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Supramolecular ligands in transition metal catalysis

TOOLS FOR CATALYST ENCAPSULATION, COMBINATORIAL CATALYSIS AND CATALYST RECYCLING

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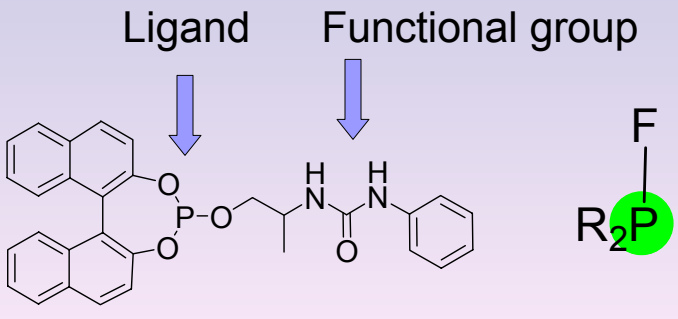
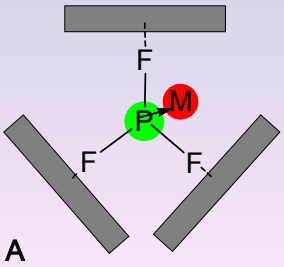
Supramolecular ligands



F =Functional Group for the assembly process

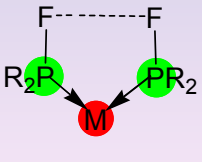
Supramolecular ligands

Catalysts encapsulation



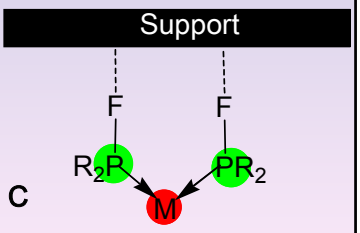
Selectivity, activity, stability

Self-assembled ligands



Selectivity, activity, stability

Catalysts Immobilization



Catalyst recycling

(JACS **2001** JACS **2004**)

F =Functional Group for the assembly process

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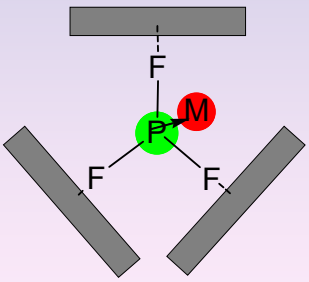
Can we encapsulate transition metals for catalysis?



- Why? Study site isolation effects
  Enzymes use cavities
- How? Literature: no examples when we started in 1999!

Other players

Raymond, Bergman

Fujita, Rebek, Sanders and others

Organic reactions in capsules

Diels Alder, isomerization, photodimerization etc.

Creation of the encapsulated transition metal catalyst using programmed building blocks: *Templated encapsulation*

Ligand-template

Vincent Slagt

Angew. Chem. Int. Ed., **2001**, *40*, 4271.

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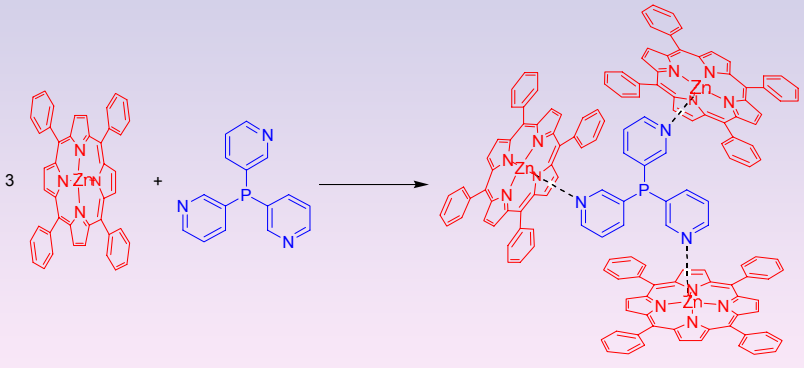
Creation of the encapsulated transition metal catalyst using programmed building blocks: *Templated encapsulation*

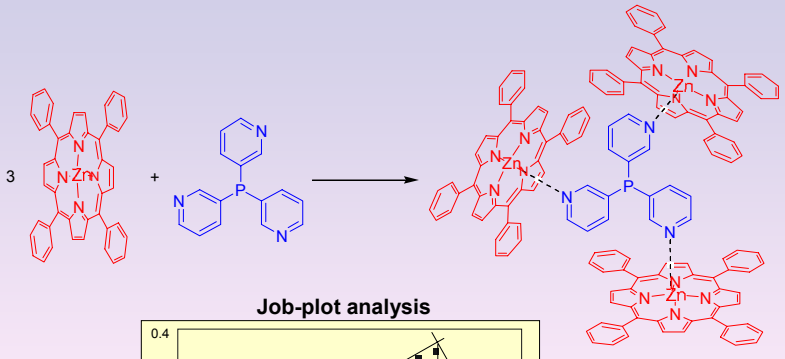


NMR titrations (shifts of 6ppm)
UV-vis titrations (Q-bands unique)

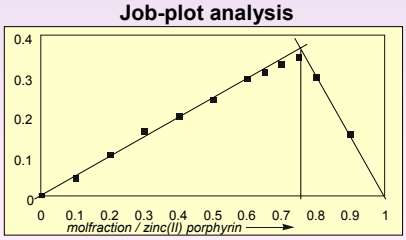
Vincent Slagt

Angew. Chem. Int. Ed., **2001**, *40*, 4271.

Templated encapsulation of Tris-pyridyl phosphine



Job-plot analysis



$K_3 > K_2 > K_1$

Program of
Prof Hunter

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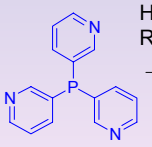
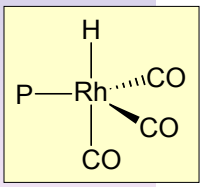
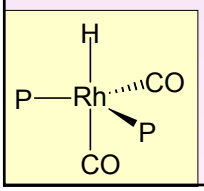
Enforced ligand dissociation from Rhodium complexes:



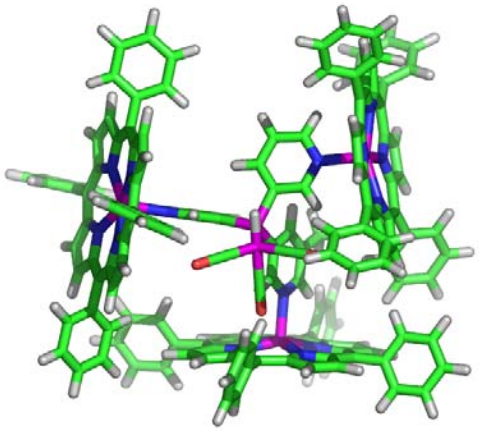
3 eq Porphyrin
H_2/CO
$RhAcac(CO)_2$



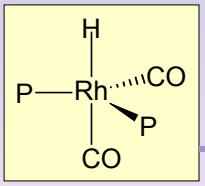
H_2/CO
$RhAcac(CO)_2$

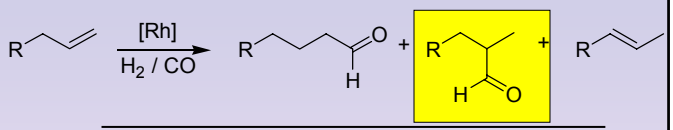


^1H and ^{31}P –NMR
HP-IR

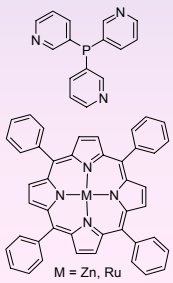


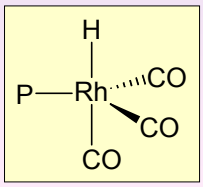
Hydroformylation of 1-octene at 25 °C





	TOF (h^{-1})	l/b	branched	2-octene
No Porphyrin	**11**	**2.8**	**25.6%**	3.4%
Zn(II) Porphyrin	**126**	**0.6**	**61.9%**	1.0%





From HP-IR: $HRh(P)(CO)_3$

Angew. Chem. Int. Ed., **2001**, *40, 4271.*

Vincent Slagt

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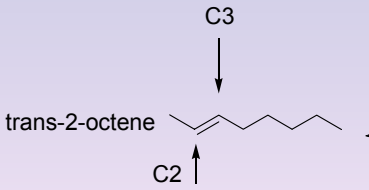
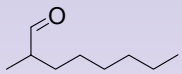
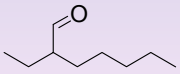
Hydroformylation of internal alkenes: Selectivity provided by the encapsulation



[Rh]
CO/H_2

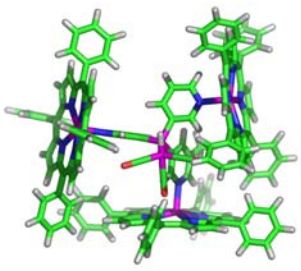


2-methyl-octanal **2**



2-ethyl-heptanal **3**

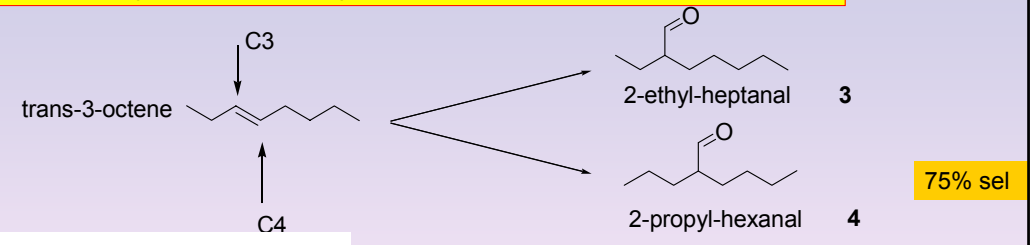
90% sel

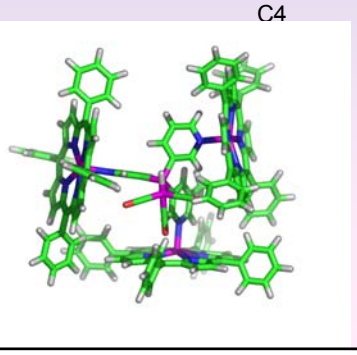


Mark Kuil

J. Am.Chem. Soc., **2006**, 11344

Hydroformylation of internal alkenes: Selectivity provided by the encapsulation





Selectivity also observed for:
2-hexene, 3-hexene
2-nonene, 3-nonene

Mark Kuil *J. Am.Chem. Soc.*, **2006**, 11344

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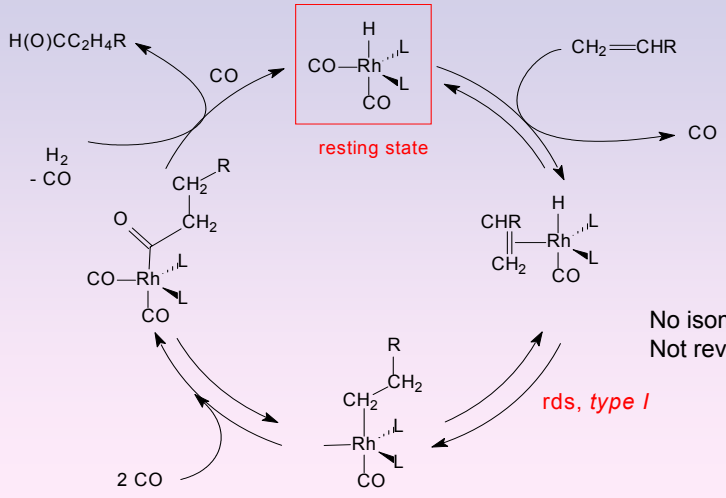
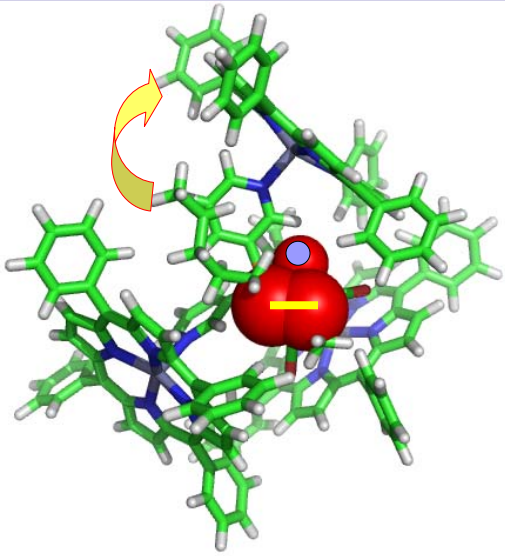
Hydroformylation; catalytic cycle for *type I* Kinetics



No isomerization
Not reversible at 25 and 40 C

Selectivity provided by the encapsulation: hindered rotation?



