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Rhodium/diene-catalyzed asymmetric arylation of *N*-Boc-protected α,β-unsaturated δ-lactam with arylboronic acids: enantioselective synthesis of 4-aryl-2-piperidinones

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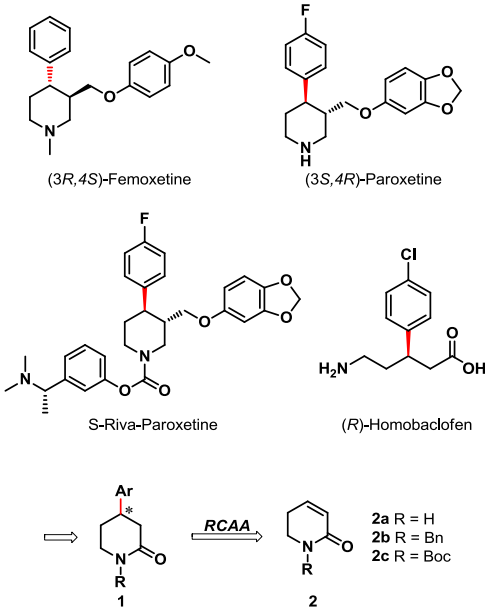
ABSTRACT

Utilizing toluene/isopropanol (20:1 to 40:1) as a solvent and KHF_2 as an additive, the rhodium/diene-catalyzed asymmetric arylation (RCAA) reaction of arylboronic acids to *N*-Boc-protected α,β-unsaturated δ-lactam proceeded smoothly to afford chiral 4-aryl-2-piperidinones with high to excellent yields (up to 94%) and enantioselectivities (up to >99% ee). Further conversion of adduct (*R*)-1-(*tert*-butyloxycarbonyl)-4-(4-chlorophenyl)-2-piperidone to (*R*)-Homobaclofen hydrochloride was also presented.

1. Introduction

Rhodium-catalyzed asymmetric arylation (RCAA) reactions provide one of the most straightforward and powerful ways to introduce aryl fragments into specific molecules in an enantioselective manner. During the last decade, significant efforts have been devoted to the discovery of novel chiral ligands and catalytic systems.[1] On the other hand, exploring suitable aryl-acceptors is also a major focus in this field. We have previously reported the RCAA of arylboronic acids to α,β-unsaturated γ-lactams with excellent enantioselectivities (usually over 97% ee) and demonstrated much better enantioselectivities for lactams with electron-withdrawing *N*-Boc-protecting group than its *N*-Bn- or *N*-PMB-analogues.[2] Herein, we wish to extend this asymmetric methodology to *N*-Boc-protected α,β-unsaturated δ-lactam, affording a novel and efficient entry to optically active 4-aryl-2-piperidinones.

Optically pure 4-aryl-2-piperidinones (**1**) are key intermediates for the synthesis of pharmacologically active molecules such as Femoxetine,[3] Paroxetine,[3a,4] *S*-Riva-Paroxetine,[5] and Homobaclofen[6] (Scheme 1). Despite considerable efforts have been made for the synthesis of **1**,[7] reports on catalytic asymmetric arylation variants have been rare.[8] In 2001, Hayashi and co-workers first



Scheme 1. Pharmacologically active 4-aryl-piperidine derivates and RCAA to α,β-unsaturated δ-lactams.

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described the RCAA reaction to α,β-unsaturated δ-lactam **2a** and *N*-Bn-protected α,β-unsaturated δ-lactam **2b**.[9] However, in order to suppress the fast hydrolysis of the arylboronic acids, the large excess amount of arylboroxines was necessarily used in place of arylboronic acids for the completion of the reaction possibly due to the relatively lower aryl-accepting capability of **2a** and **2b**. To address these disadvantage and pursue more reactive aryl-acceptor,[10] we started to explore rhodium/diene-catalyzed asymmetric arylation of arylboronic acids to *N*-Boc-protected α,β-unsaturated δ-lactam **2c**.

2. Results and discussion

2.1. Evaluation of chiral bicyclo[3.3.0]octadiene ligands and optimization of reaction conditions

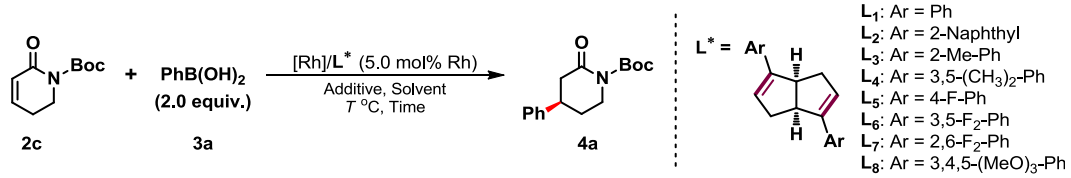
At the outset, various chiral bicyclo[3.3.0]octadiene ligands (**L_1**–**L_8**) have been examined in the RCAA of phenylboronic acid (**3a**) to **2c** using $[Rh(C_2H_4)_2Cl]_2$[11] as a precatalyst (Table 1, entries 1–8). Taking into account the results in both enantioselectivity and yield, the chiral diene ligand, (*S*,*S*)-1,3a,4,6a-tetrahydro-3,6-diphenylpentalene (**L_1**, (*S*,*S*)-Ph-thpe),[12] provided the best outcome (Table 1, entry 1). The application of chiral diene ligands **L_2**–**L_4** bearing more sterically hindered aromatic groups led to different levels of erosion in enantioselectivities (Table 1, entries 2–4). Additionally, significant losses in yields were observed when either the electron-deficient diene ligands (**L_5**–**L_7**) or electron-sufficient diene ligand (**L_8**) were employed, albeit a little bit higher enantioselectivity was reached for the reaction using ligand **L_8** (Table 1, entries 5–8).

