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Highly Enantioselective Allylation of Aromatic α-Keto Phosphonates Catalyzed by Chiral *N,N′*-Dioxide-Indium(III) Complexes

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Abstract: The ramipril derivative *N,N′*-dioxide **3g**-indium(III) complex was found to be an efficient catalyst for the allylation of the aromatic α-keto phosphonates. The corresponding α-hydroxy phosphonates were obtained with high yields (up to 98%) and high enantioselectivities (up to 91% *ee*). A bifunctional catalyst system was described with an *N*-oxide as Lewis base activating tetraallyltin and indium as Lewis acid activating aromatic α-keto phosphonates. A possible catalytic cycle has been proposed to explain the mechanism of the reaction.

Keywords: allylation; chiral *N,N′*-dioxides; enantioselectivity; α-hydroxy phosphonate; indium

Introduction

The enantioselective allylation of carbonyl compounds is a powerful and important method for the asymmetric synthesis of enantiomerically enriched homoallylic alcohols.[1] The chiral α-hydroxy phosphonic acid derivatives have important biologically activity.[2] They are widely used for pharmaceutical applications, such as anticancer[3] and antivirus activities.[4] And they are also enzyme inhibitors of renin,[5] or human immunodeficiency virus (HIV) protease and polymerase.[6] Only a few stereoselective syntheses of α-hydroxy phosphonates were reported including the asymmetric reduction of α-keto phosphonates,[7] the asymmetric oxidation of benzyl phosphonates[8] and the asymmetric hydrophosphonylation of carbonyl compounds.[9] Recently, α-hydroxy phosphonates and α-hydroxy-β-nitro phosphonates were obtained by Zhao and co-workers through the asymmetric aldol and Henry reactions of α-keto phosphonates.[10,11] The cyanosilylation[12a] and cross-benzoin reactions[12b] of α-keto phosphonates were also developed by Demir and co-workers. However, the asymmetric allylation of α-keto phosphonates has still not been described so far.[13] Therefore, it is very desirable to develop an asymmetric synthesis of α-hydroxy allylic phosphonates.

Chiral *N*-oxides have been disclosed as ligands in many asymmetric procedures that have not yet achieved higher levels of efficiency.[14] We previously reported a chiral *N,N′*-dioxide as the highly efficient organocatalyst for the cyanation reaction with moderate to high enantioselectivities.[15–18] Metal complexes of chiral *N*-oxides could also give good results in the cyanation[19], allylation and Henry reactions[20] of carbonyl compounds. Herein, we report the first asymmetric allylation of aromatic α-keto phosphonates catalyzed by the chiral *N,N′*-dioxide **3g**-In(III) complex.

Results and Discussion

Allylstannane reagents are efficient in allylation of ketones.[21] We initiated the allylation of α-keto phosphonates with tetraallylstannane using the chiral (*S*)-pipecolic acid derivative *N,N′*-dioxide **1a** (Figure 1) as organocatalyst, which exhibited excellent yields and high enantioselectivities in the asymmetric Strecker reaction of phosphinoyl ketoimines.[16b] However, no product was obtained in the allylation of α-keto phosphonates (Table 1, entry 1).

Following the concept of bifunctional catalysis, indium(III) reagents was chosen as central metal to

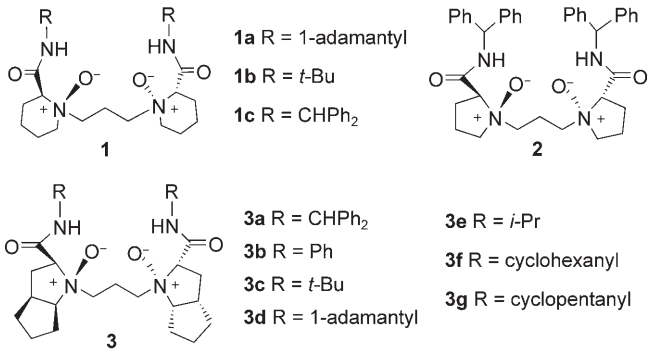
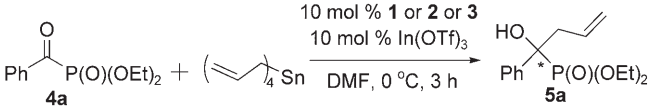


Figure 1. Ligands screened for the asymmetric allylation.

Table 1. Asymmetric allylation of α-keto phosphonate **4a** catalyzed by chiral *N,N′*-dioxide-In(III) complexes.[a]



Entry	Ligand	Yield [%][b]	*ee* [%][c]
1[d]	**1a**	N.R.[e]	-
2	**1a**	77	31
3	**1b**	88	48
4	**1c**	76	60
5	**2**	81	31
6	**3a**	74	69
7	**3b**	69	29
8	**3c**	79	70
9	**3d**	67	66
10	**3e**	67	83
11	**3f**	85	84
12	**3g**	88	85

