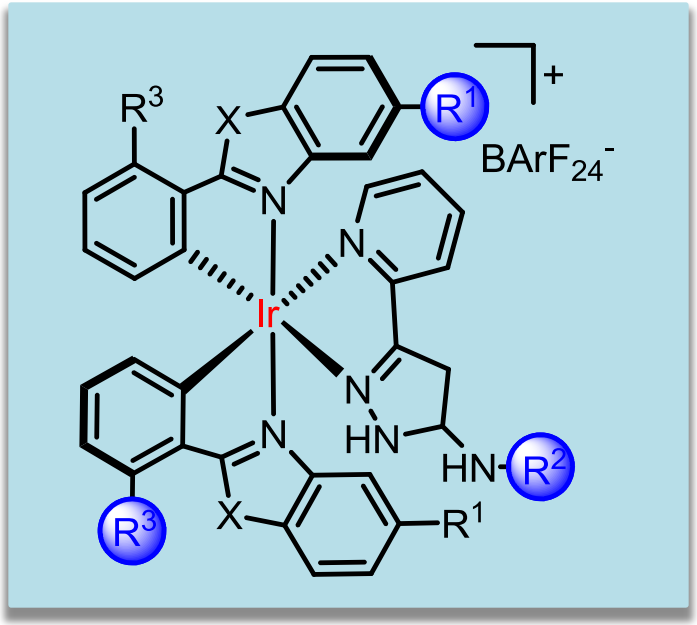
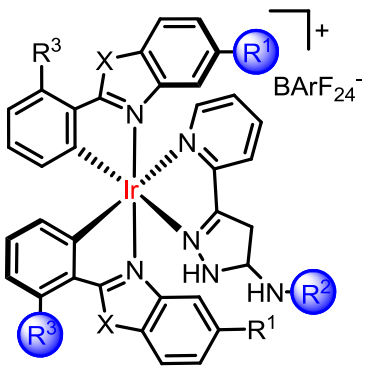
A Class of Chiral Octaheral Iridium(III) Complexes Bearing Achiral Ligands

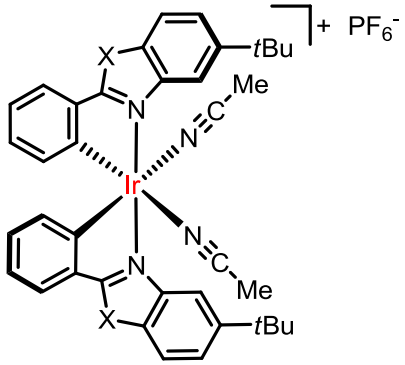


Qinghe Liu
Hu Group Meeting
January 19th 2015

Contents

- Part 1: Synthesis of enantiomerically pure iridium complexes

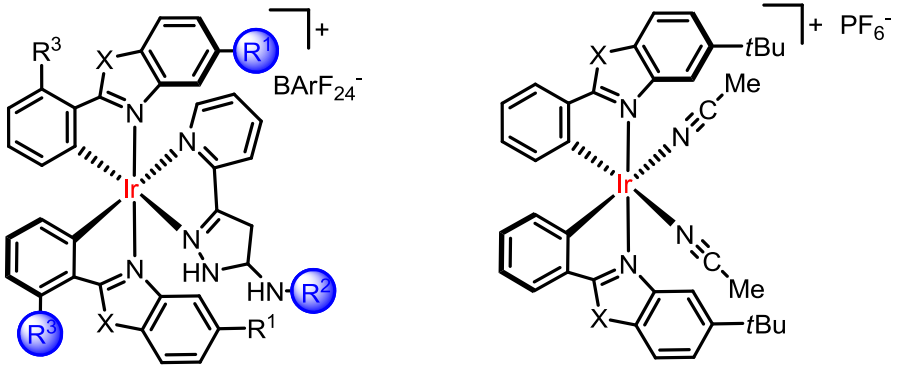




- Part 2: Asymmetric catalysis with these iridium complexes
- Part 3: conclusion

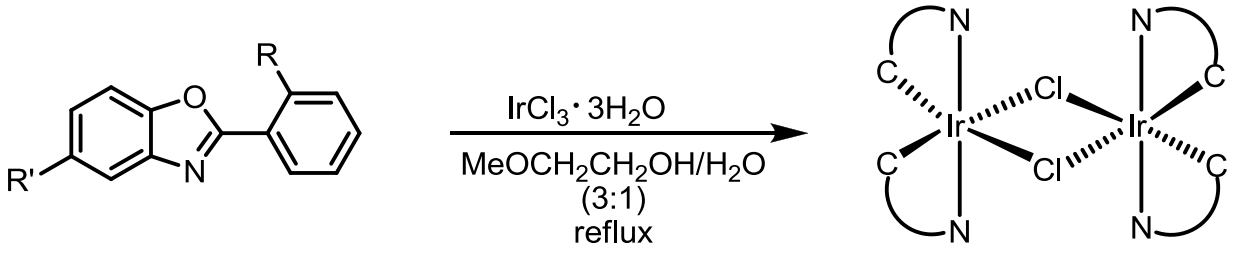
Contents

- Part 1: Synthesis of enantiomerically pure iridium complexes

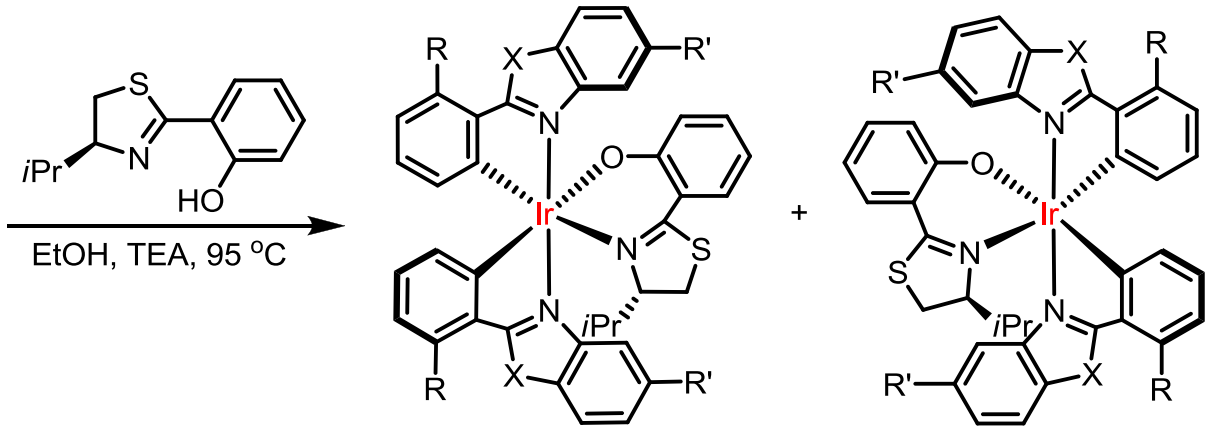


- Part 2: Asymmetric catalysis with these iridium complexes
- Part 3: conclusion

synthesis of iridium complexes



R = H, R' = CH_2OH;
R = Ph, R' = CH_2OH;
R = 3,5-$Me_2C_6H_4$, R' = CH_2OH;
R = H, R' = H



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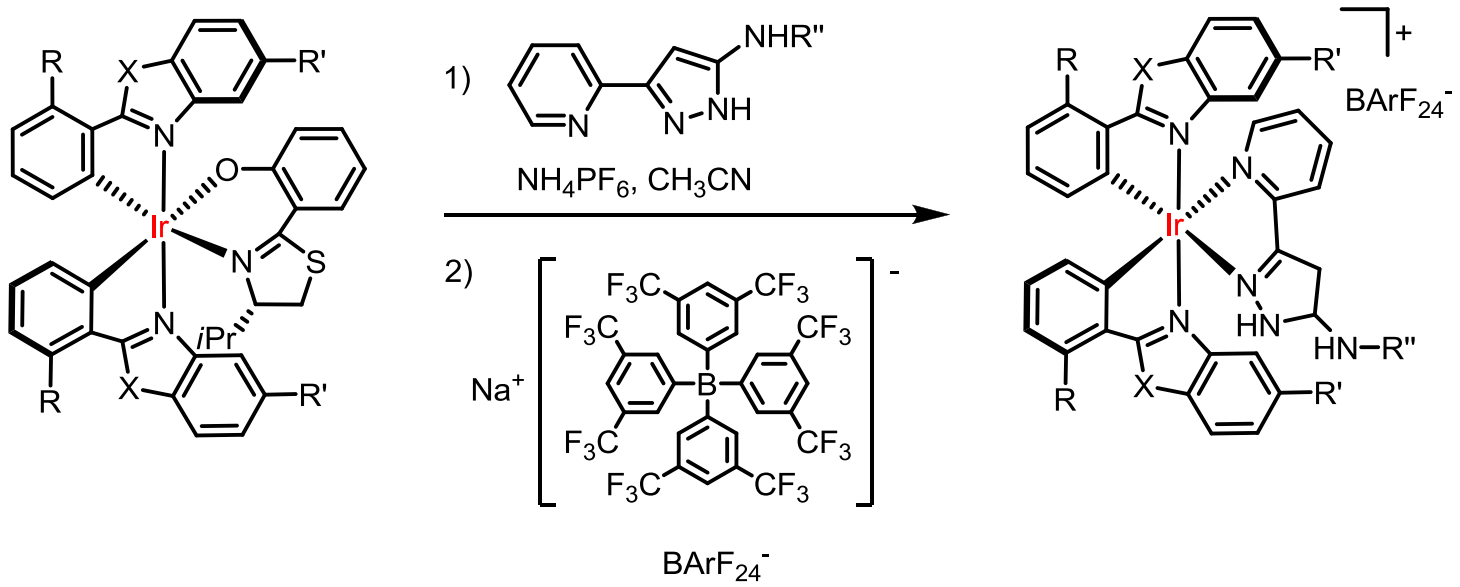
Nonoyama, G. *Bull. Chem. Soc. Jpn*. **1974**, *47*, 767.
Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

synthesis of iridium complexes

- First Generation:

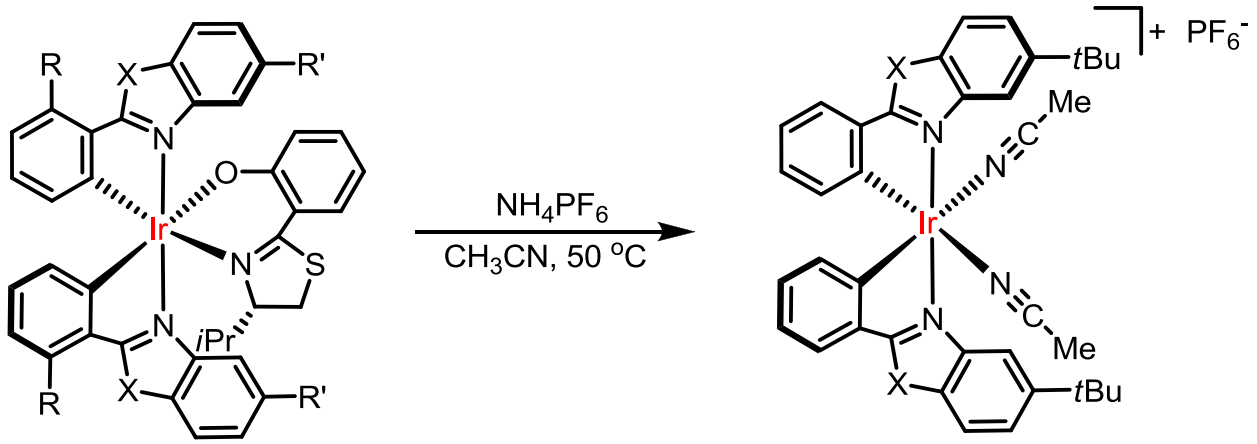


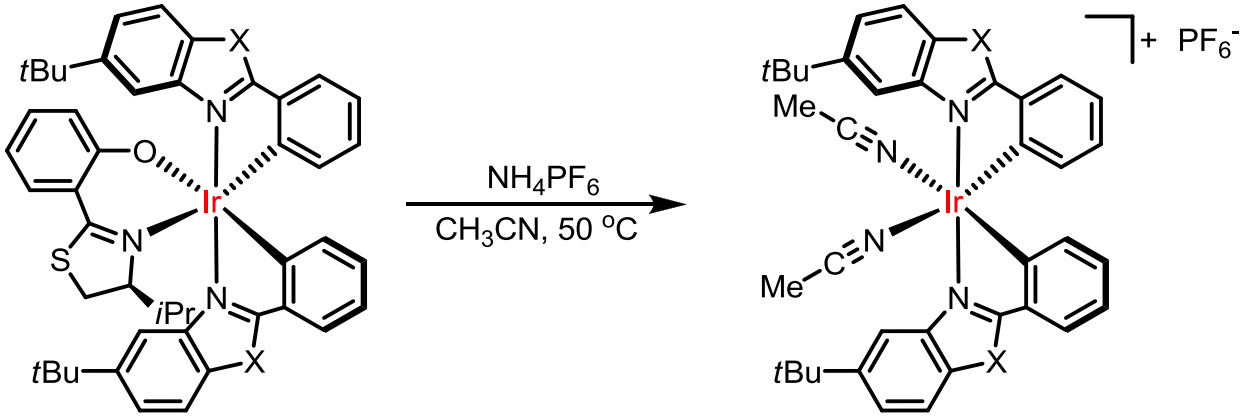
R = H, R' = CH_2OH, R" = H;
R = H, R' = CH_2OH, R" = *n*Bu;
R = H, R' = CH_2OH, R" = Ph;
R = H, R' = CH_2OH, R" = $COCF_3$;
R = Ph, R' = CH_2OH, R" = $COCF_3$;
R = 3,5-$Me_2C_6H_4$, R' = CH_2OH, R" = $COCF_3$;
R = H, R' = H, R" = Ph

Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

synthesis of iridium complexes

- Sencond Generation:





Huo, H.; Meggers, E. *J. Am. Chem. Soc*. **2014**, *136*, 2990.

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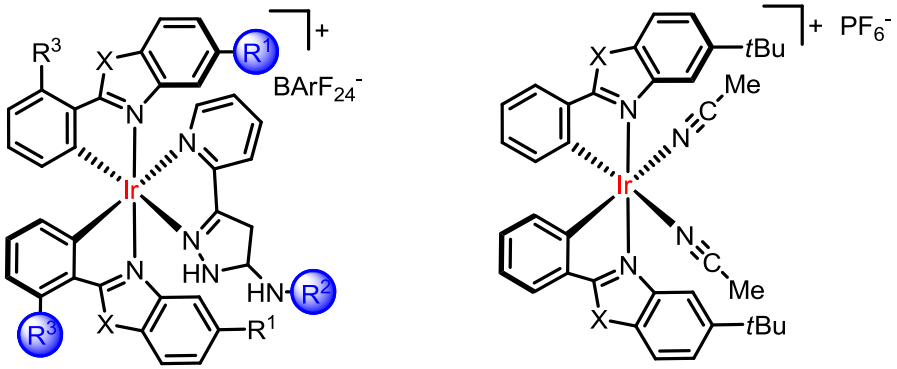
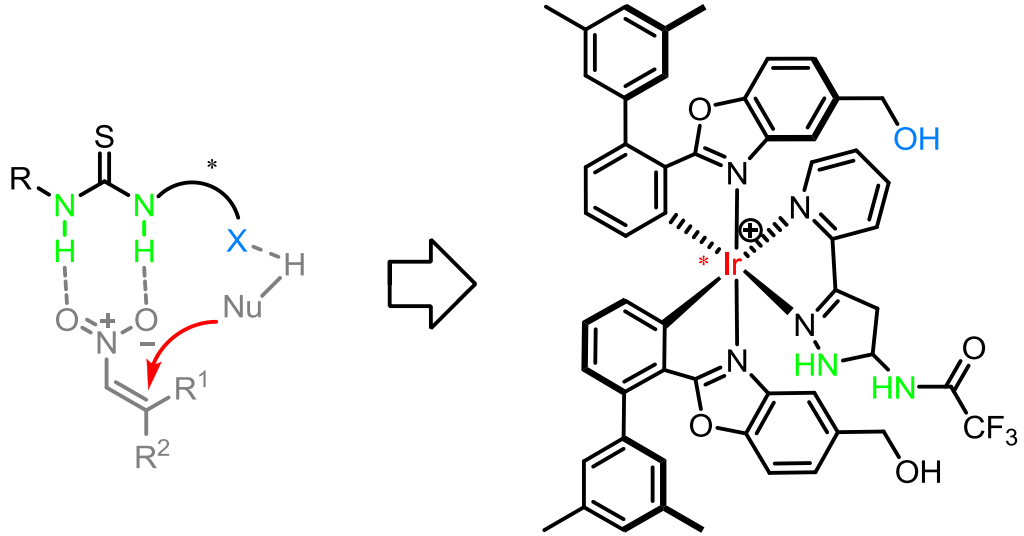
- Part 1: Synthesis of enantiomerically pure iridium complexes



- Part 2: Asymmetric catalysis with these iridium complexes
- Part 3: conclusion

asymmetric catalysis with complexes

■ Bifunctional hydrogen-bonding asymmetric organocatalysis as inspiration for a chiral-at-metal iridium.



Organic H-Bonding Catalyst

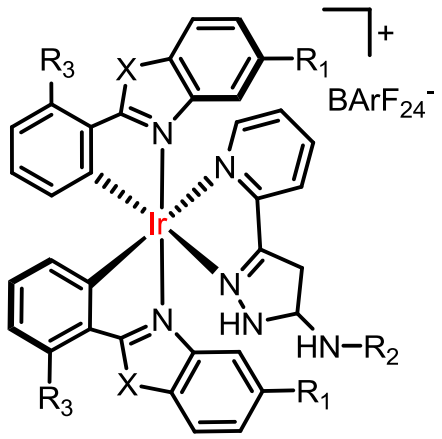
Chiral-At-Metal Octahedral H-Bonding Catalyst

■ The coordinated pyrazole acts as a double hydrogen bond donor to a nitroalkene, whereas a hydroxymethyl substituent on a benzoxazole serves as a hydrogen-bond acceptor for the mucleophile.

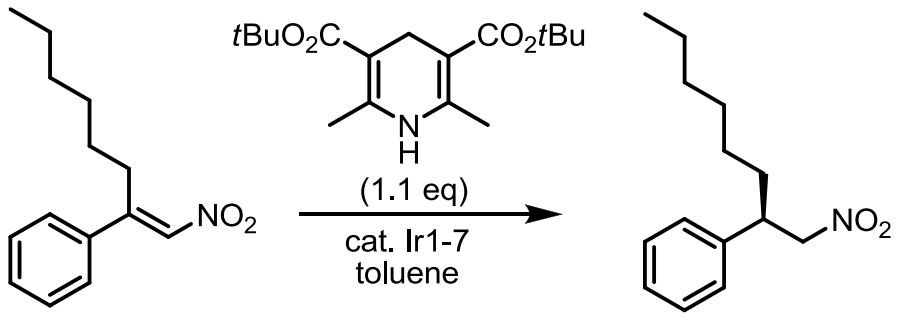
Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

asymmetric catalysis with complexes

■ Development of inert chiral-at-metal Ir(III) complexes for the asymmetric transfer hydrogenation of nitroalkene with Hantzsch ester.



