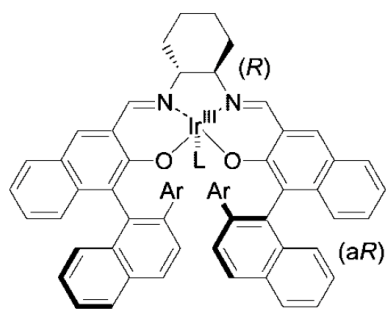
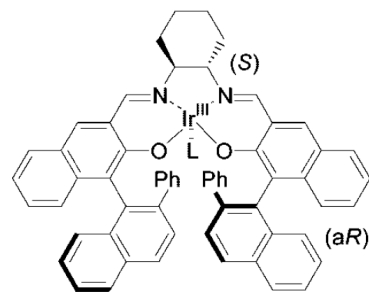


# Construction of Aryliridium – Salen Complexes: Enantio- and *Cis*-Selective Cyclopropanation of Conjugated and Nonconjugated Olefins

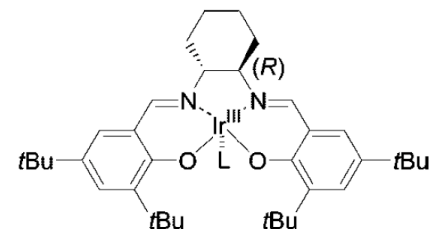
Katsuki *et al.* *JACS* ASAP.



- 2 : L= *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, Ar= Ph
- 3 : L= *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, Ar= H
- 4 : L= C<sub>6</sub>H<sub>5</sub>, Ar= Ph



- 5 : L= *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>



- 6 : L= *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>

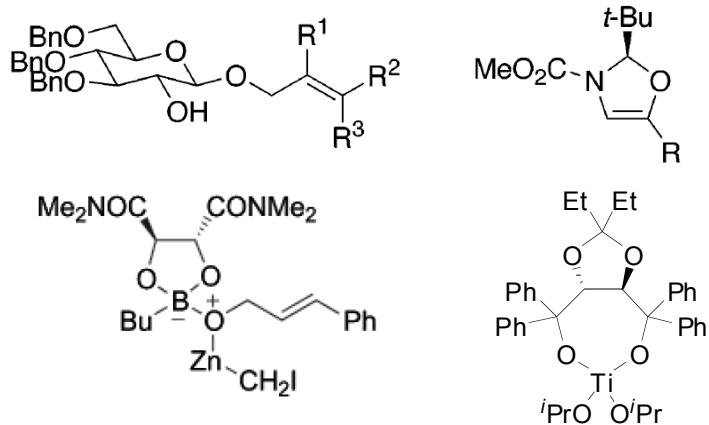
Marija Manojlović

Wipf Group Current Literature Meeting

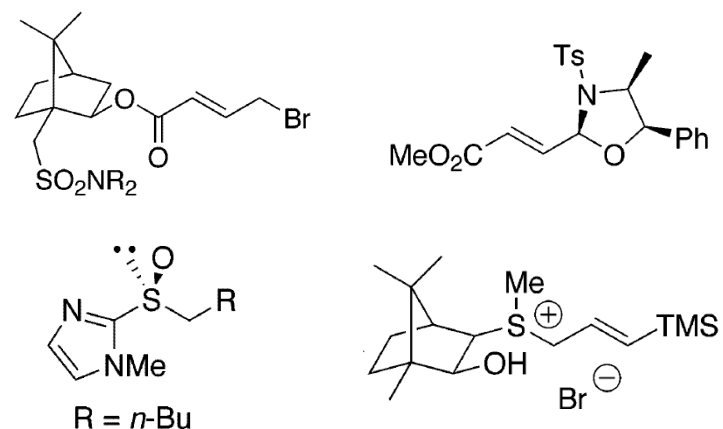
7-19-08

# Asymmetric Cyclopropanation

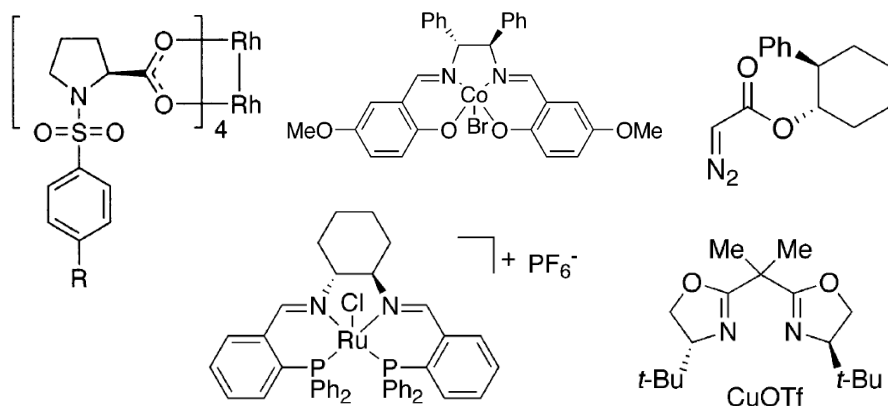
## Halometalmethyl mediated



## Michael Initiated Ring Closure

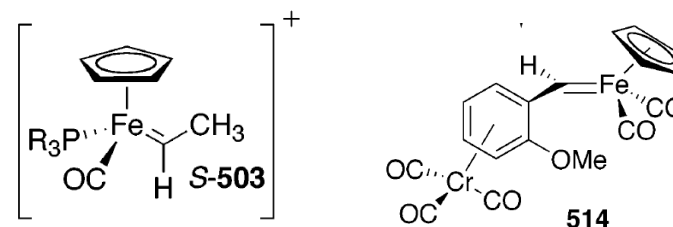


## Transition Metal Catalyzed Decomposition of Diazomethane



## Other Methods

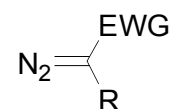
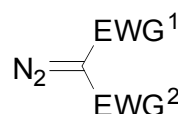
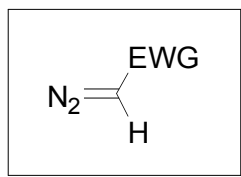
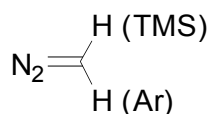
- Enzyme catalyzed kinetic resolution
- Chiral Stoichiometric Carbenes



Chem. Rev. **2003**, 103, 977.

