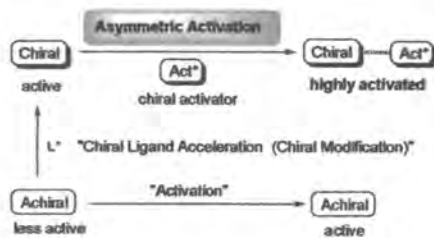
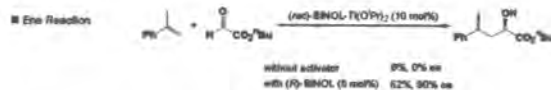
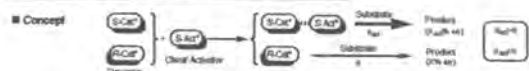


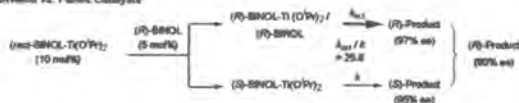
Asymmetric Catalysis



Asymmetric Activation of Racemic Catalyst

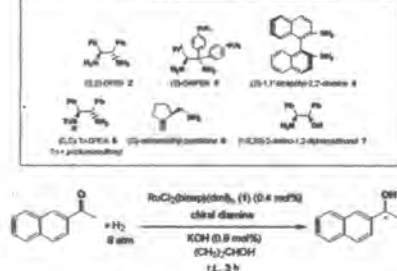


Activated vs. Parent Catalysts



K. Mikami, S. Matsukawa, *Nature* 1997, 386, 613
Emerald 1996, 1, 50

Screening of Chiral Activator for Asymmetric Activation

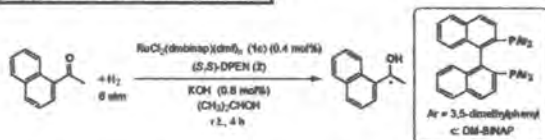


Ohkuma, T.; Oeda, H.; Hamaguchi, S.; Ikariya, T.; Noyori, R. *JACS*, 117, 2673 (1995)

Screening of Chiral Activator for Asymmetric Activation

Entry	R ₁ / R ₂ / R ₃	chiral activator	% ee	yield (%)
1	racemic	(S,S)-2, 0.2 mol%	38 (R)	91
2	racemic	(S,S)-2, 0.4 mol%	79 (R)	99
3	racemic	(S)-3, 0.2 mol%	23 (R)	99
4	(S)	(S)-3, 0.4 mol%	76 (R)	99
5	racemic	(S)-4, 0.2 mol%	4 (R)	53
6	(S)	(S)-4, 0.4 mol%	39 (R)	47
7	racemic	(S,S)-5, 0.2 mol%	1 (R)	3
8	(S)	(S,S)-5, 0.4 mol%	-	N.B.
9	racemic	(S)-6, 0.2 mol%	4 (R)	96
10	(S)	(S)-6, 0.4 mol%	69 (R)	>99
11	racemic	(1 <i>R</i> ,2 <i>S</i>)-7, 0.2 mol%	5 (R)	1
12	(S)	(1 <i>R</i> ,2 <i>S</i>)-7, 0.4 mol%	7 (R)	6

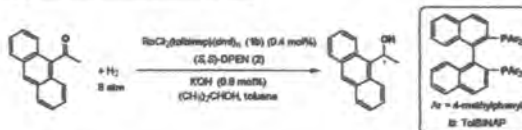
Hydrogenation of 1'-Acetonaphthone



Entry	DM-BINAP	temp. (°C)	(S,S)-DPEN (2)	% ee	yield (%)
1	Racemic	r.t.	0.2 mol%	79 (R)	99
2	Racemic	r.t.	0.4 mol%	80 (R)	99
3	(S)	r.t.	0.4 mol%	>99 (R)	99
4	(R)	r.t.	0.4 mol%	56 (S)	99
5 ^{a)}	Racemic	-35	0.4 mol%	90 (R)	95
6 ^{a)}	(S)	-35	0.4 mol%	>99 (R)	99
7 ^{a)}	(R)	-35	0.4 mol%	62 (S)	54

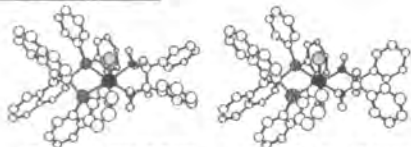
a) Reaction time is 7 hours.

