Supramolecular Concepts in Homogeneous Catalysis

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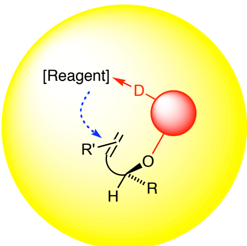
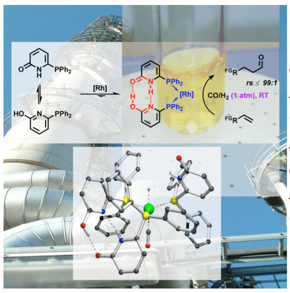
Research Topics in the Breit Group: Synthesis & Catalysis

■ *Reagent-Directing Groups (RDG) in Synthesis*



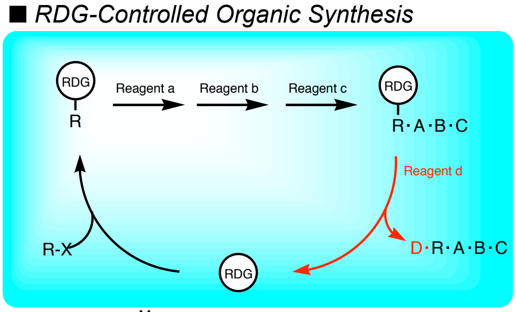
• ***Hydroformylation***
Acc. Chem. Res. **2003**, *36*, 264; *JACS* **2004**, *126*, 10244.
• ***Conjugate Addition***
Chem. Rev. ***2008**, in print.*
• ***Allylic Substitution***
Angew. Chem. **2004**, *43*, 3874; *ibid.* **2004**, *43*, 3878; *Angew. Chem.* **2005**, *117*, 5401; Chem. Eur. J. **2006**, 12, 6669.

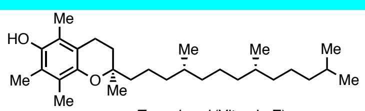
■ *Bioinspired Self-Assembly of Molecular Catalysts*



JACS **2003**, *125*, 6608*;*
Angew. Chem. **2005**, *117*, 1666 (selected as "Hot Paper")
Angew. Chem. **2006**, *118*, 1629;
JACS **2006**, *128*, 4188
Angew. Chem. **2007**, *119*, 1629 (selected as "Hot Paper")
Chem.Commun. **2008**, 844.

■ *RDG-Controlled Organic Synthesis*

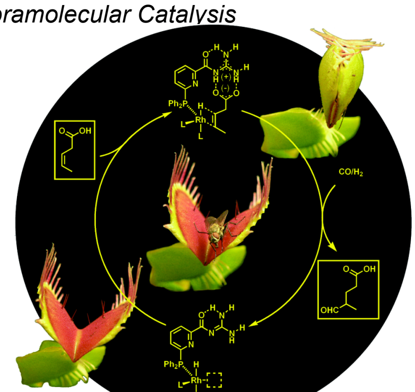




α-Tocopherol (Vitamin E)

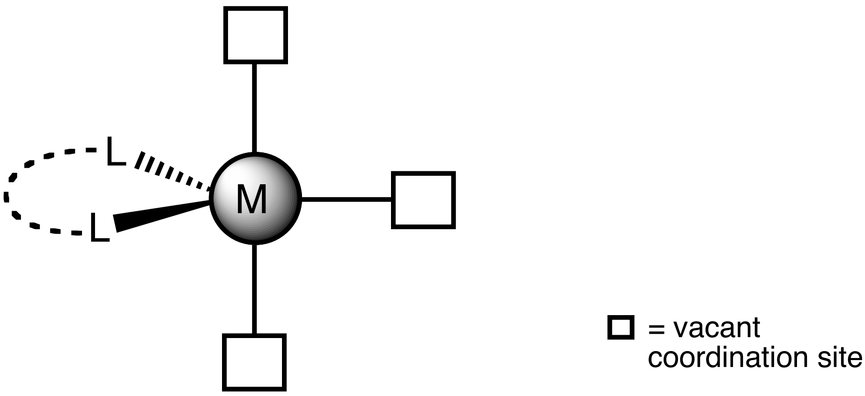
Angew. Chem. **2007**, *119*, 8824, (selected as "Hot Paper")

■ *Supramolecular Catalysis*



Angew. Chem. **2008**, *120*, 317 & ibid, 4010 "Hot Paper"

Homogeneous Metal Catalysis

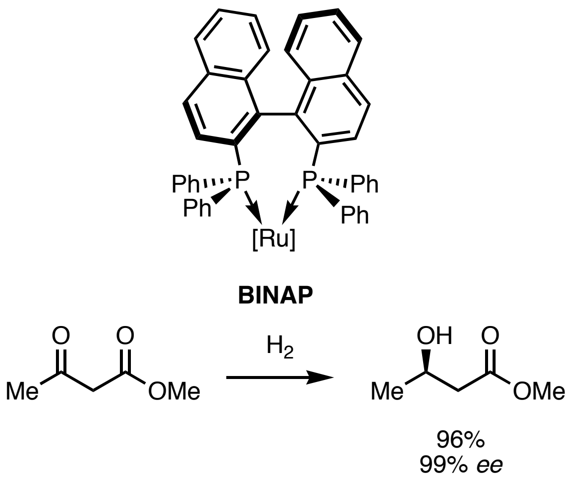


Selectivity through

- Choice of Transition Metal
- "Spectator Ligands" - Sterics/Electronics
- Secondary Interactions between Substrate and Catalyst

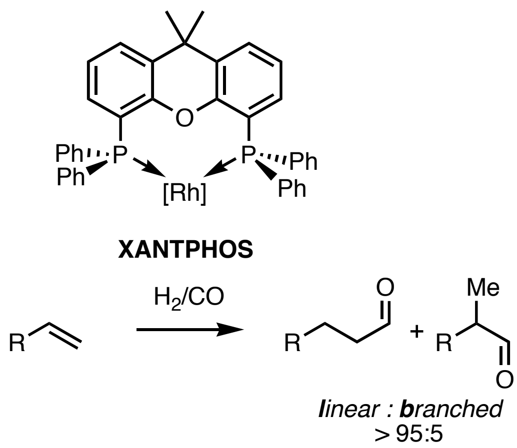
Bidentate Ligands in Homogeneous Metal Complex Catalysis

- Enantioselectivity



Noyori

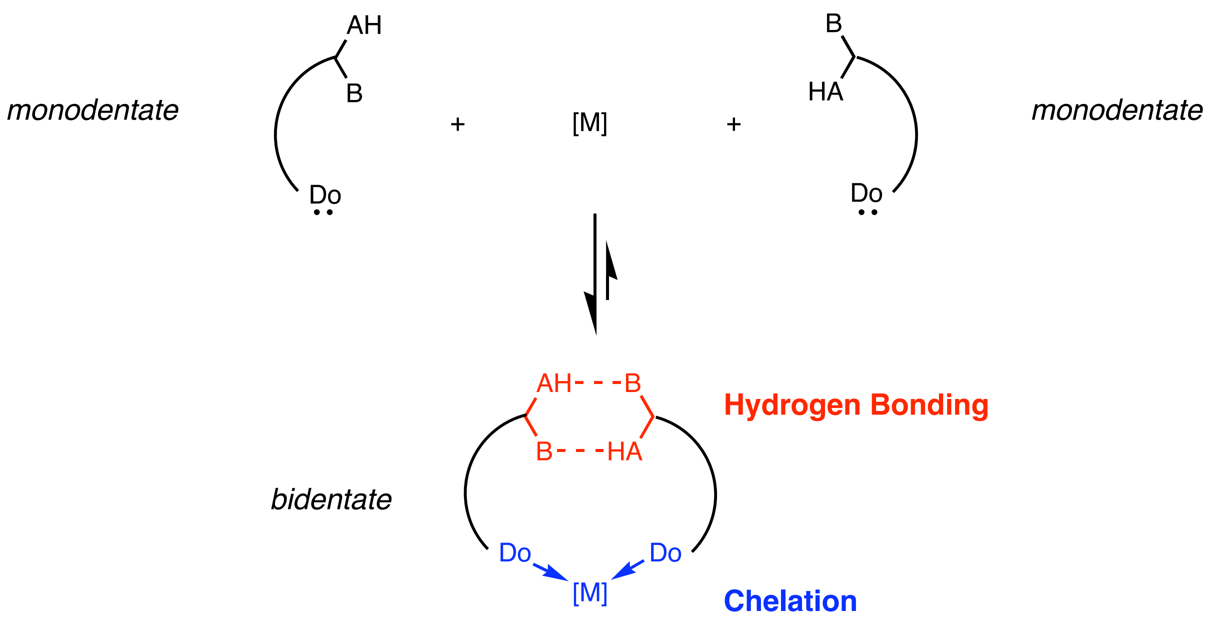
- Regioselectivity



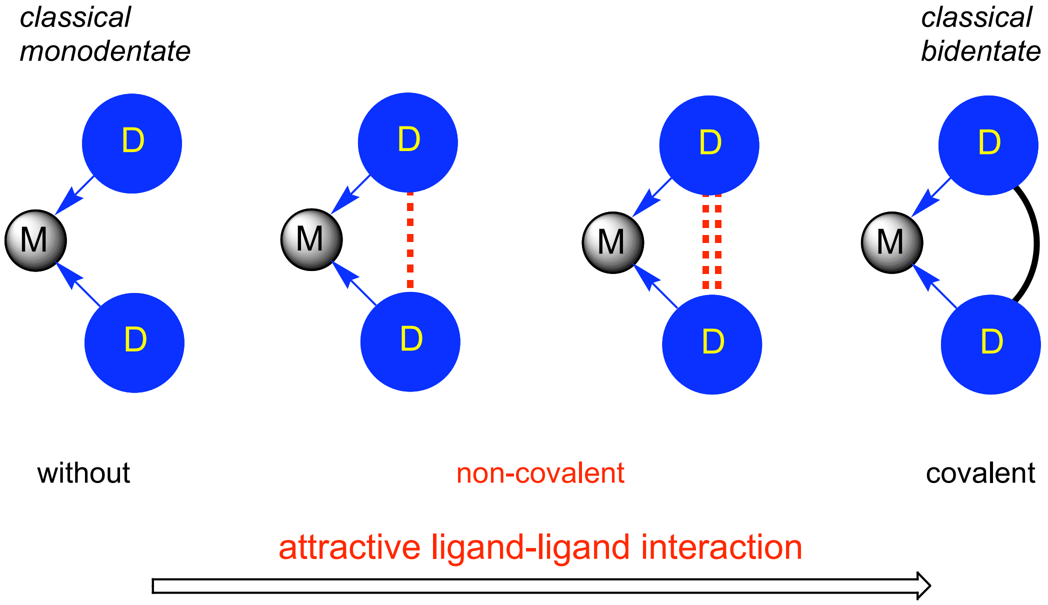
van Leeuwen

Advantage:	Superior Selectivities
Disadvantages:	Multistep Synthesis, Costs

From Monodentate to Bidentate Ligands through Hydrogen Bonding



Emulation of Chelation through Self-Assembly of Monodentate Ligands



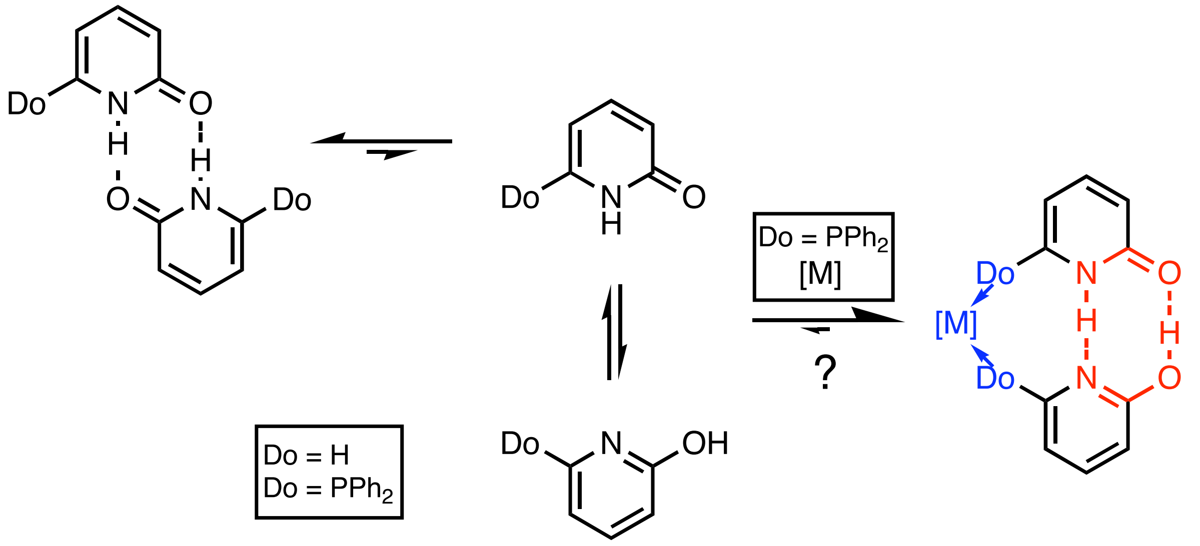
Ionic Interactions
van Leeuwen (2007)

Hydrogen Bonding
Breit (2003)

Coordinative Bonding
Reek, van Leeuwen (2003)
Takacs (2004)

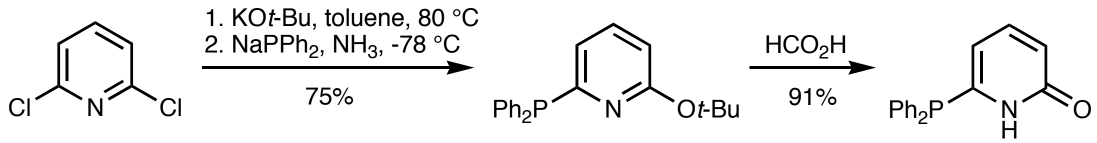
B. Breit, *Angew. Chem. Int. Ed.* **2005**, *44*, 6816-25.

