2004 / 1 / 7
Literature Seminar
Tomofumi Kinoshita (M1)

Philosophies on Catalyst Tuning

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philosophy ?

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0. Introduction

Synthesis of Chiral Bisphosphines with Tunable Bite Angles and Their Applications in Asymmetric Hydrogenation of β-Ketoesters

Zhaoguo Zhang, Hu Qian, James Longmire, and Xumu Zhang*

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BINAP-type ligands with various dihedral angles were synthesized, and their ability for hydrogenation of β-ketoesters were tested. → next page.

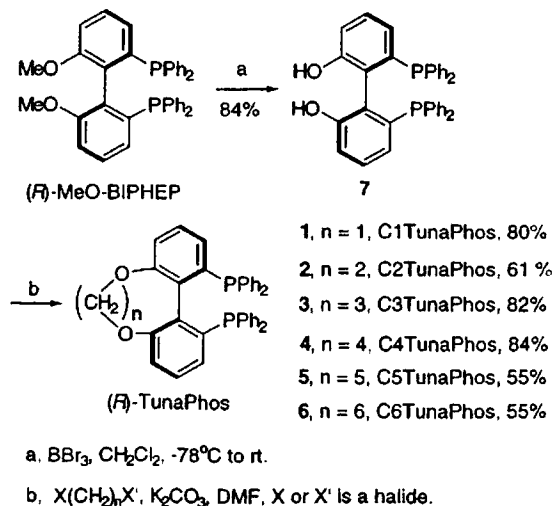*JOC, 2000, 65, 6223.*

Scheme 1. Synthesis of CnTunaPhos Ligands

(R)-MeO-BIPHEP   7

1, n = 1, C1TunaPhos, 80%
2, n = 2, C2TunaPhos, 61 %
3, n = 3, C3TunaPhos, 82%
4, n = 4, C4TunaPhos, 84%
5, n = 5, C5TunaPhos, 55%
6, n = 6, C6TunaPhos, 55%

(R)-TunaPhos

a, BBr_3, CH_2Cl_2, -78°C to rt.

b, $X(CH_2)_nX'$, K_2CO_3, DMF, X or X' is a halide.

Table 1. Calculated Dihedral Angles of Chiral Bisphosphines

phosphine	1	2	3	4	5	6	MeO-BIPHEP	BINAP
dihedral angle[a] (deg)	60	74	77	88	94	106	87	87

Table 2. Ru-Catalyzed Asymmetric Hydrogenation of β-Ketoesters[a]

$$R^1 \underset{R^2}{\overset{O \quad O}{\bigwedge\bigwedge}} OR^3 + H_2 \text{ (750 psi)} \xrightarrow[\text{Chiral Phosphine (1.2 mol\%), in MeOH}]{[Ru(C_6H_6)Cl_2]_2 \text{ (0.5 mol\%)}} R^1 \underset{R^2}{\overset{OH \quad O}{\bigwedge\bigwedge}} OR^3 \quad (\% \text{ ee})$$

Entry	Substrate	1	2	3	4	5	6	MeO-BIPHEP	BINAP
1	OMe	90.9	90.8	97.7	99.1	97.1	96.5	97.9	98.4
2	OPr^i	90.1	90.8	97.7	99.3	96.8	96.3	98.8	98.2
3	OBu^t	90.0	93.9	99.0	99.2	96.8	95.9	98.5	97.6
4	OEt	89.9	93.8	99.0	99.0	96.9	95.9	98.5	97.5
5	Ph ··· OEt	76.8	71.4	72.0	82.3	78.5	60.5	74.8	78.4
6	OEt	79.6 (46.1% syn) 93.9 (53.9% anti)	85.6 (45.7) 95.6 (54.3)	95.5 (45.5) 98.5 (54.5)	95.8 (45.6) 98.7 (54.4)	92.5 (44.2) 98.0 (55.8)	90.7 (46.5) 97.5 (53.5)	95.2 (45.9) 98.1 (54.1)	91.3 (46.8) 95.7 (53.2)
7	OEt	87.9	89.7	95.2	96.8	94.7	91.9	97.5	93.4

[a] Hydrogenation was performed as described in the text. All reactions were complete in >99% conversion, and ee's were determined by chiral GC.

4 seems to be best catalyst .....

Planar-Chiral Pyridine N-Oxides, a New Family of Asymmetric Catalysts: Exploiting an η⁵-C₅Ar₅ Ligand to Achieve High Enantioselectivity[1]

Beata Tao, Michael M.-C. Lo, and Gregory C. Fu*

Department of Chemistry
Massachusetts Institute of Technology
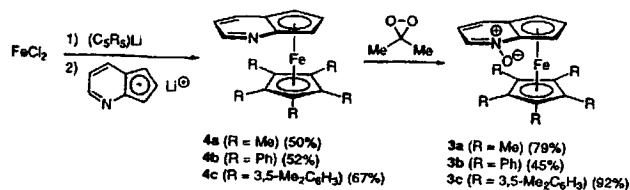*Cambridge. Massachusetts 02139*

JACS, 2001, 123, 353

Increased steric demand gave higher enantioselectivity ...

4a (R = Me) (50%)
4b (R = Ph) (52%)
4c (R = 3,5-Me₂C₆H₃) (67%)

3a (R = Me) (79%)
3b (R = Ph) (45%)
3c (R = 3,5-Me₂C₆H₃) (92%)

Figure 1. Synthesis of planar-chiral pyridine N-oxides.

Table 1. Desymmetrization of cis-Stilbene Oxide Catalyzed by Planar-Chiral Pyridine N-Oxides

entry	catalyst	temperature	ee (%)
1	3a	rt	11
2	3b	rt	25
3	3b	−78 °C	60
4	3c	rt	68
5	3c	−78 °C	92
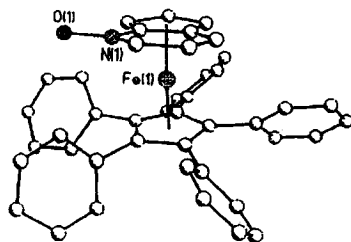
Figure 2. X-ray crystal structure of (−)-3b·MeOH (for clarity, the MeOH is omitted).
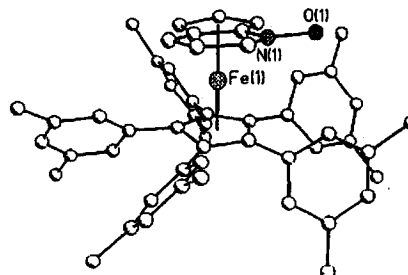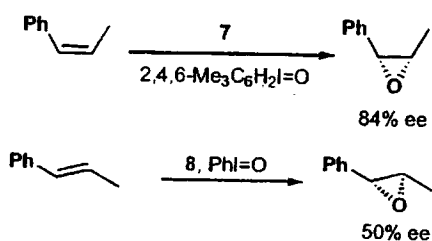

Figure 3. X-ray crystal structure of (+)-3c·TsOH (for clarity, the TsOH is omitted).