Hydrogenation of 9-Acetylanthracene



Entry	TolBINAP	(S,S)-DPEN	temp. (°C)	time (h)	% ee	yield (%)
1	racemic	0.4 mol%	r.t.	18	78 (R)	28
2	racemic	0.4 mol%	80	10	80 (R)	99
3	(R)	0.4 mol%	r.t.	18	80 (R)	27
4	(R)	0.4 mol%	80	10	81 (R)	99
5	(S)	0.4 mol%	80	10	41 (R)	91

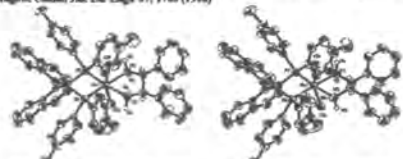
BINAP-Ru(II)/DPEN Complex



(R)-BINAP-Ru(II)/(R,R)-DPEN

(R)-BINAP-Ru(II)/(S,S)-DPEN

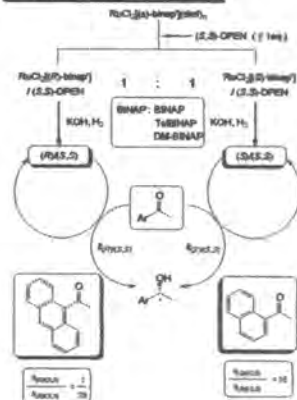
Deaton, H.; Ohtsuka, T.; Mizuta, K.; Yokozawa, E.; Kozawa, M.; Katsuyama, E.; England, A. F.; Ikariya, T.; Noyori, M. *Angew. Chem., Int. Ed. Engl.* 27, 1763 (1998)



RuCl₂[(R)-tolbinap]/(R,R)-dpem

RuCl₂[(R)-tolbinap]/(S,S)-dpem

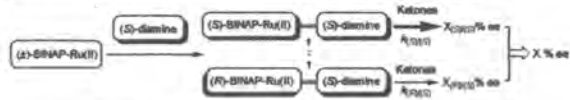
Substrate-Dependent Kinetic Feature



Asymmetric Activation / Deactivation of Racemic Ru(II) Catalyst

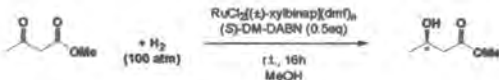
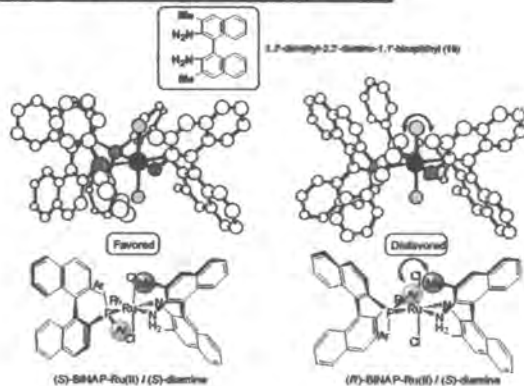


Problems of Asymmetric Activation of Racemic Ru(II) Catalyst



- 1) Non-selective formation of activated complexes
- 2) Enantioselectivity critically depend on a substrate

Binaphthyldiamine Derivative for Selective Complexation

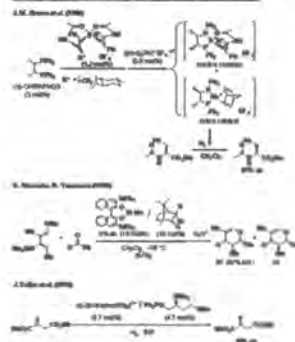


Hydrogenation of methyl 3-oxobutanoate by racemic BINAP-Ru(II) catalysts through asymmetric deactivation.

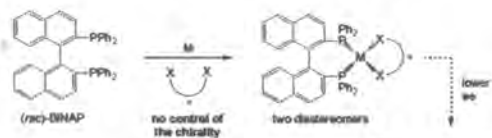
Cat.	(S)-DM-DABN	% ee ^a	% yield ^b
(S)-BINAP-Ru(II)	0.5eq	99.3 (R)	quant.
(R)-BINAP-Ru(II)	none	99.9 (R)	quant.

