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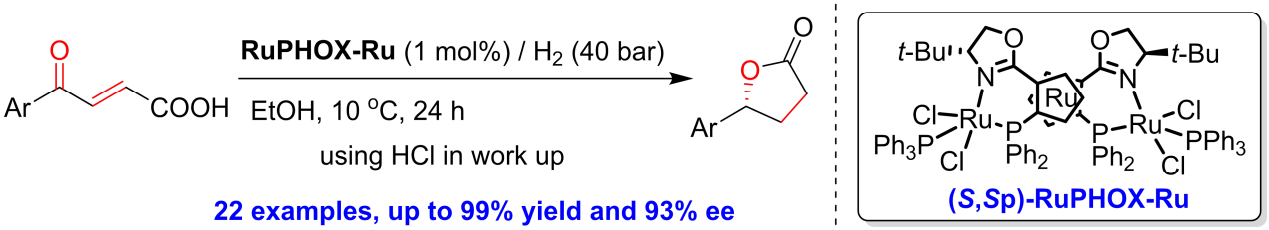

22 examples, up to 99% yield and 93% ee

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Synthesis of Chiral γ-Lactones via a RuPHOX-Ru Catalyzed Asymmetric Hydrogenation of Aroylacrylic Acids

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ABSTRACT

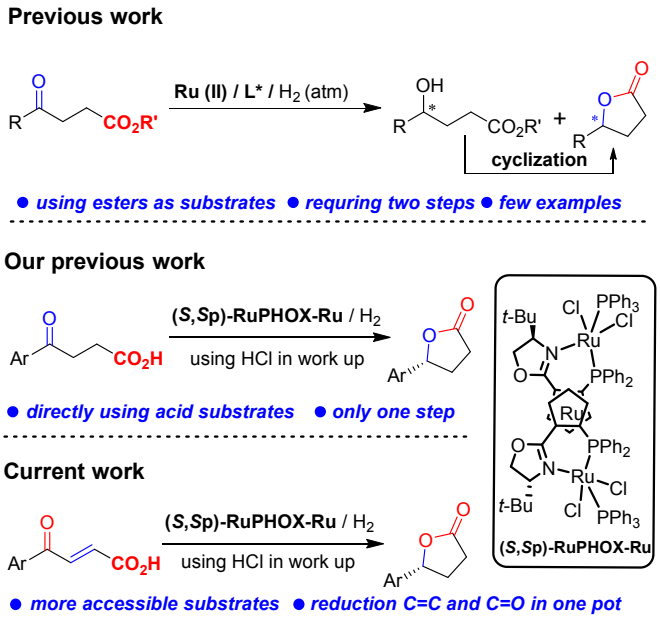
An asymmetric hydrogenation of aroylacrylic acids catalyzed by RuPHOX-Ru catalyst has been developed, affording the corresponding chiral γ-lactones in high yields and with up to 93% ee. The methodology has the advantage of utilizing easily accessible substrates and has therefore expand the scope of the resulting chiral γ-lactones. Furthermore, high catalytic efficiency was achieved in that the reduction of both the C=C and C=O double bonds was achieved in one step. The current work provides an alternative and convenient pathway for the synthesis of a wide range of chiral γ-lactones.

1. Introduction

In both academic laboratories and industrial applications, chiral metal-catalyzed asymmetric catalytic hydrogenation reactions provide one of the most cost effective and eco-friendly methods for the production of a vast array of structurally diverse and enantiomerically pure compounds.[1] Due to its low cost and high availability, Ru-catalyzed asymmetric hydrogenation has received much attention and has been employed in a number of industrial processes ranging from kilogram to ton scales.[2]

Chiral γ-lactone skeletons are present in numerous natural products, biologically active compounds and drugs,[3] and the efficient synthesis of such skeletons has been realized via the Ru-catalyzed asymmetric hydrogenation of γ-keto esters (Scheme 1).[4] However, these reactions always give a mixture of the desired cyclic γ-lactones and undesired uncyclized γ-hydroxy esters, and an additional cyclization is needed to afford only the cyclic product. In addition, harsh reaction conditions are required and only a limited substrate scope has been explored.

We previously developed a chiral phosphino-oxazoline ligand, RuPHOX, which showed excellent catalytic behaviors in several types of asymmetric catalysis, in particular Ru-catalyzed asymmetric hydrogenation.[5] Subsequently, the ruthenocene-based ruthenium-complex, RuPHOX-Ru, has been synthesized and used directly in the asymmetric hydrogenation of many types of substrates bearing either C=O or C=C bonds.[6] Just recently, the asymmetric hydrogenation of γ-aryl ketone acids, instead of γ-keto esters, was achieved using the RuPHOX-Ru catalyst, providing chiral γ-lactones directly in up to 99% yield and with up to 97% ee (Scheme 1).[6j] Although chiral γ-lactones can be obtained in one step under mild reaction conditions, a limitation still remains. The synthesis of the hydrogenation substrates, γ-aryl ketone acids, is via Friedel-Crafts reaction and the scope of substituents is therefore limited to the position of the substituents on the aromatic ring. Almost simultaneously, we have realized an efficient RuPHOX-Ru-catalyzed asymmetric hydrogenation of chromones in which both the C=C and C=O doubled



Scheme 1 Synthesis of chiral γ-lactones.

