Jingbo Xiao
November 27, 2004

Hydrogen Bond Mediated Enantioselectivity of Radical Reactions

Tobias Aechtner, Martina Dressel, Thorsten Bach*

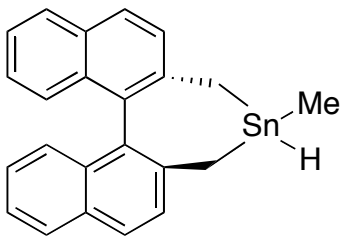
**Lehrstuhl für Organische Chemie I, Technische Universität München,
Lichtenbergstrasse 4, 85747 Garching, Germany**

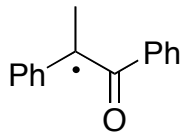
***Angew. Chem., Int. Ed.* 2004, *43*, 5849-5851**

Jingbo Xiao
November 27, 2004

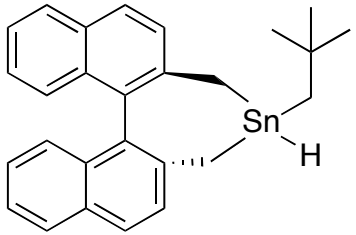
Enantioselectivity of H-Transfer Radical Reactions

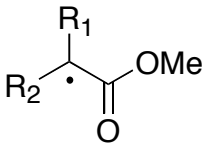
1. Reagent control process-Prochiral radical reacts with a chiral reagent