Cat	R_1	R_2	R_3
Ir1	CH_2OH	H	H
Ir2	CH_2OH	*n*Bu	H
Ir3	CH_2OH	Ph	H
Ir4	CH_2OH	$COCF_3$	H
Ir5	CH_2OH	$COCF_3$	Ph
Ir6	CH_2OH	$COCF_3$	3,5-$Me_2C_6H_3$
Ir7	H	Ph	H

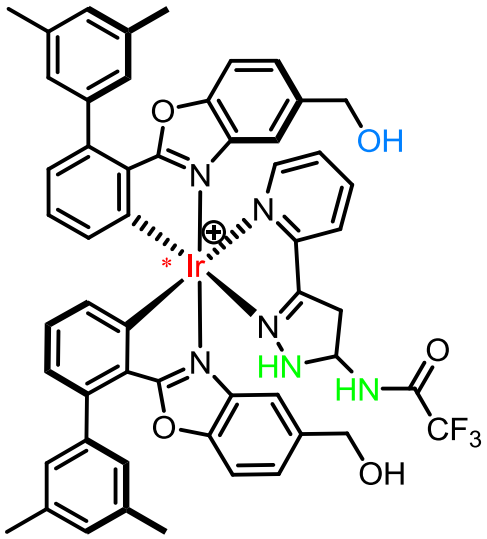


entry	cat.	loading (mol %)	t (h)	conv. (%)	ee (%)
1	Ir1	20	22	92	63
2	Ir2	20	24	82	70
3	Ir3	20	22	94	84
4	Ir4	20	7	96	90
5	Ir5	20	1	100	99
6	Ir5	1	20	96	98
7	Ir6	1	14	94	99
8	Ir7	20	20	<20	0

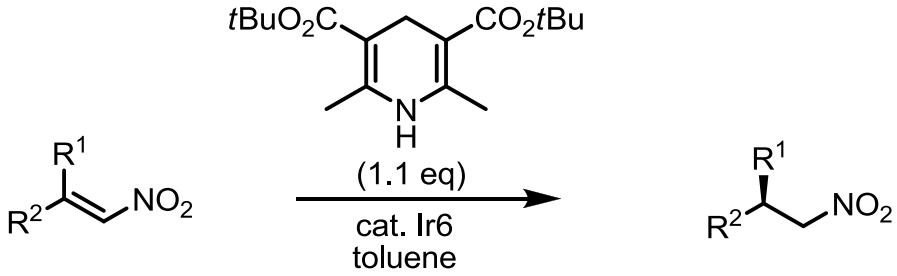
Chen, L.;. Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

asymmetric catalysis with complexes

- Scope of the asymmetric transfer hydrogenation with Ir6.



Ir6

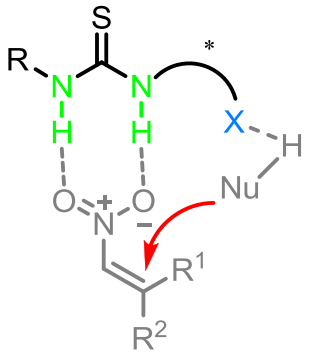


entry	R^1, R^2	loading (mol %)	t (h)	yield. (%)	ee (%)
1	*n*Hex, Ph	1	18	94	99
2	*n*Pr, Ph	1	24	96	98
3	iPr, Ph	1	24	92	96
4	Me, Ph	1	22	91	95
5	Me, *p*-MePh	1	24	95	95
6	Me, *p*-ClPh	1	24	93	94
7	Me, *m*-ClPh	1	24	91	93
8	Me, 2-naphthyl	1	24	96	96
9	*n*Hex, Ph	0.3	72	95	97
10	*n*Hex, Ph	0.1	96	89	94

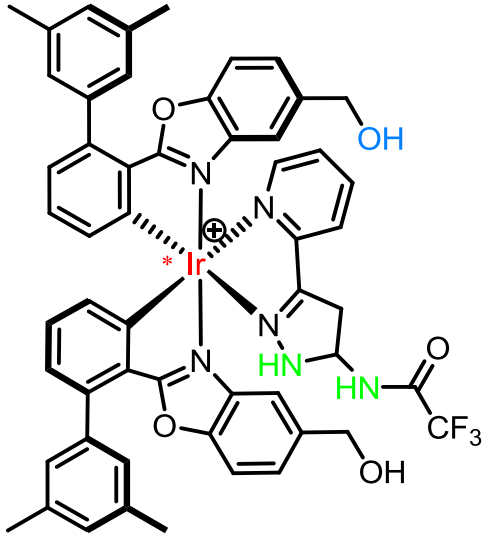
Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

asymmetric catalysis with complexes

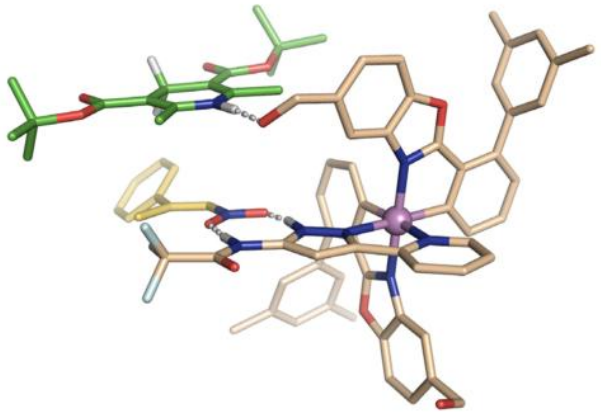
- Proposed a model of ternary complex formed by catalyst, nitroalkene, and Hantzsch ester leading to the transition state..



Organic
H-Bonding Catalyst



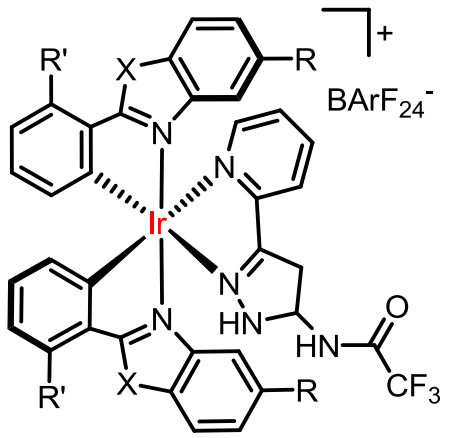
Chiral-At-Metal Octahedral
H-Bonding Catalyst



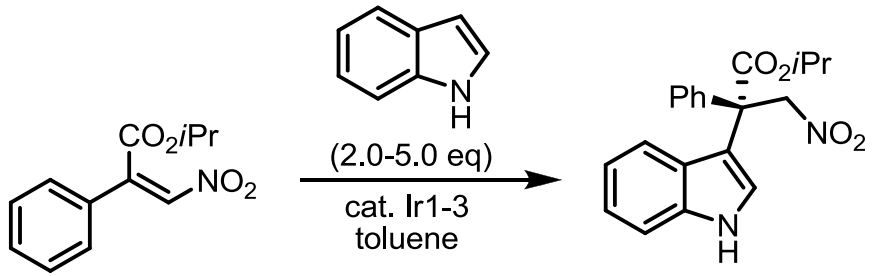
Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

asymmetric catalysis with complexes

■ Development of a chiral-at-metal Ir(III) complex for the enantioselective Fiedel-Crafts alkylation of indole with the nitroalkene.



Cat	R	R'
Ir1	CH_2OH	3,5-Me_2Ph
Ir2	$CONEt_2$	3,5-Me_2Ph
Ir3	$CONEt_2$	N-carbazolyl

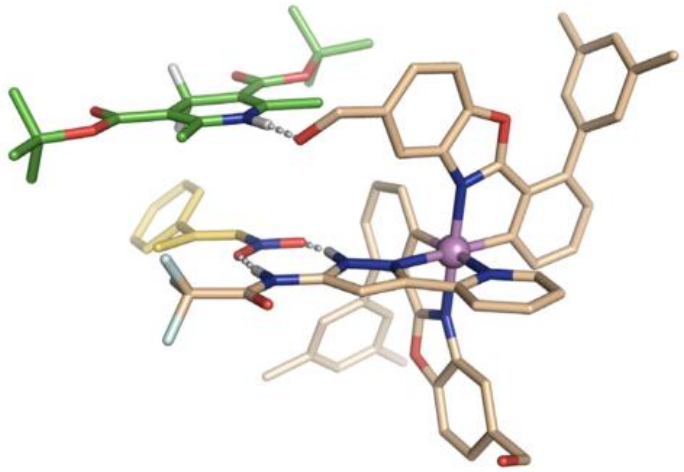


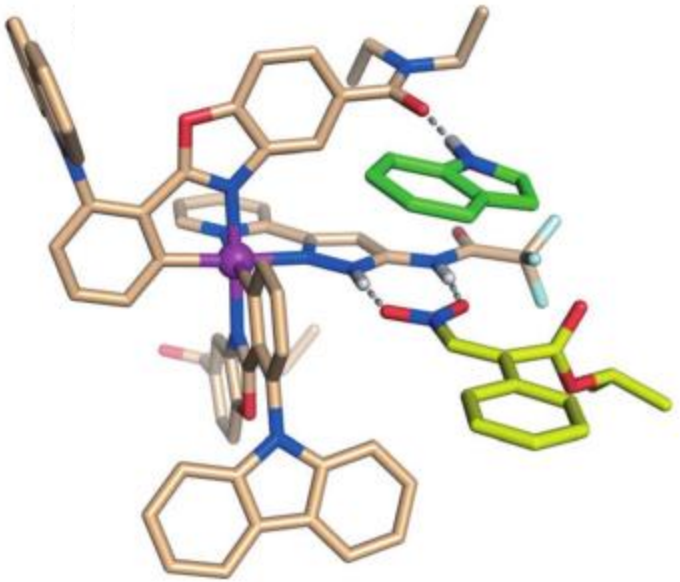
entry	cat.	conditions	t (h)	conv. (%)	ee (%)
1	Ir1 (5 mol%)	alkene (1M), indole (2 eq)	72	71	70
2	Ir2 (5 mol%)	alkene (1M), indole (2 eq)	24	87	96
3	Ir2 (2 mol%)	alkene (1M), indole (2 eq)	58	77	93
4	Ir3 (2 mol%)	alkene (1M), indole (2 eq)	36	97	98
5	Ir3 (1 mol%)	alkene (2M), indole (2 eq)	24	93	96
6	Ir3 (1 mol%)	alkene (1M), indole (2 eq)	24	98	96
7	Ir3 (1 mol%)	alkene (2M), indole (2 eq)	<12	100	96

Chen, L.; Meggers, E. *Angew. Chem., Int. Ed*. **2013**, *52*, 14021.

asymmetric catalysis with complexes

■ Proposed a model of ternary complex composed of catalyst, nitroalkene, and indole leading to the transitions state.



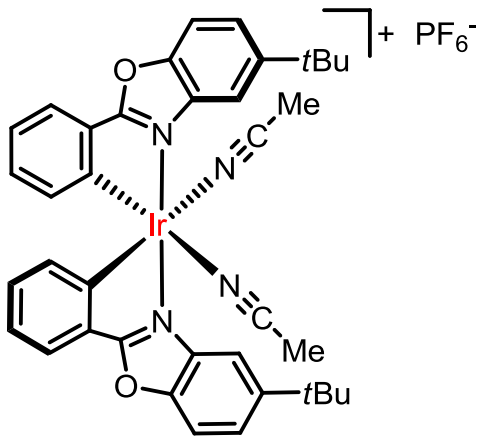


Chen, L.; Meggers, E. *J. Am. Chem. Soc*. **2013**, *135*, 10598.

