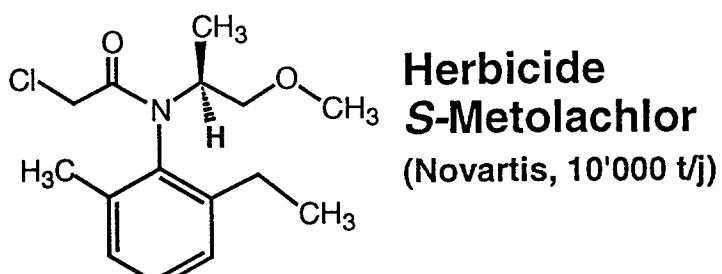
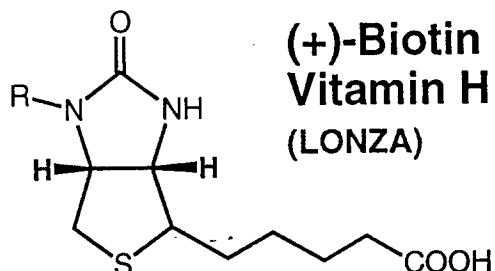
Dr. Volker Gramlich
Dr. Michael Wörle
Arianna Martelletti
Dr. Fabio Zürcher

} X-ray crystallography

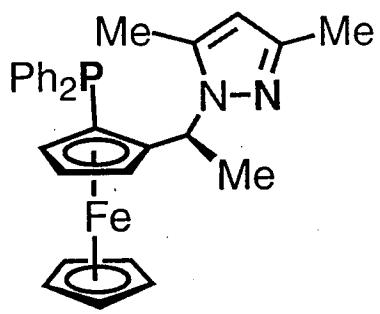
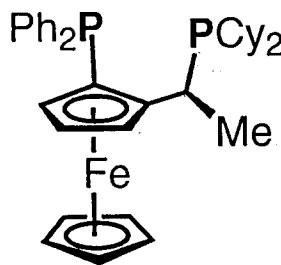
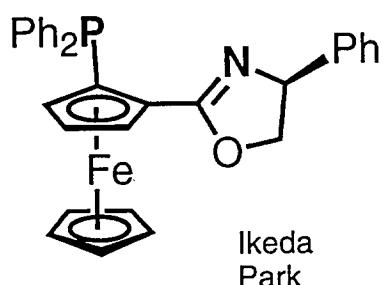
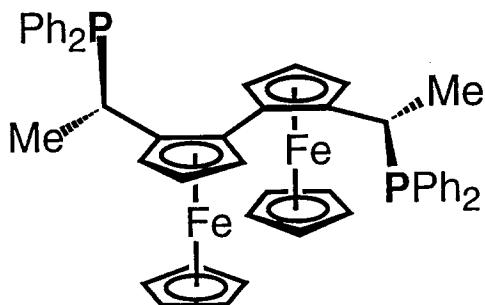
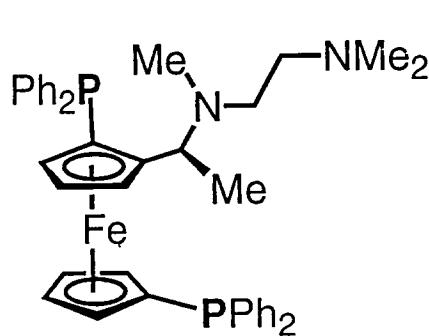
Dr. Peter Blöchl, IBM Research Laboratories
Dr. Pierluigi Barbaro, CNR Firenze, Italy

ETH
Swiss National Science Foundation
Novartis Ltd. (former Ciba-Geigy Ltd.)
LONZA Ltd., Givaudan Roure Ltd.

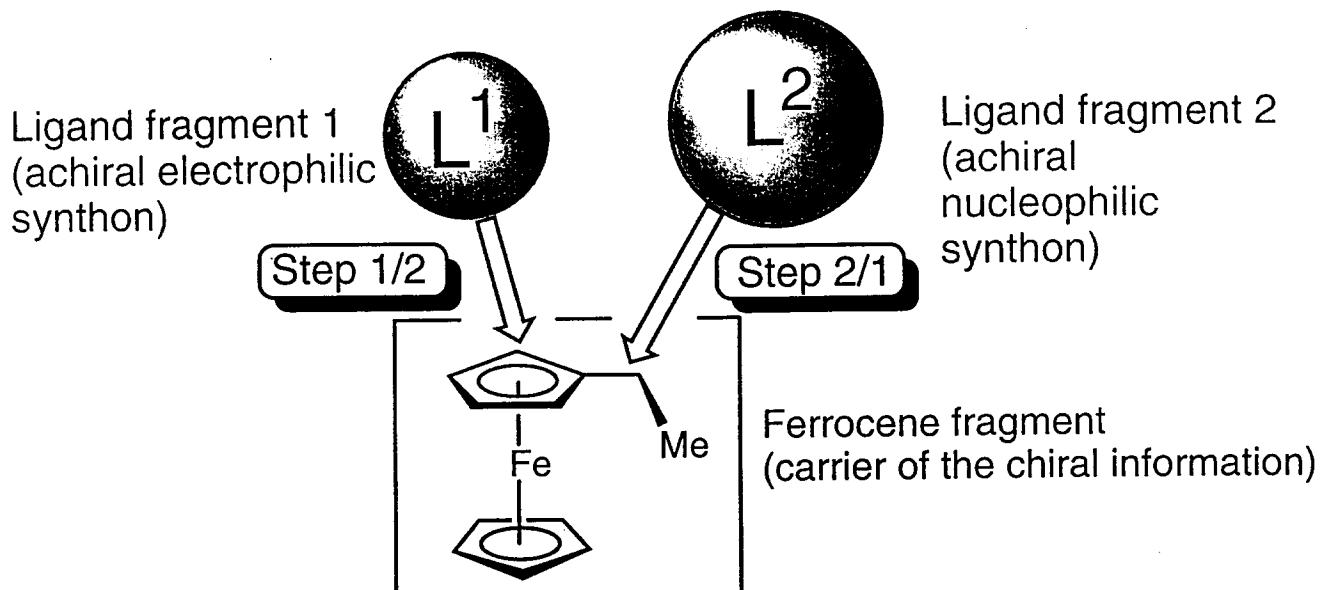
Production-Scale Application of Ferrocenyl Ligands in Catalytic Asymmetric Hydrogenations



Chiral Ferrocenyl Ligands - Some Representatives

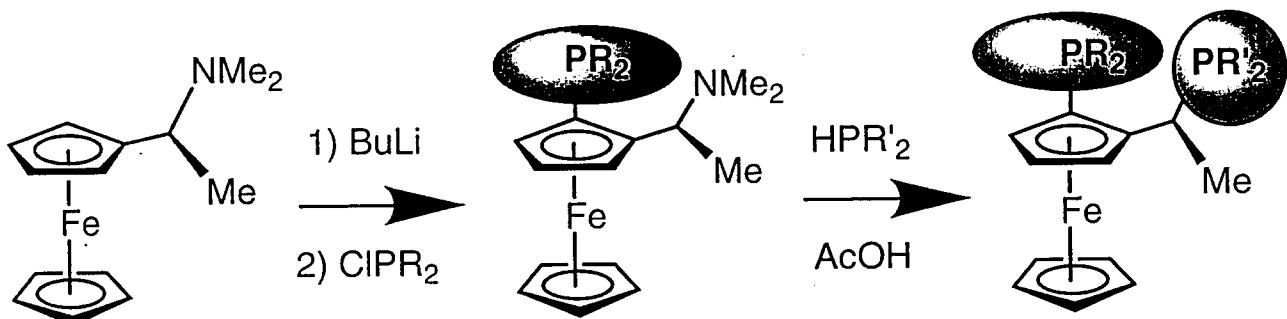


General Strategy for the Synthesis of New Ferrocenyl Ligands



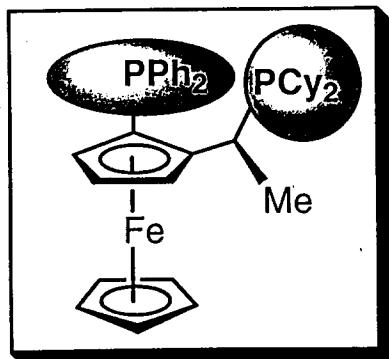
The assembly of the three components occurs in two consecutive stereoselective (-specific) synthetic steps

An Easily Accessible Class of Chiral Chelating Ferrocenyl Ligands



The prototype:

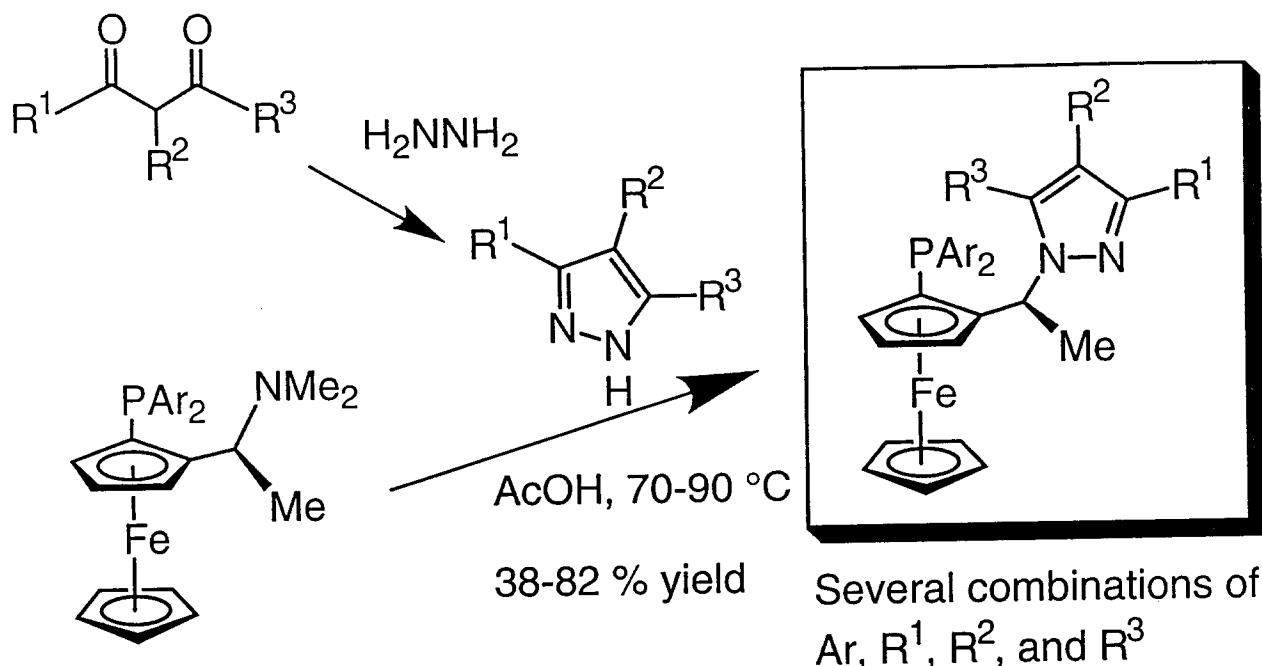
(S)-(R)-Josiphos



→ High yields of crystalline products

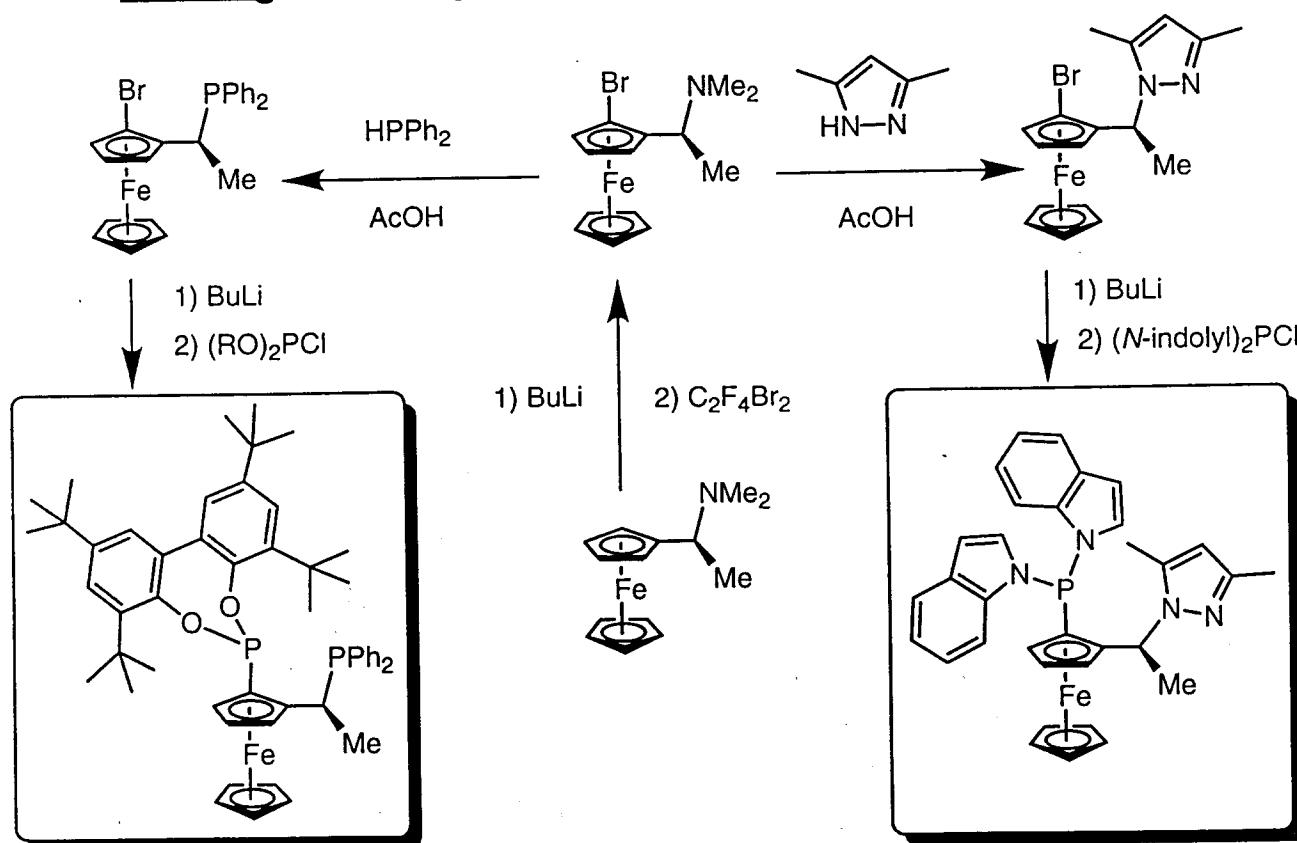
→ Many combinations of PR₂ and PR'₂

Synthesis of Pyrazole-Containing Ferrocenyl Ligands



A. Togni et al., *Organometallics* 1995, 14, 5415.

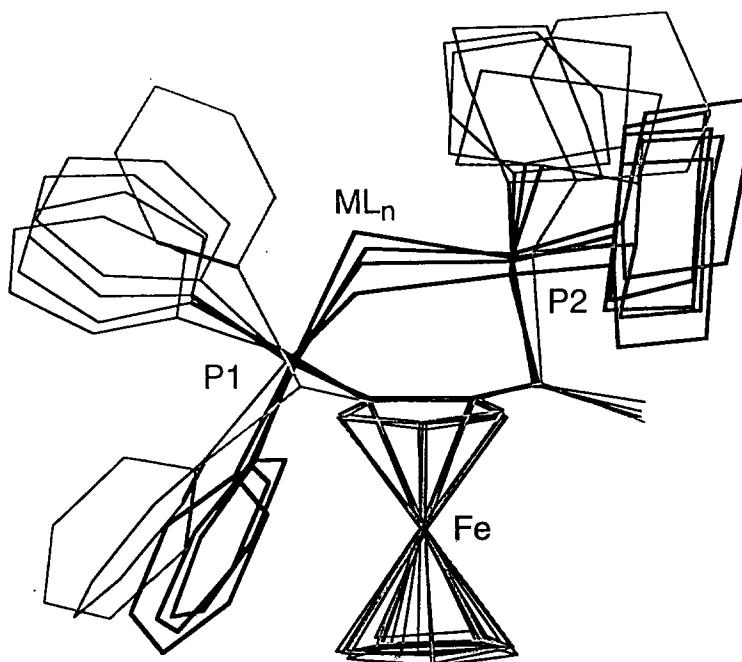
New Ligands Prepared by the "Inverse Sequence"