[a] Unless other specified, all reactions were carried out in the air, 10 mol % ligand, 10 mol % $In(OTf)_3$, 0.1 mmol α-keto phosphonate **4a**, 1.1 equivs. tetraallylstannane, 1.0 mL DMF, 0 °C for 3 h.
[b] Isolated yields.
[c] Determined by HPLC on a Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.
[d] Without $In(OTf)_3$.
[e] N.R. = no reaction.

methyl-derived *N,N′*-dioxides **1b** and **1c** (Table 1, entries 3 and 4). When (*S*)-pipecolic acid-based *N,N′*-dioxide **1c** was displaced by the L-proline derivative *N,N′*-dioxide **2**, the enantioselectivity was sharply decreased to 31 % *ee* (Table 1, entry 5). Excitingly, when the (*S*)-ramipril acid derivative *N,N′*-dioxide **3a** was used, the enantioselectivity was improved to 69 % *ee* (Table 1, entry 6). Inspired by these results, (*S*)-ramipril acid derivative *N,N′*-dioxides **3a–g** (Figure 1) were tested. The experimental results revealed that *N,N′*-dioxide **3b** bearing a phenyl moiety was disadvantageous for the enantioselectivity (Table 1, entry 7), while the *N,N′*-dioxides bearing an aliphatic amide (**3c–g**) gave good enantioselectivities (Table 1, entries 8–11). Especially, the enantioselectivity was greatly increased to 85 % *ee* with the cyclopentanyl-based *N,N′*-dioxide **3g** as the ligand (Table 1, entry 12).

Other parameters were also investigated. Firstly, central metals were evaluated and the results are listed in Table 2. The reactivity and enantioselectivity

Table 2. Central metal effects on the allylation of α-keto phosphonate **4a**.[a]

Entry	Central metal	Yield [%][b]	*ee* [%][c]
1	$Cu(OTf)_2$	67	-18[e]
2	$Zn(OTf)_2$	N.R.[d]	-
3	$Yb(OTf)_3$	N.R.[d]	-
4	$Sc(OTf)_3$	N.R.[d]	-
5	$In(OTf)_3$	88	85
6	$InBr_3$	81	15
7	$InCl_3$	84	0
8	$In(OAc)_3$	N. R.[d]	-

[a] All reactions were carried out in 10 mol % **3g**, 10 mol % metal reagent, 0.1 mmol α-keto phosphonate, 1.1 equivs. tetraallylstannane, 1.0 mL DMF, 0 °C for 3 h.
[b] Isolated yields.
[c] Determined by HPLC on a Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.
[d] N.R. = no reaction.
[e] The opposite enantiomer was produced.

activate α-keto phosphonates, which had been proved to be efficient in the allylation of the carbonyl compounds.[13,20,21a–d] The results are listed in Table 1. The results indicated that 10 mol % **1a**-$In(OTf)_3$ complex could successfully catalyze the enantioselective allylation of α-keto phosphonate in 77 % yield with 31 % *ee* (Table 1, entry 2). Encouraged by this result, a series of *N,N′*-dioxides was synthesized and applied in the asymmetric allylation of α-keto phosphonates. As shown in Table 1, the enantioselectivities were remarkably increased by changing the adamantyl-derived *N,N′*-dioxide **1a** into *tert*-butyl- or diphenyl-

were largely dependent on the central metals. The **3g**-$Cu(OTf)_2$ complex delivered only moderate yield and low enantioselectivity (Table 2, entry 1), while the complexes with $Zn(OTf)_2$, $Yb(OTf)_3$ and $Sc(OTf)_3$ as central metals, could not even catalyze the allylation of α-keto phosphonates (Table 2, entries 2–4). Furthermore, the counter-anion also affected the reactivity and enantioselectivity (Table 2, entries 5–8). Indium bearing a halogen gave rather low enantioselectivities with good reactivity (Table 2, entries 6 and 7). In the presence of **3g**-$In(OAc)_3$ complex, no α-hydroxy phosphonate was detected (Table 2, entry 8).

Subsequently, the molar ratio of ligand **3g** to In(OTf)$_3$ was examined and the results are shown in Table 3. Decreasing the molar ratio [**3g**/In(OTf)$_3$] from 1:1 to 1:2 led to a negative effect (Table 3, entries 1–3). When the molar ratio was increased from 1:1 to 3:2, the reactivity was slightly decreased and the enantioselectivity was maintained (Table 3, entry 4). However, when the molar ratio was further increased to 2:1, the enantioselectivity was reduced to 82% *ee* (Table 3, entry 5).

Table 3. Effects of the ratio of ligand to In(OTf)$_3$ on the allylation of α-keto phosphonate **4a**.[a]

Entry	**3g** [mol%]	In(OTf)$_3$ [mol%]	Yield [%][b]	*ee* [%][c]
1	5	10	72	71
2	7.5	10	71	79
3	10	10	88	85
4	15	10	84	85
5	20	10	79	82

[a] All reactions were carried out in 0.1 mmol α-keto phosphonate **4a**, 1.1 equivs. tetraallylstannane, 1.0 mL DMF, 0 °C for 3 h.
[b] Isolated yields.
[c] Determined by HPLC on Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.