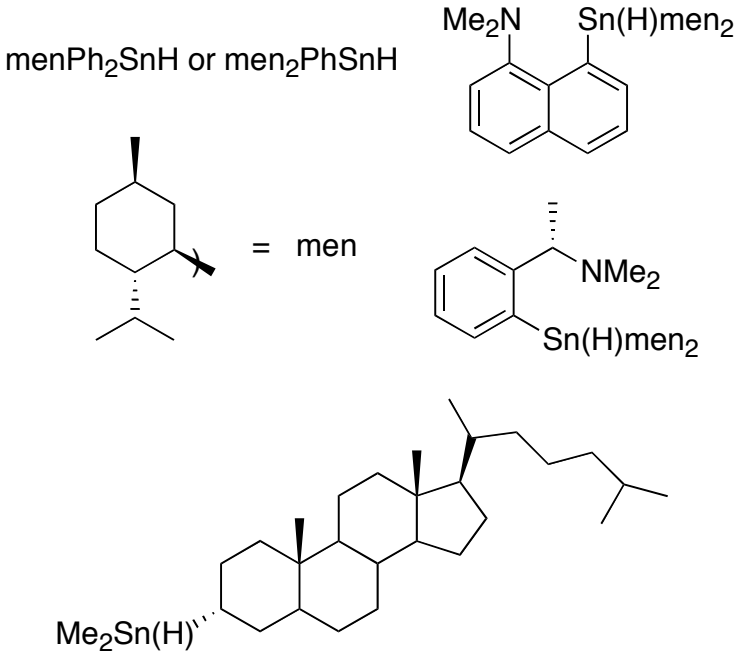
ee 11% - 41%





ee 16% - 64%

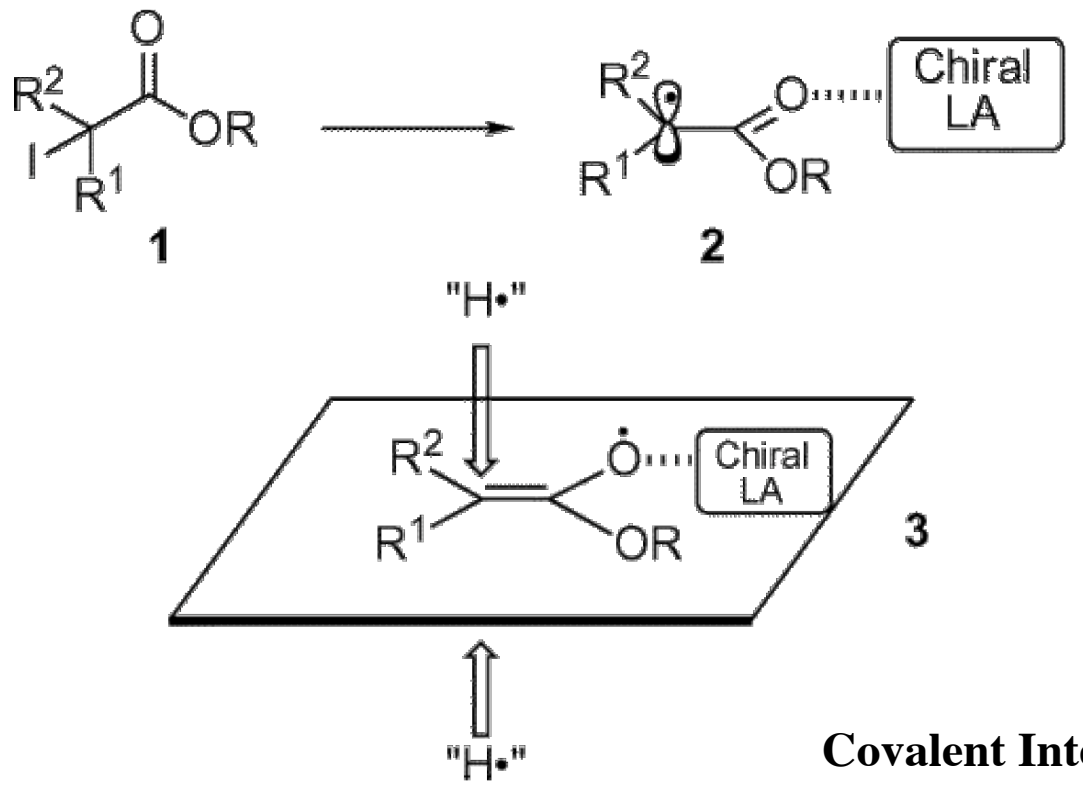
Tetrahedron: Asym. **1996**, *7*, 2417. *Tetrahedron: Asym.* **2003**, *14*, 3069.



Selectivity was improved a lot (up to 96% ee) by adding LA such as Cp_2ZrCl_2

Chem. Commun. **1999**, 1665.