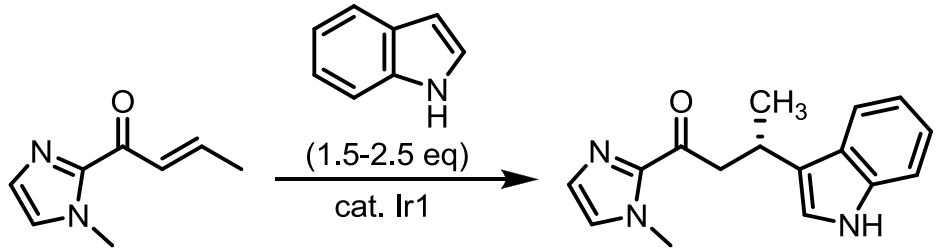
Chen, L.; Meggers, E. *Angew. Chem., Int. Ed*. **2013**, *52*, 14021.

asymmetric catalysis with complexes

■ Enantioselective Friedel-Crafts addition of indole to α, β-unsaturated imidazole catalyzed by Ir(III) complex.



Ir1



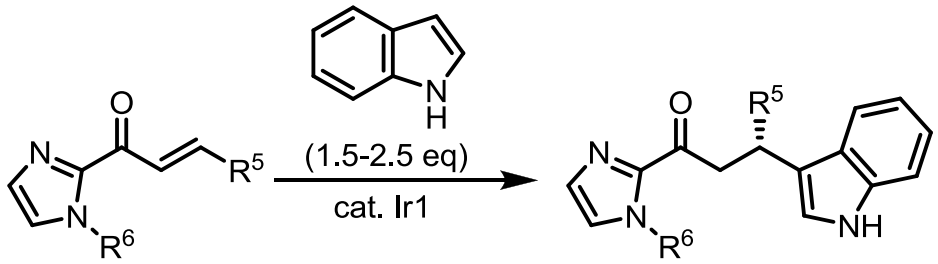
entry	solvent	conditions	t (h)	conv. (%)	ee (%)
1	MeCN	indole (1.5 eq, 0.75 M), rt	20	35	95
2	MeOH	indole (1.5 eq, 0.75 M), rt	20	70	95
3	CH_2Cl_2	indole (1.5 eq, 0.75 M), rt	20	90	94
4	THF	indole (1.5 eq, 0.75 M), rt	20	85	96
5	THF	indole (2.5 eq, 2.5 M), rt	20	100	96
6	THF	as entry 5 plus air	20	100	96
7	THF	as entry 5 plus air and 1% H_2O	20	88	96
8	THF	indole (2.5 eq, 2.5 M), 0 ^oC	36	100	97

■ Substitution of the chiral auxiliary ligand by two acetonitrile ligands..

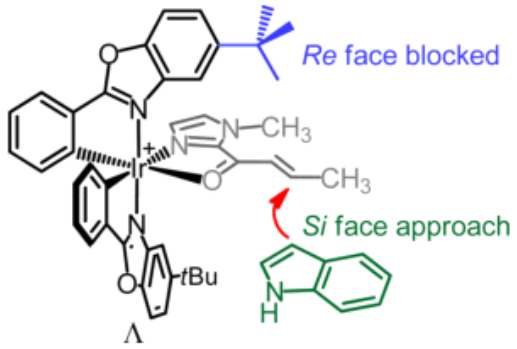
Huo, H.; Meggers, E. *J. Am. Chem. Soc*. **2014**, *136*, 2990.

asymmetric catalysis with complexes

■ Enantioselective Friedel-Crafts addition of indole to α, β-unsaturated imidazole catalyzed by Ir(III) complex.

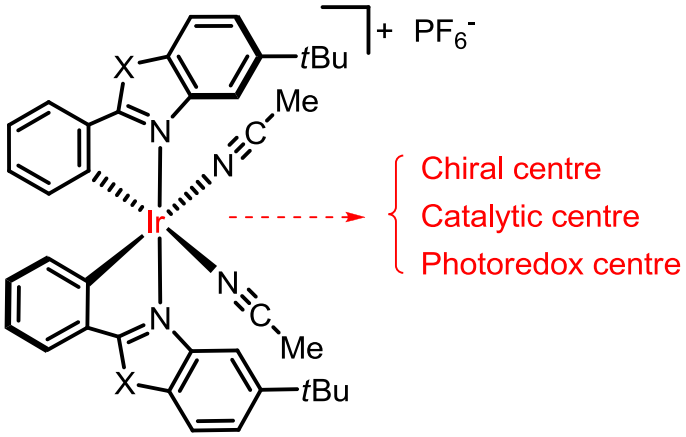


entry	R^5, R^6	loading (mol %)	T (^oC)	t (h)	yield. (%)	ee (%)
1	Et, Me	2.0	0	48	89	96
2	*n*Bu, Me	2.0	rt	20	97	91
3	*i*Pr, Me	2.0	rt	48	78	93
4	Ph, Me	1.0	rt	16	98	93
5	CO_2Et, Me	1.0	rt	24	97	98
6	Me, *i*Pr	1.0	rt	24	99	97
7	Me, *i*Pr	0.5	rt	44	97	97
8	Me, *i*Pr	0.25	rt	60	91	97



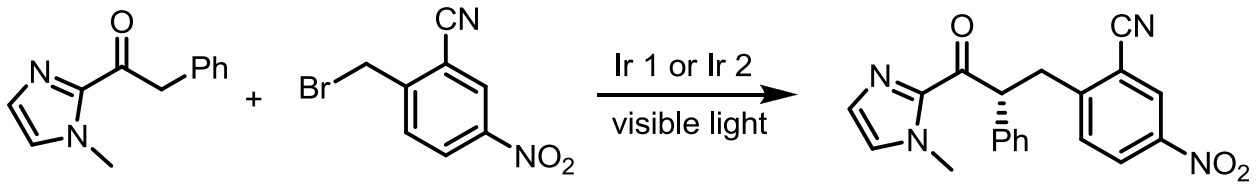
■ One face of the alkene is sterically shielded by one of the tert-butyl groups.

Huo, H.; Meggers, E. *J. Am. Chem. Soc*. **2014**, *136*, 2990.



Ir 1 (X = O), Ir 2 (X = S)

■ The possibility that these chiral Lewis acids intertwine chiral enolate catalysis with photoredox radical ion chemistry?

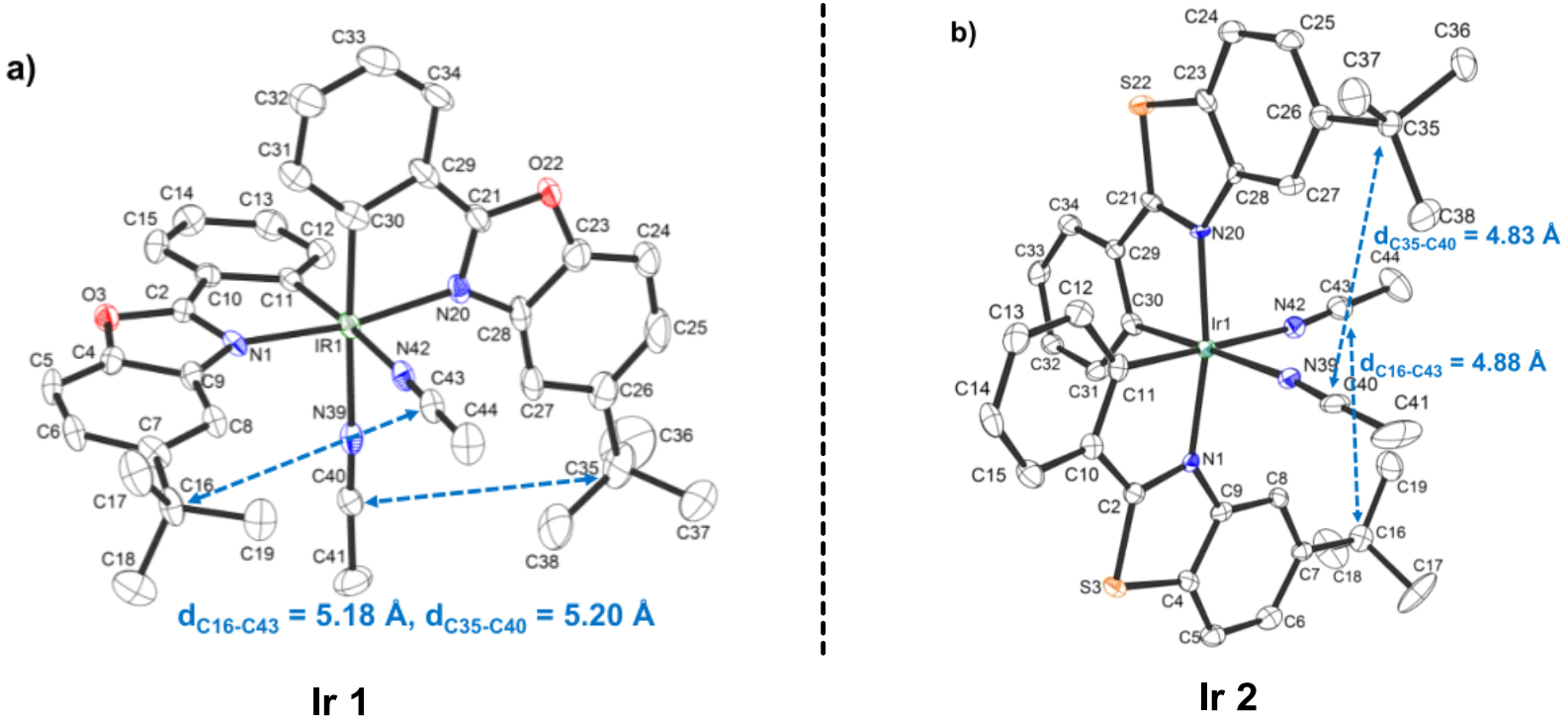


entry	solvent	illumination	conditions	t (h)	conv. (%)	ee (%)
1	Ir 1 (5 mol%)	visible light	imidazole(0.3M, 3eq), MeOH, rt	20	85	95
2	Ir 1 (2 mol%)	visible light	Na_2HPO_4, imidazole(1.2M, 3eq)	3	97	95
3	Ir 2 (2 mol%)	visible light	same as above	1.5	100	99
4	Ir 2 (0.5 mol%)	visible light	same as above	4.5	97	98
5	Ir 2 (2 mol%)	dark	same as above	1.5	<5	n.d.
6	none	visible light	same as above	16	0	n.a.

