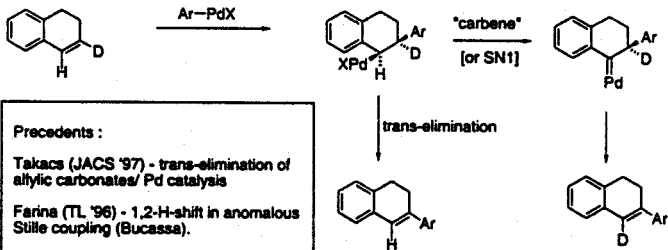


Summary Slides

IASOC 2000

John M. Brown

Mechanisms for 2-arylation in Heck reactions of dihydronaphthalene

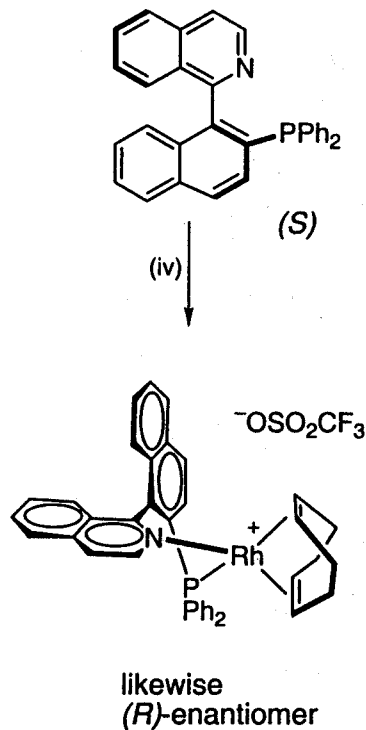
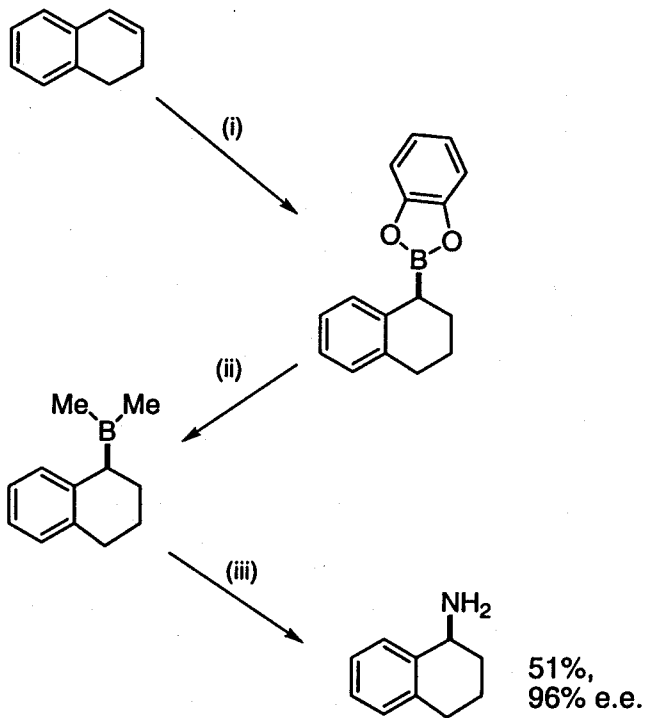


Precedents :

Takacs (JACS '97) - trans-elimination of allylic carbonates/ Pd catalysis

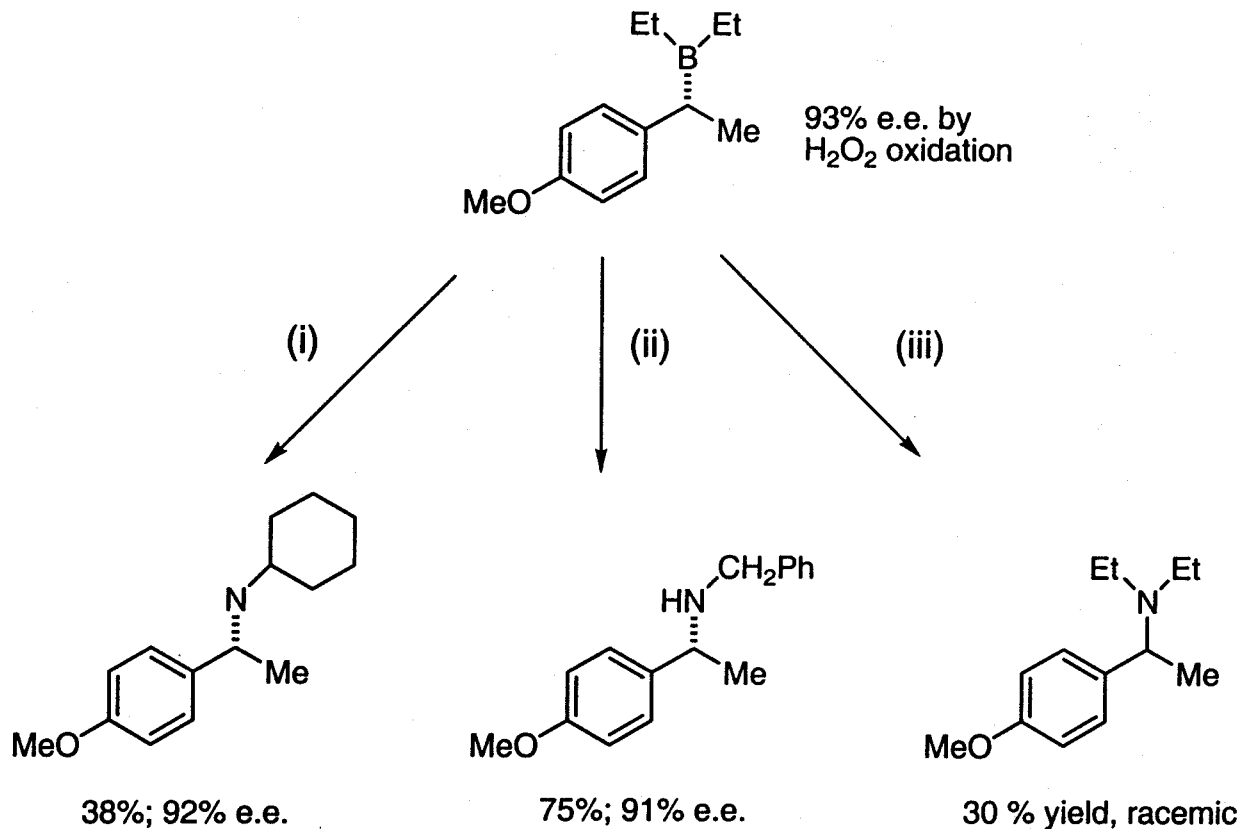
Farina (TL '96) - 1,2-H-shift in anomalous Stille coupling (Bucassa).