^a Determined by chiral HPLC analysis (CHIRALCELL OB-H) after conversion to methyl 3-benzoyloxobutanoate. ^b Determined by GC analysis (TC-1701).

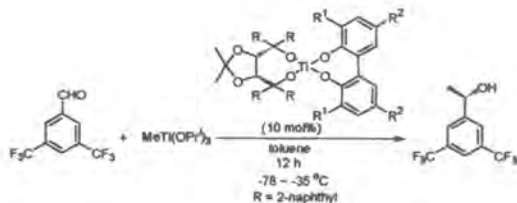
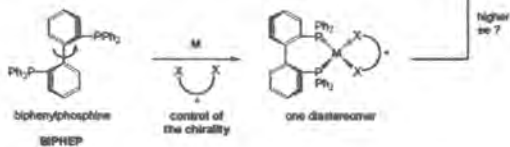
Asymmetric Deactivation of Racemic Catalyst



Tropos vs Atropos Phosphine Ligands for Asymmetric Catalysis



Atropos (*Atropos*, She who cannot be turned)

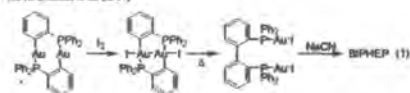


3,3'-Modified BIPOLate/TADDOLate-Ti complexes

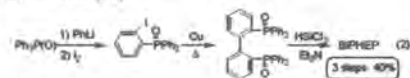
R ¹	R ²	% Yield	(% ee)
Ph	H	36	69
p-MeO-Ph	H	40	65
Me	H	56	88
MeO	Me	60	100

Synthesis of BIPHEP itself

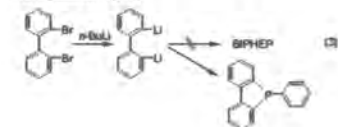
M. A. Bennett et al. (1987)



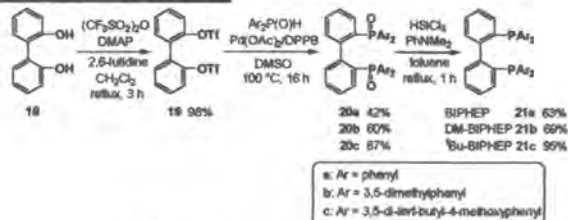
M. Schlosser et al. (1996)



T. S. Mirman et al. (1989)

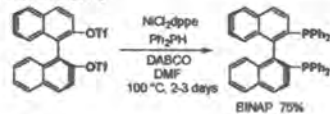


Synthesis of BIPHEP Derivative

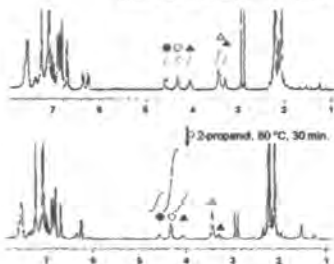
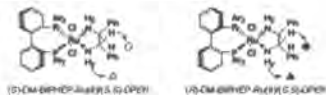


a: Ar = phenyl
b: Ar = 3,5-dimethylphenyl
c: Ar = 3,5-di-*tert*-butyl-4-methoxyphenyl

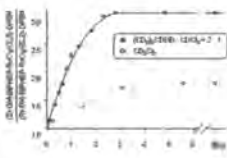
Ch. D. et al. (1994)



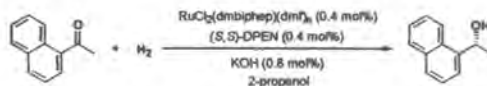
Tropos Nature of Ruthenium(II) Catalysts



