STEREO GROUP MEETING: 11/25/2013

Angewante Communications

Enantioselective Sulfonation of Enones with Sulfonyl Imines by Cooperative N-Heterocyclic-Carbene/ Thiourea/ Tertiary-Amine Multicatalysis

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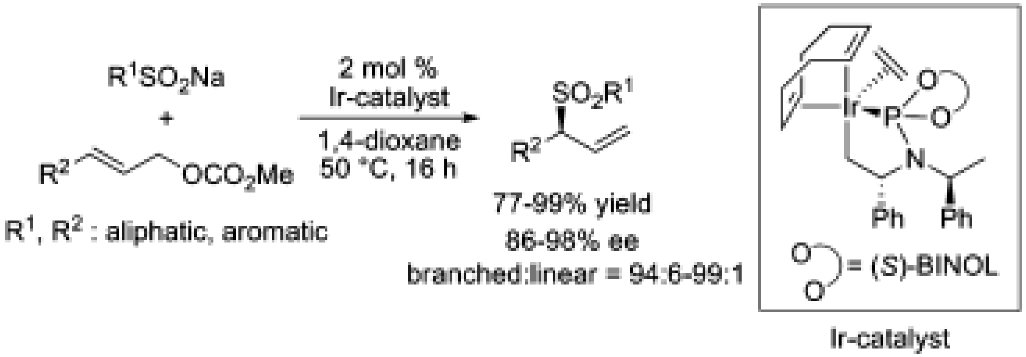
Angew. Chem. Int. Ed. **2013**, *52*, 12354 –12358

REPORTER: Yajun REN

Why I choose this paper?

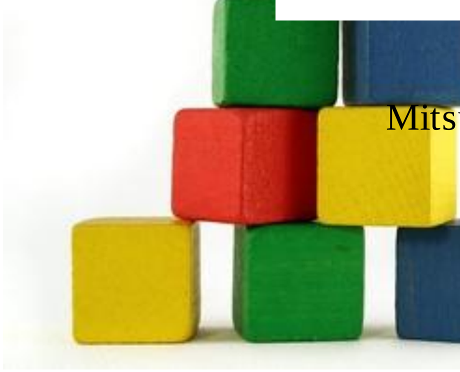
- It is the first organocatalytic enatioselective sulfonation of α,β-unsaturated ketones
- Two organic catalysts containing three catalytic moieties an NHC, a thiourea and a tertiary amine operate in an cooperative manner