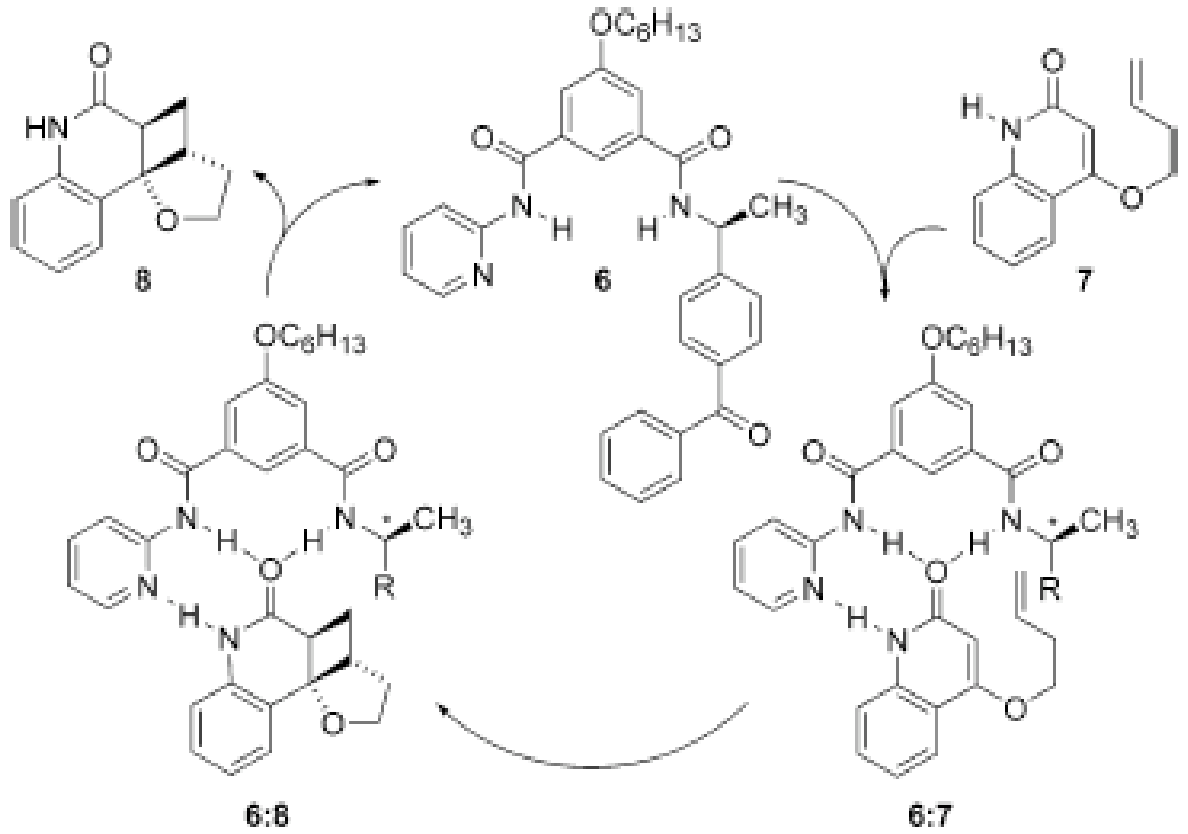
2. Substrate control process-Chelate complex of the substrate and chiral LA



Covalent Interaction

Chem. Rev. **2003**, *103*, 3263.