Tropos Catalyst at Room Temperature



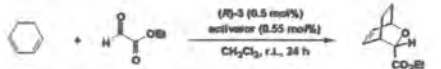
Hydrogenation of 1'-acetonaphthone



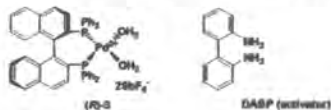
Phosphine	S/S,S/R/S,S ^{b)}	H ₂ (atm)	T (°C)	t (h)	% ee	Yield (%)
DM-BIPHEP	1 : 1	8	28	4	63	>99
DM-BIPHEP	2 : 1	8	28	4	73	>99
DM-BIPHEP	3 : 1	8	28	4	84	>99
(<i>z</i>)-DM-BINAP	(1 : 1)	8	28	4	80	>99
DM-BIPHEP	3 : 1	40	-35	12	92	>99
(<i>z</i>)-DM-BINAP	(1 : 1)	40	-35	7	89	>99

a) Hydrogenation was performed without pre-heat. b) The ratio of (S)-phosphine-Ru(S,S)-DPEN/(R)-phosphine-Ru(S,S)-DPEN was determined by ¹H NMR analysis. c) DM-BIPHEP-Ru(S,S)-DPEN in 2-propanol was pre-heated at 80 °C for 30 min.

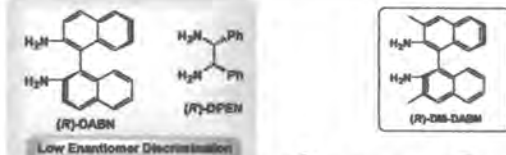
Glyoxylate-HDA Reaction by [Pd((R)-binap)(H₂O)₂](SbF₆)₂ through Asymmetric Activation



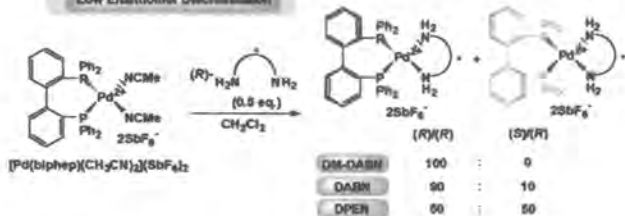
entry	activator	yield(%)	% ee (endo)
1	none	trace	-
2	DABP	71	>99 (1R,3S,4S)



Ability of Enantiomer Discrimination by Diamines

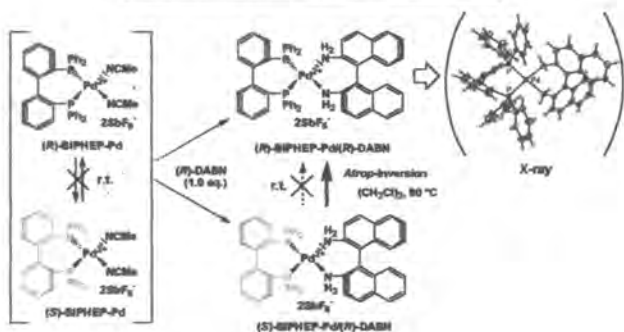


Low Enantiomer Discrimination

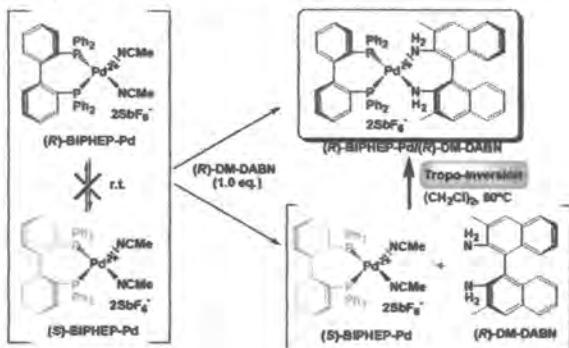


DM-DABN	100	:	0
DABN	90	:	10
DPEH	60	:	50

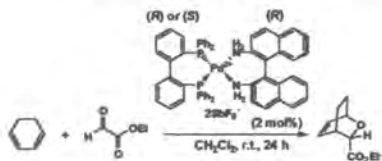
Atrop-inversion of BIPHEP-Pd Complex using DABN



Tropo-inversion of Palladium(II) Complex using DM-DABN

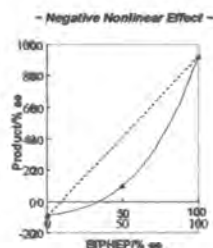


Glyoxylate-HDA Reaction using BIPHEP-Pd/DABN Complex

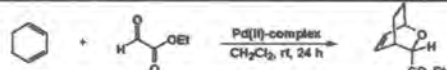


entry	(R)/(R) : (S)/(R)	yield(%)	% ee (endo) ^{a)}
1	50 : 50	84	8 (1S,3R,4R)
2	75 : 25	81	10 (1R,3S,4S)
3	100 : 0	75	82 (1R,3S,4S)

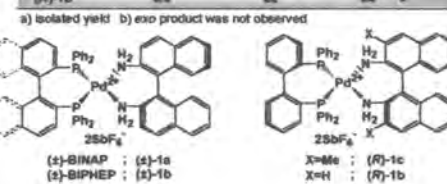
a) exo product was not observed.