Various solvents were screened in the presence of 10 mol% **3g**-In(III) complex. The results indicated that the solvents were crucial to the enantioselectivity and reactivity. Tetrahydrofuran and acetonitrile provided good yields, but the enantioselectivities were low (Table 4, entries 2 and 3). When toluene, dichloromethane or diethyl ether were used, low yields were obtained (Table 4, entries 4–6). This was probably because the catalyst was not soluble in these solvents. In terms of yield and enantioselectivity, DMF exhibited the best performance for the asymmetric allylation of α-keto phosphonates (Table 4, entry 1).

Table 4. Solvent effects on the allylation of α-keto phosphonate **4a**.[a]

Entry	Solvent	Yield [%][b]	*ee* [%][c]
1	DMF	88	85
2	THF	79	15
3	CH_3CN	80	14
4	Toluene	21	0
5	CH_2Cl_2	36	26
6	Et_2O	64	5

[a] All reactions were carried out in 10 mol% **3g**, 10 mol% In(OTf)$_3$, 0.1 mmol α-keto phosphonate **4a**, 1.1 equivs. tetraallylstannane, 1.0 mL solvent, 0 °C for 3 h.
[b] Isolated yields.
[c] Determined by HPLC on a Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.

To improve the enantioselectivity and reactivity, the reaction temperature and substrate concentration were checked and the results are presented in Table 5. The temperature affected both the reactivity and the enantioselectivity (Table 5, entries 1–4). When the temperature rose from 0 to 25 °C, the enantioselectivity was somewhat reduced although the reaction time was shortened to 1 h (Table 5, entry 1 *vs.* 2). Fortunately, when the reaction temperature was decreased to −20 °C, the α-hydroxy phosphonate was obtained in 87% yield with 90% *ee* (Table 5, entry 3). However, on further decreasing the temperature to −45 °C, lower reactivity and enantioselectivity were obtained (Table 5, entry 4). The substrate concentration was also a key factor. When the substrate concentration was increased to 0.2 M, a 95% yield was given and the enantioselectivity remained unchanged (Table 5, entry 5). Other concentrations were disadvantageous (Table 5, entries 6–8).

Table 5. Temperature and concentration effects on the allylation of α-keto phosphonate **4a**.[a]

Entry	*T* [°C]	Concentration [mol/L]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	25	0.1	1	88	81
2	0	0.1	3	88	85
3	−20	0.1	16	87	90
4	−45	0.1	48	16	83
5	−20	0.2	8	95	90
6	−20	0.4	7.5	92	85
7	−20	0.5	7.5	93	86
8	−20	0.05	12.5	87	86

[a] Unless other specified, all reactions were carried out in 10 mol% **3g**, 10 mol% In(OTf)$_3$, 0.1 mmol α-keto phosphonate **4a**, 1.1 equivs. tetraallylstannane in DMF.
[b] Isolated yields.
[c] Determined by HPLC on a Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.

Next, the catalyst loading and allylic reagents were evaluated. Decreasing the catalyst loading caused a notable drop in reactivity and enantioselectivity (Table 6, entry 1). On increasing the catalyst loading from 10 mol% to 20 mol%, both the yield and enantioselectivity were not changed (Table 6, entries 2–4). Meanwhile, the allylic source was screened. The allyltributylstannane gave good enantioselectivity but low reactivity (Table 6, entry 5). Allylic silicon reagents could not give the product (Table 6, entries 6 and 7). Hence, the optimal conditions were 10 mol% In(OTf)$_3$, 10 mol% **3g**, 0.2 M α-keto phosphonate in DMF at −20 °C.

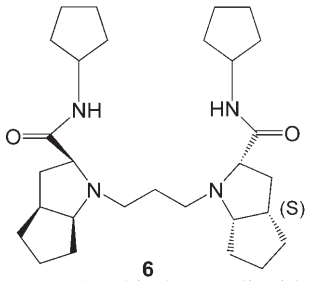
Table 6. Catalyst loading and allyl reagents effects on the allylation of α-keto phosphonate **4a**.[a]

Entry	Catalyst loading [mol%]	Allyl reagents	*t* [h]	Yield [%][b]	*ee* [%][c]
1	5	tetraallylstannane	26	91	85
2	10	tetraallylstannane	8	95	90
3	15	tetraallylstannane	6	94	90
4	20	tetraallylstannane	5	96	90
5	10	allyltributylstannane	8	<5	86
6	10	allyltriethoxysilane	8	trace	N.D.[d]
7	10	allyltrichlorosilane	8	trace	N.D.[d]

[a] Unless other specified, all reactions were carried out in 0.1 mmol α-keto phosphonate **4a**, 1.1 equivs. allyl reagents, 0.5 mL DMF at −20 °C.
[b] Isolated yields.
[c] Determined by HPLC on Chiralcel OJ-H column, and the major enantiomer was produced with the same configuration according to the HPLC analysis.
[d] Not detected.