# Transition Metal Catalyzed Decomposition of Diazoalkanes

Four main types of diazoalkanes:



Transition metals used:

hydrogen 1 H 1.0079																	helium 2 He 4.0026	
lithium 3 Li 6.941	beryllium 4 Be 9.0122																	neon 10 Ne 20.180
sodium 11 Na 22.990	magnesium 12 Mg 24.305																	argon 18 Ar 39.948
potassium 19 K 39.098	calcium 20 Ca 40.078	scandium 21 Sc 44.956	titanium 22 Ti 47.867	vanadium 23 V 50.942	chromium 24 Cr 51.996	manganese 25 Mn 54.938	iron 26 Fe 55.845	cobalt 27 Co 58.933	nickel 28 Ni 58.693	copper 29 Cu 63.546	zinc 30 Zn 65.38	gallium 31 Ga 69.723	germanium 32 Ge 72.61	arsenic 33 As 74.922	selenium 34 Se 78.96	bromine 35 Br 79.904	krypton 36 Kr 83.80	
rubidium 37 Rb 85.468	strontium 38 Sr 87.62	yttrium 39 Y 88.906	zirconium 40 Zr 91.224	niobium 41 Nb 92.906	molybdenum 42 Mo 95.94	technetium 43 Tc 98	ruthenium 44 Ru 101.07	rhodium 45 Rh 101.07	paladium 46 Pd 106.36	silver 47 Ag 107.87	cadmium 48 Cd 112.41	indium 49 In 114.82	tin 50 Sn 118.71	antimony 51 Sb 121.76	tellurium 52 Te 127.60	iodine 53 I 126.90	xenon 54 Xe 131.29	
cesium 55 Cs 132.91	barium 56 Ba 137.33	lanthanum 57-70 Lu 174.97	hafnium 71 Hf 178.49	tantalum 72 Ta 180.95	tungsten 73 W 183.84	reuterium 74 Re 186.21	osmium 75 Os 192.22	iridium 76 Ir 192.22	platinum 77 Pt 195.08	gold 78 Au 196.97	mercury 79 Hg 200.59	thallium 80 Tl 204.38	lead 81 Pb 207.2	bismuth 82 Bi 208.98	polonium 83-84 Po [209]	astatine 85 At [210]	radon 86 Rn [222]	
francium 87 Fr [223]	radium 88 Ra [226]	actinium 89-102 Lr [260]	rutherfordium 103 Rf [261]	dubnium 104 Db [262]	seaborgium 105 Sg [266]	bohrium 106 Bh [264]	hassium 107 Hs [265]	meitnerium 108 Mt [268]	darmstadtium 109 Ds [271]	roentgenium 110 Rg [272]	unbinilium 111 Uub [273]	untrium 112 Uut [277]	ununquadium 114 Uuq [289]					

- In most cases mechanism is believed to proceed through metal carbene.

- Cu, Rh, Ru and Co metal carbenes react faster with electron-rich alkenes; Pd carbenes are optimal for electron-deficient alkene.

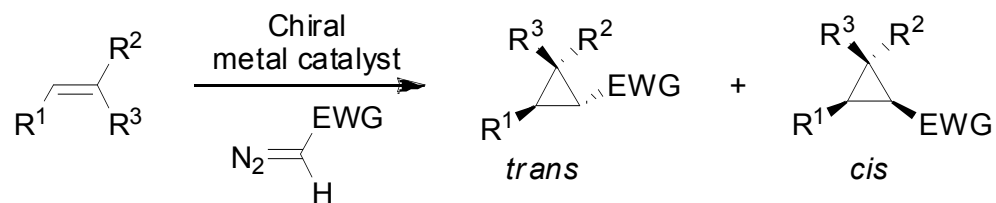
\* Lanthanide series

lanthanum 57 La 138.91	cerium 58 Ce 140.12	praseodymium 59 Pr 140.91	neodymium 60 Nd 144.24	promethium 61 Pm [145]	samarium 62 Sm 150.36	europium 63 Eu 151.96	gadolinium 64 Gd 157.25	terbium 65 Tb 158.93	dysprosium 66 Dy 162.50	holmium 67 Ho 164.93	erbium 68 Er 167.26	thulium 69 Tm 168.93	ytterbium 70 Yb 173.04
actinium 89 Ac [227]	thorium 90 Th 232.04	protactinium 91 Pa 231.04	uranium 92 U 238.03	neptunium 93 Np [237]	plutonium 94 Pu [244]	americium 95 Am [243]	curium 96 Cm [247]	berkelium 97 Bk [247]	californium 98 Cf [251]	einsteinium 99 Es [252]	fermium 100 Fm [257]	mendelevium 101 Md [258]	nobelium 102 No [259]

\*\* Actinide series

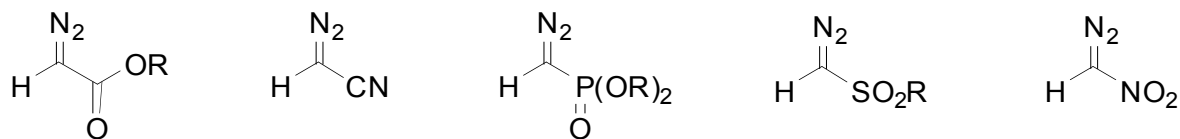
Chem. Rev. 2003, 103, 977.

# Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview



R<sup>1</sup> = Aryl or vinyl, Metal = Ru, Rh, Co, Cu, Au

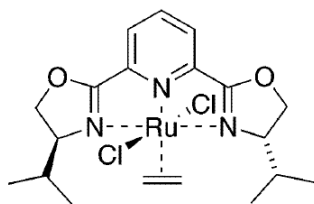
The most common carbene sources:



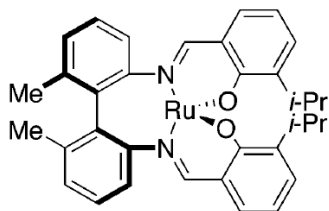
*Chem. Rev.* **2003**, 103, 977.

# Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview

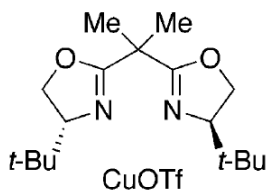
## Trans selective catalysts



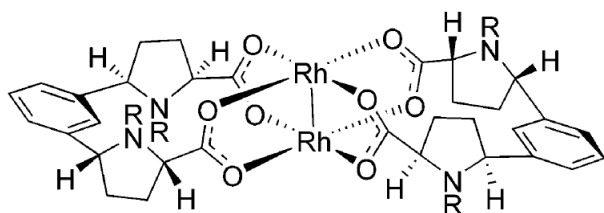
**1**



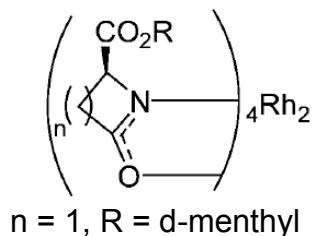
**2**



**3**

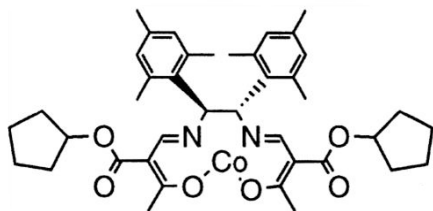


**4**



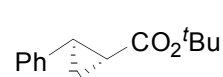
n = 1, R = d-menthyl

**5**

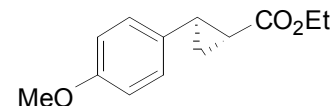


**6**

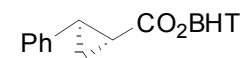
## Product scope



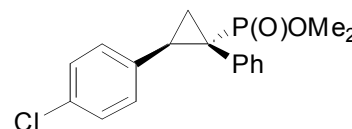
Catalyst 1, 65%  
trans : cis 97:3  
94% ee



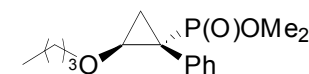
Catalyst 2, 89%  
trans : cis 96:4  
86% ee



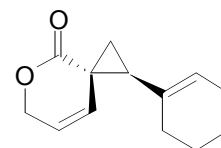
Catalyst 3, 85%  
trans : cis 94:6  
99% ee



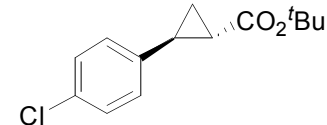
Catalyst 4, 95%  
trans : cis 99:1  
85% ee



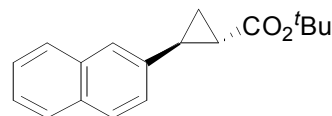
Catalyst 4, 91%  
trans : cis 72:28  
86% ee



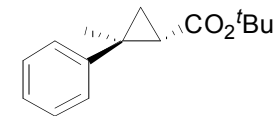
Catalyst 5, 77%  
trans : cis > 20:1  
80% ee



Catalyst 6, 93%  
trans : cis 90:10  
96% ee



Catalyst 6, 95%  
trans : cis 87:13  
96% ee



Catalyst 6, 93%  
trans : cis 47:53  
99 (93) % ee

*Chem. Rev.* **2003**, 103, 977.

