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Chiral Phebox–rhodium complexes as catalysts for asymmetric direct aldol reaction

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Abstract

Chiral bis(oxazolinyl)phenyl–rhodium complexes act as catalysts in the combination of AgOTf for direct aldol reaction of ketones and aromatic aldehydes to give the corresponding β-hydroxyketones in high *anti*-selectivity and a good to high enantioselectivity up to 91% ee.

Keywords: Rhodium; Asymmetric catalysis; Direct aldol reaction; Bisoxazoline

1. Introduction

We have demonstrated that chiral bis(oxazolinyl)phenyl–rhodium chloro complex **1a** acts as a Lewis acid catalyst for asymmetric allylation of aldehydes[1] and asymmetric Michael addition[2] of α-cyanopropionates. The aqua ligand (H_2O) on **1a** readily dissociates to provide a vacant site at the equatorial position, which can show Lewis acidity to activate carbonyl acceptors. On the other hand, we have found that the acetate ligand on **1b** can play as a Brønsted base to attain C–H bond activation reactions of arenes and acetylenes.[3] On the basis of these findings, we have envisioned that synergic action of the acidic site and the basic one can promote a direct aldol reaction of simple ketones and aromatic aldehydes as illustrated as **A** in Scheme 1. Initially, ketone may be captured on the rhodium complex by the synergic action (i) to form the corresponding rhodium–enolate (ii), which reacts with aldehyde (iii) to give the rhodium–aldolate (iv). Finally, when ketone is incorporated, the aldol product is released to regenerate the intermediate rhodium–enolate (ii).

In this context, the synergic action of acidic site and basic one on metal catalysts for asymmetric direct aldol reactions has been demonstrated by Shibasaki's group and Trost's group (Fig. 1).[4,5] Shibasaki et al. disclosed heterobimetallic La–Li tris(binaphthoxide) **2** as a catalyst for direct aldol reaction of methyl ketones and several aliphatic aldehydes.[4] Trost et al. reported dinuclear zinc catalyst **3** for the aldol coupling of aldehydes toward aryl methyl ketones or vinyl methyl ketones. Here, we report a direct aldol reaction of ketones and aromatic aldehydes catalyzed by chiral bis(oxazolinyl)phenyl–rhodium acetate complexes.[6]

2. Results and discussion

The reaction of cyclohexanone (**4**) (5.0 mmol) and *p*-nitrobenzaldehyde (**5**) (0.5 mmol) in an appropriate solvent (0.5 mL) was carried out at 60 °C for 72 h in the presence of Phebox–Rh acetate **1b** (5 mol % to aldehyde) (Scheme 2). In a toluene solution, 5 mol % of the catalyst worked well to furnish the desired aldol product **6** in 82% with 61% of *anti*-selectivity and 49% of enantioselectivity for the *anti*-product (entry 1, Table 1). Loading of cyclohexanone was decreased to 2 equiv to diminish the yield to 41% (entry 2). The reaction was extremely retarded at 40 °C; ca. 10% yield for 72 h. The reaction time was elongated to 168 h to decrease the diastereoselectivity and the enantioselectivity (entry 3). This fact may indicate that epimerization or retro-aldol process proceeds during the reaction. As other solvents, protic solvents such as methanol and isopropyl alcohol proved to

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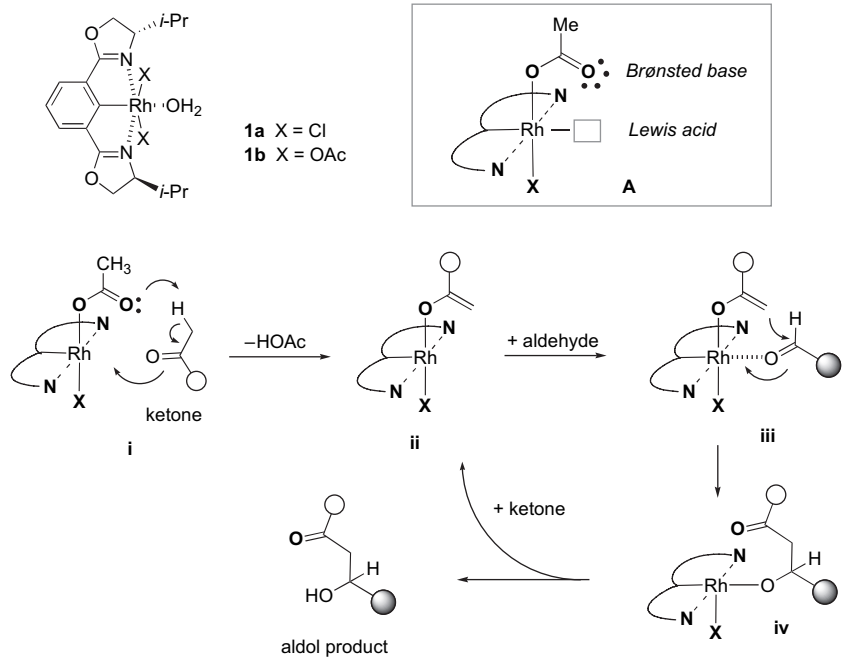


Scheme 1.