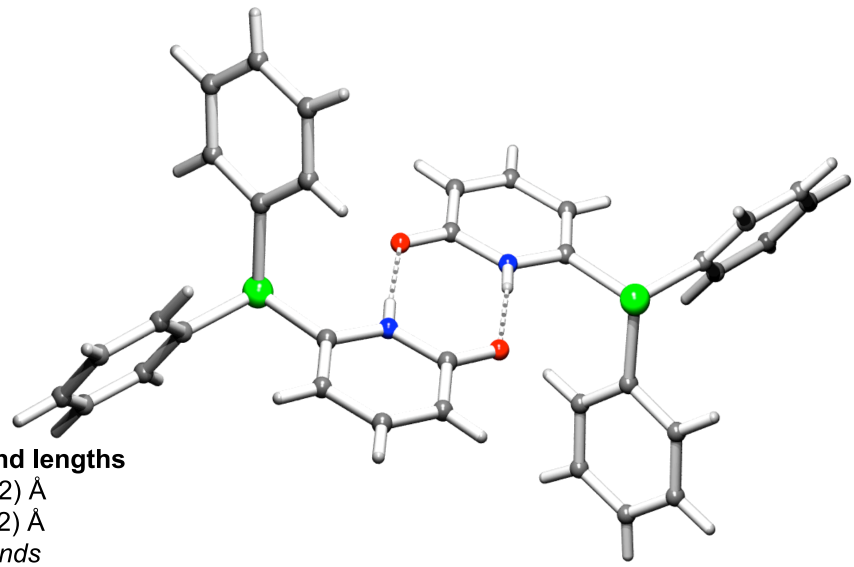
The 2-Pyridone - 2-Hydroxypyridine Tautomer System



B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608.

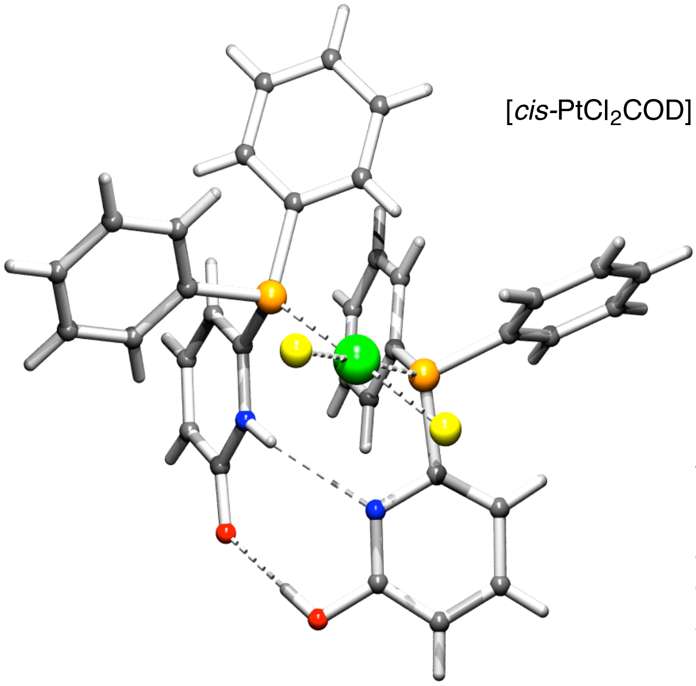
6-Diphenylphosphino-1H-pyridin-2-on (6-DPPon)





Selected bond lengths
C-O = 1.244(2) Å
C-N = 1.377(2) Å
Hydrogen Bonds
(OHN) = 2.776(1) Å

Bidentate Ligands through Self-Assembly

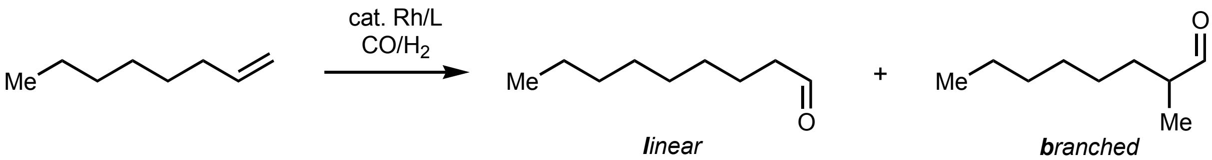


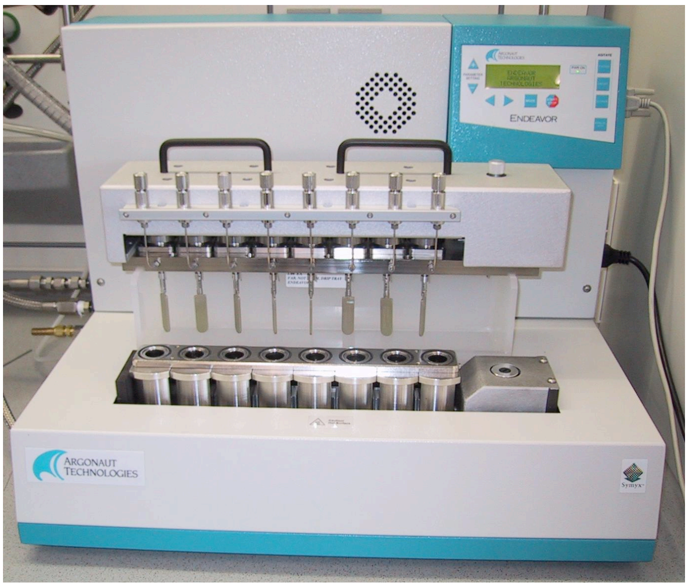
[*cis*-$PtCl_2$COD] —(2 eq 6-DPPon; CH_2Cl_2; - COD)→ [*cis*-$PtCl_2$(6-DPPon)$_2$]

Selected bond lengths and angles
P-Pt = 2.2563(6) Å and 2.2364(6) Å
P-Pt-P = 97.58°
C(15)-O(1) = 1.341(4) Å
C(45)-O(2) = 1.259(3) Å
Hydrogen Bonds
(NHN) = 3.071(3) Å
(OHO) = 2.683(3) Å

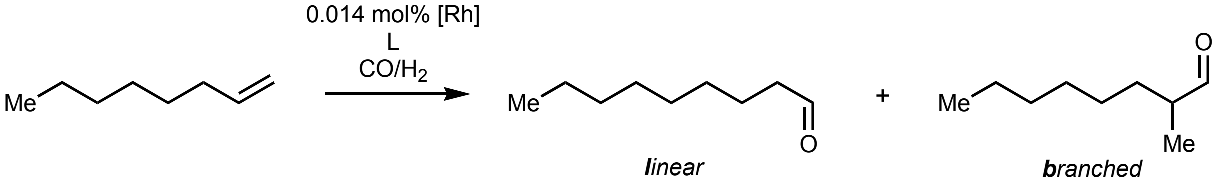
B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608.

The Test-Reaction: Hydroformylation of 1-Octene



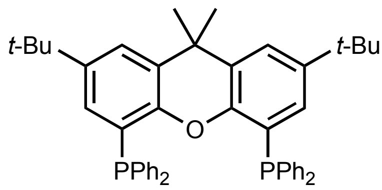


Hydroformylation of 1-Octene with the 6-DPPon/Rhodium-Catalyst

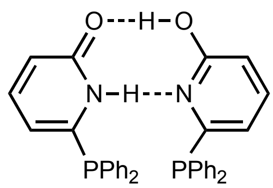


Ligand	T [°C]	Conv. [%]	Isom.[a] [%]	l : b
PPh_3	65	22	0.3	73:27
PPh_3	80	98	9	72:28
t-Bu-XANTPHOS	65	6	1	98:2
t-Bu-XANTPHOS	80	31	2	98:2
$(6\text{-DPPon})_2$	65	56	3	97:3
$(6\text{-DPPon})_2$	**80**	**96**	**8**	**96:4**

Rh:L:1-octene (1:20:7000), *c*(1-octene) = 1.4 M, 4 h, toluene, 10 bar CO/H_2 (1:1)



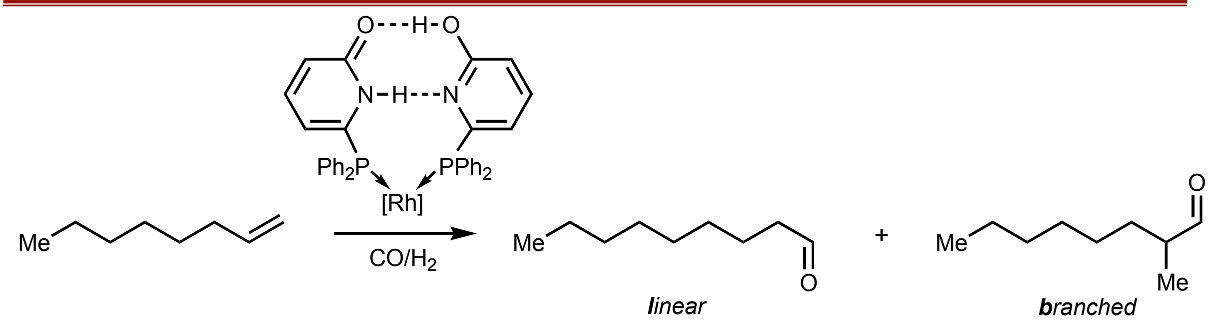
***t*-Bu-XANTPHOS**

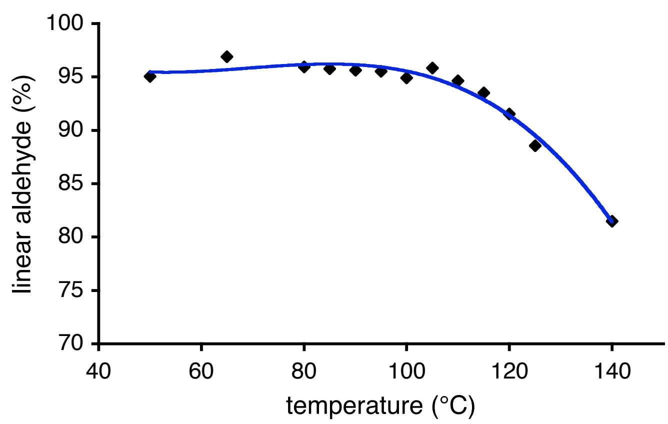


$(6\text{-DPPon})_2$

B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608.

Temperature Dependence of Regioselectivity

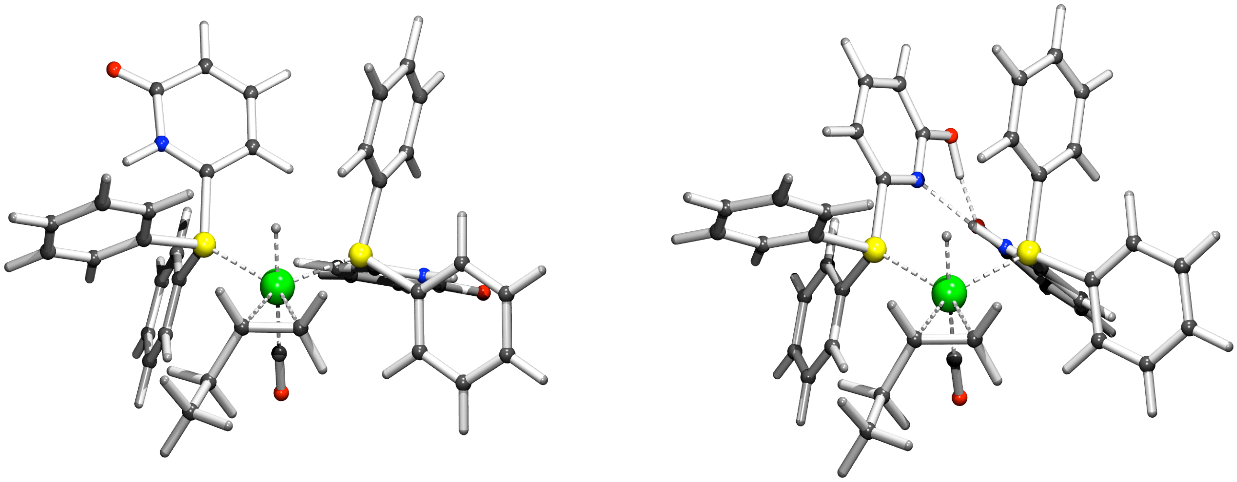




Rh:L:1-octene (1:20:7000), *c*(1-octene) = 1.4 M, 4 h, toluene, 10 bar CO/H_2 (1:1)

B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608.

DFT Calculations of the Rhodium/6-DPPon Catalyst

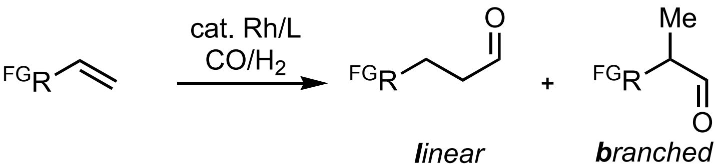


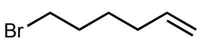
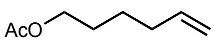
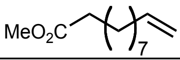
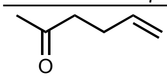
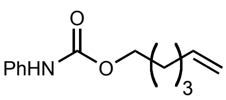
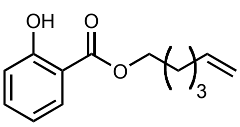
DFT (B-P86/TZVP//B-P86/SV(P))

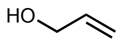
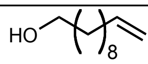
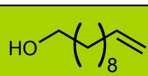
Stabilization through hydrogen-bonding:
47 kJ/mol (11.2 kcal/mol)

with A. Schäfer (BASF AG) unpublished results

Functional Group Compatibility



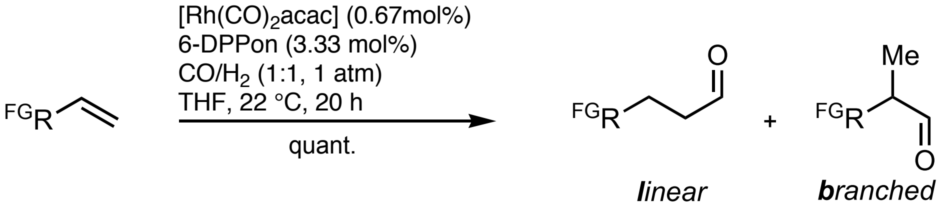
Substrate	l : b (L = 6-DPPon)	l : b (L = PPh_3)
	97:3	72:28
	96:4	71:29
	97:3	74:26
	94:6	71:29
	96:4	69:31
	95:5	70:30

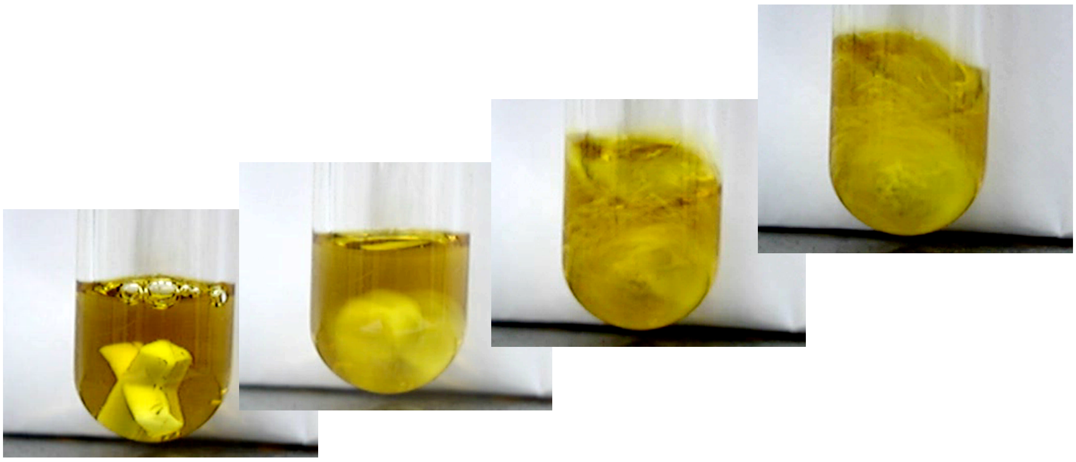
Substrate	l : b (L = 6-DPPon)	l : b (L = PPh_3)
 [a]	95:5	89:11
	96:4	77:23
 MeOH as solvent	83:17	77:23
 + 0.5 eq AcOH	81:19	-

Rh:L:alkene (1:20:1000), *c*(alkene) = 0.698 M, toluene, 10 bar CO/H_2 (1:1), 70 °C. Complete conversion in all cases after 20 h.
[a] Determined by GC or NMR analysis of the crude reaction product.
[b] Isolated as the corresponding γ-lactol.

