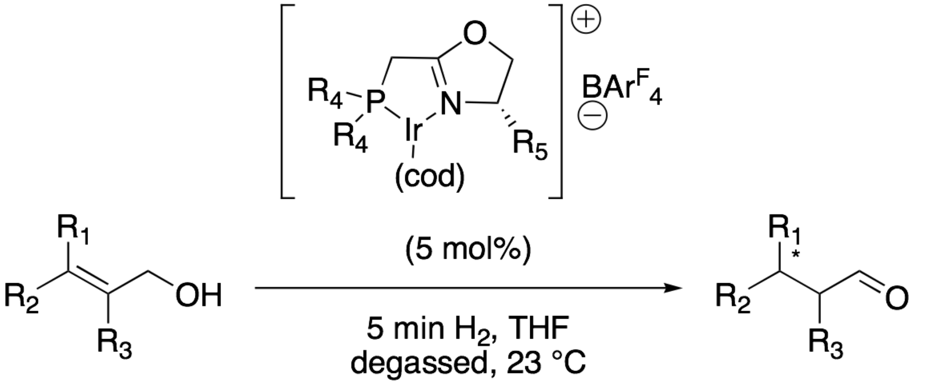
Iridium-Catalyzed Asymmetric Isomerization of Primary Allylic Alcohols