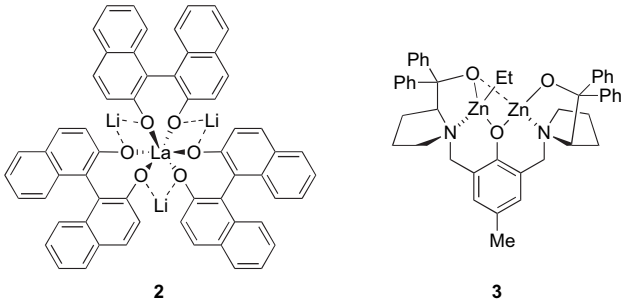
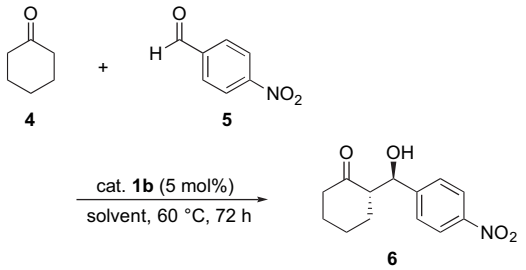


Figure 1.

be good media to produce **6** in 67–85% yields (entries 4–8). Furthermore, water did not interfere the catalysis (entry 9).[7,8]

In order to improve the stereoselectivity, we examined some of additives such as silver salts (Table 2). After several trials, we eventually found that silver triflate (5 mol %) incremented diastereoselectivity up to 13:87 of *syn*/*anti* and enantioselectivity to 81% for *anti*-product (entry 1). Addition of 10 mol % of AgOTf resulted in 87% ee (entry 2). Interestingly, trifluoromethanesulfonic acid itself also gave a similar result to entry 1 (entry 3). Other silver salts proved to be effective



Scheme 2. Direct aldol reaction with Phebox–Rh acetate catalyst.

Table 1
Direct aldol reaction of cyclohexanone and *p*-nitrobenzaldehyde catalyzed by Phebox–Rh acetate **1b**[a]

Entry	Solvent	Yield (%)	dr *syn*/*anti* (%)	ee *syn*/*anti* (%)
1	Toluene	82	39:61	27:49
2[b]	Toluene	41	31:69	36:60
3[c]	Toluene	80	49:51	14:29
4	THF	79	34:66	0:43
5	$Cl(CH_2)_2Cl$	85	35:65	2:25
6	MeCN	68	54:64	36:38
7	MeOH	80	45:55	4:48
8	*i*-PrOH	67	30:70	−2:64
9	H_2O	78	45:55	26:34

[a] Phebox–Rh **1b** (0.025 mmol, 5 mol %), *p*-nitrobenzaldehyde (0.5 mmol), cyclohexanone (5.0 mmol), solvent (0.5 mL), 60 °C, 72 h.
[b] Cyclohexanone (1.0 mmol).
[c] 168 h.

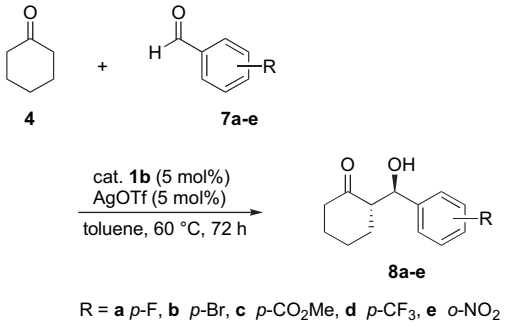
Table 2
Direct aldol reaction of cyclohexanone and *p*-nitrobenzaldehyde catalyzed by Phebox–Rh acetate **1b** in the presence of additive[a]

Entry	Additive	Yield (%)	dr *syn*/*anti* (%)	ee *syn*/*anti* (%)
1	AgOTf	78	17:83	−3:81
2[b]	AgOTf	79	13:87	−7:87
3	HOTf	79	14:86	21:83
4	$AgBF_4$	79	23:77	31:77
5	$AgPF_6$	79	22:78	11:73
6	$AgSbF_6$	76	16:84	0:66
7	$AgOSO_2Me$	81	33:67	24:60
8	AgOAc	80	33:67	31:71
9	$AgOCOCF_3$	82	30:70	9:60

[a] Phebox–Rh **1b** (0.025 mmol, 5 mol %), additive (5 mol %), *p*-nitrobenzaldehyde (0.5 mmol), cyclohexanone (5.0 mmol), toluene (0.5 mL), 60 °C, 72 h.
[b] AgOTf (10 mol %).

to some extent for diastereoselectivity (30:70 to 84:16) and enantioselectivity (60–77% for *anti*-product) (entries 4–9).