• Isn't there "catalyst tuning method" beyond just

trial and error?

- Scientific Catalyst tuning
- New Concept for tuning   ) philosophy ?
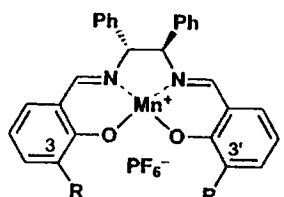
1. Catalyst tuning of Mn-Salen complex.

Review: Adv. Synth. Catal. 2002, 344, 131.

◦ first example(s)

Ph ─── / → Ph \/
       7   O
   2,4,6-Me₃C₆H₂I=O   84% ee

Ph ─── → Ph ~ /
      8, PhI=O   O
                  50% ee

7: R= t-Bu, 8: R= (S)-Ph(Et)CH

Scheme 2. Early examples of Mn(salen)-catalyzed asymmetric epoxidation.

Jacobsen et al,
   JACS, 1990, 112, 2801.

Katsuki et al,
   TL, 1990, 31, 7345.

◦ Origin of enantioselectivity ?

☆ Structure of Mn-salen complex.

(L = achiral)
enantiomeric
━━━━━━
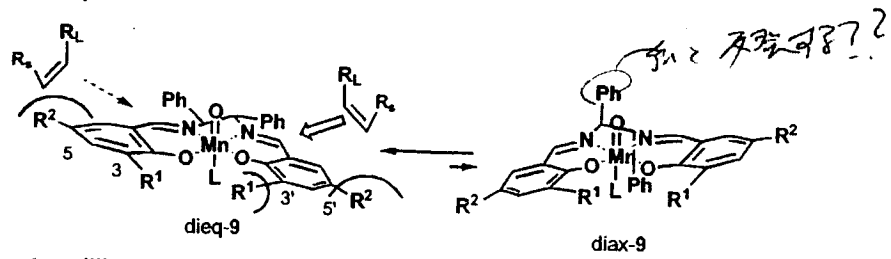diastereomeric
(L = optically active)
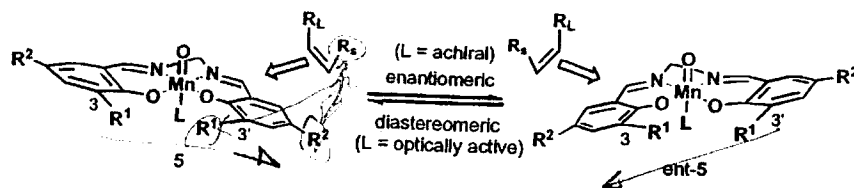
⇒ To gain enantioselectivity ...

① discrimination between R_L and R_S.

② change equilibrium toward one isomer.

○ In the first system ...

Scheme 3. Conformational equilibration of chiral oxo Mn(salen)s.

($R^2 = H$)

{ ○ Steric Repulsion between R^2 and R_L

  ○ dieq-9 is stable than diax-9

⇒ enantioselective epoxidation was possible.
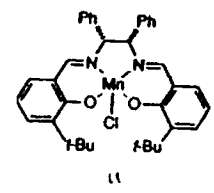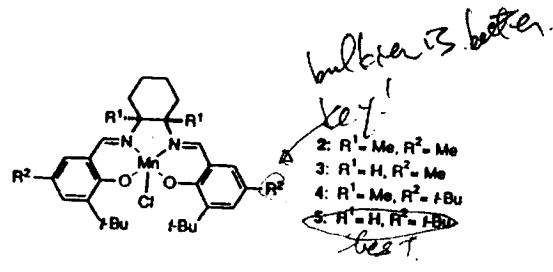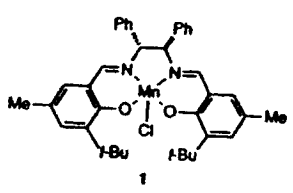
⟼ Ligand Tuning.

(1) **Highly Enantioselective Epoxidation Catalysts Derived from 1,2-Diaminocyclohexane[†]**

JACS, 1991, 113, 7064.

Eric N. Jacobsen,* Wei Zhang, Alexander R. Muci, James R. Ecker, and Li Deng

Roger Adams Laboratory, Department of Chemistry University of Illinois, Urbana, Illinois 61801
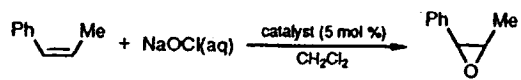
bulkier is better.

key!

2: $R^1 = Me$, $R^2 = Me$
3: $R^1 = H$, $R^2 = Me$
4: $R^1 = Me$, $R^2 = t$-Bu
5: $R^1 = H$, $R^2 = t$-Bu
best

Larger substituent is introduced on aromatic ring.

first catalyst
(84% ee)

Better selectivity was obtained with catalyst 5, as expected.

Table I. Asymmetric Epoxidation of *cis*-β-Methylstyrene with Catalysts 1–5

$$Ph\text{—}Me + NaOCl(aq) \xrightarrow[CH_2Cl_2]{catalyst (5 mol \%)} Ph\text{—}Me$$

entry	catalyst	yield,[a] %	ee, %	epoxide config'n
1	(R,R)-1	88	84	1R,2S-(+)
2	(S,S)-2	54	49	1S,2R-(-)
3	(S,S)-3	87	80	1S,2R-(-)
4	(S,S)-4	56	55	1S,2R-(-)
5	(S,S)-5	81	92	1S,2R-(-)

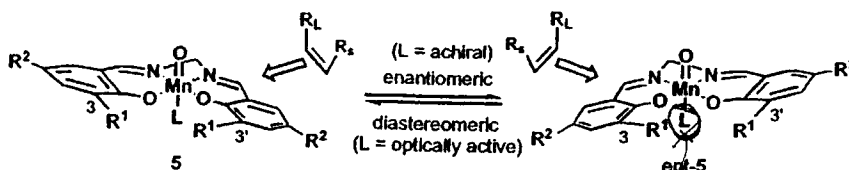[a] Determined by GC by integration against an internal quantitative standard.

(2) **Dynamic Control of Ligand Conformation: Asymmetric Epoxidation Using Achiral (Salen)manganese(III) Complex**

Keishi Miura, Tsutomu Katsuki*

Department of Molecular Chemistry, Graduate School of Science, Kyushu University 33, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan
Fax +81 (92) 642 2607
Received 1 March 1999

, The other method for change equilibrium between S and ent-S.