Next several reaction parameters including additives, solvents, and temperature were screened in order to further improve both enantioselectivity and yield by directly utilizing more reactive $[Rh(\mathbf{L_1})OH]_2$ as the catalyst. We found that a base additive such as Et_3N, Na_2CO_3 or $NaHCO_3$ was destructive to the high yields, possibly due to the decomposition of the substrate **2c** or product **4a** under basic conditions (Table 1, entries 9–11). In our previous report on RCAA of arylboronic acids to nitroalkenes, the acidic additive KHF_2 showed remarkably helpful to enhance the yields.[13] Accordingly, excellent yield and enantioselectivity were achieved, when KHF_2 applied as an additive in this case (Table 1, entry 12). To our delight, the switch of co-solvent from toluene/water to toluene/isopropanol dramatically improved the yield and enantioselectivity (92% yield, 95% ee), probably due to the suppression of corresponding protodeboration (Table 1, entry 16).[14] Moreover, the RCAA reaction could proceed smoothly at room temperature and maintain the same excellent results (Table 1, entry 18). Several attempts to change the co-solvents led to lower yields (Table 1, entries 13–15 and 17).

2.2. RCAA of arylboronic acids to *N*-Boc-protected α,β-unsaturated δ-lactam

With the optimal reaction conditions in hand, the scope of RCAA to **2c** was investigated using various arylboronic acids with diverse steric and electronic properties. The results are summarized in Table 2. Most 4-substituted phenylboronic acids gave excellent yields (90–93%) and enantioselectivities (92–93% ee, Table 2, entries 2–6). The reaction of 4-bromophenylboronic acid (**3g**, Table 2, entry 7) resulted in a little lower yield, which might be attributed to its relatively lower reactivity and faster protodeboration.[9] The same observation was also met with 3-chlorophenylboronic acid (**3h**), however, the enantioselectivity was still excellent (96% ee, Table 2, entry 8). It should be noted that the reactions were carried out in the absence of KHF_2 additive for the electron-deficient arylboronic acids at 40 °C (Table 2, entries 5–8). High yields and excellent enantioselectivities were achieved for the 3-substituted arylboronic acids (Table 2, entries 8–10). As for the more sterically hindered 2-substituted arylboronic acids, the reactions could still proceed at room temperature, giving excellent enantioselectivities albeit a little loss in yields (Table 2, entries 12 and 13). Especially, for 1-naphthylboronic acid (**3n**), it reached excellent yield and perfect enantioselectivity (>99% ee, Table 2, entry 14).

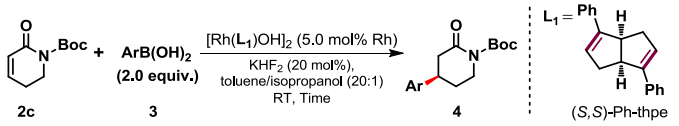
Table 1
Evaluation of chiral bicyclo[3.3.0]octadiene ligands and optimization of reaction conditions[a]



Entry	Catalyst	Additive[b]	Co-solvent	*T* (°C)	Time	Yield[c] (%)	ee[d] (%)
1	$[Rh(C_2H_4)_2Cl]_2$/**L_1**	KHF_2	Toluene/H_2O (20:1)	40	24 h	55	90
2	$[Rh(C_2H_4)_2Cl]_2$/**L_2**	KHF_2	Toluene/H_2O (20:1)	40	24 h	37	87
3	$[Rh(C_2H_4)_2Cl]_2$/**L_3**	KHF_2	Toluene/H_2O (20:1)	40	24 h	61	70
4	$[Rh(C_2H_4)_2Cl]_2$/**L_4**	KHF_2	Toluene/H_2O (20:1)	40	24 h	44	89
5	$[Rh(C_2H_4)_2Cl]_2$/**L_5**	KHF_2	Toluene/H_2O (20:1)	40	24 h	9	73
6	$[Rh(C_2H_4)_2Cl]_2$/**L_6**	KHF_2	Toluene/H_2O (20:1)	40	24 h	12	77
7	$[Rh(C_2H_4)_2Cl]_2$/**L_7**	KHF_2	Toluene/H_2O (20:1)	40	24 h	Trace	n.d.
8	$[Rh(C_2H_4)_2Cl]_2$/**L_8**	KHF_2	Toluene/H_2O (20:1)	40	24 h	23	92
9	$[Rh(\mathbf{L_1})(OH)]_2$	Et_3N	Toluene/H_2O (20:1)	40	24 h	76	94
10	$[Rh(\mathbf{L_1})(OH)]_2$	Na_2CO_3	Toluene/H_2O (20:1)	40	30 h	37	91
11	$[Rh(\mathbf{L_1})(OH)]_2$	$NaHCO_3$	Toluene/H_2O (20:1)	40	16 h	19	77
12	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Toluene/H_2O (20:1)	40	6 h	93	92
13	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Dioxane/H_2O (20:1)	40	9 h	50	94
14	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Toluene/MeOH (20:1)	40	23 h	41	88
15	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Toluene/EtOH (20:1)	40	23 h	53	90
16	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	toluene/*i*-PrOH (20:1)	40	45 min	92	95
17	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Toluene/*t*-BuOH (20:1)	40	36 h	74	96
18	$[Rh(\mathbf{L_1})(OH)]_2$	KHF_2	Toluene/*i*-PrOH (20:1)	rt	2 h	92	95

[a] The reaction was carried out with **2c** (0.2 mmol), phenylboronic acid **3a** (0.4 mmol), $[Rh(C_2H_4)_2Cl]_2$ (0.0050 mmol)/diene (**L_1**–**L_8**) (0.011 mmol, 1.1 equiv to Rh) or $[Rh(\mathbf{L_1})OH]_2$ (0.0050 mmol), and additive in 2 mL of co-solvent at 40 °C or rt, unless otherwise noted.
[b] Additives of 20 mol %.
[c] Yield of isolated product.
[d] Determined by chiral HPLC analysis.