Other benzaldehydes **7a–e** with electron-withdrawing groups were examined to give moderate yields in 44–75% (Scheme 3, Table 3). The reaction with *p*-CF_3 substituted benzaldehyde gave higher diastereoselectivity of 89% for *anti*-product and enantioselectivity up to 86% (entry 4). The case of *o*-NO_2 substituted aldehyde resulted in 90% of *anti*-selectivity (entry 5).[9]



Scheme 3. Direct aldol reaction of substituted benzaldehydes with Phebox–Rh catalyst.

Next, we examined the reaction of cyclopentanone (**9**) (5.0 mmol) as an enolate source under the same condition described in entry 1 of Table 2 (Scheme 4). The reaction with *p*-NO_2, *p*-CO_2Me, and *o*-NO_2 substituted benzaldehydes (**5**, **7c**, and **7e**) smoothly took place to give the corresponding aldol products in 54–75% yields. The high diastereoselectivity over 80% for *anti* and the high enantioselectivity up to 91% were obtained.

Acetone (**11**) (1.0 mL, no solvent) in turn was chosen to give the aldol product **12a** in 63% with 74% ee under the same condition described in entry 2 of Table 2 (Scheme 5). The reaction with *o*-nitrobenzaldehyde **7e** resulted in 61% of **12b** with 81% ee (Scheme 5). Several acyclic ketones such as diethyl ketone, acetophenone, and *tert*-butyl methyl ketones were examined, but the yields were disappointingly lower in a trace to ca. 30%.

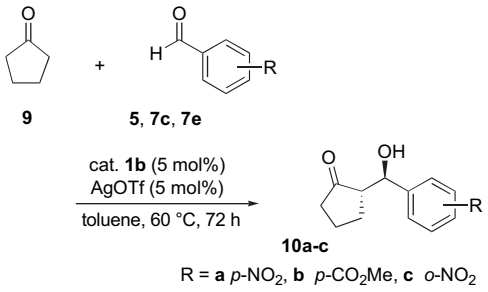
In order to determine the absolute configuration of the aldol product *anti*-**6** (>99% ee), it was subjected to preparation of the corresponding sultam derivative **14** (Scheme 6). The molecular structure of **14** could be determined by X-ray analysis to show the absolute configuration of 2*S*,3*R* (Fig. 2).

On the basis of confirmation of the absolute configuration, the transition state is hypothetically proposed in Figure 3. The C–C bond formation may take place between *Re*-face of the enolate and *Re*-face of the aldehyde through the cyclic transition state to furnish 2*S*,3*R* absolute configuration. The counter anion effect described in Table 2 can be elucidated by the transition state, in which X ligands such as OTf or PF_6, etc. can

Table 3
Direct aldol reaction of cyclohexanone and substituted benzaldehyde catalyzed by Phebox–Rh acetate **1b** in the presence of AgOTf[a]

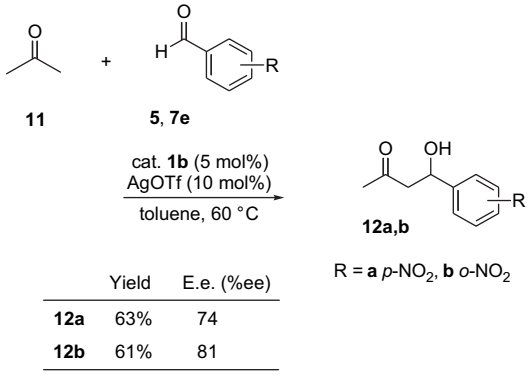
Entry	Aldehyde **7** (R)	Yield (%)	dr *syn*/*anti* (%)	ee *syn*/*anti* (%)
1	*p*-F	42	27:73	5:68
2	*p*-Br	48	17:83	10:79
3	*p*-CO_2Me	68	17:83	12:84
4[b]	*p*-CF_3	57	11:89	16:86
5[b]	*o*-NO_2	75	10:90	–:66

[a] Phebox–Rh **1b** (0.025 mmol, 5 mol %), AgOTf (10 mol %), substituted benzaldehyde (0.5 mmol), cyclohexanone (5.0 mmol), toluene (0.5 mL), 60 °C, 72 h.
[b] AgOTf (5 mol %).