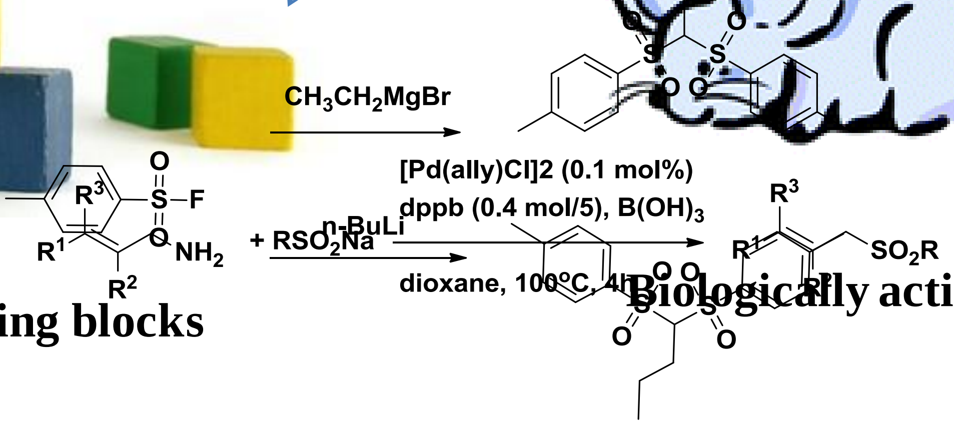
CONTEXT

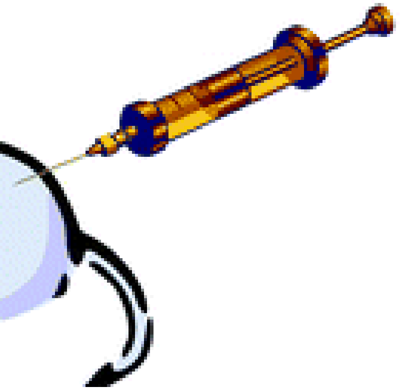


sulfones

Mitsuhiro Ueda and John F. Hartwig, *Org.* Lett. **2010**, *12*, 92-94







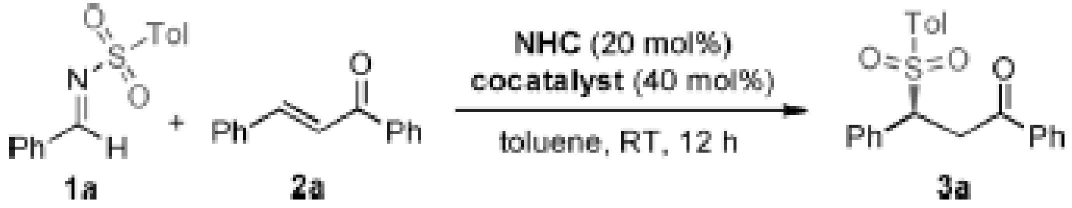
Synthetic building blocks

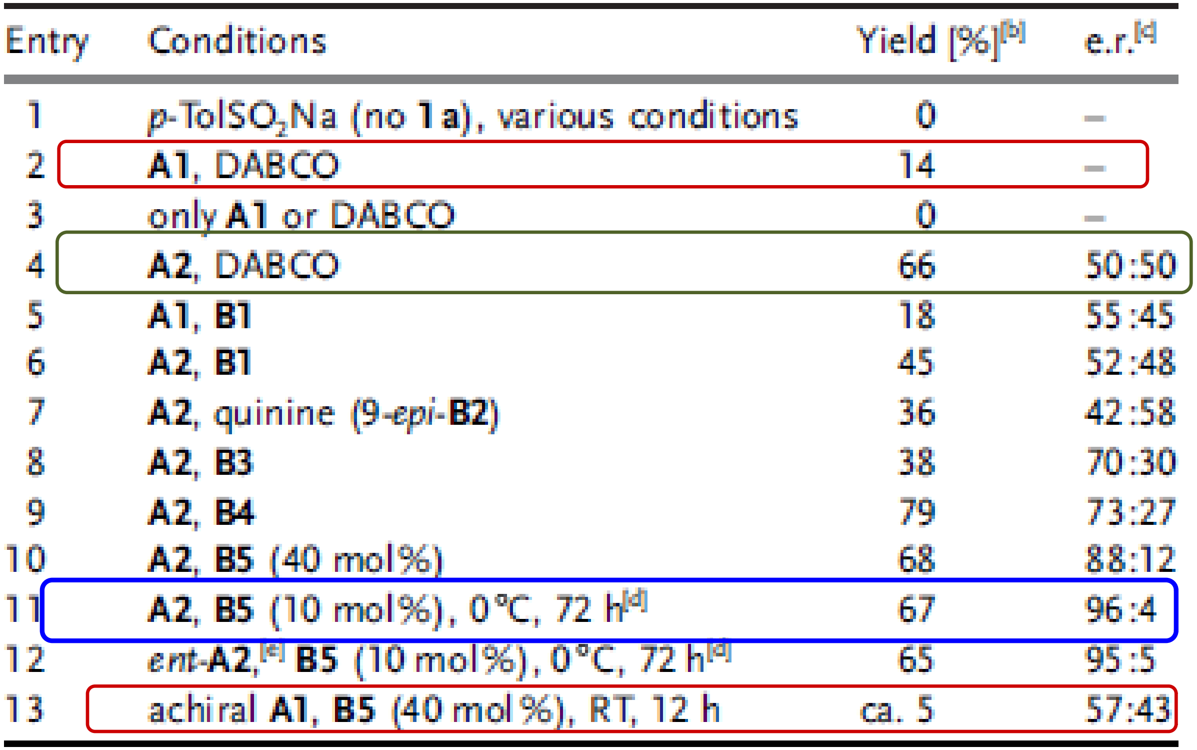
Biologically active agents for drugs

Wu, Y. Chen, M.-B. Li, M.-G. Zhou, S.-K. Tian, *J. Am. Chem. Soc.* **2012**, *134*, 14694