B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608.

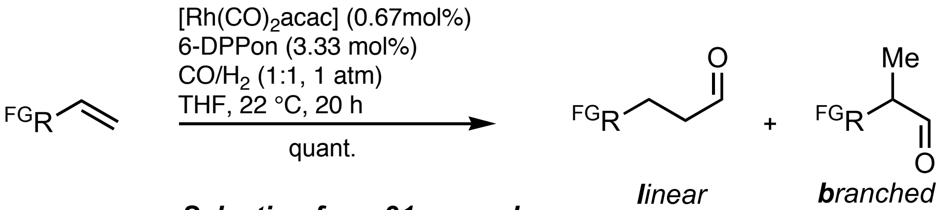
First Regioselective Room Temperature/Ambient Pressure Hydroformylation



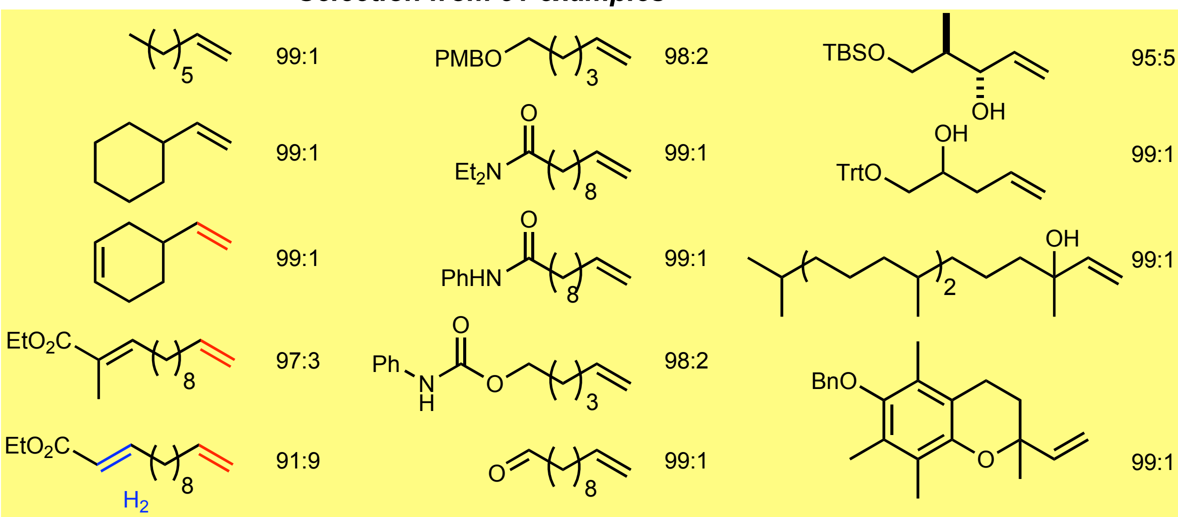


W. Seiche, A. Schuschkowski, B. Breit, *Adv. Synth. Cat.* **2005**, *347*, 1488.

First Regioselective Room Temperature/Ambient Pressure Hydroformylation

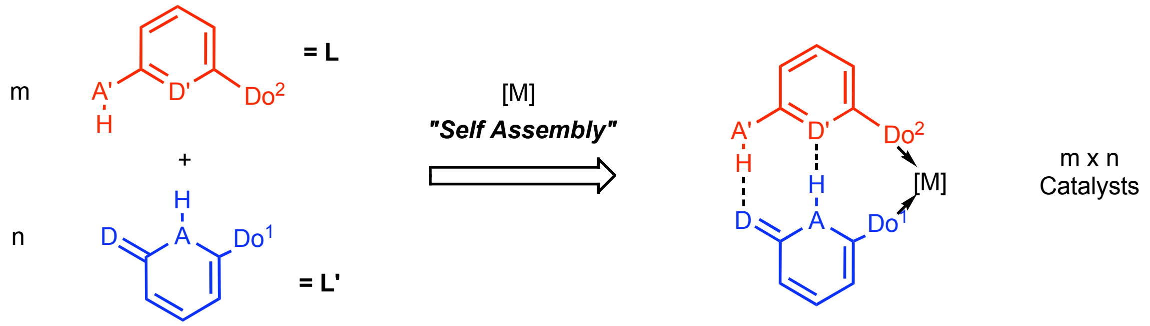


Selection from 31 examples



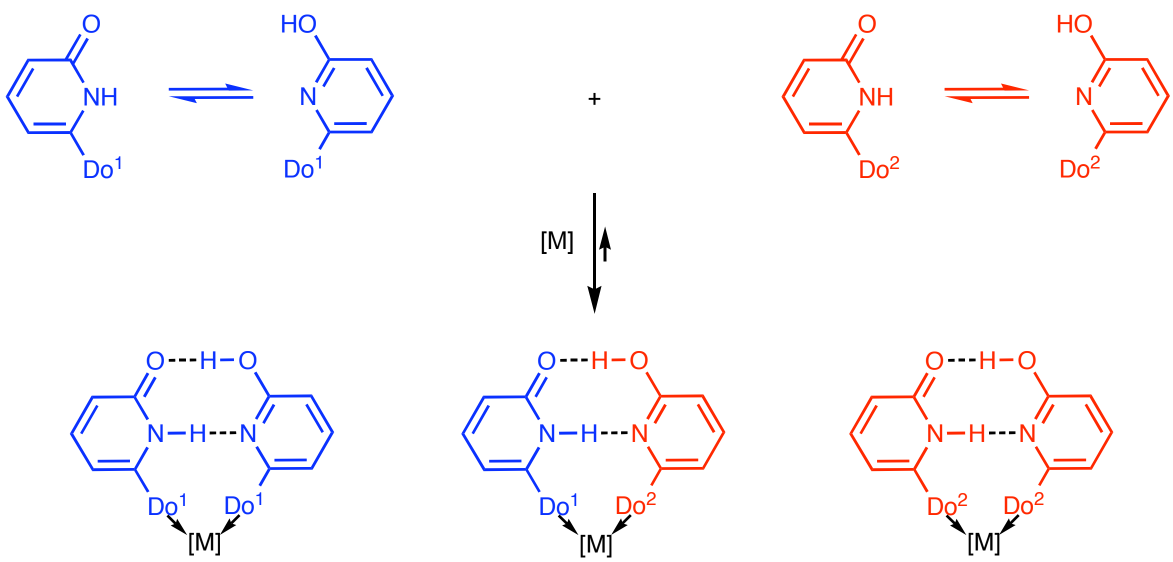
W. Seiche, A. Schuschkowski, B. Breit, *Adv. Synth. Cat.* **2005**, *347*, 1488.

Catalyst Library through "Self Assembly"



	L_1	L_2	L_3	...	L_m
L'_1	L'_1-L_1	L'_1-L_2	L'_1-L_3	...	L'_1-L_m
L'_2	L'_2- L_1	L'_2-L_2	L'_2-L_3	...	L'_2-L_m
L'_3	L'_3- L_1	L'_3-L_2	L'_3-L_3	...	L'_3-L_m
...	...	...	...	...	...
L'_n	L'_n- L_1	L'_n-L_2	L'_n-L_3	...	L'_n-L_m

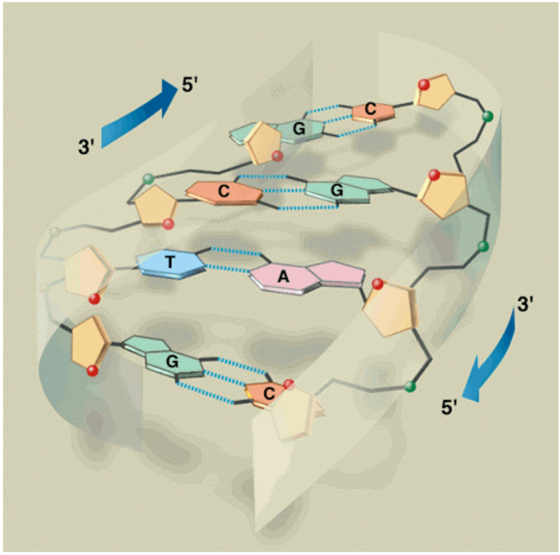
The Problem

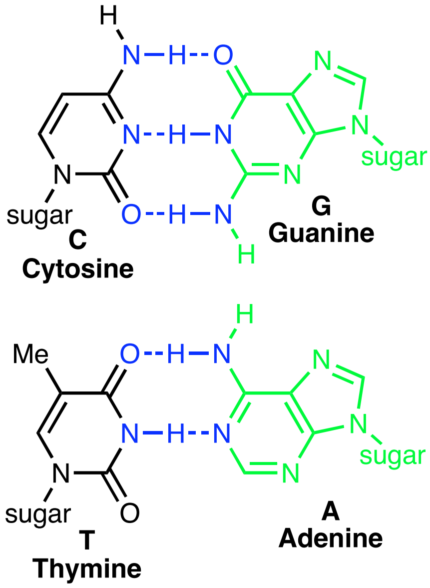


1 : 2 : 1

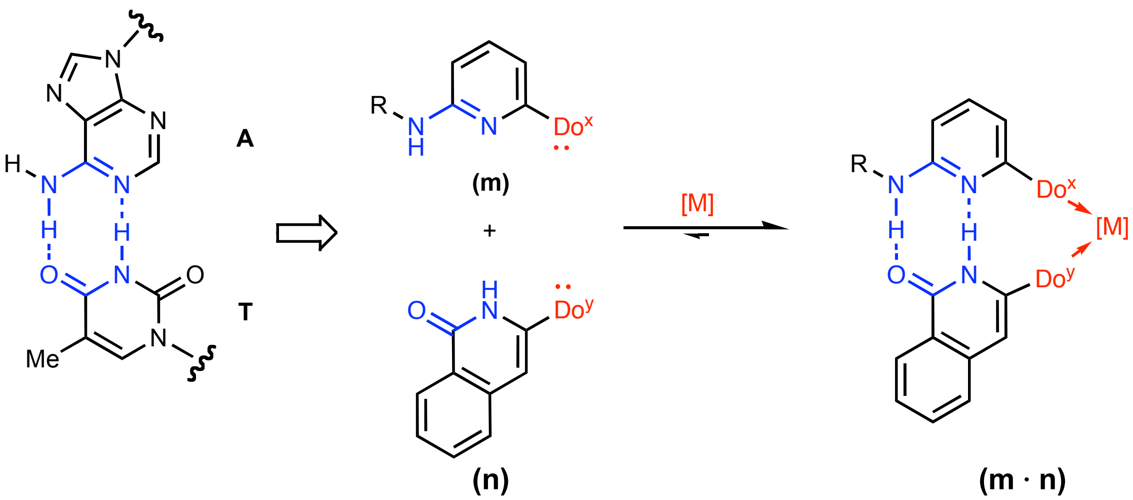
statistical mixture

Complementary Hydrogen-Bonding: A Lesson from Nature



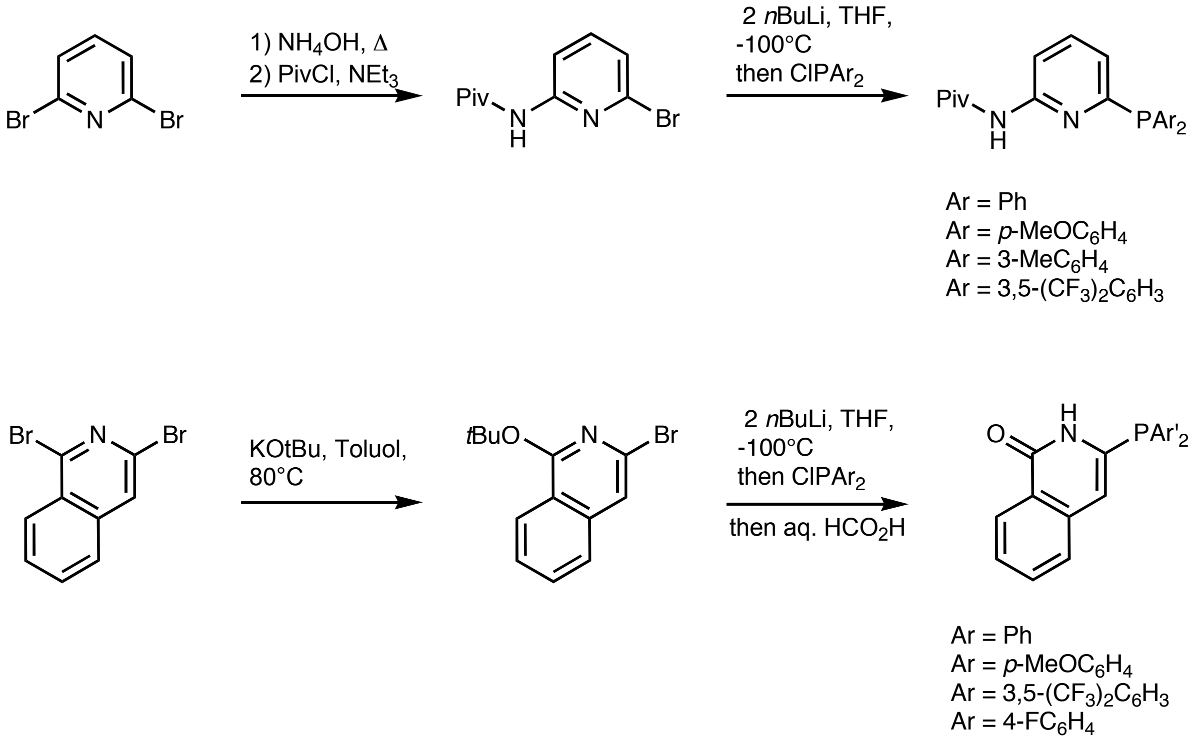


An A-T Base Pair Model for Catalyst "Self Assembly"



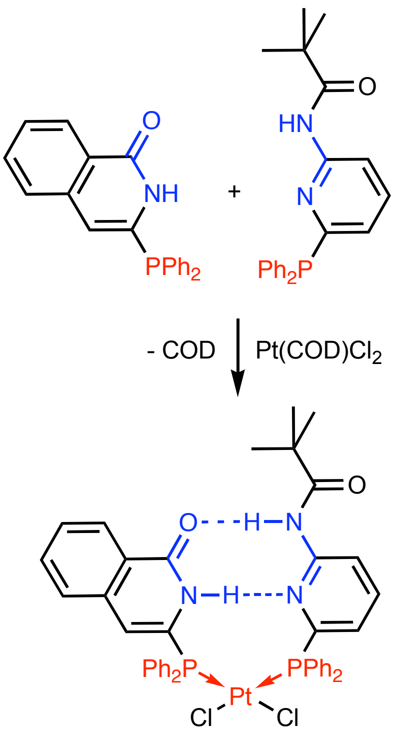
B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640.