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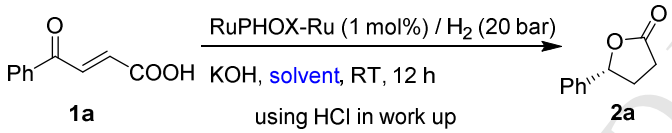
bonds could be reduced under the same reaction conditions.[6i] In this manuscript we report a RuPHOX-Ru-catalyzed asymmetric hydrogenation of aroylacrylic acids, the precursors of which can be easily obtained from various substituted acetophenones and glyoxylic acid, for the synthesis of chiral γ-lactones (Scheme 1).

2. Results and discussion

Our investigation began with benzoylacrylic acid (**1a**) which was chosen as the model hydrogenation substrate. The hydrogenation was conducted in different solvents employing 1 mol% of RuPHOX-Ru in the presence of KOH under 20 bar H_2 pressure at room temperature for 12 h (Table 1). Generally, protic solvent have proven to be beneficial to many asymmetric hydrogenation reactions. MeOH was therefore used first in the reaction with the desired γ-lactone product **2a** being obtained in 74% yield and 35% ee (entry 1). Full conversion and 68% ee were afforded when EtOH was adopted as a solvent (entry 2). The use of *n*-PrOH provided the same conversion but a slightly lower enantioselectivity than that of EtOH (entry 3). Similar ee but a sharp decrease in conversion was observed when *i*-PrOH was used as a solvent (entry 4). The use of *n*-BuOH as a solvent gave comparable results to that of *n*-PrOH (entry 5). Poor conversion of the corresponding product **2a** was observed when aprotic solvents, such as CH_2Cl_2 and THF, were employed in the above reaction (entries 6 and 7). Reduction in protic solvents was better than in aprotic solvents, with EtOH giving the best results.

Table 1 Screening of solvents[a]

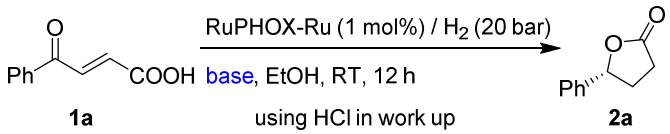


Entry	Solvent	Yield (%)[b]	ee (%)[c,d]
1	MeOH	74	35
2	EtOH	>99	68
3	*n*-PrOH	>99	57
4	*i*-PrOH	60	64
5	*n*-BuOH	>99	59
6	CH_2Cl_2	18	ND
7	THF	-	ND

[a]Conditions: **1a** (0.25 mmol), RuPHOX-Ru (1 mol%), KOH (2.0 equiv), and solvent (2 mL) under 20 bar H_2 pressure at RT for 12 h. [b] Determined by ^{1}H NMR spectroscopy. [c]Enantioselectivity was determined by HPLC using a chiral AS-H column. [d]The absolute configuration of **2a** was determined as *R*-configuration by comparing the specific rotation with reported data.[6j]

The effect of different bases on the reaction was then investigated (Table 2). First, alkali hydroxides were tested and KOH gave the best results (entries 1~4). Next, potassium containing compounds, with weaker or stronger alkalinity than that of KOH, were used (entries 5~8). Slightly inferior results were obtained with *t*-BuOK as a base (entry 5). However, a sharp decrease in reaction activity was observed when the reaction was carried out in the presence of K_2CO_3, $KHCO_3$ and KOAc (entries 6~8). Finally, the organic base Et_3N was also examined and only a trace amount of the desired product was obtained (entry 9). The amount of KOH was examined in the reaction. The desired product was obtained in only 34% yield when 1.0 equiv of KOH was used (entry 10); higher amounts had no influence on the reaction (entry 11). Therefore, the best results were obtained when the asymmetric hydrogenation was conducted with 2 equiv of KOH in EtOH.

Table 2 Screening of base[a]

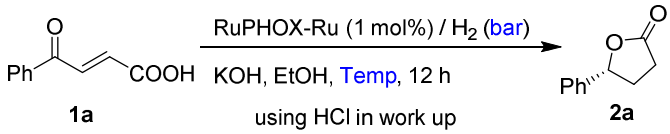


Entry	Base	Yield (%)[b]	ee (%)[c,d]
1	$LiOH•H_2O$	>99	63
2	NaOH	>99	62
3	KOH	>99	68
4	$CsOH•H_2O$	>99	52
5	*t*-BuOK	>99	64
6	K_2CO_3	5	ND
7	$KHCO_3$	8	ND
8	KOAc	trace	ND
9	Et_3N	trace	ND
10[e]	KOH	34	65
11[f]	KOH	>99	66

[a] Conditions: **1a** (0.25 mmol), RuPHOX-Ru (1 mol%), base (2.0 equiv), and EtOH (2 mL) under 20 bar hydrogen pressure at RT for 12 h. [b] Determined by ^{1}H NMR spectroscopy. [c]Enantioselectivity was determined by HPLC using a chiral AS-H column. [d]The absolute configuration of **2a** was determined as R-configuration by comparing the specific rotation with reported data.[6j] [e] 1.0 equiv of base. [f] 3.0 equiv of base.