*⇒ Use of chiral optical ligand (4)
↳ conf. の 4(R)が 7-じゃ?*

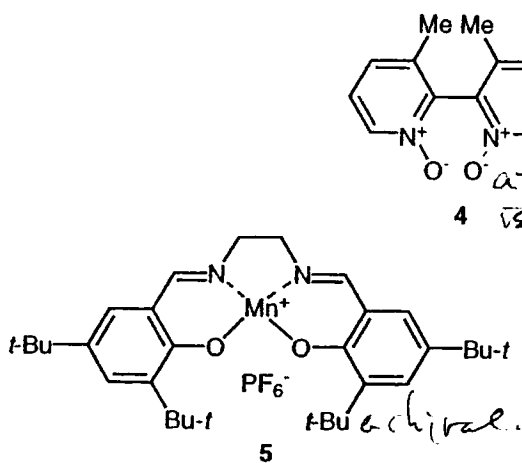*, enantioselectivity was obtained with achiral ligand S*

Table 1. AE of 2,2-dimethylchromene derivatives with achiral complex 5 as a catalyst in the presence of N,N'-dioxide (+)-4.[a]

entry	substrate	time	yield (%)	% ee[b]	config[c]
1	O$_2$N / AcHN	24	65	82	3S, 4S
2[e]	"	24	58	82	3S, 4S
3[d]	"	48	90	83	3S, 4S
4[d,e]	"	48	29	86	3S, 4S
5	NC	48	59	77	3S, 4S
6[f]	"	24	51	78	3S, 4S
7		48	60	78	3S, 4S
8[e]	"	24	41	84	3S, 4S

a) The reaction was carried out in dichloromethane at -20 °C in the presence of 4 (5 mol%) and 5 (4 mol%) unless otherwise mentioned.
b) Enantiomeric excess was determined by HPLC (DAICEL CHIRALCEL OJ, hexane/2-propanol=1/1).
c) Configuration was determined by the comparison of the elution order with the authentic samples.
d) The reaction was carried out in dichloroethane.
e) The reaction was carried out employing 20 mol% of 4.
f) The reaction was carried out employing 10 mol% of 4.

(3)

What is the Origin of Highly Asymmetric Induction by a Chiral (Salen)manganese(III) Complex? Design of a Conformationally Fixed Complex and Its Application to Asymmetric Epoxidation of 2,2-Dimethylchromenes
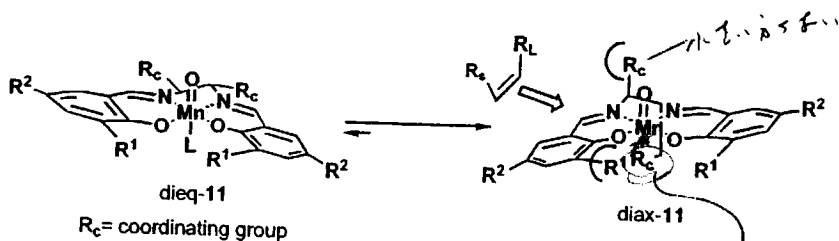
Yoshio N. Ito and Tsutomu Katsuki*

Department of Chemistry, Faculty of Science, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan
Received 9 March 1998; revised 6 April 1998; accepted 8 April 1998
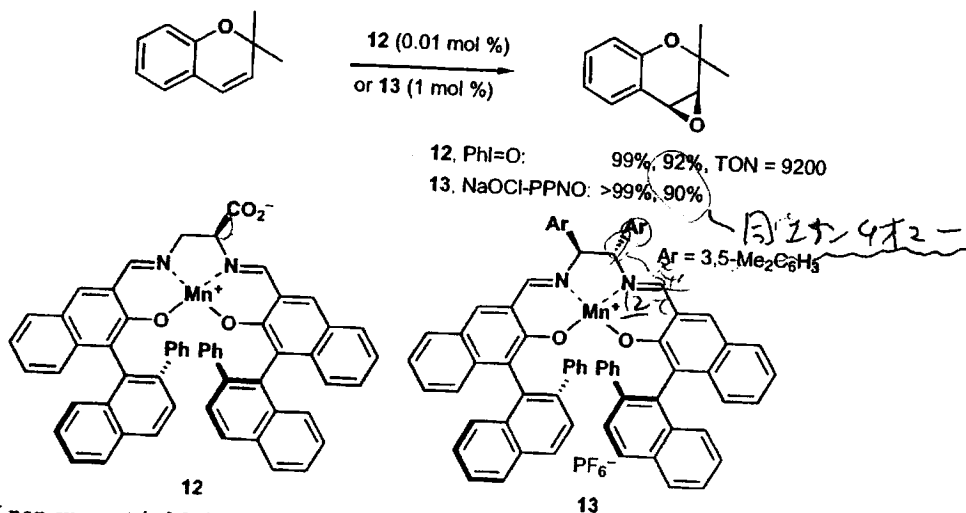
Mn-salen ligand exist in equilibrium.
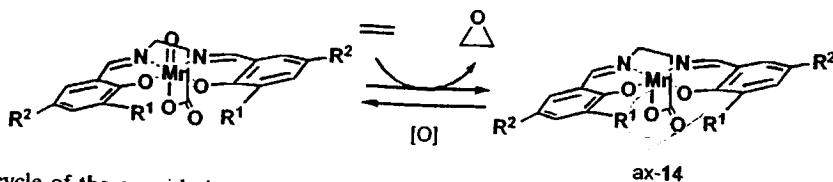
⇒ How to lock conformation?
⇓
internal axial ligand.

Scheme 5. Conformation of oxo Mn(salen) bearing a coordinating group.

dieq-11
R_c = coordinating group
diax-11

coordination 的力を使く.

With internal axial ligand (Rc), conformation can be locked as diax-11. (and gave opposite enantiomer)

12 (0.01 mol %)
or 13 (1 mol %)

12, PhI=O: 99%, 92%, TON = 9200
13, NaOCl-PPNO: >99%, 90%

Ar = 3,5-Me$_2$C$_6$H$_3$

Scheme 6. Catalysis of non-symmetric Mn(salen) 12 and of symmetric Mn(salen) 13.
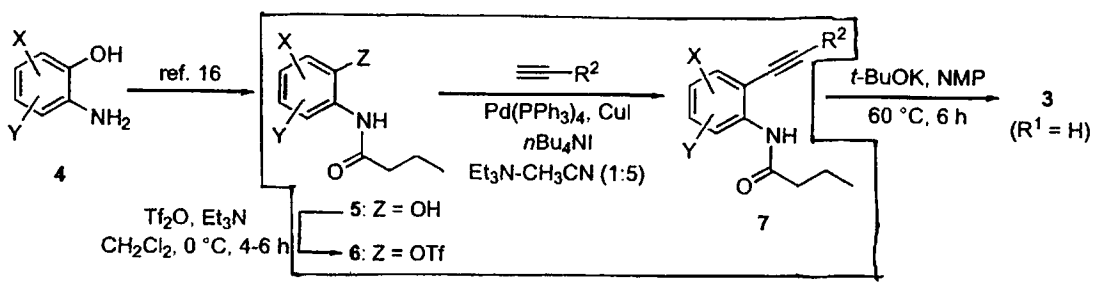

Scheme 7. Catalytic cycle of the epoxidation with Mn(salen) bearing a coordinating group.

ax-14

12 and 13 (posessing inverse chirality at ethylenediamine part) gave same enantiomer.