Table 2
RCAA of arylboronic acids to 1-*N*-Boc-2-oxo-5,6-dihydropyridine (**2c**)[a]



Entry	**3** (Ar=)	Time	Yield[f] (%)	ee[g] (%)
1	**3a** (Ph)	2 h	92	95
2	**3b** (4-Me–Ph)	8 h	90	93
3[b]	**3c** (4-*t*-Bu-Ph)	45 min	92	92
4	**3d** (4-MeO–Ph)	2 h	91	93
5[b]	**3e** (4-F–Ph)[c,d,e]	10 min	93	93
6[b]	**3f** (4-Cl–Ph)[c,d,e]	10 min	92	92
7[b]	**3g** (4-Br-Ph)[c,d,e]	25 min	80	93
8[b]	**3h** (3-Cl–Ph)[c,d,e]	25 min	76	96
9[b]	**3i** (3-Me–Ph)	2 h	94	94
10[b]	**3j** (3-MeO–Ph)	1.5 h	90	95
11	**3k** (2-Naphthyl)	8 min	85	96
12	**3l** (2-MeO–Ph)	1.5 h	84	96
13	**3m** (2-Me–Ph)	2 h	88	97
14	**3n** (1-Naphthyl)	6 min	92	>99

[a] The reaction was carried out with **2c** (0.2 mmol), arylboronic acid **3** (0.4 mmol), [Rh(**L**$_1$)OH]$_2$ (0.0050 mmol), and KHF_2 (0.04 mmol) in 2 mL of toluene/isopropanol (20:1) at rt, unless otherwise noted.
[b] At 40 °C.
[c] Arylboronic acids of 3 equiv.
[d] No additive.
[e] Toluene/isopropanol (40:1).
[f] Yield of isolated product.
[g] Determined by chiral HPLC analysis.

The absolute configuration of arylated adducts **4** was unambiguously assigned as *R* by comparison of optical rotation of the known Boc-protected piperidinone (*R*)-**4f**,[6] which was further confirmed by X-ray crystal structure of (*R*)-**4g** (Fig. 1).

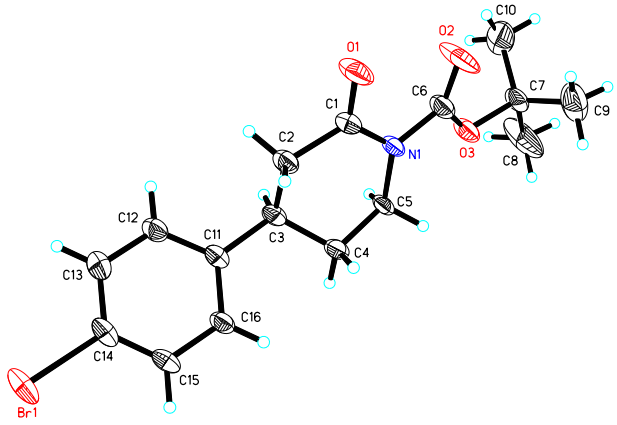
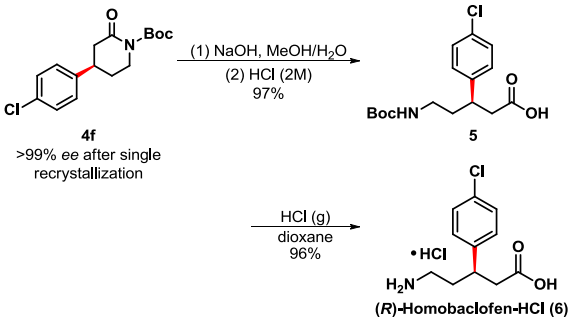


Fig. 1. X-ray crystal structure of **4g**.

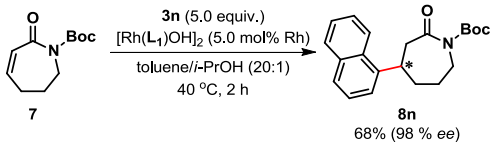
2.3. Asymmetric synthesis of (*R*)-Baclofen and RCAA to *N*-Boc-protected α,β-unsaturated ε-lactam

The chiral adducts, 4-aryl-2-piperidinones (**4**) are very useful building blocks for assembling some bioactive compounds.[3–6] Thus, the synthetic application of this methodology is demonstrated by a simple synthesis of a $GABA_B$ receptor agonist, (*R*)-Homobaclofen hydrochloride.[6] After a single recrystallization, the optical pure adduct **4f** was obtained with >99% ee and then converted to (*R*)-Homobaclofen in two steps in 93% overall yield (Scheme 2).

Further extension of this methodology to *N*-Boc-protected α,β-unsaturated ε-lactam (**7**) was also successful. Boronic acid of 5.0 equiv was required in this case, owing to the low reactivity of ε-lactam substrate. As shown in Scheme 3, the RCAA of 1-naphthyl-boronic acid (**3n**) provided chiral 4-aryl ε-lactam **8n** in 68% yield and 98% ee.



Scheme 2. Asymmetric synthesis of (*R*)-Baclofen hydrochloride **6**.



Scheme 3. RCAA to 1-*N*-Boc-7-oxo-2,3,4,7-tetrahydro-1*H*-azepine (**7**).

3. Summary

In summary, we have developed a RCAA of arylboronic acids to *N*-Boc-protected α,β-unsaturated δ-lactam or ε-lactam using a chiral diene, (*S*,*S*)-Ph-thpe as ligand. Utilizing toluene/isopropanol as solvent and KHF_2 as additive, the reaction proceeded uniformly with high to excellent yields and enantioselectivities, affording a synthetically useful chiral 4-aryl-2-piperidinones.