Encouraged by the above results, the scope of the asymmetric allylation of aromatic α-keto phosphonates was investigated under the optimal conditions. As summarized in Table 7, excellent yields (80–98%) and high enantioselectivities (86–91% *ee*) were obtained (Table 7, entries 1–14). When the stereohindance of the ester alkyl group was increased from the smaller Me and Et to the larger *i*-Pr, the enantioselectivities were slightly decreased (Table 7, entries 1–3). With either electron-withdrawing or the electron-donating group on the *p*- or *m*-position of the aromatic ring of the α-keto phosphonates, high enantioselectivities (87–91% *ee*) could be obtained (Table 7, entries 4–14). However, *o*-substituted aromatic α-keto phosphonates gave somewhat lower enantioselectivities (Table 7, entries 15 and 16). The presence of a disubstituted aromatic ring led to the corresponding α-hydroxy phosphonate in good yield and moderate enantioselectivity (Table 7, entry 17).

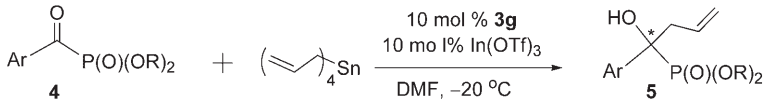
To gain a preliminary insight into the mechanism, a C_2-symmetric amide, compound **6** (Figure 2), which is the precursor of the chiral *N,N′*-dioxide **3g**, was synthesized.



6

Figure 2. Precursor of the chiral *N,N′*-dioxide **3g**.

Table 7. Scope of the enantioselective allylation of aromatic α-keto phosphonates.[a]



Entry	Ar	R	Product	*t* [h]	Yield [%][b]	*ee* [%][c]
1	Ph	Et	**5a**	8	95	90
2	Ph	Me	**5b**	8	85	90
3	Ph	*i*-Pr	**5c**	8	88	86
4	4-ClC_6H_4	Et	**5d**	10	84	91
5	4-ClC_6H_4	Me	**5e**	7	86	90
6	4-$MeOC_6H_4$	Et	**5f**	8.5	86	90
7	4-$MeOC_6H_4$	Me	**5g**	10	80	91
8	4-MeC_6H_4	Me	**5h**	10	94	91
9	4-MeC_6H_4	Et	**5i**	10	98	89
10	4-*t*-BuC_6H_4	Et	**5j**	8	94	88
11	3-$MeOC_6H_4$	Me	**5k**	9	82	91
12	3-MeC_6H_4	Et	**5l**	8	91	88
13	3-MeC_6H_4	Me	**5m**	8	90	87
14	3-BrC_6H_4	Me	**5n**	8	80	88
15	2-ClC_6H_4	Et	**5o**	9.5	98	78
16	2-ClC_6H_4	Me	**5p**	7	90	74
17	2,6-$F_2C_6H_3$	Et	**5q**	9	82	68

[a] Unless other specified, all reactions were carried out in 10 mol% **3g**, 10 mol% $In(OTf)_3$, 0.1 mmol α-keto phosphonate, 1.1 equivs. tetraallylstannane, 0.5 mL DMF at −20 °C.
[b] Isolated yields.
[c] The *ee* values were determined by chiral HPLC and the absolute configuration of major enantiomer was not determined.

thesized. Some experiments were carried out and the results are listed in Table 8. No α-hydroxy phosphonates were observed with chiral *N,N′*-dioxide **3g** or amide **6** as the organocatalyst, respectively (Table 8, entries 1 and 3). The $In(OTf)_3$ coordinated with amide **6** as the catalyst could catalyze the allylation of α-keto phosphonates with 75% yield, but the product **5a** was a racemate (Table 8, entry 4). This fact illuminated that the *N*-oxide and the central metal played a key role for this reaction. In addition, on decreasing the amount of the tetraallylstannane to 0.5 equivs. and 0.3 equivs., the reaction proceeded smoothly with 62% yield and 78% *ee* and 41% yield and 67% *ee*, respectively (Table 8, entries 5 and 6). This showed that one molecule of tetraallylstannane could provide more than one allyllic group. When less than 1.0 equiv. tetraallylstannane was used, the *ee* values changed as the conversion increased (Table 8, entries 7 and 8), which means that the tin center is involved in the enantiodetermining step.

Based on these experimental results, a plausible catalytic cycle of the enantioselective allylation of aromatic α-keto phosphonate was proposed as described in Figure 3. First, chiral *N,N′*-dioxide **3g** coordinated with $In(OTf)_3$ to form the possible complex A.[21a,b,22] Then one of the *N,N′*-dioxides coordinated with the tin atom of tetraallylstannane to form the possible complex **B**, enhancing the nucleophilicity of the allylic reagent.[23] One of the activated allylic groups might be transferred from the tin atom to the indium atom as the other one of the *N,N′*-dioxides did take part in the coordination, so as to form an allylic indium complex (complex **C**).[20,24] As a central metal, the indium activated the α-keto phosphonate and formed the possible complex **D**.[24a,25] At last, the activated allylic group preferred to attack the activated α-keto phosphonate **4a** and the product **5a** was obtained after general work-up. Simultaneously, complex **A** was also regenerated and another catalytic cycle began.