H. Fukuda, F. J. Frank, W. E. Truce, *J. Org. Chem.* **1963**, *28*, 1420

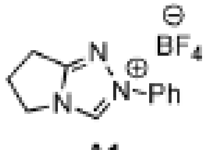
Table 1: Optimization of the reaction conditions.[a]



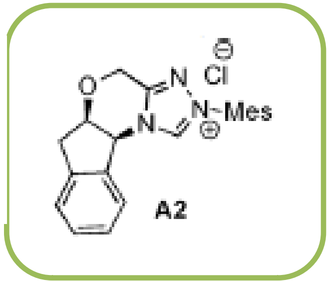


Entry	Conditions	Yield [%][b]	e.r.[c]
1	*p*-TolSO$_2$Na (no **1a**), various conditions	0	–
2	**A1**, DABCO	14	–
3	only **A1** or DABCO	0	–
4	**A2**, DABCO	66	50:50
5	**A1**, **B1**	18	55:45
6	**A2**, **B1**	45	52:48
7	**A2**, quinine (9-*epi*-**B2**)	36	42:58
8	**A2**, **B3**	38	70:30
9	**A2**, **B4**	79	73:27
10	**A2**, **B5** (40 mol%)	68	88:12
11	**A2**, **B5** (10 mol%), 0°C, 72 h[d]	67	96:4
12	*ent*-**A2**,[e] **B5** (10 mol%), 0°C, 72 h[d]	65	95:5
13	achiral **A1**, **B5** (40 mol%), RT, 12 h	ca. 5	57:43

NHC Precucor :

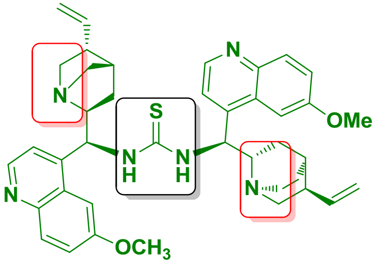


A1

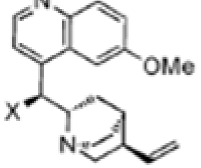


A2

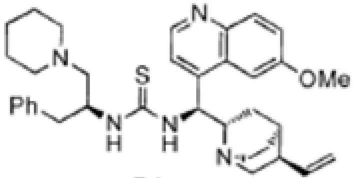
Cocatalyst:



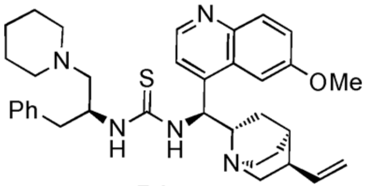
B5



X = NH$_2$, **B1**
X = OH, **B2**

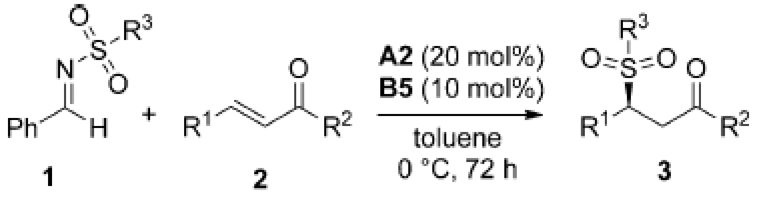


B4



B4

Table 2: Examples of the sulfonation reaction.[a]