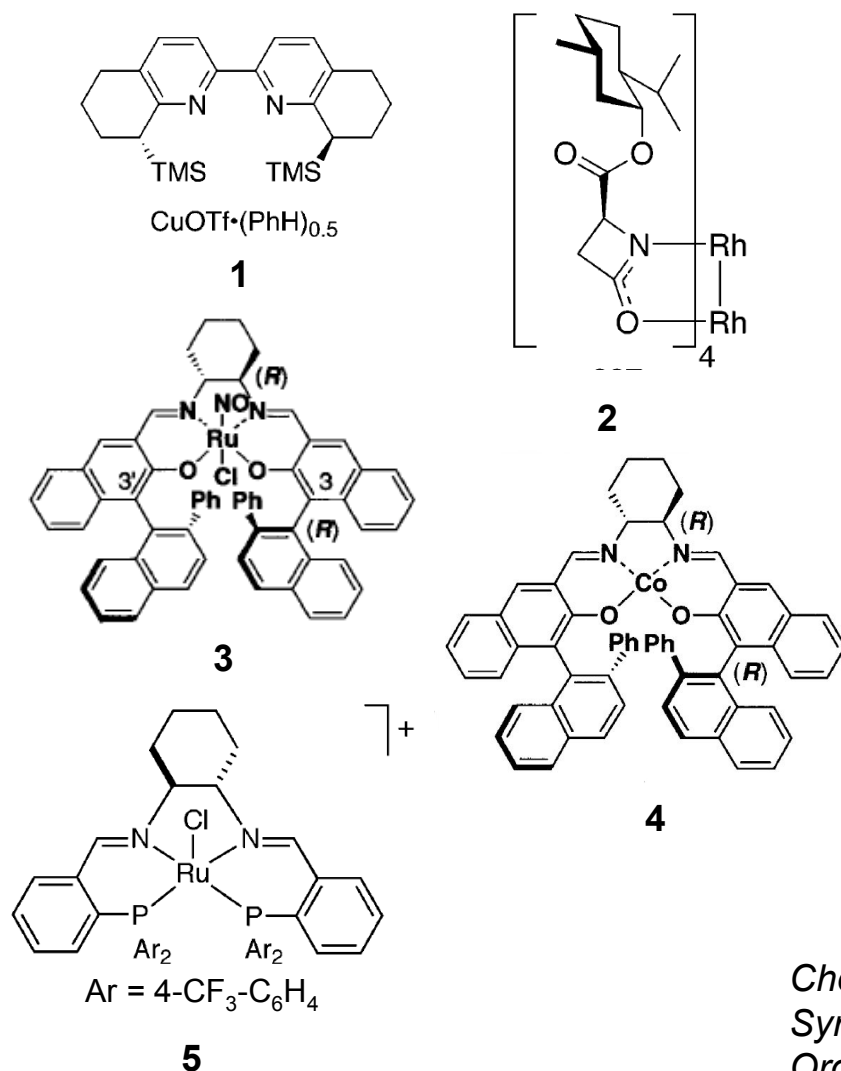
*Org. Lett.* **2006**, 8, 3437.

*ACIE* **1992**, 31, 430.

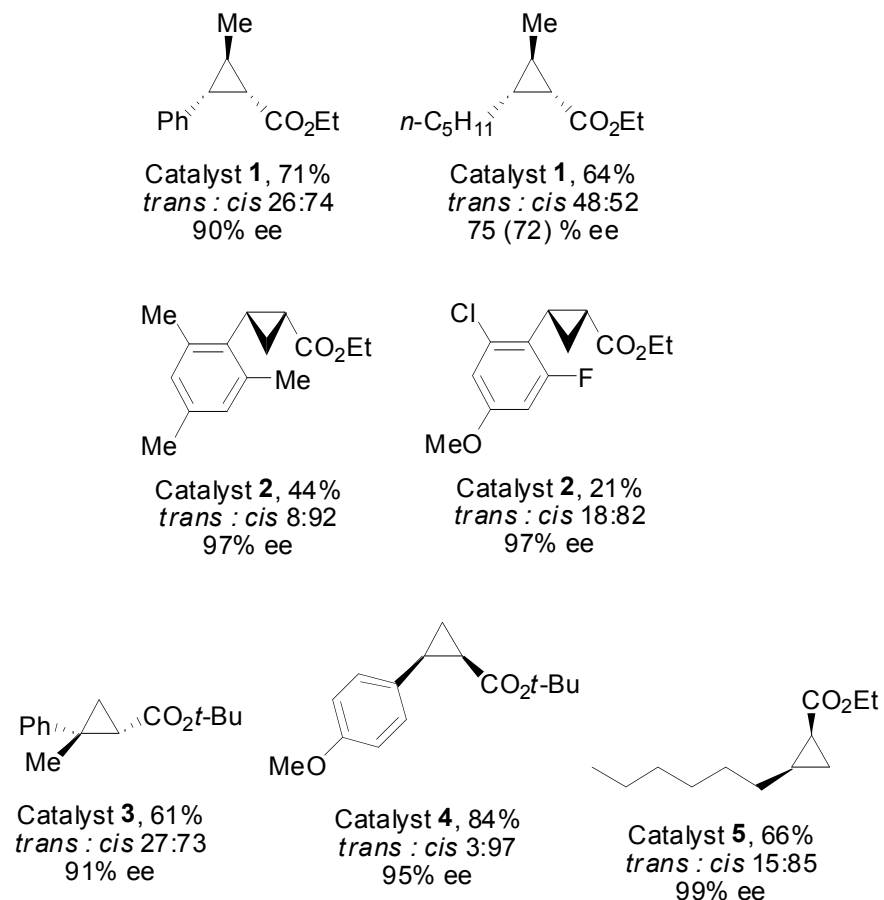
*Bull. Chem. Soc. Jpn.* **2001**, 74, 2139.

# Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview

## Cis selective catalysts



## Product scope



*Chem. Rev.* **2003**, *103*, 977.

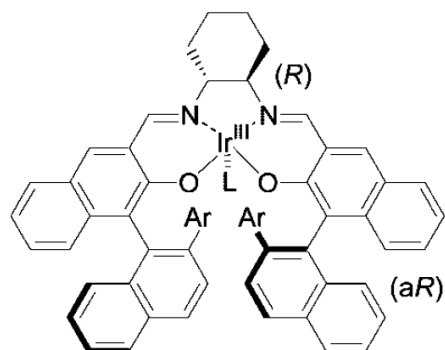
*Synlett* **1993**, 638.

*Synlett* **1999**, 1793.