Hydrogen Bond Mediated Enantioselective Photo-reaction



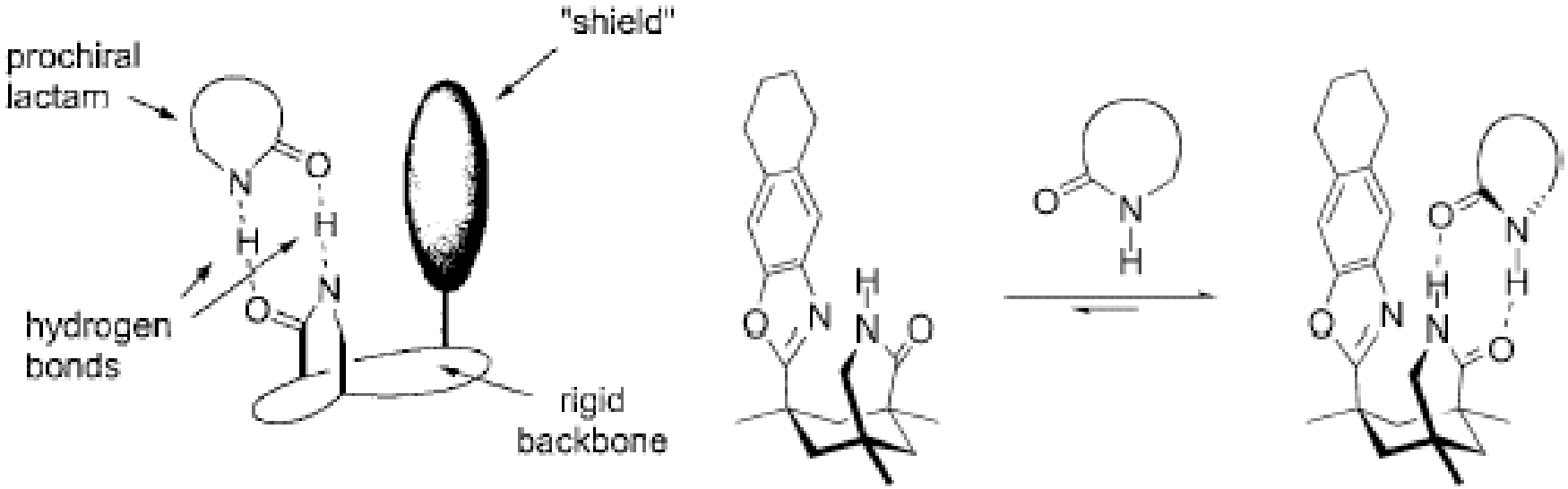
Noncovalent Interaction

100 mol% 22% ee
25 mol% 19% ee

J. Org. Chem. **2003**, *68*, 15.

Jingbo Xiao
November 27, 2004

Hydrogen Bond Mediated Enantioselective Reactions

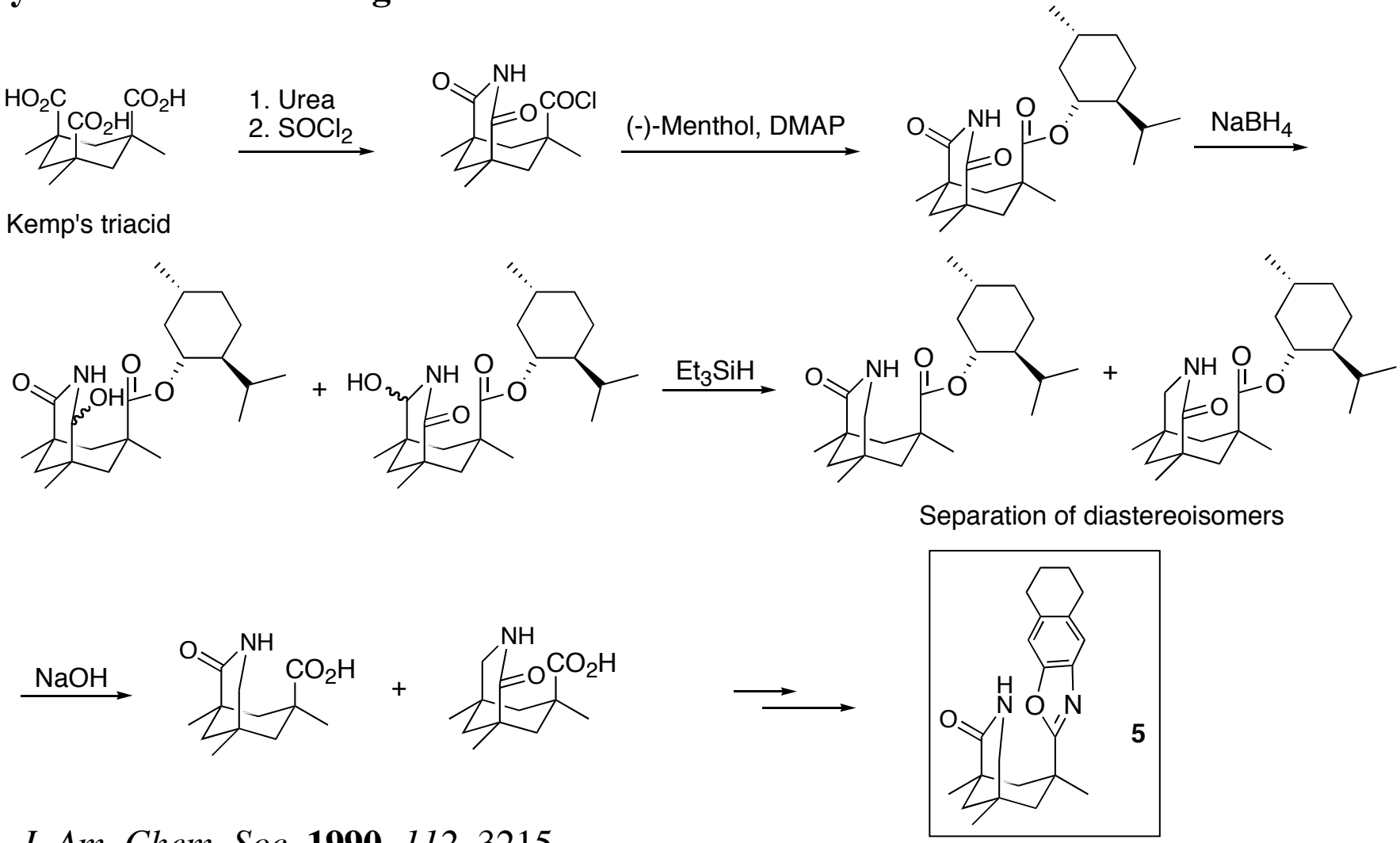


5

Noncovalent Interaction

Jingbo Xiao