Mark Kuil

J. Am.Chem. Soc., **2006**, 11344

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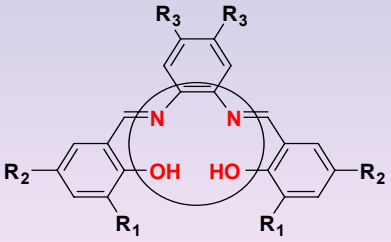
What's next?

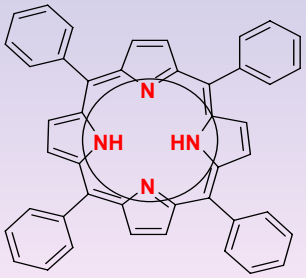
- Extend to other (more accessible) building blocks
- Extend to other reactions

Alternative building blocks for porphyrins: salphen complexes

(salphen = *N,N'*-phenylene-bis{salicylideneimine})



vs



- Great similarity with porphyrins
- Tunable Electronic/Steric features
- Cheap Starting Materials
- Synthetically accessible

→ Several Chiral analogues known

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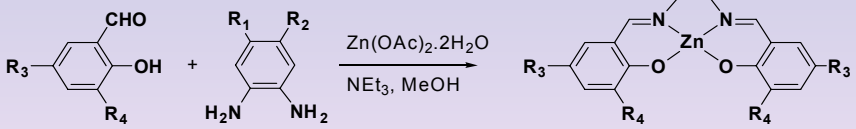
Multi-component one-pot synthesis

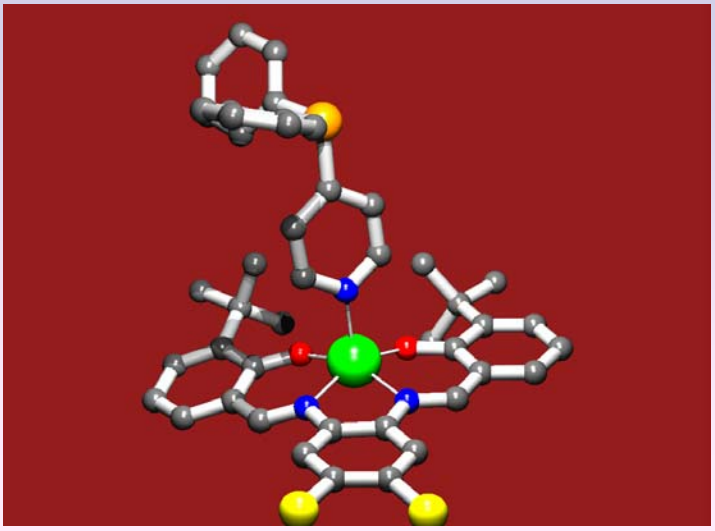


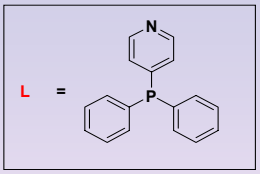
94%	$R_1 = R_2 = Cl$; $R_3 = R_4 = t$Bu
100%	$R_1 = Cl$; $R_2 = H$; $R_3 = R_4 = t$Bu
85%	$R_1 = CF_3$; $R_2 = H$; $R_3 = R_4 = t$Bu
86%	$R_1 = R_2 = Cl$; $R_3 = H$; $R_4 = t$Bu
91%	$R_1 = R_2 = Cl$; $R_3 = Br$; $R_4 = t$Bu
98%	$R_1 = R_2 = H$; $R_3 = Cl$; $R_4 = Cl$

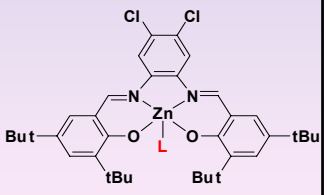
Chem. Eur. J., **2005**, *11* 4743
Eur. J. Inorg. Chem. **2005**, 4626–4634

Arjan Klei

X-ray structure of 1:1 Zn-Saphen-Ligand Assembly







UV vis titration
$K=4 \times 10^5\ M^{-1}$

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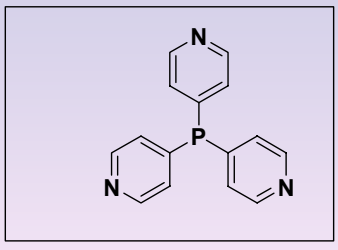
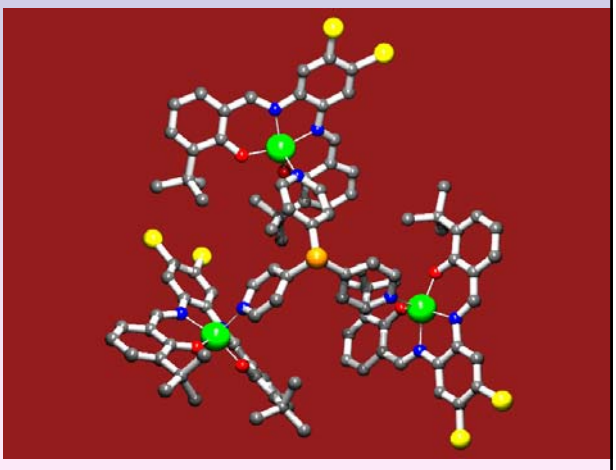
The X-ray structure of 3:1 assembly !





UV-vis titrations:
3:1 complex in solution
Structure confirmed by NMR

Chem. Commun. **2005**, 3661

Arjan Kleij

Similar behavior as porphyrin assemblies:

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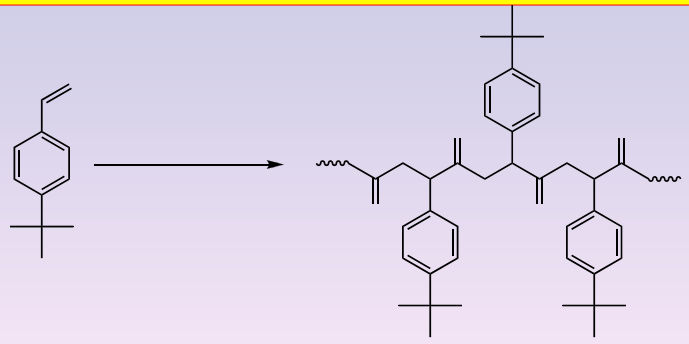
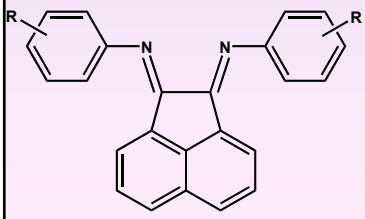
New reactions: CO-styrene co-polymerization



Polymer length
stereoregularity



M. Brookhart, et al., *J. Am. Chem. Soc.* **1994**, *116*, 3641.
M. Brookhart, etal *J. Am. Chem. Soc.* **1992**, *114*, 5894..
Macchioni, et al. *Chem.--Eur. J.* **2007**, *13*, 1570.
Macchioni,et al *Chem. Commun.* **2005**, 92.
J. Durand, B. Milani, *Coord. Chem. Rev.* **2006**, *250*, 542.

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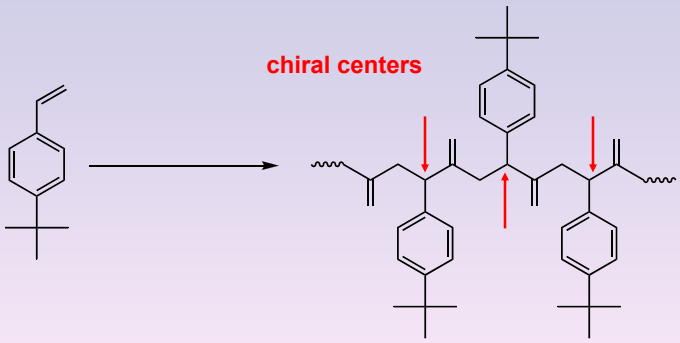
CO-styrene co-polymerization



Polymer length
stereoregularity

two successive centers with same chirality (RR or SS): like (*l*)
two successive centers with opposite chirality (RS or SR): unlike (*u*)

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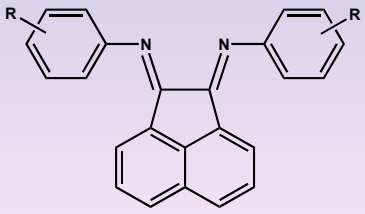
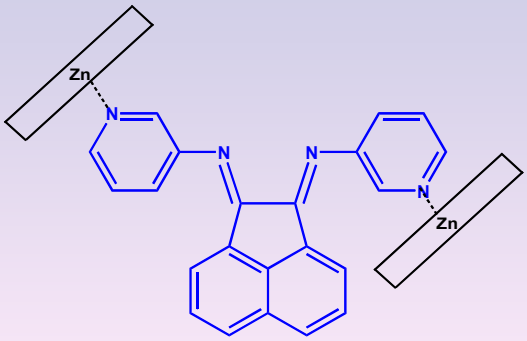
Traditional vs supramolecular BIAN ligands





Traditional BIAN ligand:
tunable via
synthetic modification

pyridyl modified BIAN ligand:
tunable via
supramolecular assembly

Jitte Flapper *Angew. Chem.* **2007** 8590

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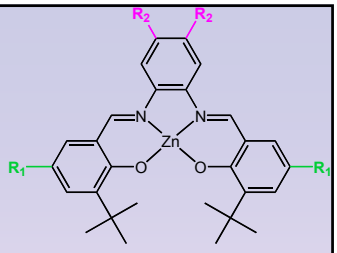
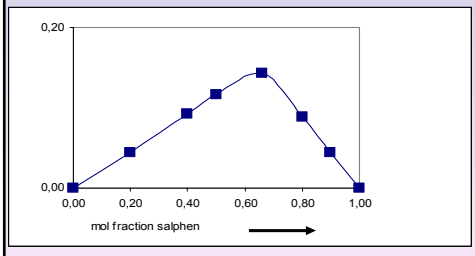
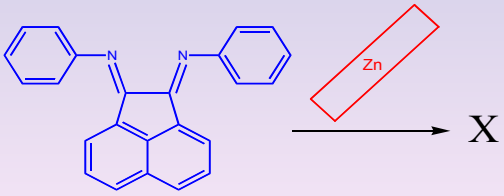
Assembly with zinc(II) salphen

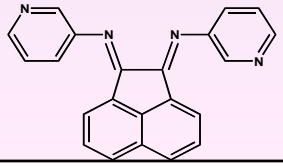


Job-plot analysis





a 1:2 complex



no complexation
with Ph-BIAN

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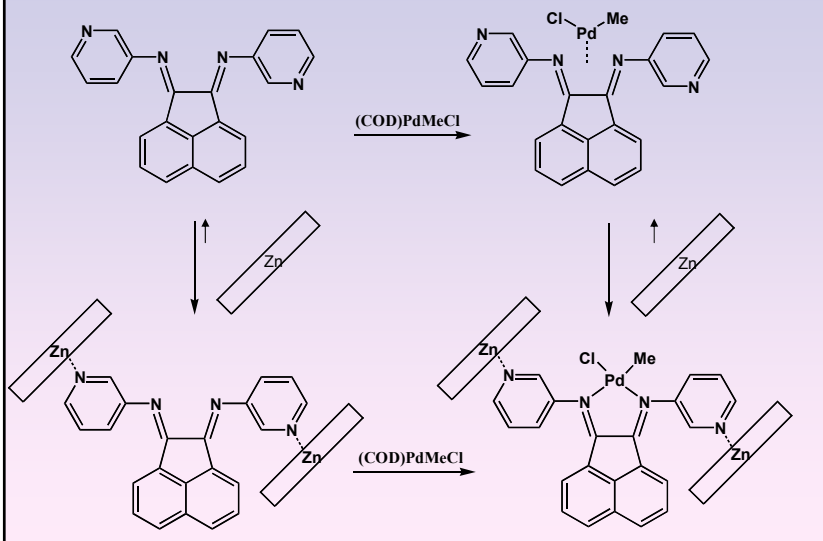
complex: selectivity based on sterics and chelate effect

