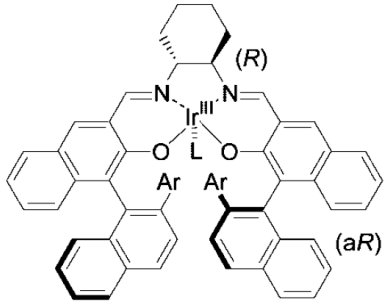
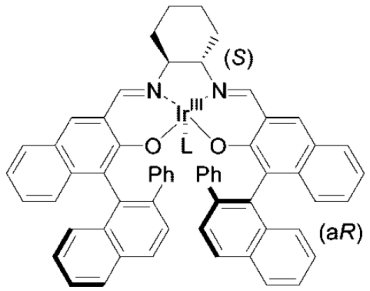
Construction of Aryliridium – Salen Complexes: Enantio- and *Cis*-Selective Cyclopropanation of Conjugated and Nonconjugated Olefins

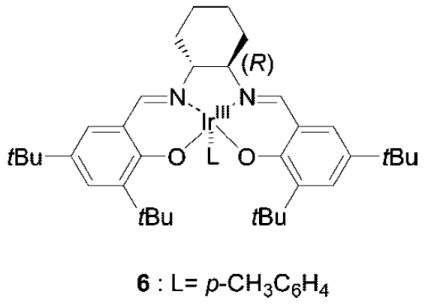
Katsuki *et al. JACS ASAP.*



2 : L= *p*-$CH_3C_6H_4$, Ar= Ph
3 : L= *p*-$CH_3C_6H_4$, Ar= H
4 : L= C_6H_5, Ar= Ph



5 : L= *p*-$CH_3C_6H_4$



6 : L= *p*-$CH_3C_6H_4$

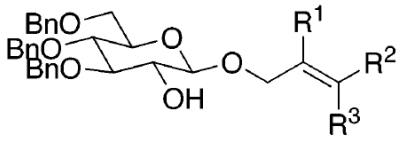
Marija Manojlović

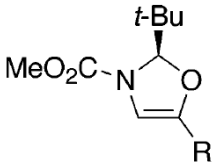
Wipf Group Current Litarature Meeting

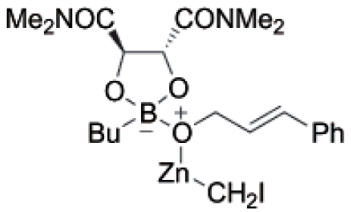
7-19-08

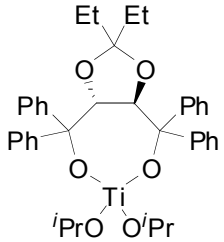
Asymmetric Cyclopropanation

Halometalmethyl mediated

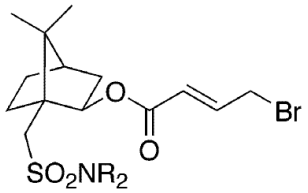


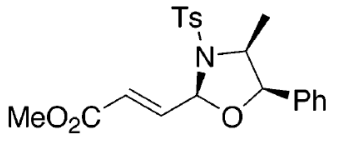


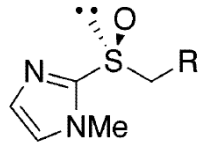




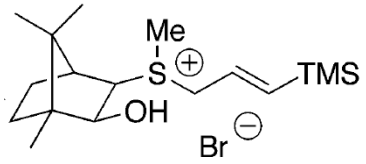
Michael Initiated Ring Closure



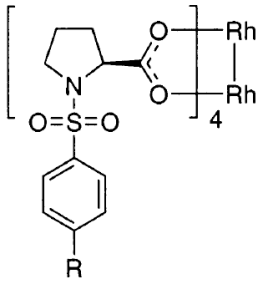


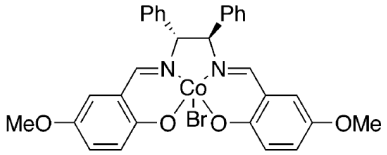


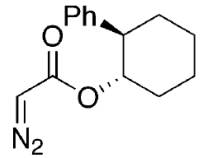
R = *n*-Bu

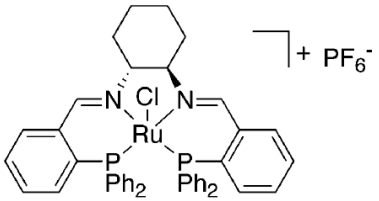


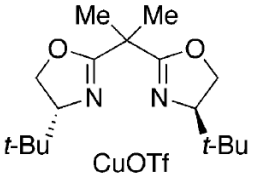
Transition Metal Catalyzed Decomposition of Diazomethane





