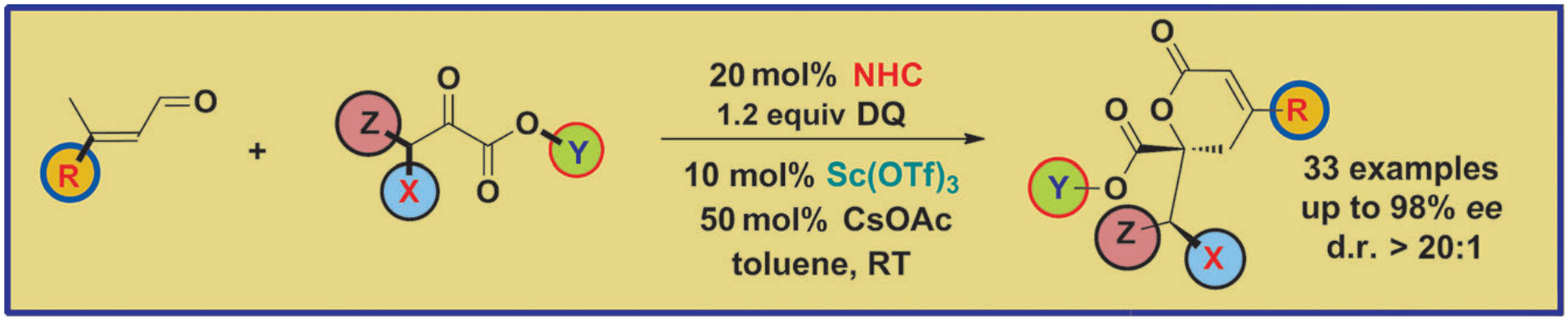
RCC *by* **Prashant Borkar**

(2nd *December 2014*)

"Intermolecular Dynamic Kinetic Resolution Cooperatively Catalyzed by an *N*-Heterocyclic Carbene and a Lewis Acid"

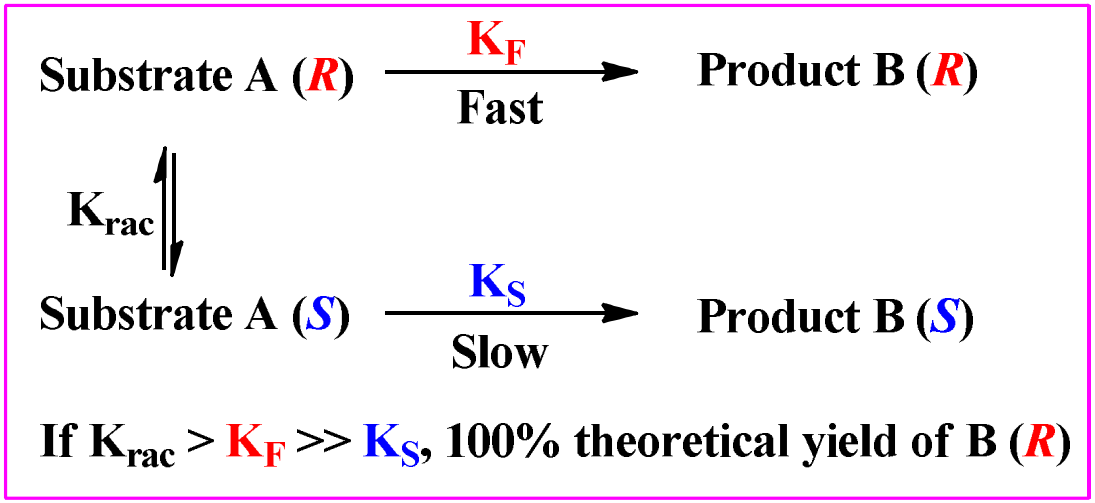
Authors: Zijun Wu, Fangyi Li, and Jian Wang*



Angew. Chem. Int. Ed. 2014, **DOI: 10.1002/anie.201410030**

Introduction

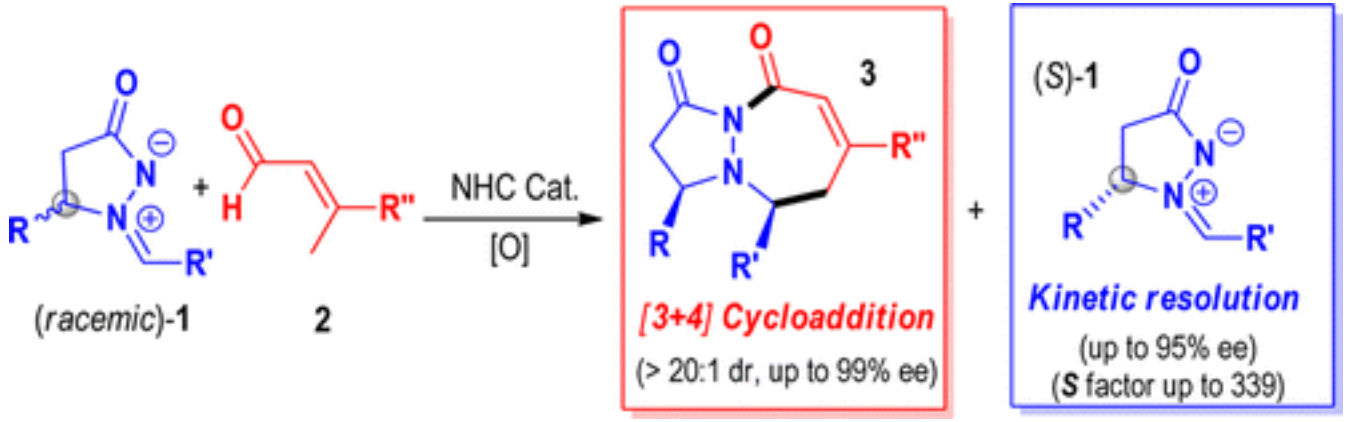
- Organocatalytic Dynamic Kinetic Resolution (DKR) processes are emerging as significant complementary methods for the conversion of racemic starting materials to products with excellent enantio- and/or diastereocontrol.
- Dynamic Kinetic Resolution (DKR) has proven to be a powerful strategy in asymmetric synthesis, allowing the stereoconvergent transformation of both enantiomers of a racemic substrate into a single enantiomer of a target molecule.
- This approach thus overcomes the limitation of traditional kinetic resolutions, which provide a maximum chemical yield of 50% for a particular enantiomer. In contrast, the theoretical yield of an efficient DKR is up to 99%.