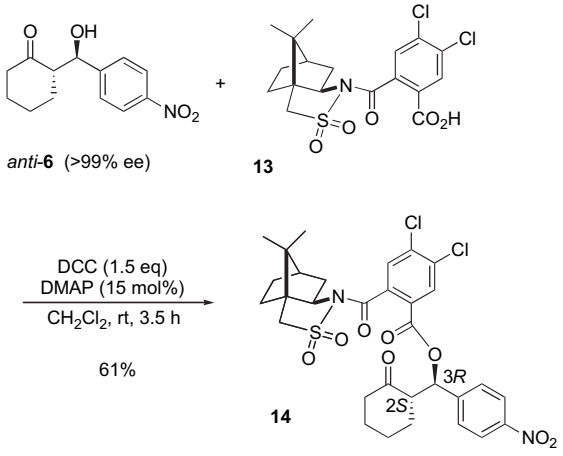
	Yield (%)	dr *syn*/*anti* (%)	ee *syn*/*anti* (%)
10a	75	20:80	72:91
10b	62	13:87	41:88
10c	54	14:86	11:84

Scheme 4.



	Yield	E.e. (%ee)
12a	63%	74
12b	61%	81

Scheme 5.



Scheme 6.

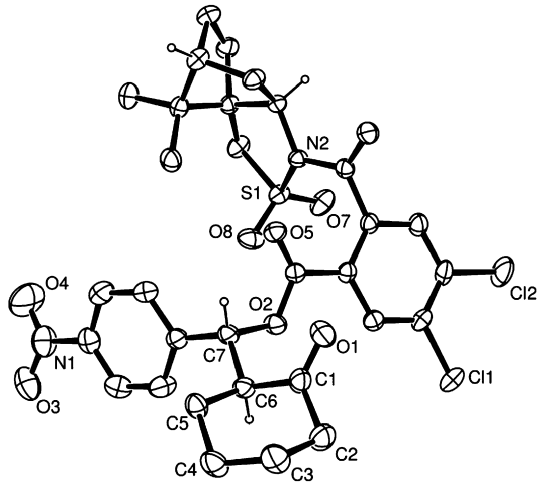


Figure 2. X-ray analysis of **14**.

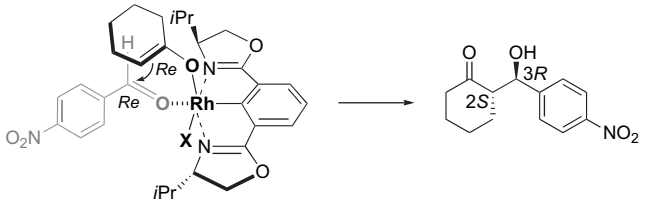


Figure 3. Proposed transition state.

influence the stereochemical course of the approaching aldehyde.[10]

3. Conclusion

We can demonstrate that chiral Phebox–Rh acetate complex exhibits catalytic activity for asymmetric direct aldol reaction to show high *anti*-selectivity and high enantioselectivity. It is thought that the complex can act as synergic catalyst with Lewis acid site and Brønsted base site to promote facile enolate-formation and successive aldol reaction. The transition state model is also proposed on the basis of the absolute and relative stereochemistry of the product. Thus, we can disclose a new type of reaction with transition metal complex having acid–base bifunctional sites.

4. Experimental

4.1. General

NMR spectra were obtained in $CDCl_3$ solution at 25 °C on spectrometers (^1H, 300 MHz and 500 MHz; ^{13}C, 75 MHz and 125 MHz). ^1H NMR chemical shifts are reported in δ units, in parts per million relative to the singlet at 7.26 ppm for chloroform. IR spectra were recorded with a JASCO FT/IR-230 spectrometer. Elemental analysis was performed with a Yanaco MT-6. Phebox–Rh catalyst **1b** was synthesized by the method reported by us.[11]

4.2. Typical aldol reactions

4.2.1. The aldol reaction of cyclohexanone (*4*) and *p*-nitrobenzaldehyde (*5*) (entry 2, Table 2)

The catalyst **1b** (13.5 mg, 0.025 mmol), AgOTf (12.9 mg, 0.050 mmol), and *p*-nitrobenzaldehyde (75.6 mg, 0.50 mmol) were placed in a flask. Then, cyclohexanone (0.50 mL, 5.0 mmol) and toluene (0.5 mL) were added under an argon atmosphere. The mixture was stirred at 60 °C for 72 h. The reaction mixture was introduced to silica gel column with hexane–ethyl acetate (3:1) to give the desired aldol product **6** in 79% yield (98.7 mg, 0.395 mmol).