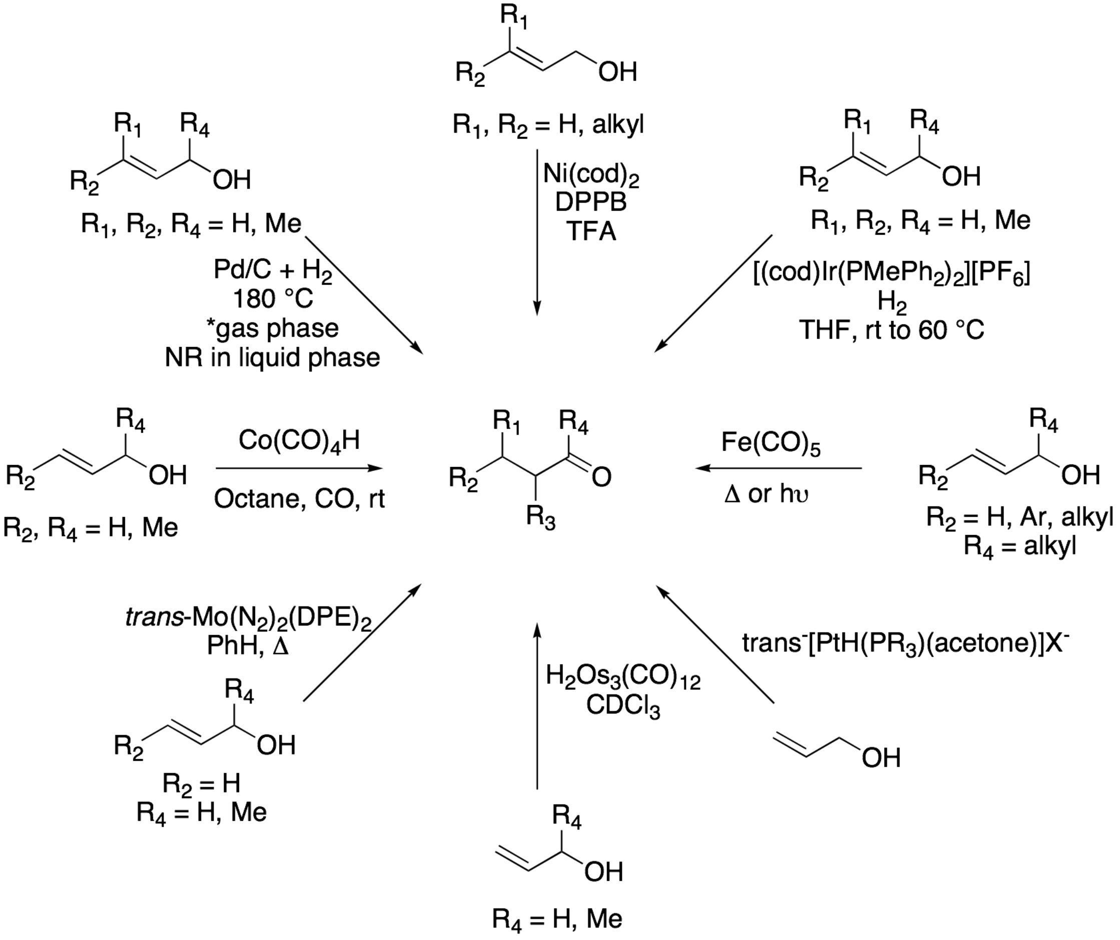


Luca Mantilli, David Gérard, Sonya Torche, Céline Besnard, and Clément Mazet

Angew. Chem. Int. Ed. **2009**, *Early View*

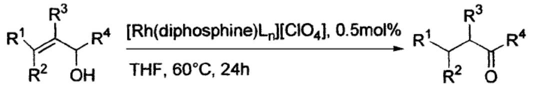
Nate Ware, Wipf Group Current Literature 06/20/09

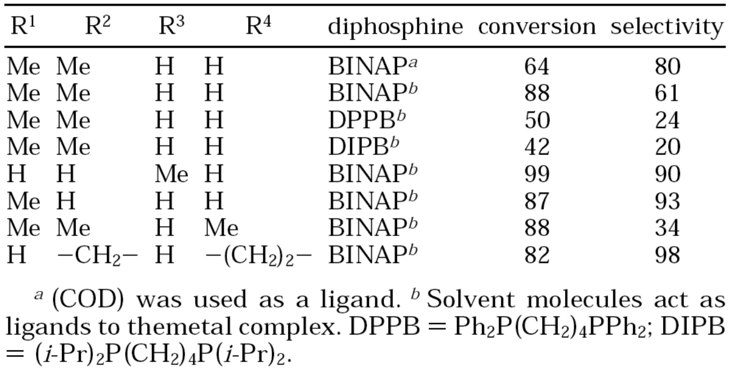
Metal Catalyzed Isomerizations of Allylic Alcohols to Carbonyl Compounds



Chem. Rev., **2003**, 103, 27

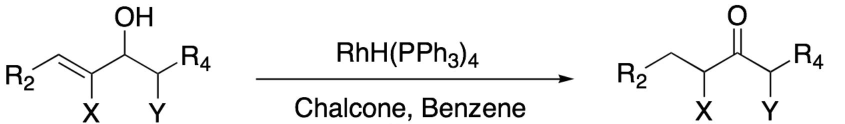
Rhodium and Ruthenium Isomerizations





R^1	R^2	R^3	R^4	diphosphine	conversion	selectivity
Me	Me	H	H	BINAP[a]	64	80
Me	Me	H	H	BINAP[b]	88	61
Me	Me	H	H	DPPB[b]	50	24
Me	Me	H	H	DIPB[b]	42	20
H	H	Me	H	BINAP[b]	99	90
Me	H	H	H	BINAP[b]	87	93
Me	Me	H	Me	BINAP[b]	88	34
H	$-CH_2-$	H	$-(CH_2)_2-$	BINAP[b]	82	98

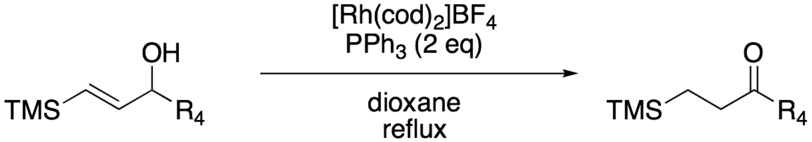
[a] (COD) was used as a ligand. [b] Solvent molecules act as ligands to themetal complex. DPPB = $Ph_2P(CH_2)_4PPh_2$; DIPB = $(i\text{-}Pr)_2P(CH_2)_4P(i\text{-}Pr)_2$.