2. Halide effects on Catalyst Tuning

∘ Can you explain following observation?

✱ Sonogashira Coupling.

Scheme 2.

Table 1. Effects of additives on the cross-coupling of triflate **6a** (X = Y = H) with phenylacetylene[a]

Entry	Additive (mol%)	t (h)	7a (R^2=Ph, %)	Entry	Additive (mol%)	t (h)	7a (R^2=Ph, %)
1	None[b]	17	29	5	n-Bu$_4$NI (100)	24	84
2	n-Bu$_4$NBr (100)[b]	24	58	6	n-Bu$_4$NI (150)	24	91
3	n-Bu$_4$NBr (150)	24	62	7	n-Bu$_4$NI (300)[b]	15	91
4	n-Bu$_4$NI (50)	24	56	8	n-Bu$_4$NI (300)[c]	36	82

[a] Carried out with 10 mol% Pd(PPh$_3$)$_4$ and 30 mol% CuI in Et$_3$N–CH$_3$CN (1:5) at 20°C under N$_2$.
[b] 20% CuI was used.
[c] Pd(PPh$_3$)$_2$Cl$_2$ was used to replace Pd(PPh$_3$)$_4$.

Dai et al, TL, 2001, 42, 5275.

Authors' argument: <u>free OTf$^⊖$ deactivate catalyst</u>. and I$^⊖$ replace OTf$^⊖$. 争论点在此处

⟹ why I$^⊖$ is better than Br$^⊖$?

∘ A paper discussing halide effects:

Rhodium-Catalyzed Asymmetric Ring Opening Reactions of Oxabicyclic Alkenes: Application of Halide Effects in the Development of a General Process

Mark Lautens,* Keith Fagnou,‡ and Dingqiao Yang†

Contribution from the Davenport Research Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario, Canada M5S 3H6

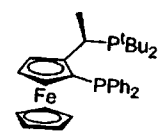Received February 24, 2003; E-mail: mlautens@alchemy.chem.utoronto.ca

JACS, 2003, 125, 14884.

Scheme 1
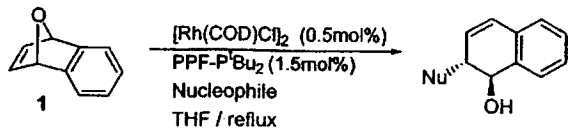
"First Generation Reaction Conditions"

PPF-P^{t}Bu$_2$

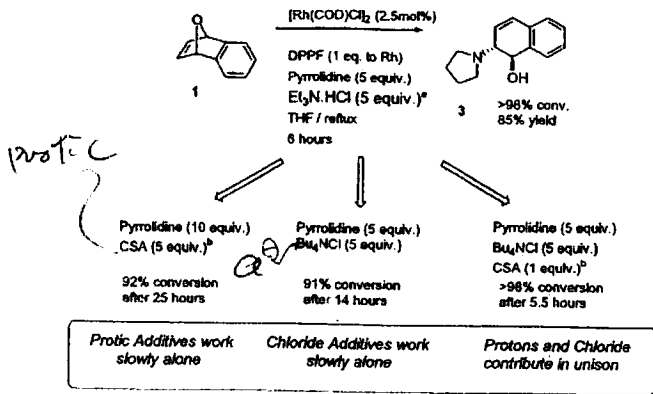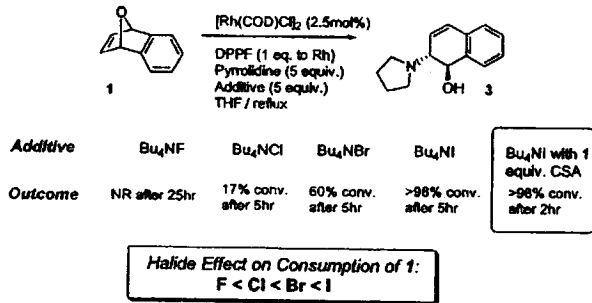| Nucleophile	Outcome
Alcohols and Phenols	>90% yield, >90%ee
Aliphatic amines	no reaction
Aromatic Amines	>90% yield, 30-74%ee
Malonates	<50% yield, 50%ee
Carboxylates	>80% yield, 30-60%ee

Aliphatic 之 aromatic amine 的反应性有 这样区别 ⟹ N.R.
Aliphatic amine suppressed this catalysis.

Scheme 2

[Rh(COD)Cl]₂ (2.5mol%)

DPPF (1 eq. to Rh)
Pyrrolidine (5 equiv.)
Et₃N·HCl (5 equiv.)ᵃ
THF / reflux
6 hours

3
>98% conv.
85% yield

Pyrrolidine (10 equiv.)
CSA (5 equiv.)ᵇ
92% conversion after 25 hours

Pyrrolidine (5 equiv.)
Bu₄NCl (5 equiv.)
91% conversion after 14 hours

Pyrrolidine (5 equiv.)
Bu₄NCl (5 equiv.)
CSA (1 equiv.)ᵇ
>98% conversion after 5.5 hours

| Protic Additives work slowly alone | Chloride Additives work slowly alone | Protons and Chloride contribute in unison |

Protic C

CA⊖

ᵃ Conditions: Substrate, [Rh(COD)Cl]₂ (2.5 mol %) and dppf (5 mol %) were dissolved inTHF and stirred at room temperature for 3−5 min. The halide additive was then added and the mixture heated and at first sign of reflux, pyrrolidine (5 equiv.) was added. ᵇ In reactions using CSA, it was added immediately after the addition of the pyrrolidine nucleophile.

Scheme 3

1

[Rh(COD)Cl]₂ (2.5mol%)

DPPF (1 eq. to Rh)
Pyrrolidine (5 equiv.)
Additive (5 equiv.)
THF / reflux

3

Additive	Bu₄NF	Bu₄NCl	Bu₄NBr	Bu₄NI	Bu₄NI with 1 equiv. CSA
Outcome	NR after 25hr	17% conv. after 5hr	60% conv. after 5hr	>98% conv. after 5hr	>98% conv. after 2hr

| Halide Effect on Consumption of 1: F < Cl < Br < I |

In presence of Et₃N·HCl, this catalysis worked well.

and H⊕ and Cl⊖ are revealed to work synergestically.

I⊖ worked best, whereas F⊖ couldn't promote reaction.