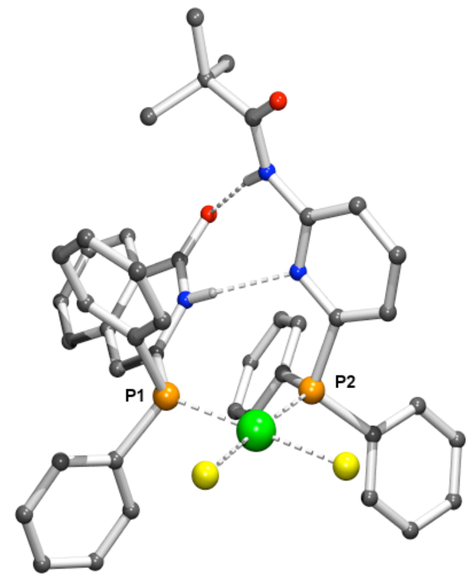
Synthesis of Aminopyridine and Isoquinolone Platforms



B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640.

Catalyst "Self Assembly" - Solid State

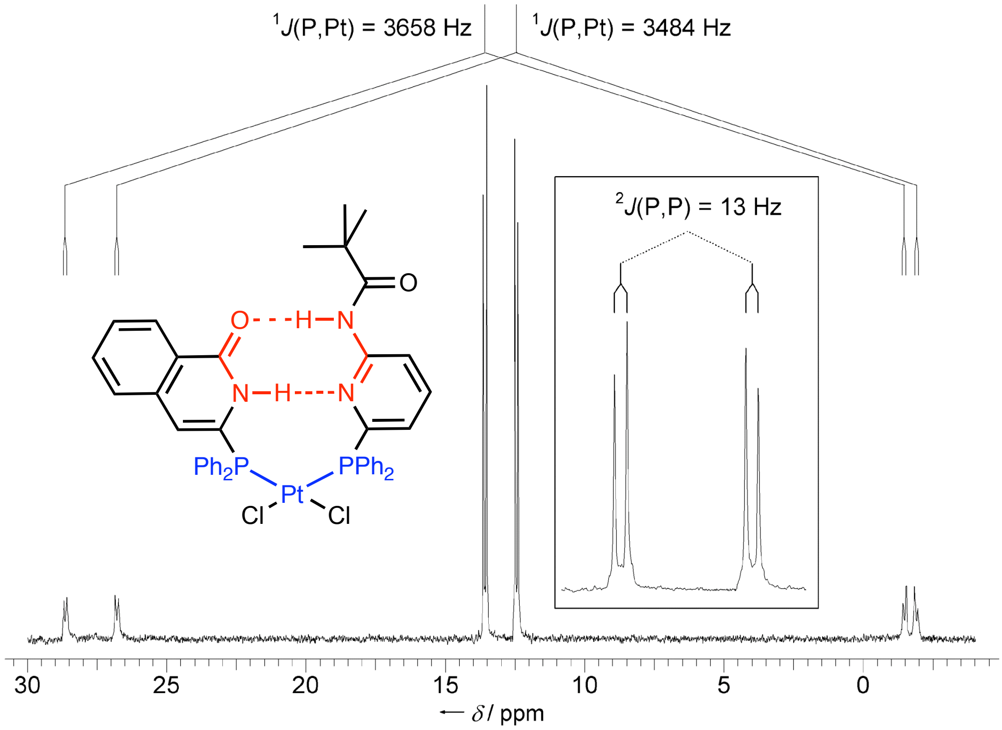




Selected bond lengths and angles:
Pt-P1 2.2486(5) Å; Pt-P2 2.2437(5) Å;
P1-Pt-P2 102.896(18)°;
N-H···N 2.932(2) Å, 163(2)°; O···H-N 2.977(2) Å, 172(2)°

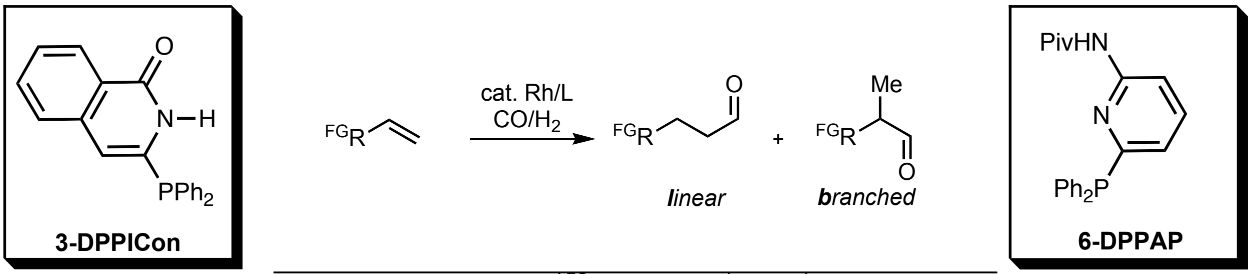
B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640.

Catalyst "Self Assembly" - in Solution ^{31}P NMR



B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640.

Hydroformylation of Terminal Alkenes

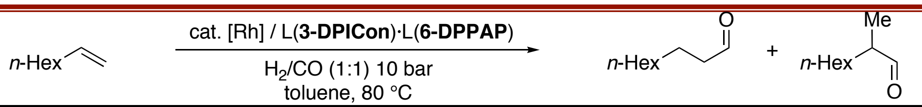


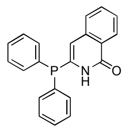
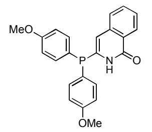
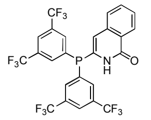
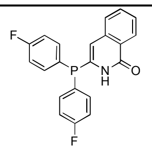
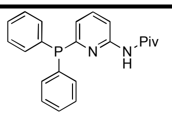
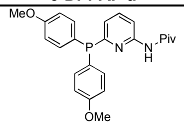
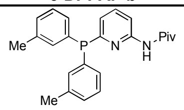
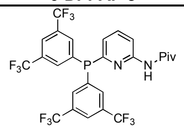
Ligand	FGR	l:b	Conversion (%)
3-DPPICon	$CH_3(CH_2)_5$	76:24	quant.
6-DPPAP	$CH_3(CH_2)_5$	72:28	quant.
3-DPPICon · 6-DPPAP	$CH_3(CH_2)_5$	94:6	quant.
3-DPPICon · 6-DPPAP	$HO(CH_2)_9$	95:5	quant.
3-DPPICon · 6-DPPAP	$MeO_2C(CH_2)_8$	94:6	quant.
3-DPPICon · 6-DPPAP	$AcO(CH_2)_4$	93:7	quant.

Conditions: [Rh(CO)$_2$acac]:ligand:substrate (1:20:1000), 10 bar CO/H_2 (1:1), toluene (c_0(alkene) = 0.7 M), 70 °C, 20 h.

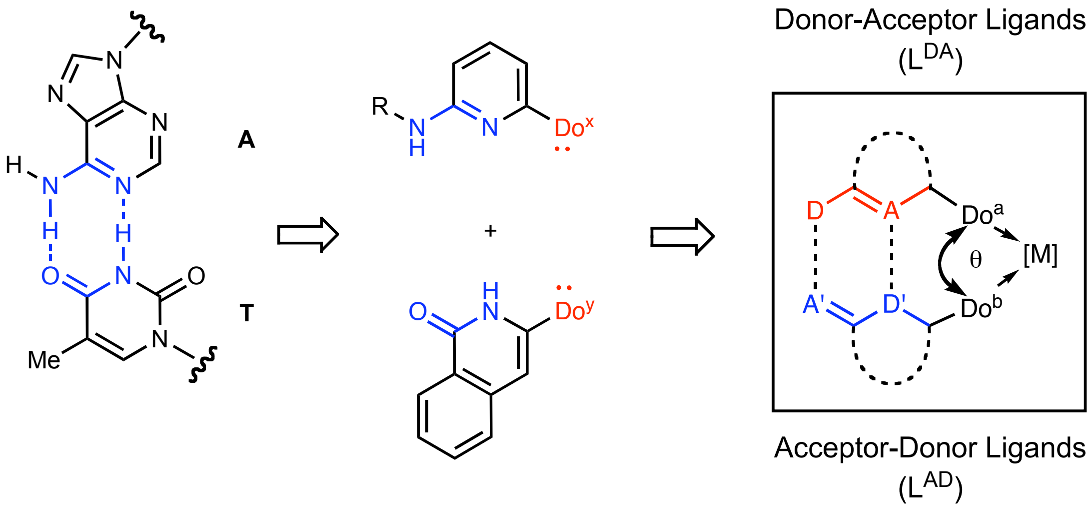
B. Breit, W. Seiche, *Angew. Chem. Int. Ed.* **2005**, *44*, 1640.

4 x 4 "Self-Assembled" Ligand Library - Hydroformylation



Ligand l:b TOF [h^{-1}]	 3-DPICon a	 3-DPICon b	 3-DPICon c	 3-DPICon d
 6-DPPAP a	2425 h^{-1}[b] 94:6[c]	1040 h^{-1} 94:6	2732 h^{-1} 96:4	2559 h^{-1} 95:5
 6-DPPAP b	2033 h^{-1} 93:7	1058 h^{-1} 92:8	1281 h^{-1} 96:4	1772 h^{-1} 94:6
 6-DPPAP c	3537 h^{-1} 94:6	1842 h^{-1} 93:7	1808 h^{-1} 96:4	2287 h^{-1} 94:6
 6-DPPAP d	7439 h^{-1} 96:4	2695 h^{-1} 95:5	7465 h^{-1} 94:6	**8643 h^{-1}** **96:4**

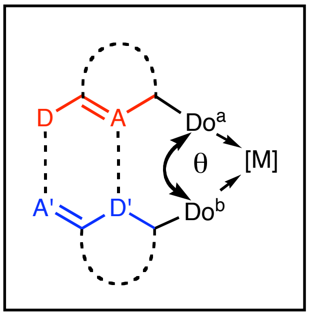
Extension of the Concept: New Heterocyclic A-T Emulating Templates



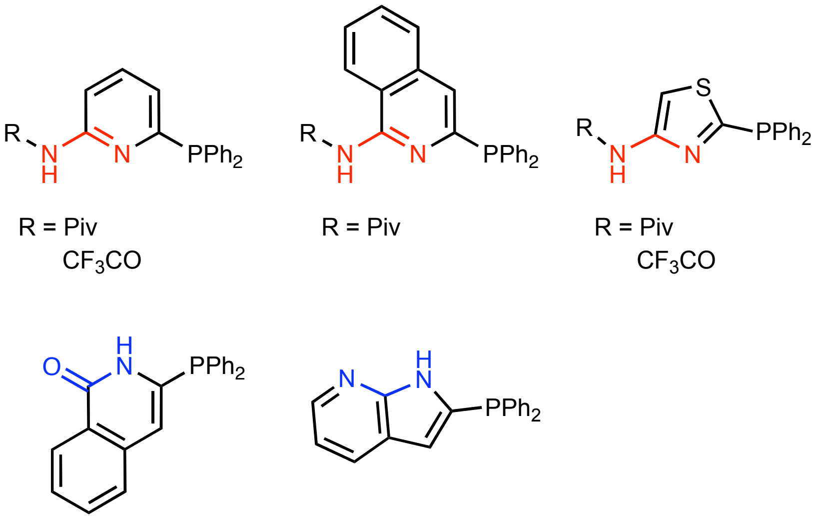
C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

Extension of the Concept: New Heterocyclic A-T Emulating Templates

Donor-Acceptor Ligands
(L^{DA})

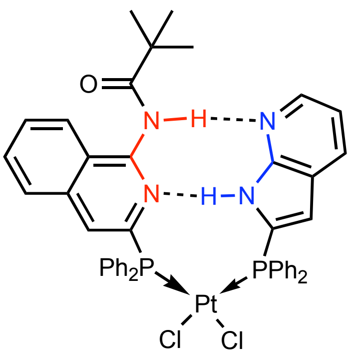


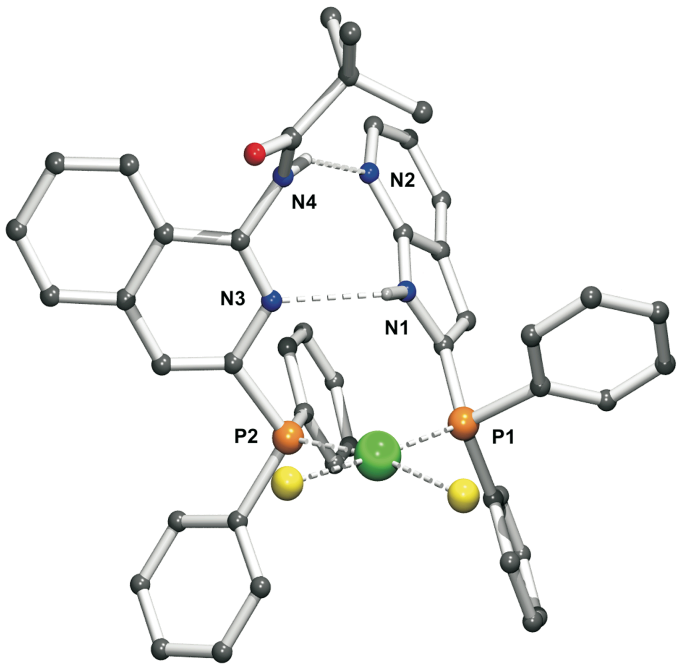
Acceptor-Donor Ligands
(L^{AD})