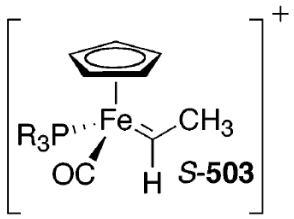


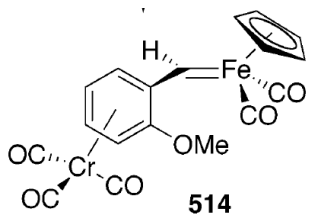




Other Methods

- Enzyme catalyzed kinetic resolution
- Chiral Stoichiometric Carbenes



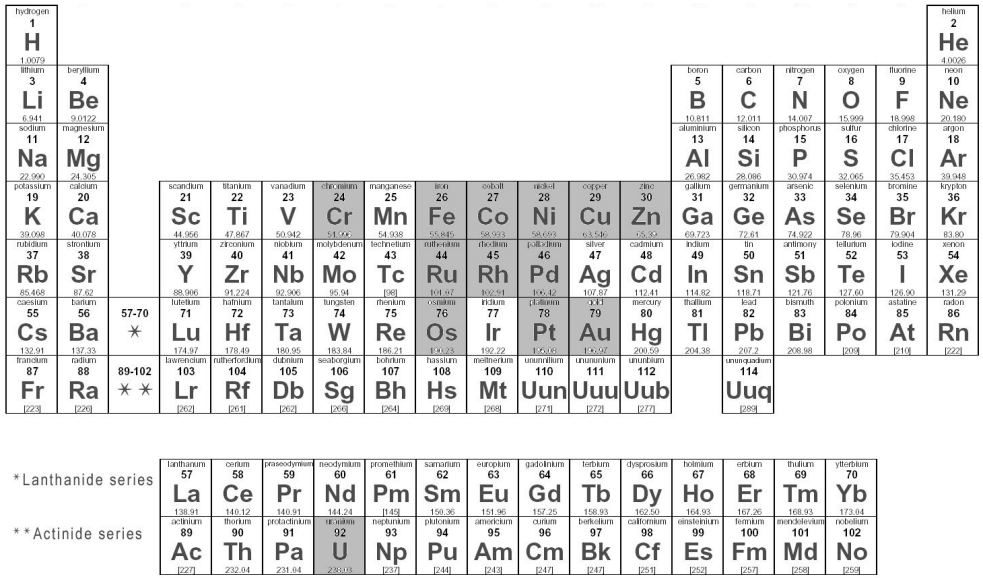


Chem. Rev. **2003**, *103*, 977.

Transition Metal Catalyzed Decomposition of Diazoalkanes

Four main types of diazoalkanes:

Transition metals used:

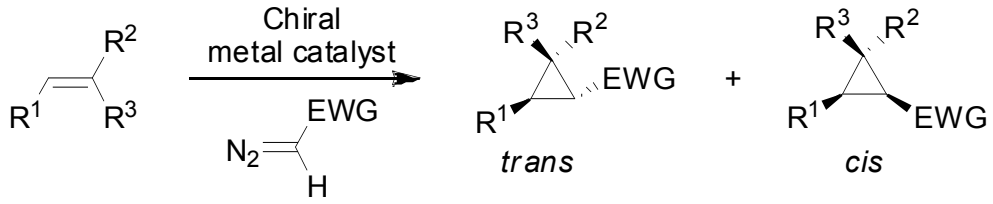


- In most cases mechanism is believed to proceed through metal carbene.