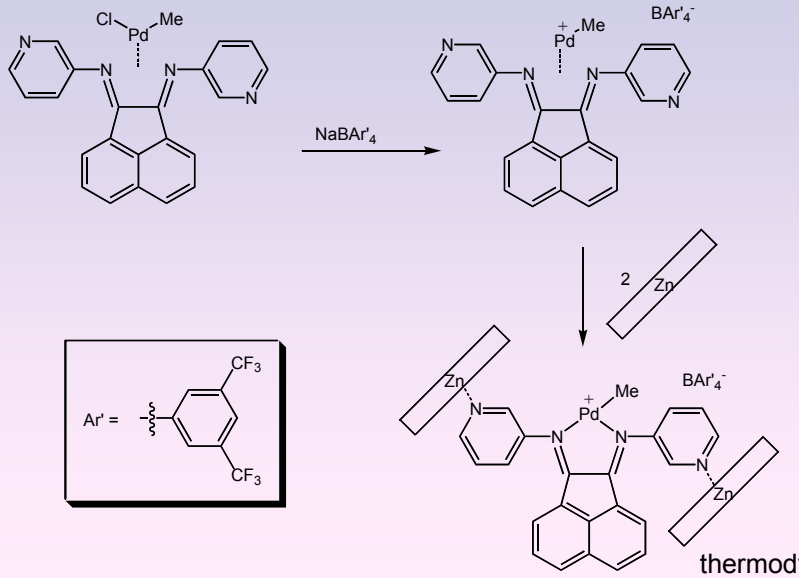


mixture of palladium complexes

One complex: selective palladium coordination!

thermodynamic product

cationic palladium complex



precursor for different complexes

active Complex pure

thermodynamic product

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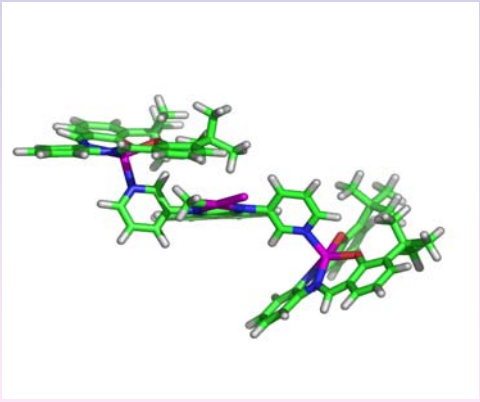
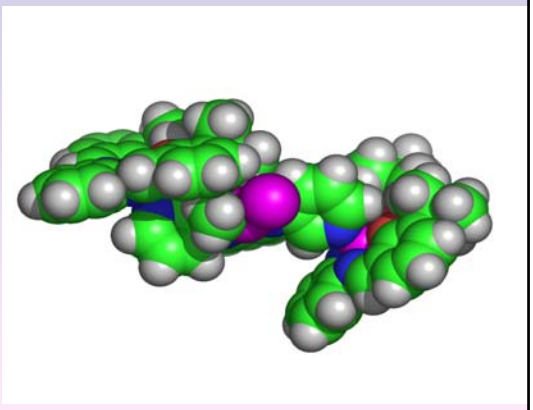
Salphen encapsulated palladium complex: molecular modeling





PM3 optimized structure

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CO / *p*-^{t}Bu-Styrene copolymerization

Supramolecular ligand syndiotactic polymers

cat	Zn-salph	equiv Zn	activity gCP/gPd	Mw (Mw/Mn)	stereoregularity		
					% II	% ul/lu	%uu
***m*Py-BIAN**	-	0	0	-	-	-	-
***m*Py-BIAN**	D	2.0	411	$104 \cdot 10^3$ (2.2)	<1	13	87

Traditional ligand atactic polymer

Ph-BIAN	-	0	284	$35 \cdot 10^3$ (1.2)	18	57	25
Ph-BIAN	D	2.0	92	$18 \cdot 10^3$ (1.4)	17	56	27

salphen is essential for activity and selectivity

Polymer Analysis
GPC
^{1}H-NMR
^{13}C-NMR

conditions:
12.5 µmol Pd-comp
1.0 ml *p*-^{t}BuStyrene
1.5 ml CH_2Cl_2
10 bar CO
16 h
25°C

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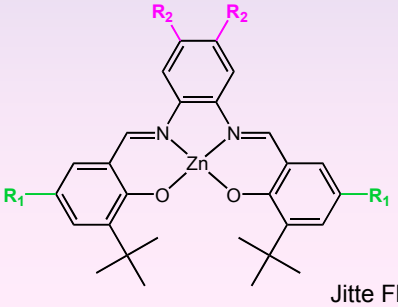
Supramolecular tunable copolymerization catalyst

Zn-salph	equiv Zn	activity gCP/gPd	Mw (Mw/Mn)	stereoregularity		
				% ll	% ul/lu	%uu
A	2.0	98	$44 \cdot 10^3$ (1.9)	2	27	71
B	"	184	$58 \cdot 10^3$ (1.9)	<1	21	79
C	"	259	$118 \cdot 10^3$ (2.9)	<1	15	85
D	"	411	$104 \cdot 10^3$ (2.2)	<1	13	87

tunable catalyst

high activity
high selectivity

salphens		
#	R_1	R_2
A	H	Cl
B	*t*Bu	Cl
C	H	H
D	*t*Bu	H



conditions:
12.5 µmol Pd-complex
1.0 ml *p*-^{t}BuStyrene
1.5 ml CH_2Cl_2
10 bar CO
16 h
25°C

Jitte Flapper *Angew. Chem.* **2007** 8590

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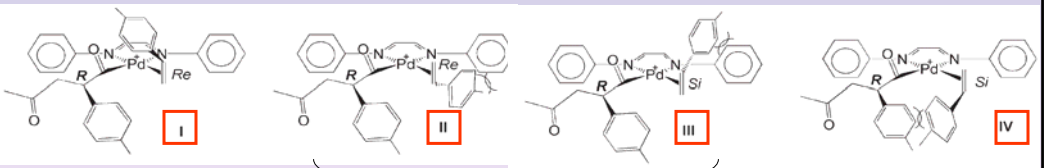
Stereocontrol mechanism (Carfagna *et. Al)*

4 possible intermediate species, leading to:

l-triad *u*-triad *u*-triad *l*-triad



no unfavorable interactions

unfavorable interaction with *ortho*-aryl substituents

unfavorable interactions

experiment:
ortho-aryl substituents → l-triads (isotactic polymer)
no *ortho*-aryl substituents → atactic polymer

Carla Carfagna et. al. *Chem. Commun.*, **2007**, 4540

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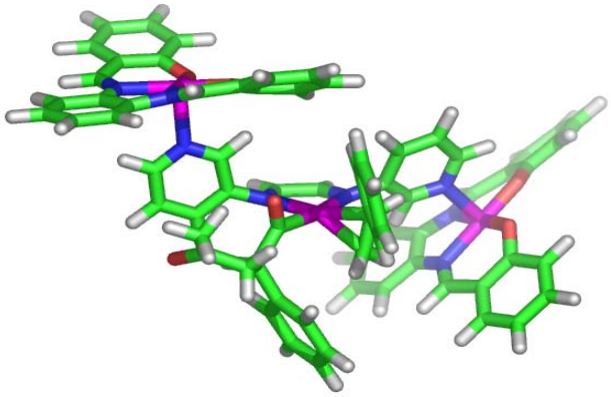
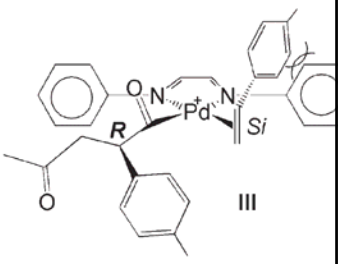
PM3-optimized structure supramolecular ligand





PM3 calculated structure of encapsulated intermediate **I**

intermediate **III** Favored ⟶ U-select

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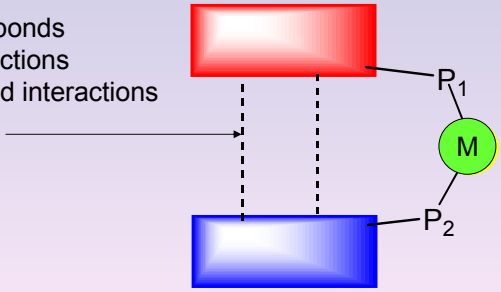
More about capsules

Koblenz *Chem Soc Rev* **2008**

Kleij *Chem Commun* **2005**
Kleij *Inorg Chem* **2005**
Kleij *Chem. Eur. J* **2006**

A supramolecular strategy to make bidentate ligands

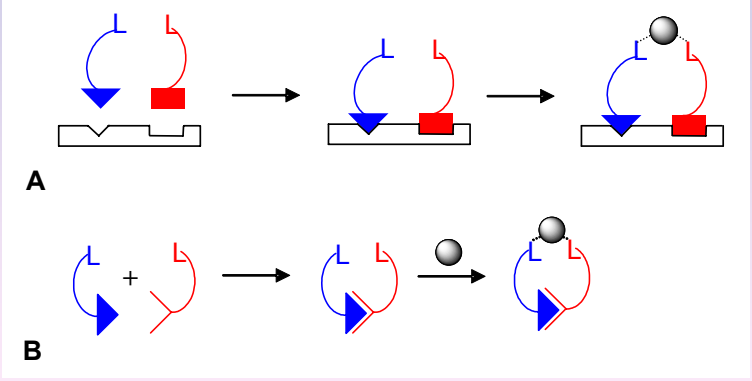
Hydrogen bonds
Ionic interactions
Metal-ligand interactions



Other early players in the field: Breit et al. *J. Am. Chem. Soc.*, **2003**, 6608
Takacs et al. *J. Am. Chem. Soc.*, **2004**, 4494

Reviews: *Org. Biomol. Chem.* ***2005***, *3, 2371*
Angew. Chem., **2005**, *44*, 6816
Dalton Trans., **2006**, 3385.

Two strategies for the formation of chelating ligands



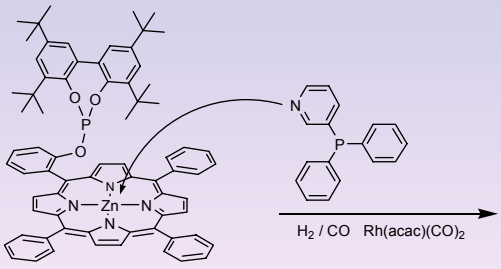
3-component
Template approach

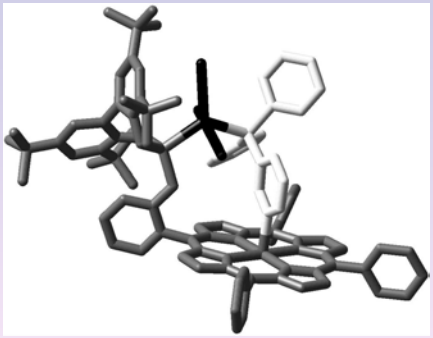
2-component
Direct approach

Ideal approach to make ligand/catalyst libraries!