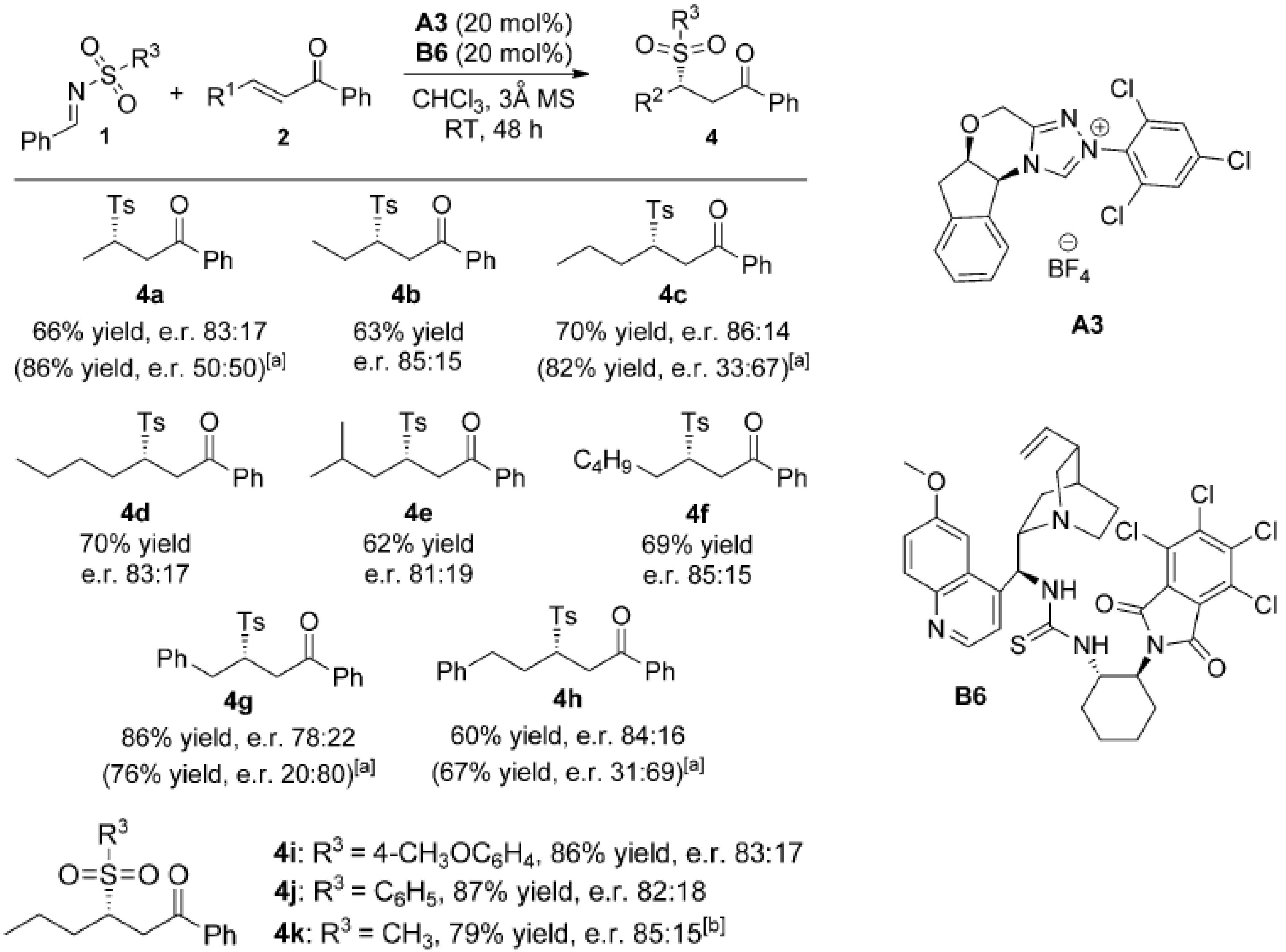


1 + **2** → **3**

1a : $R^3 = 4\text{-}MeC_6H_4$
1b : $R^3 = Ph$
1c : $R^3 = 4\text{-}MeOC_6H_4$
1d : $R^3 = Me$
1e : $R^3 = 4\text{-}NO_2C_6H_4$