Subsequently, we screened the H_2 pressure and reaction temperature with the aim of improving the ee of **2a**. As shown in Table 3, enantioselectivity increased when the H_2 pressure was increased from 20 to 40 bar (entries 1~3). Further increasing the H_2 pressure resulted in inferior results (entry 4). Next, the asymmetric hydrogenation was carried out under 40 bar H_2 pressure at a lower reaction temperature (entries 5~7). Full conversion and 84% ee were observed when the reaction was conducted at a temperature of 10 °C (entry 5). Low reaction activity or poor enantionselectivity were observed when the reaction was conducted at a lower temperature (entries 6 and 7). The optimal reaction conditions were found to be carrying out the reaction in the presence of KOH (2.0 equiv) under 40 bar of hydrogen in EtOH at 10 °C over 24 h.

Table 3 Screening of hydrogen pressure and temperature[a]



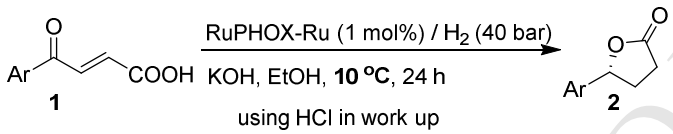
Entry	H_2 (bar)	Temp (°C)	Yield (%)[b]	ee (%)[c,d]
1	20	r.t.	>99	66
2	30	r.t.	>99	75
3	40	r.t.	>99	78
4	50	r.t.	>99	72
5[e]	40	10	>99	84
6[f]	40	5	92	84
7[g]	40	0	90	27

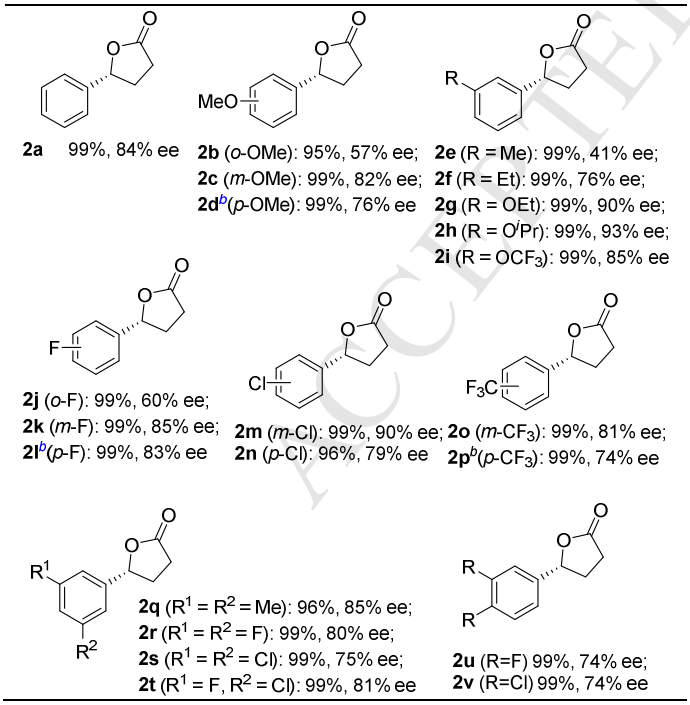
[a]Conditions: **1a** (0.25 mmol), RuPHOX-Ru (1 mol%), KOH (2.0 equiv), and EtOH (2 mL). [b]Determined by ^{1}H NMR spectroscopy. [c]Enantioselectivity was determined by HPLC using a chiral AS-H column. [d]The absolute configuration of **2a** was determined as *R*-

configuration by comparing the specific rotation with reported data.[6j] [c] [g] The reaction was carried out for 24 h.