November 27, 2004

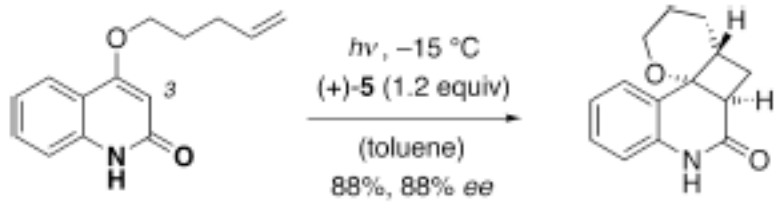
Synthesis of Chiral Ligand 5



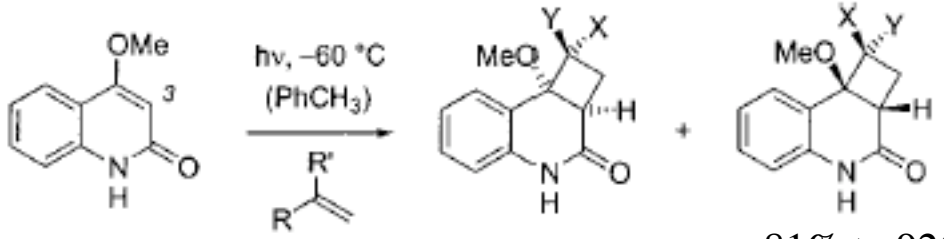
J. Am. Chem. Soc. **1990**, *112*, 3215.
Synthesis **2001**, 1395.

Jingbo Xiao
November 27, 2004

Applications of Chiral Ligand 5

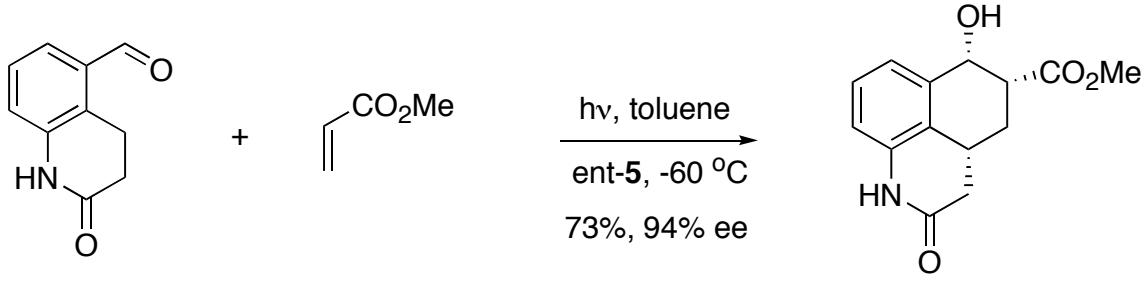


Angew. Chem., Int. Ed. **2000**, *39*, 2302.