C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

Catalyst "Self Assembly" - Solid State

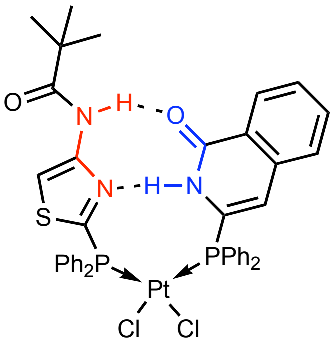


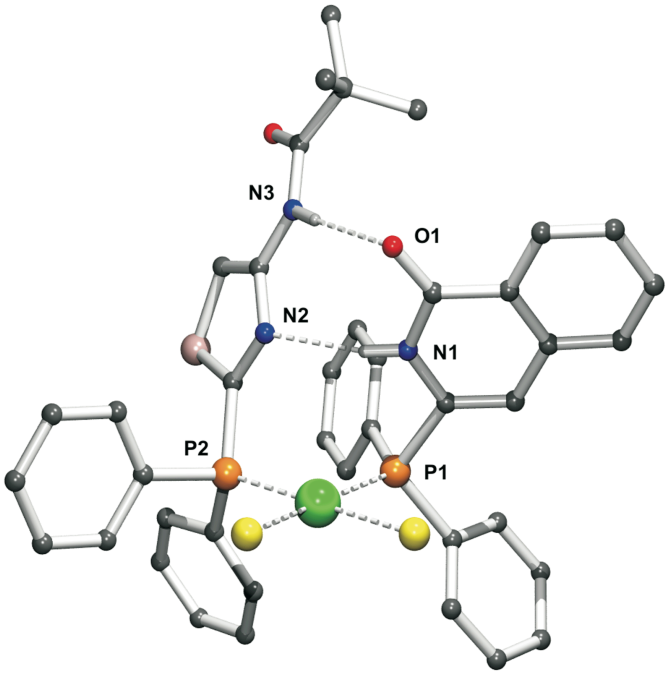


Selected bond lengths and angles:
Pt-P1 2.2417(6) Å; Pt-P2 2.2517(6) Å;
P1-Pt-P2 99.01(2)°;
N1-H···N3 129.0°; N4-H···N2 153.7°

C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

Catalyst "Self Assembly" - Solid State

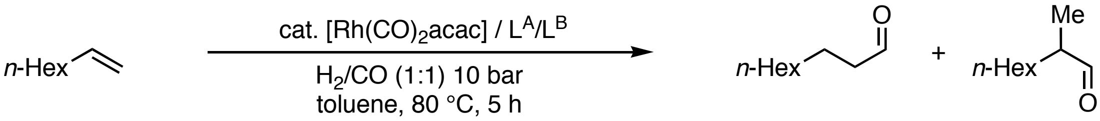




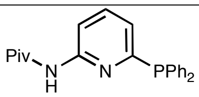
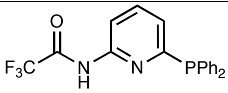
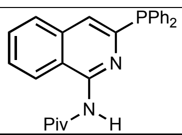
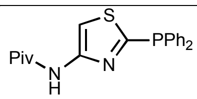
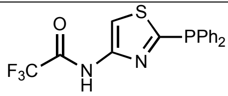
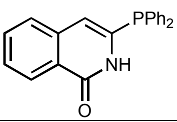
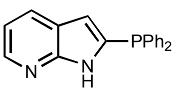
Selected bond lengths and angles:
Pt-P1 2.2609(5) Å; Pt-P2 2.2331(6) Å;
P1-Pt-P2 97.42(2)°;
N1-H···N2 159.0°; N3-H···O1 166.0°

C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

Ligand Backbone Modification: A Methanol-Stable Self-Assembly Platform

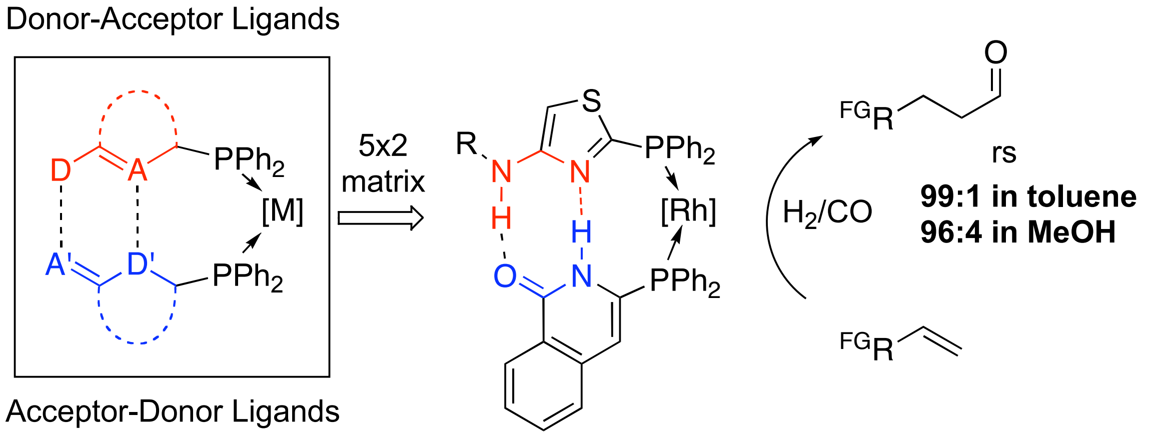


MeOH

L^A/L^B l:b TOF [h^{-1}]					
	93.4:6.6 82:18 (MeOH)	96.2:3.8 79:21 (MeOH)	95.2:4.8	**98.3:1.7** **97:3 (MeOH)**	**99.4:0.6** **96:4 (MeOH)**
	89.0:11.0	96.2:3.8	96.6:5.4	95.3:4.7	99.1.0.9 85:15 (MeOH)

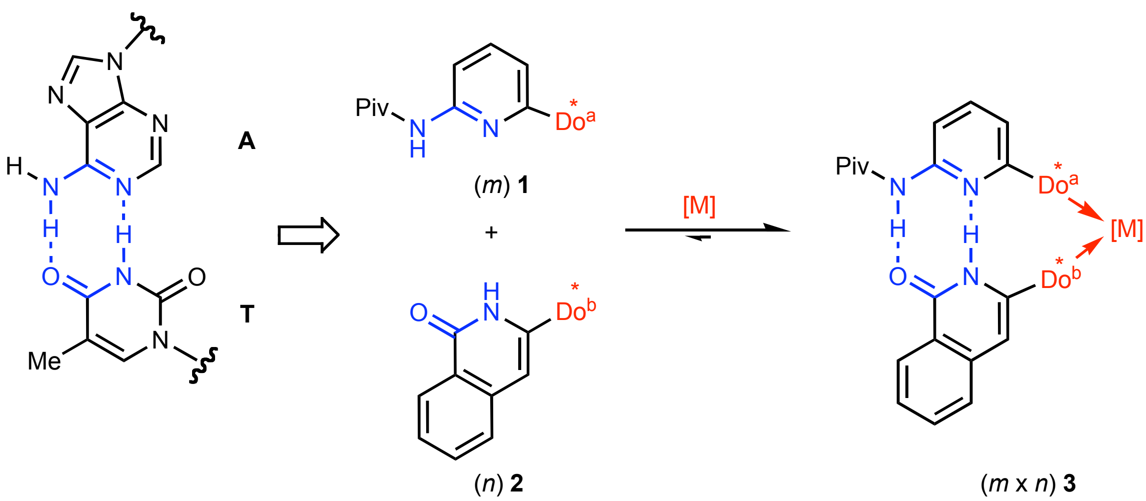
C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

Ligand Backbone Modification: A Methanol-Stable Self-Assembly Platform



C. Waloch, J. Wieland, M. Keller, B. Breit, *Angew. Chem. Int. Ed.* **2007**, *46*, 3037.

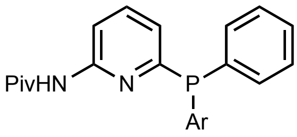
"Self Assembly" of Chiral Bidentate Ligands



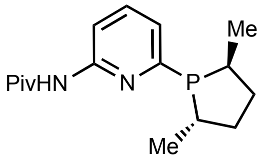
Do^a, Do^b = PAr_1Ar_2, $P(OR)_2$

M. Weis, C. Waloch, W. Seiche, B. Breit, *JACS* **2006**, *128*, 4188.

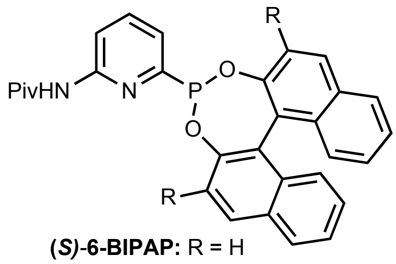
Library of Chiral Phosphine & Phosphonite Ligands



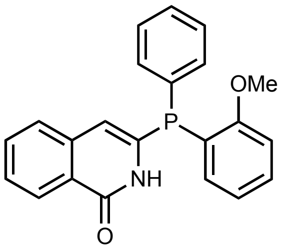
6-APPAP: Ar = *o*-Anisyl
6-NPPAP: Ar = 1-Naphthyl



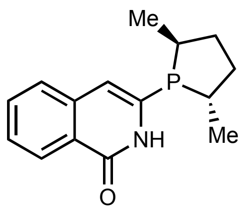
(*S*,*S*)-6-DMPAP



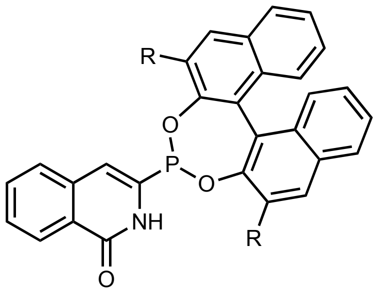
(*S*)-6-BIPAP: R = H
(*S*)-6-MBIPAP: R = Me
(*S*)-6-TBIPAP: R = *p*-Tol



3-APICon



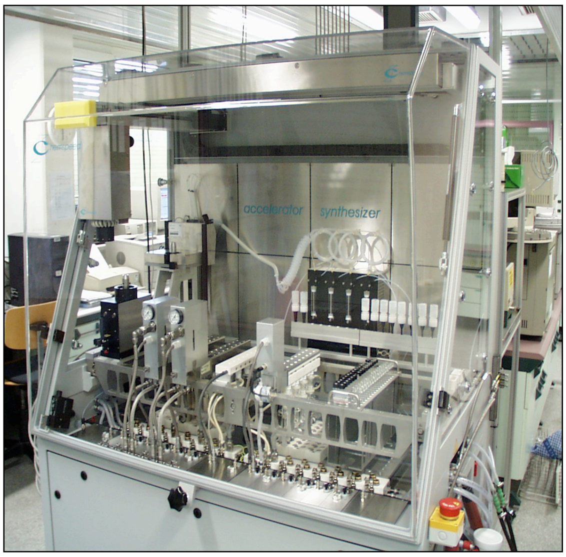
(*S*,*S*)-3-DMPICon



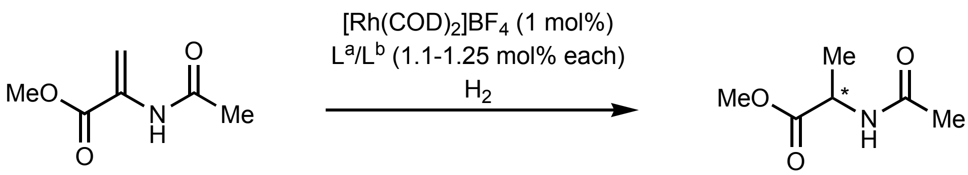
(*R*), (*S*)-3-BIPICon: R = H
(*S*)-3-MBIPICon: R = Me

M. Weis, C. Waloch, W. Seiche, B. Breit, *JACS* **2006**, *128*, 4188.

Parallel-Screening of a 8x10 Catalyst Matrix for Asymmetric Hydrogenation



- Parallel reactor: 6 blocks à 16 reactors
- Adjustment of individual rxn. conditions
- Automated 4 needle dossage system
- Automated sample collection & analysis

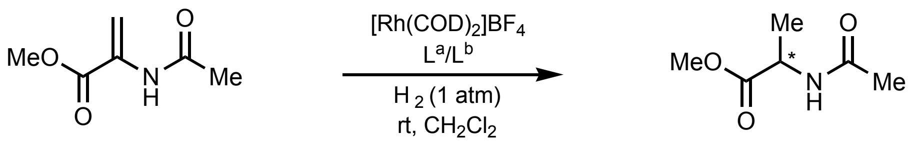


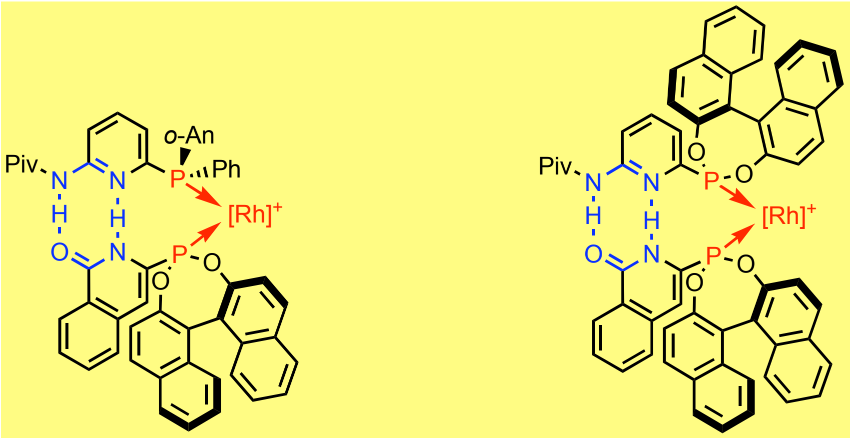
with C. Waloch, M. Weis & C. Jäkel (BASF AG) unpublished results