With the optimal reaction conditions identified, the generality of the present asymmetric hydrogenation was investigated with various substrates (Table 4). First, substrates with an electron-donating OMe group located at different positions on the phenyl ring were examined. The desired products **2b-2d** were obtained in quantitative yields and with approximately 80% ees. The best catalytic behaviors were observed for a substrate bearing a meta-substituent (**2c**). Therefore, several substrates bearing meta-substituted groups were synthesized and applied in the above reaction (**2e-2i**). The desired products were obtained in high yields and good to excellent enantioselectivities. When O^{i}Pr was the substituent, the corresponding product was obtained in 93% ee (**2h**). Subsequently, substrates with electron-withdrawing groups located at different positions on the phenyl ring were also examined (**2j-2p**). A similar phenomenon was observed in which substrates bearing meta-substituted groups gave the best results (**2k**, **2m** and **2o**). A substrate with a Cl atom at the meta-position of the phenyl ring gave the corresponding product in 90% ee (**2m**). Due to the fact that the most promising results were obtained for substrates with meta-position substituents, disubstituted substrates with electron-donating and/or electron-withdrawing substituents at both the meta-positions were next examined. All the substrates gave their corresponding products with approximately 80% ee and in quantitative yields (**2q-2t**). Finally, substrates bearing two electron-withdrawing substituents on the phenyl ring were also employed in the reaction, affording high yields and moderate enantioselectivities (**2u-2v**).

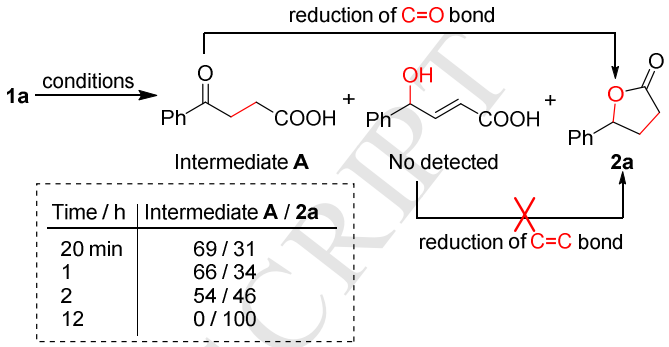
Table 4 Scope of substrates **1**[a]





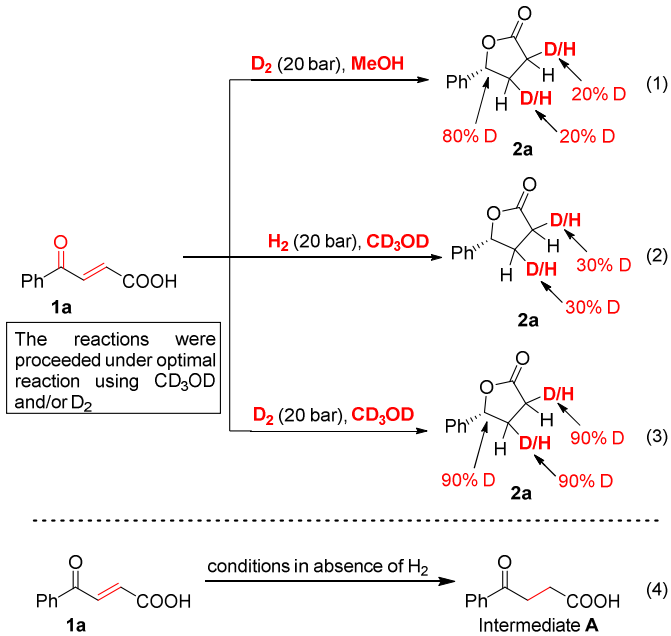
[a]Using the optimal reaction conditions shown in Table 3; Ees were determined by chiral HPLC analysis of **2** using a AS-H column; Absolute configuration of **2** was determined as *R*-configuration by comparing the specific rotation with **2a**. [b]The reaction was carried out at RT.

To explore the reaction pathway, the asymmetric hydrogenation was carried out with KOH under 20 bar hydrogen in EtOH solvent at RT and was quenched at different times. After 20 min reaction time, the raw material **1a** disappeared and a ratio of 69/31 between intermediate **A** and the terminal product **2a** was observed. No intermediate **B** was found at all. The conversion from intermediate **A** to product increased only slowly, even after 1 h or 2 h, and full conversion of **2a** was not observed until 12 h. These results indicate that the hydrogenation of C=C double bond is faster than that of C=O double bond during the reaction.



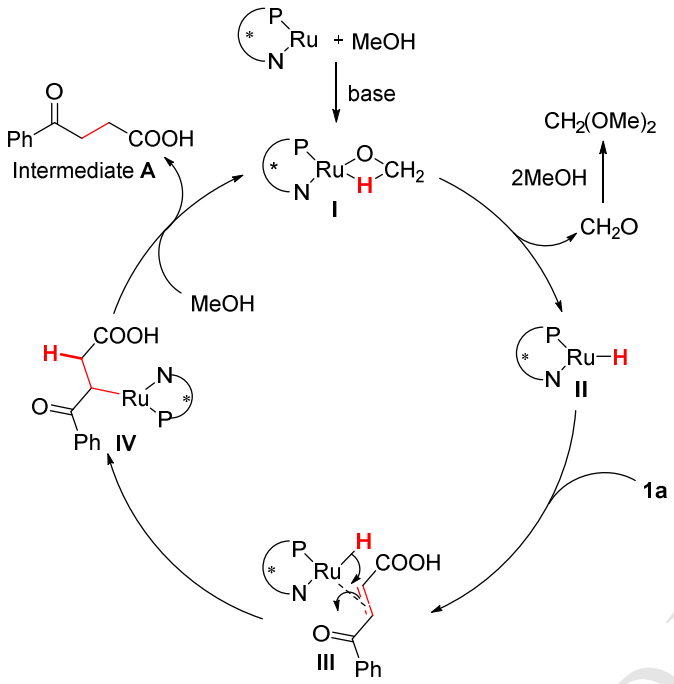
Scheme 2 Possible pathways for asymmetric hydrogenation.