Conclusions

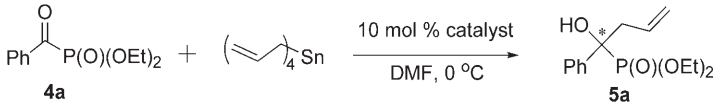
In summary, we have developed the first highly enantioselective allylation of aromatic α-keto phosphonates using a chiral indium complex, which was prepared from indium(III) trifluoromethanesulfonate and the C_2-symmetric (*S*)-ramipril acid derivative *N,N′*-dioxide **3g**. Under the mild conditions, high yields (up to 98%) and high enantioselectivities (up to 91% *ee*) were obtained for a range of aromatic α-keto phosphonates. Attractive features of the current method include the catalyst preparation with readily available materials, mild reaction conditions and convenient procedure with the tolerance of moisture and air. A possible catalytic cycle has been proposed. Future efforts will be focused on the application of α-hydroxy phosphonates and enhancement of the enantioselectivity.

Experimental Section

Typical Procedure for the Preparation of the Chiral *N,N′*-Dioxide (3g)

To a solution of (*S*)-Boc-ramipril acid (1.021 g, 4 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (0.62 mL, 4.4 mmol), isobutyl chloroformate (576 mg, 4.4 mmol) at 0 °C under stirring. After 15 min, cyclopentylamine (0.377 g, 4.4 mmol) was added. The reaction mixture was allowed to warm to ambient temperature and checked by TLC. The mixture was washed with 1 N $KHSO_4$, saturated $NaHCO_3$, brine, dried over anhydrous $MgSO_4$ and concentrated. To the residue in CH_2Cl_2 (4 mL) was added TFA (4 mL) and stirred was continued until the reaction was finished. Then, the solvent was

Table 8. Control experiment for mechanism studies.[a]



Entry	Ligand (mol%)	$In(OTf)_3$ (mol%)	Tetraallylstannane (equivs.)	*t* (h)	Yield [%][b]	*ee* [%][c]
1	**3g** (10)	-	1.1	3	N. R.	-
2	**3g** (10)	10	1.1	3	88	85
3	**6** (10)	-	1.1	3	N. R.	-
4	**6** (10)	10	1.1	3	75	0
5	**3g** (10)	10	0.5	8	62	78
6	**3g** (10)	10	0.3	24	41	67
7	**3g** (10)	10	0.4	12	60	78
8	**3g** (10)	10	0.4	18	70	69

[a] All reactions were carried out in 0.1 mmol α-keto phosphonate **4a**, 1.0 mL DMF at 0 °C.
[b] Isolated yields.
[c] Determined by HPLC on a Chiralcel OJ-H column.