Hydroboration / amination : (Mark Hooper; Elena Fernandez)



(i) catecholborane, 0.2-1% catalyst, 20°C, thf, 1 h.; (ii) 2 MeMgCl (3M in thf), 20°C, 30 min;
(iii) 3 H₂NOSO₃H, thf, 10 h; (iv) CODRhacac, Me₃SiOSO₂CF₃, thf then pentane

Route to secondary amines : Kenji Maeda


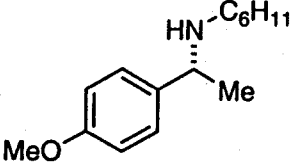
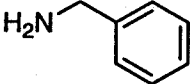
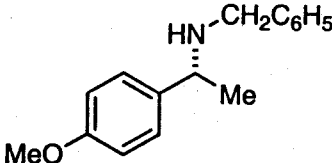
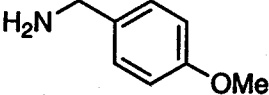
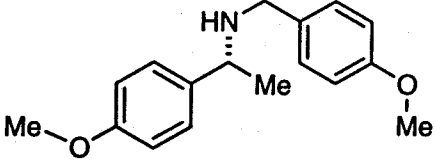
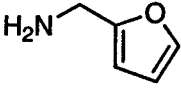
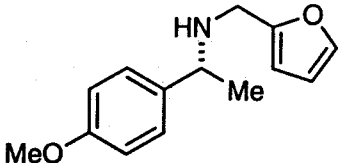


(i) $\text{C}_6\text{H}_{11}\text{NHOSO}_3\text{H}$, diglyme, 24 h, 20°C ;

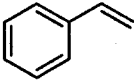
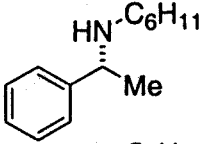
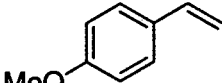
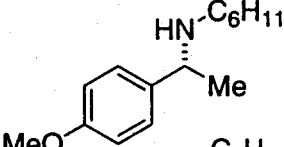
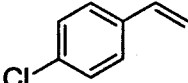
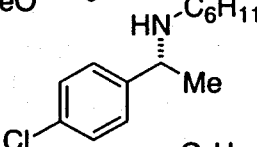
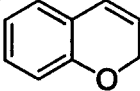
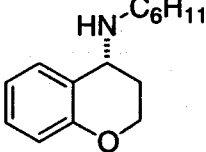
(ii) PhCH_2NHCl (ex. PhCH_2NH_2 , aq. NaOCl in situ), 0°C , 5 min then 20°C , 1 h;

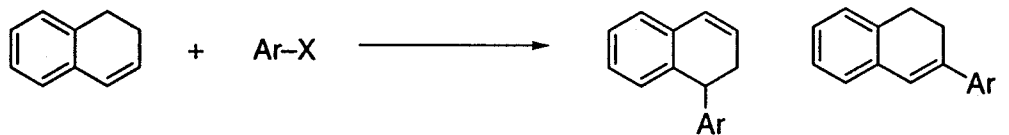
(iii) Et_2NHCl (ex. Et_2NH , aq. NaOCl), *.

Amination of p-methoxystyrene

Reactant	Product	Yield and E.e.
		82% yield, 92% e.e.
		75% yield, 91% e.e.
		77% yield, 90% e.e.
		76% yield, 91% e.e.

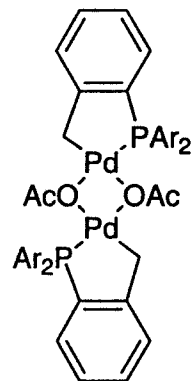
Amination with cyclohexylamine

Reactant	Product	Yield and E.e.
		71% yield, 87% e.e.
		82% yield, 92% e.e.
		50% yield, 78% e.e.
		47% yield, 87% e.e.