G. Pioda

Josiphos and its Complexes

Very similar conformations in the solid state and in solution



X-ray structures of
5 different compounds:

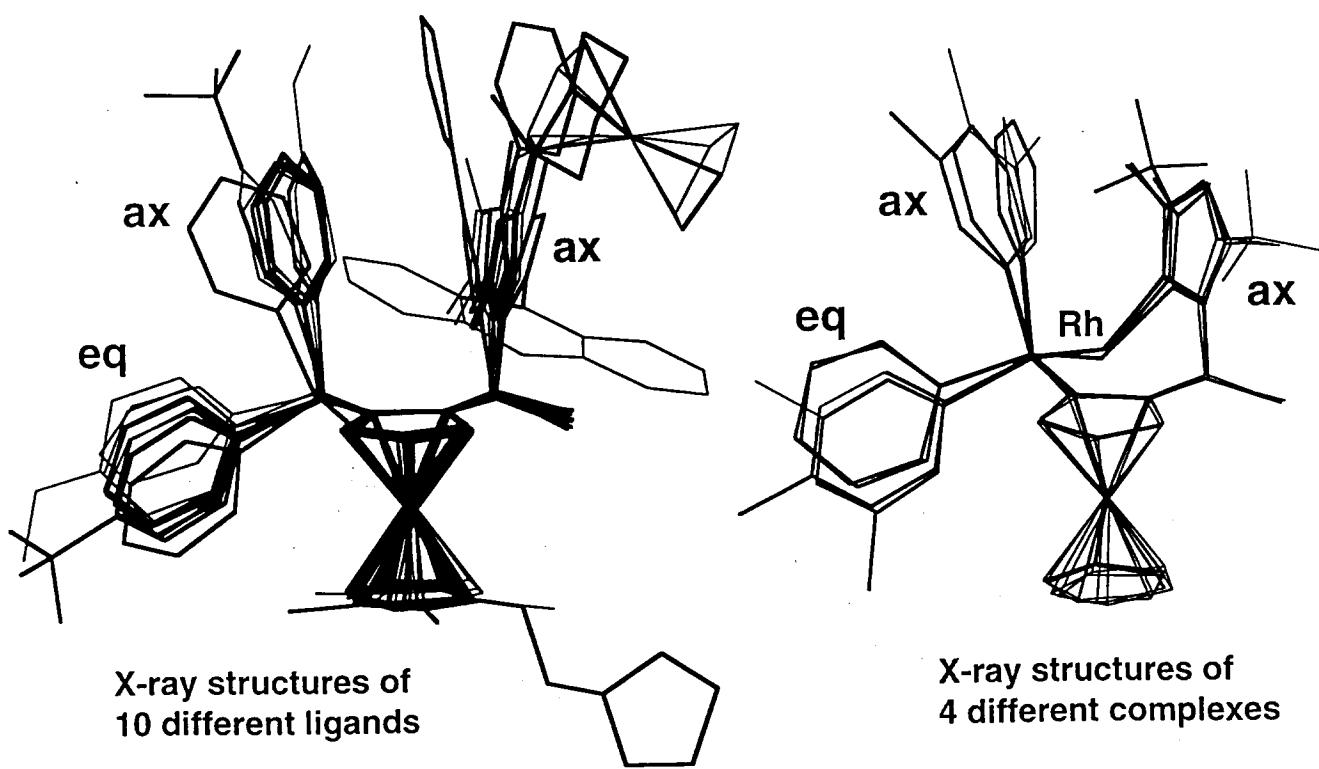
Josiphos
and complexes with
 $M = \text{Pd, Pt, Rh, Ru}$

Bite angle
 $P\text{-}M\text{-}P = 93^\circ\text{--}96^\circ$

A. Togni et al., *Inorg. Chim. Acta* 1994, 222, 213

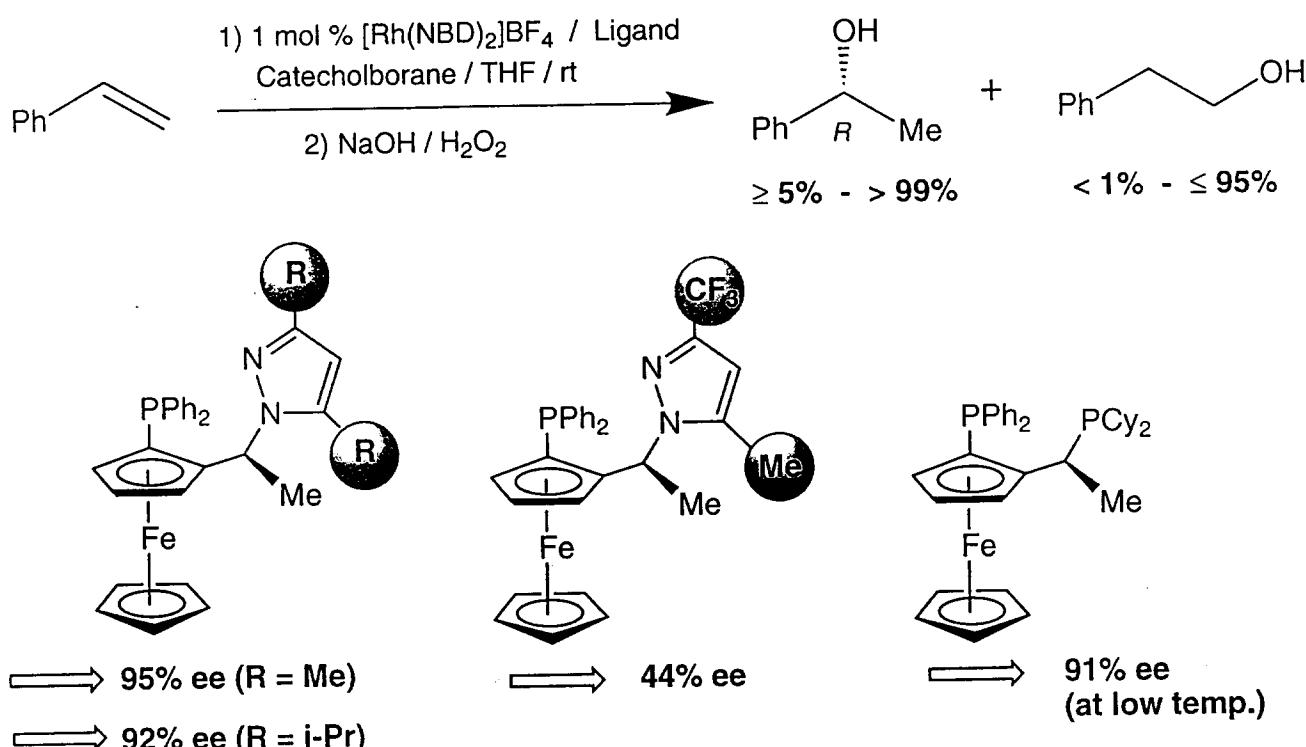
Conformation of Pyrazole-Containing Ferrocenyl Ligands

X-ray crystallographic and 2-D NMR studies in solution
confirm typical conformation in both free ligands and their complexes

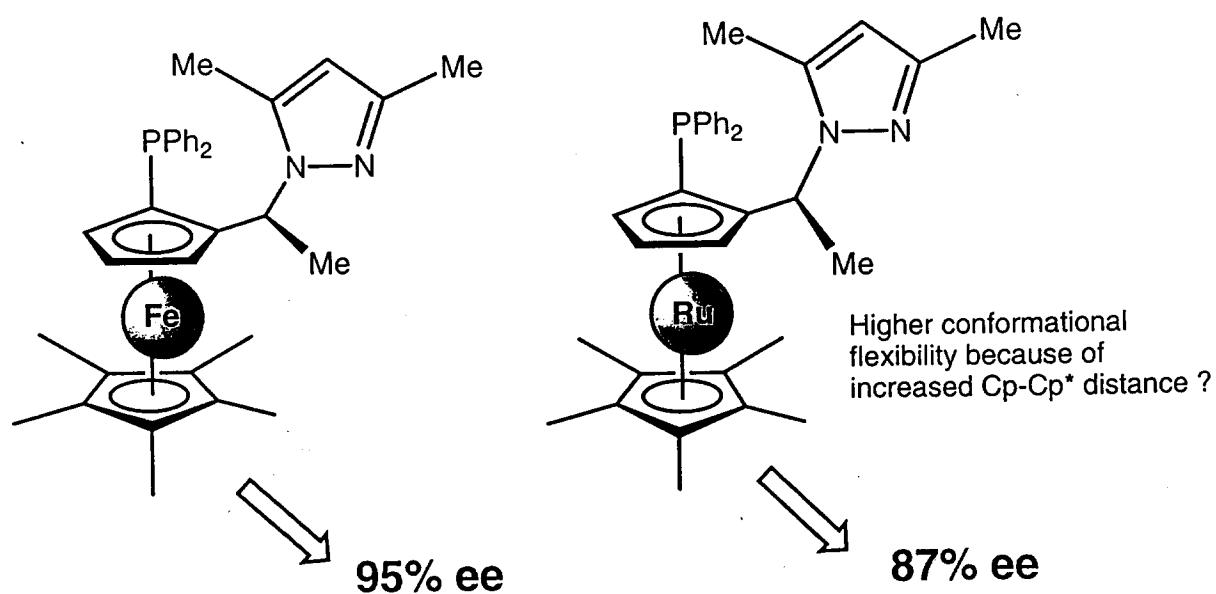


Pyrazolylphosphines in the Rh-Catalyzed Hydroboration of Olefins

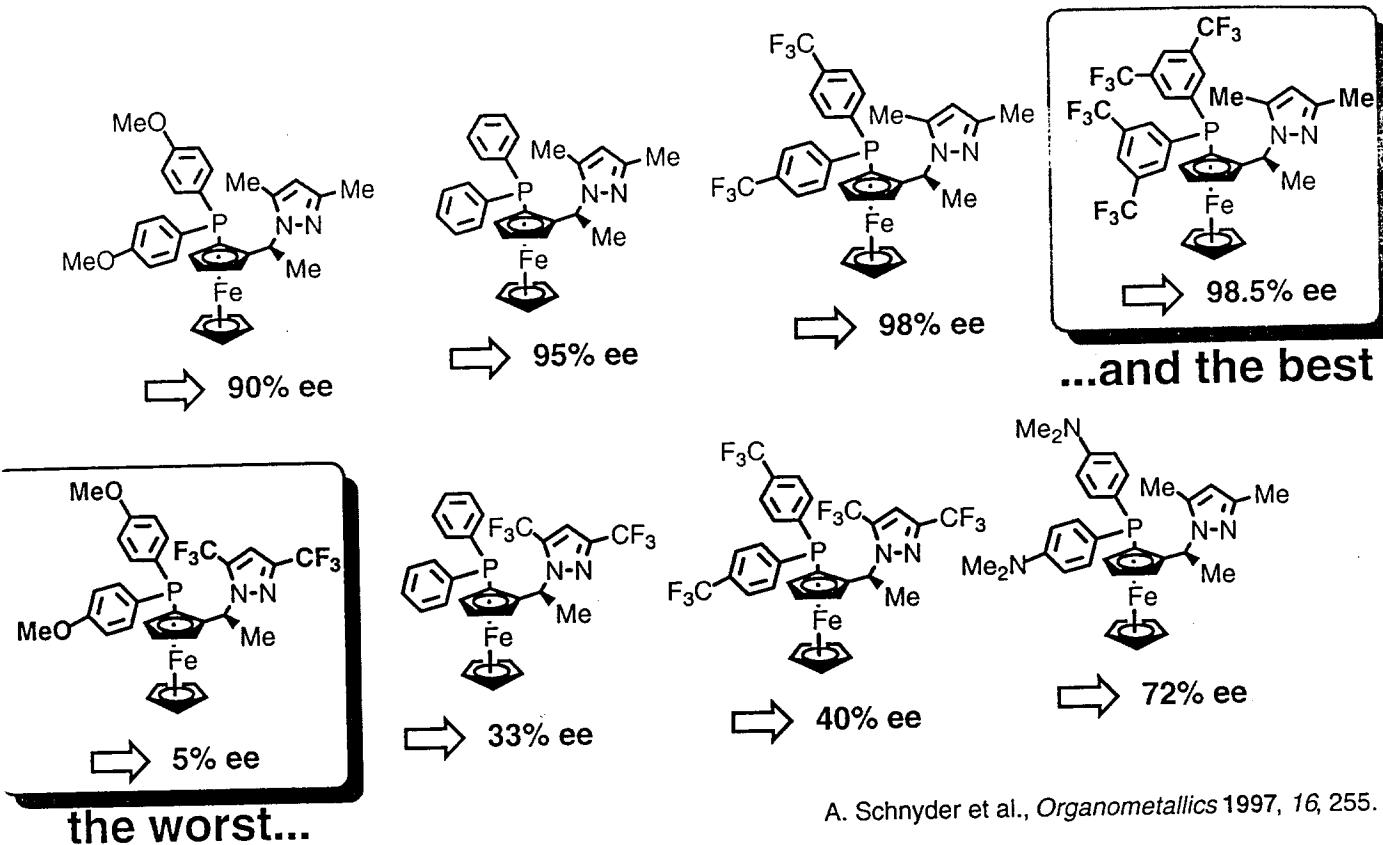
Strong Electronic Effects on Enantioselectivity



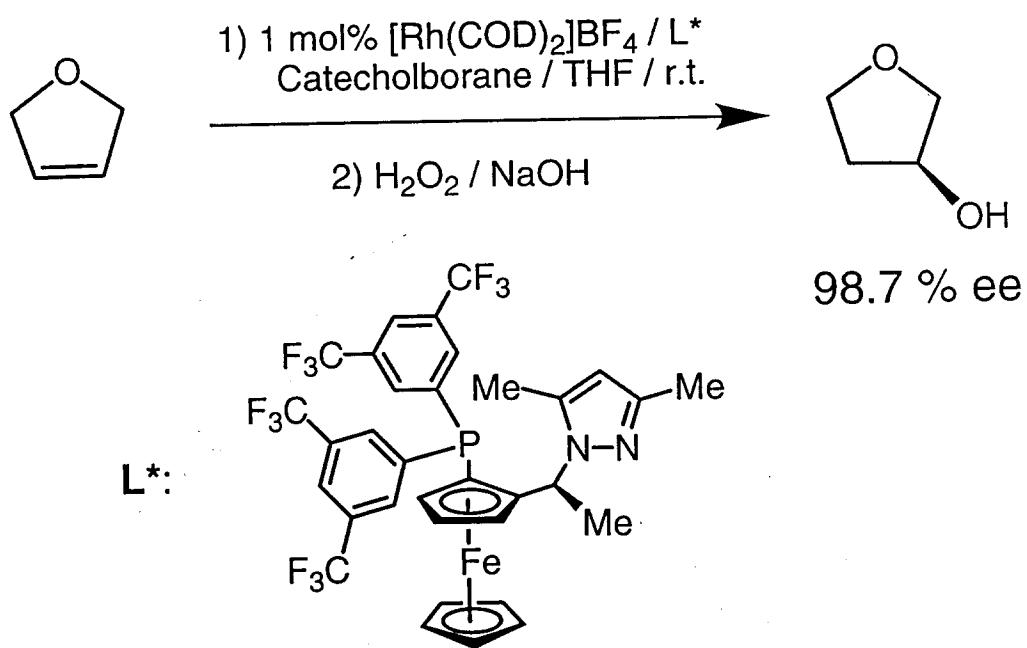
Different Stereoselectivity in the Rh-Catalyzed Hydroboration of Styrene Utilizing Ferrocenyl and Ruthenocenyl Ligands