R_2, R_4 = H, alkyl
a: X = TMS, Y = H, alkyl
b: X = H, alkyl, Y = TMS

67 - 99%

TL, **1985**, 25, 769

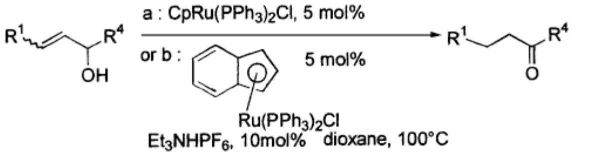


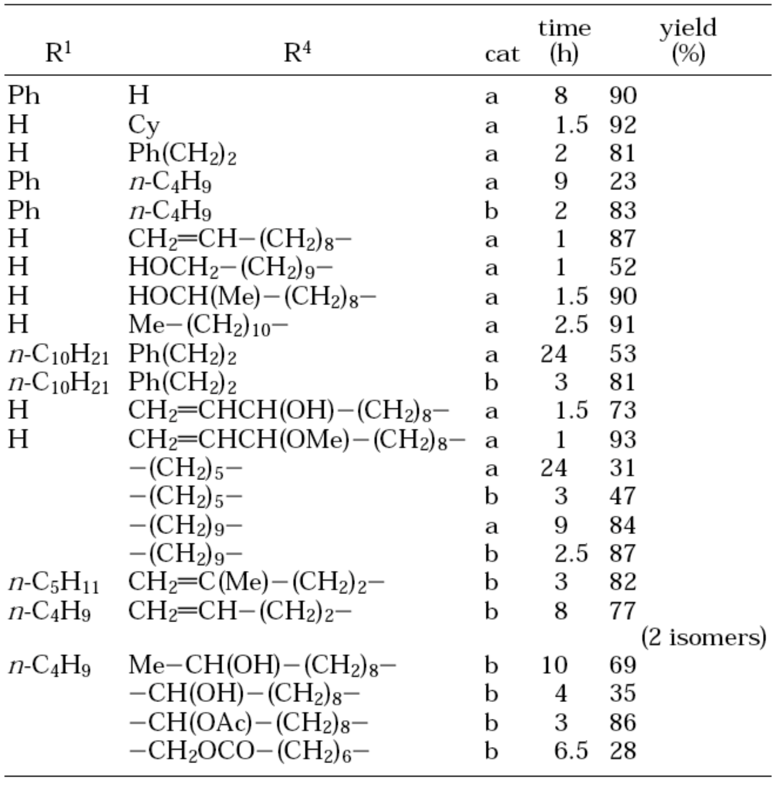
R_4 = alkyl, aryl

85 - 100%

JOC, **1995**, 60, 3045

Chem. Rev., **2003**, 103, 27

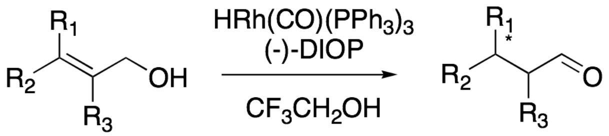




R^1	R^4	cat	time (h)	yield (%)
Ph	H	a	8	90
H	Cy	a	1.5	92
H	$Ph(CH_2)_2$	a	2	81
Ph	$n\text{-}C_4H_9$	a	9	23
Ph	$n\text{-}C_4H_9$	b	2	83
H	$CH_2{=}CH-(CH_2)_8-$	a	1	87
H	$HOCH_2-(CH_2)_9-$	a	1	52
H	$HOCH(Me)-(CH_2)_8-$	a	1.5	90
H	$Me-(CH_2)_{10}-$	a	2.5	91
$n\text{-}C_{10}H_{21}$	$Ph(CH_2)_2$	a	24	53
$n\text{-}C_{10}H_{21}$	$Ph(CH_2)_2$	b	3	81
H	$CH_2{=}CHCH(OH)-(CH_2)_8-$	a	1.5	73
H	$CH_2{=}CHCH(OMe)-(CH_2)_8-$	a	1	93
	$-(CH_2)_5-$	a	24	31
	$-(CH_2)_5-$	b	3	47
	$-(CH_2)_9-$	a	9	84
	$-(CH_2)_9-$	b	2.5	87
$n\text{-}C_5H_{11}$	$CH_2{=}C(Me)-(CH_2)_2-$	b	3	82
$n\text{-}C_4H_9$	$CH_2{=}CH-(CH_2)_2-$	b	8	77 (2 isomers)
$n\text{-}C_4H_9$	$Me-CH(OH)-(CH_2)_8-$	b	10	69
	$-CH(OH)-(CH_2)_8-$	b	4	35
	$-CH(OAc)-(CH_2)_8-$	b	3	86
	$-CH_2OCO-(CH_2)_6-$	b	6.5	28