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

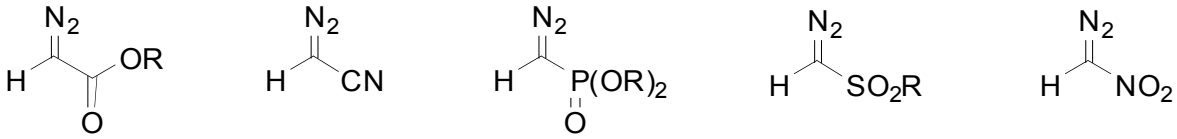
Chem. Rev. **2003**, *103*, 977.

Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview



R^1 = Aryl or vinyl, Metal = Ru, Rh, Co, Cu, Au

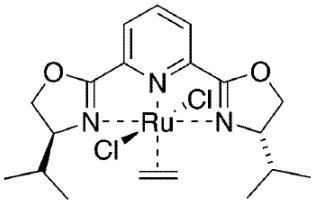
The most common carbene sources:



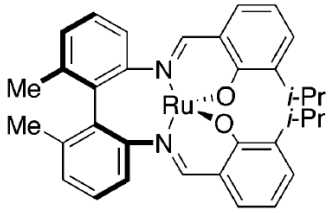
Chem. Rev. **2003**, *103*, 977.

Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview

Trans selective catalysts



1



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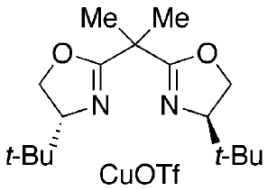
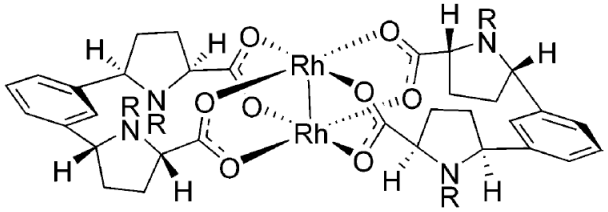


3



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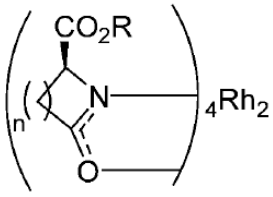
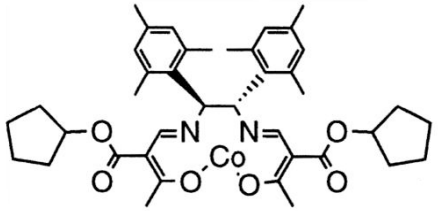


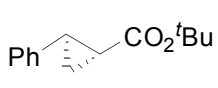
n = 1, R = d-menthyl

5

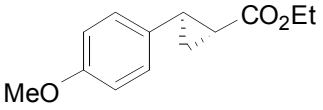


6

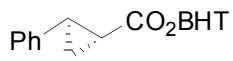
Product scope



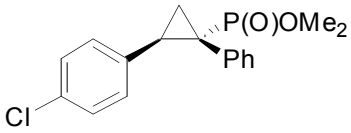
Catalyst **1**, 65%
trans : cis 97:3
94% ee



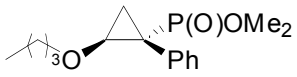
Catalyst **2**, 89%
trans : cis 96:4
86% ee



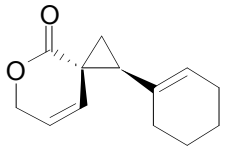
Catalyst **3**, 85%
trans : cis 94:6
99% ee



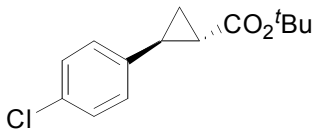
Catalyst **4**, 95%
trans : cis 99:1
85% ee



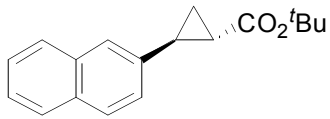
Catalyst **4**, 91%
trans : cis 72:28
86% ee



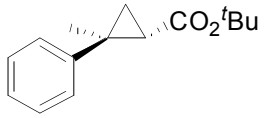
Catalyst **5**, 77%
trans : cis > 20:1
80% ee



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



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

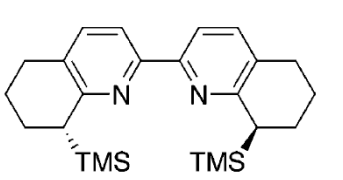


Catalyst **6**, 93%
trans : cis 47:53
99 (93) % ee

Chem. Rev. **2003**, *103*, 977. *ACIE* **1992**, *31*, 430.
Org. Lett. **2006**, *8*, 3437. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 2139.