Scheme: Dynamic Kinetic Resolution (DKR) process

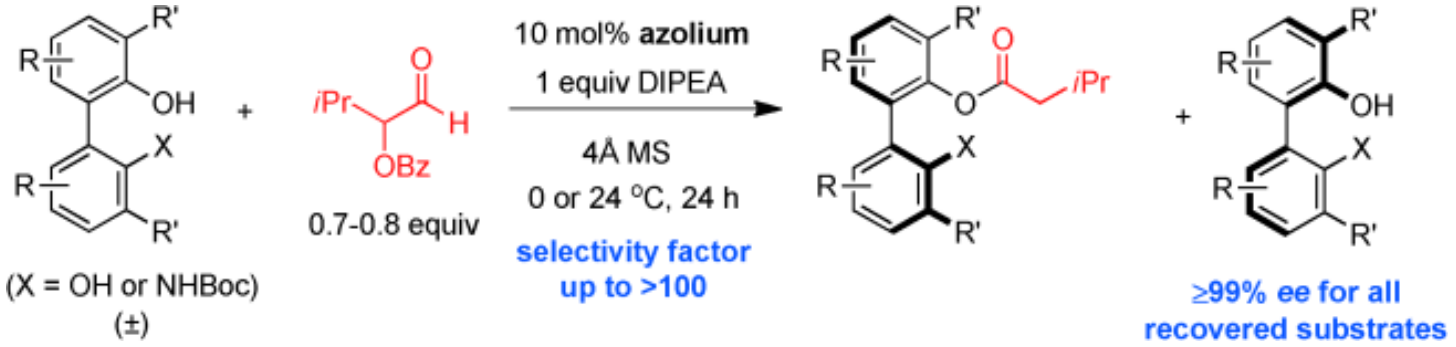
Previous reports on chiral NHC-catalyzed resolutions

KR of azomethine imines



Chi and et.al., J. Am. Chem. Soc. **2014**, *136*, 1214.

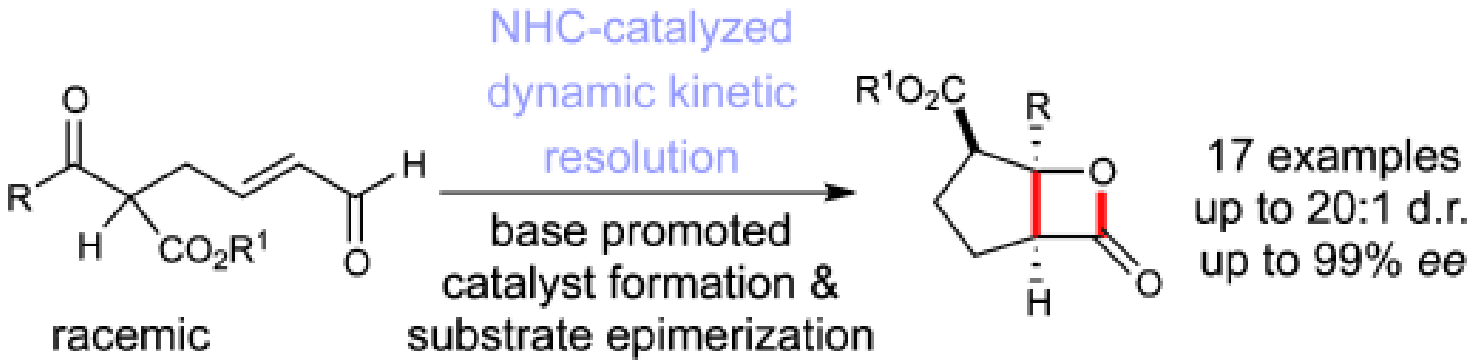
KRs of through Atroposelective esterification



Zhao and co-workers, Angew. Chem. Int. Ed. **2014,** *53*, 11041.