JACS, **1993**, 115, 2027

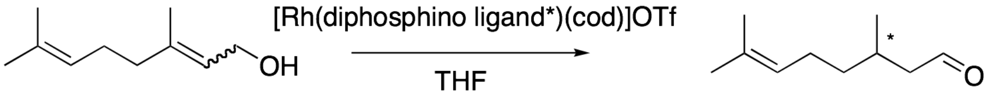
Asymmetric Isomerizations



R_1, R_2, R_3 = H, alkyl

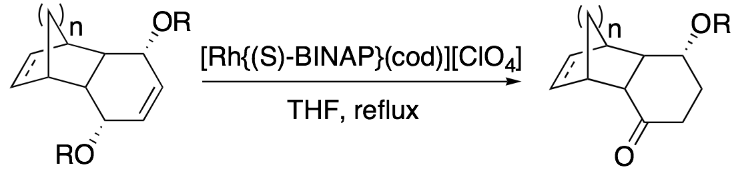
ee = < 4%

Gazz. Chim. Ital., **1976**, 106, 1131



BINAP, biaryl, ferrocenyl = *ee*'s from 4 - 61%

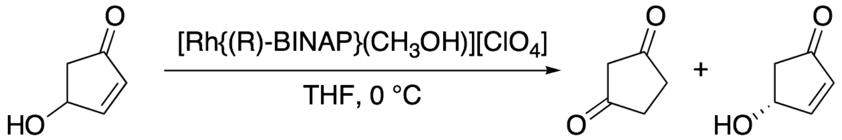
Helv. Chim Acta., **2001**, 84, 230



R = TMS, TES, TBDMS
n = 1, 2

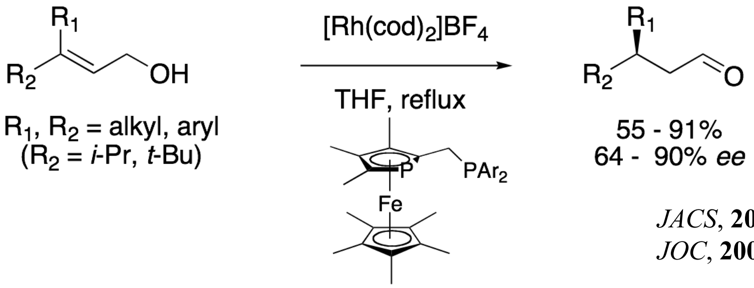
70 - 100%
93 - 97.5% *ee*

ACIE, **1995**, 34, 2287



91% *ee*

TL, **1987**, 28, 4719



R_1, R_2 = alkyl, aryl
(R_2 = *i*-Pr, *t*-Bu)

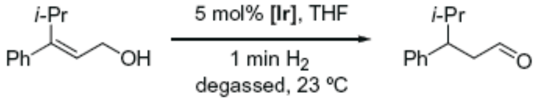
Ar = Ph, *o*-Tol

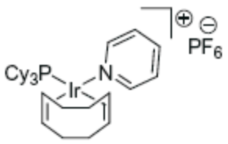
55 - 91%
64 - 90% *ee*

JACS, **2000**, 122, 9870
JOC, **2001**, 84, 230

Chem. Rev., **2003**, 103, 27

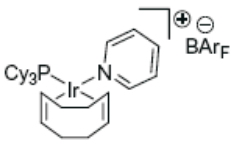
Ir Catalyzed Isomerizations in the Mazet Group