4. Experimental

4.1. General methods

All solvents were dried before use following the standard procedures. Unless otherwise indicated, all starting materials were obtained from commercial suppliers and were used without further purification. The ^1H and ^{13}C NMR spectra were recorded on 300 or 400 MHz spectrometer in the indicated solvents. Chemical shifts are reported in δ (ppm) referenced to an internal TMS standard for ^1H NMR and $CDCl_3$ (δ=77.05 ppm) for ^{13}C NMR. Optical rotations were measured on a JASCO P-1030 polarimeter.

4.2. General procedure for RCAA of arylboronic acid to 1-*N*-Boc-2-oxo-5,6-dihydropyridine (2c)

A dried Schlenk flask was charged with arylboronic acid (**3**, 0.4 mmol), [Rh(**L**$_1$)(OH)]$_2$ (**L**$_1$=(*S*,*S*)-Ph-thpe, 3.8 mg, 0.005 mmol), KHF_2 (3.2 mg, 0.04 mmol), and 1 mL of anhydrous toluene under argon. The resulting mixture was stirred at room temperature for 30 min. 1-*N*-Boc-2-oxo-5,6-dihydropyridine[15] (**2c**, 39.4 mg, 0.2 mmol) in toluene (1 mL) was added. Seven minutes later, 0.1 mL of isopropanol was added. After being stirred at room temperature for 2 h, the reaction was quenched with saturated aq NH_4Cl, extracted with ethyl acetate (20 mL×3), and the combined organic phases were washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel (300–400 mesh) column chromatography to afford **4**.

*4.2.1. (R)-1-(tert-Butyloxycarbonyl)-4-phenyl-2-piperidone (**4a**, Table 2, entry 1).* White solid, 50.7 mg, 92% yield; mp 95.1–96.6 °C; $[\alpha]_D^{27}$ +16.7 (*c* 1.00, $CHCl_3$) for 95% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36–7.33 (m, 2H), 7.27–7.19 (m, 3H), 3.88 (dt, *J*=12.8, 4.4 Hz, 1H), 3.62 (ddd, *J*=12.8, 10.8, 4.0 Hz, 1H), 3.16–3.09 (m, 1H),

2.84 (ddd, J=17.2, 5.2, 2.0 Hz, 1H), 2.64 (dd, J=17.2, 11.2 Hz, 1H), 2.22–2.17 (m, 1H), 2.01–1.91 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.4, 152.8, 143.2, 128.9, 127.0, 126.5, 83.0, 45.7, 42.1, 38.4, 30.4, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 298.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{16}H_{21}NO_3Na^{\oplus}$ 298.1414, found 298.1413; IR (KBr) ν (cm^{-1}) 3057, 2996, 2932, 1717, 1701, 1603, 1494, 1302, 1147, 890, 760, 701; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 30.5 min (S), 34.8 min (R).

*4.2.2. (R)-1-(tert-Butyloxycarbonyl)-4-(4-methylphenyl)-2-piperidone (**4b**, Table 2, entry 2).* White solid, 52.1 mg, 90% yield; mp 94.7–95.0 °C; $[\alpha]_D^{28}$ +13.2 (c 1.00, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.15 (d, J=8.0 Hz, 2H), 7.09 (d, J=8.0 Hz, 2H), 3.86 (dt, J=12.8, 4.4 Hz, 1H), 3.61 (ddd, J=12.8, 11.2, 4.4 Hz, 1H), 3.13–3.05 (m, 1H), 2.82 (ddd, J=17.2, 5.2, 2.0 Hz, 1H), 2.61 (dd, J=17.2, 11.2 Hz, 1H), 2.33 (s, 3H), 2.19–2.16 (m, 1H), 1.99–1.88 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.5, 152.8, 140.2, 136.6, 129.5, 126.3, 83.0, 45.7, 42.2, 38.1, 30.5, 28.1, 21.0; ESI-MS: $[M+Na]^{\oplus}$ 312.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_3Na^{\oplus}$ 312.1570, found 312.1581; IR (KBr) ν (cm^{-1}) 3050, 2974, 2923, 1708, 1516, 1457, 1393, 1295, 1152, 855, 808, 785; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 17.9 min (S), 21.4 min (R).

4.2.3. (R)-1-(tert-Butyloxycarbonyl)-4-(4-(tert-butyl)phenyl)-2-piperidone (4c, Table 2, entry 3). White solid, 61.0 mg, 92% yield; mp 121.1–122.3 °C; $[\alpha]_D^{28}$ +12.1 (c 1.00, $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36 (d, J=8.4 Hz, 2H), 7.13 (d, J=8.4 Hz, 2H), 3.87 (dt, J=12.4, 4.8 Hz, 1H), 3.61 (ddd, J=13.2, 10.8, 4.4 Hz, 1H), 3.14–3.06 (m, 1H), 2.83 (ddd, J=17.2, 5.2, 2.0 Hz, 1H), 2.62 (dd, J=16.8, 11.2 Hz, 1H), 2.22–2.15 (m, 1H), 1.99–1.89 (m, 1H), 1.55 (s, 9H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.6, 152.8, 149.9, 140.1, 126.1, 125.7, 83.0, 45.7, 42.1, 37.9, 34.5, 31.3, 30.5, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 354.2; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{20}H_{29}NO_3Na^{\oplus}$ 354.2040, found 354.2024; IR (KBr) ν (cm^{-1}) 3008, 2959, 2867, 1713, 1518, 1459, 1369, 1294, 1153, 830, 780; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 12.2 min (S), 14.0 min (R).