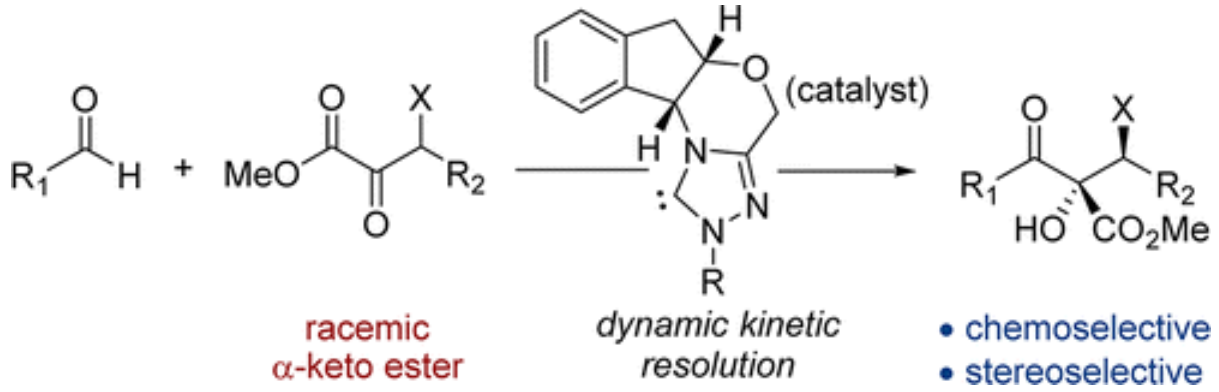
Reports on DKRs Using chiral NHC ligands

Intramolecular DKR



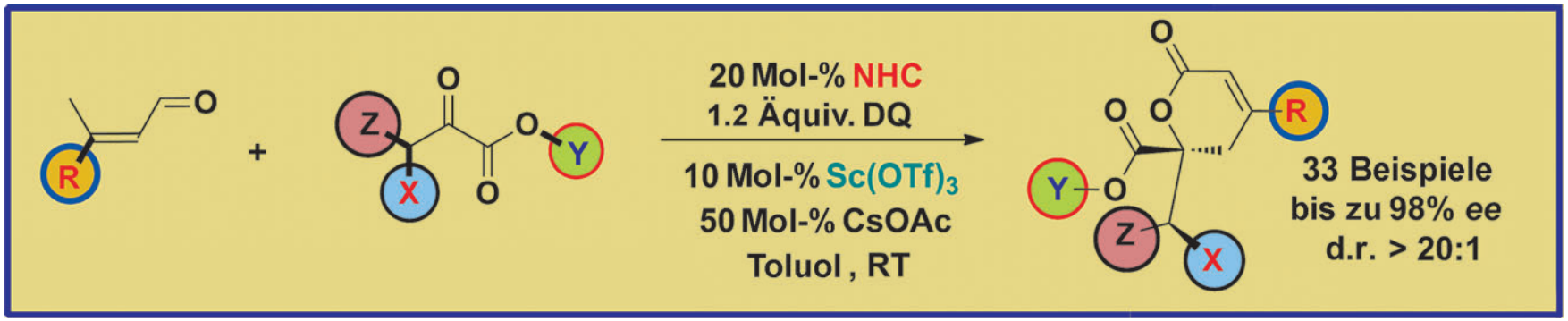
Scheidt, *Angew. Chem. Int. Ed.* **2012,** *51*, 7309.

Asymmetric Cross-Benzoin Addition

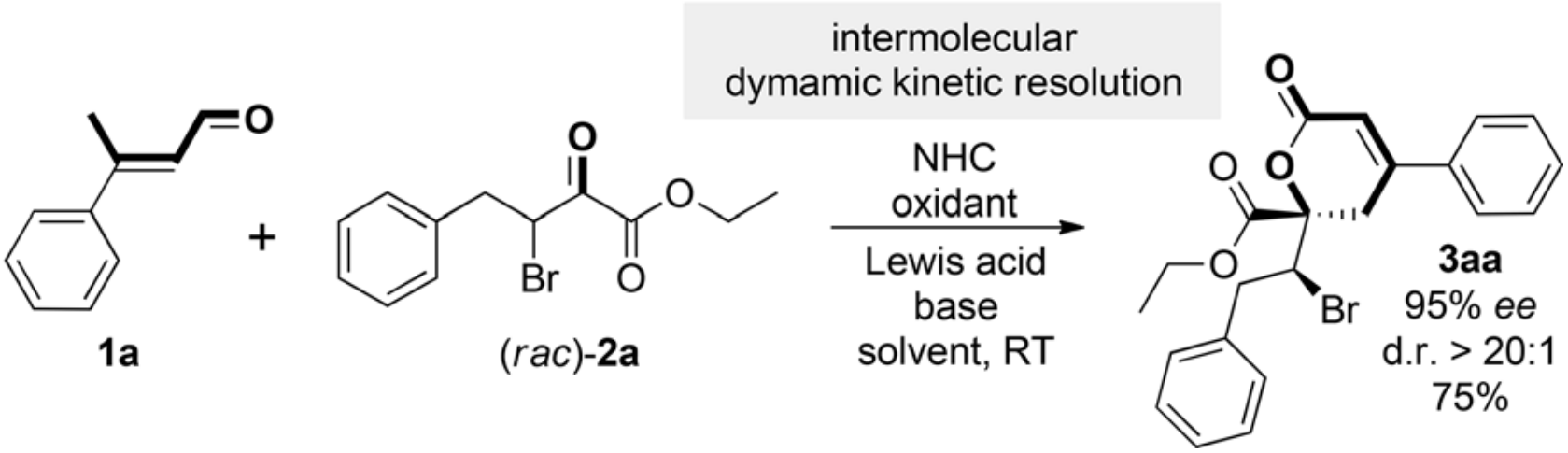


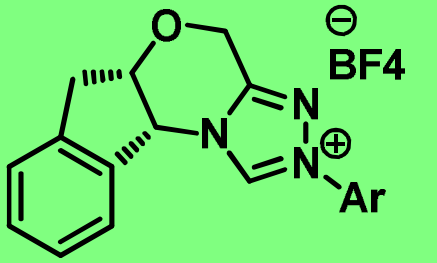
Johnson, J. Am. Chem. Soc. **2014**, *136*, 14698.