Huo, H.; Meggers, E. *Nature* **2014**, *515*, 100.

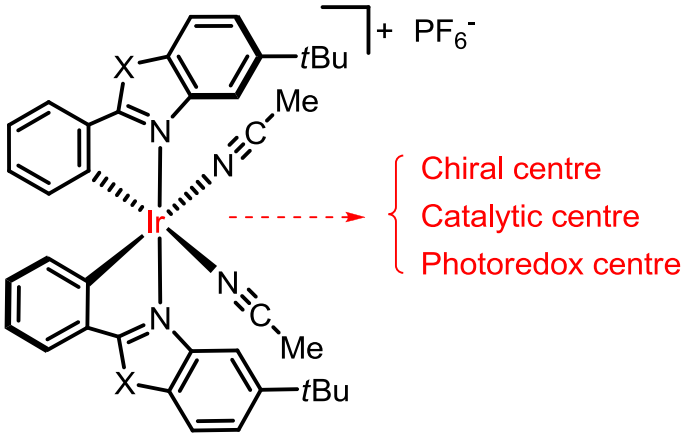
asymmetric catalysis with complexes

■ Distances between the quaternary carbon atoms of the tert-butyl groups and the nitrile carbons of the neighboring acetonitrile.



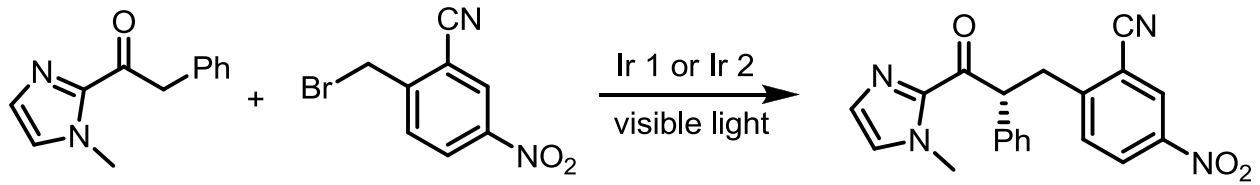
Ir 1 **Ir 2**

Huo, H.; Meggers, E. *Nature* **2014**, *515*, 100.



Ir 1 (X = O), Ir 2 (X = S)

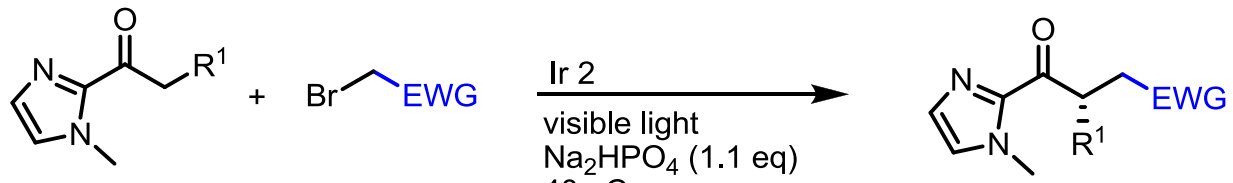
■ The possibility that these chiral Lewis acids intertwine chiral enolate catalysis with photoredox radical ion chemistry?

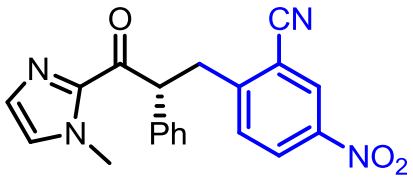


entry	solvent	illumination	conditions	t (h)	conv. (%)	ee (%)
1	Ir 1 (5 mol%)	visible light	imidazole(0.3M, 3eq), MeOH, rt	20	85	95
2	Ir 1 (2 mol%)	visible light	Na_2HPO_4, imidazole(1.2M, 3eq)	3	97	95
3	Ir 2 (2 mol%)	visible light	same as above	1.5	100	99
4	Ir 2 (0.5 mol%)	visible light	same as above	4.5	97	98
5	Ir 2 (2 mol%)	dark	same as above	1.5	<5	n.d.
6	none	visible light	same as above	16	0	n.a.

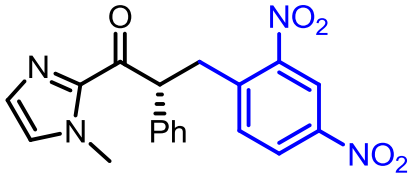
Huo, H.; Meggers, E. *Nature* **2014**, *515*, 100.

asymmetric catalysis with complexes

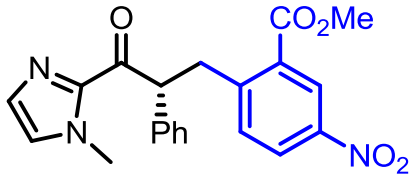




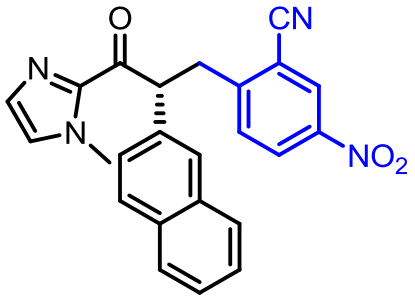
1.5 h, 100% yield, 99% e.e.



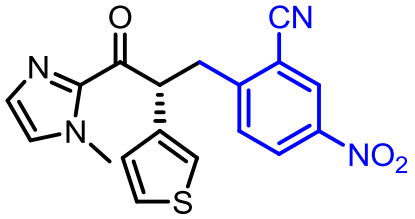
2 h, 97% yield, 99% e.e.



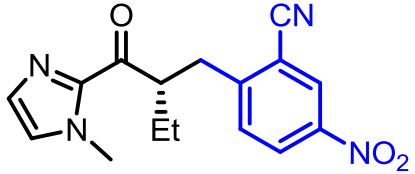
2 h, 98% yield, 99% e.e.



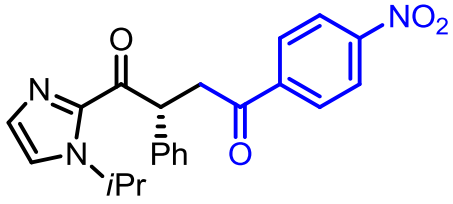
2 h, 99% yield, 98% e.e.



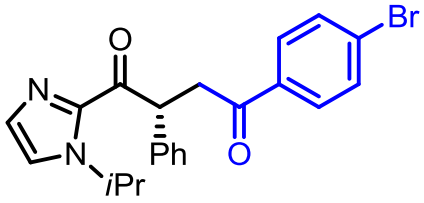
2 h, 99% yield, 97% e.e.



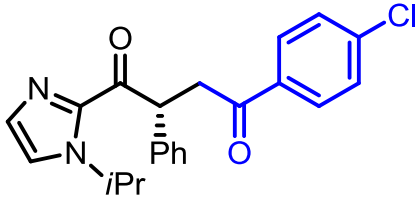
36 h, 84% yield, 91% e.e.



6 h, 91% yield, 90% e.e.