4.2.2. The aldol reaction of cyclopentanone (*9*) and *p*-methoxycarbonylbenzaldehyde (*7c*) (Scheme 4)

The catalyst **1b** (13.5 mg, 0.025 mmol), AgOTf (6.4 mg, 0.025 mmol), and *p*-methoxycarbonylbenzaldehyde (82.1 mg, 0.50 mmol) were placed in a flask. Then, cyclopentanone (0.443 mL, 5.0 mmol) and toluene (0.5 mL) were added under an argon atmosphere. The mixture was stirred at 60 °C for 72 h. The reaction mixture was introduced to silica gel column with hexane–ethyl acetate (4:1) to remove the catalyst. The residue was again purified by silica gel column chromatography with 1:1 hexane–chloroform to give the desired aldol product **10b** in 62% yield (76.7 mg, 0.31 mmol).

4.3. Analytical data of the aldol products

4.3.1. Compound *6*

White solids. ^1H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.3–1.5 (m, 1H), 1.5–1.8 (m, 3H), 1.82 (m, 1H), 2.12 (m, 1H), 2.40 (m, 1H), 2.5–2.7 (m, 2H), 4.09 (d, J=3.0 Hz, 1H, O*H*), 4.90 (dd, J=3.0, 8.4 Hz, C*H*OH), 7.50 (d, J=8.4 Hz), 8.20 (d, J=8.4 Hz); for *syn*, 3.20 (br, 1H, O*H*), 5.48 (br s, 1H, C*H*OH); ratio of *syn*/*anti* 13:87. ^{13}C NMR (75 MHz, $CDCl_3$) for *anti*, 24.82, 27.77, 30.86, 42.74, 57.19, 73.95, 123.3, 127.6, 147.2, 148.0, 214.23; for *syn*, 24.93, 26.06, 28.01, 42.72, 56.83, 70.10, 123.3, 126.4, 146.7, 148.8, 213.6. IR (KBr disk) ν 3650–3300 (br), 1698, 1524, 1347 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.64; H, 6.08; N, 5.63. Chromatography: DAICEL CHIRALPAK AD-H, eluent: hexane/2-propanol (90:10) (1.0 mL/min), retention time: 17.5 min (*syn*, minor), 20.3 min (*syn*, major), 22.5 min (*anti*, minor), 29.8 min (*anti*, major, 2*S*,3*R*); for *anti*-(2*S*,3*R*), 87% ee, for *syn*, 7% ee; diastereomer ratio, *syn*/*anti*=13:87. The data of ^1H NMR are in accordance with the previously reported ones by Takabe and Barbas.[7c]

4.3.2. Compound *8a*

White solids. ^1H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.3 (m, 1H), 1.5–1.9 (m, 4H), 2.1 (m, 1H), 2.3–2.7 (m, 3H), 3.99 (d, J=3.0 Hz, 1H, O*H*), 4.77 (dd, J=2.7, 9.0 Hz, 1H, C*H*OH), 7.03 (m, 2H), 7.28 (m, 2H); for *syn*, 3.04 (br, 1H, O*H*), 5.36 (br s, 1H, C*H*OH). IR (KBr disk) ν 3650–3300 (br), 1698, 1509, 1224 cm^{-1}. Anal. Calcd for $C_{13}H_{15}FO_2$: C, 70.25; H, 6.80. Found: C, 70.48; H, 6.91. Chromatography: DAICEL CHIRALPAK AD-H, eluent: hexane/2-propanol

(90:10) (1.0 mL/min), retention time: 8.5 min (*syn*, major), 9.6 min (*syn*, minor), 12.6 min (*anti*, minor), 13.9 min (*anti*, major); for *anti*, 68% ee, for *syn*, 5% ee; diastereomer ratio, *syn*/*anti*=27:73.

4.3.3. Compound **8b**

White solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.3 (m, 1H), 1.5–1.9 (m, 4H), 2.1 (m, 1H), 2.3–2.6 (m, 3H), 3.99 (d, J=2.4 Hz, O*H*), 4.75 (dd, J=2.4, 8.4 Hz, 1H, C*H*OH), 7.20 (m, 2H), 7.45 (m, 2H); for *syn*, 3.07 (br, 1H, O*H*), 5.34 (br s, 1H, C*H*OH). ^{13}C NMR (75 MHz, $CDCl_3$) for *anti*, 24.86, 27.87, 30.88, 42.75, 57.35, 74.14, 121.5, 128.5, 131.2, 139.7, 214.7. IR ($CHCl_3$) ν 3650–3300 (b), 1689 cm^{-1}. Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34. Found: C, 55.13; H, 5.35. Chromatography: DAICEL CHIRALPAK AD-H, eluent: hexane/2-propanol (90:10) (1.0 mL/min), retention time: 9.0 min (*syn*, minor), 10.6 min (*syn*, major), 14.1 min (*anti*, minor), 16.4 min (*anti*, major); for *anti*, 79% ee, for *syn*, 10% ee; diastereomer ratio, *syn*/*anti*=17:83. The data of ^{1}H NMR are in accordance with the previously reported ones by Takabe and Barbas.[7c]