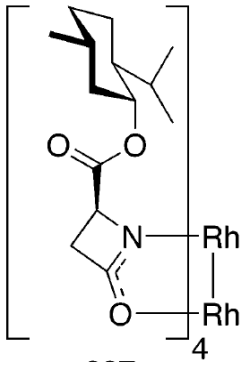
Transition Metal Catalyzed Asymmetric Carbene Transfer Cyclopropanation - Overview

Cis selective catalysts



$CuOTf\cdot(PhH)_{0.5}$

1



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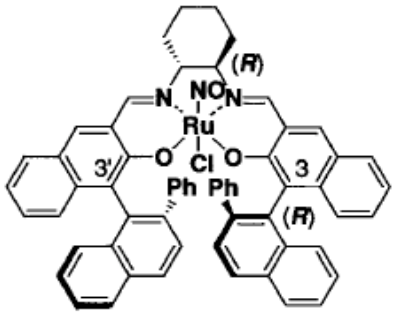

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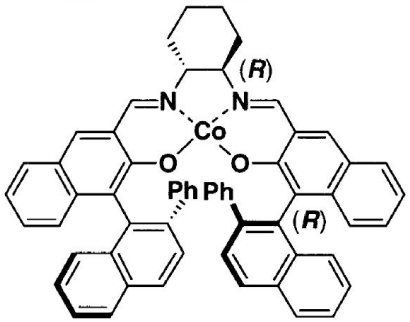

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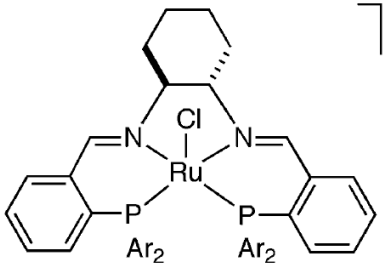
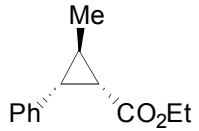


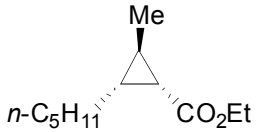
Ar = 4-CF_3-C_6H_4

5

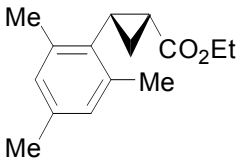
Product scope



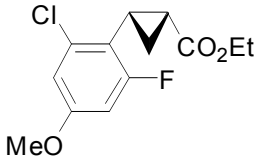
Catalyst **1**, 71%
trans : cis 26:74
90% ee



Catalyst **1**, 64%
trans : cis 48:52
75 (72) % ee

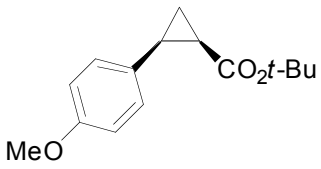


Catalyst **2**, 44%
trans : cis 8:92
97% ee

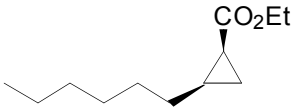


Catalyst **2**, 21%
trans : cis 18:82
97% ee

Catalyst **3**, 61%
trans : cis 27:73
91% ee



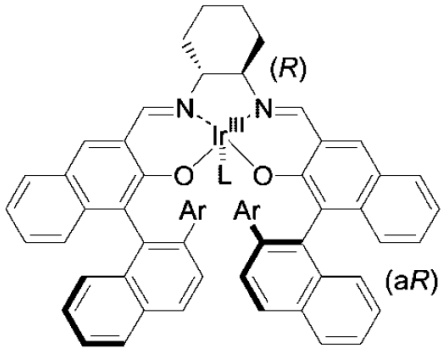
Catalyst **4**, 84%
trans : cis 3:97
95% ee



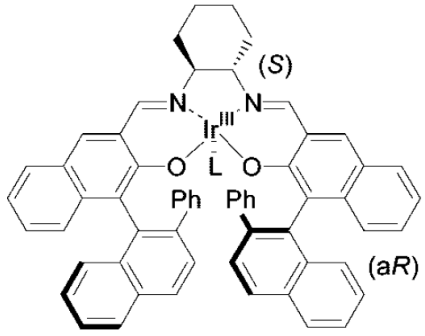
Catalyst **5**, 66%
trans : cis 15:85
99% ee

Chem. Rev. **2003**, *103*, 977. *Synlett* **1993**, 638.
Synlett **1999**, 1793. *Tetrahedron Lett.* **2000**, *41*, 3647.
Organometallics **2001**, *20*, 2120.