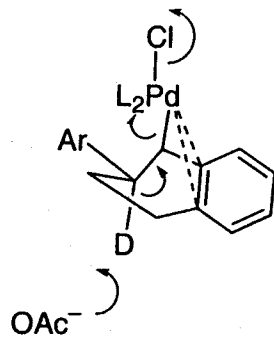
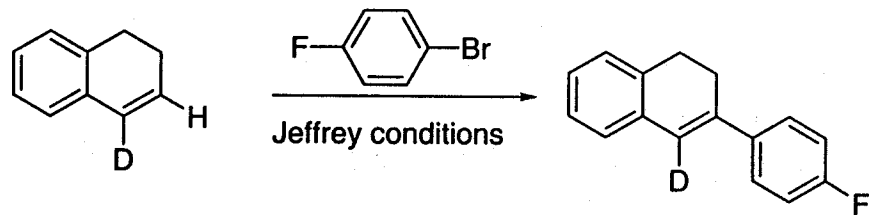
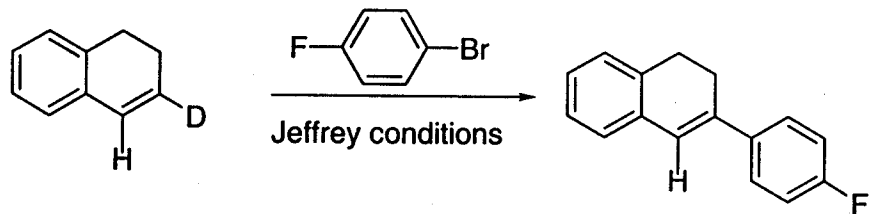


Ar = Ph	X = I	Condition A	3 : 2
Ar = 3,4-Cl ₂ Ph	X = I	Condition A	1 : 1
Ar = 4-FPh	X = Br	Condition B	1 : 1
Ar = 4FPh	X = Br	Condition C	1 : 20

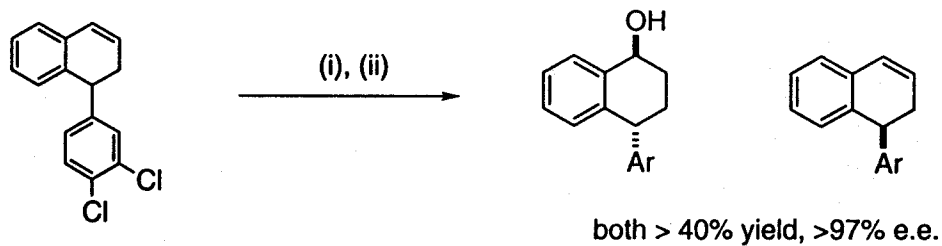
Conditions : **A**, 1 mol% Pd(OAc)₂, P(o-tol)₃, Et₃N, CH₃CN, reflux; **B**, 1 mol% complex **1**, NaOAc, DMA, 140°C; **C**, 5 mol% Pd(OAc)₂, Bu₄NOAc, DMF, 80°C



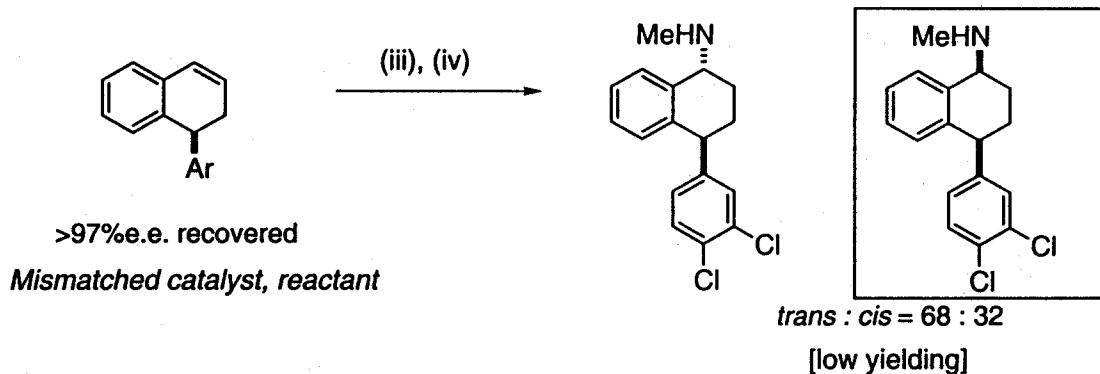
1, Ar = o-tol



Step 1

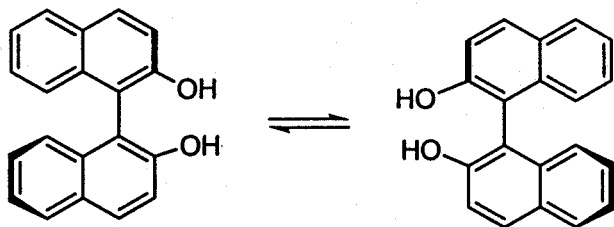


Step 2

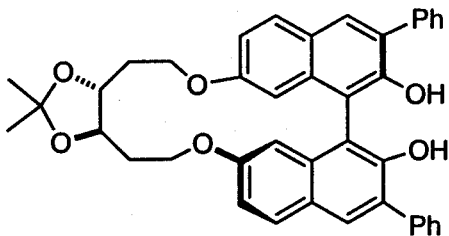


Conditions : (i) Catecholborane (0.6 eq.), *S*-QuinapRh catalyst, C_7H_8 , 2 h., (ii) H_2O_2 , NaOH, H_2O ; (iii) Catecholborane (1.2 eq.), *S*-QuinapRh catalyst, C_7H_8 , 48 h.; (iv) Et_2Zn , C_7H_8 , then MeNHCl (in situ), Et_2O .