To further elucidate the mechanism of the reaction, we conducted deuterium labelling experiments using CD_3OD and/or D_2. Approximately 25% deuterium incorporation was observed when the reaction was conducted in both MeOH and CD_3OD, revealing that the C=C double bond is reduced via a competitive process, including both hydrogenation and transfer hydrogenation (Scheme 3, eq 1 and 2). However, the C=O double bond is hydrogenated solely by H_2 or D_2 according to the corresponding deuterium labelling ratios. As expected, the reaction of **1a** in only CD_3OD under 20 bar of D_2 gave 90% deuterated product at both the C=C and C=O double bonds (eq 3). We have also carried out the reaction under the optimal reaction conditions but in the absence of H_2. Only intermediate **A**, of which the C=C double bond is reduced, was observed after 12 h, proving a transfer hydrogenation mechanism (eq 4). The above results reveal that of the different double bonds are reduced via different processes and the chiral center is formed exclusively via hydrogenation rather than transfer hydrogenation.



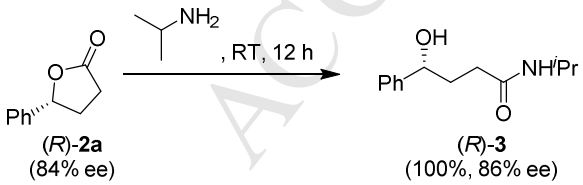
Scheme 3 Deuterium labelling experiments.

On the basis of the above experimental results and according to previously reported work,[7] a possible transfer hydrogenation reaction pathway has been proposed, as depicted in Scheme 4. First, the chiral catalyst RuPHOX-Ru reacts with MeOH to generate Ru-methoxide **I**, which subsequently gives a Ru-hydride **II** via the elimination of one molecule of HCHO. The hydrogenated substrate **1a** then coordinates to the Ru-hydride **II** to give **III**, which immediately undergoes hydride transfer process, affording the resulting intermediate **IV**. Finally, **IV** is protonated by MeOH to give the intermediate **A**, releasing the Ru-methoxide **I**.



Scheme 4 Proposed pathway for intermediate **A**.

Compound **2a** can be transformed to several different chiral building blocks, biologically active compounds and drugs, which have been disclosed in our previous work.[6j] It can also be reacted with isopropylamine directly, in the absence of solvent, over 10 h to afford 4-hydroxy-*N*-isopropyl-4-phenyl-butyramide **3** in quantitative yield and with 86% ee (Scheme 5). Compound **3** can efficiently increase the plasma levels of HDL in a cholesterol fed rat model and is useful for treating diseases such as atherosclerosis.[8]



Scheme 5 The formation of **3**.

3. Conclusions

In summary, we have developed a convenient RuPHOX-Ru-catalyzed asymmetric hydrogenation of aroylacrylic acids, providing the corresponding chiral γ-lactones in up to 99% yield and 93% ee. The methodology has the advantage of using easily accessible substrates and therefore expands the scope of the resulting chiral γ-lactones. Furthermore, high catalytic efficiency was achieved; reduction of both the C=C and C=O double bonds can proceed in one step. Mechanistic studies revealed that different types of double bonds are reduced via different hydrogenation process and that the chiral center is formed exclusively via hydrogenation rather than transfer hydrogenation.

4. Experimental section

4.1. General

All hydrogenation reactions were performed in an autoclave under an atmosphere of hydrogen, and the workup was carried out in air. Solvents were degassed using standard procedures. Commercially available reagents were used without further purification. Column chromatography was performed using 100-200 mesh silica gel. Melting points were measured with SGW X-4 micro melting point apparatus and the thermometer was uncorrected. NMR spectra were recorded on a Varian MERCURY plus-400 spectrometer with TMS as an internal standard. Enantioselectivity was measured by a high performance liquid chromatography (HPLC) using Daicel Chiralcel AS-H column and OX-H column with *n*-hexane/*i*-PrOH as eluent.