A.J. Sandee, J.N.H. Reek, *Dalton Trans.*, **2006**, 3385

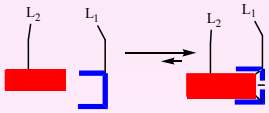
Supramolecular phosphine-phosphite ligands: direct approach





HP-NMR, HP-IR

Strong chelate effect



J. Am. Chem. Soc., **2004**, *126* 4056

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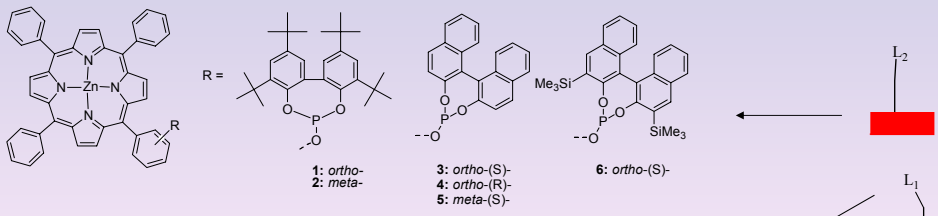
Initial study: A ligand library by just Mixing 8x6=48

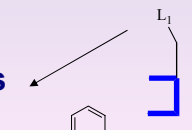
phosphite-zinc(II)porphyrin ligand building blocks



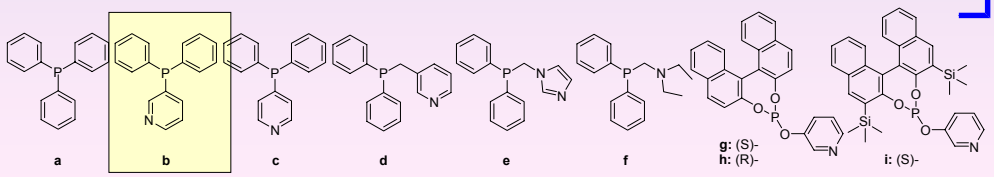
1: *ortho-*
2: *meta-*

3: *ortho*-(S)-
4: *ortho*-(R)-
5: *meta*-(S)-

6: *ortho*-(S)-



Phosphorus/nitrogen ligand building blocks

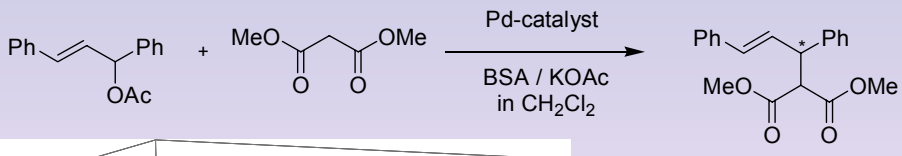


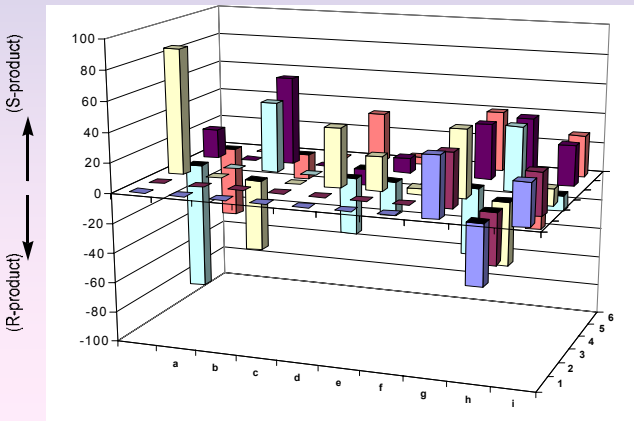
a **b** **c** **d** **e** **f** **g:** (S)- **h:** (R)- **i:** (S)-

Vincent Slagt

J. Am. Chem. Soc., **2004**, *126* 4056

Palladium-catalyzed allylic alkylation:





Ee between 85 and -85

For kinetic resolution see:
Jiang *Chem Commun* **2007**

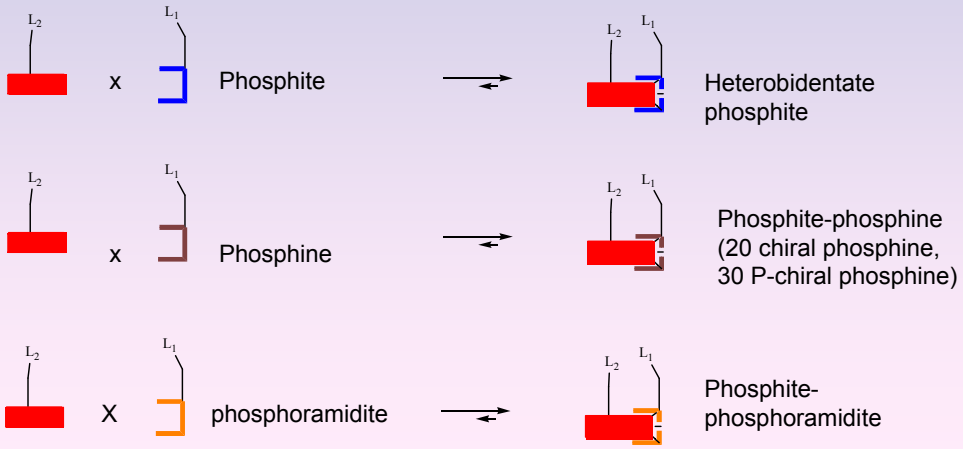
Vincent Slagt

Diversity by mixing

40 building blocks, 391 bisP-ligands,
6 ligand classes!

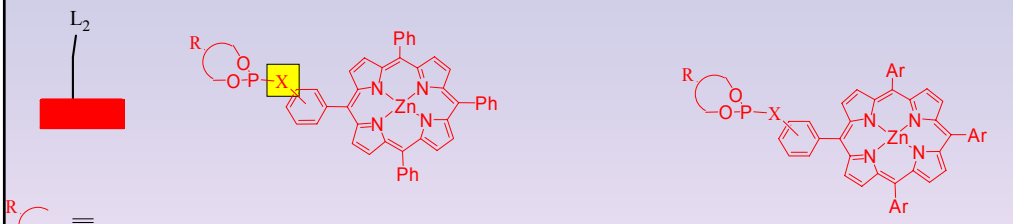
Phosphite/
Phosphoramidite

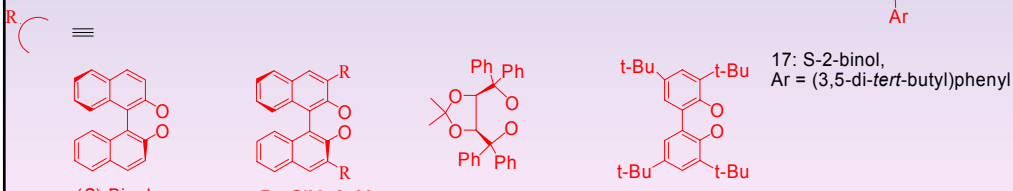
3 types of P-donors



Elsbeth Goudriaan *Eur JOC in press* **2008**

Library development: acceptor-type building blocks





(*S*)-Binol

R= SiMe3, Me

(*R, R*)-Taddol

bis(3, 5-di-*t*-Bu)-biphenyl

17: S-2-binol,
Ar = (3,5-di-*tert*-butyl)phenyl

X=O

1: S-2-binol
2: R-2-binol
3: S-2-silylbinol
4: R-2-silylbinol
5:S-3-binol
6:R-3-binol
7:S-3-silylbinol
8:R-3-silylbinol
9:3-(R,R)-Taddol
10:3-(bis(3, 5-di-t-Bu)-biphenyl)
15:S-2-dimethylbinol
16:S-3-dimethylbinol

X=NH

11:S-3-binolphosphoramidite
12:R-3-binolphosphoramidite
13:S-2-binolphosphoramidite
14:R-2-binolphosphoramidite

Elsbeth Goudriaan *Eur JOC in press* **2008**

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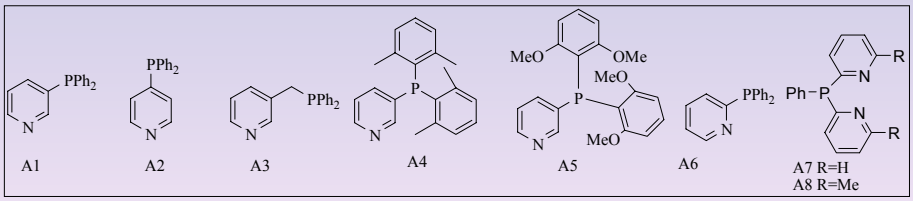
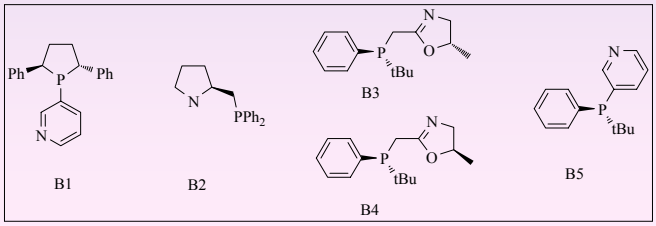
Library development: donor-type building blocks

Class A: achiral phosphines



A1 A2 A3 A4 A5 A6 A7 R=H A8 R=Me

Class B: (P-)chiral phosphines

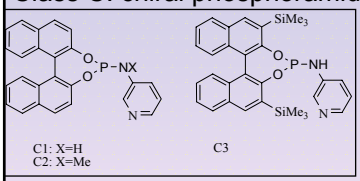


B1 B2 B3 B4 B5

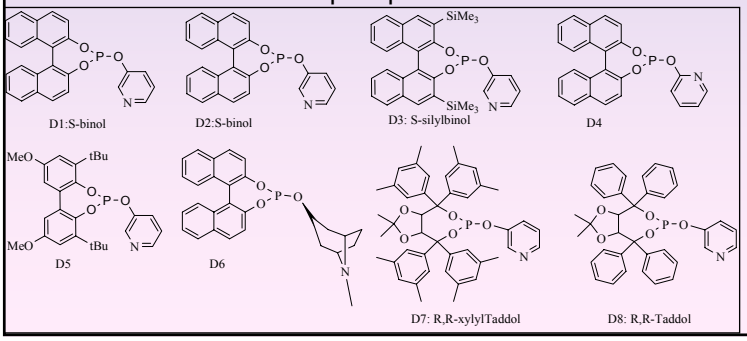
Elsbeth Goudriaan *Eur JOC in press* **2008**

Library development: donor-type building blocks

Class C: chiral phosphoramidites



Class D: chiral and achiral phosphites



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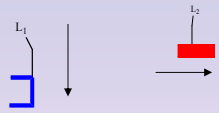
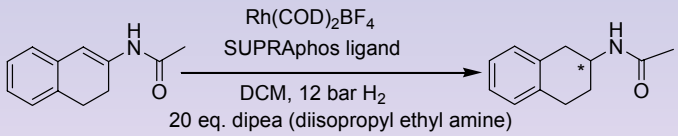
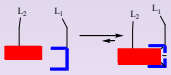
The current library: summary

	**Chiral porphyrin phosphites : *12***	**Achiral porphyrin phosphites : *1***	**Chiral porphyrin phosphoramidites : *4***	**Total**
Achiral phosphines : 8	96	8	32	136 (A)
Chiral phosphines : *5*	60	5	20	85 (B)
Achiral phosphites : *1*	12	1	4	17 (D)
Chiral phosphites : 6	72	6	24	102 (D)
Chiral phosphoramidites : *3*	36	3	12	51 (C)
Total	276	23	92	391

Hydrogenation of *N*-(3, 4-dihydro-2-naphthalenyl)-acetamide





Only a few selective catalysts known based on ruthenium,

(L. Renaud, P. Dupau, A. -E. Hay, M. Guingouain, P. H. Dixneuf, C. Bruneau, *Adv. Synth. Catal.* **2003**,)

Rhodium catalysts generally result in low to moderate ee's (<72%).

Reactions were performed at DSM.