Ligand Electronic Tuning: From 5% to 98.5% ee in the Rh-Catalyzed Hydroboration of Styrene with Catecholborane



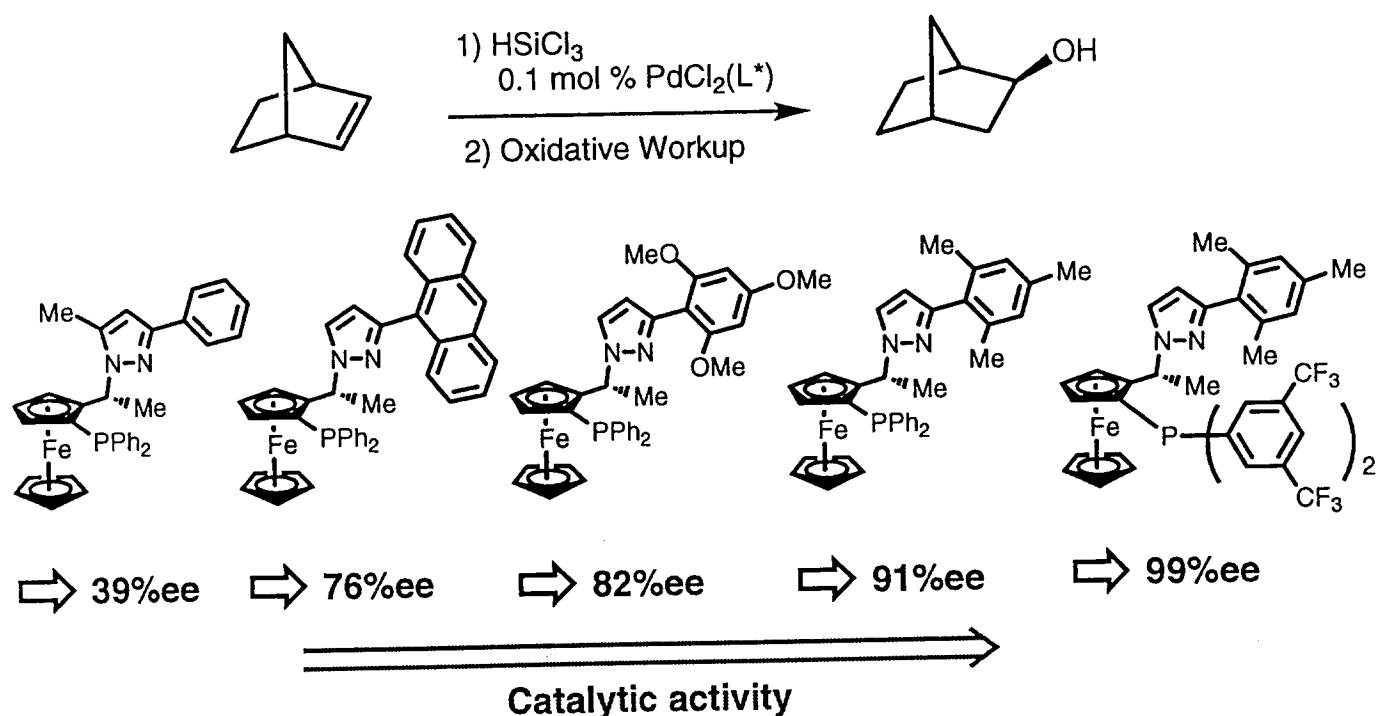
Avoiding the Problem of Regioselectivity in the Rh-Catalyzed Hydroboration...



O. Werbitzky (LONZA Ltd.), A. Schnyder

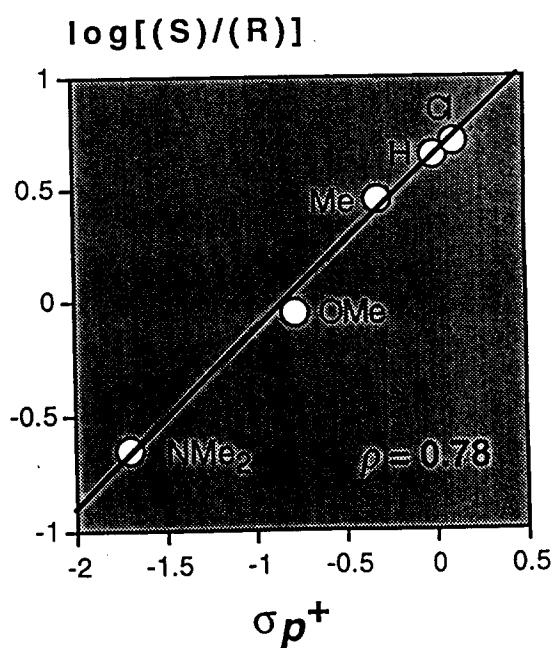
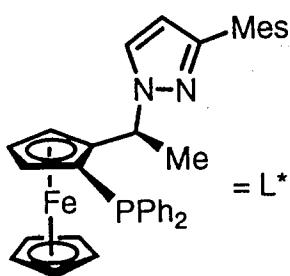
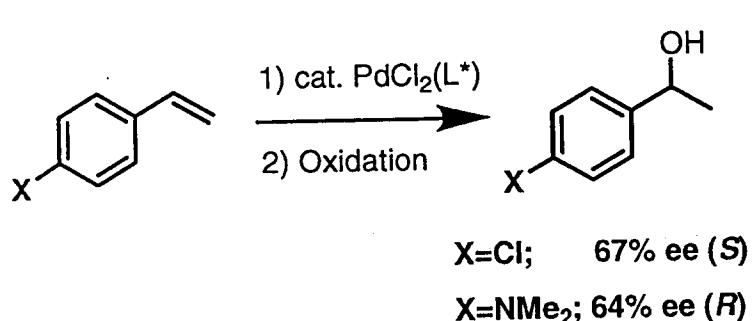
'Pyrazole-Phosphine Ligands in the Pd-Catalyzed Hydrosilylation of Olefins

Steric and electronic tuning of pyrazole and phosphine ligand fragments

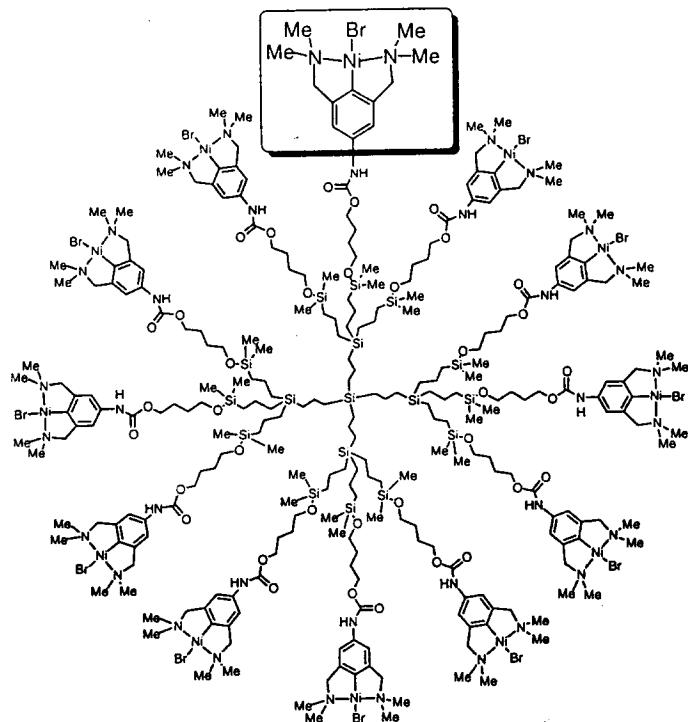


Linear Free-Energy Relationship for the Hydrosilylation of *p*-Substituted Styrenes

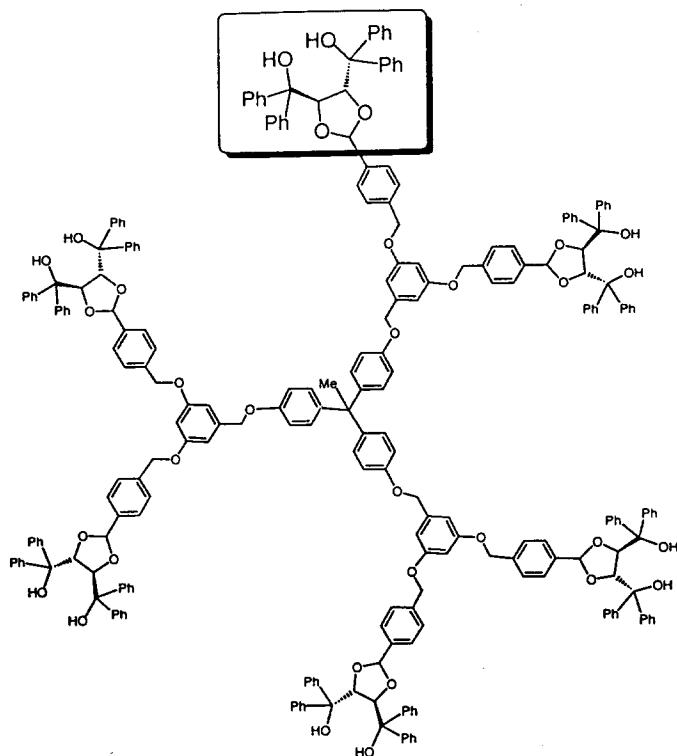
Correlation of $\log[(S)/(R)]$ with σ_p^+ indicates the development of a positive charge in the transition state of the enantioselectivity-determining step



Dendrimers with Peripheral Catalyst Units

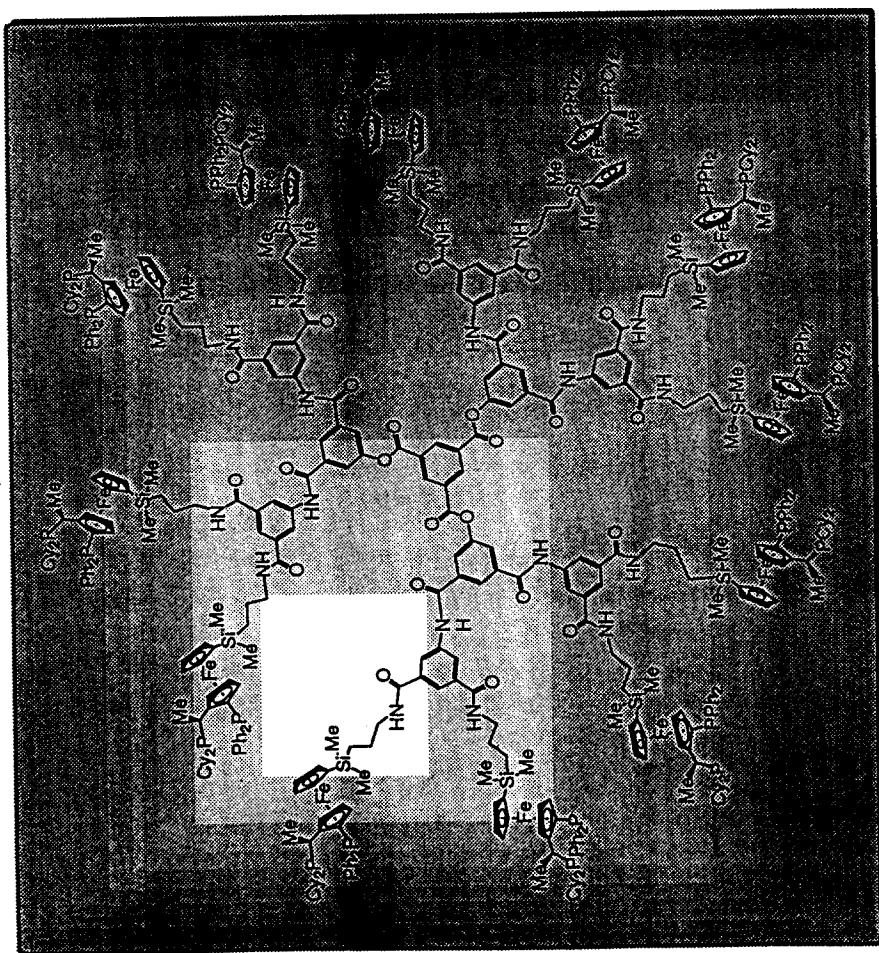
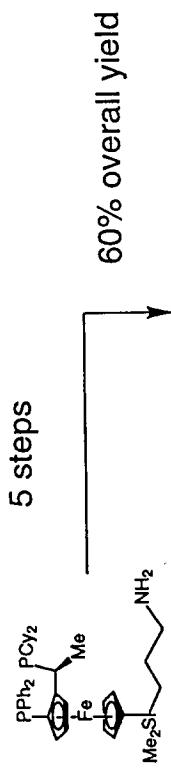


G. van Koten et al. *Nature* 1994, 372, 659



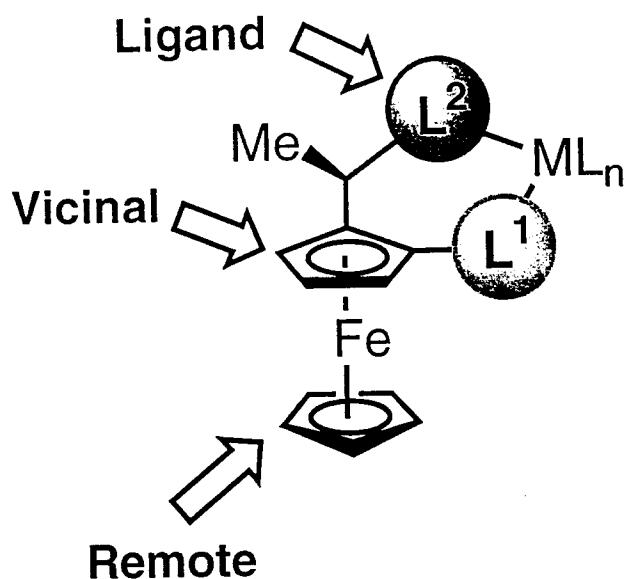
D. Seebach et al. *Helv. Chim. Acta* 1996, 79, 1710

Nanoscopic Catalysts for Asymmetric Synthesis Twelve Equivalent Ligands on a Dendrimer



G2-12-JA
C₅₇₃H₇₀₈Fe₁₂N₁₈O₂₄P₂₄Si₁₂ (MW=9982.6)