4.2. General procedure for RuPHOX-Ru-catalyzed asymmetric hydrogenation

In a nitrogen-filled glovebox, a hydrogenation tube was charged with a stirring bar, **1** (0.25 mmol), RuPHOX-Ru (4.3 mg, 1 mol%) and KOH (20 mg, 2.0 equiv). EtOH (2 mL) were then injected into the hydrogenation tube using a syringe. The hydrogenation tube was then placed in an autoclave. The system was evacuated and filled with hydrogen 3 times. The autoclave was then charged with hydrogen to 40 bar hydrogen pressure, and the reaction mixture was stirred at 10 °C for 24 h. After releasing the hydrogen, the reaction mixture was acidified with 3 M HCl solution and extracted with EtOAc (3 × 5 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The conversion of the substrate was determined by ^{1}H NMR analysis by using the above crude product. After purification via column chromatography, the ee value of the pure product was determined by HPLC using the Chiralcel AS-H column.

The corresponding racemic product was obtained using Pd/C and MeOH in an autoclave under 20 bar hydrogen pressure at RT.

*(R)-5-Phenyldihydrofuran-2(3H)-one (**2a**)*[6j]

Colorless oil (40.1 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.32 (m, 5H), 5.51 (t, J = 7.2 Hz, 1H), 2.71–2.63 (m, 3H), 2.23–2.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 139.4, 128.7, 128.4, 125.3, 81.2, 30.9, 28.9; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 14.8 min, t_{R2} = 17.7 min], ee = 84%; $[\alpha]_{25}^{D}$ = +26.59 (*c* 1.50, $CHCl_3$).

*(R)-5-(2-Methoxyphenyl)dihydrofuran-2(3H)-one (**2b**)*[9b]

Colorless oil (45.6 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (m, 2H), 6.96 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 5.75 (t, J = 6.8 Hz, 1H), 3.83 (s, 3H), 2.72–2.58 (m, 3H), 2.14–2.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 156.0, 129.3, 128.0, 125.6, 120.6, 110.5, 77.9, 55.3, 29.3, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 15.2 min, t_{R2} = 17.6 min], ee = 57%; $[\alpha]_{25}^{D}$ = +10.41 (*c* 0.94, $CHCl_3$).

*(R)-5-(3-Methoxyphenyl)dihydrofuran-2(3H)-one (**2c**)*[6j]

Colorless oil (47.9 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.24 (m, 1H), 6.90–6.82 (m, 3H), 5.50–5.43 (m, 1H), 3.79 (s, 3H), 2.68–2.55 (m, 3H), 2.23–2.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 159.9, 141.0, 129.8, 117.3, 113.8, 110.7, 81.0, 55.3, 30.9, 28.9; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-

PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 18.6 min, t_{R2} = 23.0 min], ee = 82%; $[\alpha]_{25}^{D}$ = +15.27 (*c* 0.34, $CHCl_3$).

*(R)-5-(4-Methoxyphenyl)dihydrofuran-2(3H)-one (**2d**)*[9d]

Colorless oil (47.9 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.23 (m, 2H), 6.92–6.89 (m, 2H), 5.47–5.42 (m, 1H), 3.81 (s, 3H), 2.67–2.58 (m, 3H), 2.23–2.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 159.7, 131.1, 126.9, 114.1, 81.3, 55.3, 30.9, 29.2; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 14.0 min, t_{R2} = 19.0 min], ee = 76%; $[\alpha]_{25}^{D}$ = +31.10 (*c* 0.69, $CHCl_3$).

*(R)-5-(3-Tolyl)dihydrofuran-2(3H)-one (**2e**)*[6j]

Colorless oil (44.0 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.22 (m, 1H), 7.14–7.07 (m, 3H), 5.48–5.44 (m, 1H), 2.65–2.58 (m, 3H), 2.35 (s, 3H), 2.21–2.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 139.3, 138.5, 129.1, 128.6, 125.9, 122.3, 81.3, 30.9, 28.9, 21.4; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 90/10, 210 nm, 0.8 mL/min, t_{R1} = 23.6 min, t_{R2} = 31.0 min], ee = 41%; $[\alpha]_{25}^{D}$ = +22.46 (*c* 0.33, $CHCl_3$).

*(R)-5-(3-Ethylphenyl)dihydrofuran-2(3H)-one (**2f**)*

Colorless oil (47.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.28 (m, 1H), 7.19–7.16 (m, 2H), 7.15–7.12 (m, 1H), 5.51–5.48 (m, 1H), 2.69–2.63 (m, 5H), 2.23–2.16 (m, 1H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 144.9, 139.3, 128.7, 128.0, 124.7, 122.5, 81.4, 31.0, 29.0, 28.8, 15.5; IR (KBr) cm^{-1}: 2964, 1774, 1631, 1362, 1181, 1138, 1023, 797, 703; HRMS (ESI): calcd for $C_{12}H_{14}O_2$ $[M+Na]^+$: 213.0886, found 213.0886; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 11.8 min, t_{R2} = 14.7 min], ee = 76%; $[\alpha]_{25}^{D}$ = +18.18 (*c* 0.67, $CHCl_3$).