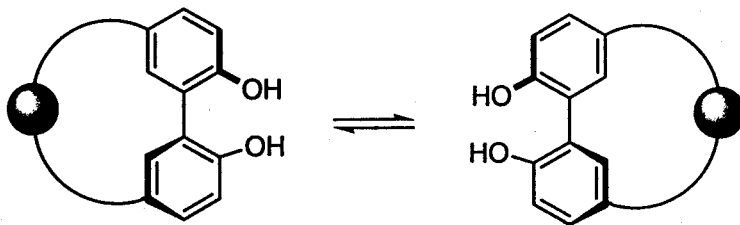
Ligands prepared by resolution procedures



Ligand needs to be resolved; racemisation very slow at $>100^{\circ}\text{C}$

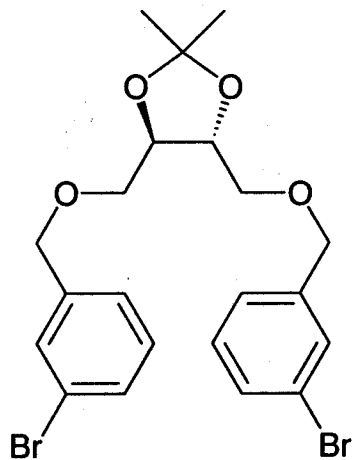


Diastereoselective biaryl synthesis
[Lipshutz, TL. 1998]



Fast interconversion; X perturbs equilibrium

Successful cyclisation method



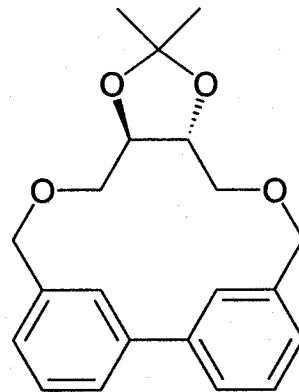
ex R,R-tartrate

Ni(OAc)₂, 2,2'-bipyridyl

NaH, KI

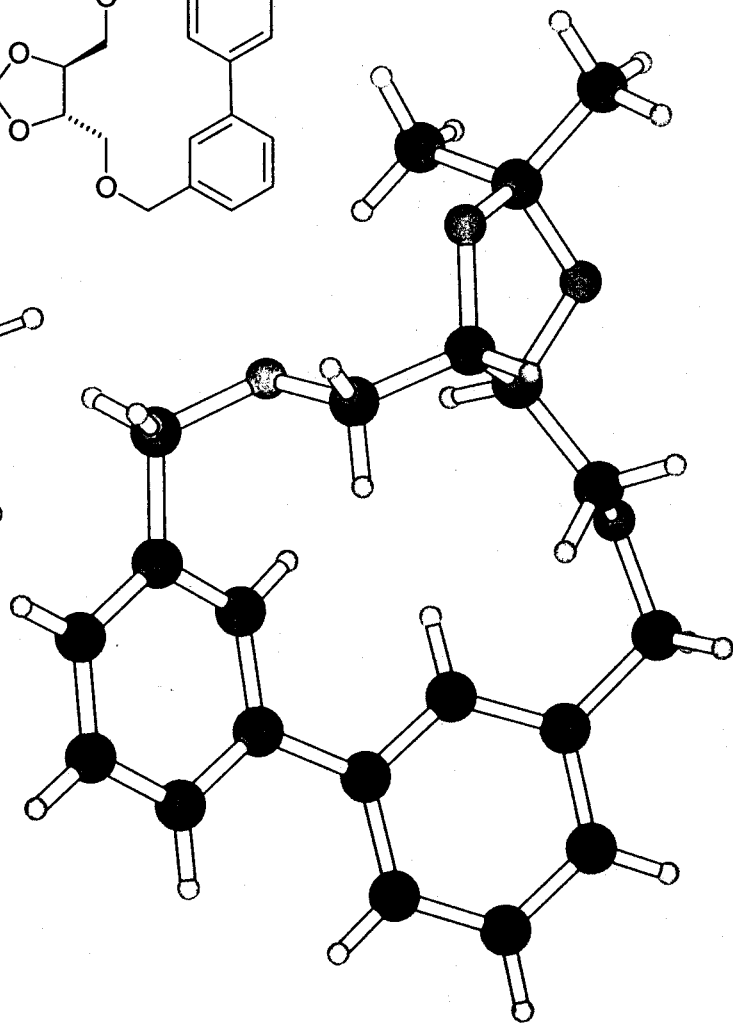
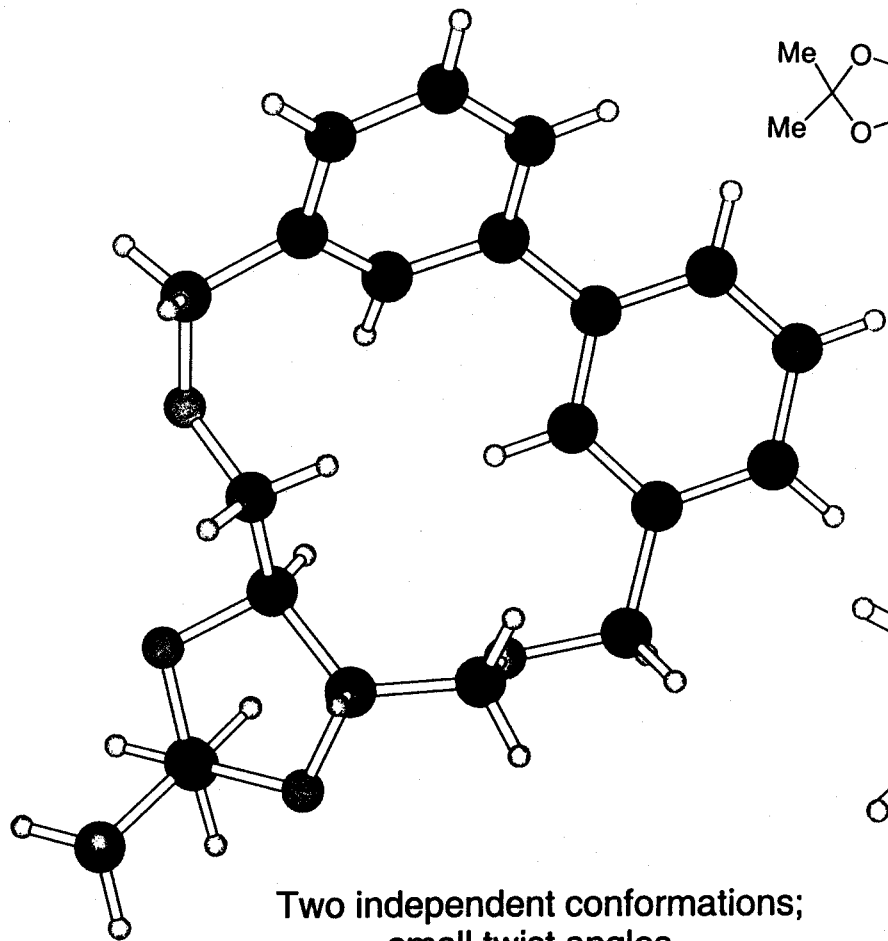
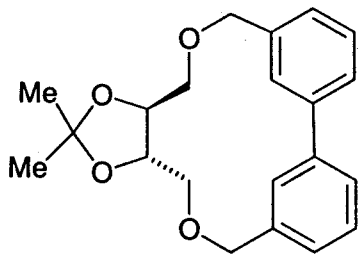