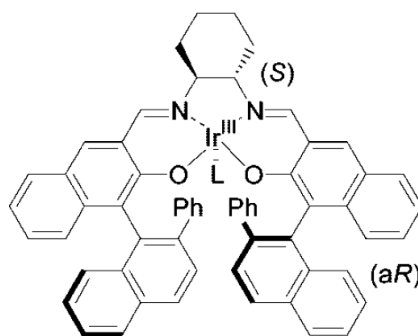
*Tetrahedron Lett.* **2000**, *41*, 3647.

*Organometallics* **2001**, *20*, 2120.

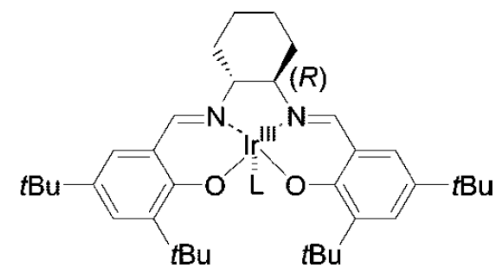
# Title Paper – Aryliridium-Salen Complexes



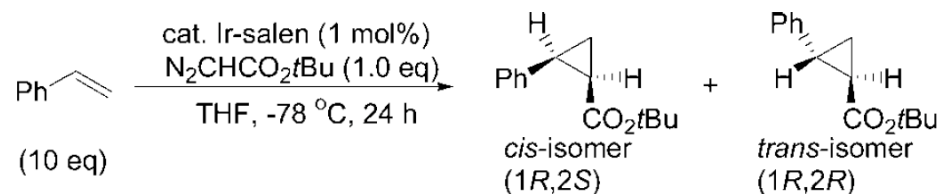
- 2** : L = *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, Ar = Ph  
**3** : L = *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, Ar = H  
**4** : L = C<sub>6</sub>H<sub>5</sub>, Ar = Ph



- 5** : L = *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>



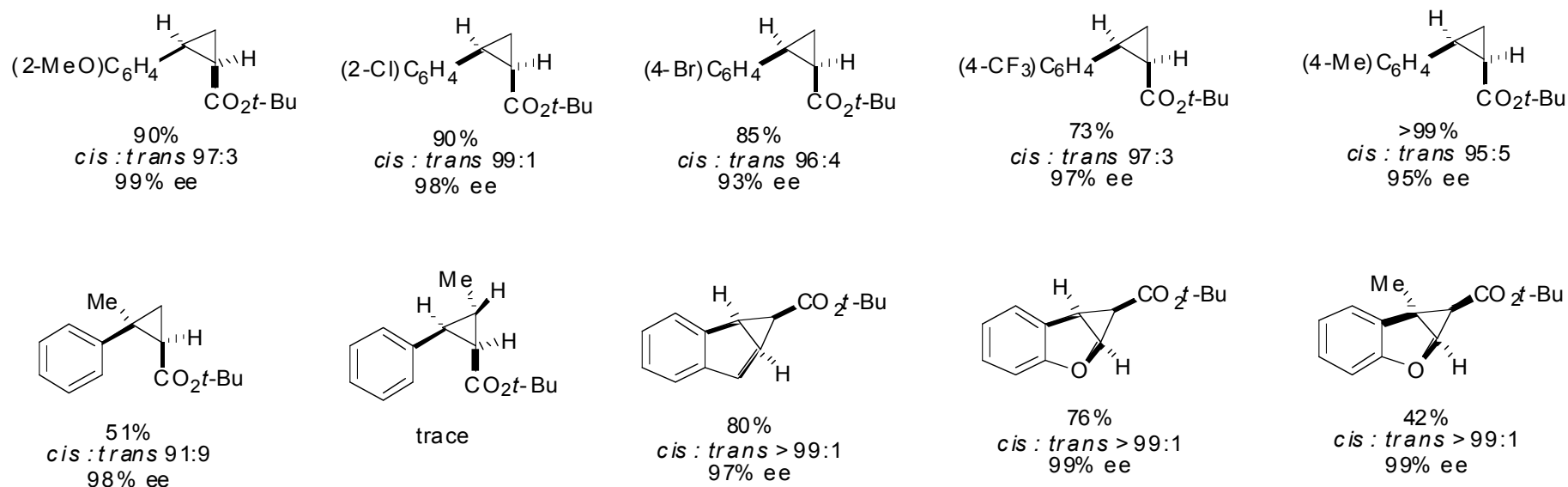
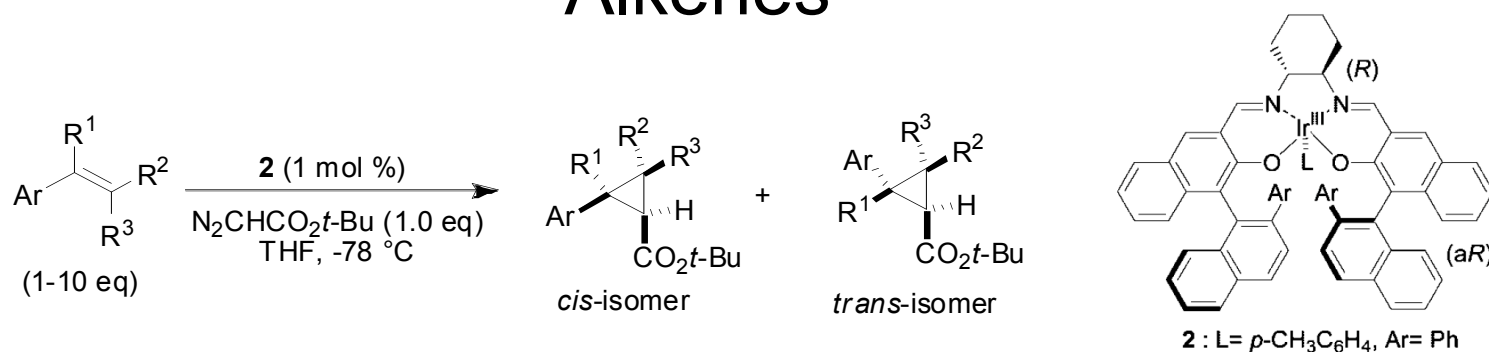
- 6** : L = *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>