*(R)-5-(3-Ethoxyphenyl)dihydrofuran-2(3H)-one (**2g**)*[6j]

Colorless oil (51.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.27 (m, 1H), 6.89–6.80 (m, 3H), 5.50–5.42 (m, 1H), 4.02 (q, *J* = 6.4 Hz, 2H), 2.66–2.58 (m, 3H), 2.20–2.12 (m, 1H), 1.39 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 159.2, 140.9, 129.8, 117.2, 114.3, 111.3, 81.0, 63.5, 30.9, 28.9, 14.8; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 17.2 min, t_{R2} = 21.2 min], ee = 90%; $[\alpha]_{25}^{D}$ = +9.77 (*c* 0.54, $CHCl_3$).

*(R)-5-(3-Isopropoxyphenyl)dihydrofuran-2(3H)-one (**2h**)*[6j]

Colorless oil (55.0 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.23 (m, 1H), 6.85–6.82 (m, 3H), 5.46–5.43 (m, 1H), 4.58–4.51 (m, 1H), 2.64–2.57 (m, 3H), 2.20–2.12 (m, 1H), 1.31 (d, *J* = 5.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 158.2, 141.0, 129.8, 117.1, 115.4, 112.8, 81.0, 69.9, 30.9, 28.9, 22.0; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 12.2 min, t_{R2} = 14.3 min], ee = 93%; $[\alpha]_{25}^{D}$ = +13.01 (*c* 0.83, $CHCl_3$).

*(R)-5-(3-(Trifluoromethoxy)phenyl)dihydrofuran-2(3H)-one (**2i**)*[6j]

Colorless oil (61.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.20–7.15 (m, 2H), 5.51–5.46 (m, 1H), 2.71–2.62 (m, 3H), 2.20–2.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.3, 149.5, 141.8, 130.3, 123.4, 120.7, 120.3 (q, *J* = 256.2 Hz), 117.9, 80.0, 30.8, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 85/15, 210 nm, 0.8 mL/min, t_{R1} = 13.5 min, t_{R2} = 17.4 min], ee = 85%; $[\alpha]_{25}^{D}$ = +28.18 (*c* 0.55, $CHCl_3$).

*(R)-5-(2-Fluorophenyl)dihydrofuran-2(3H)-one (**2j**)*[9c]

Colorless oil (45.0 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (t, *J* = 7.6 Hz, 1H), 7.35–7.27 (m, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 10.0 Hz, 1H) , 5.73 (t, *J* = 7.2 Hz, 1H), 2.75–2.63 (m, 3H), 2.23–2.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 159.6 (d, *J* = 245.6 Hz), 130.0 (d, *J* = 8.1 Hz), 126.9 (d, *J* = 12.6 Hz), 126.5 (d, *J* = 3.8 Hz), 124.4 (d, *J* = 3.6 Hz), 115.6 (d, *J* = 20.7 Hz), 76.2 (d, *J* = 3.3 Hz), 29.7, 28.5; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 11.9 min, t_{R2} = 14.4 min], ee = 60%; $[\alpha]_{25}^{D}$ = +14.32 (*c* 0.35, $CHCl_3$).

*(R)-5-(3-Fluorophenyl)dihydrofuran-2(3H)-one (**2k**)*[6j]

Colorless oil (45.0 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (m, 1H), 7.10–6.96 (m, 3H), 5.50–5.43 (m, 1H), 2.67–2.57 (m, 3H), 2.18–2.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 162.9 (d, *J* = 245.6 Hz), 142.0 (d, *J* = 7.3 Hz), 130.4 (d, *J* = 8.1 Hz), 120.7 (d, *J* = 2.9 Hz), 115.3 (d, *J* = 20.9 Hz), 112.3 (d, *J* = 22.6 Hz), 80.2, 30.8, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 14.8 min, t_{R2} = 18.2 min], ee = 85%; $[\alpha]_{25}^{D}$ = +14.67 (*c* 0.43, $CHCl_3$).

*(R)-5-(4-Fluorophenyl)dihydrofuran-2(3H)-one (**2l**)*[6j]

Colorless oil (45.0 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (t, *J* = 5.6 Hz, 2H), 7.04 (t, *J* = 8.0 Hz, 2H), 5.46-5.43 (m, 1H), 2.67–2.57 (m, 3H), 2.18–2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 162.6 (d, *J* = 245.8 Hz), 135.1 (d, *J* = 3.1 Hz), 127.2 (d, *J* = 8.3 Hz), 115.7 (d, *J* = 21.6 Hz), 80.6, 31.0, 29.0; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 15.9 min, t_{R2} = 19.2 min], ee = 83%; $[\alpha]_{25}^{D}$ = +36.69 (*c* 0.63, $CHCl_3$).

*(R)-5-(3-Chlorophenyl)dihydrofuran-2(3H)-one (**2m**)*[6j]

Colorless oil (49.0 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.27 (m, 3H), 7.21–7.16 (m, 1H), 5.48–5.42 (m, 1H), 2.69–2.59 (m, 3H), 2.19–2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 141.4, 134.7, 130.1, 128.5, 125.4, 123.3, 80.2, 30.8, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 98/2, 210 nm, 0.8 mL/min, t_{R1} = 74.7 min, t_{R2} = 101.8 min], ee = 90%; $[\alpha]_{25}^{D}$ = +23.59 (c 0.44, $CHCl_3$).