THF / 60°C

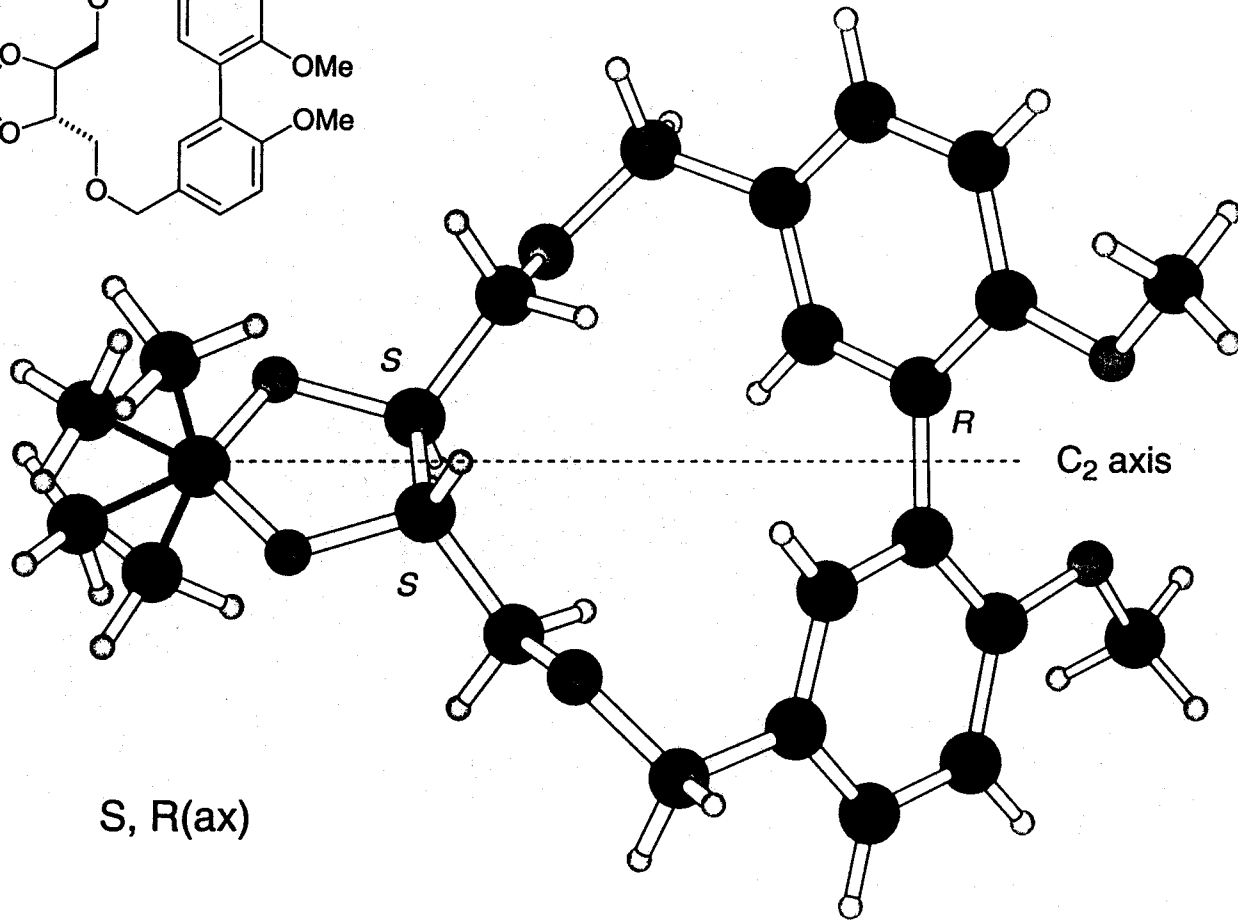
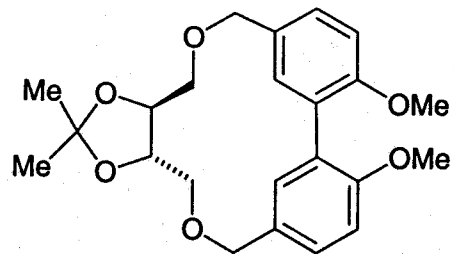