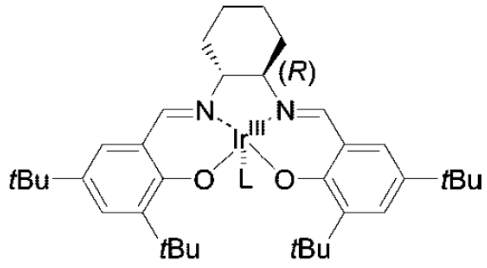
Title Paper – Aryliridium-Salen Complexes



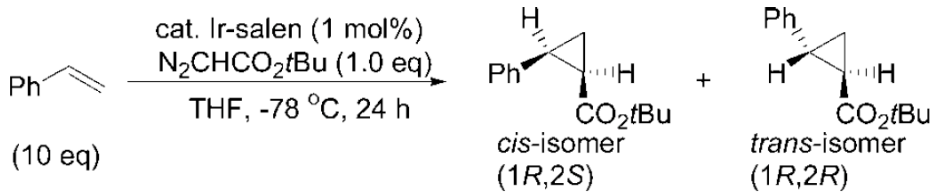
2 : L= *p*-$CH_3C_6H_4$, Ar= Ph
3 : L= *p*-$CH_3C_6H_4$, Ar= H
4 : L= C_6H_5, Ar= Ph



5 : L= *p*-$CH_3C_6H_4$



6 : L= *p*-$CH_3C_6H_4$



entry	catalyst	yield/%[b]	*cis*:*trans*[c]	% ee_{cis}[d]	% ee_{trans}[d]
1	**2**	99	>99:1	>99[e]	
2	**3**	44	41:59	63[e]	60[f]
3	**4**	99	>99:1	98[e]	
4	**5**	43	58:42	−37[g]	70[f]
5	**6**	25	29:71	1	1

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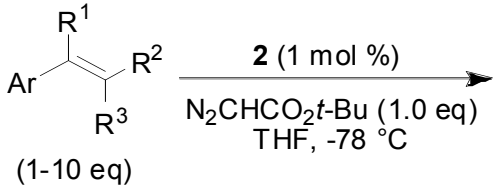
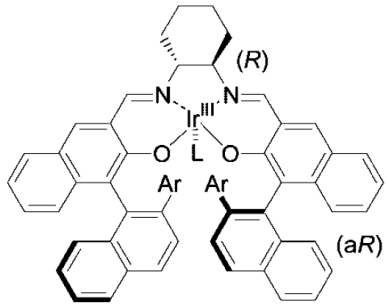
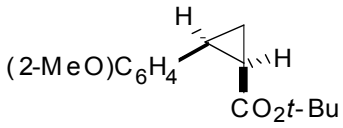
Title Paper – Cyclopropanation of Conjugated Alkenes