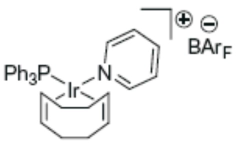
1

4h
conv. = 74%



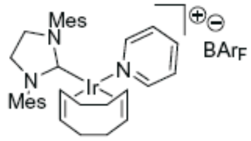
2

4h
conv. > 99%



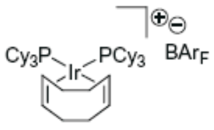
3

14h
conv. < 5%



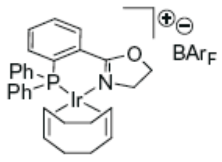
4

14h
conv. < 5%



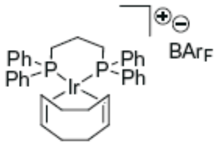
5

14h
conv. < 5%



6

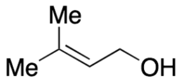
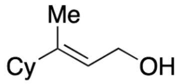
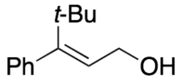
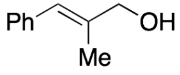
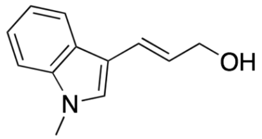
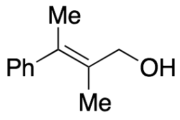
14h
conv. < 5%



7

14h
conv. < 5%

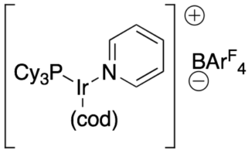
Selected Substrate Scope

substrate	**2** (mol%)	time (hr)	conversion (%)
	0.25	0.5	>99
	0.25	2	95
	5	16	>99
	0.5	1	>99
	1	2	>99
	10	22	98

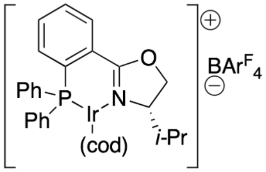
Conversion determined by ^{1}H NMR

L. Mantilli, C. Mazet, *Chimia,* **2009.** 63, 35
L. Mantilli, C. Mazet, *Tetrahedron Lett.,* **2009.** 50, 4141

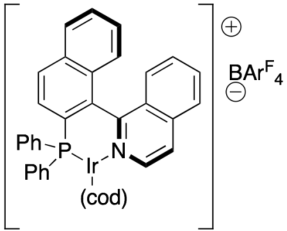
Title Paper - Catalyst Development



1



2



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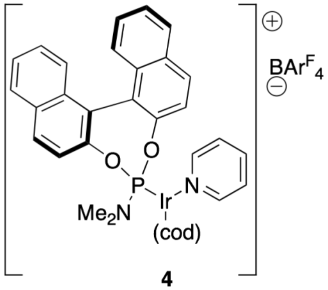

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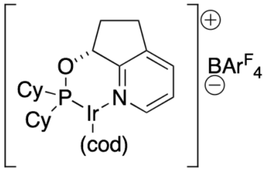

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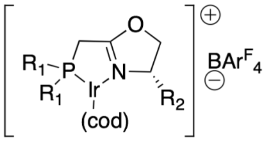
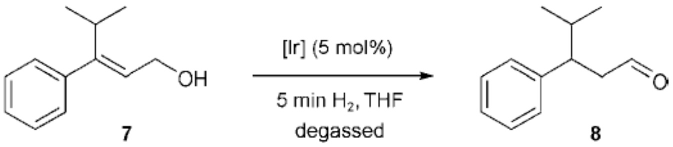


6a: R_1 = Cy ; R_2 = *i*-Pr
6b: R_1 = *t*-Bu ; R_2 = *i*-Pr
6c: R_1 = Cy ; R_2 = CH_2Ph
6d: R_1 = *t*-Bu ; R_2 = CH_2Ph
6e: R_1 = Cy ; R_2 = Ph
6f: R_1 = *t*-Bu ; R_2 = Ph
6g: R_1 = 1-Ad ; R_2 = Ph
6h: R_1 = Cy ; R_2 = *t*-Bu
6i: R_1 = *t*-Bu ; R_2 = *t*-Bu
6j: R_1 = 1-Ad ; R_2 = *t*-Bu

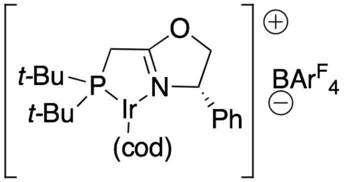
L. Mantilli, et. al., *ACIE,* **early view**