Entry	1	R^1	R^2	3	Yield [%]	e.r.
1[b]	1a	Ph	Ph	3a	69	96:4
2[c]	1a	$4\text{-}MeOC_6H_4$	Ph	3b	60	90:10
3	1a	$3\text{-}NO_2C_6H_4$	Ph	3c	76	89:11
4	1a	$4\text{-}ClC_6H_4$	Ph	3d	49	95:5
5	1a	$4\text{-}MeC_6H_4$	Ph	3e	54	94:6
6	1a	$4\text{-}NO_2C_6H_4$	Ph	3f	84	> 99:1
7	1a	Ph	$4\text{-}MeOC_6H_4$	3g	64	97:3
8	1a	Ph	$4\text{-}ClC_6H_4$	3h	79	97:3
9[b]	1a	Ph	$4\text{-}BrC_6H_4$	3i	77	> 99:1
10	1a	Ph	2-naphthyl	3j	57	91:9
11	1a	$4\text{-}ClC_6H_4$	$4\text{-}ClC_6H_4$	3k	52	99:1
12	1a	Ph	2-furyl	3l	63	95:5
13	1b	Ph	Ph	3m	52	96:4
14	1c	Ph	Ph	3n	67	92:8
15	1d	Ph	Ph	3o	44	73:27
16[c]	1e	Ph	Ph	3p	13	93:7
17	1a	COOEt	Ph	3q	50	50:50
18[c]	1a	Ph	Me	3r	30	77:23
19	1a	*n*Bu	Me	3s	58	60:40
20	1a	Me	Ph	4a	86	50:50

Scheme 1 **Examples of the sulfonation of aliphatic enones**



4a 66% yield, e.r. 83:17 (86% yield, e.r. 50:50)[a]

4b 63% yield e.r. 85:15

4c 70% yield, e.r. 86:14 (82% yield, e.r. 33:67)[a]

4d 70% yield e.r. 83:17

4e 62% yield e.r. 81:19

4f 69% yield e.r. 85:15

4g 86% yield, e.r. 78:22 (76% yield, e.r. 20:80)[a]

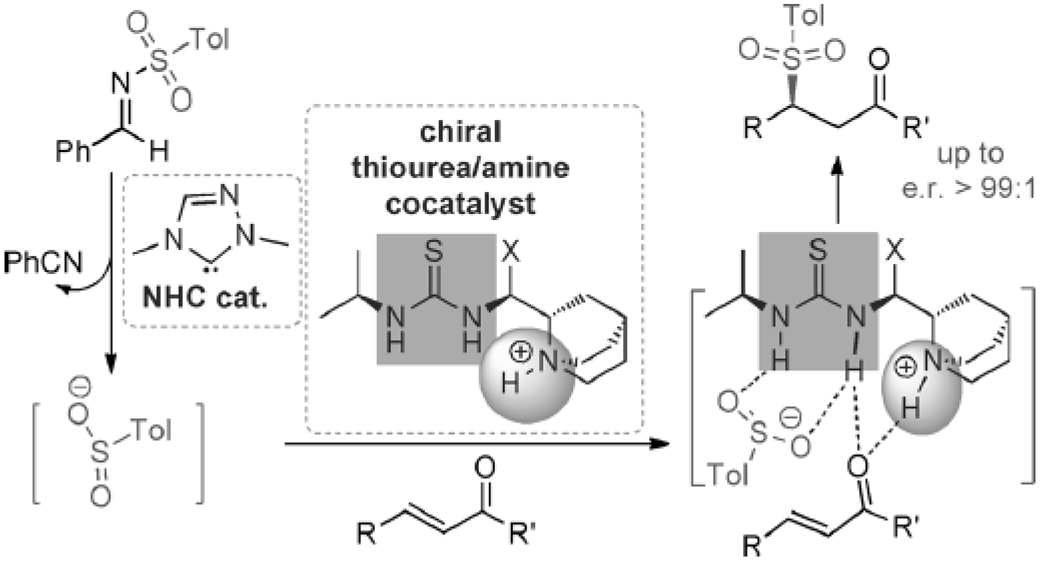
4h 60% yield, e.r. 84:16 (67% yield, e.r. 31:69)[a]