Scheme 7

I⊖ can =⊃ path or 3 2 Ir-C⊖
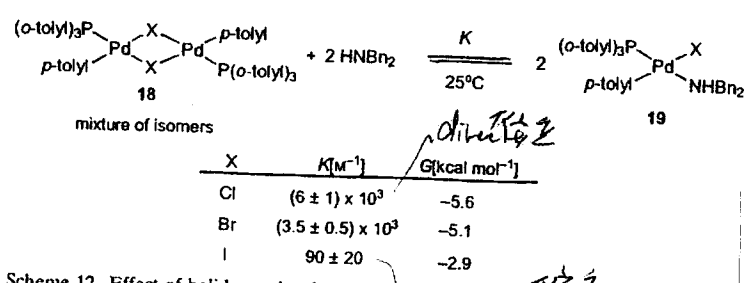
(a) Substrate binding on the exo-face (displacement of a halide ligand or dimer bridge cleavage): (b) oxidative insertion; (c) protonation of the rhodium alkoxide; (d) nucleophilic attack and product liberation; (e) amine binding; (f) amine ligand protonation and nucleophilic displacement by a halide nucleophile; (g) dimer formation with loss of a halide ligand; (h) dimer cleavage by nucleophilic displacement with a halide; (i) α-oxidation of the amine ligand.

⊃ The authors' hypothesis for the role of ⟹ H⊕ + X⊖

with H⊕ and X⊖, poisoned catalyst 67 could be converted to active 69.

⟹ Again, why I⊖ work better than F⊖ ?

○ For Halide effects in transition metal catalysis:
 Review: Lautens et al, Angew. Chem. Int. Ed.
 2002, 41, 26.

Scheme 12. Effect of halide on the cleavage of dimer.

X	K [M^{-1}]	G [kcal mol^{-1}]
Cl	$(6 \pm 1) \times 10^3$	−5.6
Br	$(3.5 \pm 0.5) \times 10^3$	−5.1
I	90 ± 20	−2.9

Pd/I$^{\ominus}$ dimer is stable toward cleavage by amine.

⇒ The reasons.

① Donor ability of lone pair electrons is highest with I.
 ⇒ 18 is the most stable in the case of I.

② L—Pd(X)(NHBn$_2$)L ⟺ Steric interaction is the most severe with large I.
 ⇒ disfavor cleavage.

Size, σ-bond donation, *trans* effect, bond strengths to late / low oxidation state metals
F Cl Br I
π-bond donation, bond strengths to early / high oxidation state metals

Scheme 1. Trends in the properties of halide ligands.

⇒ 63 → 62 (last page) is slowered.
 therefore active 62 can be at higher concentration.

○ Attempt to understand other system:

Effect of Ligands and Additives on the Palladium-Promoted Carbonylative Coupling of Vinyl Stannanes and Electron-Poor Enol Triflates

Simona Ceccarelli,[†] Umberto Piarulli,[‡] and Cesare Gennari*,[†]

Dipartimento di Chimica Organica e Industriale, Università di Milano, Centro CNR (Sost. Org. Nat.), via Venezian 21, 20133 Milano, Italy, and Dipartimento di Scienze Mat. Fis. e Chimiche, Università degli Studi dell'Insubria, via Lucini 3, 22100 Como, Italy

cesare@iumchx.chimorg.unimi.it

JOC, 2000, 65, 6254.

6

7a R' = Bu
7b R' = Me

[Pd(0)], CO
Ligand, Additive(s)
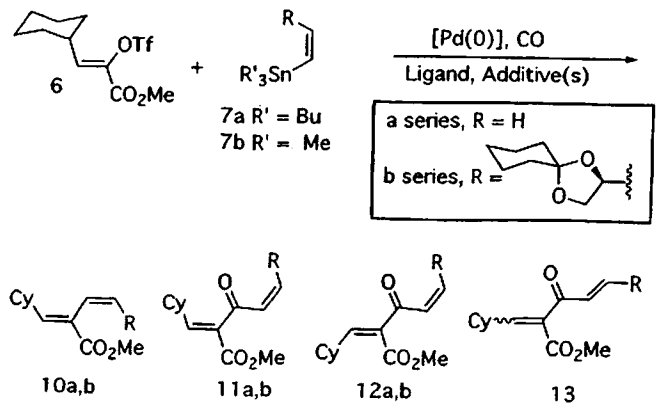
a series, R = H
b series, R =

10a,b   11a,b   12a,b   13

Table 1. Palladium Catalyzed Coupling of Vinyl Triflate 6 and Tributylvinylstannane 7a in the Presence of Carbon Monoxide at Atmospheric Pressure

| entry	solvent, T, time	catalyst	additives	yield, %[uncatalyzed −CO] 10a	yield, % +CO, desired 11a + 12a
1	THF, 55 °C, 7 h	Pd(PPh$_3$)$_4$ (5%)	LiCl (3 equiv)	15	13[a] (73:27)[b]
2	NMP, RT, 5 h	Pd(PPh$_3$)$_4$ (5%)	LiCl (3 equiv)	39	60 (79:21)[b]
3	NMP, RT, 4 h	Pd(PPh$_3$)$_4$ (5%)	LiCl (3 equiv), CuI (10%)	17	79 (72:28)[b]
4	NMP, RT, 35 min	Pd$_2$dba$_3$ (5%); As(Ph)$_3$ (20%)	LiCl (3 equiv)	19	81 (82:17)[b]
5	NMP, RT, 6 min	Pd$_2$dba$_3$ (5%); As(Ph)$_3$ (20%)	LiCl (3 equiv), CuI (10%)	<1	74[c] (80:20)[b]
6	NMP, RT, 15 h	Pd(PPh$_3$)$_4$ (5%)	CuI (10%)	—	—[d]
7	NMP, RT, 17 h	Pd$_2$dba$_3$ (5%); As(Ph)$_3$ (20%)	CuI (10%)	—	—[d]

[a] Plus 71% recovered starting material. [b] Ratio determined by integration of the methyl signals in the ^{1}H NMR spectrum. [c] Plus 25% recovered starting material. [d] Pd black precipitates immediately after addition of substrates.
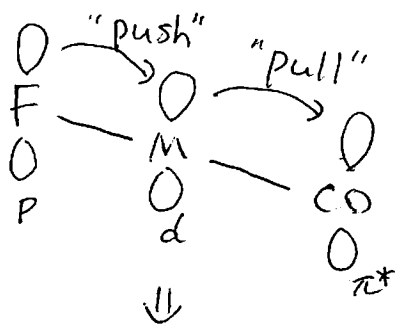
Addition of CuI increased desired product 11a + 12a.

10a: product without CO-insertion.

11a + 12a: product with CO (desired)

∘ push-pull interaction
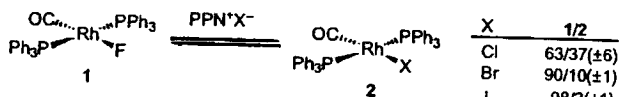
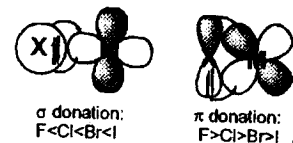Scheme 5. Effect of push-pull interactions on the hard/soft character of a transition metal complex.

bond is strengthened.