60%, 1 mmolar scale

P. Caubere, 1989



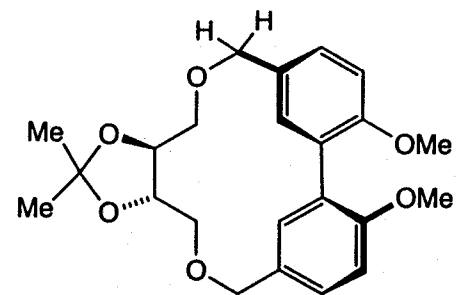
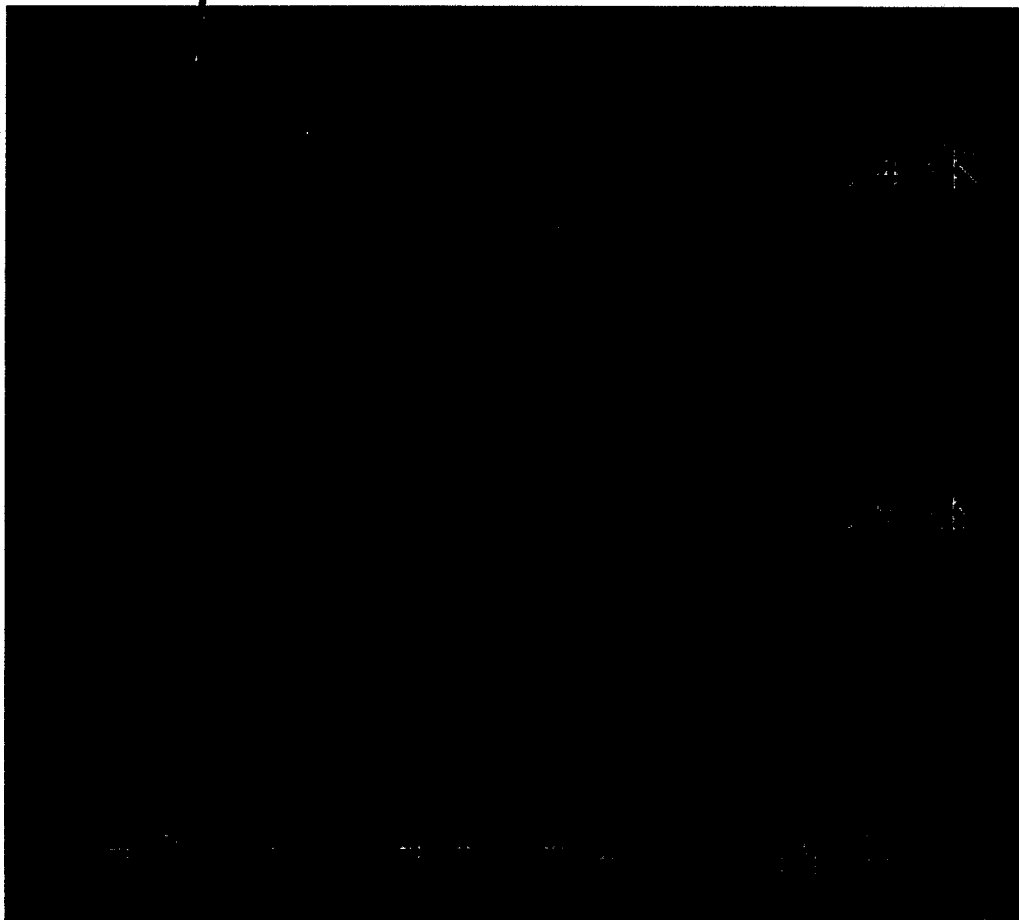
Two independent conformations;
small twist angles



Threitol cyclophane

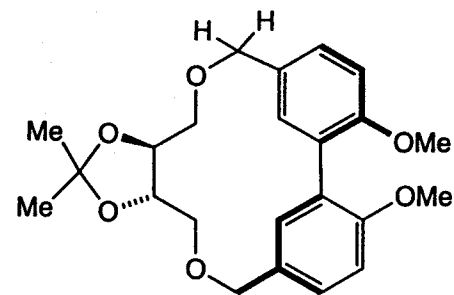
R

S

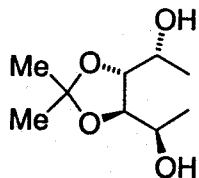


S

$^1\text{H NMR}$

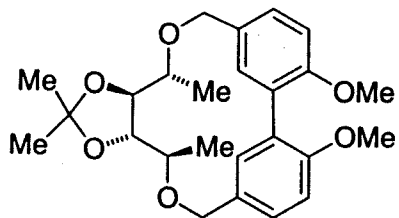


R

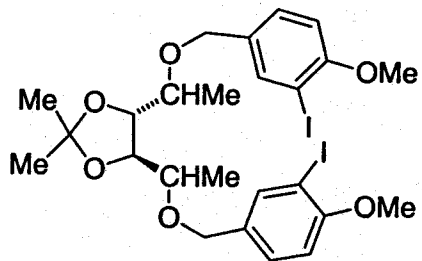


ex mannitol

$\text{Ni}(\text{PPh}_3)_4$ DMF



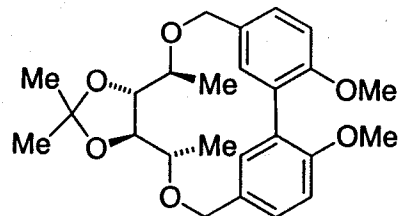
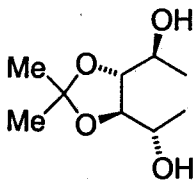
45-60%