Hydrogenation of Acetamidoacrylate

	(*S*)-6-BIPAP	(*S*)-6-MBIPAP	(*S*)-6-TBIPAP	(*S*,*S*)-6-DMPAP	(+)-6-APPAP	(–)-6-APPAP	(+)-6-NPPAP	(–)-6-NPPAP	(+)-2-APPAT	(–)-2-APPAT	+ (*S*) – (*R*)
(*S*)-3-BIPICon	95	94	20	33	49	48	28	45	75	52	>90%
(*R*)-3-BIPICon	91	18	73	17	-54	-50	-58	-52	-55	-80	>80%
(*S*)-3-MBIPICon	94	57	49	-13	-1	4	7	8	-19	25	>70%
(*S*,*S*)-6-DMPICon	80	57	31	44	42	37	61	62	40	41	>50%
2-PAIND	85	42	-79	41	7	-10	4	-3	-6	5	>30%
3-DPICon	77	45	-70	-39	-6	1	-1	0	-19	31	0-29%
(+)-3-APICon	72	23	-66	-15	0	-15	-4	5	-7	17	
(–)-3-APICon	73	45	-31	-3	-2	6	-2	3	-11	7	

Asymmetric Hydrogenation of Acetamidoacrylate - The Winners



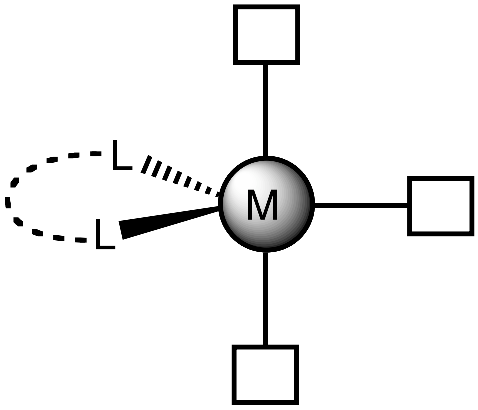


94% *ee*

99% *ee* (Substrate : Cat = 1000 : 1)

M. Weis, C. Waloch, W. Seiche, B. Breit, *JACS* **2006**, *128*, 4188.

Homogeneous Metal Catalysis

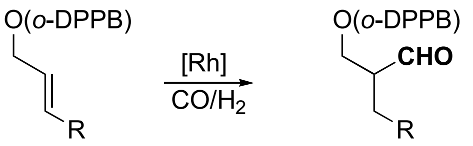


□ = vacant coordination site

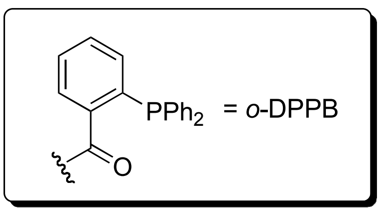
Selectivity through
- Choice of Transition Metal
- "Spectator Ligands" - Sterics/Electronics
- Attractive Interactions between Substrate and Catalyst

Selectivity through Attractive Catalyst/Substrate Interaction - Chelation with Catalyst-Directing Groups

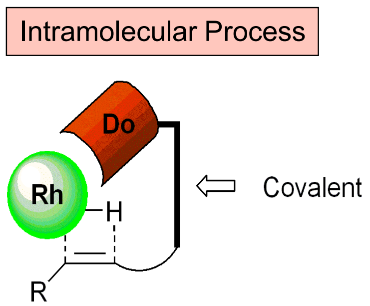
- Directed branched-selective Hydroformylation of terminal and internal Alkenes



rs up to 98 : 2



Catalyst-Directing Group (CDG)



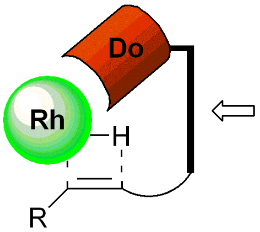
+ Selectivity

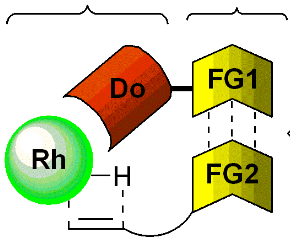
+ Activity

− Stoichiometric Amounts of covalent CDG

B. Breit, *Acc. Chem. Res.* **2003**, *36*, 264-275; B. Breit, C. Grünanger, O. Abillard, *Eur. J. Org. Chem.* **2007**, 2497-2503.

Supramolecular Catalyst: Concept



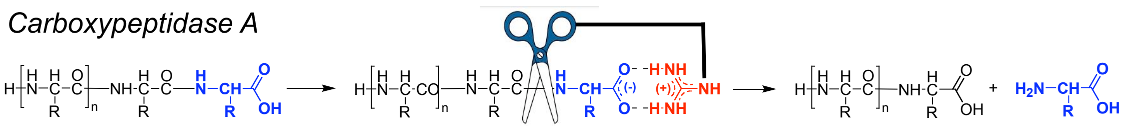


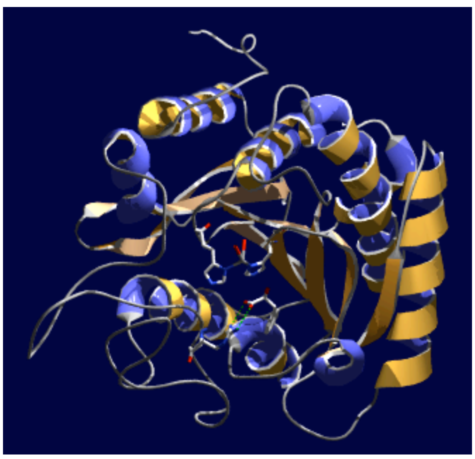
T. Smejkal, B. Breit, *Angew. Chem.* **2008**, *120*, 317.

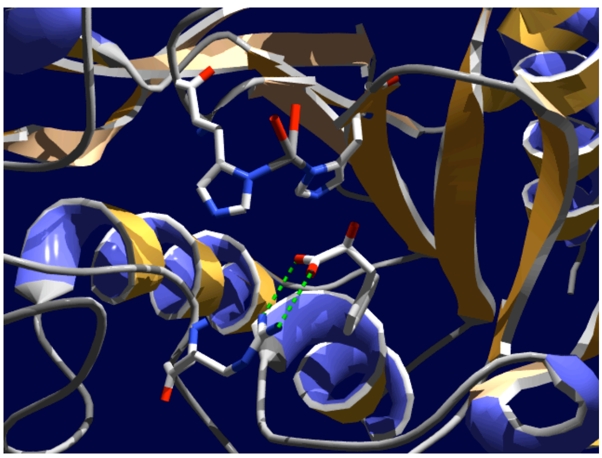
Selectivity through Attractive Catalyst/Substrate Interaction - Molecular Recognition

stabilization of TS‡

Carboxypeptidase A



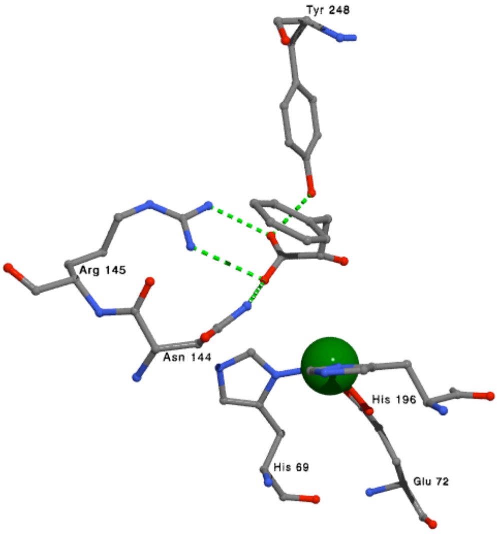


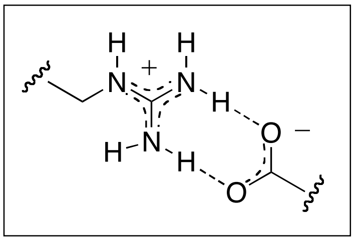


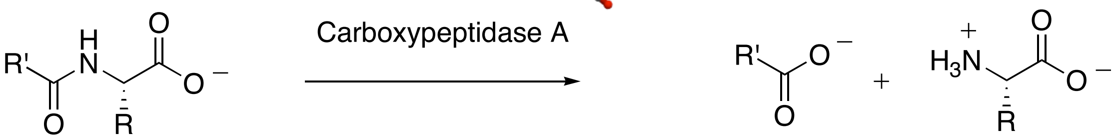
Selectivity (typically very high)

Activity (up to 10^{20} faster)

Supramolecular Catalyst: Carboxypeptidase A

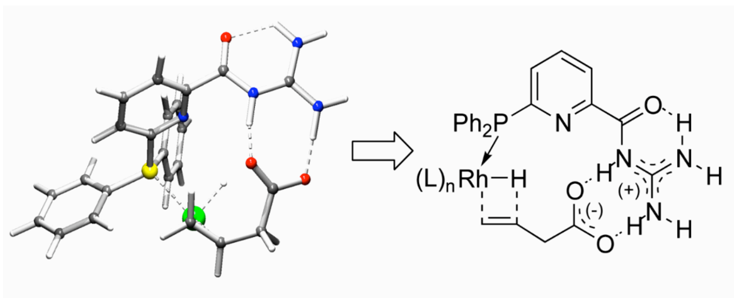




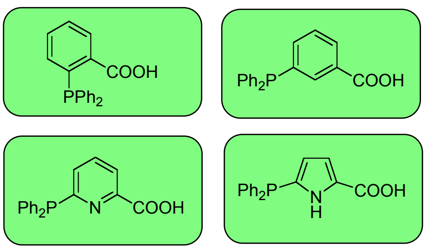


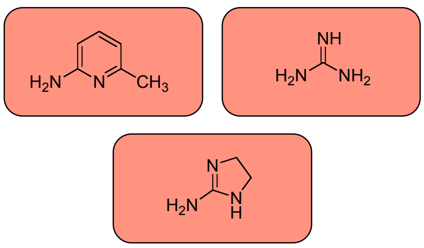
Catalyst Design

Molecular Modeling



Fragment Based Synthesis - Building Blocks

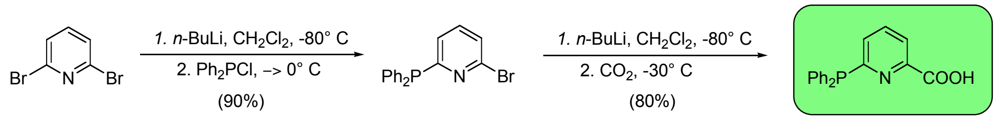


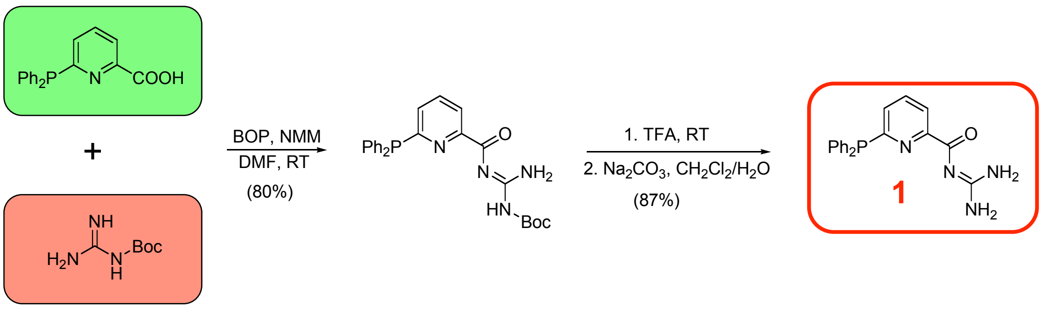


T. Smejkal, B. Breit, *Angew. Chem.* **2008**, *120*, 317.

Catalyst Design

Synthesis:

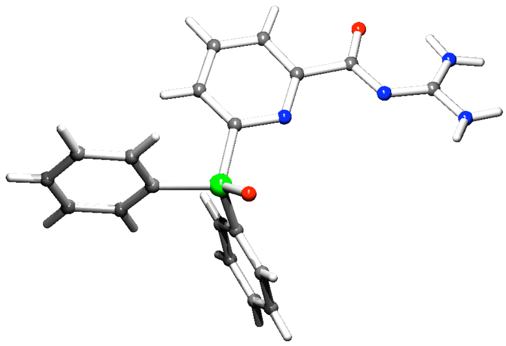


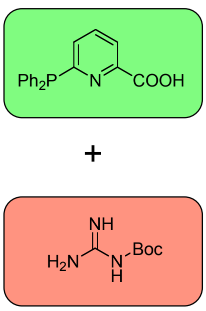


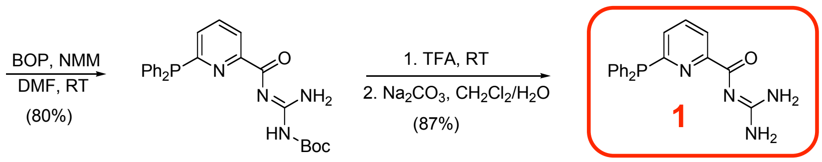
T. Smejkal, B. Breit, *Angew. Chem.* **2008**, *120*, 317.

Catalyst Design

Synthesis:

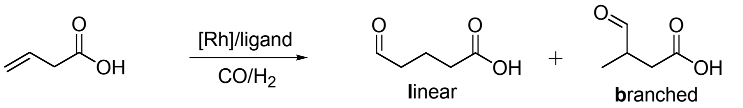






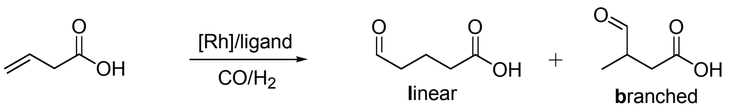
T. Smejkal, B. Breit, *Angew. Chem.* **2008**, *120*, 317.