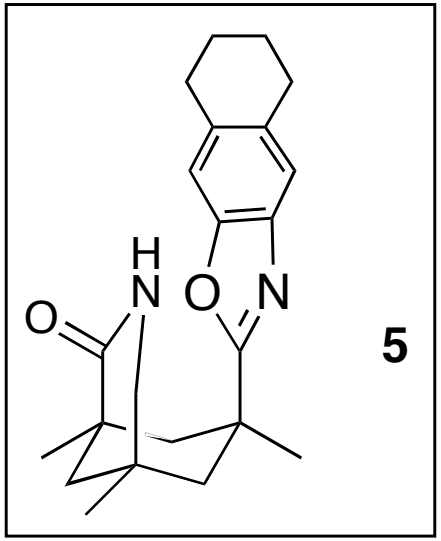


J. Am. Chem. Soc. **2002**, *124*, 7982.

ee 81% to 92%

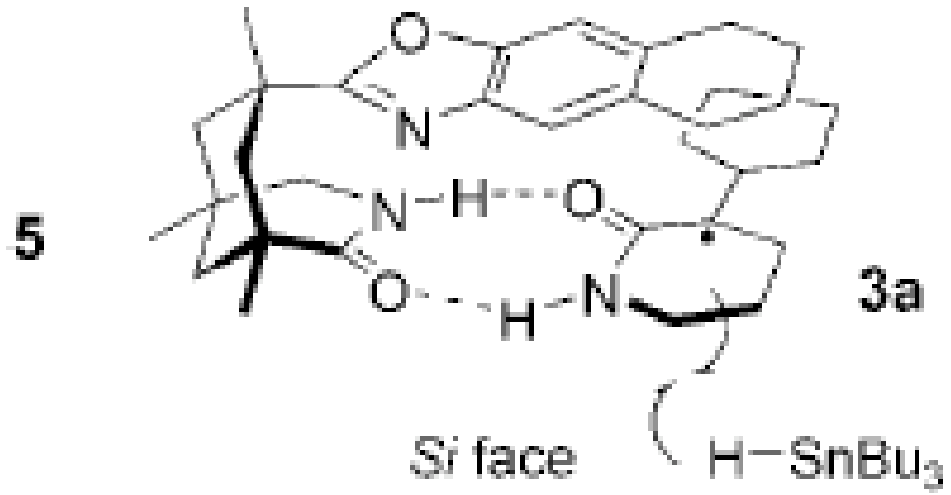


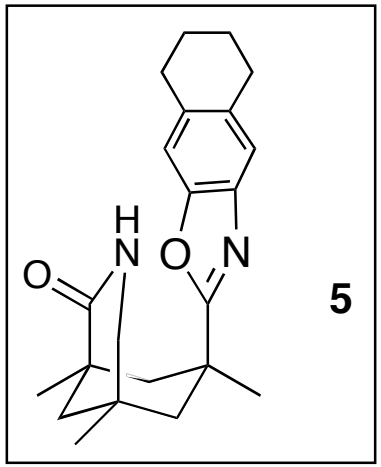
Angew. Chem., Int. Ed. **2003**, *42*, 3693.
Chem. Eur. J. **2004**, *10*, 2173.