*4.2.4. (R)-1-(tert-Butyloxycarbonyl)-4-(4-methoxyphenyl)-2-piperidone (**4d**, Table 2, entry 4).* White solid, 55.6 mg, 90% yield; mp 87.4–87.6 °C; $[\alpha]_D^{27}$ +14.1 (c 1.00, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.12 (d, J=8.4 Hz, 2H), 6.88 (d, J=8.4 Hz, 2H), 3.88–3.83 (m, 1H), 3.80 (s, 3H), 3.64–3.57 (m, 1H), 3.11–3.04 (m, 1H), 2.81 (dd, J=16.8, 5.6 Hz, 1H), 2.59 (dd, J=17.2, 11.2 Hz, 1H), 2.18–2.14 (m, 1H), 1.97–1.86 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.6, 158.6, 152.8, 135.3, 127.4, 114.2, 83.0, 55.3, 45.6, 42.4, 37.6, 30.6, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 328.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_4Na^{\oplus}$ 328.1519, found 328.1512; IR (KBr) ν (cm^{-1}) 2982, 2936, 1767, 1716, 1612, 1513, 1345, 1248, 1150, 838, 768; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 43.2 min (S), 54.8 min (R).

*4.2.5. (R)-1-(tert-Butyloxycarbonyl)-4-(4-fluorophenyl)-2-piperidone (**4e**, Table 2, entry 5).* White solid, 54.6 mg, 93% yield; mp 76.9–77.1 °C; $[\alpha]_D^{29}$ +162.1 (c 0.99, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.16 (dd, J=8.4, 5.2 Hz, 2H), 7.03 (t, J=8.4 Hz, 2H), 3.87 (dt, J=13.2, 4.4 Hz, 1H), 3.61 (ddd, J=12.8, 11.2, 4.4 Hz, 1H), 3.15–3.07 (m, 1H), 2.82 (ddd, J=16.8, 5.6, 2.0 Hz, 1H), 2.59 (dd, J=17.2, 11.2 Hz, 1H), 2.20–2.15 (m, 1H), 1.98–1.88 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.2, 161.8 (d, J_{CF}=244.3 Hz), 152.7, 138.9 (d, J_{CF}=3.6 Hz), 128.0 (d, J_{CF}=8.0 Hz), 115.7 (d, J_{CF}=21.1 Hz), 83.2, 45.5, 42.3, 37.8, 30.5, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 298.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{16}H_{20}NO_3FNa^{\oplus}$ 316.1319, found 316.1327; IR (KBr) ν (cm^{-1}) 2981, 2926, 1709, 1604, 1513, 1400, 1368, 1298, 1149, 837, 770; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 27.5 min (S), 29.0 min (R).

*4.2.6. (R)-1-(tert-Butyloxycarbonyl)-4-(4-chlorophenyl)-2-piperidone[6] (**4f**, Table 2, entry 6).* White solid, 57.0 mg, 92% yield; mp 106.0–106.8 °C; $[\alpha]_D^{29}$ +15.4 (c 1.00, $CHCl_3$) for 92% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.31 (d, J=8.4 Hz, 2H), 7.13 (d, J=8.4 Hz, 2H), 3.87 (dt, J=12.8, 4.4 Hz, 1H), 3.61 (ddd, J=12.8, 11.2, 4.4 Hz, 1H), 3.15–3.07 (m, 1H), 2.82 (ddd, J=16.8, 5.2, 1.6 Hz, 1H), 2.58 (dd, J=16.8, 11.2 Hz, 1H), 2.20–2.16 (m, 1H), 1.98–1.88 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.0, 152.7, 141.6, 132.8, 129.0, 127.9, 83.2, 45.5, 42.0, 37.9, 30.3, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 332.0; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{16}H_{20}NO_3ClNa^{\oplus}$ 332.1024, found 332.1036; IR (KBr) ν (cm^{-1}) 3419, 2977, 2931, 1768, 1667, 1494, 1389, 1365, 1310, 1159, 846, 777; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 32.5 min (S), 36.9 min (R).

*4.2.7. (R)-1-(tert-Butyloxycarbonyl)-4-(4-bromophenyl)-2-piperidone (**4g**, Table 2, entry 7).* White solid, 56.7 mg, 80% yield; mp 98.2–98.7 °C; $[\alpha]_D^{28}$ +11.2 (c 1.00, $CHCl_3$) for 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.46 (d, J=8.4 Hz, 2H), 7.08 (d, J=8.4 Hz, 2H), 3.87 (dt, J=13.2, 4.4 Hz, 1H), 3.61 (ddd, J=13.2, 10.8, 4.4 Hz, 1H), 3.13–3.05 (m,1H), 2.82 (ddd, J=17.2, 5.6, 2.0 Hz, 1H), 2.58 (dd, J=17.2, 11.2 Hz, 1H), 2.21–2.14 (m, 1H), 1.97–1.87 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.0, 152.7, 142.1, 132.0, 128.2, 120.8, 83.2, 45.5, 41.9, 38.0, 30.2, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 376.0; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{16}H_{20}NO_3BrNa^{\oplus}$ 376.0519, found 376.0509; IR (KBr) ν (cm^{-1}) 3064, 2977, 2931, 1767, 1667, 1489, 1400, 1301, 1158, 845, 828, 775; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; n-hexane/i-propanol=90:10; flow rate=0.7 ml/min; retention time: 37.4 min (S), 45.4 min (R).

X-ray structural data for 4g (CCDC 888969)

Crystal data	
$C_{16}H_{20}BrNO_3$	F_{000}=728
M_r=354.24	D_{calcd}=1.446 Mg/m^3
Monoclinic, $C2$	Mo Kα radiation
Hall symbol: none	Cell parameters from 1330 reflections
a=22.956(5) Å	λ=0.717073 Å
b=7.7296(15) Å	θ=1.80–26.00°
c=9.2996(18) Å	μ=2.535 mm^{-1}
α=90°	T=293(2) K
β=99.558(4)°	Prismatic, colorless
γ=90°	0.311×0.215×0.167 mm
V=1627.2(5) Å^3	Z=4
Data collection	
Bruker SMART APEX diffractometer	1330 Reflections with $I>2\sigma(I)$
Radiation source: fine-focus sealed tube	R_{int}=0.0319
Graphite	θ_{max}=26.00°
φ and ω scans	h=−27→28
Absorption correction: empirical	k=−9→9
T_{min}=0.53517, T_{max}=1.00000	l=−11→5
Refinement	
Refinement on F^2	H atoms treatment: constrained
Matrix type: full	$w = 1/[\sigma^2(F_o^2) + (0.0282P)^2 + 0.0000P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2>2\sigma(F^2)]$=0.0449	$(\Delta/\sigma)_{max}$=0.004
$wR(F^2)$=0.1029	$\Delta\rho_{max}$=0.488 e Å^{-3}
S=0.990	$\Delta\rho_{min}$=−0.60 e Å^{-3}
3191 Reflections	Absolute structure: Flack HD (1983)
193 Parameters	Absolute structure parameter: 0.025(15)
1 Restraints	