Trans-position of CO ligand became "hard" through push-pull interaction.
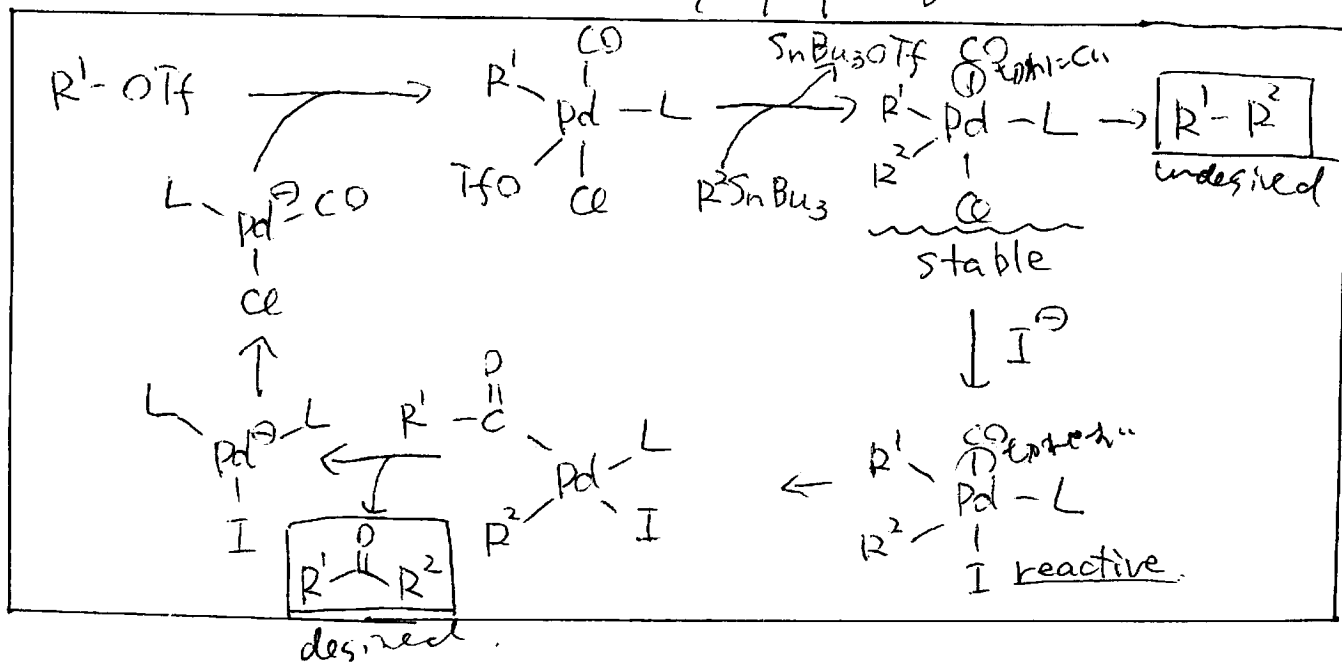
Electronegativity	
F	3.98
Cl	3.16
Br	2.96
I	2.66

σ donation: F<Cl<Br<I

π donation: F>Cl>Br>I

Scheme 2. Electronic properties of halide ligands.

∘ Reason of CuI effect : My proposal

3. Other interesting examples.
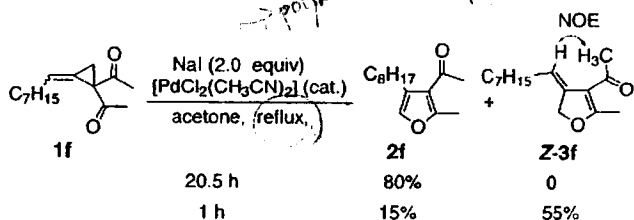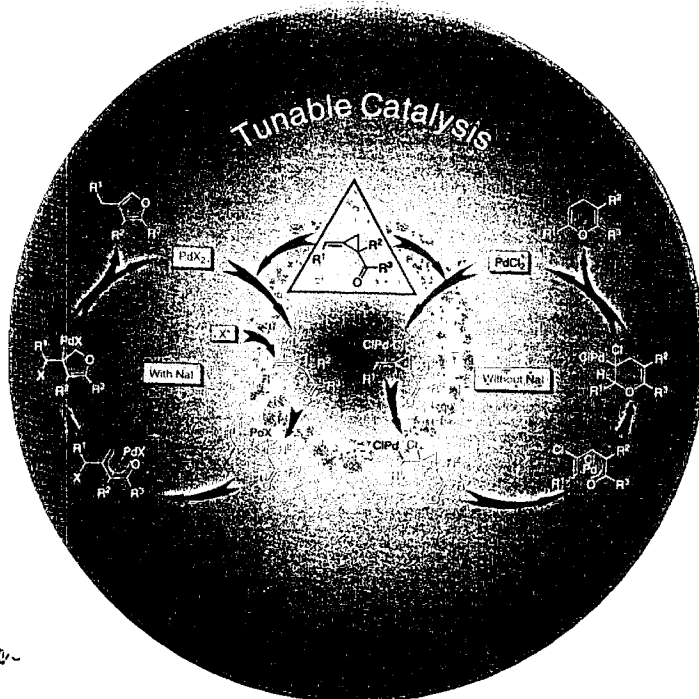
Regioselective Cyclization

Tuning the Regioselectivity in the Palladium(II)-Catalyzed Isomerization of Alkylidene Cyclopropyl Ketones: A Dramatic Salt Effect**
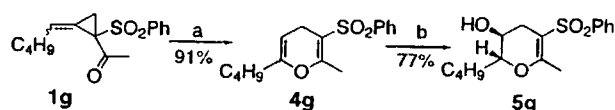
Shengming Ma and *Junliang Zhang*

isomerization of polysubstituted Pd(II)

NOE

	2f	Z-3f
20.5 h	80%	0
1 h	15%	55%

Scheme 2. The Pd^{II}-catalyzed cycloisomerization reaction of 1f under Conditions A.
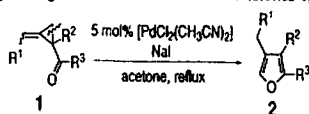
Scheme 3. The Pd^{II}-catalyzed isomerization reaction of 1g under Conditions B and the subsequent hydroboration–oxidation reaction. a) 5 mol% [PdCl$_2$(CH$_3$CN)$_2$], acetone, RT, 5 min; b) 1. BH$_3$·SMe$_2$, THF, 0 °C→RT, 1 h; 2. NaOH–H$_2$O$_2$, 0 °C→RT, 6 h.

li

with NaI   **without NaI**

I⊖ changed the shape of product completely!