4.3.4. Compound **8c**

White solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.3 (m, 1H), 1.5–1.9 (m, 4H), 2.1 (m, 1H), 2.3–2.6 (m, 3H), 3.91 (s, 3H, CH_3O), 4.83 (d, J=8.7 Hz, 1H, C*H*OH), 7.36 (m, 2H), 8.01 (m, 2H); for *syn*, 5.44 (br s, 1H, C*H*OH); *syn*/*anti*=17:83. IR ($CHCl_3$) ν 3650–3300 (br), 1718, 1692 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.53; H, 6.99. Chromatography: DAICEL CHIRALCEL OD-H, eluent: hexane/2-propanol (95:5) (1.0 mL/min), retention time: 16.6 min (*syn*, minor), 18.5 min (*syn*, major), 20.1 min (*anti*, major), 23.2 min (*anti*, minor); for *anti*, 84% ee, for *syn*, 12% ee. The data of ^{1}H NMR are in accordance with the previously reported ones by Takabe and Barbas.[7c]

4.3.5. Compound **8d**

White solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.3 (m, 1H), 1.5–1.9 (m, 4H), 2.1 (m, 1H), 2.3–2.7 (m, 3H), 4.85 (d, J=8.4 Hz, 1H, C*H*OH), 7.44 (m, 2H), 7.61 (m, 2H); for *syn*, 5.44 (br, 1H, C*H*OH); *syn*/*anti*=11:89. IR (KBr disk) ν 3650–3300 (br), 1699, 1326 cm^{-1}. Anal. Calcd for $C_{14}H_{15}F_3O_2$: C, 61.76; H, 5.55. Found: C, 61.58; H, 5.56. Chromatography: DAICEL CHIRALPAK AD-H, eluent: hexane/2-propanol (90:10) (1.0 mL/min), retention time: 7.0 min (*syn*, minor), 8.0 min (*syn*, major), 10.1 min (*anti*, minor), 12.5 min (*anti*, major); for *anti*, 86% ee, for *syn*, 16% ee.

4.3.6. Compound **8e**

Pale yellow solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.5–1.9 (m, 5H), 2.1 (m, 1H), 2.3–2.5 (m, 2H), 2.78 (m, 1H), 4.1 (br, 1H, O*H*), 5.45 (d, J=6.9 Hz, 1H, C*H*OH), 7.43 (t, J=8.2 Hz, 1H), 7.64 (t, J=8.2 Hz, 1H), 7.77 (d, J=8.2 Hz, 1H), 7.85 (d, J=8.2 Hz, 1H); for *syn*, 5.96 (br s, 1H, C*H*OH); *syn*/*anti*=10:90. ^{13}C NMR (75 MHz, $CDCl_3$) for *anti*, 25.11, 27.90, 31.23, 42.90, 57.32, 69.72, 123.9, 128.2, 128.8, 132.8, 148.4, 214.4. IR (KBr disk) ν 3650–3300 (br), 1701, 1523, 1344 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.61; H, 6.14; N, 5.62. Chromatography: DAICEL CHIRALPAK AD-H, eluent: hexane/2-propanol (97:3) (1.0 mL/min), retention time: 48.9 min (*anti*, major), 52.0 min (*anti*, minor); for *anti*, 66% ee, for *syn*, not determined. The data of ^{1}H NMR are in accordance with the previously reported ones by Takabe and Barbas.[7c]

4.3.7. Compound **10a**

White solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.55 (m, 1H), 1.6–1.9 (m, 2H), 2.05 (m, 1H), 2.2–2.6 (m, 3H), 4.77 (s, 1H, O*H*), 4.84 (d, J=9.3 Hz, 1H, C*H*OH), 7.53 (d, J=8.7 Hz, 2H), 8.21 (d, J=8.7 Hz, 2H); for *syn*, 5.42 (br, 1H, C*H*OH); ratio of *syn*/*anti* 20:80. ^{13}C NMR (75 MHz, $CDCl_3$) for *anti*, 20.55, 27.00, 38.71, 55.15, 74.41, 123.5, 127.1, 147.4, 148.4, 221.6. IR (KBr disk) ν 3600–3300 (br), 1722, 1521, 1348 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.37; H, 5.59; N, 5.96. Chromatography: DAICEL CHIRALPAK AS-H, eluent: hexane/2-propanol (80:20) (1.0 mL/min), retention time: 8.5 min (*syn*, major), 9.9 min (*anti*, minor), 11.9 min (*anti*, major), 27.1 min (*syn*, minor); for *anti*, 91% ee, for *syn*, 72% ee. The data of ^{1}H NMR are in accordance with the previously reported ones by Takabe and Barbas.[7c]