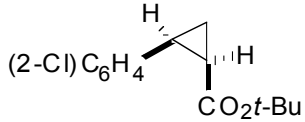




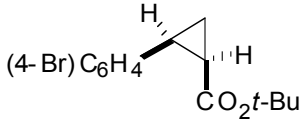
2 : L= *p*-$CH_3C_6H_4$, Ar= Ph



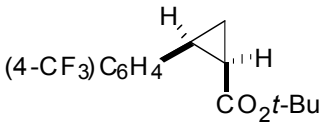
90%
cis : *trans* 97:3
99% ee



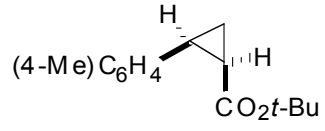
90%
cis : *trans* 99:1
98% ee



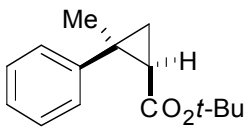
85%
cis : *trans* 96:4
93% ee



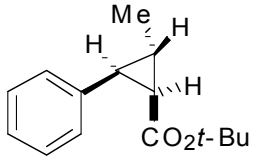
73%
cis : *trans* 97:3
97% ee



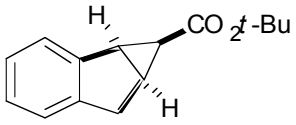
>99%
cis : *trans* 95:5
95% ee



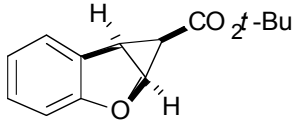
51%
cis : *trans* 91:9
98% ee



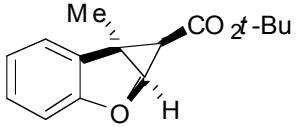
trace



80%
cis : *trans* > 99:1
97% ee



76%
cis : *trans* > 99:1
99% ee



42%
cis : *trans* > 99:1
99% ee

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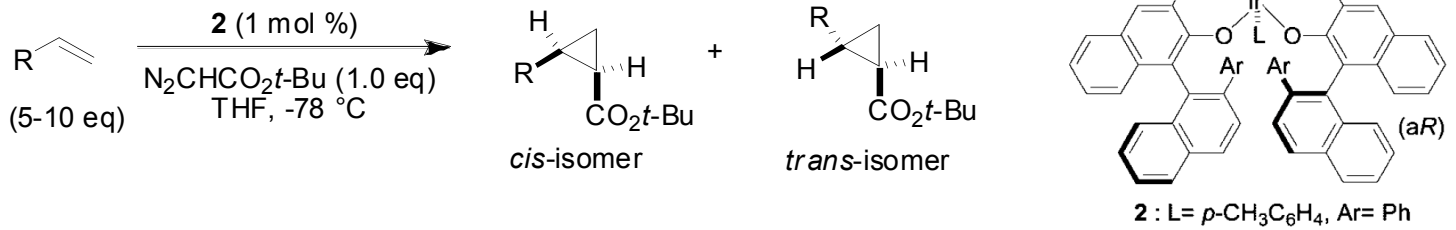
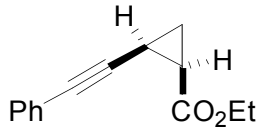
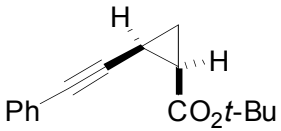
Title Paper – Cyclopropanation of Dienes and Eneynes

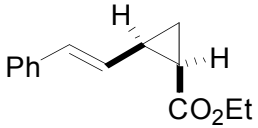




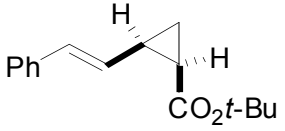
84%
cis : trans 93:7
95% ee



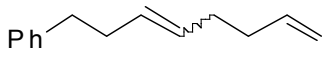
90%
cis : trans 95:5
93% ee



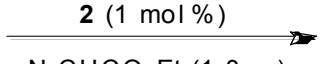
99%
cis : trans 79:21
94% ee

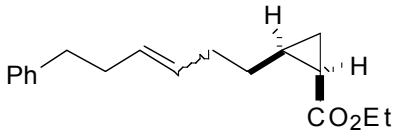


> 99%
cis : trans 75:25
97% ee

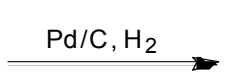


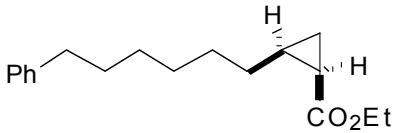
9:1 E/Z mixture



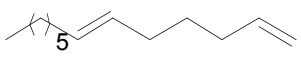


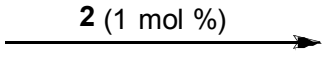
74% yield
Terminal : Internal > 99:1
cis : trans = 90 :10