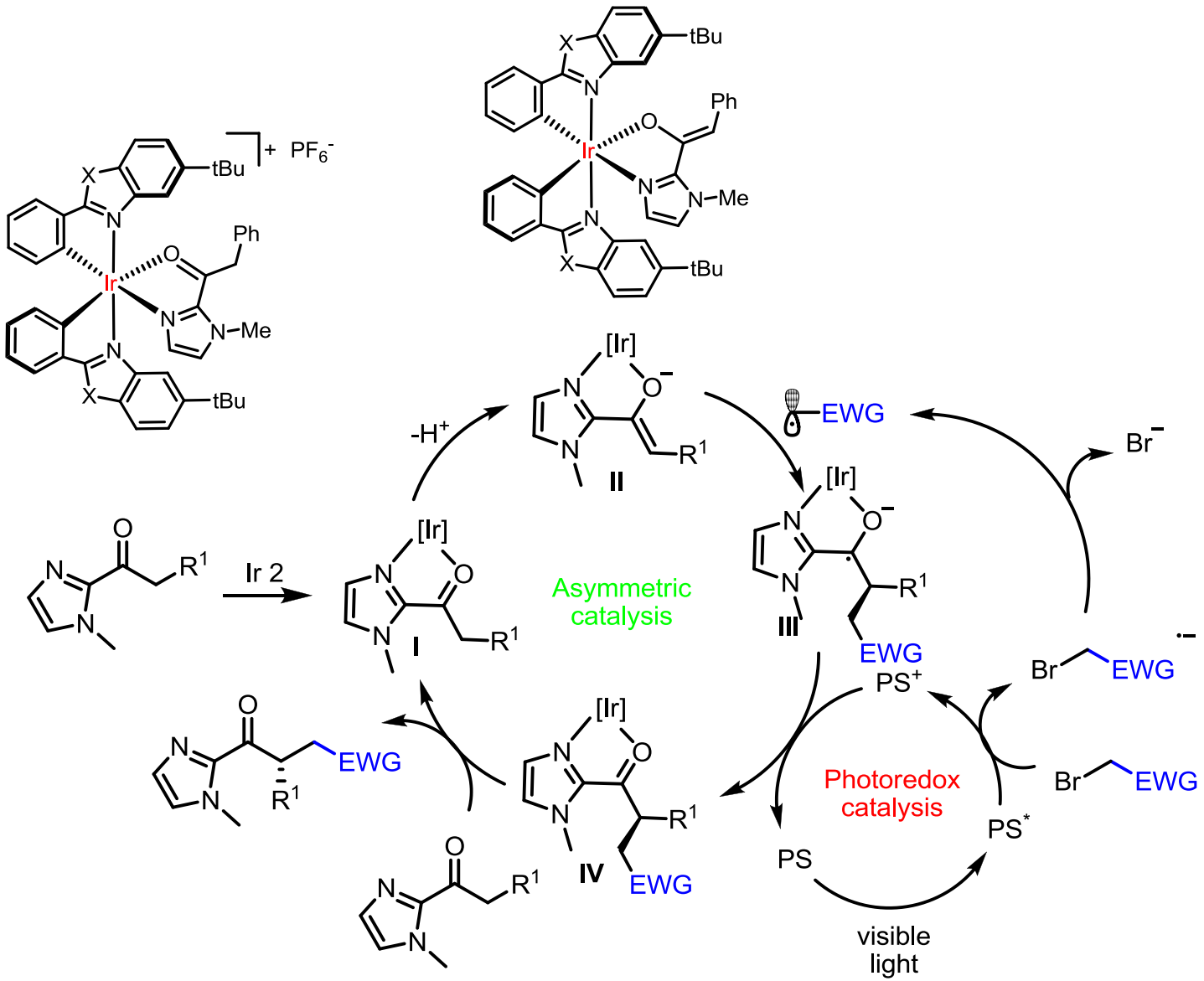


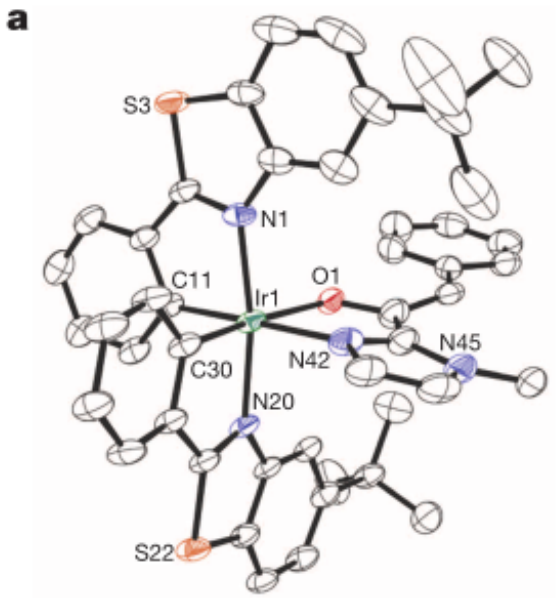
2 h, 86% yield, 91% e.e.

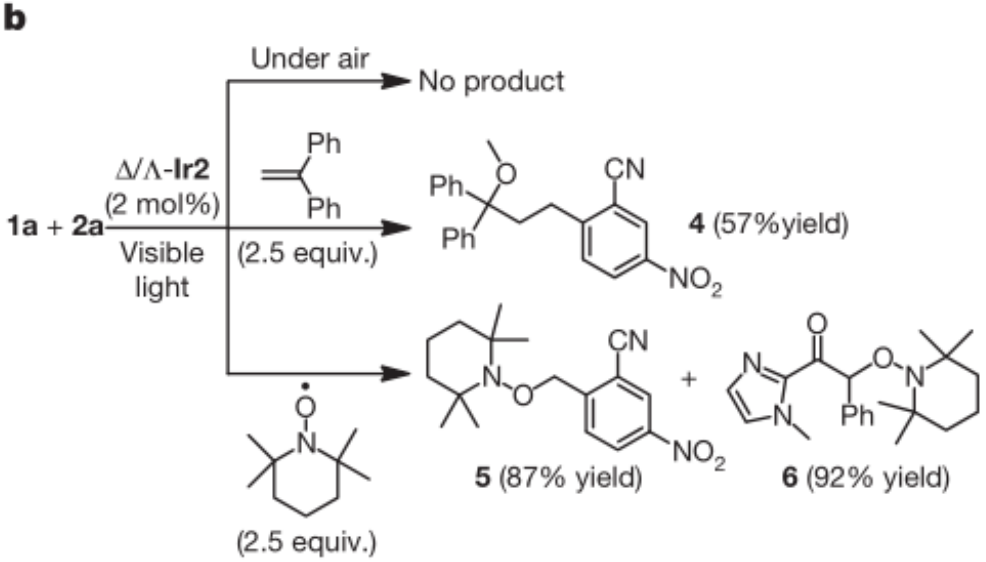


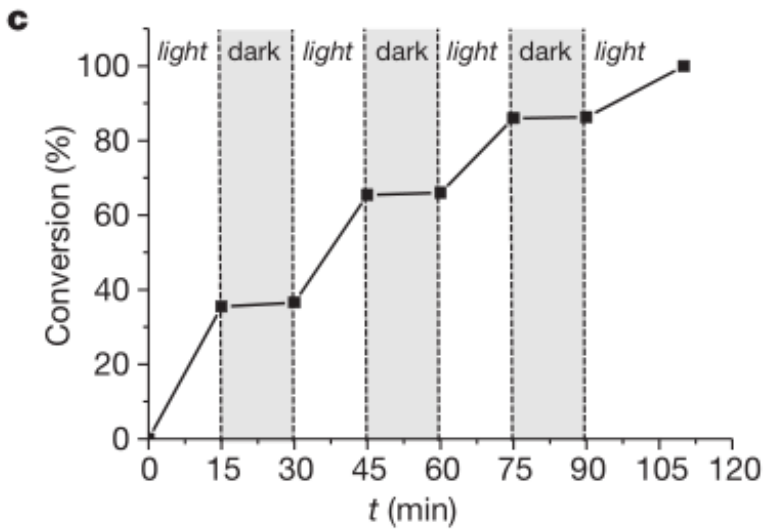
24 h, 91% yield, 91% e.e.

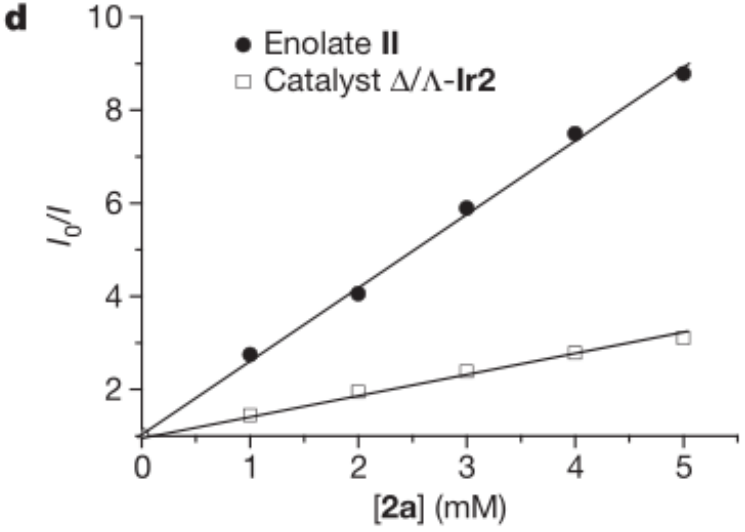
asymmetric catalysis with complexes



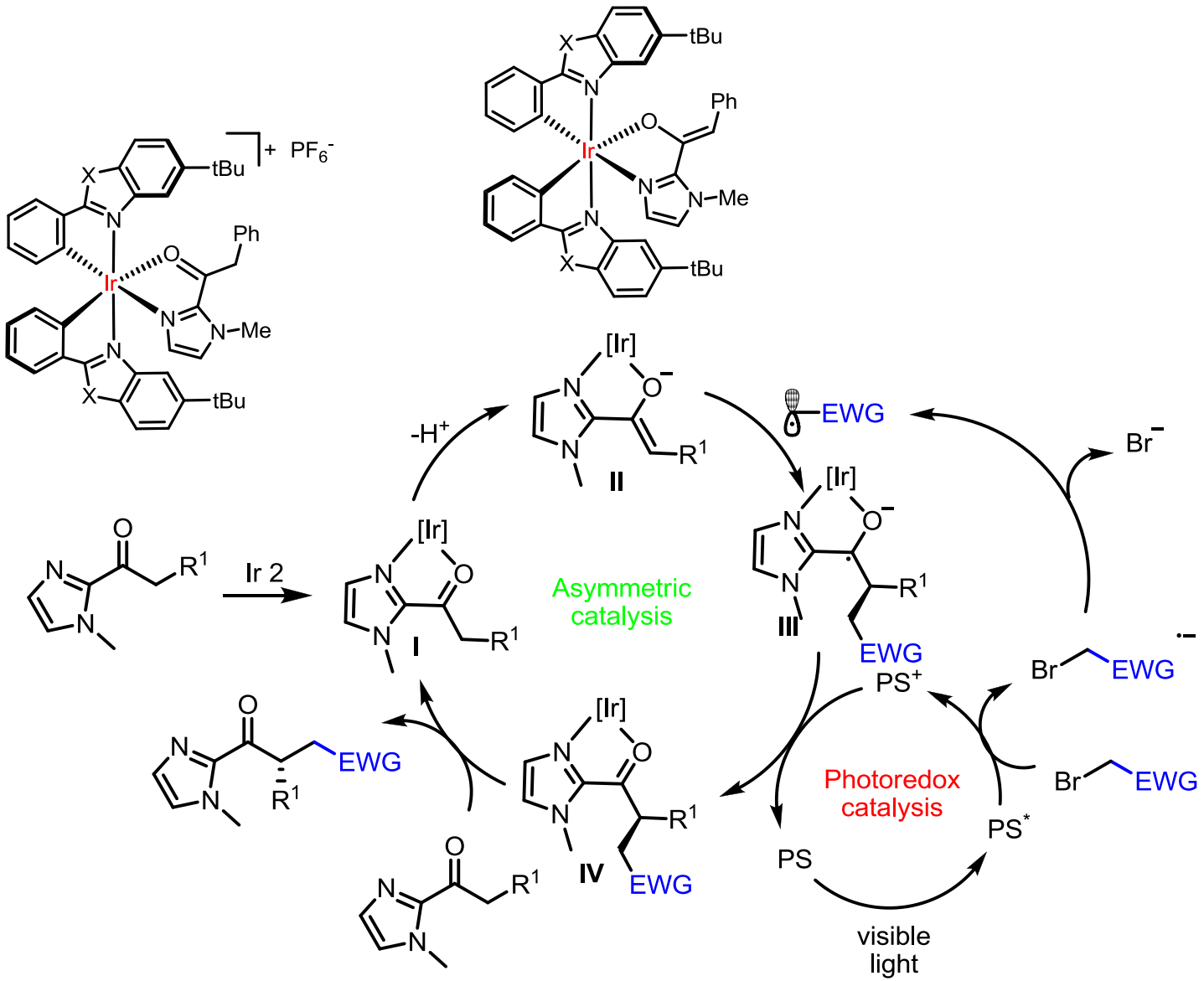

a
S3
N1
C11
Ir1
O1
N45
C30
N42
N20
S22


b
Under air
No product
1a + 2a
Δ/Λ-Ir2
(2 mol%)
Visible
light
Ph
Ph
(2.5 equiv.)
Ph
O
Ph
CN
NO2
4 (57%yield)
O
N
(2.5 equiv.)
CN
N
O
NO2
5 (87% yield)
O
N
O
N
N
Ph
6 (92% yield)


c
light
dark
light
dark
light
dark
light
Conversion (%)
0
20
40
60
80
100
0
15
30
45
60
75
90
105
120
t (min)