4.3.8. Compound **10b**

White solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.50 (m, 1H), 1.6–1.8 (m, 2H), 2.0 (m, 1H), 2.2–2.6 (m, 3H), 3.91 (s, 3H, C*H*$_3$O), 4.77 (d, J=9.0 Hz, 1H, C*H*OH), 7.39 (d, J=8.1 Hz), 8.00 (d, J=8.1 Hz); for *syn*, 5.35 (d, J=2.4 Hz, 1H, C*H*OH); ratio of *syn*/*anti* 13:87. IR (KBr disk) ν 3650–3300 (br), 1710, 1280 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.71; H, 6.55. Chromatography: DAICEL CHIRALCEL OJ-H, eluent: hexane/2-propanol (92:8) (1.0 mL/min), retention time: 23.5 min (*anti*, major), 27.1 min (*syn*, major), 32.1 min (*syn*, minor), 35.8 min (*anti*, minor); for *anti*, 88% ee, for *syn*, 41% ee.

4.3.9. Compound **10c**

Pale yellow solids. ^{1}H NMR (300 MHz, $CDCl_3$) for *anti*, δ 1.7–1.9 (m, 3H), 2.05 (m, 1H), 2.3–2.6 (m, 3H), 5.45 (d, J=8.7 Hz, 1H, C*H*OH), 7.44 (t, J=8.0 Hz, 1H), 7.66 (t, J=8.0 Hz, 1H), 7.80 (d, J=8.0 Hz, 1H), 7.81 (t, J=8.0 Hz, 1H); for *syn*, 5.92 (br, 1H, C*H*OH); ratio of *syn*/*anti* 14:86. ^{13}C NMR (75 MHz, $CDCl_3$) for *anti*, 20.66, 26.73, 38.75, 55.51, 69.08, 123.8, 128.4, 128.8, 132.9, 136.0, 148.1, 221.5. IR ($CHCl_3$) ν 3600–3300 (br), 1735, 1525, 1346 cm^{-1}. FAB-HRMS: [(M+1)$^+$] *m*/*z*, found: 236.0919; calcd ($C_{12}H_{14}NO_4$): 236.0923. Chromatography: DAICEL CHIRALCEL OD-H, eluent: hexane/2-propanol (95:5) (1.0 mL/min), retention time: 12.6 min (*syn*, minor), 16.3 min (*syn*, major), 21.6 min (*anti*, major), 24.3 min (*anti*, minor); for *anti*, 84% ee, for *syn*, 11% ee.

4.3.10. Compound **12a**

White solids; mp, 59–62 °C. ^{1}H NMR (300 MHz, $CDCl_3$), δ 2.23 (s, 3H), 2.84 (m, 2H), 2.87 (br, 1H), 5.26 (m, 1H), 7.53 (d, J=8.7 Hz, 2H), 8.20 (d, J=8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 30.84, 51.56, 68.87, 123.5, 126.2, 147.0, 149.7, 208.1. IR (KBr disk) ν 3650–3200 (br), 1708, 1515 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.46; H, 5.34; N, 6.68. FAB-HRMS: [(M+1)$^+$] m/z, found: 210.0756; calcd ($C_{10}H_{12}NO_4$): 210.0766. Chromatography: DAICEL CHIRALCEL OJ-H, eluent: hexane/2-propanol (80:20) (0.5 mL/min), retention time: 25.8 min (major), 28.8 min (minor); 74% ee; DAICEL CHIRALPAK AS-H, eluent: hexane/2-propanol (70:30), the former (major), the latter (minor); $[\alpha]_D^{25}$ +58.6 (c 1.0, $CHCl_3$); lit.[12] $[\alpha]_D^{20}$ +66.2 (c 0.5, $CHCl_3$); the absolute configuration was assigned as R; the references were cited in Ref. 12.

4.3.11. Compound **12b**

Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ 2.25 (s, 3H), 2.73 (dd, J=9.9, 18.0 Hz, 1H), 3.15 (d, J=18.0 Hz, 1H), 3.7 (br, 1H), 5.68 (d, J=9.9 Hz, 1H), 7.44 (t, J=8.1 Hz, 1H), 7.67 (t, J=8.2 Hz, 1H), 7.90 (d, J=8.2 Hz, 1H), 7.96 (d, J=8.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), 30.57, 51.12, 65.59, 124.2, 127.9, 128.0, 133.6, 138.1, 146.8, 208.3. IR ($CHCl_3$) ν 3600–3300 (br), 1712, 1526, 1348 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.02; H, 5.30; N, 6.69. Chromatography: DAICEL CHIRALPAK AS-H, eluent: hexane/2-propanol (80:20) (1.0 mL/min), retention time: 7.6 min (minor), 8.8 min (major); 81% ee; $[\alpha]_D^{23}$ −100.5 (c 0.36, $CHCl_3$).