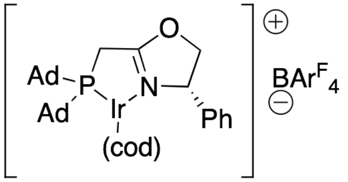
Entry[a]	Catalyst	*T* [°C]	*t* [h]	Conv. [%][b]	*ee* [%][c]
1	(*S*)-**2**	23	18	< 5	n.d.
2	(*R*)-**3**	23	18	< 5	n.d.
3	(*S*)-**4**	23	18	< 5	n.d.
4	(*R*)-**5**	23	18	19[d]	5 (*S*)
5	(*S*)-**6a**	23	18	98	11 (*R*)
6	(*S*)-**6b**	23	18	75	28 (*S*)
7	(*S*)-**6c**	23	2	> 99	30 (*S*)
8	(*S*)-**6d**	23	2	> 99	45 (*S*)
9	(*R*)-**6e**	23	2	> 99	75 (*R*)
10	(*R*)-**6f**	23	2	> 99	84 (*R*)
11	(*R*)-**6f**	−10	4	> 99	90 (*R*)
12	(*R*)-**6f**	−30	14	> 99	90 (*R*)
13	(*R*)-**6f**	−50	22	85	90 (*R*)
14	(*R*)-**6g**	23	4	95	91 (*R*)
15	(*R*)-**6g**	23	14	20	90 (*R*)[e]
16	(*R*)-**6g**	−10	22	6	93 (*R*)
17	(*S*)-**6h**	23	12	> 99	89 (*S*)
18	(*S*)-**6i**	23	12	98	95 (*S*)
19	(*S*)-**6j**	23	22	75	97 (*S*)

[a] Reported results are the average of at least two runs. [b] Determined by GC or ^1H NMR methods. [c] Determined by GC or SFC methods using a chiral stationary phase. Absolute configuration (shown in parentheses) based on the sign of the optical rotation and by comparison with literature data. See Ref. [3b]. [d] The remaining 81% is a 2:1 mixture of *E*/*Z* isomers of **7**. [e] 2.5 mol% of the catalyst used. n.d. = not determined.