Jingbo Xiao
November 27, 2004

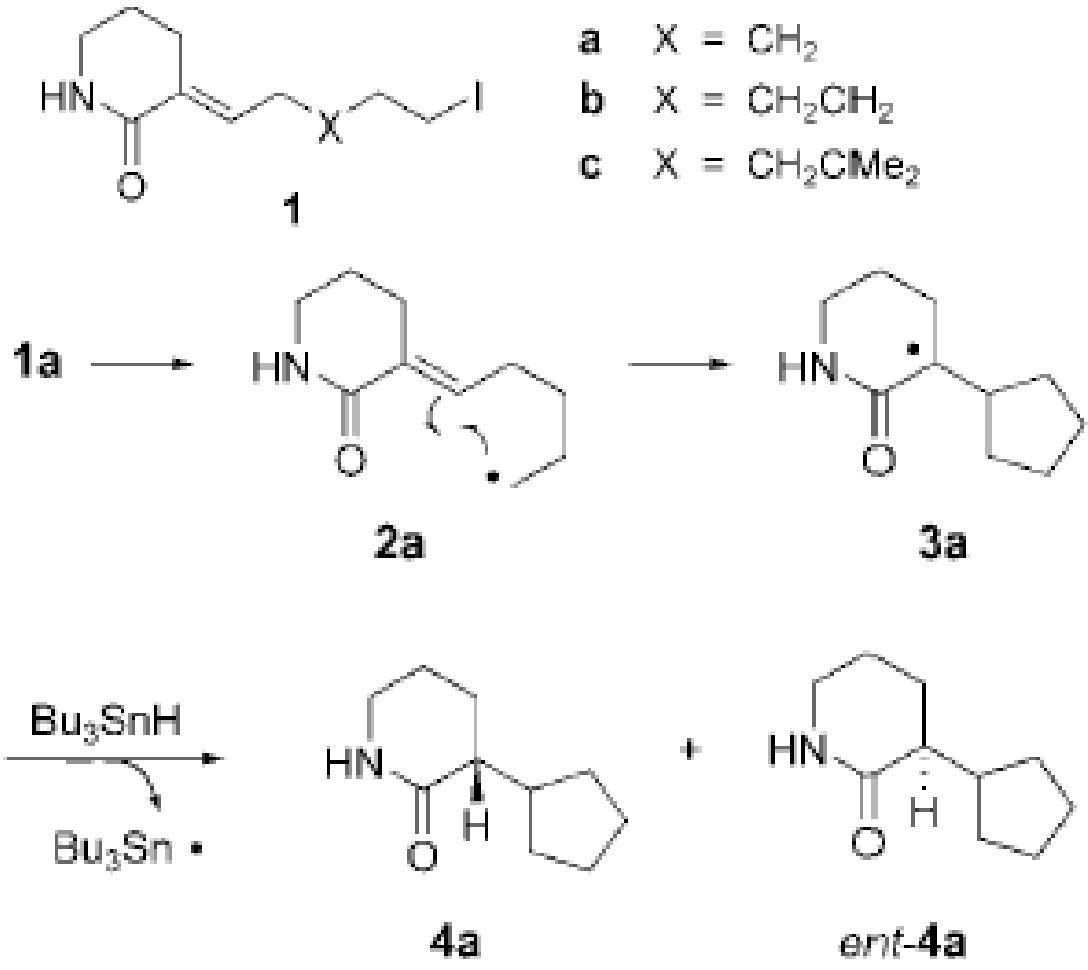
New Application of Chiral Ligand 5 - Chiral H-Transfer Radical Reaction





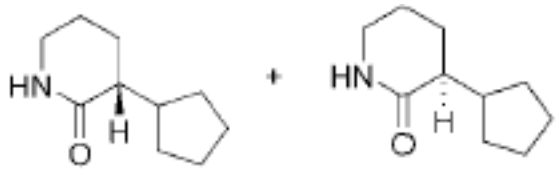
Angew. Chem., Int. Ed. **2004**, *43*, 5849.

Investigated System: 5-*exo*-Cyclization



Angew. Chem., Int. Ed. **2004**, *43*, 5849.