X.B. Jang, Elsbeth Goudriaan

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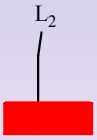
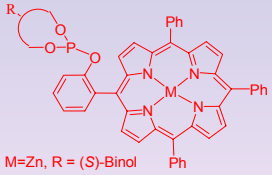
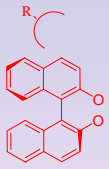
Building blocks for the hydrogenation of enamide

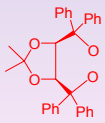




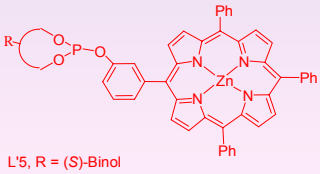
L'1, M=Zn, R = (*S*)-Binol
L'2, M=Zn,R= (*R, R*)-Taddol
L'3, M=Zn,R = bis(3, 5-di-*t*-Bu)-biphenyl
L'4 = M=H,H, R = (*S*)-Binol



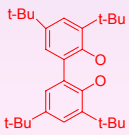
(*S*)-Binol



(*R, R*)-Taddol



L'5, R = (*S*)-Binol
L'6, R = (*R, R*)-Taddol
L'7, R = bis(3, 5-di-*t*-Bu)-biphenyl



bis(3, 5-di-*t*-Bu)-biphenyl

X.B. Jang, Elsbeth Goudriaan

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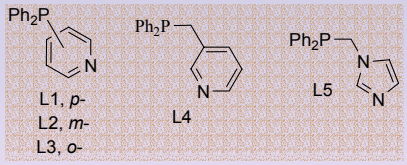
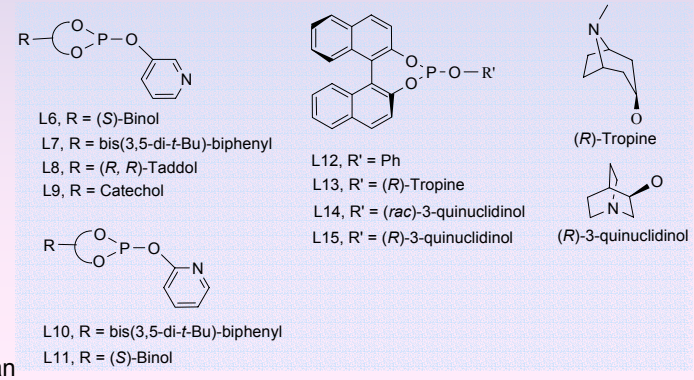
Building blocks for the hydrogenation of enamide





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Hydrogenation: 1 hit out of 60 experiments

Conversion

	L1	L2	L4	L5	L6	L7	L8	L9	L10	L11	L13	L14
L'1	44	**100**	62	5	80	40	36	20	31	**97**	86	65
L'2	5	10	2	1	8	4	7	0	9	11	21	14
L'5	38	88	29	28	67	18	19	8	9	**100**	84	**96**
L'6	48	54	70	15	59	14	83	8	9	73	**93**	90

ee

	L1	L2	L4	L5	L6	L7	L8	L9	L10	L11	L13	L14
L'1	27	**94**	47	20	13	**54**	**49**	17	11	-2	**56**	13
L'2	5	7	8	5	16	-3	6	0	3	-12	16	10
L'5	24	46	18	14	21	**52**	31	11	21	30	34	28
L'6	-1	26	-4	0	5	-7	-12	6	5	4	-9	-5

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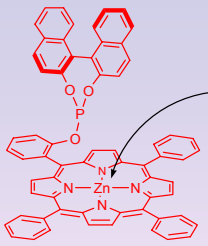
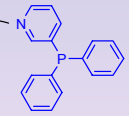
Hydrogenation of *N*-(3, 4-dihydro-2-naphthalenyl)-acetamide

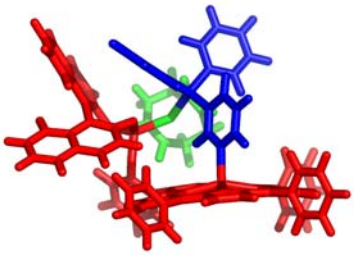


L1'

L2



$Rh(COD)_2BF_4$



Supported by NMR

		t(h)	Conv.(%)	Ee (%)
	L1'/L2	4	100	94 (+)
	L1'/PPh_3	14	56	24(+)
(No zinc)	L4'/L2	14	19	10 (+)
	L1'	3	100	20 (+)

131 ppm;

J_{P-P}=41Hz, J_{P-Rh}=263 Hz

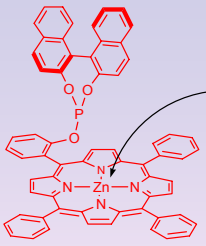
26 ppm;

J_{P-P}=41Hz, J_{P-Rh}=146 Hz

X.B. Jang, Elsbeth Goudriaan

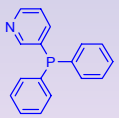
DE UNIVERSITEIT VAN AMSTERDAM UvA

Hydrogenation of *N*-(3, 4-dihydro-2-naphthalenyl)-acetamide

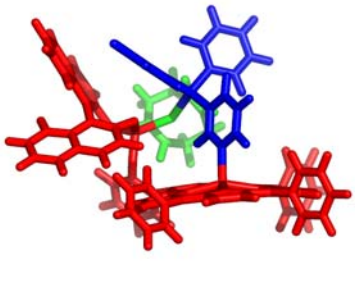


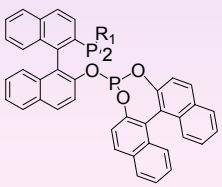
L1'

L2



$Rh(COD)_2BF_4$



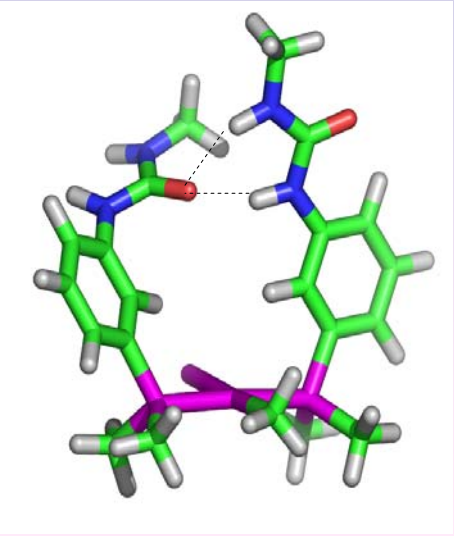


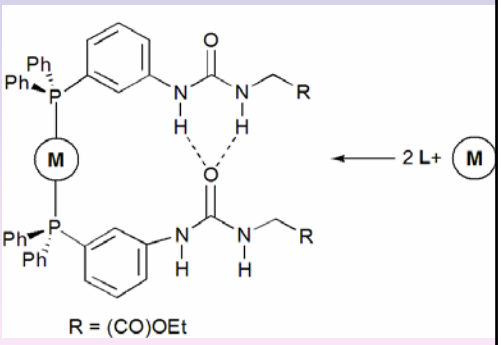
	t(h)	Conv.(%)	ee(%)
5 mol% Rh	4	100	94 (+)
1 mol% Rh	14	86	93 (+)
Binaphos	3	100	60 (+)

Angew. Chem. Int. Ed. **2006**, *45*, 1223-1227

X.B. Jang, Elsbeth Goudriaan

Extending to systems based to hydrogen bond





NMR, IR

Lisa Knight *Organometallics* **2006** *25* 954

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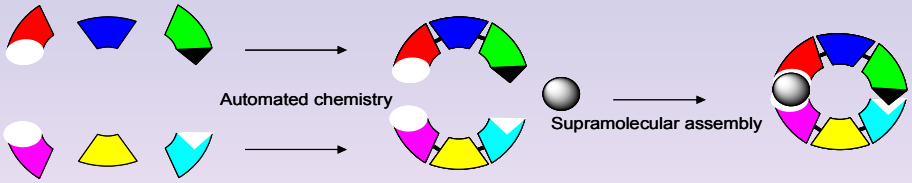
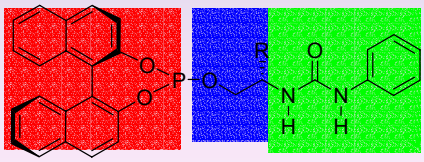
Building block approach: Modular concept



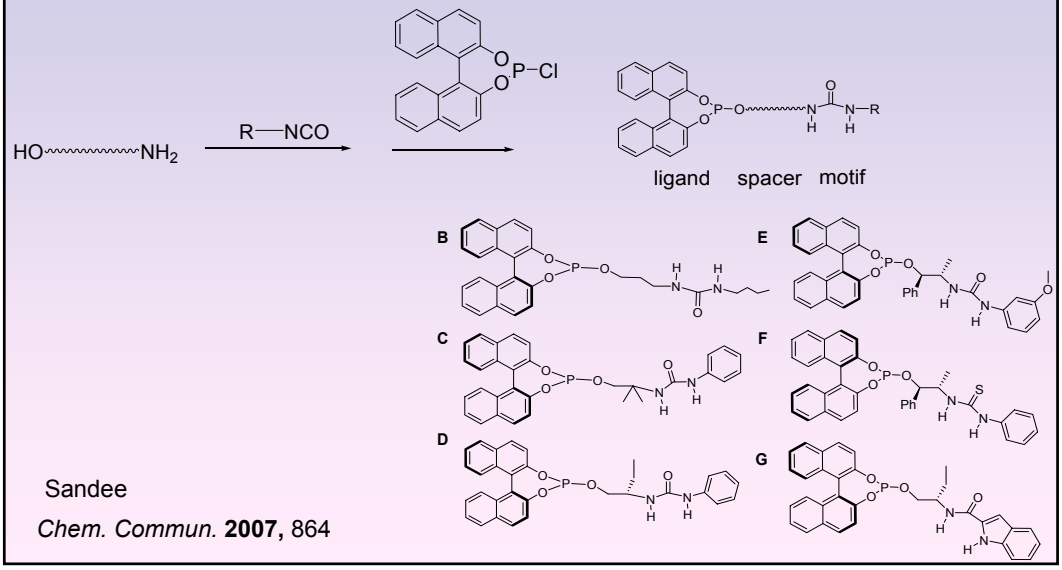


UREAPhos

Bert Sandee
Mark Kuil
Jurjen Meeuwissen

EP1816132

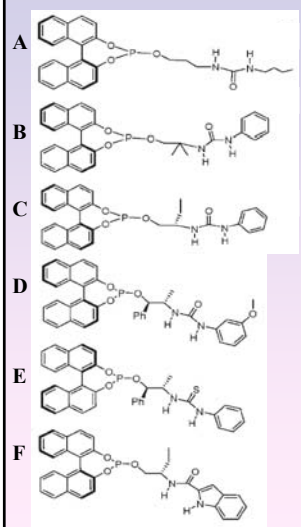
UREAphos: Supramolecular Bidentate phosphite

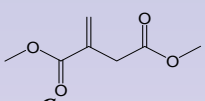


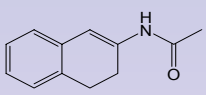
Sandee

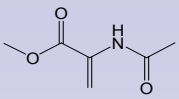
Chem. Commun. **2007,** 864

Asymmetric Hydrogenation









	Conv.	ee	Conv.	ee	Conv.	ee
A	0	0	4	4 (*R*)	0	0
B	100	16.6 (*S*)	12.3	76.5 (*R*)	100	93.6 (*R*)
C	100	46 (*S*)	4.1	60.7 (*R*)	100	92.3 (*R*)
D	100	92.7 (*S*)	34.1	52.5 (*R*)	100	82.1 (*R*)
E	100	13.8 (*R*)	0.4	37.9 (*S*)	36.9	44.6 (*S*)
F	100	95.8 (*S*)	26.1	1.5 (*R*)	–	–