Possible Anchoring Points for Spacer on Ferrocenyl Ligands



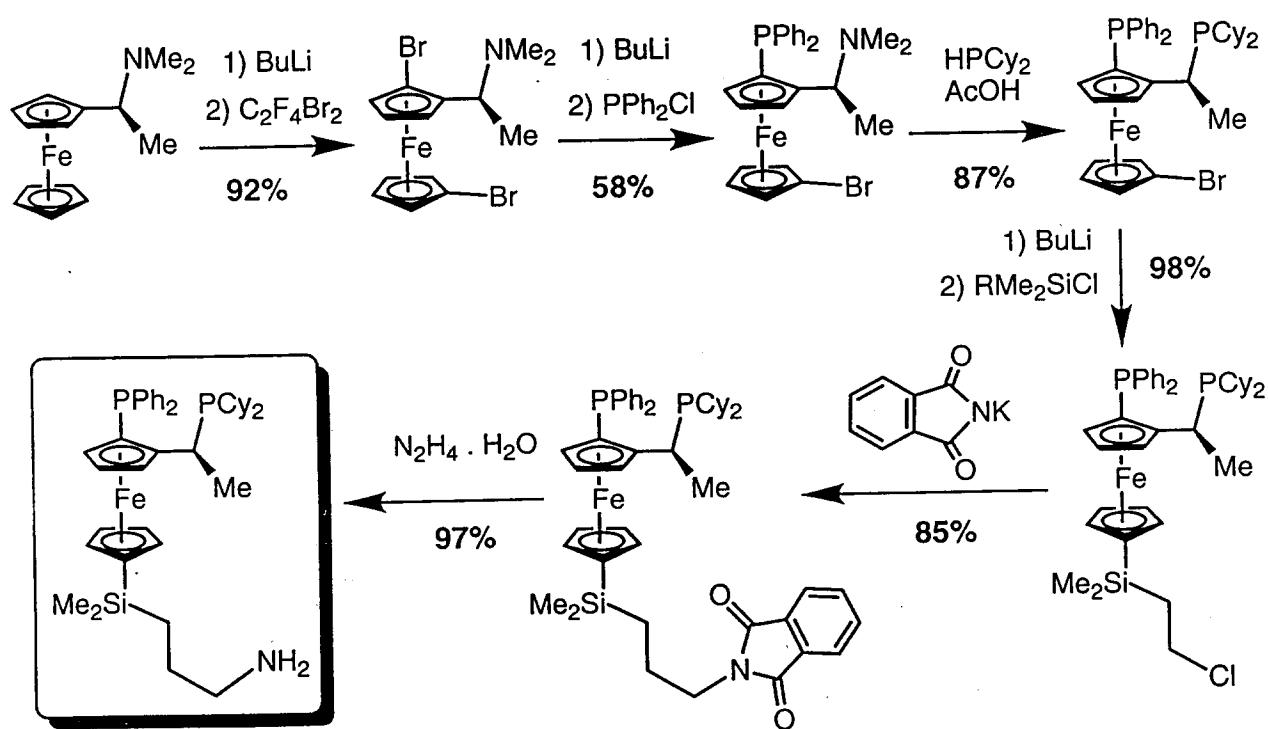
Criteria:

- Synthetic accessibility
- Possible interactions with chelate ring

Remote anchoring is best but more difficult

Anchoring

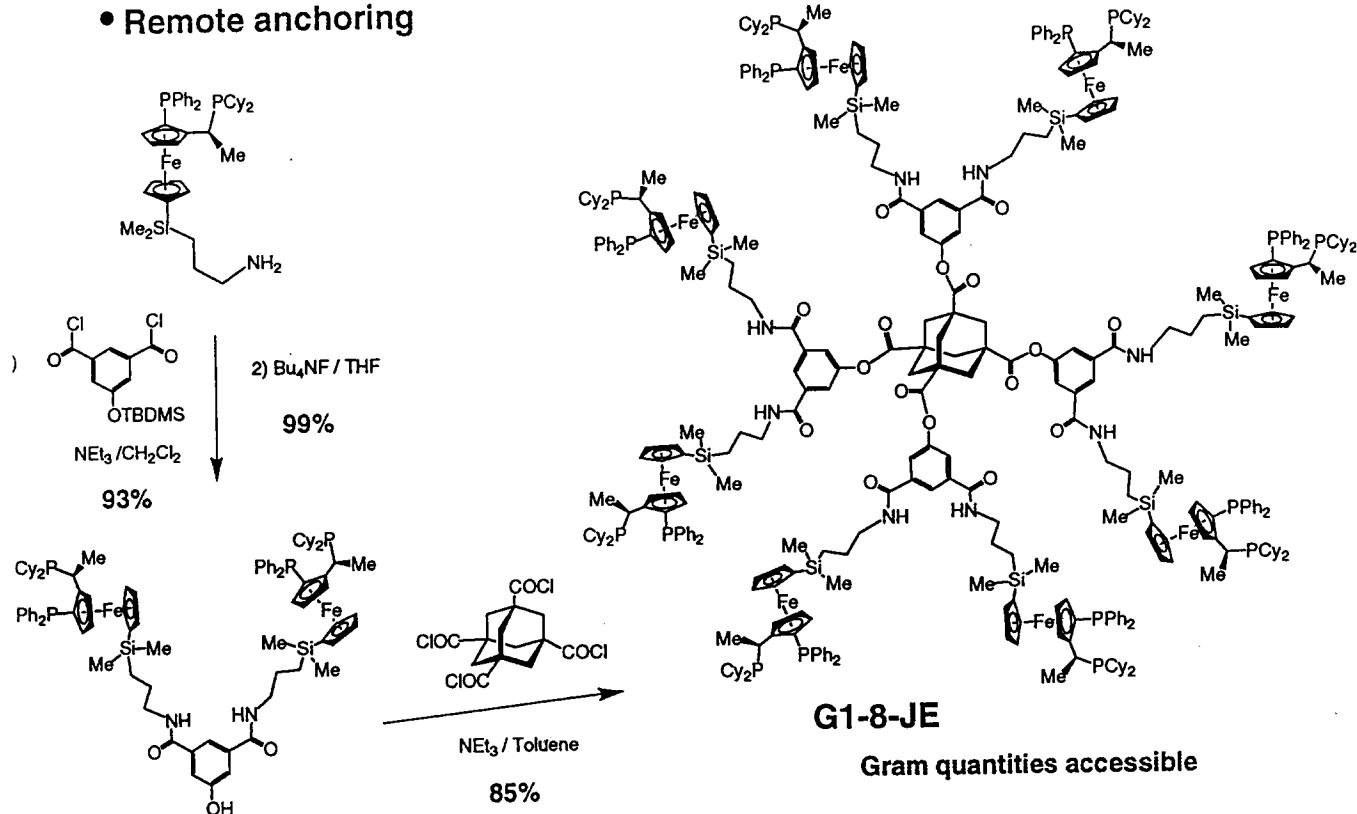
Synthesis of a Functionalized Josiphos for Dendritic Derivatives



B. Pugin, Novartis Ltd. WO 96 32,400 / EP 729969
C. Köllner, ETH

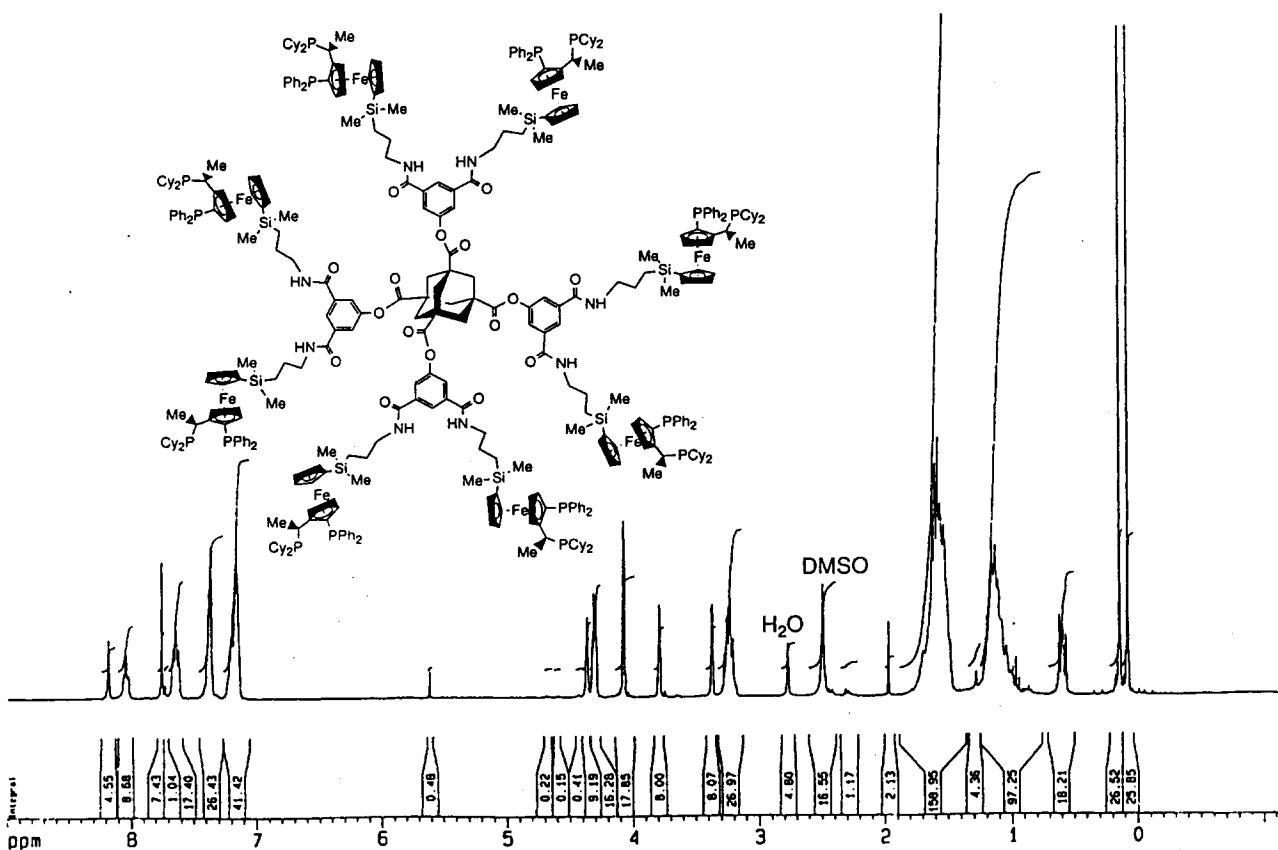
A Typical Convergent Synthesis of a G1-Josiphos Dendrimer