Investigated System-Optimize conditions



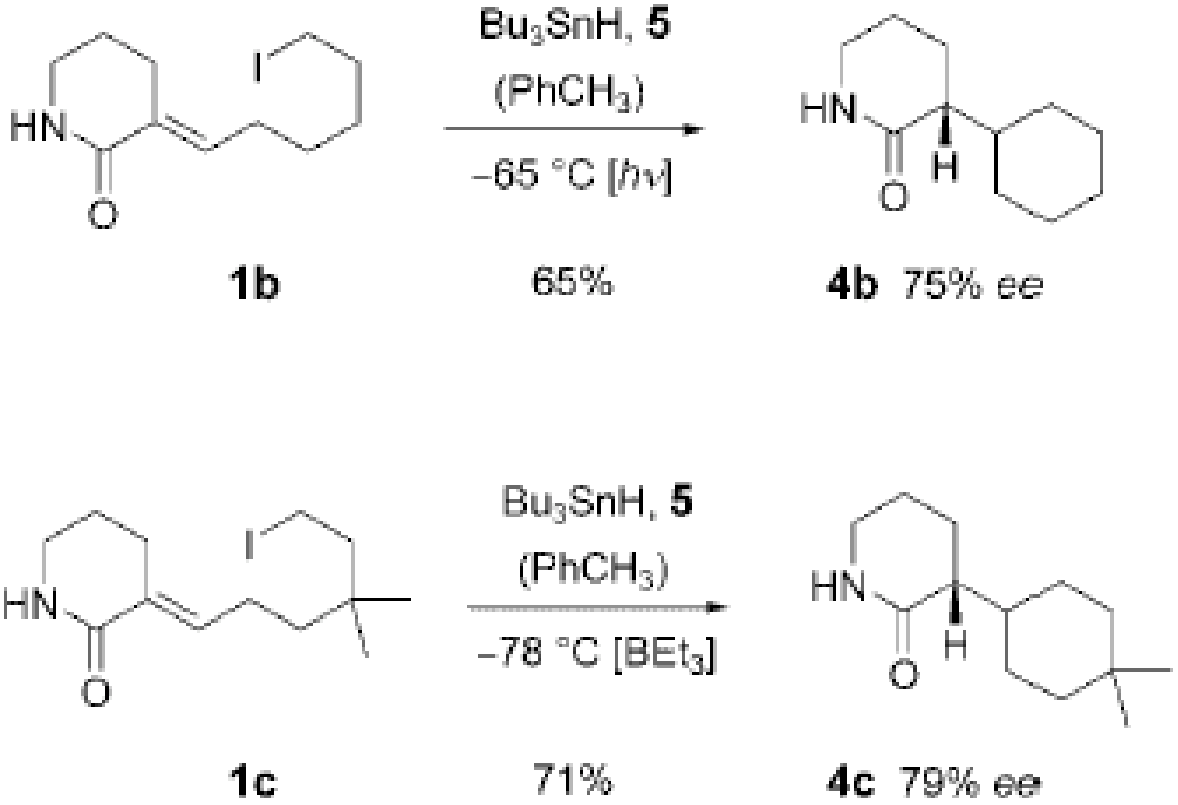
4a *ent*-**4a**

Table 1: Enantioselective radical reaction (cf. Scheme 1) of substrate **1a** to give the products **4a** and *ent*-**4a** using the chiral complexing reagent **5**.[10]

Entry	T [°C][a]	Equiv.[b]	BEt_3 [mol%]	Yield [%]	*ee* [%][c]
1	25	–	50	83	–
2	25	2.5	20	84	38
3	25	2.5	10	72	44
4	−10	1.0	50	78	20
5	−10	2.5	20	82	40
6	−10	2.5	10	79	55
7	−78	1.0	20	91	40
8	−78	2.5	50	84	41
9	−78	2.5	20	81	84

Angew. Chem., Int. Ed. **2004**, *43*, 5849.

Investigated System: 6-*exo*-Cyclization



Angew. *Chem*., *Int*. *Ed*. **2004**, *43*, 5849.

Conclusions

1. First example of hydrogen bond mediated enantioselectively radical H-transfer reaction.
2 System works for both 5- and 6- exo cyclization.
3 Stereochemistry of the products are predictable.
4 Both enantiomers of the ligand are easily prepared.

5 More than stoichiometric amount of chiral ligand needed.
6 Temperature and type of initiator are critical for the results.
7 The recycle of the ligand?