*4.2.8. (R)-1-(tert-Butyloxycarbonyl)-4-(3-chlorophenyl)-2-piperidone (**4h**, Table 2, entry 8).* White solid, 47.1 mg, 76% yield; mp 80.0–80.2 °C; $[\alpha]_D^{28}$ +13.8 (*c* 1.00, $CHCl_3$) for 96% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.30–7.19 (m, 3H), 7.08 (d, *J*=7.2 Hz, 1H), 3.89 (dt, *J*=13.2, 4.4 Hz, 1H), 3.65–3.58 (m, 1H), 3.13–3.06 (m, 1H), 2.83 (dd, *J*=16.8, 4.0 Hz, 1H), 2.60 (dd, *J*=16.8, 11.2 Hz, 1H), 2.20–2.18 (m, 1H), 1.99–1.89 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.9, 152.7, 145.2, 134.7, 130.2, 127.3, 126.8, 124.7, 83.2, 45.5, 41.9, 38.2, 30.2, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 332.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{16}H_{20}NO_3ClNa^{\oplus}$ 332.1024, found 332.1031; IR (KBr) ν (cm^{-1}) 3063, 2973, 2927, 1770, 1760, 1599, 1475, 1367, 1283, 1150, 788, 696; HPLC: Phenomenex Lux 5u Cellulose-1 (PC-1) Column; detected at 214 nm; *n*-hexane/*i*-propanol=70:30; flow rate=0.7 ml/min; retention time: 13.4 min (*S*), 14.6 min (*R*).

*4.2.9. (R)-1-(tert-Butyloxycarbonyl)-4-(3-methylphenyl)-2-piperidone (**4i**, Table 2, entry 9).* White solid, 54.4 mg, 94% yield; mp 61.9–63.2 °C; $[\alpha]_D^{28}$ +15.0 (*c* 1.00 $CHCl_3$) for 94% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.23 (t, *J*=7.6 Hz, 1H), 7.07 (d, *J*=7.6 Hz, 1H), 7.00(s, 1H), 6.99 (d, *J*=7.6 Hz, 1H), 3.87 (dt, *J*=12.8, 4.4 Hz, 1H), 3.61 (ddd, *J*=12.8, 11.2, 4.4 Hz, 1H), 3.12–3.04 (m, 1H), 2.82 (ddd, *J*=17.2, 5.2, 2.0 Hz, 1H), 2.62 (dd, *J*=17.2, 11.2 Hz, 1H), 2.35 (s, 3H), 2.21–2.14 (m, 1H), 2.00–1.90 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.5, 152.8, 143.2, 138.5, 128.8, 127.8, 127.3, 123.5, 83.1, 45.7, 42.2, 38.4, 30.4, 28.1, 21.5; ESI-MS: $[M+Na]^{\oplus}$ 312.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_3Na^{\oplus}$ 312.1570, found 312.1557; IR (KBr) ν (cm^{-1}) 3031, 1767, 1669, 1609, 1488, 1391, 1284, 1149, 849, 816, 703; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; *n*-hexane/*i*-propanol=90:10; flow rate=0.7 ml/min; retention time: 19.0 min (*S*), 20.3 min (*R*).

*4.2.10. (R)-1-(tert-Butyloxycarbonyl)-4-(3-methoxyphenyl)-2-piperidone (**4j**, Table 2, entry 10).* White solid, 55.0 mg, 90% yield; mp 48.4–48.9 °C; $[\alpha]_D^{22}$ +15.6 (*c* 0.96 $CHCl_3$) for 95% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.28–7.24 (m, 1H), 6.81–6.74 (m, 3H), 3.88 (dt, *J*=12.8, 4.4 Hz, 1H), 3.81 (s, 3H), 3.61 (ddd, *J*=12.8, 11.2, 4.4 Hz, 1H), 3.13–3.05 (m, 1H), 2.84 (ddd, *J*=17.2, 5.2, 2.0 Hz, 1H), 2.62 (dd, *J*=17.2, 11.2 Hz, 1H), 2.22–2.16 (m, 1H), 2.00–1.90 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.4, 160.0, 152.8, 144.8, 129.9, 118.8, 112.7, 112.0, 83.1, 55.2, 45.7, 42.1, 38.5, 30.3, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 328.2; HRMS (FTMS-MALDI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_4Na^{\oplus}$ 328.1519, found 328.1530; IR (KBr) ν (cm^{-1}) 3060, 3002, 2983, 2932, 1705, 1597, 1492, 1396, 1369, 1162, 790, 700; HPLC: Phenomenex Lux 5u Cellulose-1 (PC-1) Column; detected at 214 nm; *n*-hexane/*i*-propanol=50:50; flow rate=0.7 ml/min; retention time: 17.2 min (*S*), 19.0 min (*R*).