entry	catalyst	yield/% <sup>b</sup>	<i>cis:trans</i> <sup>c</sup>	% ee <sub><i>cis</i></sub> <sup>d</sup>	% ee <sub><i>trans</i></sub> <sup>d</sup>
1	<b>2</b>	99	>99:1	>99 <sup>e</sup>	
2	<b>3</b>	44	41:59	63 <sup>e</sup>	60 <sup>f</sup>
3	<b>4</b>	99	>99:1	98 <sup>e</sup>	
4	<b>5</b>	43	58:42	-37 <sup>g</sup>	70 <sup>f</sup>
5	<b>6</b>	25	29:71	1	1

Katsuki *et al.* JACS, ASAP.

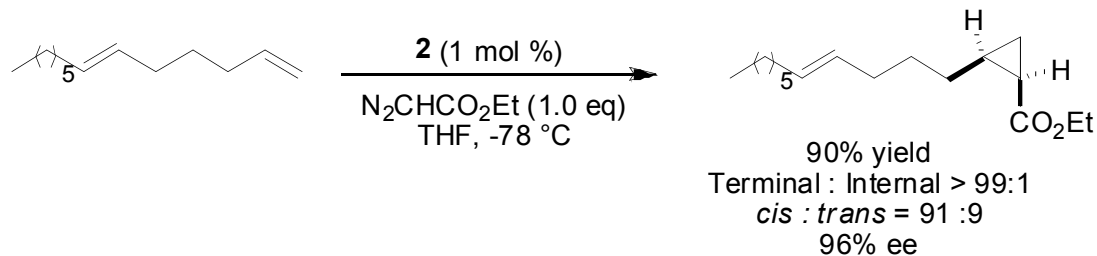
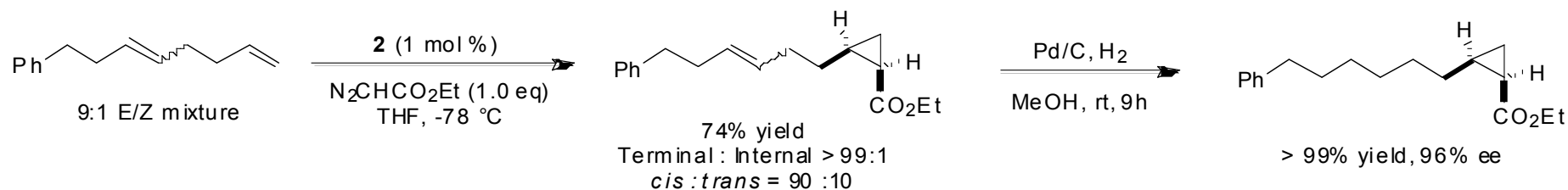
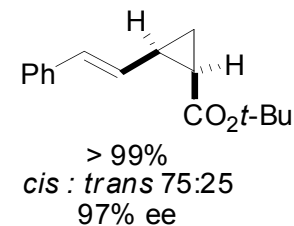
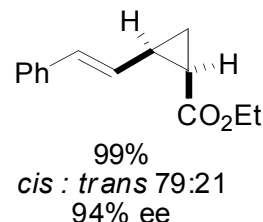
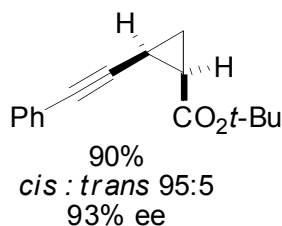
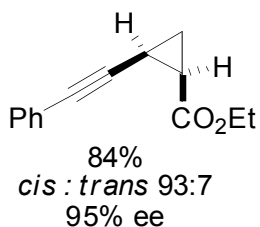
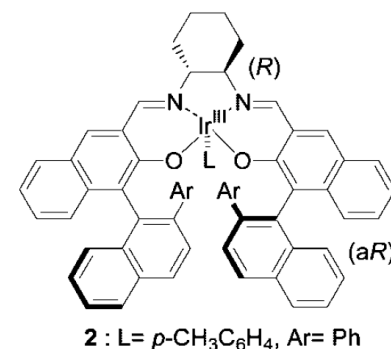
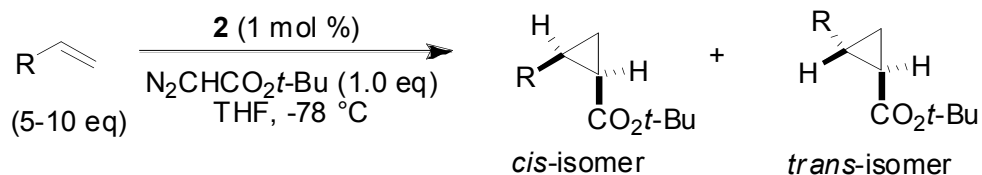
# Title Paper – Cyclopropanation of Conjugated Alkenes



Katsuki *et al.* *JACS*, ASAP.