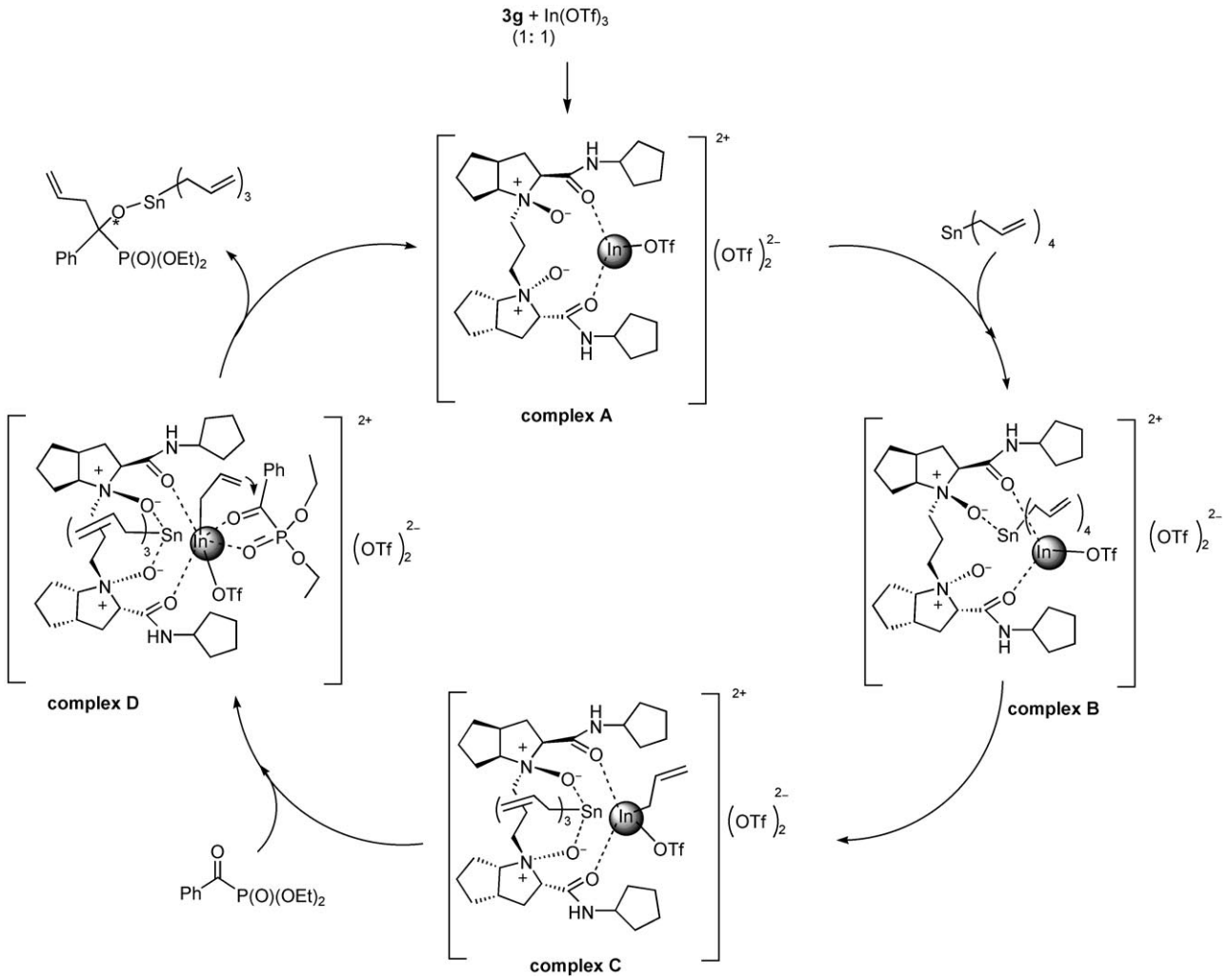


Figure 3. Proposed catalytic cycle.

evaporated, and H_2O (10 mL) was added. The pH value of the mixture was brought into the range of 8–10 by the addition of 1 N NaOH. The aqueous phase was extracted with CH_2Cl_2 (5×20 mL). The combined organic phase was washed with brine, dried over anhydrous $MgSO_4$ and evaporated under vacuum. The residue was directly used for next step. To a solution of (*S*)-ramipril-amide in CH_3CN (4 mL) was added K_2CO_3 (608 mg, 4.4 mmol) and 1,3-dibromopropane (204 μL, 2 mmol) under stirring. It was refluxed and monitored by TLC. Then, the solid was removed by filtration. The residue was concentrated and purified by silica gel column chromatography (EtOAc) to give **6** as a white solid; yield: 0.780 g (83% for 3 steps).

To a solution of **6** (0.780 g, 1.612 mmol) in CH_2Cl_2 (20 mL) was added *m*-chloroperoxybenzoic acid (0.624 g, 3.546 mmol) under stirring at −20 °C. After the reaction was finished, the misture was purified by silica gel column chromatography (MeOH/ether = 1:1) to give **3g** as a white solid; yield: 0.750 g (90%); $[\alpha]_D^{25}$: −24.4 (*c* 0.50 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.71 (d, *J* = 7.6 Hz, 2H), 4.16–4.18 (m, 2H), 3.93–3.96 (m, 2H), 3.71–3.73 (m, 2H), 3.33–3.36 (m, 2H), 3.16–3.23 (m, 2H), 2.71–2.73 (m, 2H), 2.58–2.64 (m, 2H), 2.38–2.40 (m, 4H), 2.00–2.12 (m, 2H), 1.89–1.99 (m, 6H), 1.43–1.74 (m, 18H), 1.23–1.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 166.43, 83.43, 80.42, 66.02, 50.24, 42.14, 34.51, 32.76, 32.07, 27.85, 26.42, 23.65, 19.17 ppm; HR-MS (ESI): *m/z* = 516.3678, calcd. for $C_{29}H_{48}N_4O_4$ [M + H$^+$]: 516.3676.

Typical Experimental Procedure for the Enantioselective Allylation of Aromatic α-Keto Phosphonates

To a dried tube equipped with a magnetic stirring bar were added $In(OTf)_3$ (5.6 mg, 0.01 mmol) and **3g** (5.2 mg, 0.01 mmol) in DMF (0.5 mL) to afford a clear solution, which was allowed to stir at 25 °C for 0.5 h. In sequence, the tetraallyltin (26.4 μL, 0.11 mmol) was added at 25 °C. After 0.5 h, α-keto phosphonate **4a** (24.2 mg, 0.1 mmol) was added at −20 °C. The reaction mixture was stirred at −20 °C for 8 h and directly purified by column chromatography on silica gel eluted with ether to afford product **5a** as a colorless solid with 90% *ee*; yield: 95%; mp 72–74 °C; $[\alpha]_D^{25}$: +3.13 (*c* 0.54 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.59–7.61 (m, 2H), 7.35–7.39 (m, 2H), 7.29–7.31 (m, 1H), 5.58–5.64 (m, 1H), 5.15–5.20 (m, 2H), 4.10–4.17 (m,

2H), 3.90–3.97 (m, 1H), 3.72–3.79 (m, 1H), 2.93–3.03 (m, 2H), 2.75 (d, $J=10.0$ Hz, 1H), 1.29 (t, $J=7.2$ Hz, 3H), 1.14 (t, $J=7.2$ Hz, 3H); HPLC (DAICEL CHIRALCEL OJ-H, hexane/2-propanol, 99/1, 1.0 mL), t_R (minor) = 7.038 min, t_R (major) = 7.728 min.