*4.2.11. (R)-1-(tert-Butyloxycarbonyl)-4-(naphthalen-2-yl)-2-piperidone (**4k**, Table 2, entry 11).* White solid, 55.3 mg, 85% yield; mp 104.6–105.2 °C; $[\alpha]_D^{29}$ +13.0 (*c* 1.00 $CHCl_3$) for 96% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.84–7.80 (m, 3H), 7.62 (s, 1H), 7.51–7.44 (m, 2H), 7.33 (dd, *J*=8.4, 2.0 Hz, 1H), 3.90 (dt, *J*=12.8, 4.8 Hz, 1H), 3.67 (ddd, *J*=12.8, 10.8, 4.0 Hz, 1H), 3.34–3.26 (m, 1H), 2.93 (ddd, *J*=17.2, 5.2, 2.0 Hz, 1H), 2.75 (dd, *J*=17.2, 11.2 Hz, 1H), 2.32–2.25 (m, 1H), 2.12–2.02 (m, 1H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.4, 152.8, 140.5, 133.5, 132.5, 128.7, 127.7, 127.7, 126.4, 125.9, 125.0, 124.8, 83.1, 45.6, 42.0, 38.5, 30.4, 28.0; ESI-MS: $[M+Na]^{\oplus}$ 348.2; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{20}H_{23}NO_3Na^{\oplus}$ 348.1570, found 348.1578; IR (KBr) ν (cm^{-1}) 3061, 2976, 2925, 1712, 1599, 1476, 1390, 1370, 1292, 1149, 850, 824, 750; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; *n*-hexane/*i*-propanol=90:10; flow rate=0.7 ml/min; retention time: 32.8 min (*S*), 41.6 min (*R*).

*4.2.12. (R)-1-(tert-Butyloxycarbonyl)-4-(2-methoxyphenyl)-2-piperidone (**4l**, Table 2, entry 12).* White solid, 51.3 mg, 84% yield; mp 59.7–60.6 °C; $[\alpha]_D^{22}$ +26.7 (*c* 0.91, $CHCl_3$) for 96% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.25–7.21 (m, 1H), 7.11 (dd, *J*=7.2, 1.2 Hz, 1H), 6.94 (t, *J*=7.2 Hz, 1H), 6.88 (d, *J*=8.0 Hz, 1H), 3.89–3.82 (m, 4H), 3.63 (ddd, *J*=12.8, 10.8, 4.4 Hz, 1H), 3.50–3.42 (m, 1H), 2.85 (ddd, *J*=17.2, 5.6, 1.6 Hz, 1H), 2.60 (dd, *J*=17.2, 10.8 Hz, 1H), 2.16–2.10 (m, 1H), 2.04–1.94 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.2, 156.9, 152.8, 131.3, 127.9, 126.5, 120.8, 110.6, 82.9, 55.2, 45.8, 40.7, 32.6, 28.6, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 328.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_4Na^{\oplus}$ 328.1519, found 328.1513; IR (KBr) ν (cm^{-1}) 2977, 2932, 1719, 1703, 1600, 1495, 1391, 1367, 1291, 1149, 855, 758; HPLC: Phenomenex Lux 5u Cellulose-1 (PC-1) Column; detected at 214 nm; *n*-hexane/*i*-propanol=50:50; flow rate=0.7 ml/min; retention time: 8.1 min (*S*), 9.0 min (*R*).

*4.2.13. (R)-1-(tert-Butyloxycarbonyl)-4-(2-methylphenyl)-2-piperidone (**4m**, Table 2, entry 13).* White solid, 50.9 mg, 88% yield; mp 81.4–81.8 °C; $[\alpha]_D^{29}$ +33.9 (*c* 0.95, $CHCl_3$) for 97% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.24–7.14 (m, 4H), 3.89 (dt, *J*=12.8, 4.4 Hz, 1H), 3.65 (ddd, *J*=12.8, 10.8, 4.4 Hz, 1H), 3.37–3.29 (m, 1H), 2.80 (ddd, *J*=17.2, 5.6, 2.0 Hz, 1H), 2.58 (dd, *J*=17.2, 11.2 Hz, 1H), 2.34 (s, 3H), 2.17–2.10 (m, 1H), 2.02–1.92 (m, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.7, 152.7, 141.3, 135.3, 130.8, 126.8, 126.7, 124.9, 83.1, 45.7, 41.6, 34.2, 29.5, 28.1, 19.3; ESI-MS: $[M+Na]^{\oplus}$ 312.2; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{17}H_{23}NO_3Na^{\oplus}$ 312.1570, found 312.1584; IR (KBr) ν (cm^{-1}) 3000, 2976, 2931, 1766, 1714, 1672, 1483, 1367, 1305, 1150, 855, 761; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; *n*-hexane/*i*-propanol=90:10; flow rate=0.7 ml/min; retention time: 17.8 min (*S*), 25.1 min (*R*).

*4.2.14. (R)-1-(tert-Butyloxycarbonyl)-4-(naphthalen-1-yl)-2-piperidone (**4n**, Table 2, entry 14).* White solid, 59.9 mg, 92% yield; mp 99.3–100.4 °C; $[\alpha]_D^{22}$ + .3 (*c* 1.02, $CHCl_3$) for >99% ee; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.02 (d, *J*=8.0 Hz, 1H), 7.89 (d, *J*=8.0 Hz, 1H), 7.77 (d, *J*=8 Hz, 1H), 7.57–7.45 (m, 3H), 7.33 (d, *J*=6.8 Hz, 1H), 4.00–3.92 (m, 1H), 3.87 (dt, *J*=12.8, 4.8 Hz, 1H), 3.75 (ddd, *J*=12.8, 10.4, 4.4 Hz, 1H), 3.04 (ddd, *J*=17.2, 5.2, 2.0 Hz, 1H), 2.75 (dd, *J*=17.2, 10.4 Hz, 1H), 2.39–2.32 (m,1H), 2.17–2.08 (m, 1H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.7, 152.7, 138.8, 134.0, 131.0, 129.2, 127.6, 126.4, 125.8, 125.6, 122.6, 122.4, 83.2, 45.5, 41.82 33.4, 29.8, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 348.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{20}H_{23}NO_3Na^{\oplus}$ 348.1570, found 348.1574; IR (KBr) ν (cm^{-1}) 3049, 2978, 2931, 1702, 1598, 1486, 1392, 1370, 1148, 855, 799, 773; HPLC: Phenomenex Lux 5u Cellulose-2 (PC-2) Column; detected at 214 nm; *n*-hexane/*i*-propanol=95:5; flow rate=0.7 ml/min; retention time: 42.9 min (*R*), 48.1 min (*S*).