This work



Model reaction and its optimization

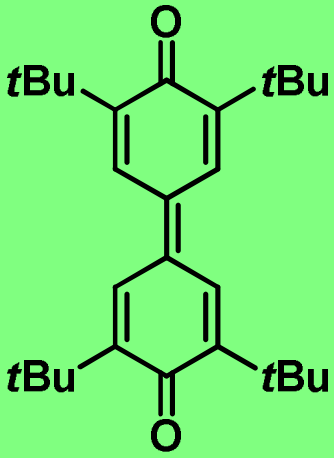




Ar = 2,6-$(C_2H_5)_2C_6H_5$

(20 mol%)

NHC



(1.2 eq DQ)

Oxidant

Lewis acid as additive = $Sc(OTf)_3$

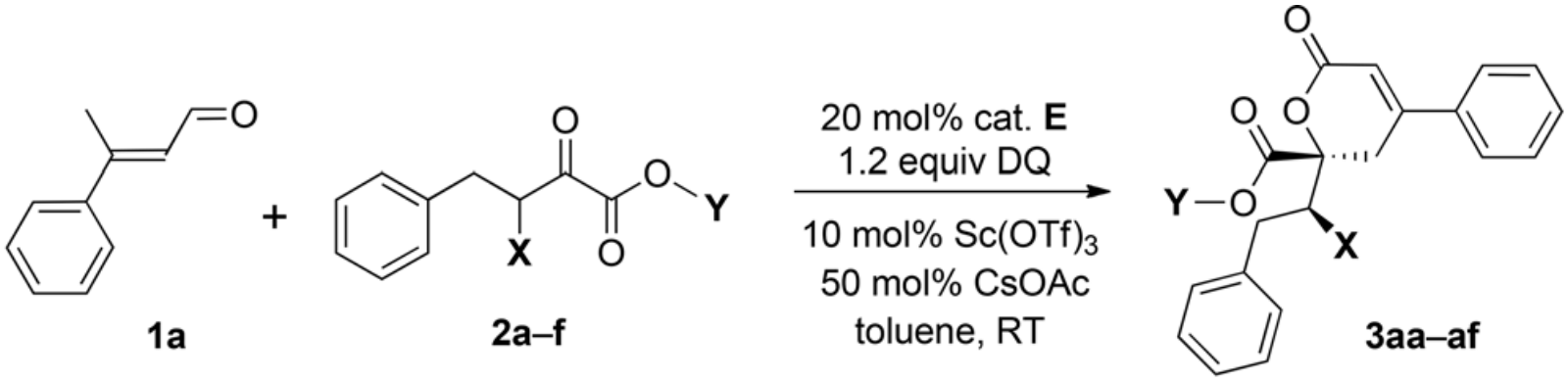
(10 mol%)

Base = CsOAc

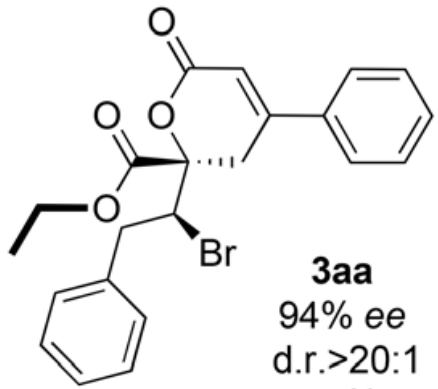
(50 mol%)