Conc. $Rh(nbd)_2BF_4$ 0.5 mM, Rh:L:Subs 1:1.2:100, DCM, RT, 10 bar H_2, 18 h

Chem. Comm., **2007**, 8, 864

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Next step: Synthesis of building blocks with the robot

at-it
New Technology to Accelerate Catalyst Discovery

BASF
The Chemical Company

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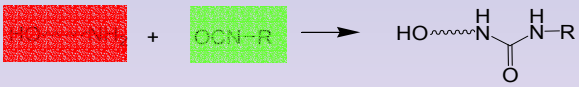
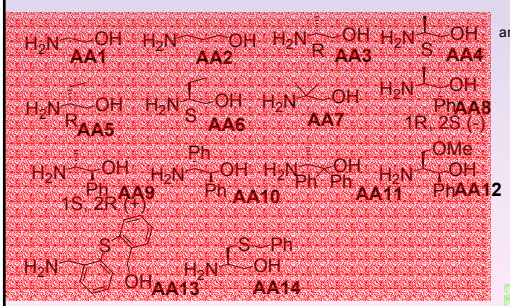
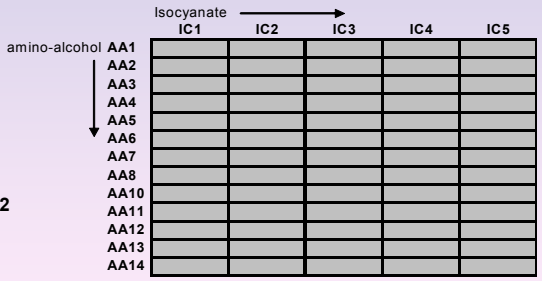
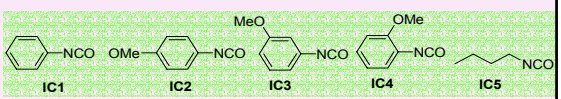
Automated ligand preparation

70 urea-alcohols
Success rate 100%









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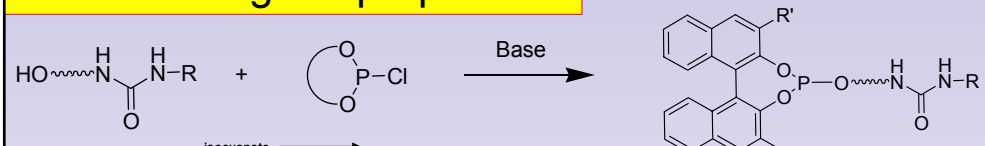
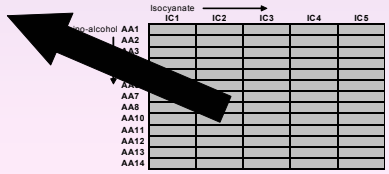
Automated ligand preparation



isocyanate

Amino-alcohol	IC1	IC2	IC3	IC4	IC5	
AA1	D1		D12			
AA2	D2		D13	D16	D20	R-bisnaphtol
AA3	D3					
AA4	D4	D8	D14	D17	D21	
AA5	D5	D9			D22	
AA6	D6	D10		D18	D23	
AA7	D7	D11	D15	D19		

	IC1	IC2	IC3	IC4	IC5	
AA1	D24	D30	D37	D44	D50	
AA2	D25	D31	D38	D45	D51	S-bisnaphtol
AA3	D26	D32	D39	D46	X	
AA4		D33			X	
AA5	D27	D34	D40	D47		
AA6	D28	D35	D41	D48		
AA7	D29	D36	D42	D49		
AA8			D43			



Large success rate

UREAPhos patent: EP1816132

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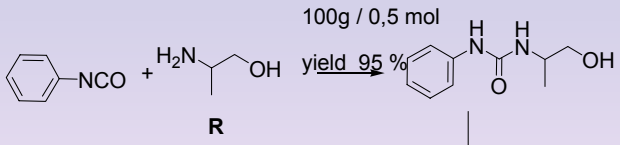
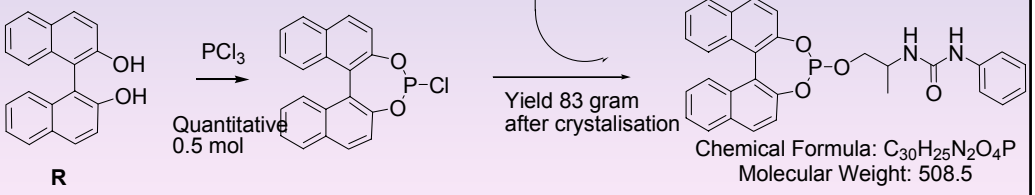
Scale-up of ligands synthesis:

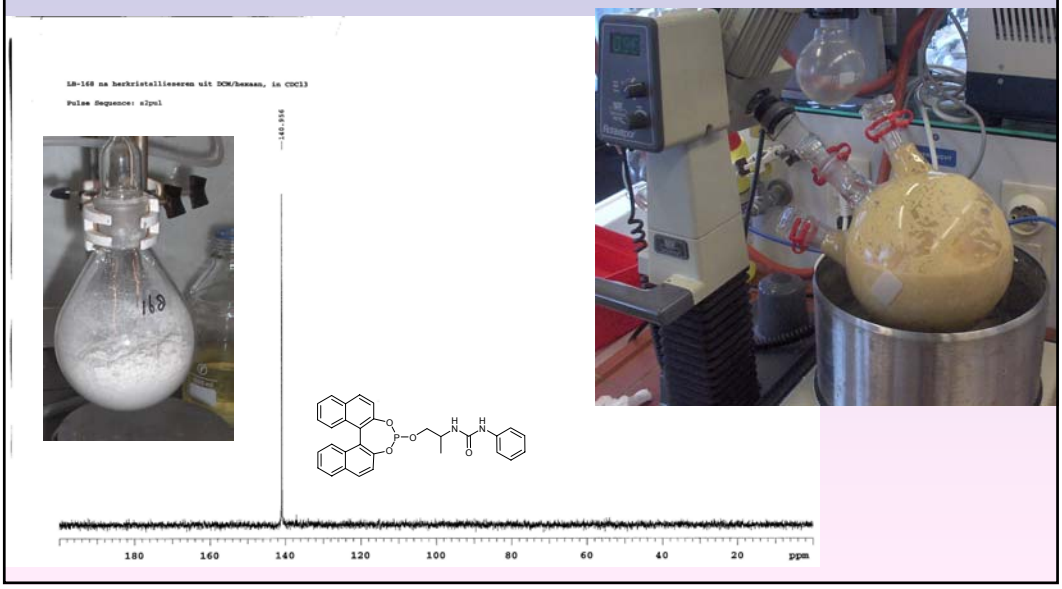




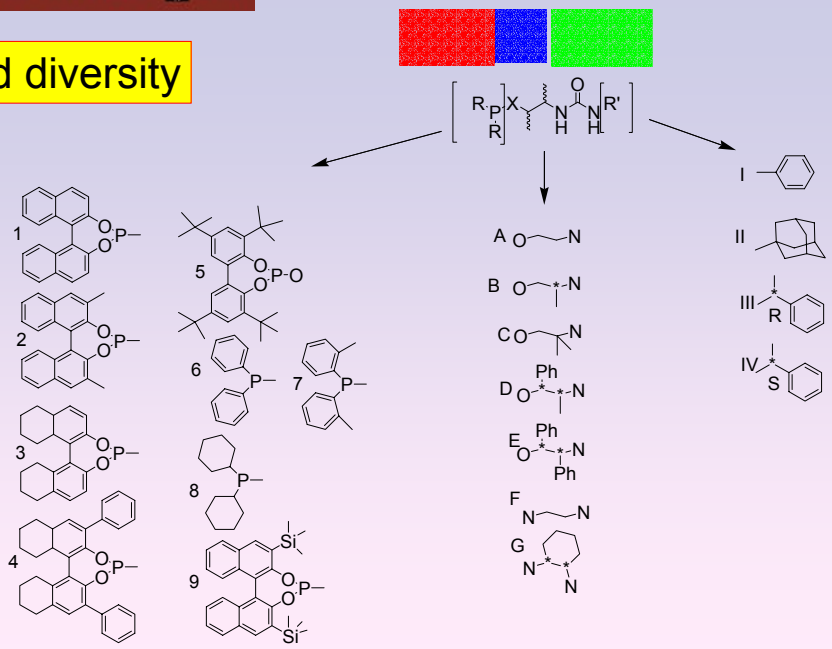
Chemical Formula: $C_{30}H_{25}N_2O_4P$
Molecular Weight: 508.5

Cat-it
New Technology to Accelerate Catalyst Discovery

Scale-up of ligands synthesis:



Scope and diversity



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Robotics for screening, optimization and kinetics

HITS

Catalyst screening 48 in parallel

Catalyst optimization kinetics 16

Mark Kuil

De Universiteit van Amsterdam UvA

Privileged ligands vs. Combinatorial ligands (or ligand design)

- Ligands form good catalysts for a wide range of substrates
- Limited tuning abilities and sometimes lengthy synthesis

Yoon, Jacobsen, *Science* **2003**, *299*, 1691

- Large ligand libraries
- Wide substrate scope achieved by screening libraries for hits
- Most ligands do not provide general solutions

Tang, Zhang, *Chem. Rev.* **2003**, *103*, 3029

Gennari and Piarulli, *Chem Rev* **2003**, *103*, 3071

Jäkel, Paciello *Chem. Rev.* **2006**, *106*, 2912

Goudriaan, Reek, *EurJIC*, **2008**, 2927

Reetz *Angew. Chem.* **2008,**

De Vries et al *Acc. Chem. Res.* **2007,** *40,* 1267

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Privileged ligands vs. Combinatorial ligands

- Ligand form good catalysts for a wide range of substrates
- Limited tuning abilities and sometimes lengthy synthesis

How to find these ligands?

- Large ligand libraries
- Wide substrate scope achieved by screening libraries for hits
- Most ligands do not provide general solutions

Availability of large ligand libraries?

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Privileged ligands *vs* Combinatorial ligands

- Usually cis-bidentate
- C2 or very unsymmetrical
- Bulky groups on P atom to transfer chirality
- Chiral elements close to substrate
- Modular to enable tuning

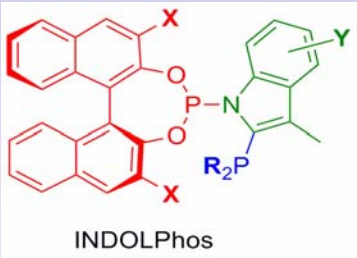
Ligand design

- Building block approach
- Large libraries
- Large diversity
- Modular to enable tuning
- More dynamic and flexible??

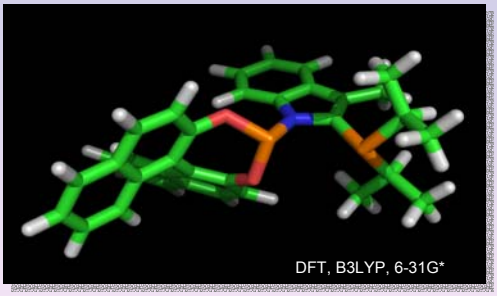
Supramolecular ligands

Blaser et al *Adv. Synth. Catal.* **2003**, p103

INDOLPhos: a new privileged Ligand?