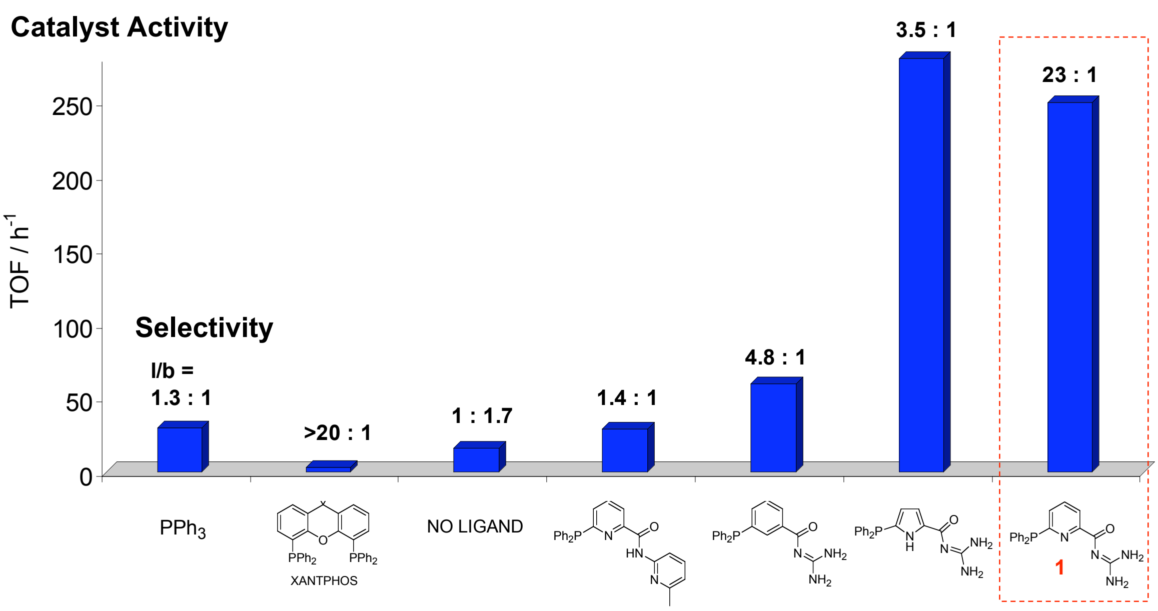
Screening



Conditions: $[Rh(CO)_2acac]$/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, THF(2 ml), 10 bar CO/H_2 (1:1), 40°C, 4 h.

Screening





Conditions: $[Rh(CO)_2acac]$/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, THF(2 ml), 10 bar CO/H_2 (1:1), 40°C, 4 h.

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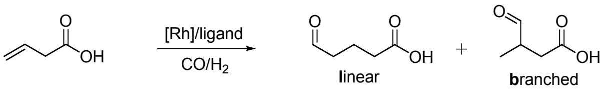
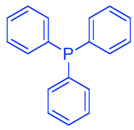
Quantification of the “Supramolecular Effect“



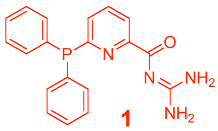
Ligand:



1.3 : **1** (TOF = 30 h^{-1})

⇩ ⇩

$k_{(rel)}$ = 1.6 | $k_{(rel)}$ = 1.25



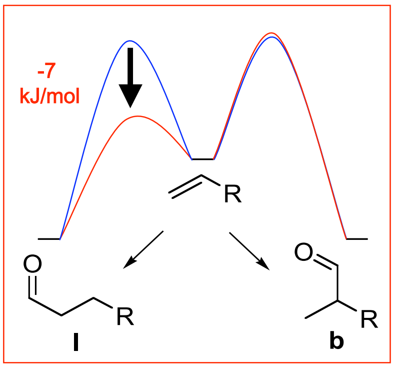
1

23 : **1** (TOF = 250 h^{-1})

⇩ ⇩

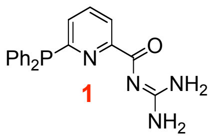
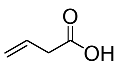
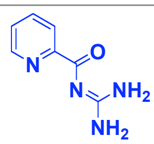
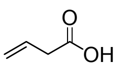
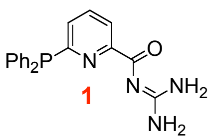
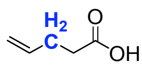
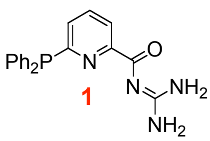
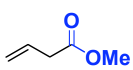
$k_{(rel)}$ = 23 | $k_{(rel)}$ = 1

Selective TS‡ stabilization:



Conditions: $[Rh(CO)_2acac]$/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, THF(2 ml), 10 bar CO/H_2 (1:1), 40°C, 4 h.

Probing Molecular Recognition

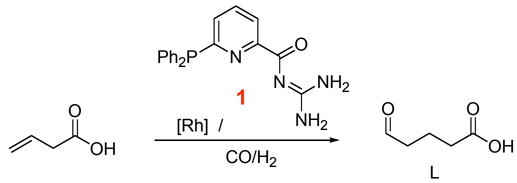
Entry	Ligand	Substrate	TOF (h^{-1})	Regioselectivity (l/b ratio)
1			250	23
2	PPh_3 / 		12	1.5
3			49	3.6
4		 (+ AcOH)	29 (34)	1.1 (1.4)

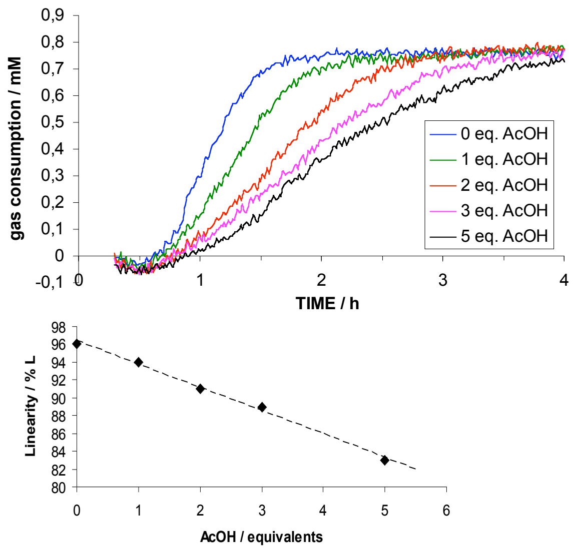
Ligand Modification (entries 1–2)

Substrate Modification (entries 3–4)

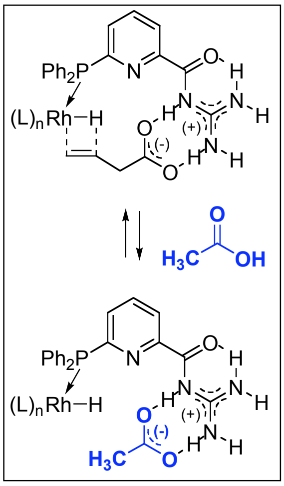
Conditions: $[Rh(CO)_2acac]$/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, THF(2 ml), 10 bar CO/H_2 (1:1), 40°C, 4 h.

Probing Molecular Recognition: Competition Experiment



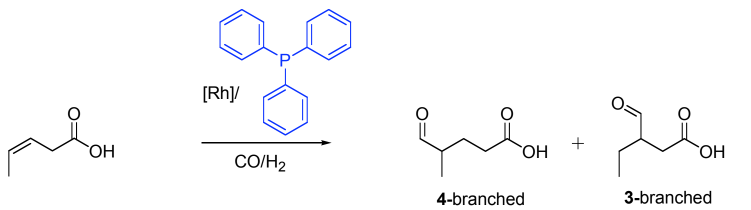


Inhibition



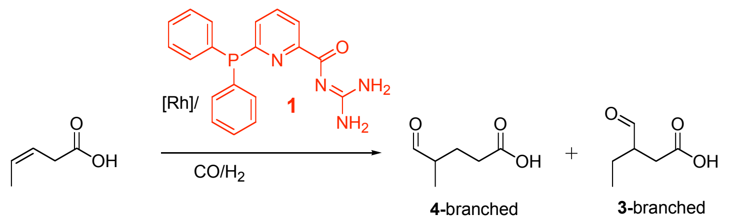
Conditions: [Rh(CO)$_2$acac]/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, THF(2 ml), 10 bar CO/H_2 (1:1), 40°C, 4 h.

Regioselective Hydroformylation of an Internal Alkene



(Conversion = 20%) 1 : 1.7

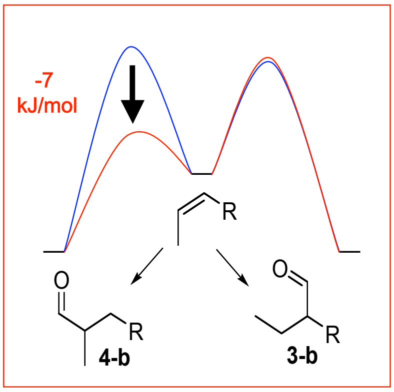
k(rel) = 1   k(rel) = 1.7



(Conversion = 80.5%) 11 : 1

k(rel) = 17.8   k(rel) = 1.6

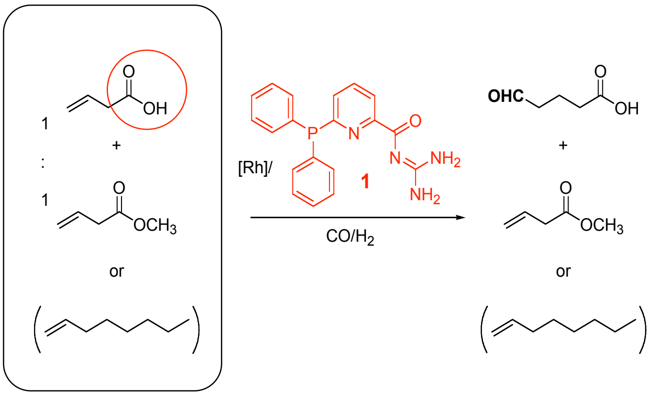
Selective TS‡ stabilization:



Conditions: [Rh(CO)$_2$acac]/ligand/substrate = 1:10:50, c_0(substrate) = 0.2 M, THF(4 ml), 6 bar CO/H_2 (1:1), RT, 68 h.

Substrate Selectivity

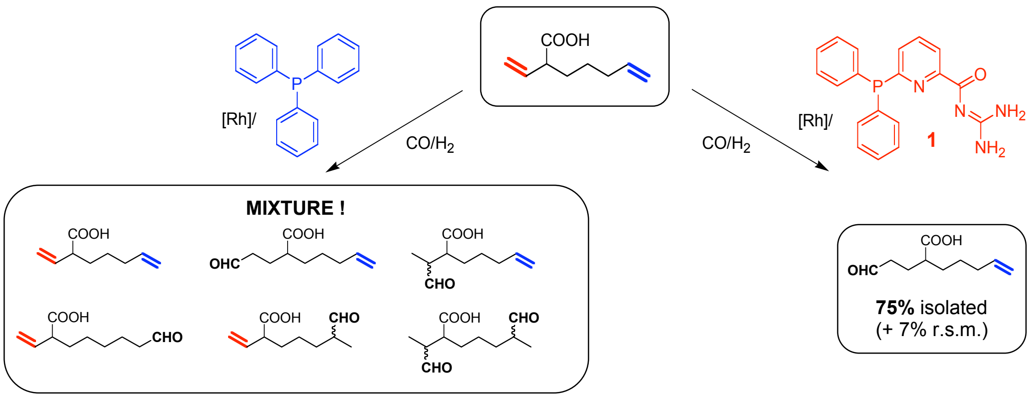
Mixture ⇨ Selective reaction of the complementary substrate

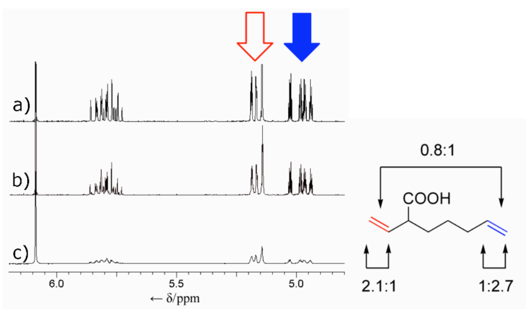


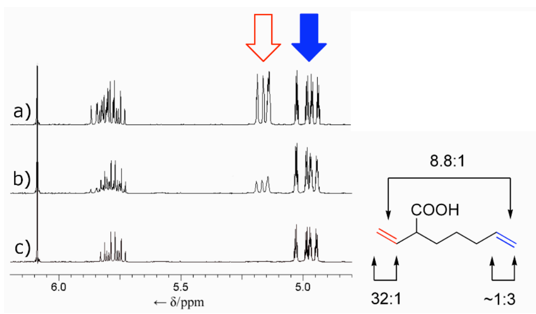
Hydroformylation $k_{(rel)}$	Regioselectivity l/b
1	50
<0.1	2.3
<0.15	3

Conditions: $[Rh(CO)_2acac]$/ligand/substrate1/substrate2 = 1:20:200:200, c_0(substrate) = 0.13 M, THF(6 ml), 4 bar CO/H_2 (1:1), RT.

Reaction Site Selectivity







Conditions: $[Rh(CO)_2acac]$/ligand/substrate = 1:10:150, c_0(substrate) = 0.2 M, THF(8 ml), 4 bar CO/H_2 (1:1), 25° C.

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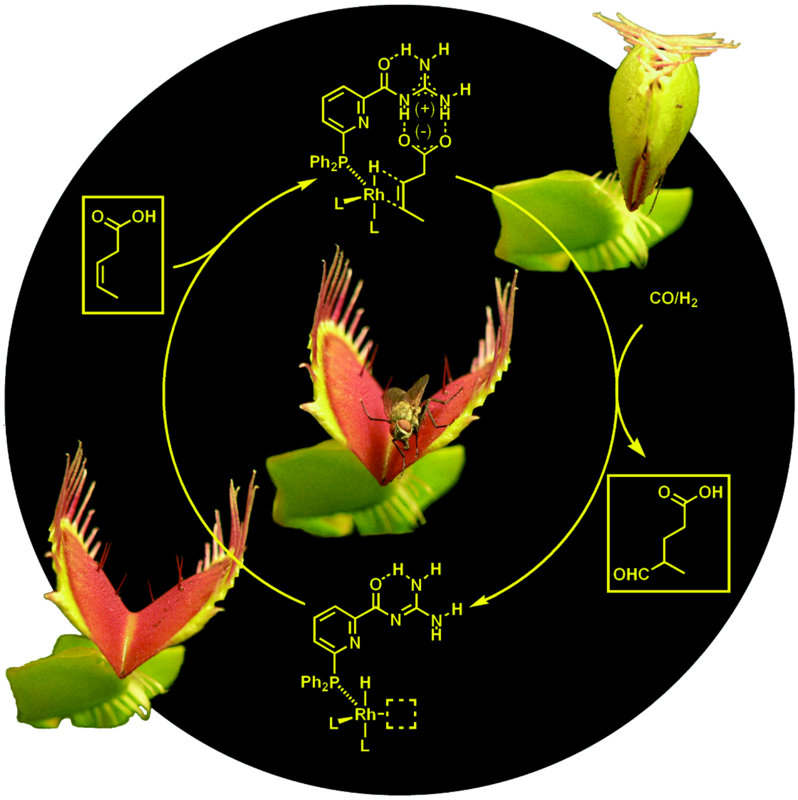
Proposed Mechanism - Trap and Bite