Solvent = Toluene

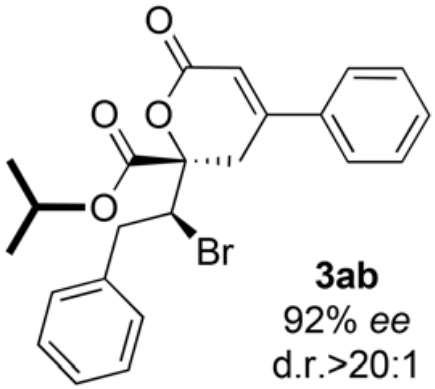
Table 1- Scope of β-halo-α-ketoesters



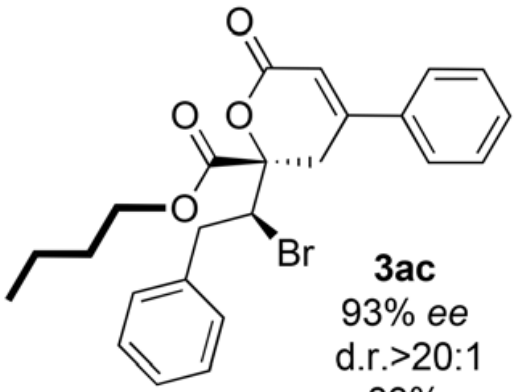
1a + **2a–f** → **3aa–af**



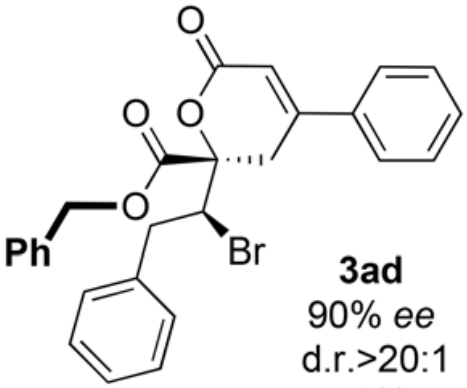
3aa
94% *ee*
d.r.>20:1
75%



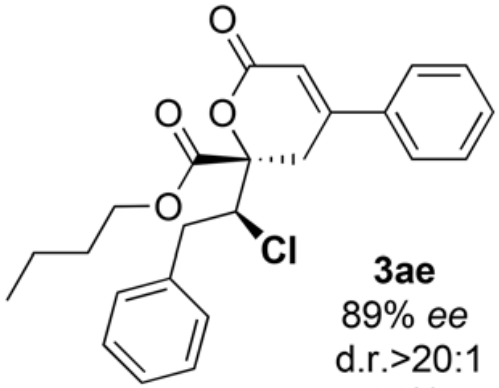
3ab
92% *ee*
d.r.>20:1
80%



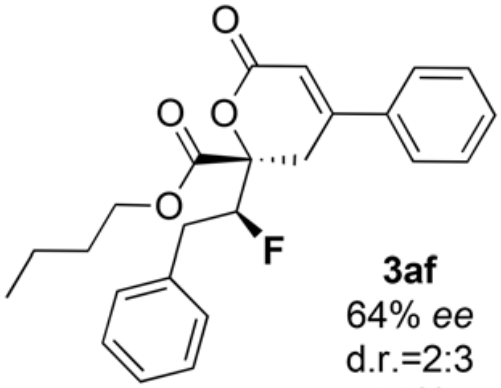
3ac
93% *ee*
d.r.>20:1
83%



3ad
90% *ee*
d.r.>20:1
76%

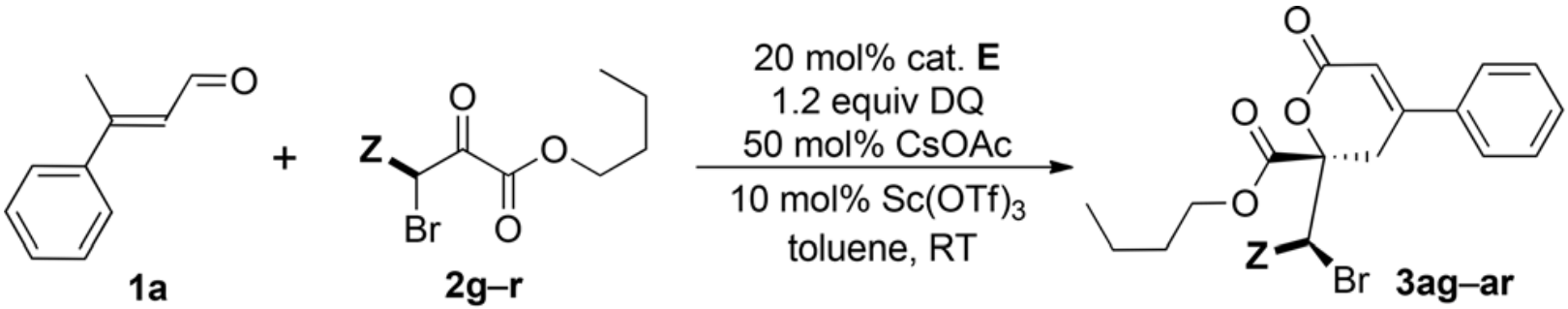


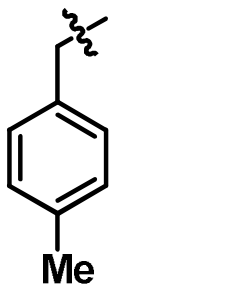
3ae
89% *ee*
d.r.>20:1
81%



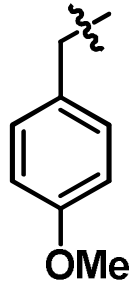
3af
64% *ee*
d.r.=2:3
80%

Table 2: Scope of other β-halo-α-ketoesters





85% ee
d.r.> 20:1,
81%



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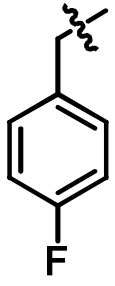

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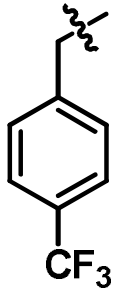
d.r.> 20:1,
79%



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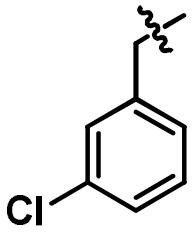
d.r.> 20:1,
86%



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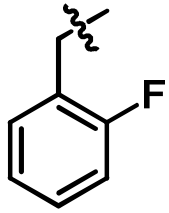

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d.r.> 20:1,
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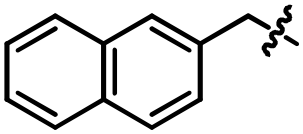

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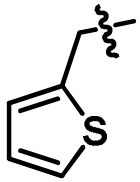
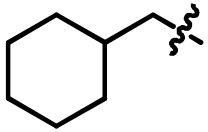