- Remote anchoring

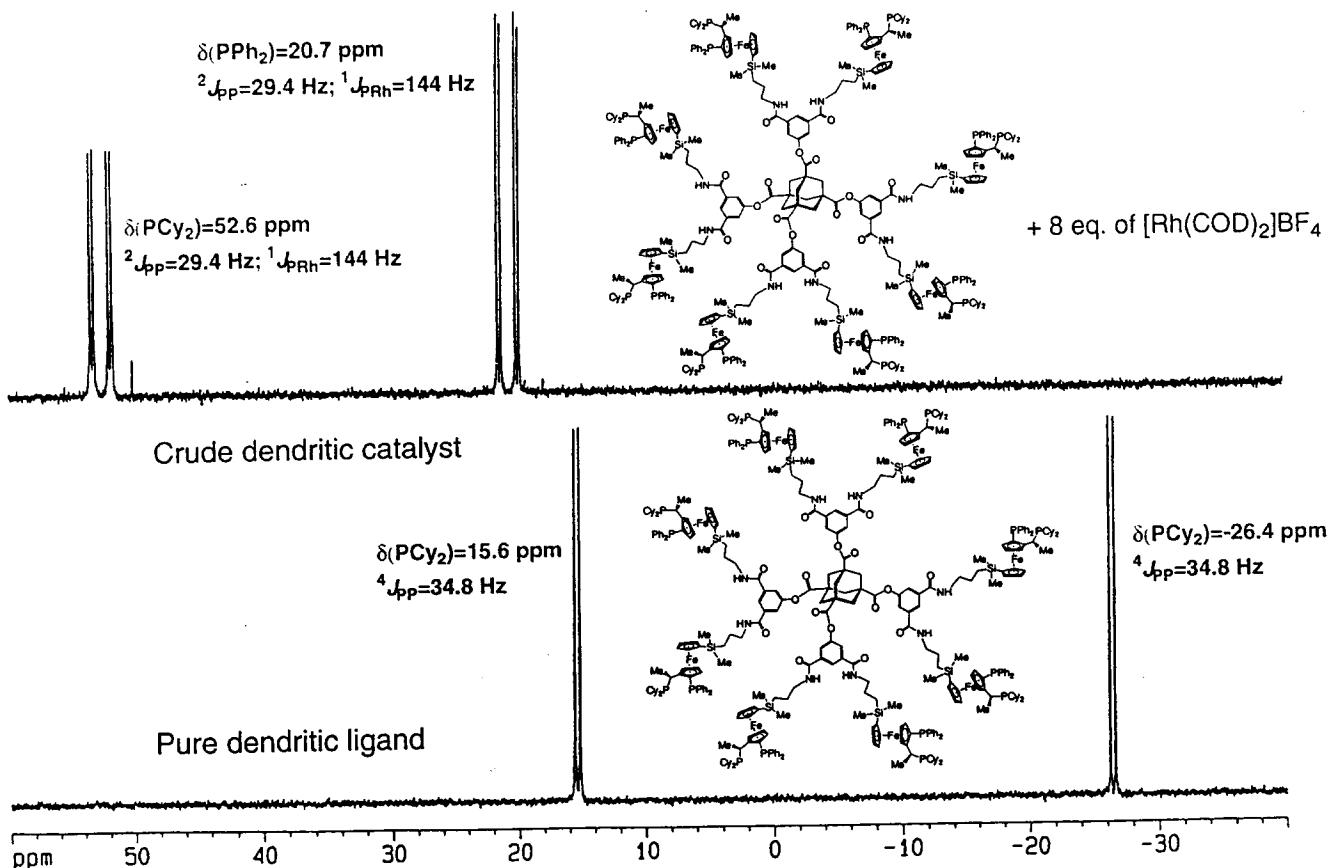


C. Köllner, B. Pugin, A. Togni *J. Am. Chem. Soc.* 1998, 120, in the press

300 MHz ^1H NMR Spectrum of G1-8-JE in DMSO-d_6 at 120°C

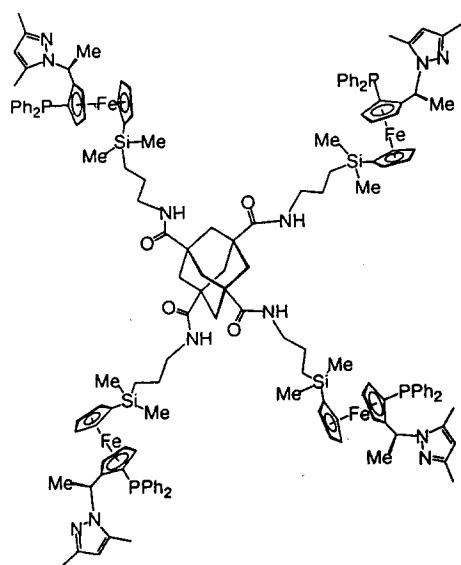


³¹P NMR spectroscopy indicates "full loading" of dendrimers with Rhodium

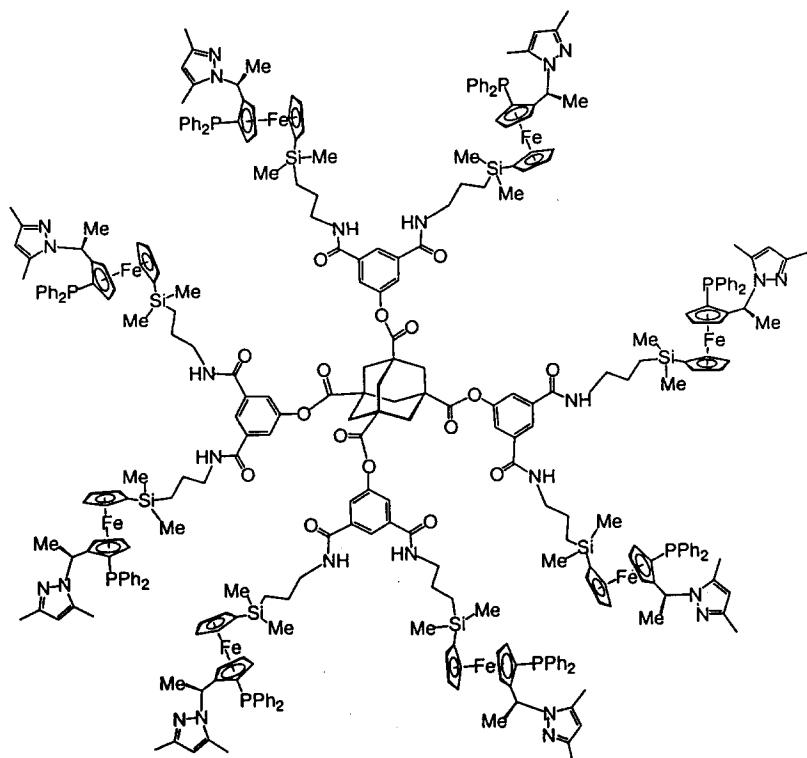


Dendrimers of P,N-Ligands

- Remote anchoring



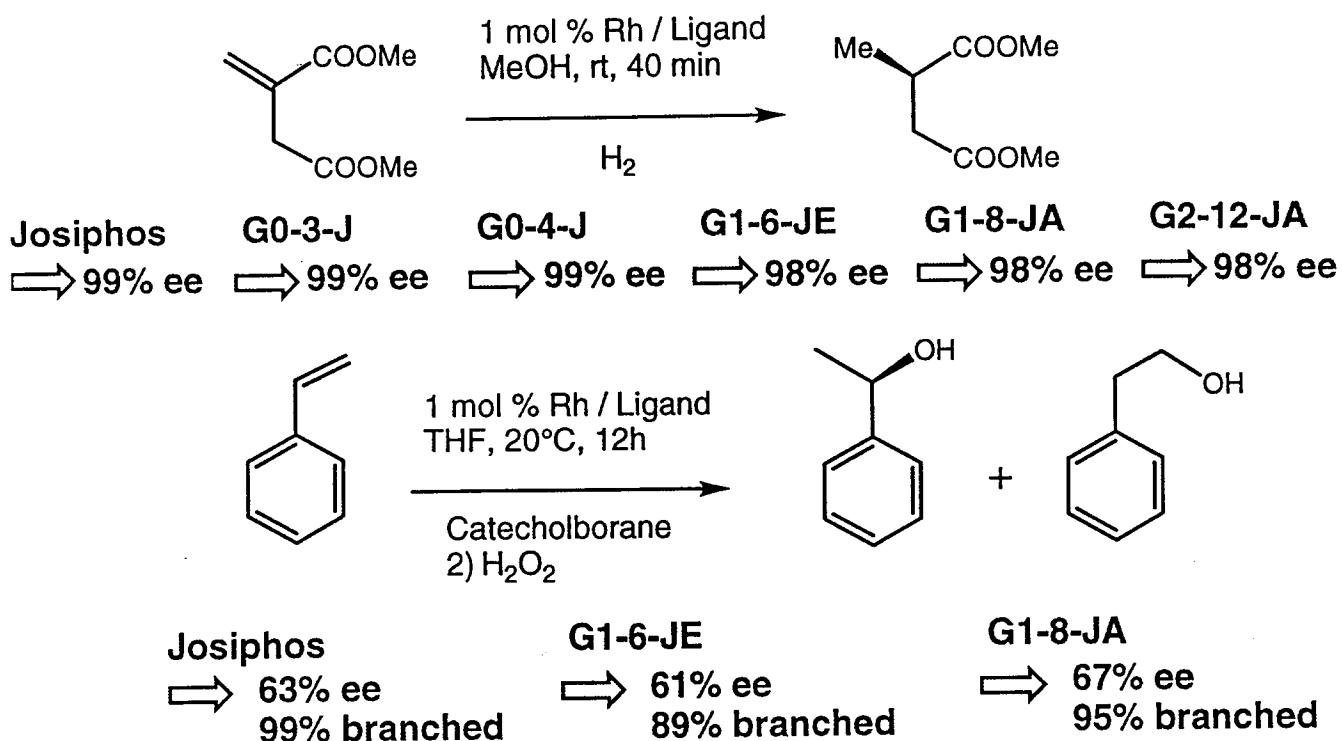
G0-4-PzP



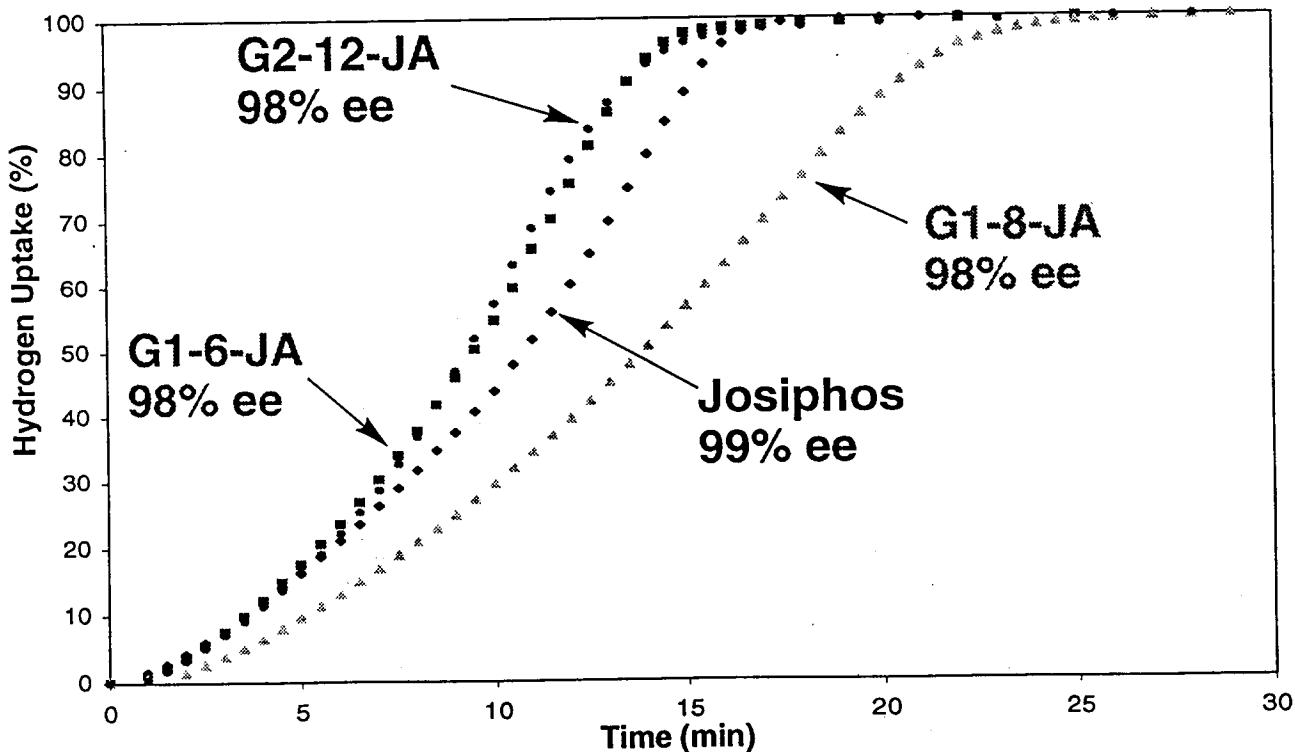
G1-8-PzPE

Application of Dendrimeric Josiphos Ligands in Asymmetric Rh-Catalyzed Hydrogenation and Hydroboration

Very similar results, as compared to corresponding mononuclear catalyst

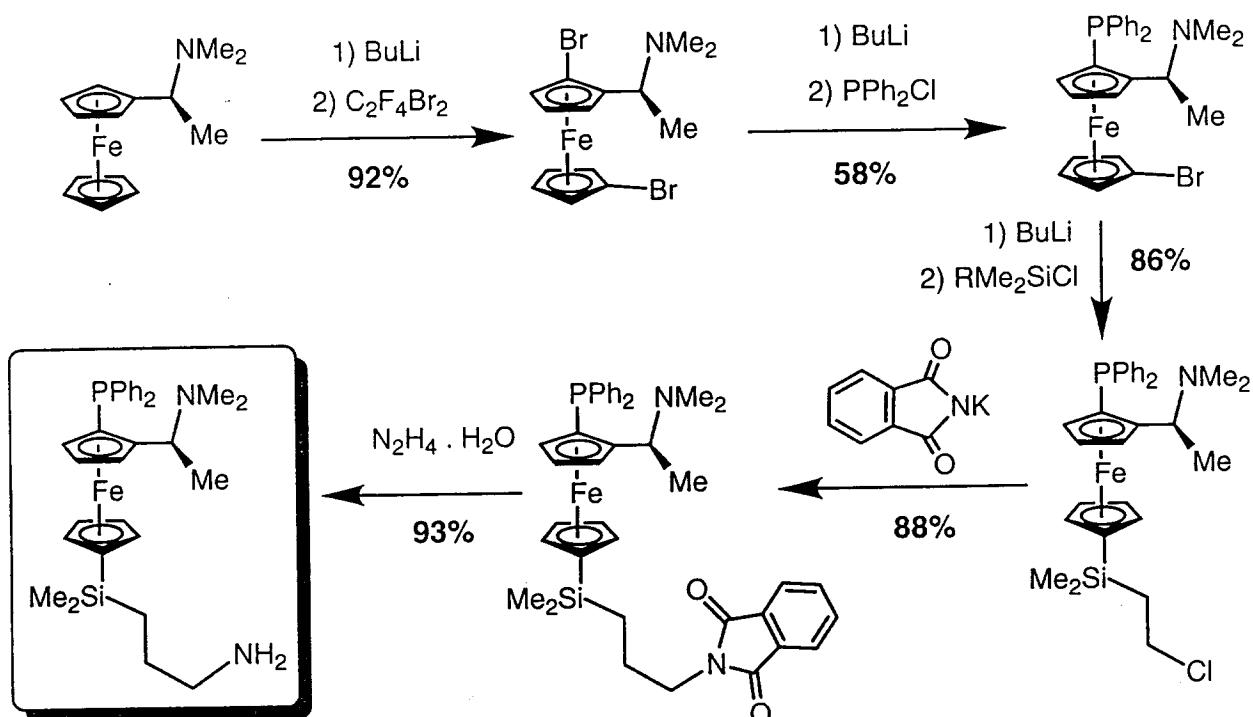


Comparison of Monomeric and Dendritic Catalysts in the Rh-Catalyzed Hydrogenation of Dimethyl Itaconate



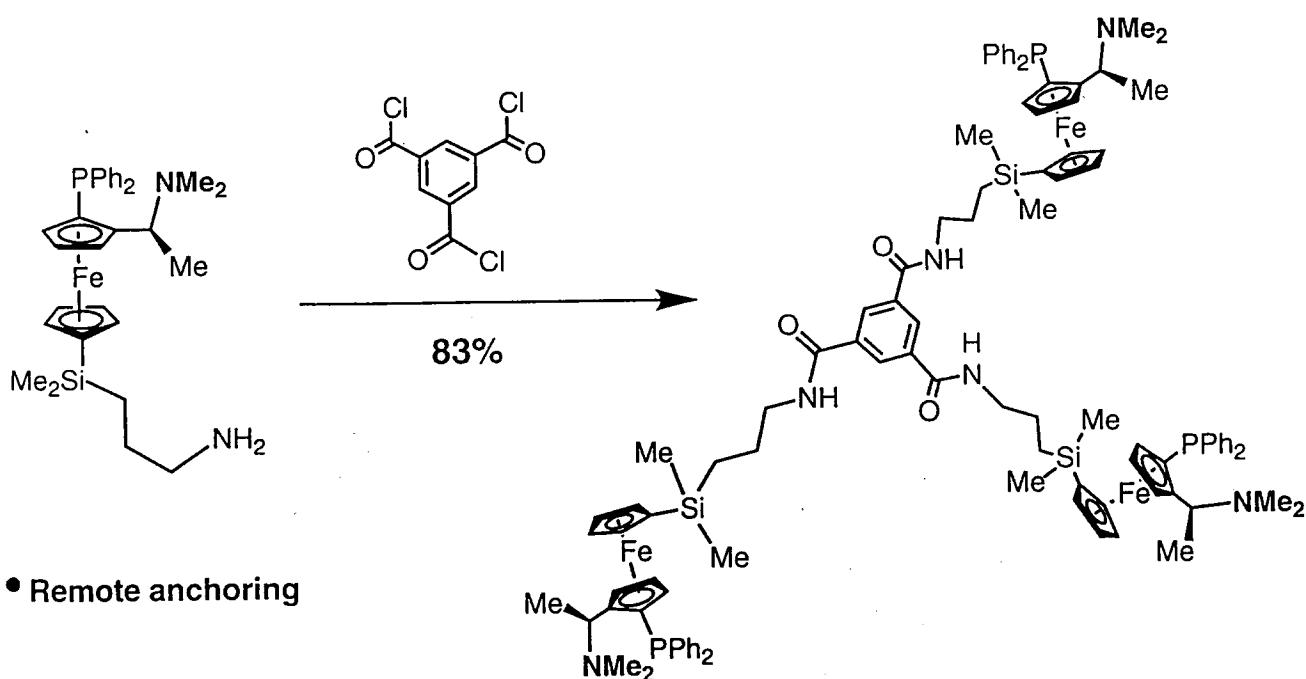
Conditions: 1mol% Rh, MeOH, 25°C, 1 atm H₂, 2 mmol/15mL

Synthesis of a Functionalized Josiphos Precursor for Dendritic Derivatives



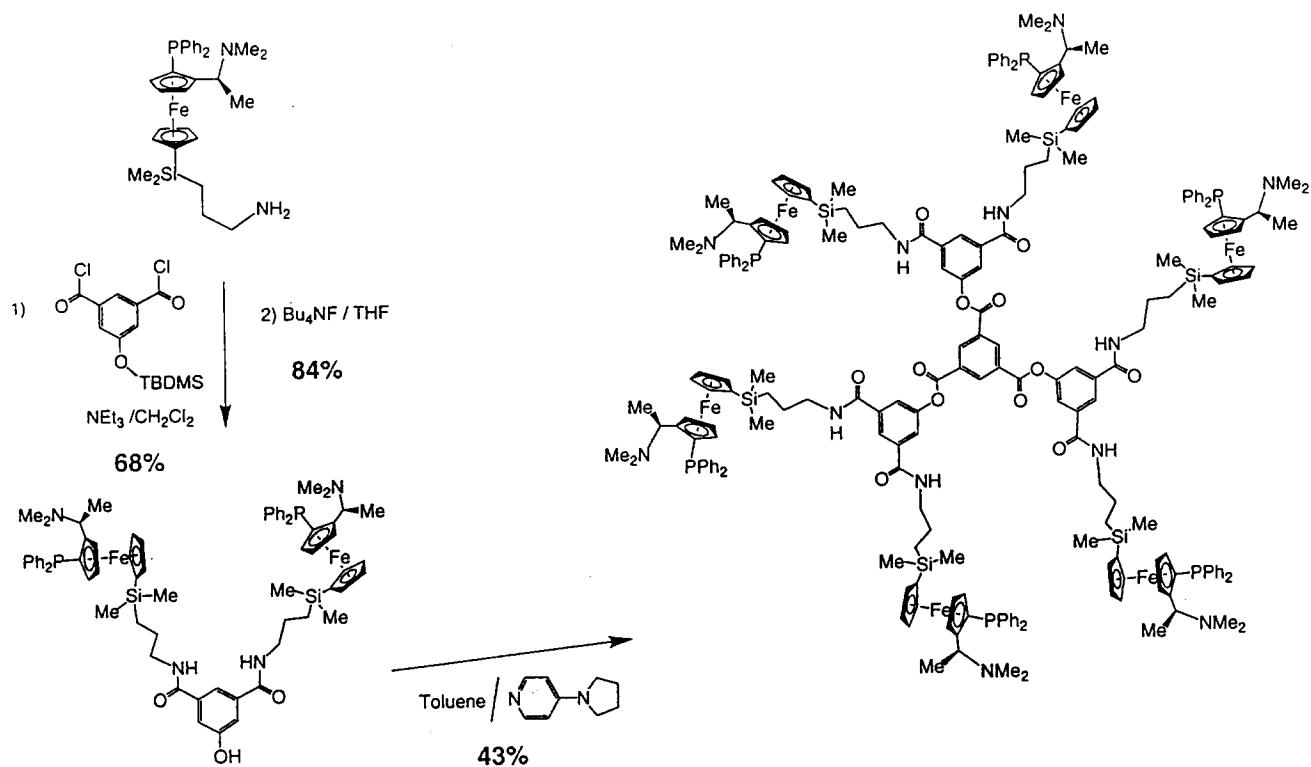
Synthesis of a Branched PPFA Derivative for "Terminal" Functionalization