4i: R^3 = 4-$CH_3OC_6H_4$, 86% yield, e.r. 83:17

4j: R^3 = C_6H_5, 87% yield, e.r. 82:18

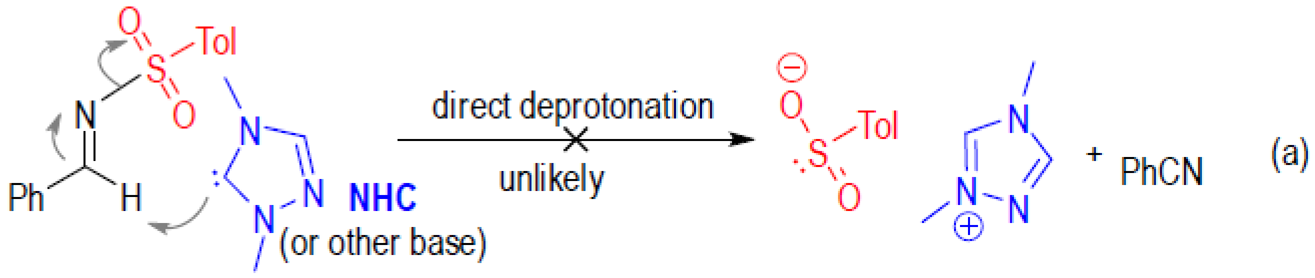
4k: R^3 = CH_3, 79% yield, e.r. 85:15[b]

Mechanism



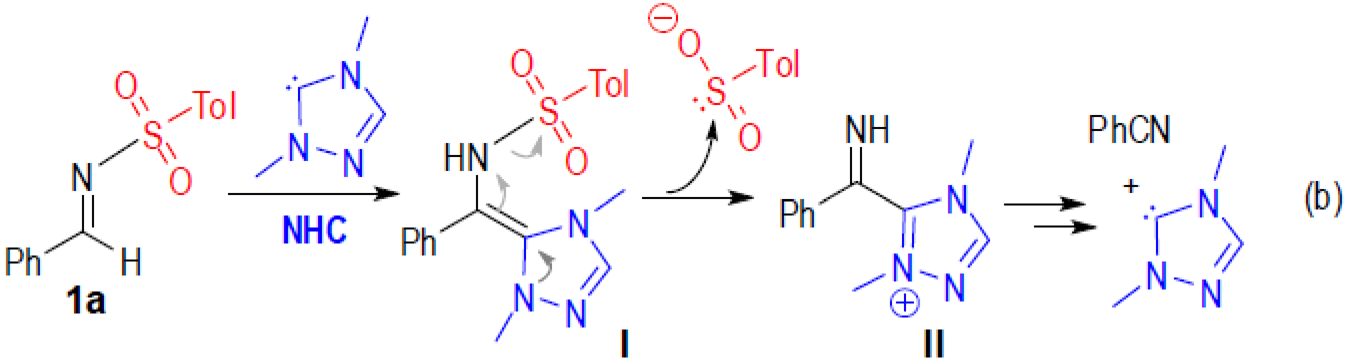
Scheme 2: Enantioselective catalytic sulfonation of enones. Tol = p-tolyl

- **the sulfinic anion is probably released from the imine substrate before its addition to the enone**



- **in the absence of an NHC, none of the product 3a was obtained when a variety of bases were used**

- **the acidity of the imine hydrogen atom is much weaker than that of the hydrogen atom on the triazolium ring of the NHC precatalyst as evidenced by H/D-exchange experiments in the presence of D2O(** ***see supporting info.)***



Conclusion

- developed the first organocatalytic enantioselective synthesis of β-sulfonyl ketones
- The sulfinic anion was generated from sulfonyl imines under NHC catalysis
- The enantioselectivity of the transformations was controlled by the use of noncovalent thiourea/tertiary-aminecocatalysts

THANK YOU FOR YOUR KIND ATTENTION!