INDOLPhos



- Rigid indole backbone offers precise control over chiral space
- Tuneable at various positions (R, X, Y)
- Inequivalent P-donor atoms enforce specific substrate binding

Jeroen Wassenaar

Wassenaar, J; Reek, J.N.H. *Dalton Trans.*, **2007**, 3750

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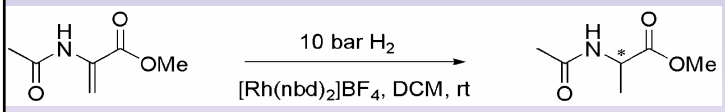
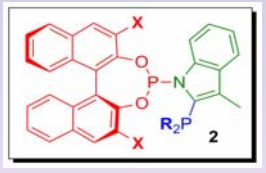
Asymmetric Hydrogenation





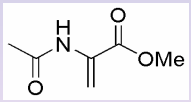
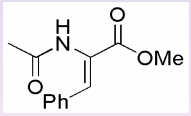
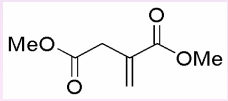
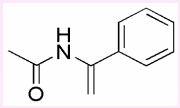
Entry	Ligand	Cat. loading (mol %)	% conv.[a]	% ee (config)
1	**2a (R=Ph, X=H)**	1	100	13 (*S*)
2	**2a (R=Ph, X=H)**	0.2	100	13 (*S*)
3	**2b (R=Ph, X=$SiMe_3$)**	1	100	36 (*R*)
4	**2c (R=*i*-Pr, X=H)**	1	100	86 (*R*)
5	**2d (R=*i*-Pr, X=Me)**	1	100	**97** (*R*)
6	**2d (R=*i*-Pr, X=Me)**	0.04	100	**97** (*R*)
7	**2e (R=Cy, X=H)**	1	100	94 (*R*)

TOF 1200/min

[a] Conversion after 16h

Wassenaar, J; Reek, J.N.H. *Dalton Trans.*, **2007**, 3750

Hydrogenation – scope: Bench mark substrates

Substrate	% conv.	% ee (config.)
	100	97 (*R*)
	100	97 (*S*)
	100	98 (*S*)
	100	94 (*S*)

Wassenaar, J; Reek, J.N.H. *Dalton Trans.*, **2007**, 3750

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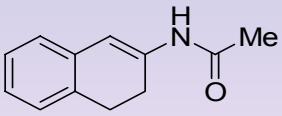
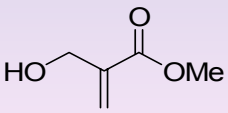
Privileged ligands vs. Combinatorial ligands
INDOLPhos against UREAPhos

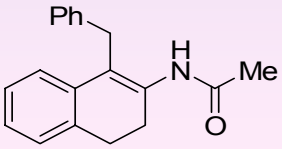
72% ee

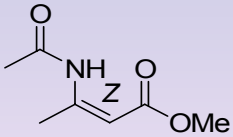
A 

90% ee

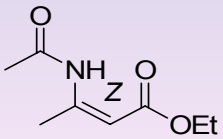
B 

52% ee
(Ru, 100 bar)

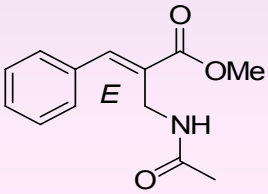
C 

D 

92% ee

E 

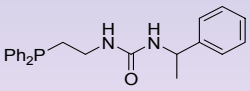
94% ee

F 

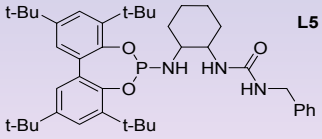
91% ee

Ureaphos Homo bidentate ligand library

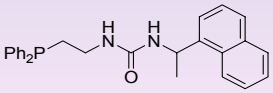
12 ligands



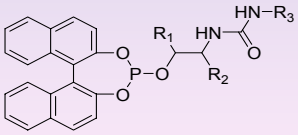
L1 (*R*)



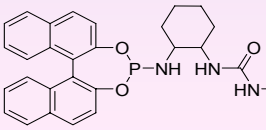
L5 (*S*,*S*)



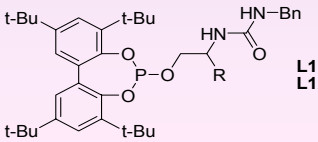
L2 (*R*)



L6 (*R*) R_1=H R_2=H R_3=Bn
L7 (*R*,*R*) R_1=H R_2=Me R_3=Bn
L8 (*R*,*R*) R_1=H R_2=Me R_3=Ph
L9 (*R*,*R*) R_1=H R_2=Me R_3=*n*-Bu
L10 (*R*,*S*,*R*) R_1=Ph R_2=Me R_3=Ph



L3 (*R*,*S*,*S*)
L4 (*R*,*R*,*R*)



L11 (*S*) R=*i*-Pr
L12 (*R*) R=Me

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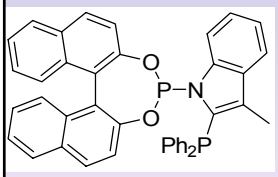
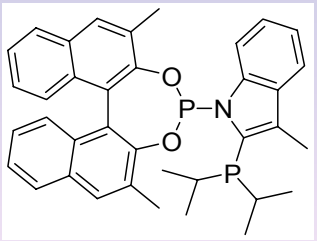
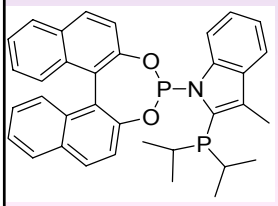
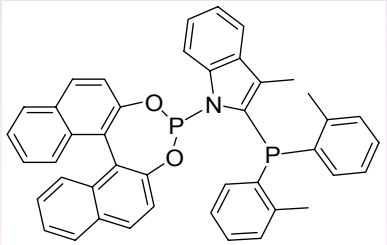
INDOLPhos ligand library

4 ligands









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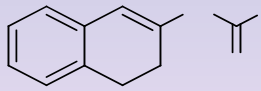
Ureaphos Homo ligand library

INDOLPhos: no reaction

Ligand	Conversion	*ee*
L1	70	*53*
L2	36	*15*
L3	3.2	*15*
L4	10	*67*
L5	<1	-
L6	18	*35*
L7	52	*13*
L8	16	*40*
L9	53	*17*
L10	12	*49*
L11	84	12
L12	18	53

← Highest ee



Optimization of conversion

Ligand	PH_2 (bar)	Temp (°C)	conv (%)	ee (%)
L8	10	25	51	47.9
L8	10	35	75	47.4
L8	25	25	71	43.1
L8	25	35	89	41.7

color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

Highest *ee* reported 90% Ru 100 bar H_2, (L. Renaud, et al., *Adv. Synth. Catal.* **2003**,)

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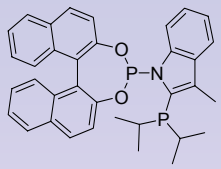
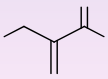
Ureaphos Homo ligand library



93% ee, TOF 6000 mol/mol/h
98 % ee at -40 C
Adv Syn Cat. **2008**

Highest ee ever reported!!

Ligand	Conversion	*ee*
L1	49	*21*
L2	<1	-
L3	67	49
L4	<1	-
L5	72	3.3
L6	80	-
L7	100	3.2
L8	88	*14*
L9	51	-
L10	100	*28*
L11	40	*74*
L12	100	*30*



color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

Rh DuPHOS highest ee reported: 90%. *Adv Syn Cat.* **2003** 185

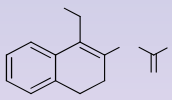
INDOLPhos : UREAPhos = 1:1

Ureaphos Homo ligand library

INDOLPhos:
conversion <4%, ee max 60%

Ligand	Conversion	*ee*
L1	6,4	26
L2	25	34
L3	5,4	13
L4	<1	-
L5	<1	-
L6	8,6	20
L7	4,6	71
L8	3,0	71
L9	3,8	72
L10	5,2	69
L11	10	*14*
L12	2,0	*44*

Highest ee ever reported!!



Optimization

reactor	pH_2 (bar)	Temp (°C)	conv (%)	ee (%)
L8	10	25	7.3	83
L8	10	35	15	85
L8	40	25	18	81
L8	40	40	84	83

color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

Highest *ee* reported 52% 100 bar H_2, MeOH, 20 hr. *Adv. Synth. Cat.* **2001**, 343

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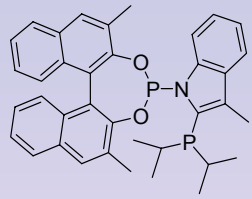
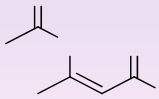
Ureaphos Homo ligand library

Ligand	Conversion	*ee*
L1	13	-
L2	4.0	-
L3	1.0	63
L4	28	64
L5	<1	-
L6	4.6	19
L7	30	*11*
L8	8.8	*33*
L9	29	*31*
L10	30	*35*
L11	97	*19*
L12	100	-



60% conv
93% ee

lit 92% ee (Beller, *Org Proc Res. Dev*. **2007**)



color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

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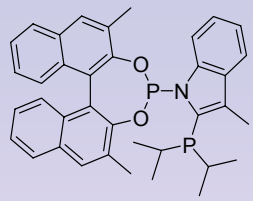
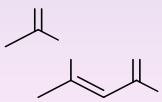
Ureaphos Homo ligand library

Ligand	Conversion	*ee*
L1	5.6	*4.4*
L2	<1	-
L3	<1	-
L4	8.4	71
L5	<1	-
L6	3.4	7.3
L7	21	*22*
L8	9.0	*29*
L9	6.0	*32*
L10	18	*13*
L11	70	*8.4*
L12	17	*9.3*



54% conv
94% ee

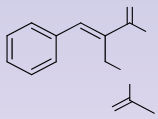
lit 94% ee, (Beller, *Org Proc Res. Dev*. **2007**)



color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

Ureaphos Homo ligand library

INDOLPhos:
conversion <1%, ee max 40%



Ligand	Conversion	*ee*
L1	<1	-
L2	<1	-
L3	1.5	*72*
L4	2.2	*83*
L5	1.0	*58*
L6	35	*38*
L7	16	*96*
L8	23	*96*
L9	18	*78*
L10	6.6	*97*
L11	24	*37*
L12	<1	-

Optimization

ligand	PH_2 (bar)	Temp (°C)	conv (%)	ee (%)
L8	10	25	28.8	94.7
L8	10	35	45.1	96.5
L8	10	45	61.4	96.5
L8	30	25	44.9	92.6
L8	30	35	63.5	94.9
L8	30	45	84.4	95.7

color conv/ ee	0-10%	10-20%	20-30%	30-40%	40-50%	50-60%	60-70%	70-80%	80-90%	90-100%

Highest reported in lit 91% ee, de Vries/Feringa *OBC* **2007**

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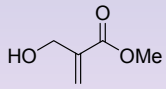
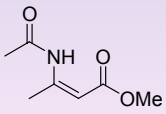
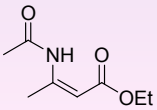
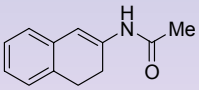
INDOLPhos : UREAPhos = 3:3

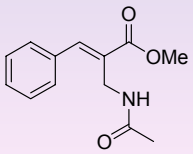
Highest ee



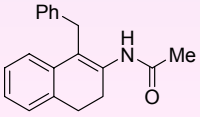








Highest ee



Highest ee

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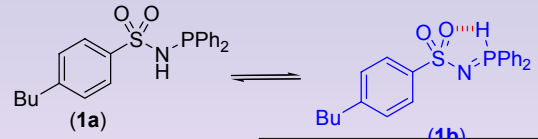
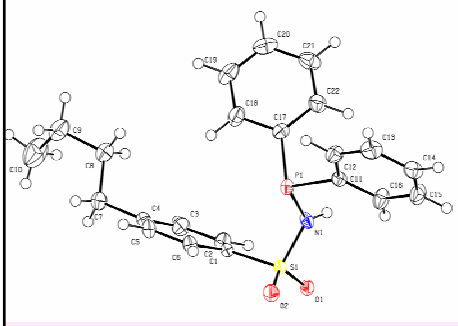
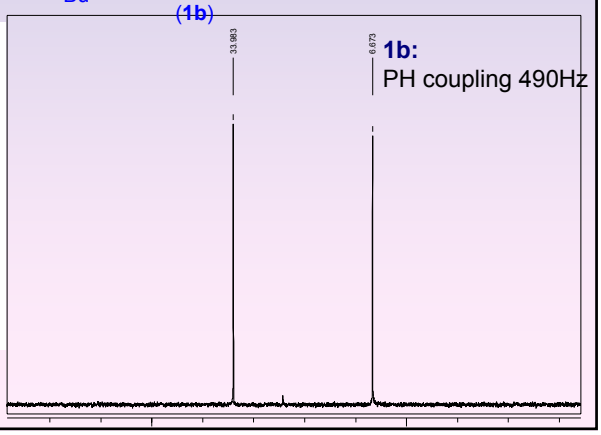
METAMORPhos: Adaptive Supramolecular Ligands