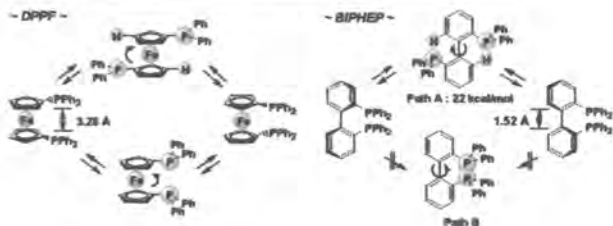
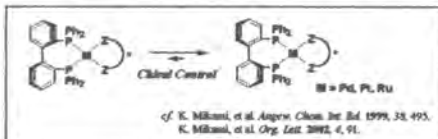
Asymmetric Hetero Diels-Alder Reaction using Palladium(II) Complexes



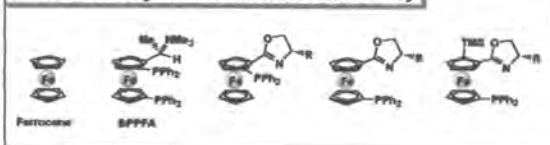
catalyst	mol(%)	yield(%) ^{a)}	ee(%) ^{b)}
(x)-1a	2	61	7 (1S,3R,4R)
(x)-1b	-	84	9 -
(R)-1c	-	89	36 (1R,3S,4S)
(R)-1b	-	75	92 -
(R)-1b	0.5	82	84 -



Flexibility of BIPHEP vs DPPF Ligands



Chiral Ferrocene Ligands with Central and Planar Chirality



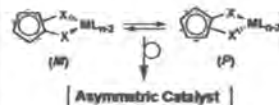
Disfavored

Favored

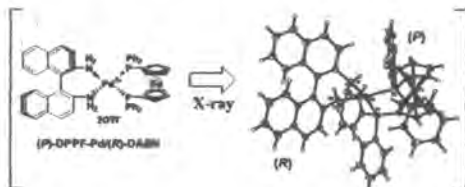


cf. W.-P. Deng, et al. *J. Am. Chem. Soc.* 2004, 126, 4508

Chiral Control of Axial Chirality?



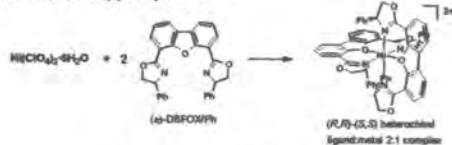
Dynamic Chiral Control of DPPF Ligand by Chiral Diamines



Structure of DPPF-Metal Complex

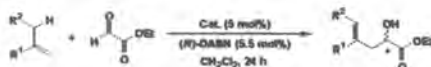


- Octahedral Nickel(II) Complex -



cf. S. Kazanets, et al. *J. Am. Chem. Soc.* 1998, 120, 3074-3088

Asymmetric Glyoxylate-Ene Reaction using DPPF-Ni Catalysts



entry	Cat.	alkene	temp(°C)	yield(%)	% ee
1	Ni(dppf)(SbF ₆) ₂		r.t.	84	90(S)
2	Ni(SbF ₆) ₂		r.t.	87	75 -
3	Ni(dppf)(ClO ₄) ₂		r.t.	52	76 -
4	Ni(dppf)(SbF ₆) ₂		r.t.	91	92 -
5	Ni(dppf)(SbF ₆) ₂		0	14	91 -
5 ^a	Ni(dppf)(SbF ₆) ₂		80	98	87 -
5 ^b	Ni(dppf)(SbF ₆) ₂		r.t.	43	48(R)

^a Reaction time was 4 hours. ^b (R)-DM-DABN was used instead of (R)-DABN.

Effects of Phosphine Ligands on Ni Complexes