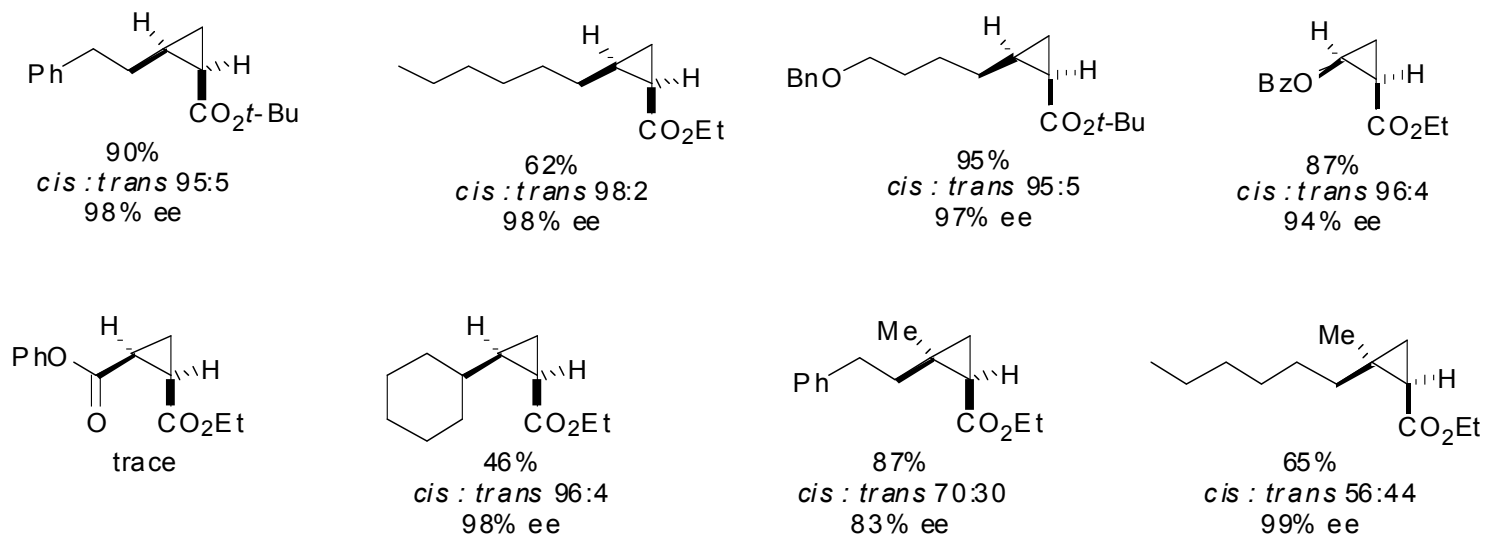
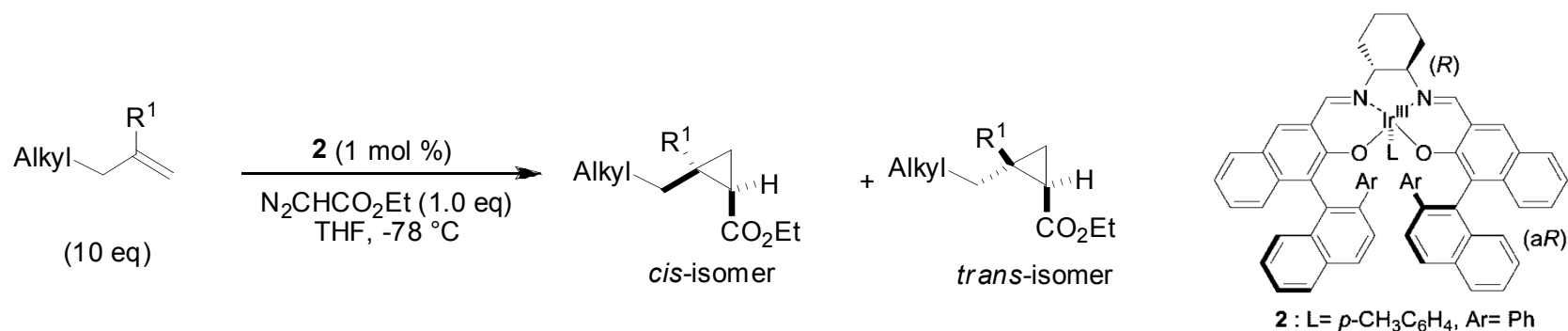


# Title Paper – Cyclopropanation of Dienes and Eneynes



Katsuki *et al.* *JACS*, ASAP.