Principle: Completion of ligand synthesis after dendrimer synthesis



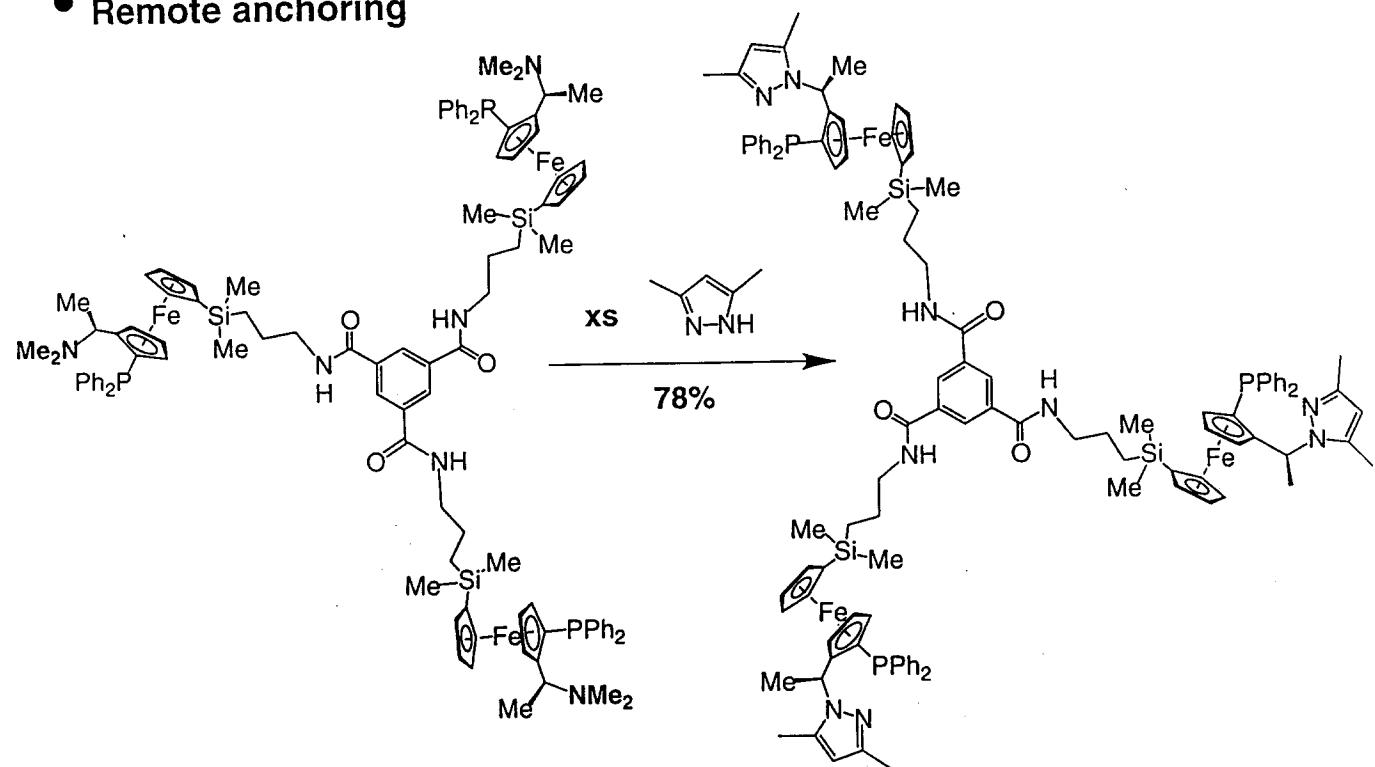
Synthesis of a G1-PPFA Derivative

- Remote anchoring

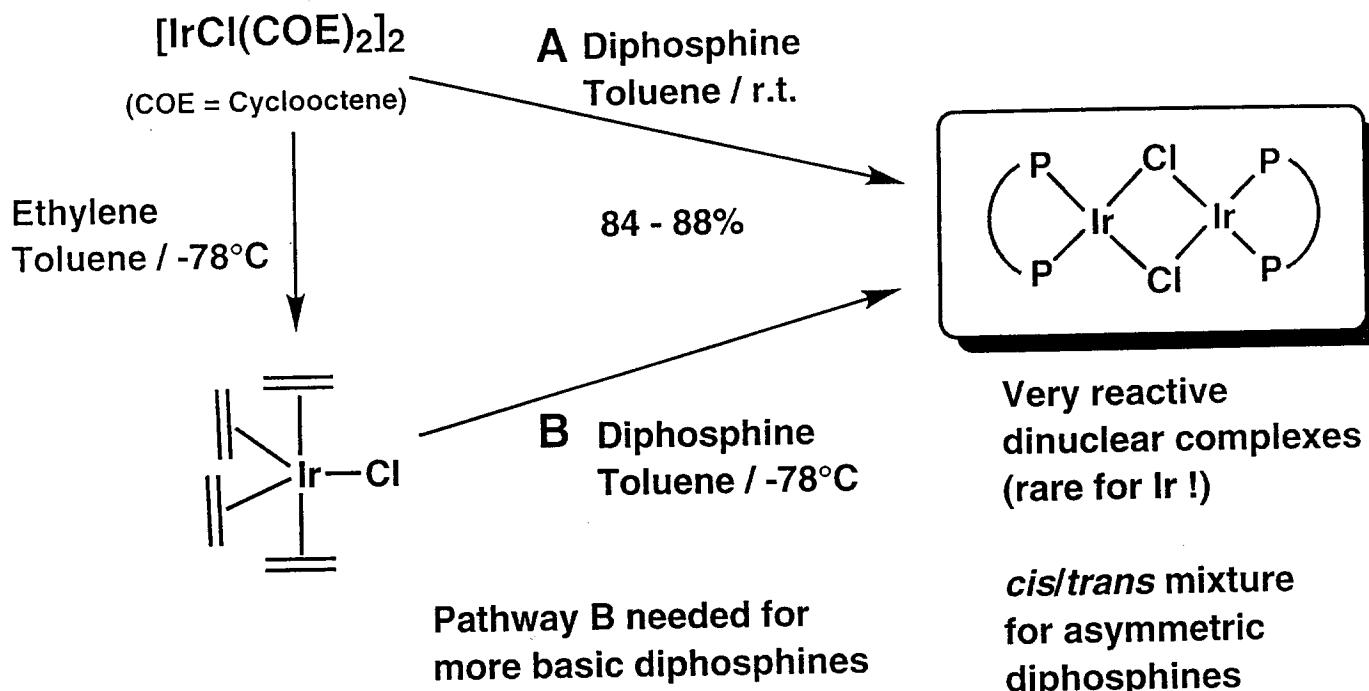


An Example of "Terminal" Functionalization of a Dendritic Ligand

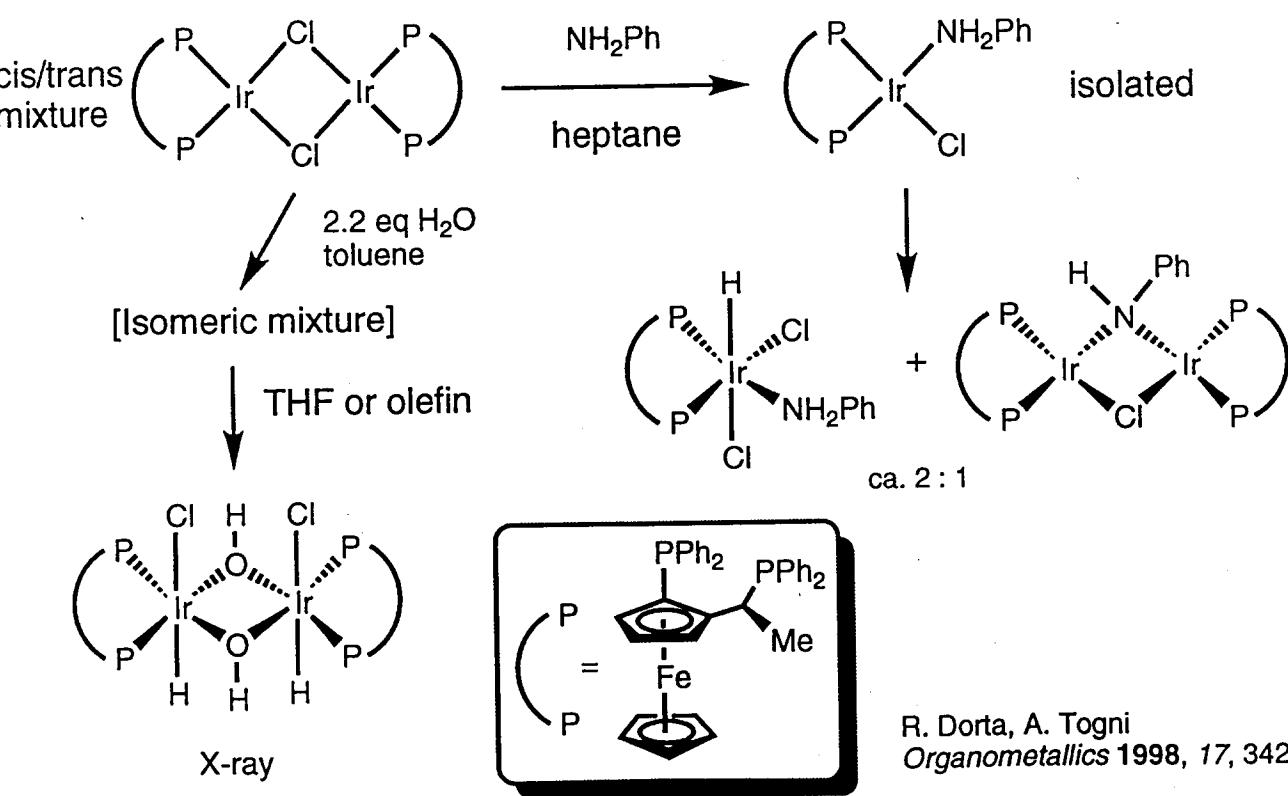
- Remote anchoring



Synthesis of Olefin-Free Ir(I) Diphosphine Complexes

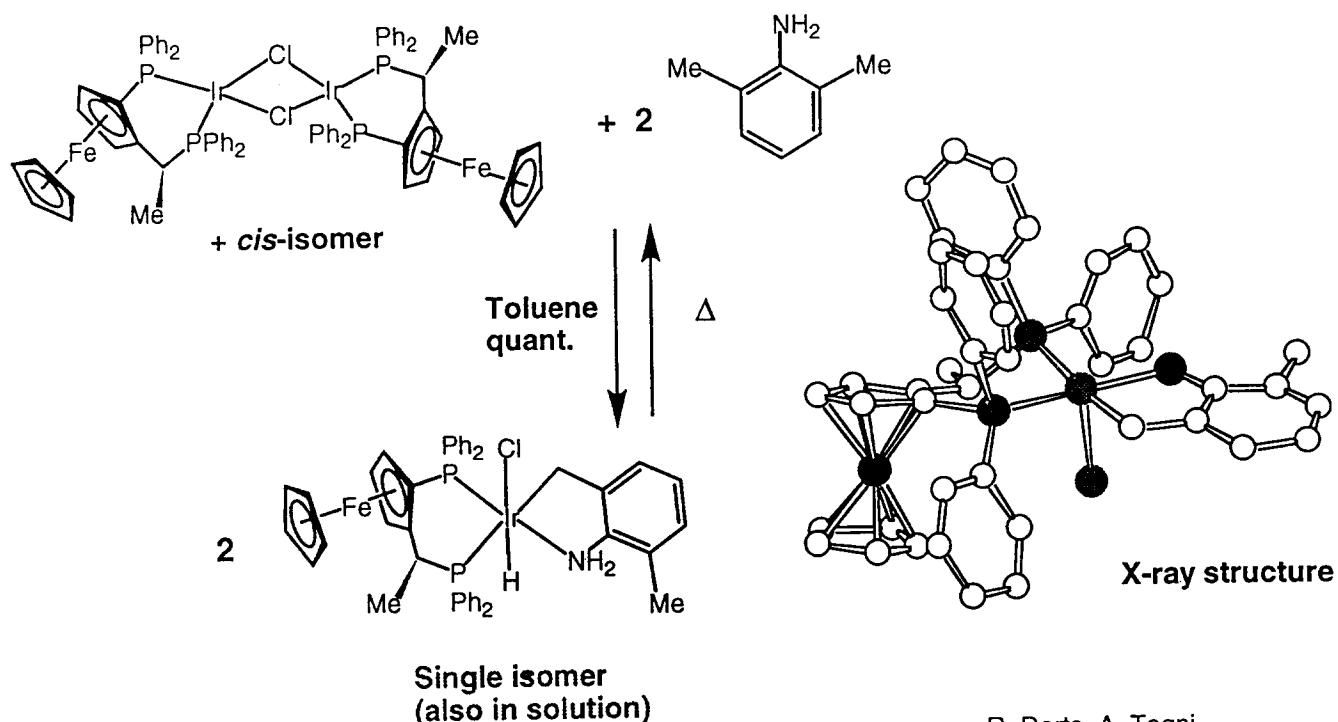


Clean O-H and N-H Bond Activation by a Dinuclear Ir(I)-Ferrocenyl Diphosphine Complex



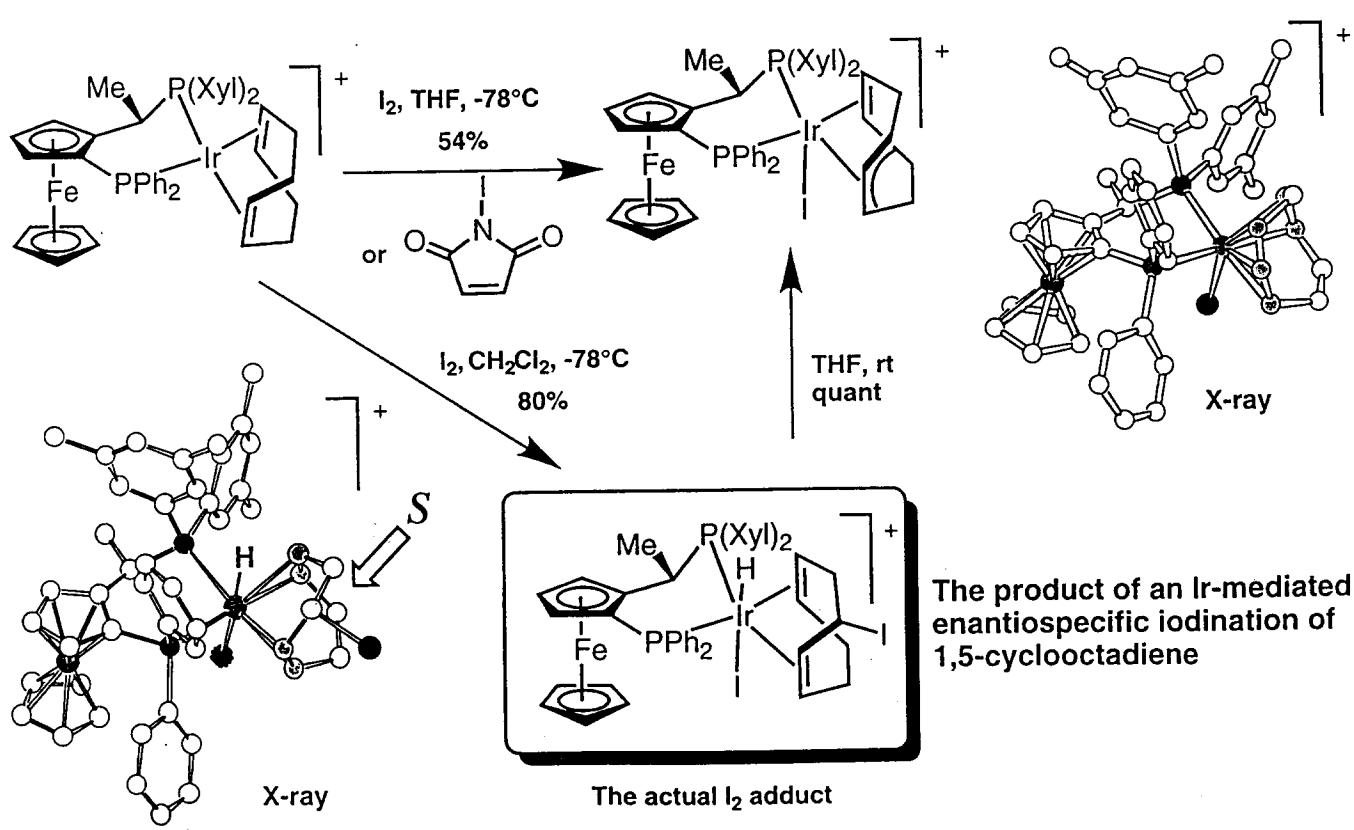
Reversible C-H Activation in 2,6-Dimethylaniline