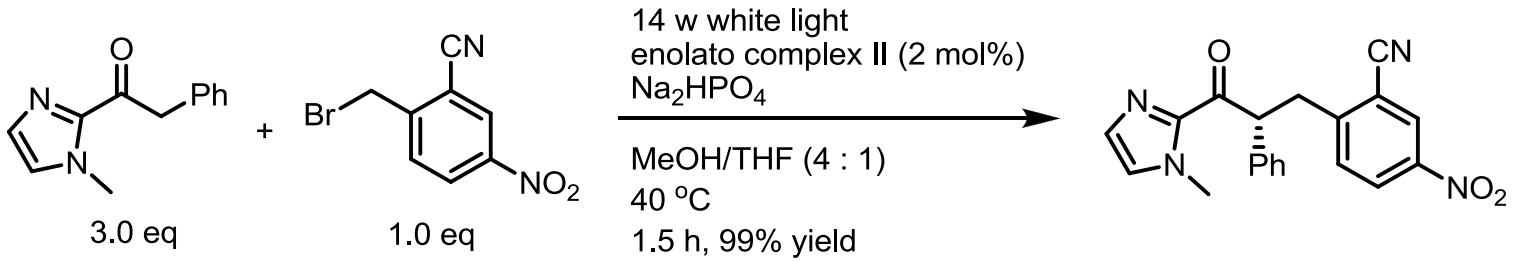

d
Enolate II
Catalyst Δ/Λ-Ir2
I0/I
2
4
6
8
10
0
1
2
3
4
5
[2a] (mM)

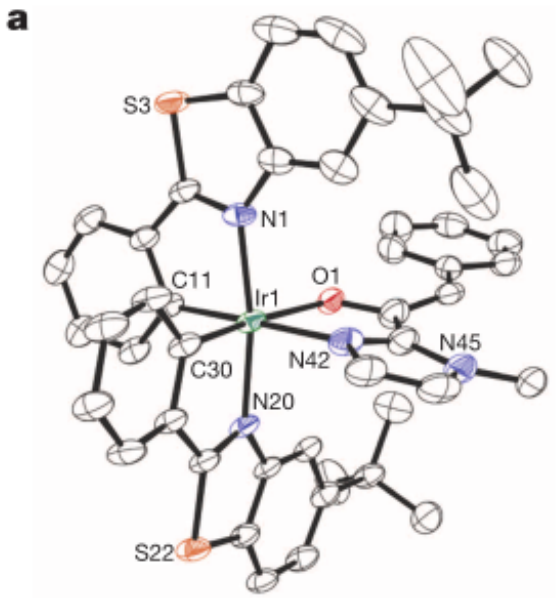
asymmetric catalysis with complexes

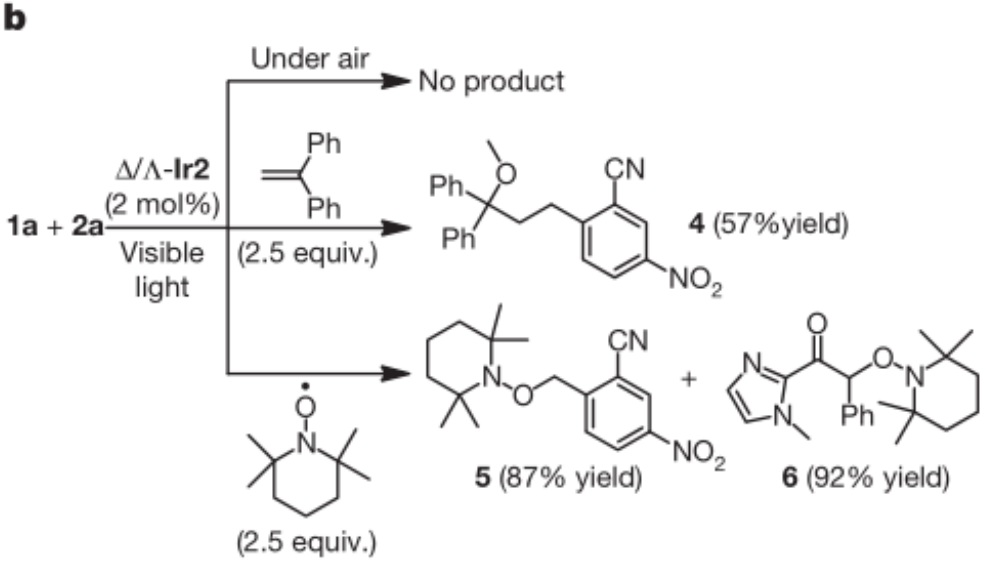


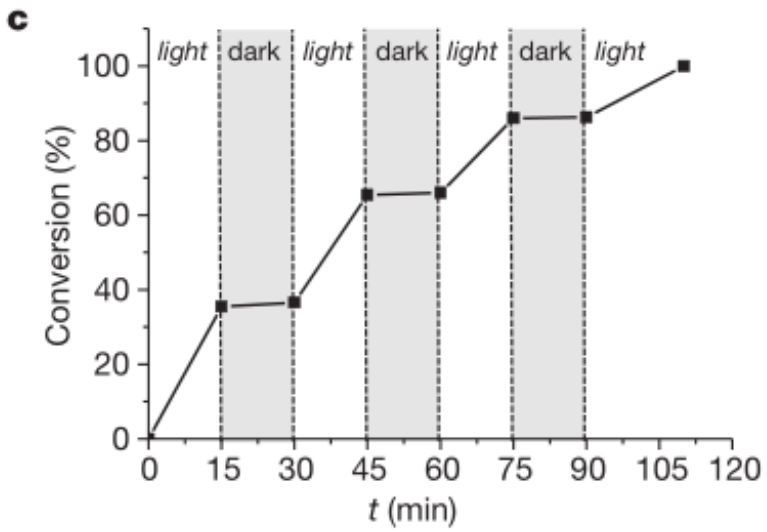
asymmetric catalysis with complexes

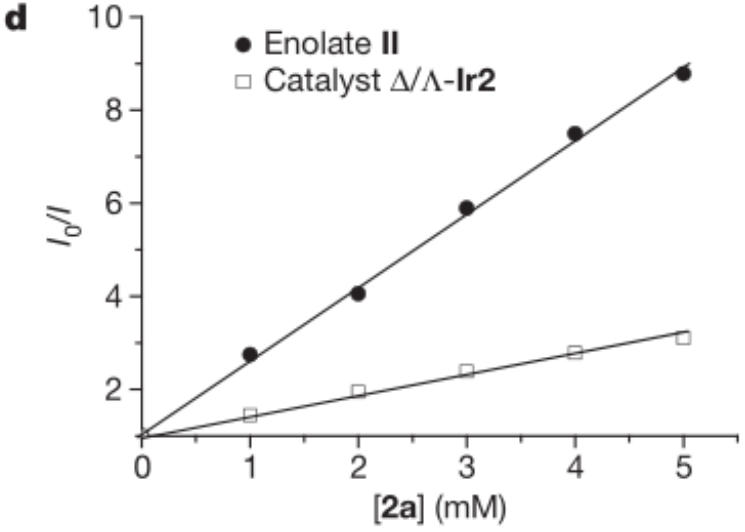
- The independently synthesized racemic enolate iridium complex **II** (intermidiate **II**) catalyzes the photoredox reaction with an identical efficiency compared to **Ir2**, thereby confirming that complex **II** (intermidiate **II**) is competent.