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References

[1] For reviews of enantioselective carbonyl allylation, see: a) Y. Yamamoto, *Acc. Chem. Res.* **1987**, *20*, 243–249; b) J. A. Marshall, *Chem. Rev.* **1996**, *96*, 31–47; c) S. E. Denmark, J. Fu, *Chem. Rev.* **2003**, *103*, 2763–2793.

[2] For review, see: O. I. Kolodiazhnyi, *Tetrahedron: Asymmetry* **2005**, *16*, 3295–3340.

[3] a) M. L. Peters, M. Leonard, A. A. Licata, *Clev. Clin. J. Med.* **2001**, *68*, 945–951; b) B. Z. Leder, H. M. Kronenberg, *Gastroenterology* **2000**, *119*, 866–869.

[4] R. Snoeck, A. Holy, C. Dewolf-Peeters, J. Van Den Oord, E. De Clercq, G. Andrei, *Antimicrob. Agents Chemother.* **2002**, *46*, 3356–3361.

[5] a) J. F. Dellaria, Jr. R. G. Maki, H. H. Stein, J. Cohen, D. Whittern, K. Marsh, D. J. Hoffman, J. J. Plattner, T. J. Perun, *J. Med. Chem.* **1990**, *33*, 534–542; b) M. Tao, R. Bihovsky, G. J. Wells, J. P. Mallamo, *J. Med. Chem.* **1998**, *41*, 3912–3916.

[6] B. Stowasser, K.-H. Budt, J.-Q. Li, A. Peyman, D. Ruppert, *Tetrahedron Lett.* **1992**, *33*, 6625–6628.

[7] a) T. Gajda, *Tetrahedron: Asymmetry* **1994**, *5*, 1965–1972; b) C. Meier, W. H. G. Laux, *Tetrahedron: Asymmetry* **1995**, *6*, 1089–1092; c) C. Meier, W. H. G. Laux, *Tetrahedron: Asymmetry* **1996**, *7*, 89–94; d) C. Meier, W. H. G. Laux, *Tetrahedron* **1996**, *52*, 589–598; e) V. V. Nesterov, O. I. Kolodyazhnyi, *Russ. J. Gen. Chem.* **2005**, *75*, 1161–1162; f) V. V. Nesterov, O. I. Kolodiazhnyi, *Tetrahedron: Asymmetry* **2006**, *17*, 1023–1026.

[8] a) D. M. Pogatchnik, D. F. Wiemer, *Tetrahedron Lett.* **1997**, *38*, 3495–3498; b) D. M. Cermak, Y. Du, D. F. Wiemer, *J. Org. Chem.* **1999**, *64*, 388–393; c) D. Skropeta, R. R. Schmidt, *Tetrahedron: Asymmetry* **2003**, *14*, 265–273.

[9] a) T. Arai, M. Bougauchi, H. Sasai, M. Shibasaki, *J. Org. Chem.* **1996**, *61*, 2926–2927; b) H. Sasai, M. Bougauchi, T. Arai, M. Shibasaki, *Tetrahedron Lett.* **1997**, *38*, 2717–2720; c) M. D. Groaning, B. J. Rowe, C. D. Spilling, *Tetrahedron Lett.* **1998**, *39*, 5485–5488; d) B. J. Rowe, C. D. Spilling, *Tetrahedron: Asymmetry* **2001**, *12*, 1701–1708; e) B. Saito, T. Katsuki, *Angew. Chem. Int. Ed.* **2005**, *44*, 4600–4602; f) D. F. Wiemer, *Tetrahedron* **1997**, *53,* 16609–16644.

[10] a) S. Samanta, C.-G. Zhao, *J. Am. Chem. Soc.* **2006**, *128*, 7442–7443; b) R. Dodda, C.-G. Zhao, *Org. Lett.* **2006**, *8*, 4911–4914.

[11] T. Mandal, S. Samanta, C.-G. Zhao, *Org. Lett.* **2007**, *9*, 943–945.

[12] a) A. S. Demir, Ö. Reis, M. Kayalar, S. Eymur, B. Reis, *Synlett* **2006**, 3329–3333; b) A. S. Demir, Ö. Reis, A. C. Iğdir, I. Esiringü, S. Eymur, *J. Org. Chem.* **2005**, *70*, 10584–10587.

[13] For a racemic example of allylation of α-keto phosphonates, see: D. Y. Kim, D. F. Wiemer, *Tetrahedron Lett.* **2003**, *44*, 2803–2805.

[14] a) B. Tao, M. M.-C. Lo, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 353–354; b) S. E. Denmark, Y. Fan, *J. Am. Chem. Soc.* **2002**, *124*, 4233–4235; c) T. Shimada, A. Kina, T. Hayashi, *J. Org. Chem.* **2003**, *68*, 6329–6337; d) J. F. Traverse, Y. Zhao, A. H. Hoveyda, M. L. Snapper, *Org. Lett.* **2005**, *7*, 3151–3154; e) A. V. Malkov, M. Bell, F. Castelluzzo, P. Kočovský, *Org. Lett.* **2005**, *7*, 3219–3222.