Table 2: Palladium(II)-catalyzed regioselective isomerization of ketones 1, which leads to furans 2.[a]

Entry	1			t	Yield of 2
	R^1	R^2	R^3	[h]	[%]
1	C$_7$H$_{15}$	CO$_2$Et	Me (1b)	10	74 (2b)
2	C$_4$H$_9$	CO$_2$Et	Me (1c)	14	74 (2c)
3	Bn	CO$_2$Et	Me (1d)	13.5	78 (2d)
4		1d		24	65 (2d)[b]
5	TBSO(CH$_2$)$_3$	CO$_2$Et	Me (1e)	26	82 (2e)
6	C$_7$H$_{15}$	COMe	Me (1f)	20.5	80 (2f)[c]
7	H	H	C$_6$H$_5$(CH$_2$)$_2$ (1h)	12	77 (2h)

[a] Unless otherwise specified, the reaction was carried out using 1 (0.25–1.5 mmol) in the presence of 5 mol% [PdCl$_2$(CH$_3$CN)$_2$] and 2 equiv of sodium iodide in 2 mL of acetone under reflux (Conditions A). [b] The reaction was carried out in the presence of 0.2 equiv of sodium iodide in 0.5 mL of acetone under reflux. [c] See the text.
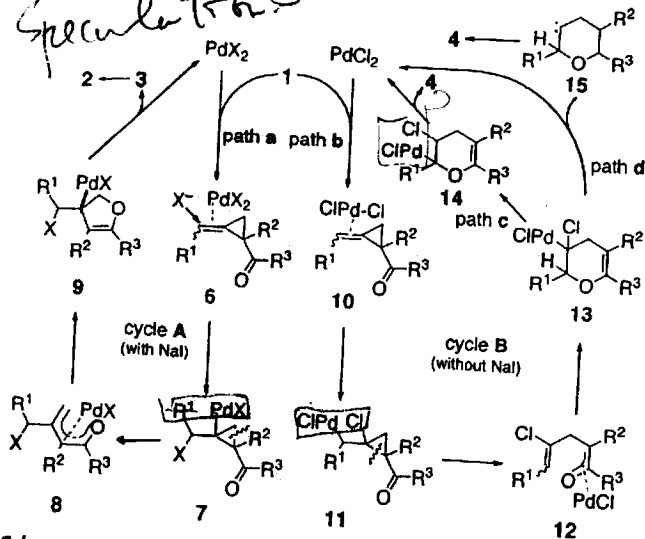
Table 3: Palladium(II)-catalyzed regioselective isomerization of the ketones 1, which leads to the 4H-pyrans 4.[a]
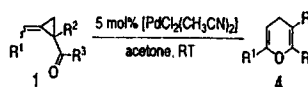
Entry	1			t	Yield of 4
	R^1	R^2	R^3	[min]	[%]
1	C$_7$H$_{15}$	CO$_2$Et	Me (1b)	15	80 (4b)
2	C$_4$H$_9$	CO$_2$Et	Me (1c)	15	75 (4c)
3	Bn	CO$_2$Et	Me (1d)	15	69 (4d)
4		1d		10	80 (4d)[b]
5	TBSO(CH$_2$)$_3$	CO$_2$Et	Me (1e)	10	85 (4e)[b]
6	C$_7$H$_{15}$	COMe	Me (1f)	40	60 (4f)
7	C$_4$H$_9$	SO$_2$Ph	Me (1g)	15	91 (4g)
8	C$_8$H$_{17}$	H	Ph (1i)	15	70 (4i)[b]

[a] Unless otherwise specified, all reactions were carried out using 1 (0.5 mmol) in the presence of 5 mol% [PdCl$_2$(CH$_3$CN)$_2$] in 2 mL of acetone at RT (Conditions B). [b] The solvent used was benzene.

— Speculation —

I° changed the regioselectivity of halopalladation and leads to different product.

Scheme 4. A plausible mechanism for the Pd^{II}-catalyzed isomerization reaction of 1.

Nickel-Catalyzed Cross-Coupling Reaction of Grignard Reagents with Alkyl Halides and Tosylates: Remarkable Effect of 1,3-Butadienes

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JACS, 2002, 124, 4222.

$$R\text{-}X \quad + \quad R'\text{-}MgX \quad \xrightarrow[\text{1,3-butadiene}]{\text{cat. NiCl}_2} \quad R\text{-}R' \qquad (1)$$

R = alkyl   R' = alkyl, aryl
X = Cl, Br, OTs
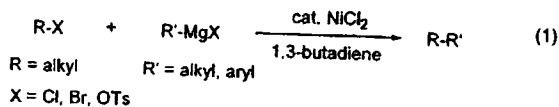
Only 1,3-butadiene type additive made catalysis ⇒ go well.

Ni^{0} *is real cat?*

Scheme 1. A Plausible Reaction Pathway

Table 1. Cross-Coupling Reaction of n-$C_{10}H_{21}Br$ with n-BuMgCl

entry	catalyst	additive	n-$C_{14}H_{30}$	decane	decenes[b]
1	NiCl$_2$		92	<1	2
2	NiCl$_2$	none	2	49	27
3	Ni(acac)$_2$		90	<1	2
4	Ni(COD)$_2$		92	<1	3
5	PdCl$_2$		38	1	3
6	NiCl$_2$		99	<1	0
7	NiCl$_2$		5	14	9
8	NiCl$_2$	COD^c	10	18	38
9	NiCl$_2$	Ph—≡—Et	3	7	23
10	NiCl$_2$	3-CF$_3$-styrene	15	25	14

Column header (GC yield (%)[a]) spans n-$C_{14}H_{30}$, decane, decenes.

[a] Conditions: n-$C_{10}H_{21}Br$ (2 mmol), catalyst (3 mol %), n-BuMgCl (1.3 equiv, 0.9 M), additive (1 equiv, 0.7 M); 25 °C; 3 h. *[b]* A mixture of 1-decene and 2-decenes. *[c]* 1,5-Cyclooctadiene.
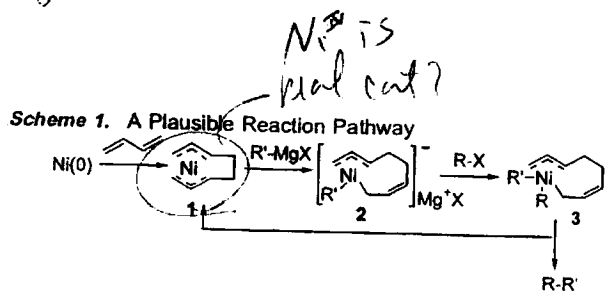
⇒ *shape of catalyst is completely changed in reaction with additive.*
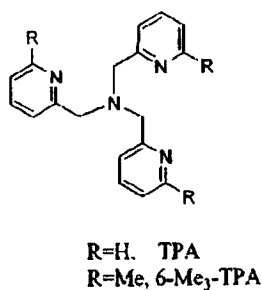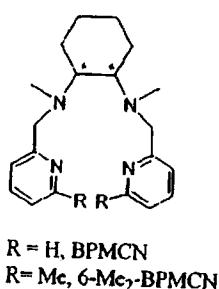
⇓

Applicable to Sequential Reaction, with changing catalyst structure?