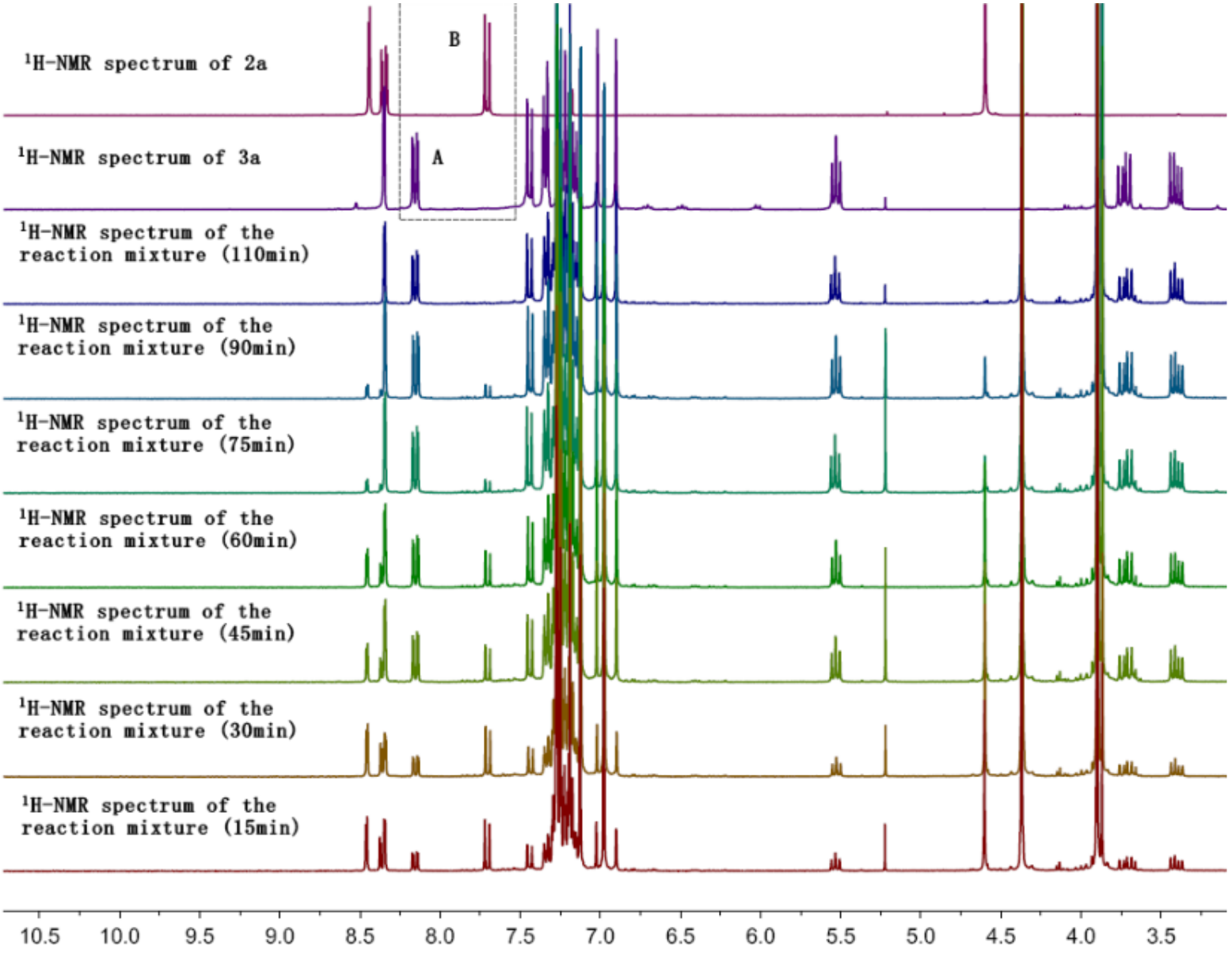

a
S3
N1
C11
Ir1
O1
N45
C30
N42
N20
S22

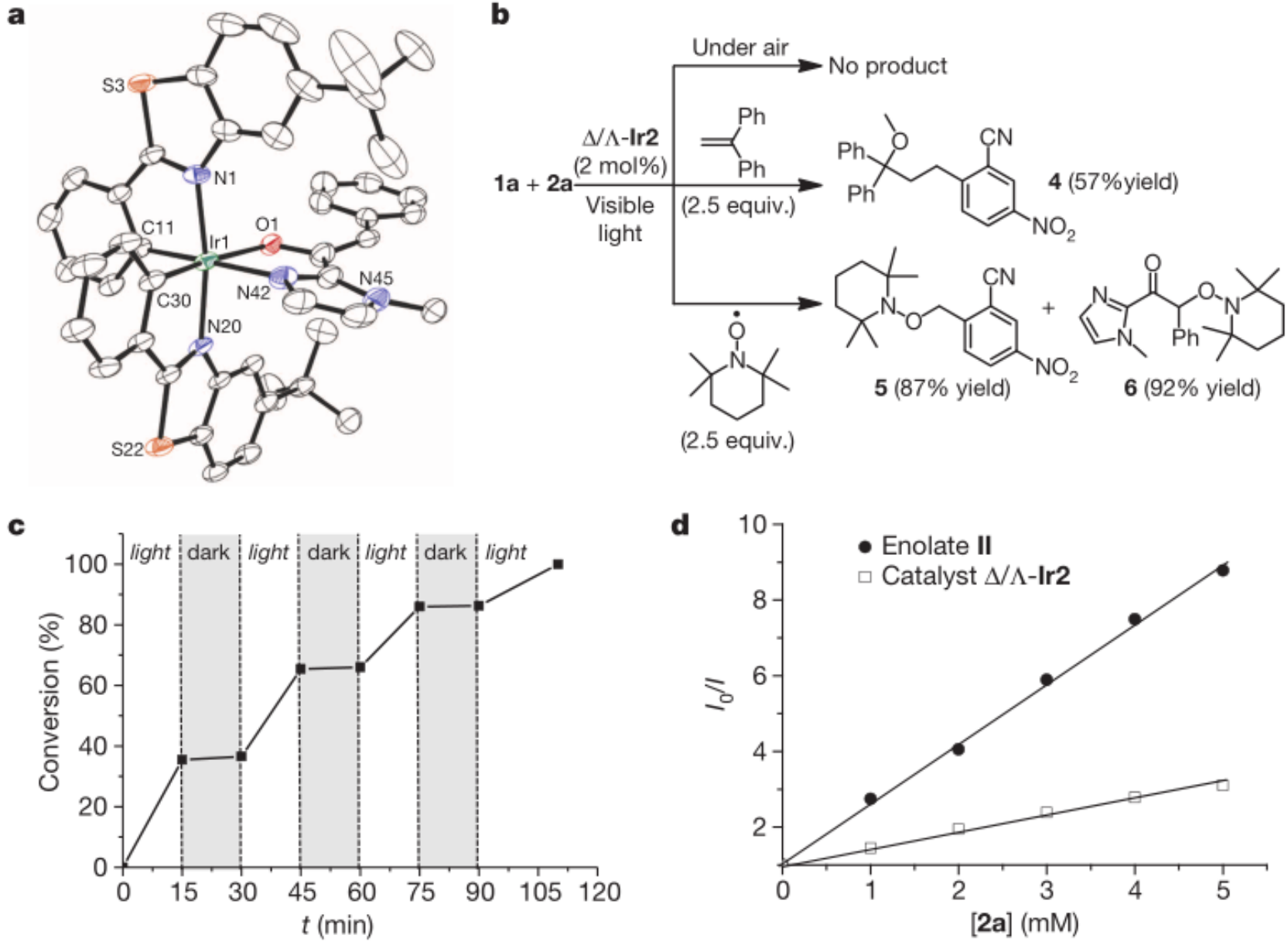

b
Under air
No product
1a + 2a
Δ/Λ-Ir2
(2 mol%)
Visible
light
Ph
Ph
(2.5 equiv.)
Ph
O
Ph
CN
NO2
4 (57%yield)
O
N
(2.5 equiv.)
CN
N
O
NO2
5 (87% yield)
O
N
O
N
N
Ph
6 (92% yield)


c
light
dark
light
dark
light
dark
light
Conversion (%)
0
20
40
60
80
100
0
15
30
45
60
75
90
105
120
t (min)


d
Enolate II
Catalyst Δ/Λ-Ir2
I0/I
2
4
6
8
10
0
1
2
3
4
5
[2a] (mM)

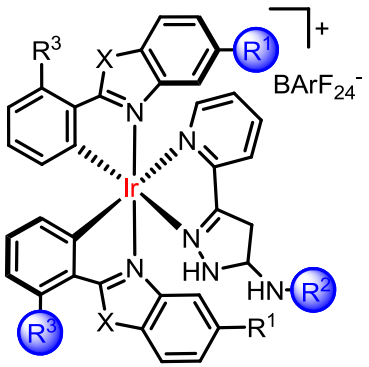
asymmetric catalysis with complexes

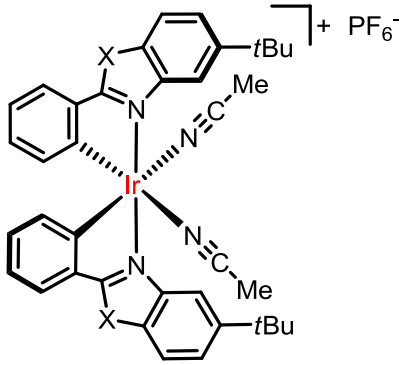



a
S3
N1
C11
Ir1
O1
N45
N42
C30
N20
S22
b
Under air
No product
1a + 2a
Δ/Λ-Ir2
(2 mol%)
Visible
light
Ph
Ph
(2.5 equiv.)
Ph
O
Ph
CN
NO2
4 (57%yield)
N
O
(2.5 equiv.)
CN
NO2
5 (87% yield)
+
O
N
N
O
N
Ph
6 (92% yield)
c
light
dark
light
dark
light
dark
light
Conversion (%)
0
20
40
60
80
100
0
15
30
45
60
75
90
105
120
t (min)
d
Enolate II
Catalyst Δ/Λ-Ir2
I0/I
2
4
6
8
10
0
1
2
3
4
5
[2a] (mM)

Contents

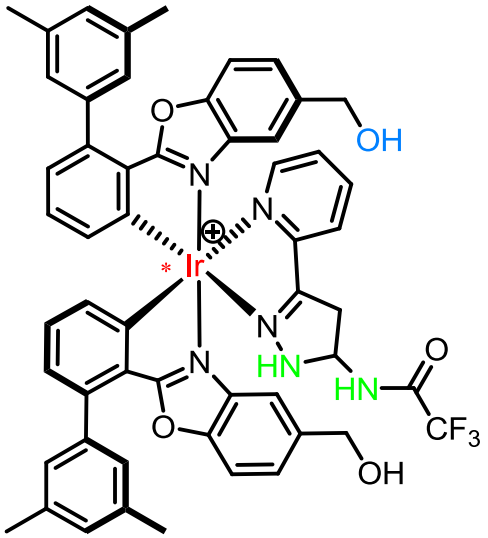
- Part 1: Synthesis of enantiomerically pure iridium complexes



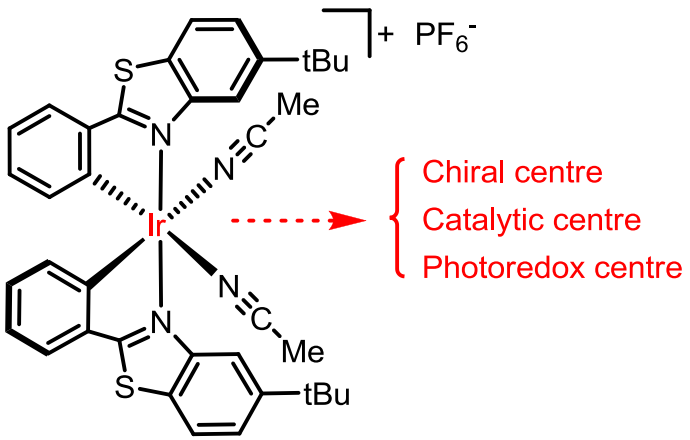


- Part 2: Asymmetric catalysis with these iridium complexes
- Part 3: conclusion

Summary and Outlook



Chiral-At-Metal Octahedral H-Bonding Catalyst



- A coordinated pyrazole acts as a double hydrogen-bond donor to a nitroalkene, and a hydroxymethyl substituent on a benzoxazole ligand serves as a hydrogen-bond acceptor for the incoming nucleophile.
- The iridium centre acts as a chiral centre, a catalytic centre, and a photoredox centre.
- Their research methods are similar with our development of fluorinated sulfone or sulfoximine reagents. They change the activity of iridium complex by regulation of the substituents, and we regular the nature of sulfone or sulfoximine reagents by changing functional groups .

Thanks for your attention