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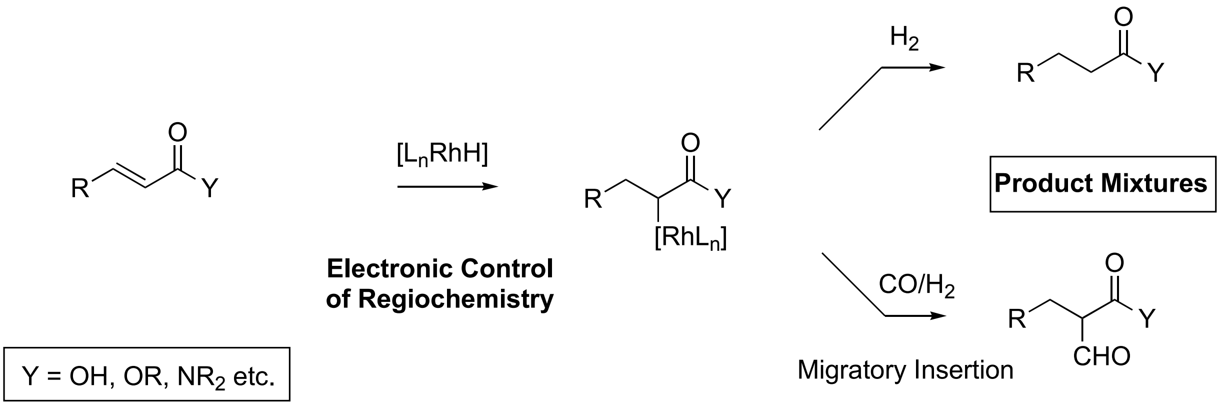
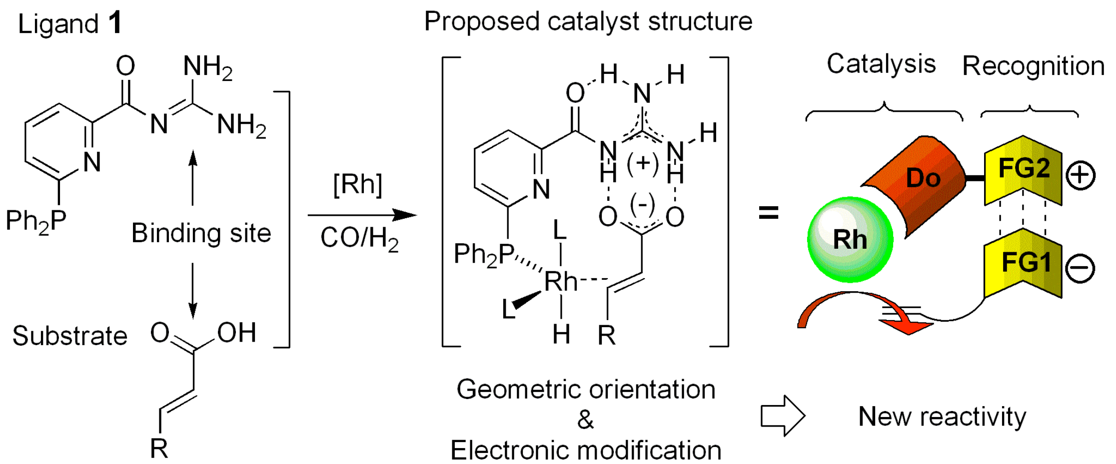
Hydroformylation of α,β-unsaturated Carboxylic Acids & Derivatives:

Chemoselectivity & Regiochemistry Issues



Supramolecular Catalyst - Electronic Modification & Reaction of Acrylic Acids

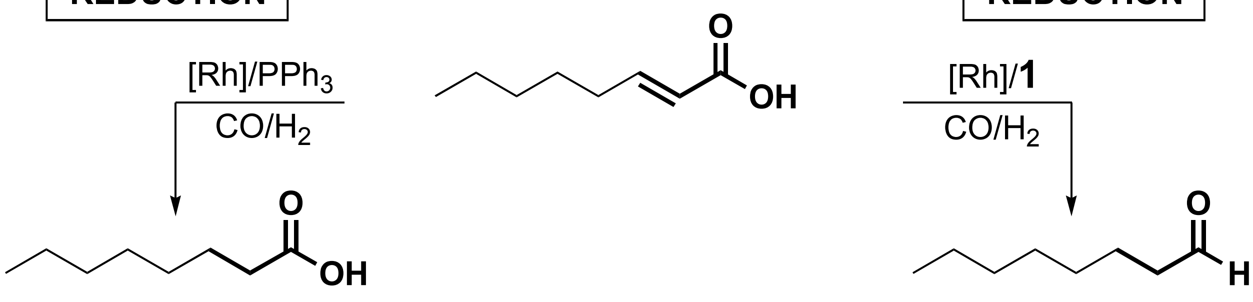


T. Smejkal, B. Breit, *Angew. Chem.* **2008**, *120*, 4010 (selected as "Hot Paper")

Supramolecular Catalyst - Hydroformylation of α,β-Unsaturated Carboxylic Acids

2-H REDUCTION

4-H REDUCTION



32% CONVERSION
>99:1

100% CONVERSION
99:1

Conditions: [Rh(CO)$_2$acac]/ligand/substrate = 1:10:200, c_0(substrate) = 0.2 M, CH_2Cl_2 (4 ml), 10 bar CO/H_2 (1:1), 25°C, 24 h.

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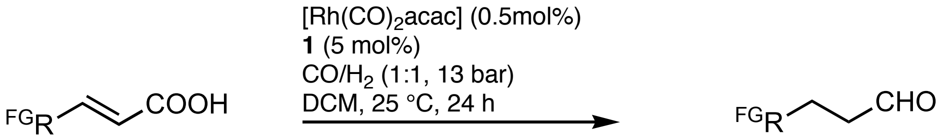
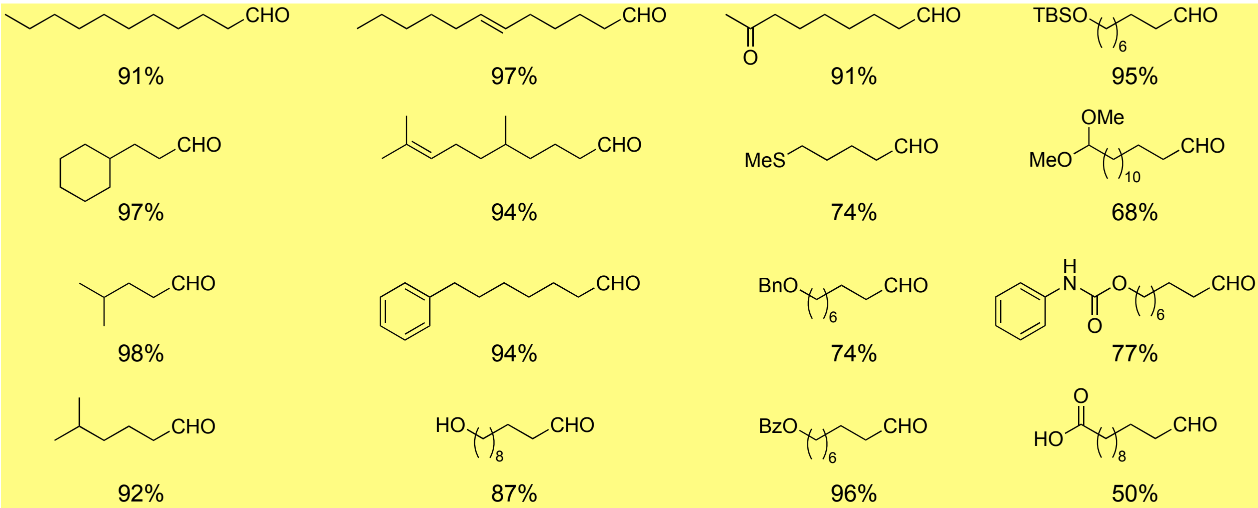
Catalytic Reduction of α,β-Unsaturated Carboxylic Acids to Aliphatic Aldehydes





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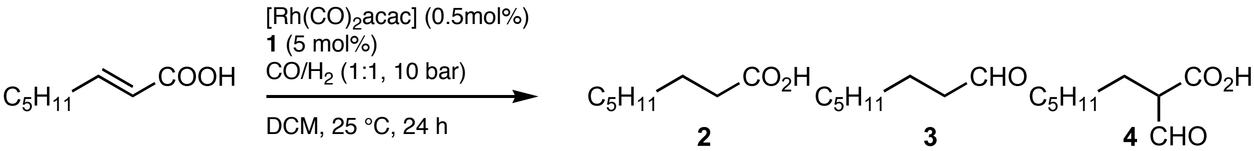
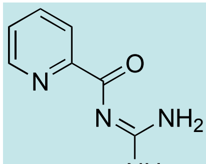
Catalyst Control Experiments

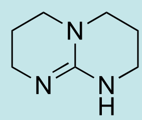


Entry	Ligand	Conversion [%]	Yield [%]
1	**1**	100	**2**(<1), **3**(94)
2	No ligand	<1	**2**(<1)
3	PPh_3	32	**2**(32)
4[b]	PPh_3	33	**2**(26), **3**(3), **4**(4)
5	$P[O(o,p\text{-}tBu_2C_6H_3)]_3$	68	**2**(33), **3**(23), **4**(12)
6[c]	PPh_3/**5** (1:1)	8	**2**(8)
7	PPh_3/Et_3N (1:1)	42	**2**(42)
8	PPh_3/**6** (1:1)	<1	**2**(<1)
9	PPh_3/Et_3N (1:20)	25	**2**(8), **3**(17)

[a] Conditions: $[Rh(CO)_2acac]$/ligand/**2** = 1:10:200, c_0(**2**) = 0.2 M, CH_2Cl_2 (4 ml), 10 bar CO/H_2 (1:1), 25°C, 24 h. [b] THF(4 ml), 40 bar CO/H_2 (1:1). [c] Formation of a suspension was observed.



5



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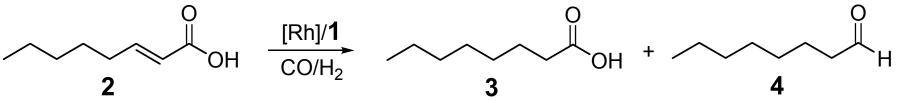
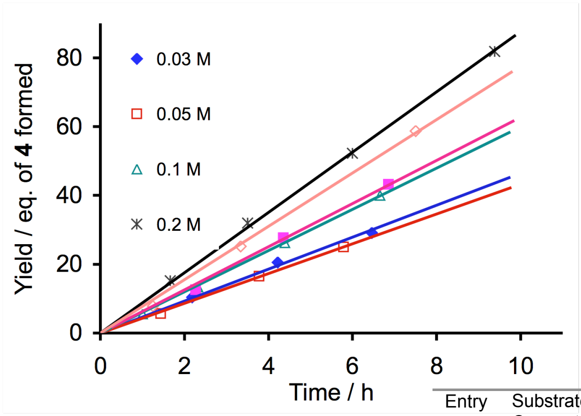
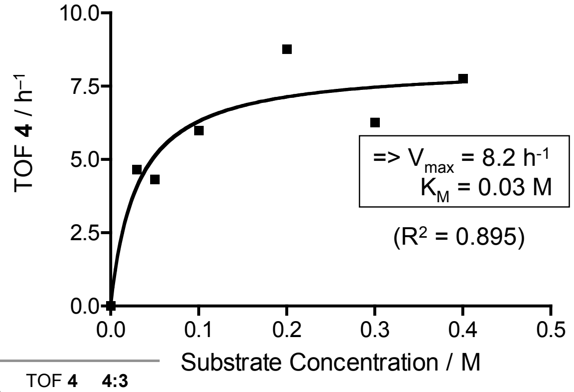
Kinetics



Conditions: [Rh(CO)$_2$acac]/**1**/**2** = 1:10:30-400, c_0(**2**) = 0.03-0.4 M, CH_2Cl_2 (8 ml), 10 bar CO/H_2 (1:1), 25°C.





Entry	Substrate **2** Concentration [M]	TOF **4** [h^{-1}]	**4:3**
1	0.03	4.65	>99:1
2	0.05	4.33	>99:1
3	0.1	5.99	>99:1
4	0.2	8.76	99:1
5	0.3	6.27	27:1
6	0.4	7.76	21:1

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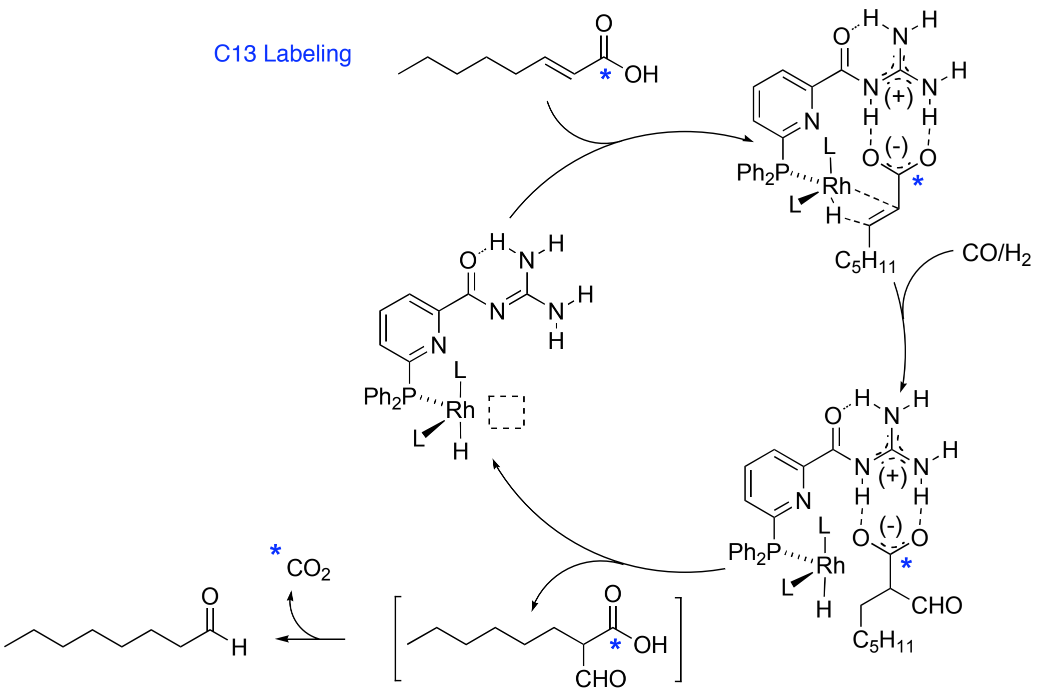
Proposed Catalytic Cycle



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