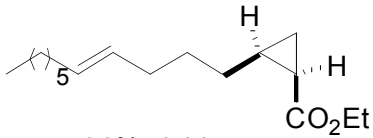




> 99% yield, 96% ee







90% yield
Terminal : Internal > 99:1
cis : trans = 91 :9
96% ee

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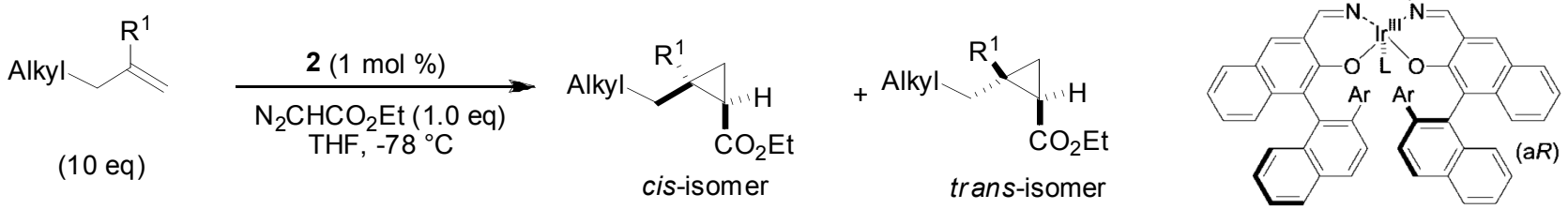
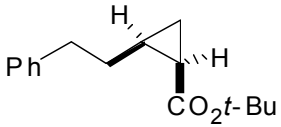
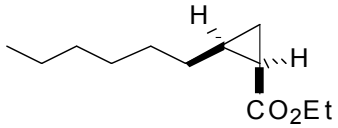
Title Paper – Cyclopropanation of Nonactivated Alkenes