4.3. Preparation of (*R*)-Baclofen hydrochloride 6

*4.3.1. (R)-5-((tert-Butoxycarbonyl)amino)-3-(4-chlorophenyl)pentanoic acid (**5**).*[6] Optically pure **4f** (135.9 mg, 69% yield, >99% ee, $[\alpha]_D^{28}$ +14.9 (*c* 0.18, CH_2Cl_2)) was obtained after single recrystallization from 197.0 mg of **4f** (92% ee) in 10 mL of hexane/EtOAc (2:1). To a solution of **4f** (52.3 mg, 0.169 mmol, >99% ee) in methanol (2.5 mL) was added an aqueous solution of NaOH (1 M, 3.0 mL), and the resulting mixture was stirred at room temperature for 30 min. The pH of the aqueous solution was adjusted to 1 using 1 M HCl. The aqueous phase was extracted with Et_2O (20 mL×3), and the combined organic phases were washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel (300–400 mesh) column chromatography to afford **5** (53.7 mg, 97%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$)

δ (ppm) 12.00 (s, 1H), 7.33 (d, J=8.4 Hz, 2H), 7.26 (d, J=8.4 Hz, 2H), 6.78 (s, 1H), 3.04–3.02 (m, 1H), 2.75–2.70 (m, 2H), 2.62–2.43 (m, 2H), 1.75–1.59 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.4, 156.0, 143.5, 131.3, 129.9, 128.6, 77.9, 41.1, 39.0, 38.5, 36.3, 28.7.

*4.3.2. (R)-Homobaclofen hydrochloride salt (**6**).* To a 4 mL of 1,4-dioxane solution of HCl (gas, 5 M) was added **5** (53.7 mg, 0.164 mmol). The resulting mixture was stirred at room temperature for 24 h and concentrated to give **6** (41.5 mg, 96%) as a yellow solid. Mp 176.8–178.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.15 (br s, 1H), 7.85 (br s, 3H), 7.38 (s, J=8.8 Hz, 2H), 7.31 (s, J=8.8 Hz, 2H), 3.11–3.09 (m, 1H), 2.68–2.62 (m, 2H), 2.55–2.42 (m, 2H), 1.92–1.79 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 173.2, 142.6, 131.6, 129.9, 128.8, 40.9, 38.7, 37.4, 33.5; ESI-MS: $[M-HCl+H]^{\oplus}$ 228.1; HRMS (FTMS-ESI): $[M-HCl+H]^{\oplus}$ calcd for $C_{11}H_{15}ClNO_2^{\oplus}$ 228.0786, found 228.0795; IR (KBr) ν (cm^{-1}) 3178(brs), 2926, 1717, 1702, 1673, 1613, 1495, 1342, 1176, 1092, 829, 707.

4.4. Preparation of 8n

*4.4.1. 1-(tert-Butyloxycarbonyl)-4-(naphthalen-1-yl)-2-oxoazepane (**8n**).* A dried Schlenk flask was charged with naphthalen-1-ylboronic acid (**3n**, 172 mg, 1.0 mmol), $[Rh(\mathbf{L_1})(OH)]_2$ ($\mathbf{L_1}$=(*S*,*S*)-Ph-thpe, 3.8 mg, 0.005 mmol), KHF_2 (3.2 mg, 0.04 mmol), and 1 mL of anhydrous toluene under argon. The resulting mixture was stirred at room temperature for 30 min. 1-*N*-Boc-7-oxo-2,3,4,7-tetrahydro-1*H*-azepine (**7**, 42.3 mg, 0.2 mmol) in 1 mL of toluene was added. Seven minutes later, 0.1 mL of isopropanol was added. After being stirred at 40 °C for 1.5 h, the reaction was quenched with saturated aq NH_4Cl, extracted with ethyl acetate (20 mL×3), and the combined organic phases were washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel (300–400 mesh) column chromatography to afford **8n** (46 mg, 68%) as a colorless oil. $[\alpha]_D^{28}$ +13.1 (*c* 1.01, $CHCl_3$) for 98% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.10 (d, J=8.4 Hz, 1H), 7.86 (d, J=8.0 Hz, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.58–7.41 (m, 3H), 7.32 (d, J=7.2 Hz, 1H), 4.42 (dd, J=15.2, 6.8 Hz, 1H), 3.77 (t, J=10.8 Hz, 1H), 3.50 (dd, J=15.2, 10.4 Hz, 1H), 3.18 (dd, J=13.2, 11.2 Hz, 1H), 2.92 (d, J=13.6 Hz, 1H), 2.26 (d, J=13.6 Hz, 1H), 2.19–2.13 (m, 1H), 1.95–1.75 (m, 2H), 1.58 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.2, 153.0, 142.1, 134.0, 130.6, 129.1, 127.3, 126.4, 125.7, 125.4, 122.9, 122.2, 83.1, 46.4, 46.0, 37.2, 35.7, 28.9, 28.1; ESI-MS: $[M+Na]^{\oplus}$ 362.1; HRMS (FTMS-ESI): $[M+Na]^{\oplus}$ calcd for $C_{21}H_{25}NO_3Na^{\oplus}$ 362.1727, found 362.1727; IR (KBr) ν (cm^{-1}) 2979, 2931, 1766, 1731, 1597, 1392, 1367, 1345, 1150, 854, 778, 753; HPLC: Phenomenex Lux 5u Cellulose-4 (PC-4) Column; detected at 214 nm; *n*-hexane/*i*-propanol=80:20; flow rate=0.7 ml/min; retention time: 13.4 min (*minor*), 14.8 min (*major*).

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