86% ee
d.r.> 20:1,
83%

87% ee
d.r.> 20:1,
70%



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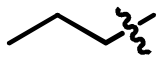
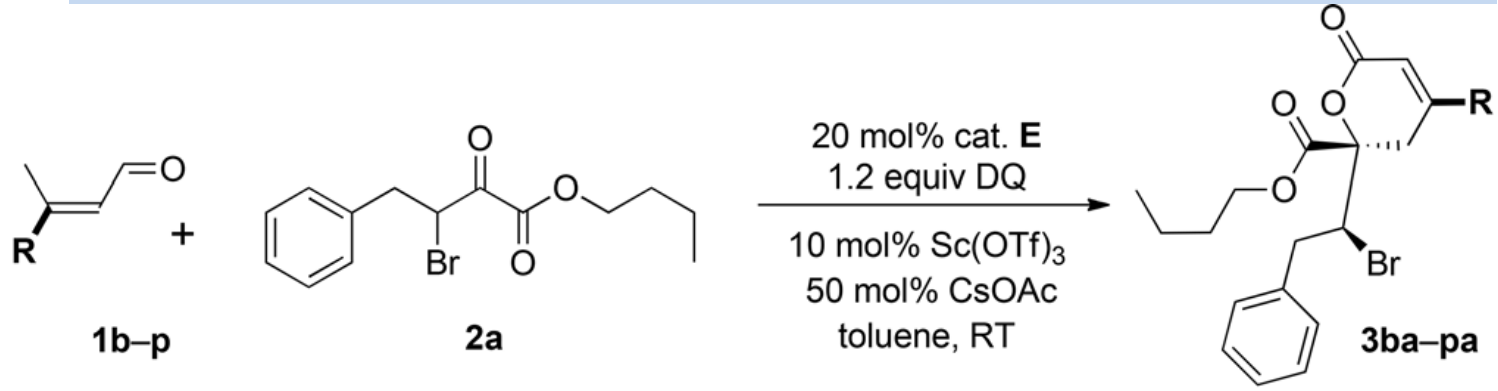
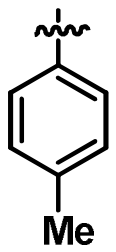


90% ee
d.r.> 20:1,
76%

91% ee
d.r.> 20:1,
77%

Table 3: The scope of α,β-unsaturated aldehydes





92% ee
d.r.> 20:1,
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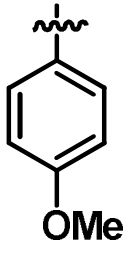

94% ee
d.r.> 20:1,
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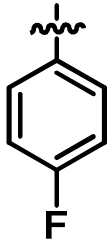

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d.r.> 20:1,
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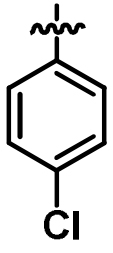

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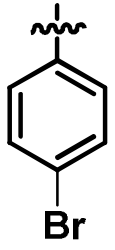
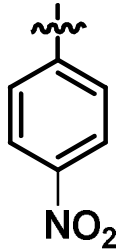


90% ee
d.r.> 20:1,
84%



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d.r.> 20:1,
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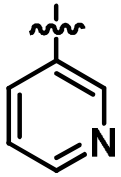

98% ee
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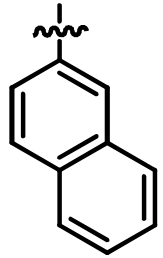

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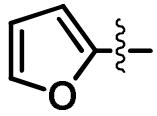
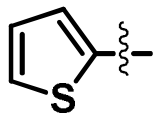


90% ee
d.r.> 20:1,
72%



90% ee
d.r.> 20:1,
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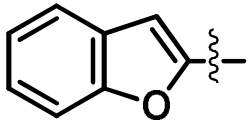

88% ee
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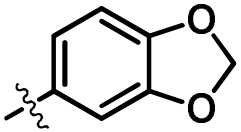

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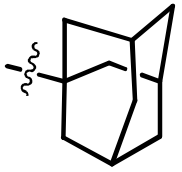
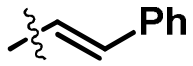