No N-H oxidative addition observed

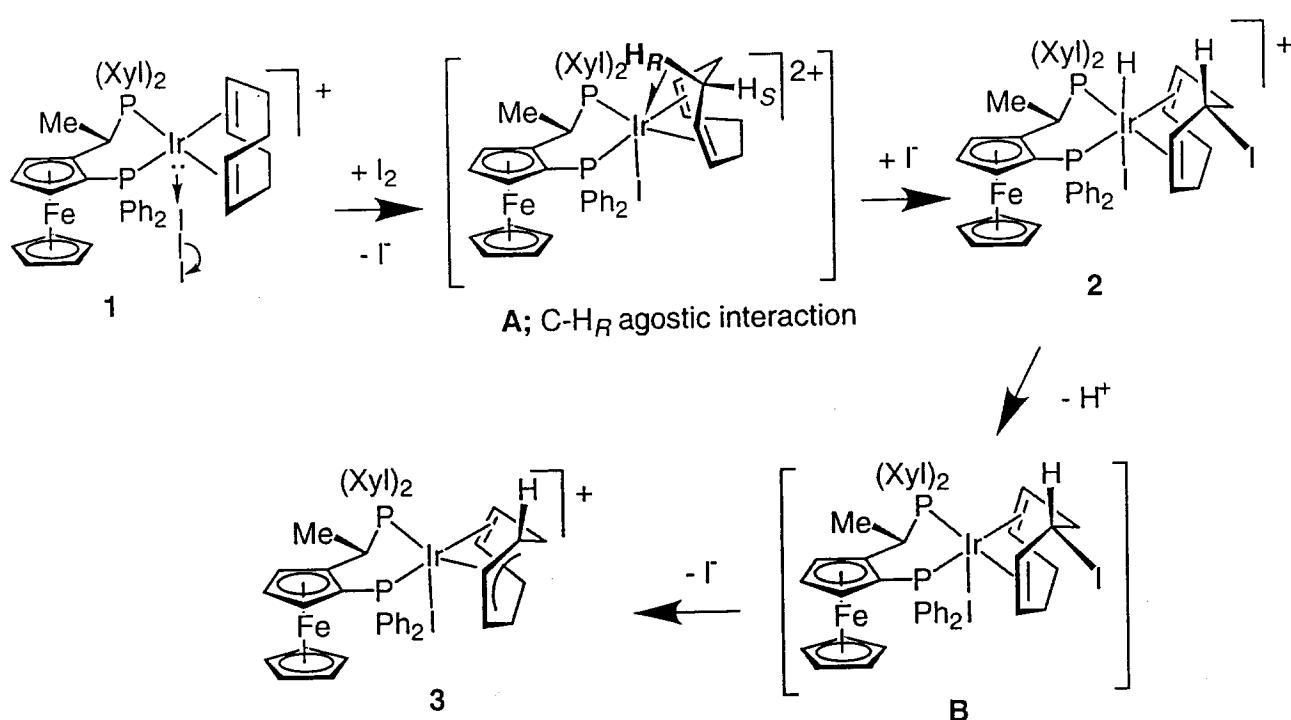


R. Dorta, A. Togni
Organometallics 1998, 17, 3423.

Reactivity of Ir(I)-COD Complexes with Iodine Enantiospecific C-H Activation / Iodination

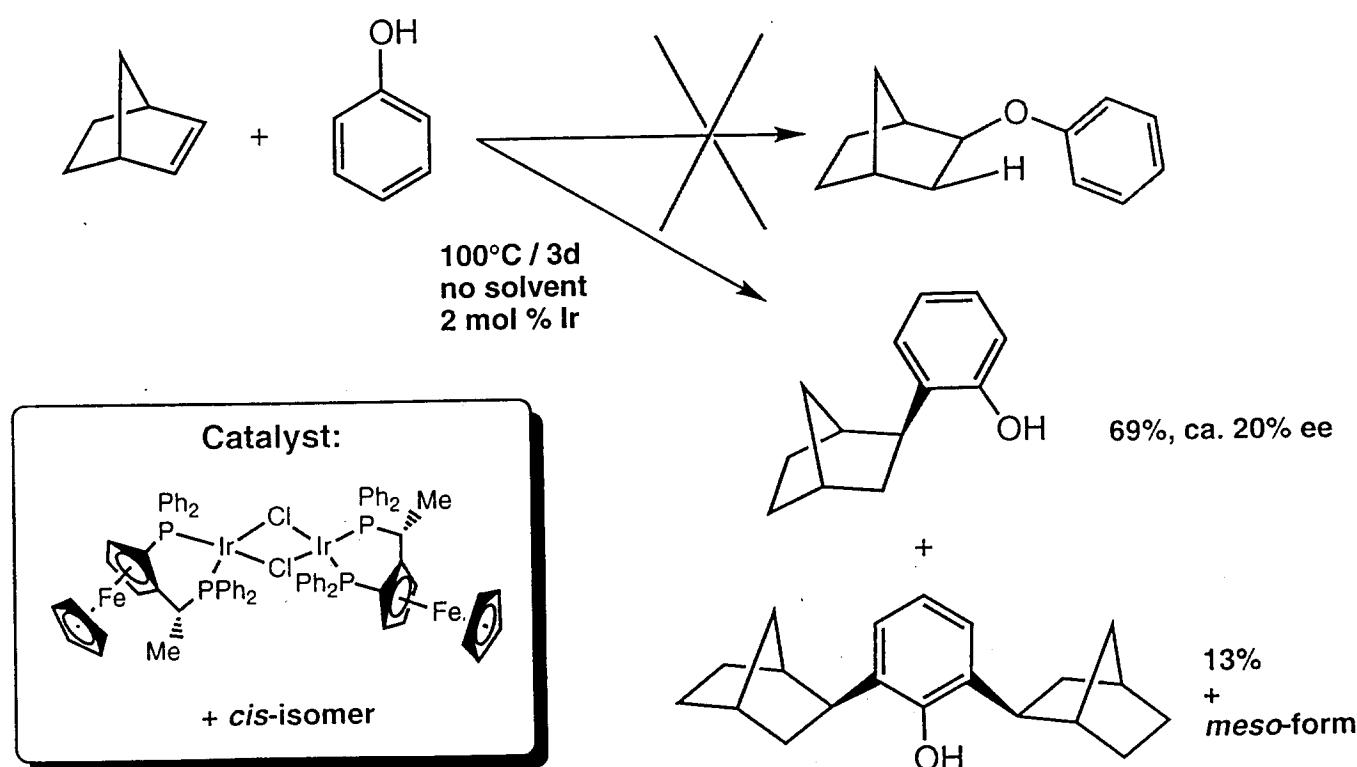
Ir-(ICOD)H⁺

A Possible Mechanistic Scheme Accounting for Allylic C-H Activation / Iodination



Attempt PhOH

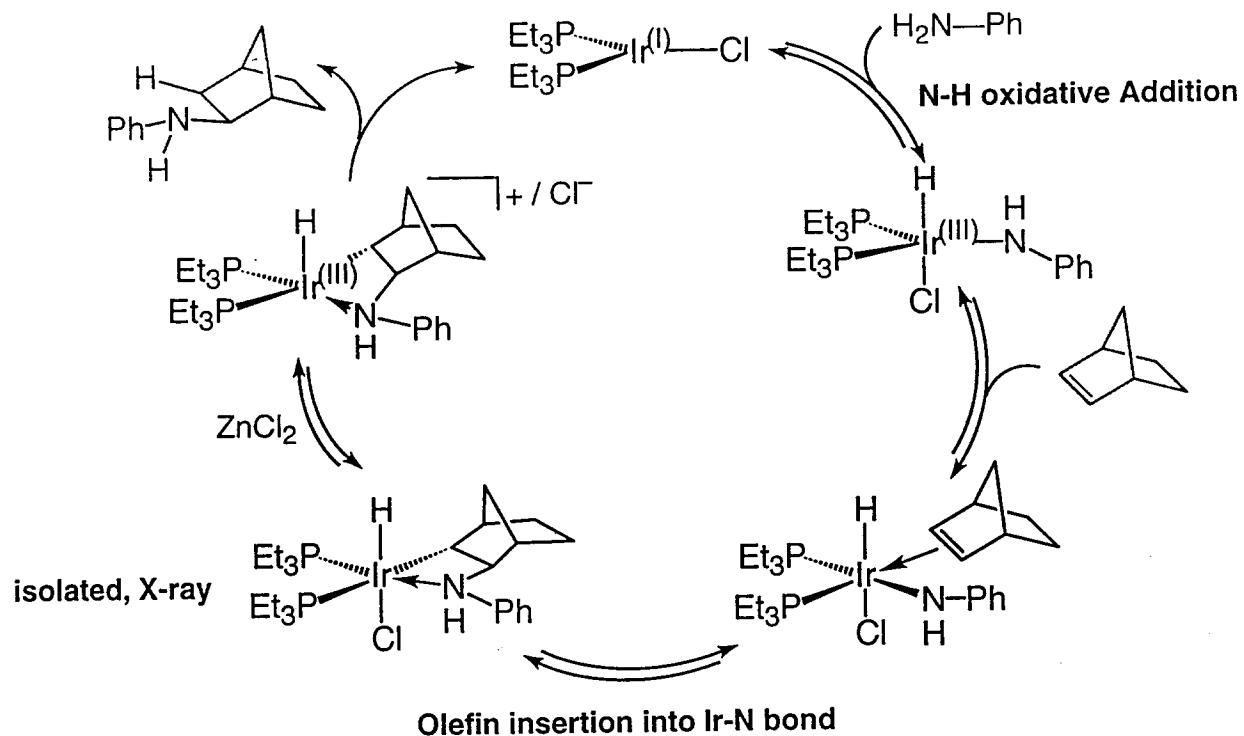
Attempted Hydrophenoxylation of Norbornene



A Well Studied Achiral Hydroamination System

The Addition of Aniline to Norbornene via N-H Activation

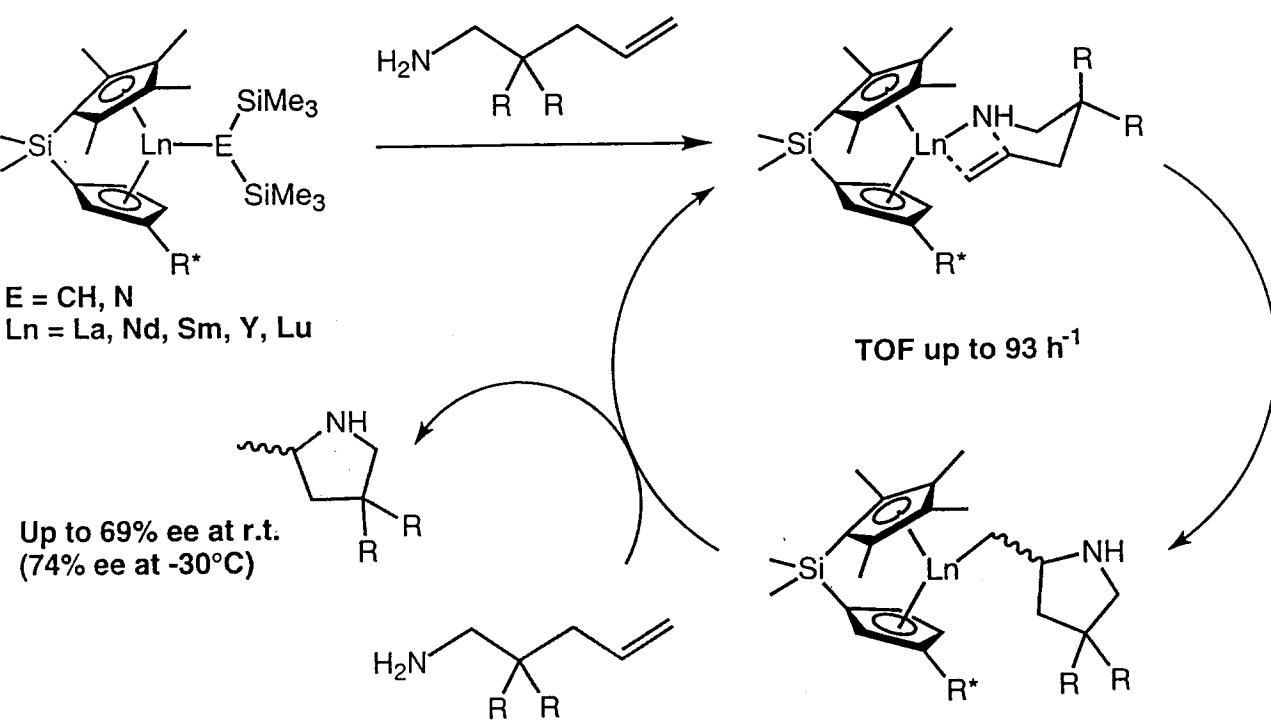
Calabrese, Casalnuovo, Milstein, *J. Am. Chem. Soc.* 1988, 110, 6738



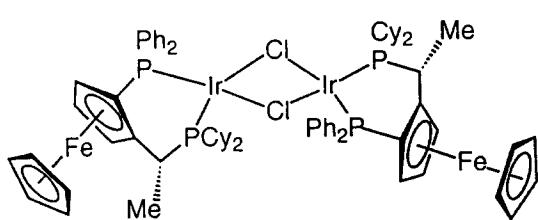
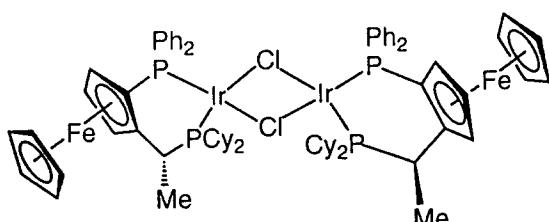
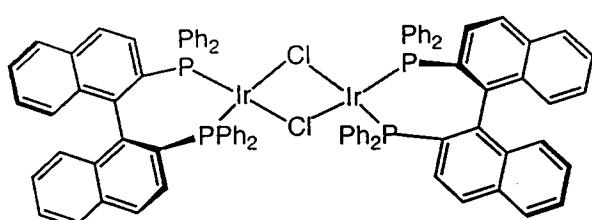
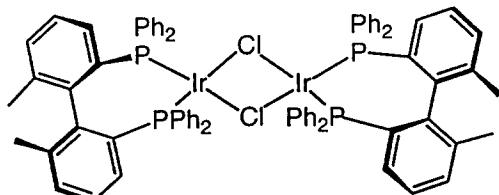
Marks