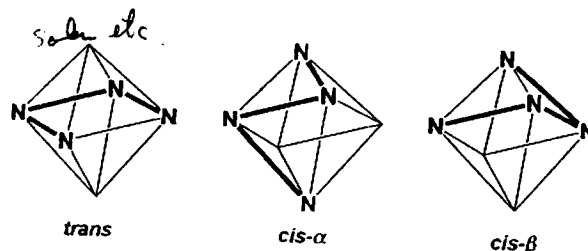# Ligand Topology Tuning of Iron-Catalyzed Hydrocarbon Oxidations**

Miquel Costas and Lawrence Que, Jr.*

tetra-coordinative ligand can take three different topologies on hexacoordinative metal.

R = H, BPMCN
R = Me, 6-Me₂-BPMCN

R=H. TPA
R=Me, 6-Me₃-TPA

Authors synthesized catalysts only different in topology.

Scheme 1. Three different topologies that can be adopted by tetradentate ligands such as N,N-bis(2-pyridylmethyl)-N,N'-dimethyl-$trans$-1,2-diaminocyclohexane (bpmcn).

trans   cis-α   cis-β

*[Fₑ⁴⁴ 'ᵈᵗⁱ 'ᵗⁱⁿ' *Xᴼᴳᵃᵗⁱⁿᵗ* *ᵗᵍⁿ'ᵗ**

$$L = [Fe^{II}(bpmcn)(OTf)_2]$$

$$X = OTf.$$

$$\alpha - L$$

$$\beta - L$$
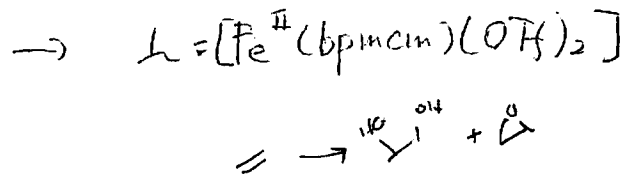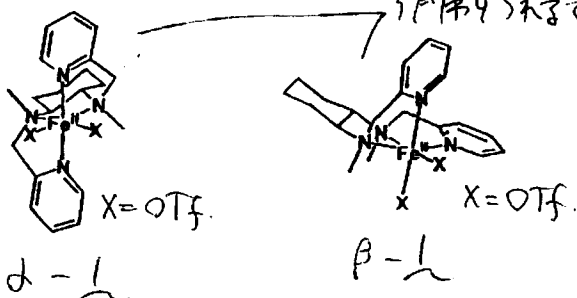
Table 1. Alkane oxidation reactivities of nonheme iron catalysts.[a]

	Fe(tpa)[b]	α-1	β-1	Fe(6-Me₃-tpa)[b]
cyclohexane				
A + K[c] (TN)[d]	3.2	5.9	1.9	1.4
[A]/[K]	5	9	0.9	1
KIE[e]	3.5	3.2	4.0	3.3
[H₂¹⁸O₂/H₂¹⁸O] (%)[f]	70/27	82/15	34/10	22/1
adamantane 3°/2°[g]	17	15	17	15
cis-DMCH[h]%RC[i]	>99%	>99%	68%	54%

[a] Reaction conditions: 0.7 mM catalyst, 7 mM H₂O₂, and 0.7 M substrate in CH₃CN at room temperature in air. H₂O₂ solution added by syringe pump over a 30-min period. [b] Data from references [5] and [6]. [c] A + K = alcohol + ketone. [d] TN = Turnover number. [e] KIE = Intermolecular kinetic isotope effect obtained from the competitive oxidation of c-C₆H₁₂/c-C₆D₁₂ to cyclohexanol. [f] ¹⁸O incorporated into cyclohexanol when H₂¹⁸O₂ was used as a oxidant/when reaction was carried out in presence of 1000 equiv of H₂¹⁸O. Other conditions as stated in [a]. [g] 3 × [1-adamantanol]/([2-adamantanol] + [2-adamantanone]). [h] DMCH = 1,2-dimethylcyclohexane. [i] %RC = 100 × (cis-$trans$)/(cis + $trans$).

Completely different reactivity was observed between α-L and β-L.

Table 2. Olefin oxidation reactivities of nonheme iron catalysts.[a]

	Fe(tpa)[b]	α-1	β-1	Fe(6-Me₃-tpa)[b]
cyclooctene				
diol + epoxide (TN)[c]	7.4	6.5	7.7	5.6
[diol]/[epoxide]	1.2:1	0.1:1	1.8:1	7.0:1
epoxide %¹⁸O [H₂¹⁸O₂/H₂¹⁸O](%)[d]	90/9	90/11	66/15	54/3
diol %¹⁸O from				
H₂¹⁸O₂ [noO/1O/2O](%)[e]	0/97/3	3/89/7	2/4/93	4/96
H₂¹⁸O [noO/1O/2O](%)[f]	13/86/1	11/88/1	97/3/0	99/1/0
cis-2-heptene				
diol + epoxide (TN)[c]	4.9	7.0	6.8	4.5
[diol]/[epoxide]	1.6:1	0.1:1	0.8:1	10:1
%RC[g] epoxide	80	>99	67	35
%RC[g] diol	96	>99	85	93
trans-2-heptene				
diol + epoxide (TN)[c]	4.8	5.7	5.6	4.1
[diol]/[epoxide]	2.2:1	0.05:1	0.6:1	13:1
%RC[g] epoxide	>99	>99	86	>99
%RC[g] diol	96	>99	81	96
1-octene				
diol + epoxide (TN)[c]	7.5	6.4	4.7	5.8
[diol]/[epoxide]	2.0:1	0.2:1	2.1:1	18:1

[a] Reaction conditions: 0.7 mM catalyst, 7 mM H₂O₂, and 0.7 M substrate in CH₃CN at room temperature in air. H₂O₂ solution added by syringe pump over a 30-min period. [b] Data from references [5] and [6]. [c] TN = Turnover number [d] ¹⁸O incorporated into cyclooctene epoxide when H₂¹⁸O₂ was used as a oxidant/when reaction was carried out in presence of 1000 equiv of H₂¹⁸O. Other conditions as stated in [a]. [e] Percentage of cis-cyclooctane-1,2-diol that contains no ¹⁸O/1 ¹⁸O atom/2 ¹⁸O atom when H₂¹⁸O₂ was used as a oxidant. Other conditions as stated in [a]. [f] Percentage of cis-cyclooctane-1,2-diol that contains no ¹⁸O/1 ¹⁸O atom/2 ¹⁸O atom when reaction was carried out in presence of 1000 equiv of H₂¹⁸O. Other conditions as stated in [a]. [g] %RC = 100 × (cis-$trans$)/(cis + $trans$).