99% ee
d.r.> 20:1,
65%

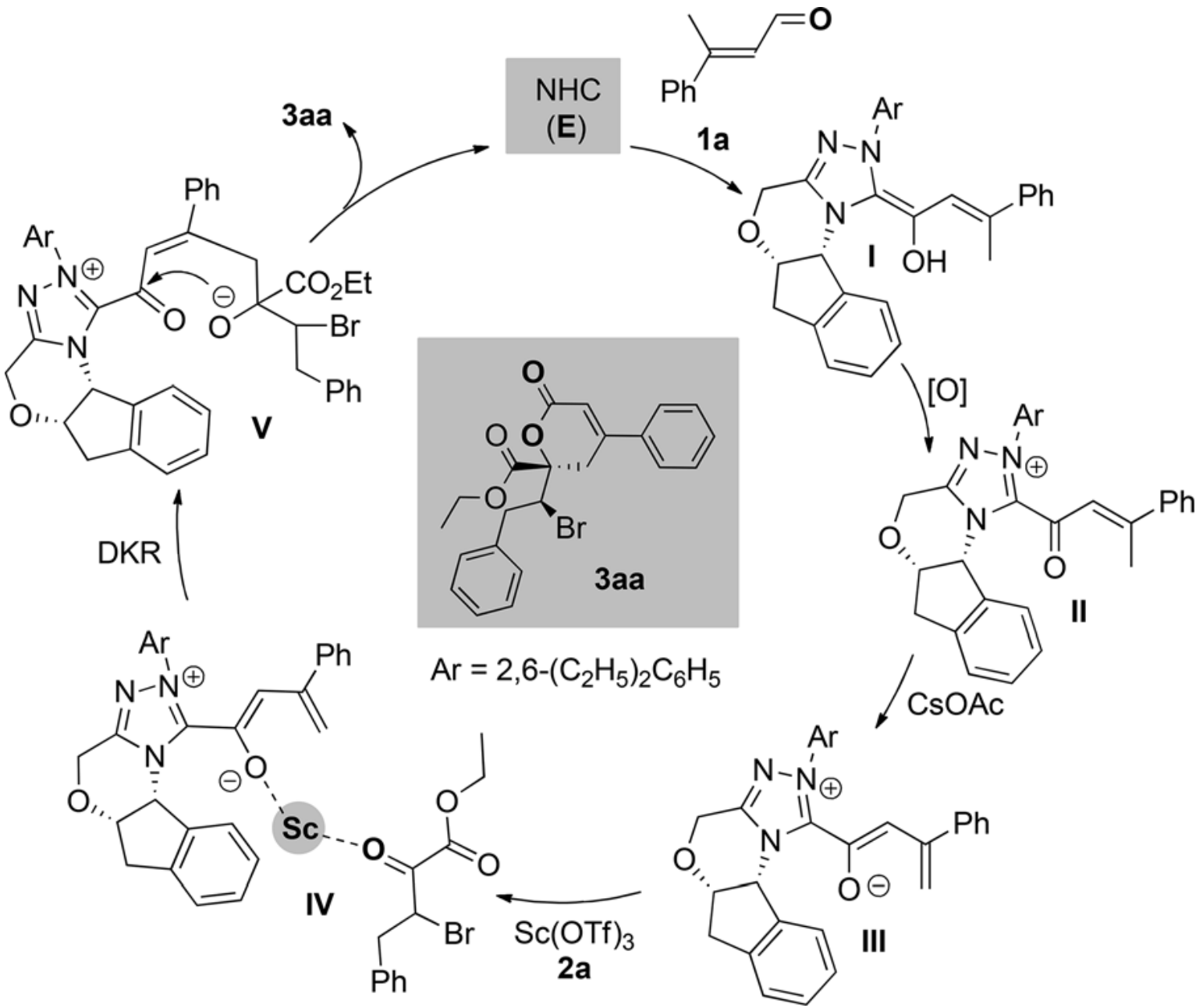


89% ee
d.r.> 20:1,
83%

Me

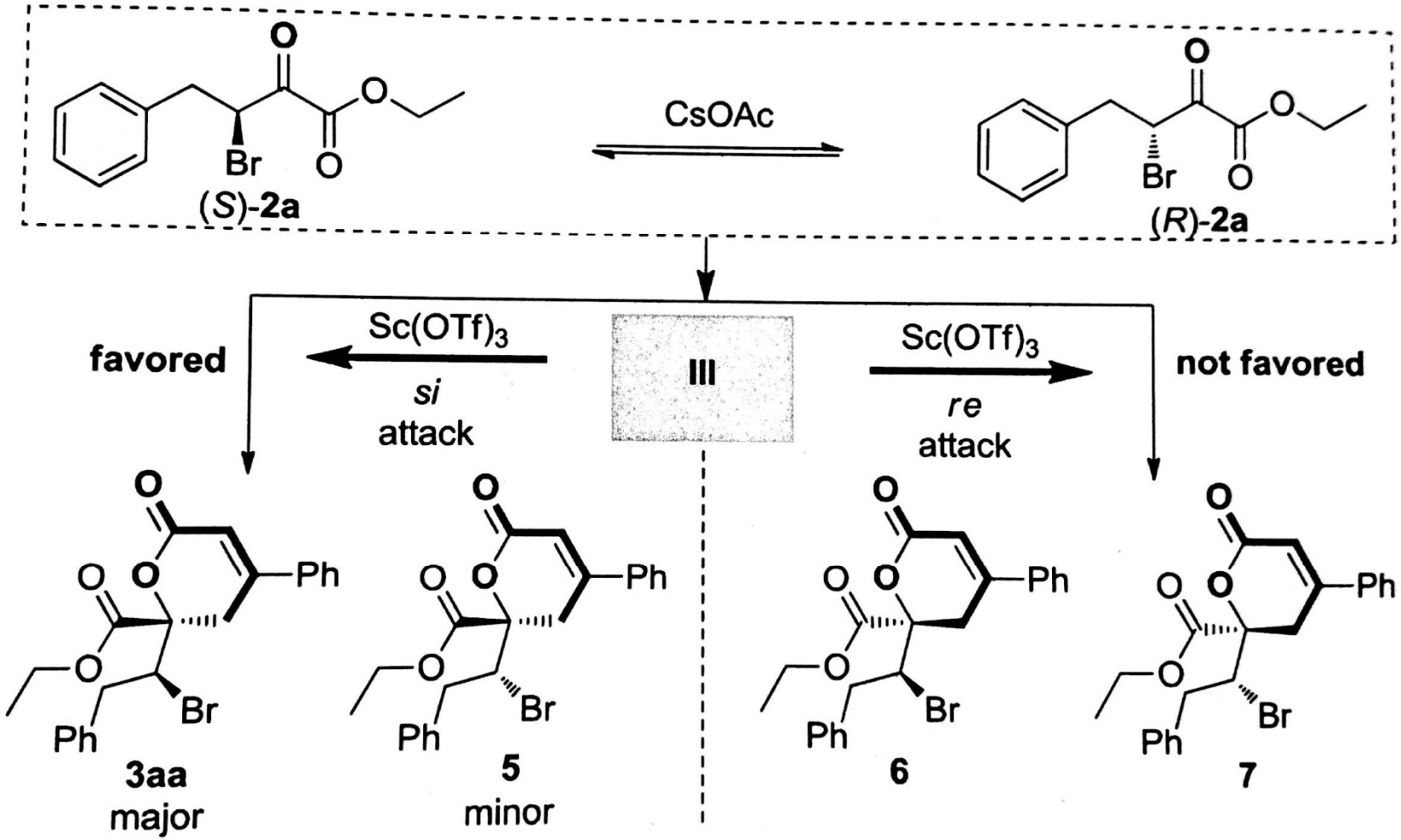
40% ee
d.r.> 20:1,
67%

Postulated Mechanism

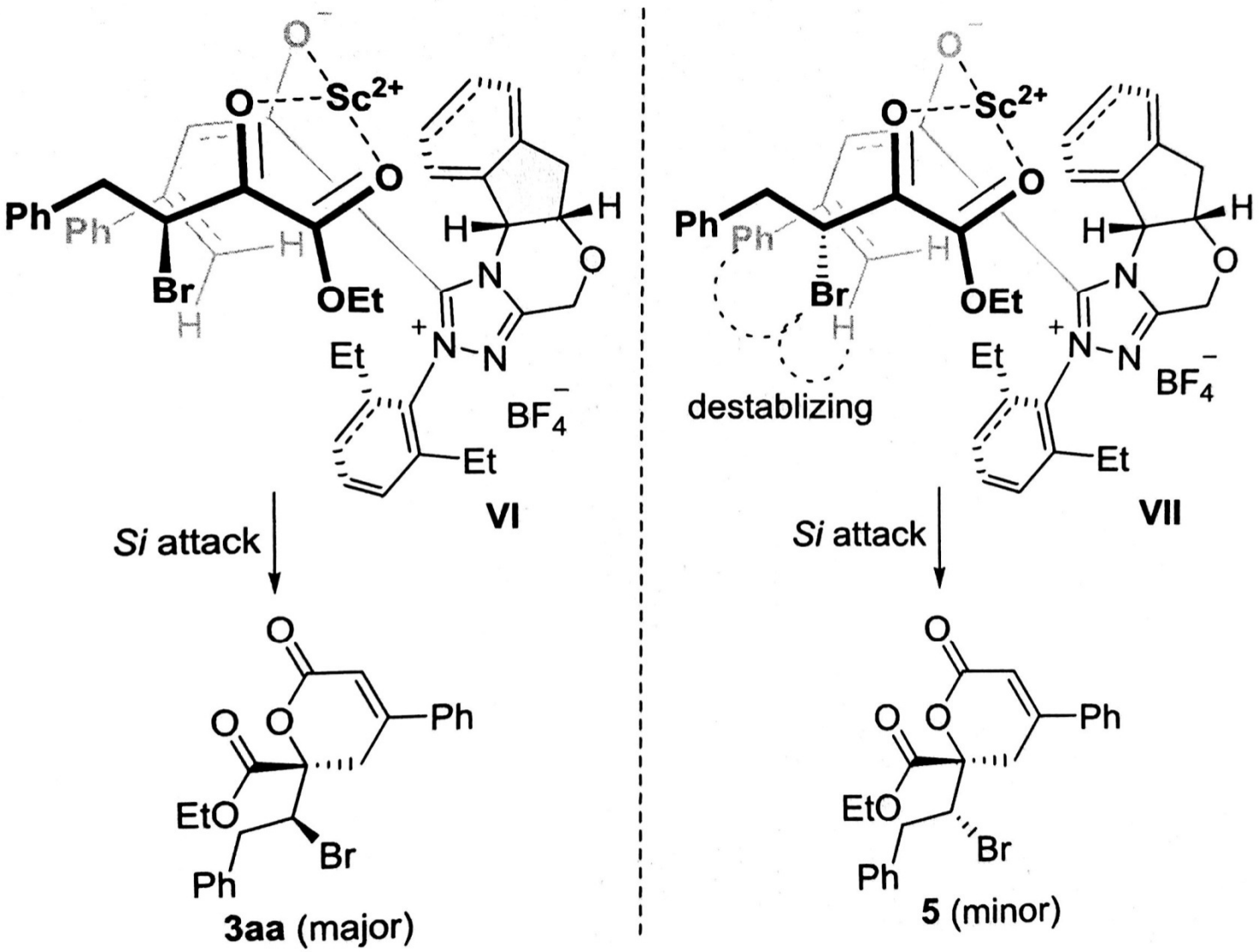


Proposed dynamic kinetic resolution (DKR) process

Scheme 1. Proposed dynamic kinetic resolution (DKR) process.



Proposed reaction transition state model



Conclusion

- **Protocol reports intermolecular dynamic kinetic resolution of β-halo-α-ketoesters through cooperative catalysis by an N-heterocyclic carbene and a Lewis acid in an oxidation/lactonization sequence.**

- **Efficient access to enantioenriched δ-lactones with two contiguous stereocenters in good to high yields with excellent diastereoselectivity.**

THANK YOU FOR YOUR KIND ATTENTION