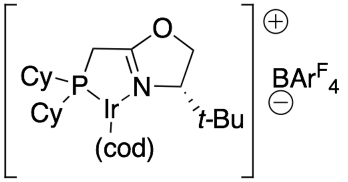
Substrate Scope



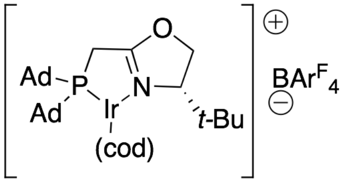
6f



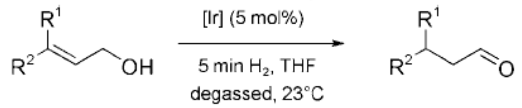
6g



6h



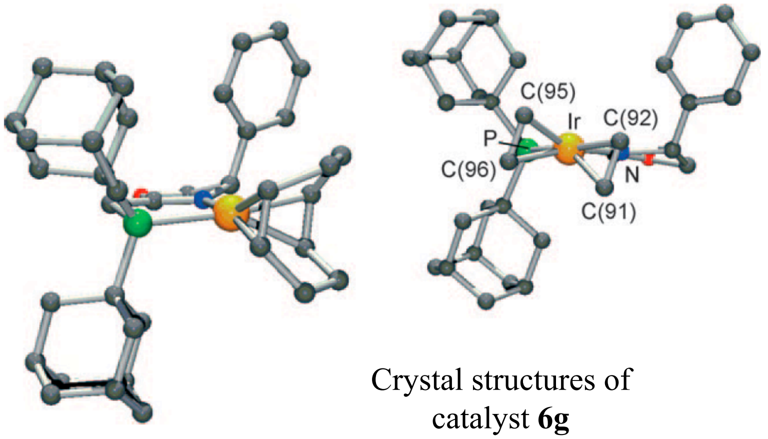
6j



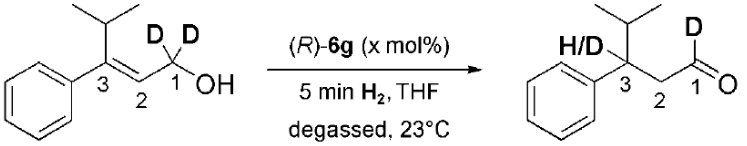
Entry[a]	Catalyst	R¹	R²	*t* [h]	Conv. [%][b]	*ee* [%][c]
1	(*R*)-**6f**	*i*Pr	4-Me-C_6H_4	22	50	56 (*R*)
2	(*R*)-**6g**	*i*Pr	4-Me-C_6H_4	22	84	86 (*R*)
3	(*S*)-**6j**	*i*Pr	4-Me-C_6H_4	22	71	95 (*S*)
4	(*R*)-**6g**	*i*Pr	4-MeO-C_6H_4	22	>99	90 (*R*)
5	(*S*)-**6j**	*i*Pr	4-MeO-C_6H_4	22	91	94 (*S*)
6	(*R*)-**6g**	*i*Pr	4-Cl-C_6H_4	22	88	82 (*R*)
7	(*S*)-**6j**	*i*Pr	4-Cl-C_6H_4	22	60	94 (*S*)
8	(*R*)-**6f**	Me	C_6H_5	22	30	34 (*S*)
9	(*R*)-**6g**	Me	C_6H_5	22	10	57 (*S*)
10	(*S*)-**6h**	Me	C_6H_5	22	<5[d]	n.d.
11	(*R*)-**6f**	Et	C_6H_5	8	35	60 (*S*)
12	(*R*)-**6g**	Et	C_6H_5	22	30	73 (*S*)
13	(*R*)-**6f**	Cy	C_6H_5	6	78	87 (*R*)
14	(*R*)-**6g**	Cy	C_6H_5	6	85	94 (*R*)
15	(*S*)-**6j**	Cy	C_6H_5	22	88	98 (*S*)
16	(*R*)-**6g**	*t*Bu	C_6H_5	22	80	99 (*R*)
17	(*S*)-**6j**	*t*Bu	C_6H_5	22	81	>99 (*S*)
18	(*R*)-**6f**	Me	Cy	22	70	60 (*S*)
19	(*R*)-**6g**	Me	Cy	22	90	68 (*S*)
20	(*S*)-**6j**	Me	Cy	18	25	76 (*R*)
21	(*R*)-**6g**	Ph	*i*Pr	22	26[e]	46 (S)
22	(*R*)-**6g**	Ph	Me	22	18	25 (R)

[a] Reported results are the average of at least two runs. [b] Determined by GC or ^{1}H NMR methods. [c] Determined by GC or SFC methods using a chiral stationary phase. Absolute configuration (shown in parentheses) based on the sign of the optical rotation and by comparison with literature data. See Ref. [3b]. [d] A 3:1 mixture of *E*/*Z* isomers was recovered. [e] The remaining 74% is a 3.5:1 mixture of *E*/*Z* isomers.