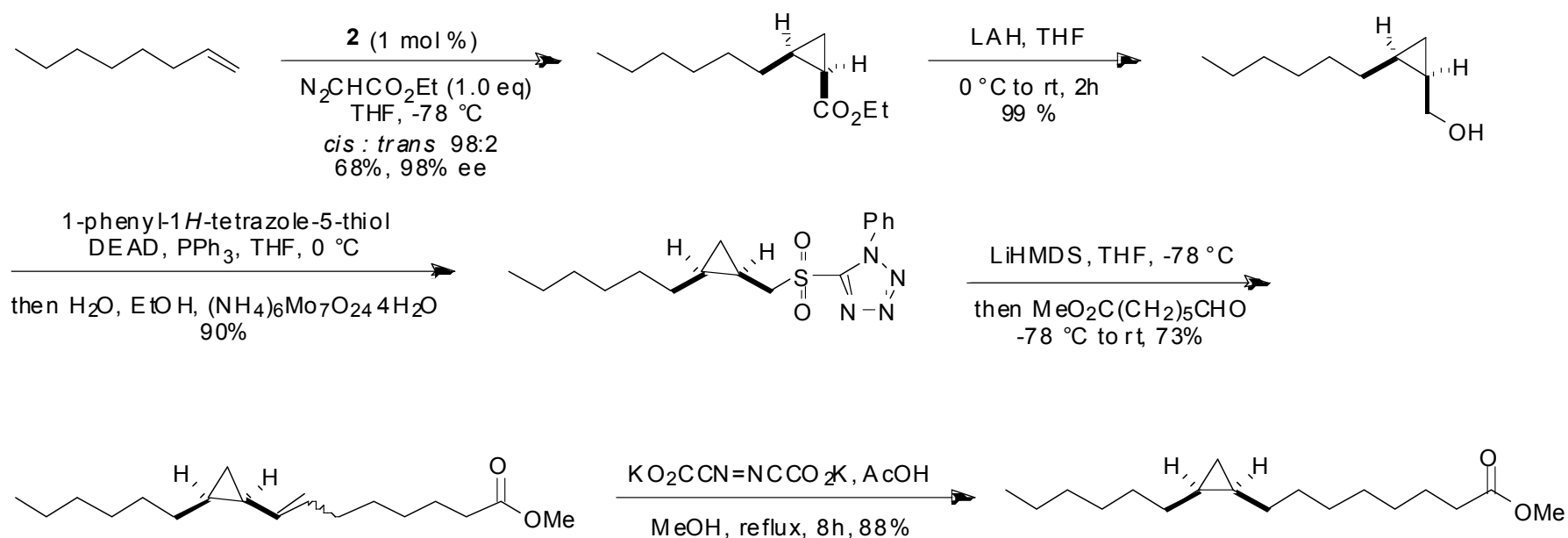
# Title Paper – Cyclopropanation of Nonactivated Alkenes



Katsuki *et al.* *JACS*, ASAP.

# Synthesis of 8-[(1*R*,2*S*)-2-hexylcyclopropyl]octanoate

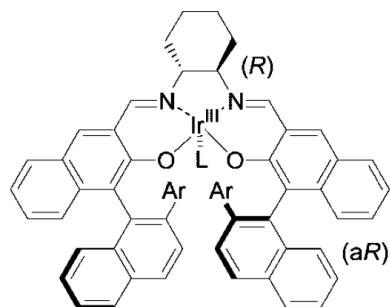
- Cyclopropyl fatty acid ester, isolated from *Escherichia coli*



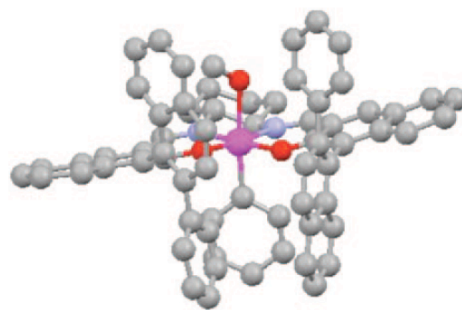
Katsuki *et al.* JACS, ASAP.

# Title Paper – Mechanistic Considerations

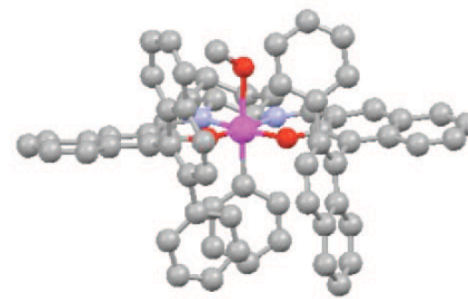
-Crystal structure of the catalyst 4



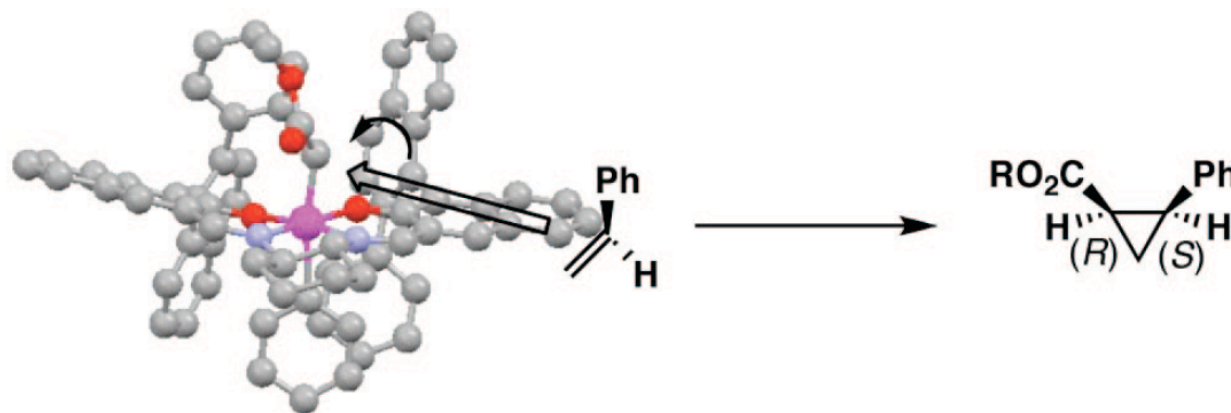
4 : L = C<sub>6</sub>H<sub>5</sub>, Ar = Ph



S1



S2



carbenoid intermediate: horizontal view from the cyclohexane side

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# Conclusions

- First stable Ir(III) salen complexes that carry apical aryl ligand were synthesized
- Two of these complexes are shown to be unique and potent catalysts for *cis*-selective asymmetric cyclopropanation
- More than 30 different *cis*-cyclopropyl esters were made in excellent yields and selectivities starting from both conjugated and unactivated alkenes
- This cyclopropanation was applied to the synthesis of natural cyclopropyl fatty acid ester