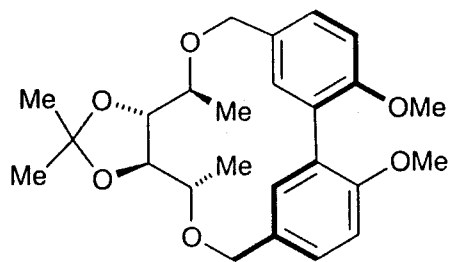
ex iditol

$\text{Ni}(\text{PPh}_3)_4$

DMF

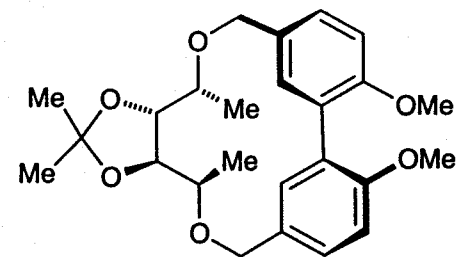


CD spectra of the diastereomers



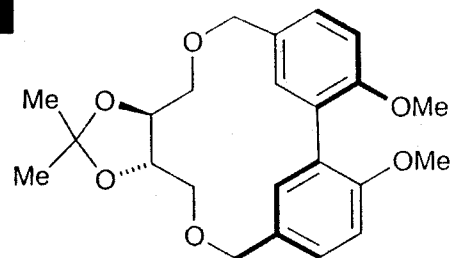
IDITOL

R



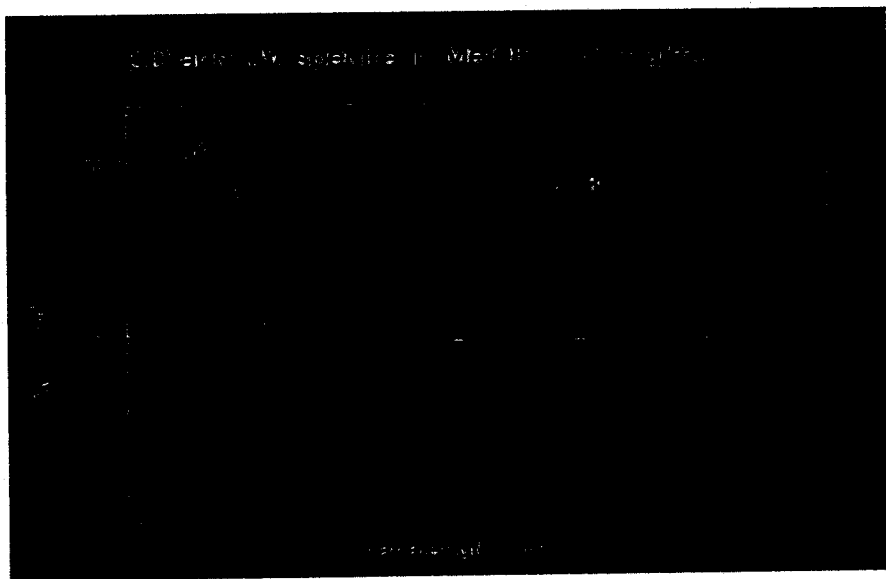
MANNITOL

S

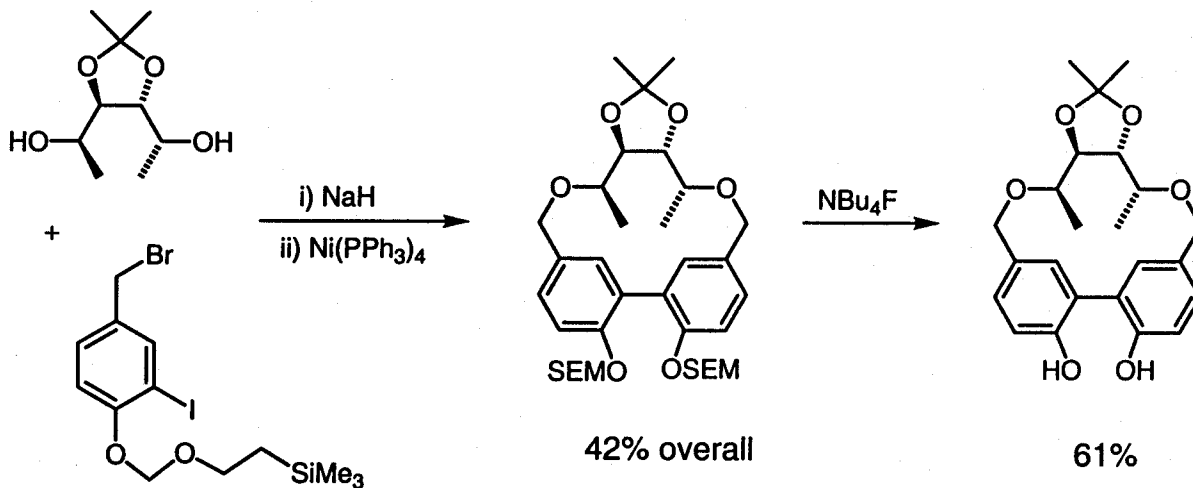


THREITOL

R

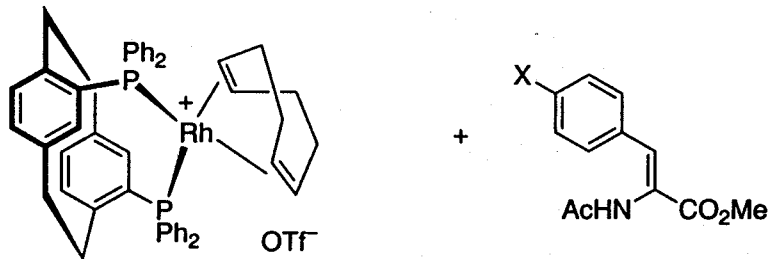


Biphenol Synthesis in the Mannitol Series



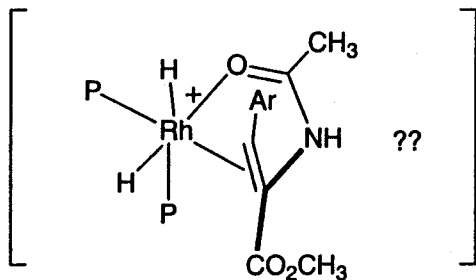
Biphenols show sharp CH₂ NMR at ambient temperature and below