4.4. Synthesis of **14**

A pure major enantiomer (ca. 99% ee) of *anti*-**6** aldol product was obtained by recrystallization in three times starting from a *syn*/*anti* mixture of **6** (ca. 80% *anti*, ca. 90% ee) using ethyl acetate. The mixture of pure and major *anti*-**6** (50 mg, 0.20 mmol), *N*-(2-carboxy-4,5-dichlorobenzoyl)-(−)-10,2-camphorsultam (TCI-1683) (130 mg, 0.30 mmol), DCC (62 mg, 0.30 mmol), and DMAP (3.7 mg) in CH_2Cl_2 (5 mL) was stirred at room temperature for 3.5 h. The mixture was introduced to the silica gel column with hexane–ethyl acetate (3:1) to give the corresponding sultam derivative **14** in 60% yield (80 mg, 0.12 mmol). White solids; mp 231.1–231.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$), δ 0.60 (br, 3H), 0.81 (s, 3H), 1.2–1.4 (m, 3H), 1.6–1.8 (m, 2H), 1.8–1.9 (m, 5H), 2.10 (m, 2H), 2.30 (m, 1H), 2.45 (m, 2H), 3.05 (m, 1H), 3.24 (d, J=14.0 Hz, 1H), 3.30 (d, J=14.0 Hz, 1H), 3.93 (m, 1H, C*H*N), 6.34 (d, J=7.5 Hz, 1H, C*H*OCO), 7.50 (s, 1H), 7.56 (d, J=7.0 Hz, 2H), 8.01 (s, 1H), 8.18 (d, J=7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.84, 19.97, 24.55, 26.36, 27.54, 29.89, 32.97, 37.42, 42.17, 44.55, 47.41, 48.36, 52.87, 54.78, 65.48, 74.80, 123.4, 127.9, 128.4, 131.4, 131.5, 134.9, 137.2, 144.9, 147.7, 162.2, 164.9, 208.6. IR (KBr disk) ν 3000–2800, 1736, 1715, 1673, 1525, 1351, 1300 cm^{-1}. FAB-HRMS: [(M+1)$^+$] m/z, found: 663.1348; calcd ($C_{31}H_{33}O_8N_2Cl_2S$): 663.1335; $[\alpha]_D^{23}$ −120.7 (c 0.45, $CHCl_3$).

4.5. X-ray analysis of sultam derivative **14**

4.5.1. X-ray diffraction study

Single crystals suitable for X-ray diffraction study were obtained from pentane/ethyl acetate solution at room temperature. The diffraction data were collected on a Brucker SMART APEX CCD diffractometer with graphite monochromated Mo Kα radiation (λ=0.71073 Å). An empirical absorption correction was applied by using SADABS. The structure was solved by direct method and refined by full-matrix least-square on F^2 using SHELXTL. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located on calculated positions and refined as rigid groups. Refinement details: empirical formula: $C_{31}H_{32}Cl_2N_2O_8S$; M_r=663.55; temperature 173(2) K; crystal system: monoclinic; space group: $P2_1$; a=11.1723(7), b=12.3376(7), c=11.1952(7) Å, β=98.6510(10)°, V=1525.58(16) Å^3, Z=2, ρ_{calcd}=1.444 Mg m^{-3}, μ=0.336 mm^{-1}, $F(000)$=692, crystal size=0.80×0.80×0.60 mm^3, θ range=1.84–27.49°; Index ranges: $-14\leq h\leq 13$, $-16\leq k\leq 15$, $-14\leq l\leq 13$; reflections collected 10,541, independent reflections 6722 [R(int)=0.0169], completeness to θ=27.49°, 99.8%; max/min transmission 1.000000/0.781362; data/restraints/parameters 6722/1/399; goodness-of-fit on F^2 1.034; final R indices [$I>2\sigma(I)$]: $R1$=0.0331, $wR2$=0.0854; R indices (all data): $R1$=0.0352, $wR2$=0.0874; largest diff. peak/hole 0.340 and −0.296 e Å^{-3}. CCDC-634997 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

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Supplementary data

LC charts of all products were listed. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.022.

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8. In place of isopropyl group of **1b**, phenyl and benzyl were examined to decrease the enantioselectivity for *anti*-product to 20–38% ee.
9. Benzaldehyde (**7**, R=H) gave a lower yield of ca. 30%.
10. We checked the ligand exchange reaction of **1b** and AgOTf (1.5–2.0 equiv) in toluene-d_8 at 60 °C in NMR tubes, respectively. The replacement of an acetate ligand by a triflate was observed to form mono-triflate substituted Phebox–Rh species in ca. 50% for 18 h in toluene-d_8.
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