[15] a) B. Liu, X. M. Feng, F. X. Chen, G. L. Zhang, X. Cui, Y. Z. Jiang, *Synlett* **2001**, 1551–1554; b) Z. G. Jiao, X. M. Feng, B. Liu, F. X. Chen, G. L. Zhang, Y. Z. Jiang, *Eur. J. Org. Chem.* **2003**, 3818–3826.

[16] a) X. Huang, J. L. Huang, Y. H. Wen, X. M. Feng, *Adv. Synth. Catal.* **2006**, *348*, 2579–2584; b) J. L. Huang, X. H. Liu, Y. H. Wen, B. Qin, X. M. Feng, *J. Org. Chem.* **2007**, *72*, 204–208.

[17] Y. H. Wen, X. Huang, J. L. Huang, Y. Xiong, B. Qin, X. M. Feng, *Synlett* **2005**, 2445–2448.

[18] B. Qin, X. H. Liu, J. Shi, K. Zheng, H. T. Zhao, X. M. Feng, *J. Org. Chem.* **2007**, *72*, 2374–2378.

[19] a) Q. H. Li, X. H. Liu, J. Wang, K. Shen, X. M. Feng, *Tetrahedron Lett.* **2006**, *47,* 4011–4014; b) Y. C. Shen, X. M. Feng, G. L. Zhang, Y. Z. Jiang, *Synlett* 1353–1355; c) Q. H. Li, L. Chang, X. H. Liu, X. M. Feng, *Synlett* 1675–1678.

[20] a) X. Zhang, D. H. Chen, X. H. Liu, X. M. Feng, *J. Org. Chem.* **2007**, *72,* 5227–5233; b) K. Zheng, B. Qin, X. H. Liu, X. M. Feng, *J. Org. Chem.* **2007**, *72*, 8478–8483; c) B. Qin, X. Xiao, X. H. Liu, J. L. Huang, Y. H. Wen, X. M. Feng, *J. Org. Chem.* **2007**, *72*, 9323–9328.

[21] a) J. Lu, M. L. Hong, S. J. Ji, Y.-C. Teo, T.-P. Loh, *Chem. Commun.* **2005**, 4217–4218; b) F. Delpech, I. A. Guzei, R. F. Jordan, *Organometallics* **2002**, *21*, 1167–1176; c) Y.-C. Teo, J.-D. Goh, T.-P. Loh, *Org. Lett.* **2005**, *7*, 2743–2745; d) Y.-C. Teo, K. T. Tan, T.-P. Loh, *Chem. Commun.* **2005**, 1318–1320; e) H. Hanawa, S. Kii, K. Maruoka, *Adv. Synth. Catal.* **2001**, *343*, 57–60; f) S. Casolari, D. D′Addario, E. Tagliavini, *Org. Lett.* **1999**, *1*, 1061–1063; g) A. Cunningham, S. Woodward, *Synlett* **2002**, 43–44; h) K. M. Waltz, J. Gavenonis, P. J. Walsh, *Angew. Chem. Int. Ed.* **2002**, *41*, 3697–3699; i) O. Prieto, S. Woodward, *J. Organomeat. Chem.* **2006**, *691*, 1515–1519; j) J. G. Kim, K. M. Waltz, L. F. Garcia, D. Kwiatkowski, P. J. Walsh, *J. Am. Chem. Soc.* **2004**, *126*, 12580–12585; k) J. G. Kim, E. H. Camp, P. J. Walsh, *Org. Lett.* **2006**, *8*, 4413–4416; l) A. J. Wooten, J. G. Kim, P. J. Walsh, *Org. Lett.* **2007**, *9*, 381–384.

[22] The NH signal of the catalyst and ligand in ^{1}H NMR has a slight shift (see Supporting Information). The catalyst prepared from $In(OTf)_3$ and **3g** in a 1:1 ratio afforded the peak at 1092.5 in HR-MS (calcd.: 1092.1).

[23] a) S. E. Denmark, J. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 2208–2216; b) Y. Hamashima, M. Kanai, M. Shibasaki,

J. Am. Chem. Soc. **2000**, *122*, 7412–7413; c) S.-K. Tian, R. Hong, L. Deng, *J. Am. Chem. Soc.* **2003**, *125*, 9900–9901; d) N. kato, D. Tomita, K. Maki, M. Kanai, M. Shibasaki, *J. Org. Chem.* **2004**, *69*, 6128–6130.

[24] a) R. Takita, Y. Fukuta, R. Tsuji, T. Ohshima, M. Shibasaki, *Org. Lett.* **2005**, *7*, 1363–1366; b) S. E. Denmark, G. L. Beutner, T. Wynn, M. D. Eastgate, *J. Am. Chem. Soc.* **2005**, *127*, 3774–3789; c) I. Shibata, H. Kato, T. Ishida, M. Yasuda, A. Baba, *Angew. Chem. Int. Ed.* **2004**, *43*, 711–714.

[25] a) L. C. Wieland, H. Deng, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 15453–15456; b) K. Endo, T. Hatakeyama, M. Nakamura, E. Nakamura, *J. Am. Chem. Soc.* **2007**, *129*, 5264–5271.