Likewise Threitol, Iditol series



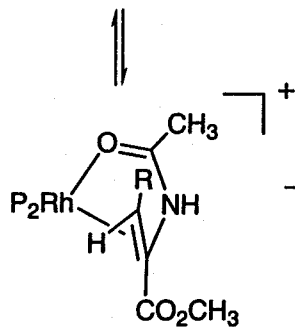
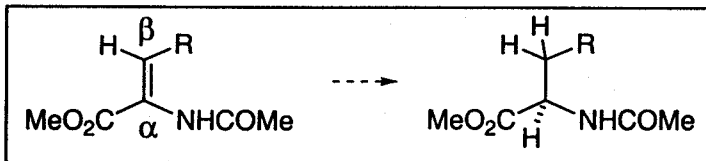
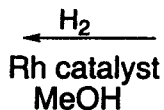
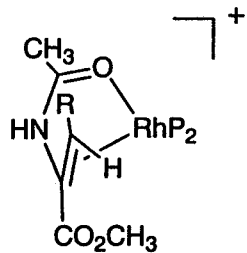
bubble through
para-H₂ (50%)

in NMR probe, -15°C

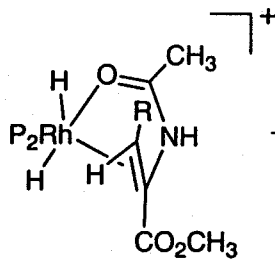


PHIP detects transients where
there is H----H coupling

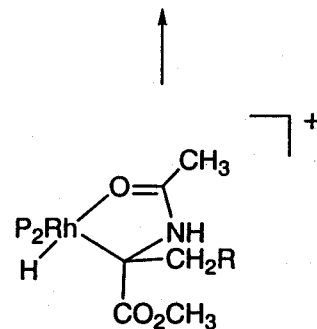
[Bargon, Giernoth U. Bonn]



enamide complexes



dihydride ???



alkylhydride

Summary of observations on the PHIP transient

The new species is associated with 1-H chemical shifts of ca. -2 and -19 ppm [-2 ppm is unusual - agostic?]

Formation is observed in the temperature range of -10°C to -25°C - occurs only when substrate remains

Concurrent with the observation of transient, polarised hydrogenation product is also seen.

Both rhodium norbornadiene and cyclooctadiene complexes can be employed.

The transient is associated with bound substrate, since different substrates give distinct spectra

Any exchange of substrate with unbound species is slow (half-life >300 ms) on the NMR time-scale

Conclusions on the PHIP-observed species

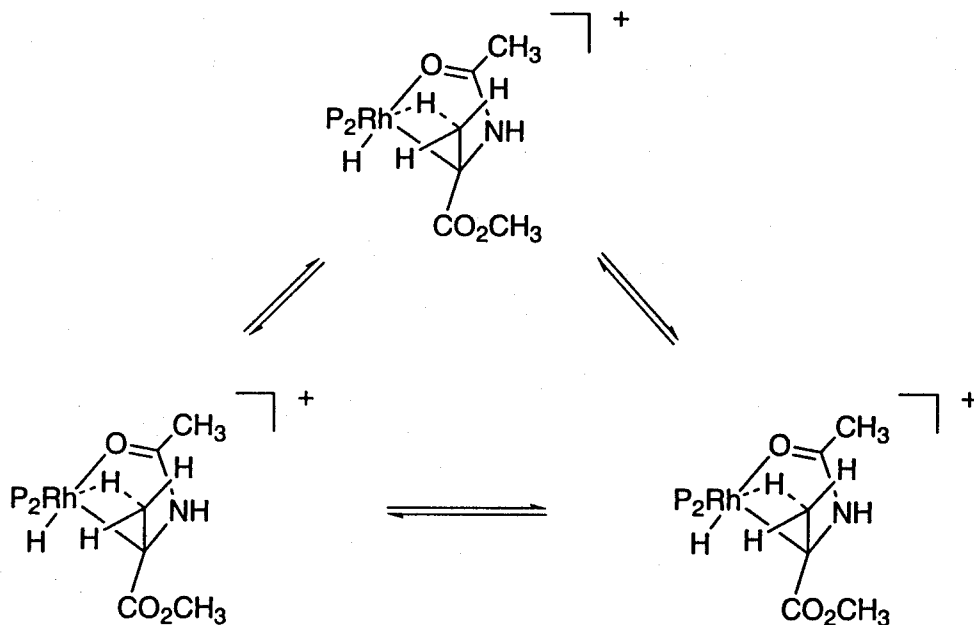
The complex is a rhodium enamide dihydride with one agostic hydrogen in flight to the beta-carbon; the second is trans- to a coordinated (enamide) oxygen

For dehydroalanine, the hydride exchanges rapidly with the beta-methylene group

The transient behaves as an intermediate in hydrogenation, being closely associated with the observation of spin-polarised product (INEPT)

Polarisation transfer to the reactant observed by INEPT requires some substrate dissociation from the transient - but does not reveal the mechanism by which this occurs.

Dynamic agostic methyl group for the dehydroalanine case



Rotation about the C_α - C_β bond is rapid on the NMR timescale