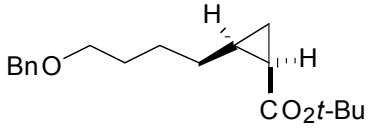




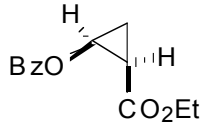
90%
cis : trans 95:5
98% ee



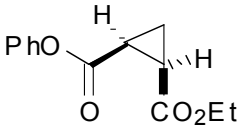
62%
cis : trans 98:2
98% ee



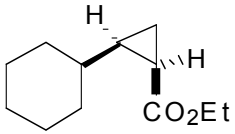
95%
cis : trans 95:5
97% ee



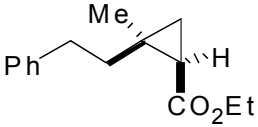
87%
cis : trans 96:4
94% ee



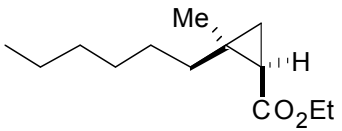
trace



46%
cis : trans 96:4
98% ee



87%
cis : trans 70:30
83% ee



65%
cis : trans 56:44
99% ee

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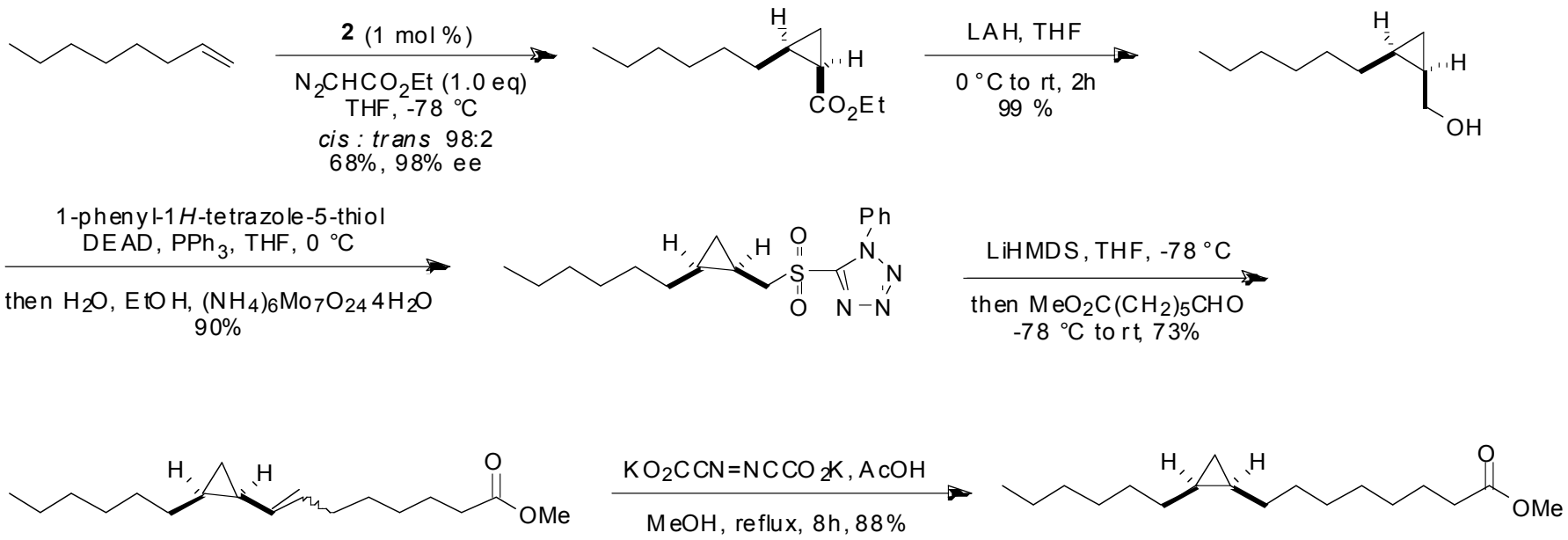
Synthesis of 8-[(1*R*,2*S*)-2-hexylcyclopropyl]octanoate

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



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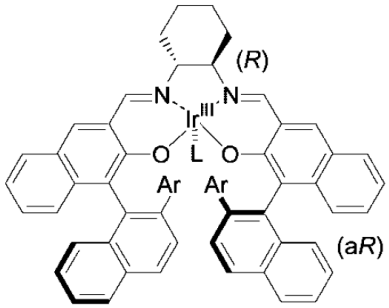
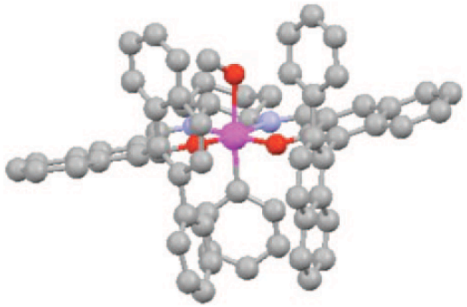
Title Paper – Mechanistic Considerations

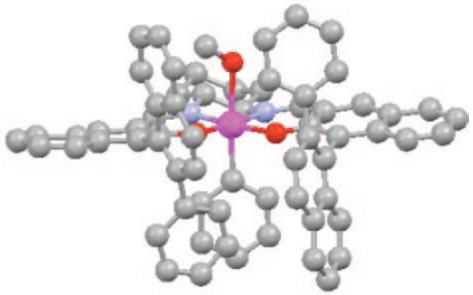
-Crystal structure of the catalyst 4



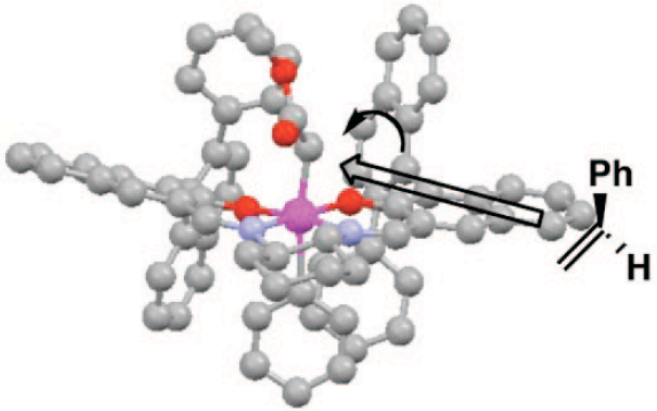
4 : L= C_6H_5, Ar= Ph



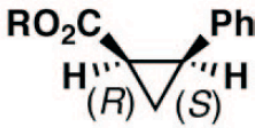
S1



S2



carbenoid inermediate: 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 strating from both conjugated and unactivated alkenes
- This cyclopropanation was applied to the synthesis of natural cyclopropyl fatty acid ester