Lanthanide-Catalyzed Asymmetric Olefin Hydroamination/Cyclization

T.J. Marks et al. *J. Am. Chem. Soc.* 1994, 116, 10241



Some of the Catalyst Precursors Used in Asymmetric Hydroamination

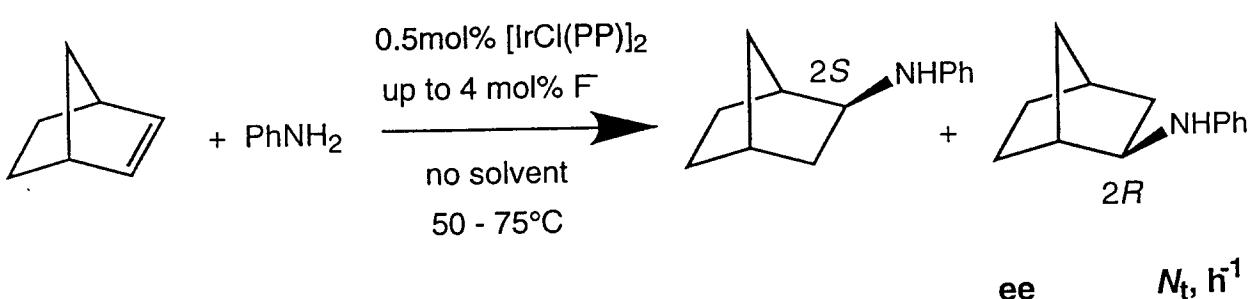
trans-[IrCl((R)-(S)-Josiphos)]₂cis-[IrCl((R)-(S)-Josiphos)]₂[IrCl((S)-BINAP)]₂ (X-ray)[IrCl((R)-Biphemp)]₂(see also: K. Tani et al. *Chem. Lett.* 1997, 1215)

R. Dorta

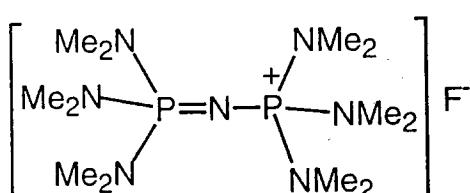
Hydroamination results

Ir-Catalyzed Asymmetric Hydroamination of Norbornene

Fluoride Effect on Activity and Selectivity

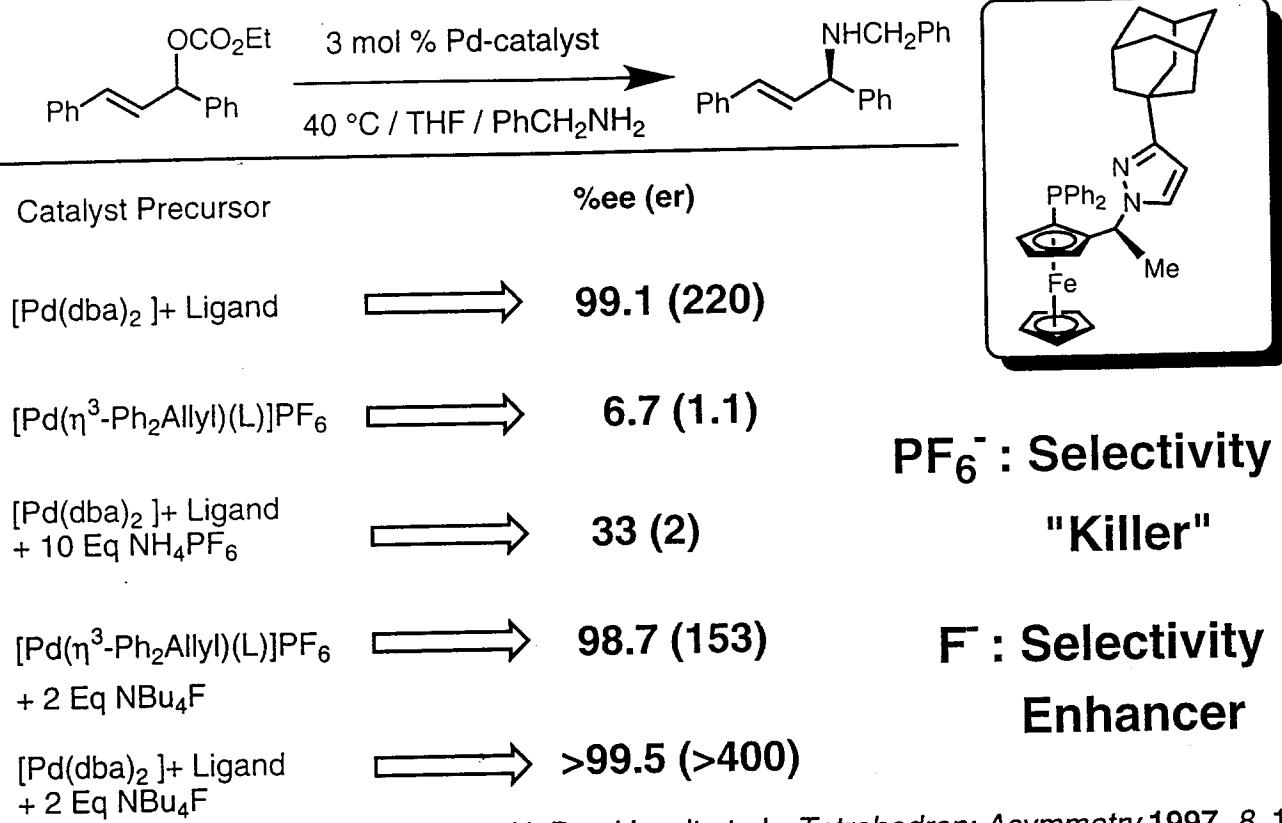


Fluoride added as:



(R)-(S)-Josiphos	60%(R)	(1.11)
(R)-(S)-Josiphos no fluoride	51%(S)	(0.17)
(R)-Biphemp	92%(S)	(0.17)
(S)-BINAP	95%(R)	(0.15)
(S)-BINAP no fluoride	57%(R)	(0.08)

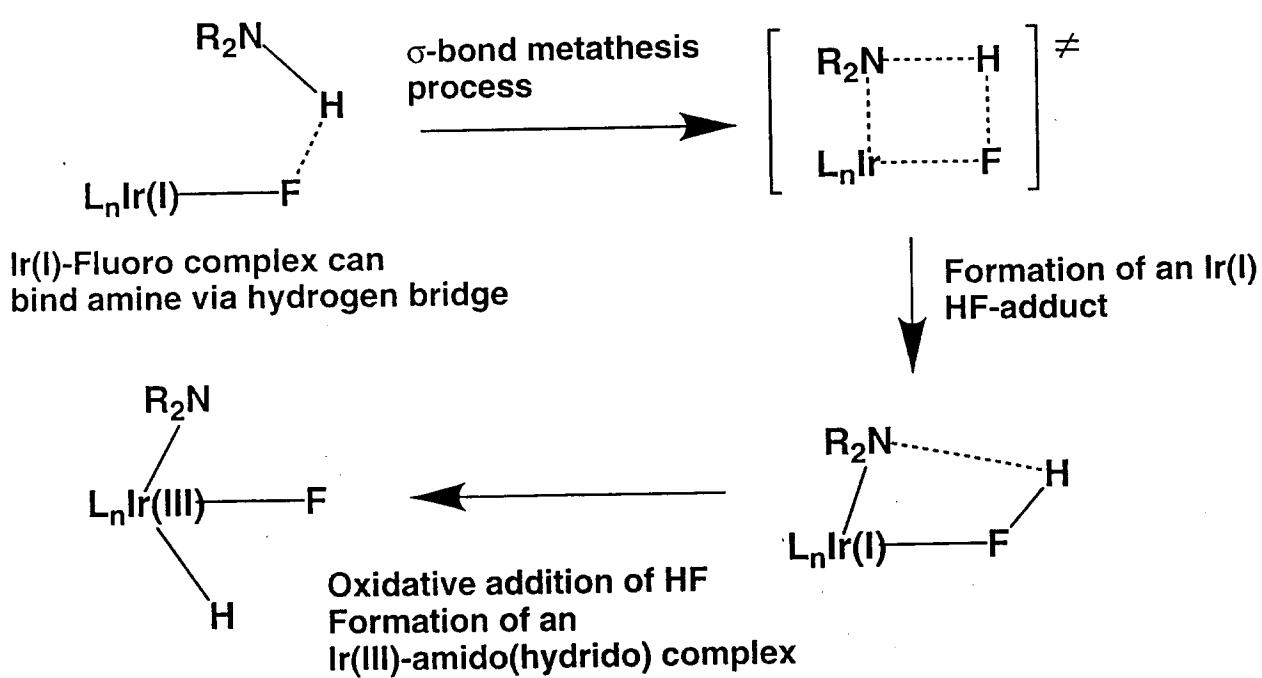
Anion Effects on Enantioselectivity in Pd-Catalyzed Allylic Amination



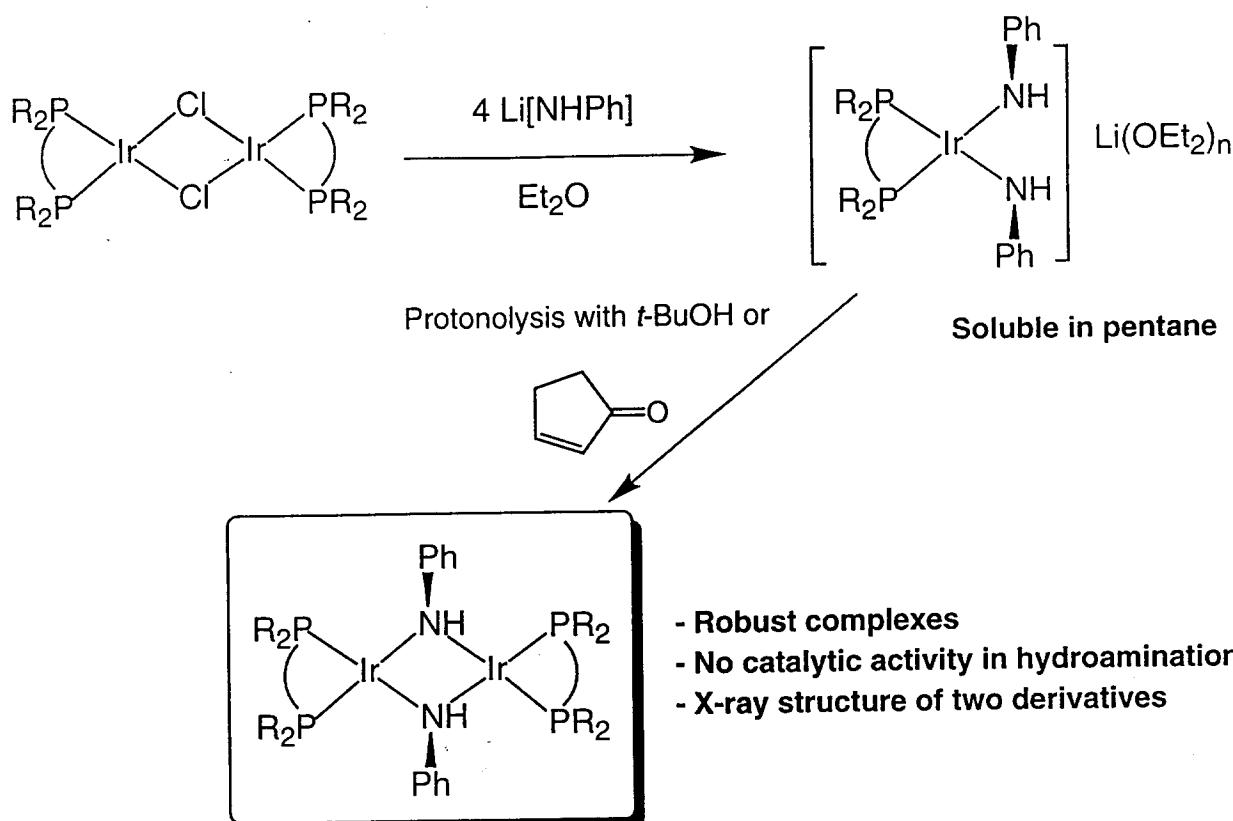
Fluoride role

A Possible Role of Fluoride in Ir-Catalyzed Hydroamination

Postulated formation of reactive fluoro complexes

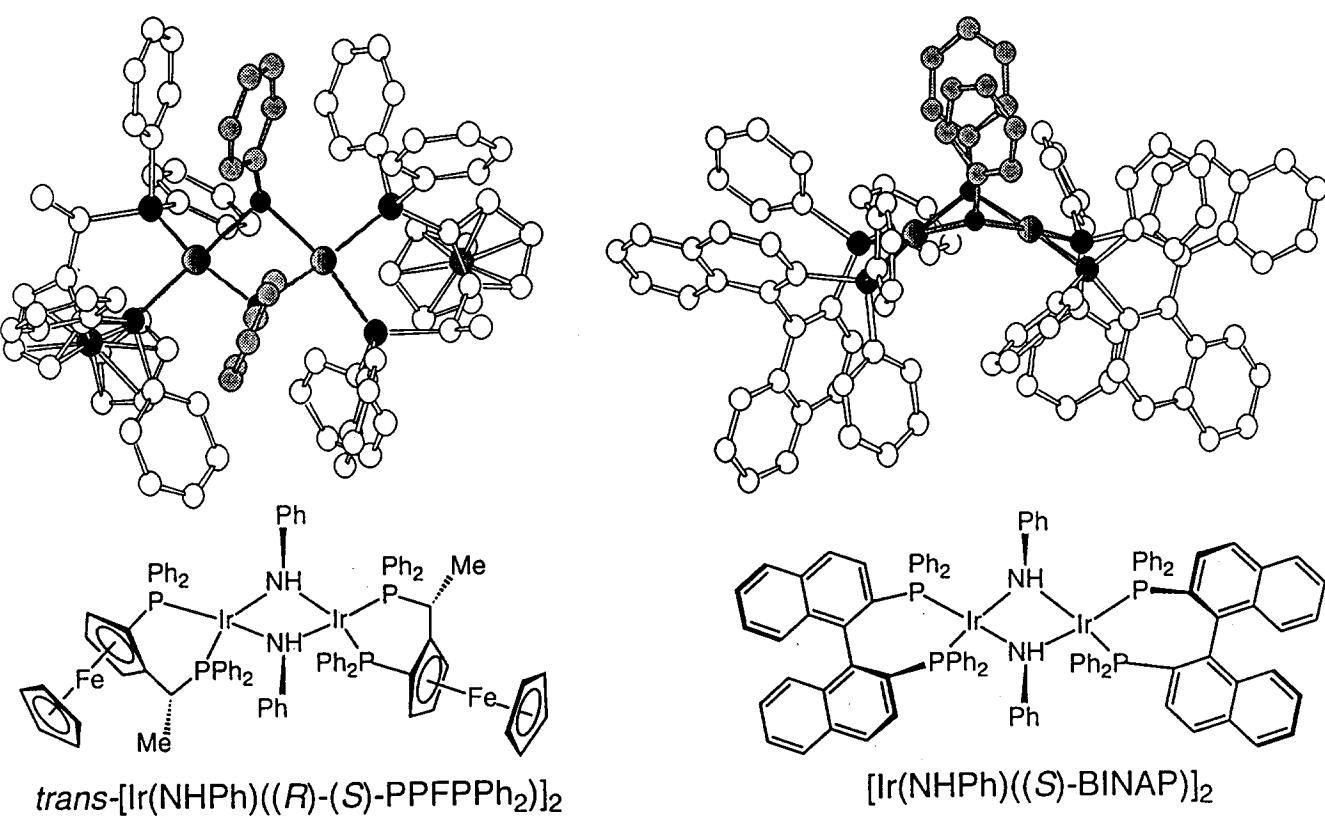


Formation of Amido Bridged Complexes via Amido Iridate(I) Derivatives



$[\text{Ir}(\text{NHPh})(\text{PP})]\text{2-cpl}$

Structures of Dinuclear Iridium-Amido Complexes



R. Dorta