Frederic Patureau



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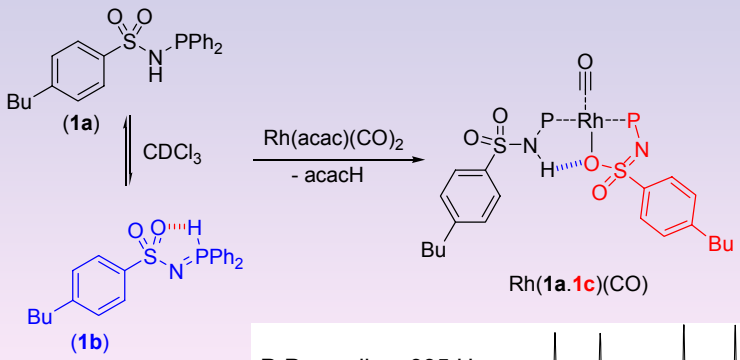
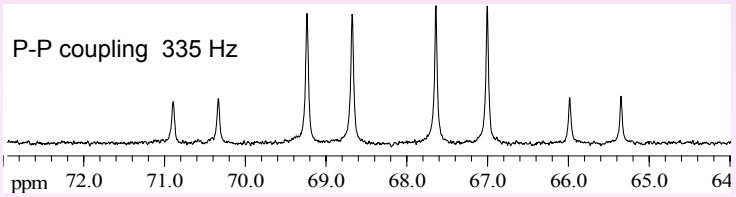
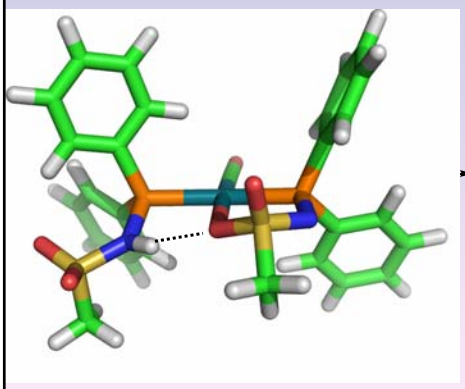
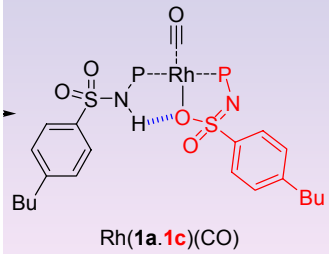
METAMORPhos: Adaptive Supramolecular Ligands





METAMORPhos: Adaptive Supramolecular Ligands





Rh(**1a**.**1c**)(CO)

DFT optimized structure, IR and NMR evidence for H-bond

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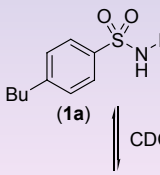
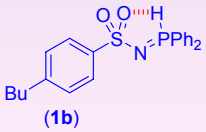
METAMORPhos: Supramolecular *heterobidentate* Ligands

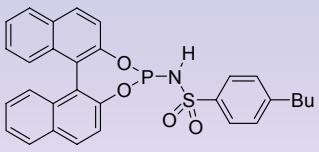


(**1a**)

$CDCl_3$

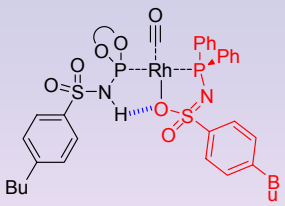


(**1b**)



R-(**2**)

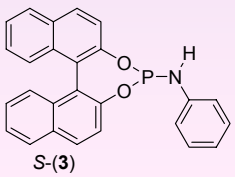
$Rh(acac)(CO)_2$



Rh(**2**.**1c**)(CO)

Selective hetero combined complex formation

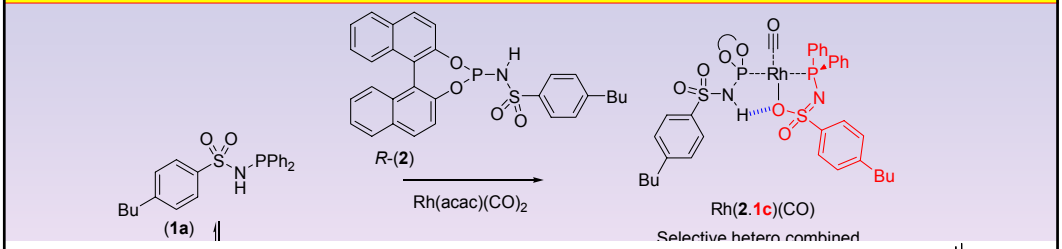
$Rh(acac)(CO)_2$

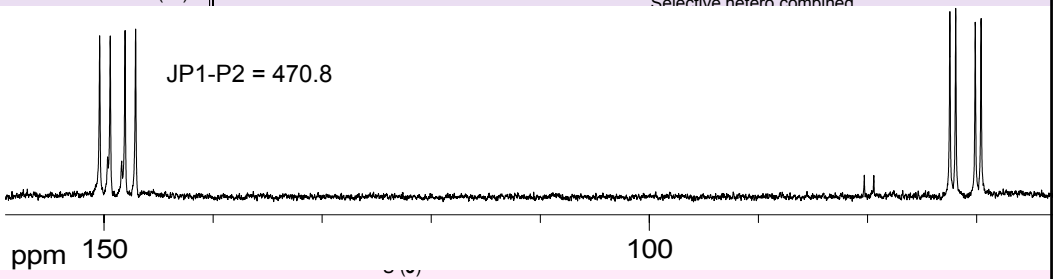


S-(**3**)

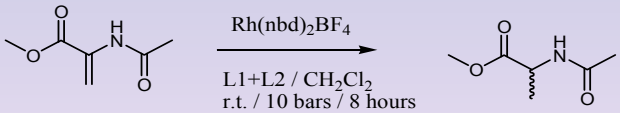
Homo combined complexes exclusively

METAMORPhos: Supramolecular *heterobidentate* Ligands

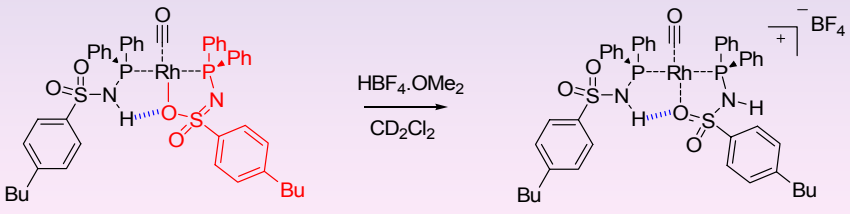




METAMORPhos: hydrogenation of MAA



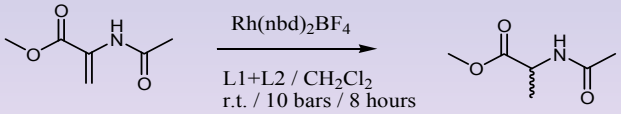
methyl-2-acetamidoacrylate



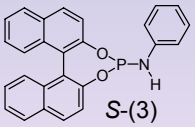
Rh(**1a**.**1c**)(CO)
INACTIVE in Hydrogenation

Rh(**1a**)$_2$(CO)BF$_4$
ACTIVE

METAMORPhos: hydrogenation of MAA

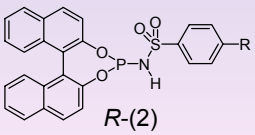


methyl-2-acetamidoacrylate

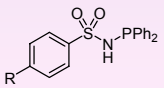


S-(3)

L^{A} [a]	L^{B} [a]	Rh[mM]	MAA/Rh	ee[%]	R/S
1	**1**	0.1	10^3	-	-
1	**2**	0.1	10^3	91.7	S
2	**2**	0.1	10^3	99.0	S
PPh_3	**PPh_3**	0.1	10^3	-	-
PPh_3	**3**	0.1	10^3	3.6	S
3	**3**	0.1	10^3	65.0	R
3	**1**	0.1	10^3	46.0	R

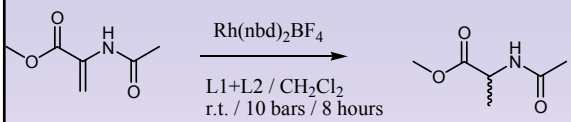


R-(2)
R = n-butyl

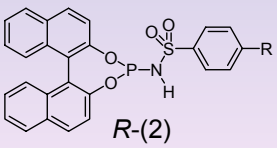


(1)

METAMORPhos: hydrogenation kinetics

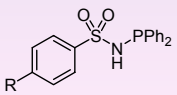


methyl-2-acetamidoacrylate



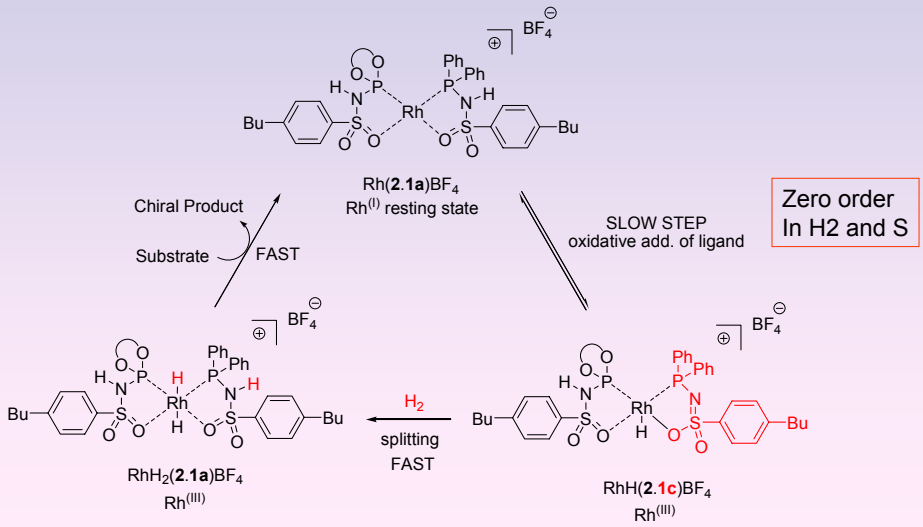
R-(2)
R = n-butyl

Cat. structure[a]	H2	substrate	Cat	T.O.F.
Rh(**1a.1c**)	P	0	P	652
Rh(**2.1c**)	**0**	**0**	P	**1186**
Rh(**2**)$_2$	P	P	P	574

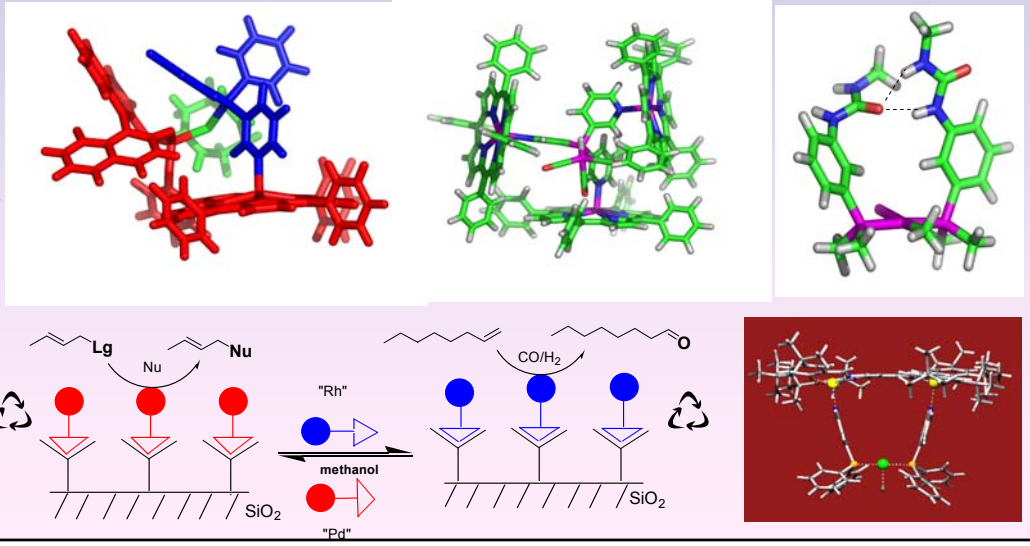


(1)

METAMORPhos: a new hydrogenation mechanism?



Supramolecular Transition metal catalysis
Fun & Functional!



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Dr. D. Tooke (UU)

DSM
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