Crystal Structure and NMR Studies of Catalyst

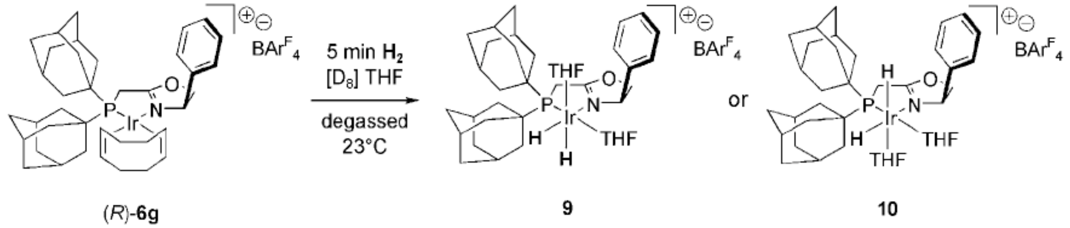


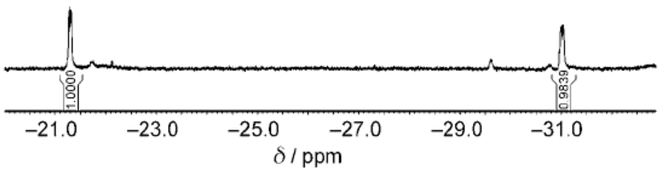
Crystal structures of catalyst **6g**



mol% [Ir]	H incorporation
5	10%
10	20%
20	40%

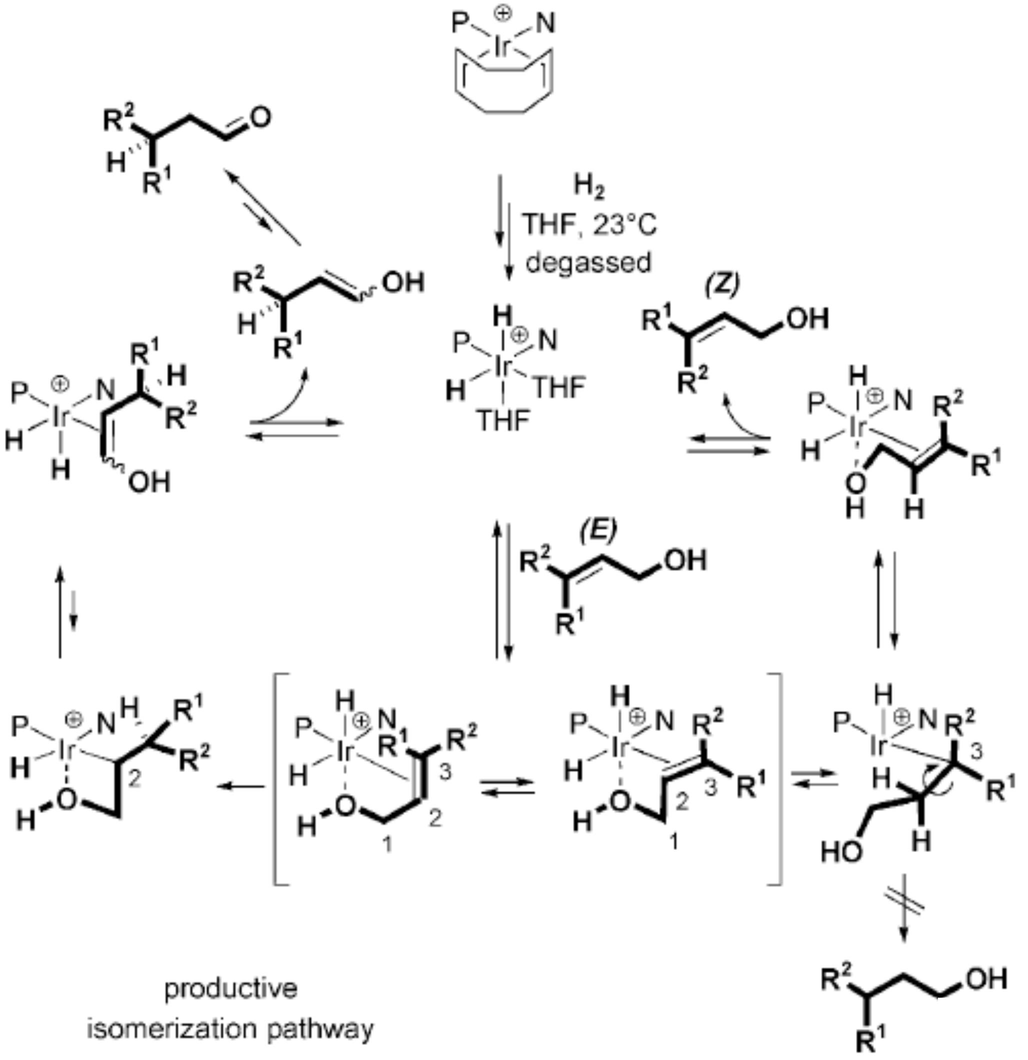
Labeling experiments using a dideuterated model substrate





^{1}H NMR of active catalyst to determine the orientation of the hydride in the complex

Catalyst Mechanism



Mechanism based on analogy with Stork and Crabtree’s studies of directed hydrogenation by Crabtree’s catalyst

Conclusions

- Developed a variety of asymmetric catalysts for the isomerization of allylic alcohols into chiral carbonyl compounds.