*(R)-5-(4-Chlorophenyl)dihydrofuran-2(3H)-one (**2n**)*[9d]

Colorless oil (47.0 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.27 (m, 2H), 7.24-7.20 (m, 2H), 5.44-5.38 (m, 1H), 2.62-2.54 (m, 3H), 2.11-2.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 137.9, 134.2, 127.8 (d, *J* = 215.3 Hz), 127.8 (d, *J* = 129.3 Hz), 80.5, 30.9, 28.9; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 90/10, 210 nm, 0.8 mL/min, t_{R1} = 25.2 min, t_{R2} = 29.5 min], ee = 79%; $[\alpha]_{25}^{D}$ = +25.96 (*c* 0.55, $CHCl_3$).

*(R)-5-(3-(Trifluoromethyl)phenyl)dihydrofuran-2(3H)-one (**2o**)*[6j]

Colorless oil (57.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.56 (m, 2H), 7.53–7.49 (m, 2H), 5.56–5.51 (m, 1H), 2.72–2.64 (m, 3H), 2.20–2.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.3, 140.4, 131.4, 131.1, 129.3, 128.5, 125.3 (q, *J* = 3.8 Hz), 122.0 (q, *J* = 3.8 Hz), 80.2, 30.9, 28.8; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 10.8 min, t_{R2} = 14.3 min], ee = 81%; $[\alpha]_{25}^{D}$ = +34.39 (*c* 0.46, $CHCl_3$).

*(R)-5-(4-(Trifluoromethyl)phenyl)dihydrofuran-2(3H)-one (**2p**)*[9d]

Colorless oil (57.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 5.55 (t, *J* = 7.6 Hz, 1H), 2.75–2.63 (m, 3H), 2.19–2.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.3, 143.4, 130.6 (d, *J* = 32.8 Hz), 125.8 (q, *J* = 3.7 Hz), 125.4, 123.9 (d, *J* = 270.7 Hz), 80.1, 30.9, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8

mL/min, t_{R1} = 10.6 min, t_{R2} = 12.7 min], ee = 74%; $[\alpha]_{25}^{D}$ = +22.25 (*c* 0.36, $CHCl_3$).

*(R)-5-(3,5-Dimethylphenyl)dihydrofuran-2(3H)-one (**2q**)*[6j]

Colorless oil (45.6 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94 (s, 1H), 6.92 (s, 2H), 5.44–5.39 (m, 1H), 2.63–2.56 (m, 3H), 2.30 (s, 6H), 2.19–2.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 139.3, 138.4, 130.0, 123.0, 81.4, 30.9, 28.9, 21.3; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 10.2 min, t_{R2} = 13.1 min], ee = 85%; $[\alpha]_{25}^{D}$ = +18.83 (*c* 0.46, $CHCl_3$).

*(R)-5-(3,5-Difluorophenyl)dihydrofuran-2(3H)-one (**2r**)*

Colorless oil (49.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87-6.81 (m, 2H), 6.77–6.70 (m, 1H), 5.46–5.43 (m, 1H), 2.72–2.61 (m, 3H), 2.16–2.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1, 164.4 (d, *J* = 12.6 Hz), 161.9 (d, *J* = 12.6 Hz), 143.5 (t, *J* = 8.9 Hz), 108.1 (d, *J* = 26.4 Hz), 108.1 (d, *J* = 11.6 Hz), 103.7 (t, *J* = 25.1 Hz), 79.5, 30.6, 28.5; IR (KBr) cm^{-1}: 2959, 2830, 2716, 1787, 1631, 1366, 1119, 785, 774; HRMS (ESI): calcd for $C_{10}H_8F_2O_2$ $[M+Na]^+$: 221.0385, found 221.0383; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 11.6 min, t_{R2} = 14.6 min], ee = 80%; $[\alpha]_{25}^{D}$ = +11.06 (*c* 0.52, $CHCl_3$).

*(R)-5-(3,5-Dichlorophenyl)dihydrofuran-2(3H)-one (**2s**)*

Colorless oil (57.3 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.30 (m, 1H), 7.23–7.21 (m, 2H), 5.45–5.41 (m, 1H), 2.72–2.63 (m, 3H), 2.17–2.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1, 142.9, 135.5, 128.5, 123.7, 79.4, 30.8, 28.6; IR (KBr) cm^{-1}: 3078, 2926, 2854, 1782, 1570, 1436, 1179, 799, 691; HRMS (ESI): calcd for $C_{10}H_8Cl_2O_2$ $[M+H]^+$: 230.9974, found 230.9981; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 85/15, 210 nm, 0.8 mL/min, t_{R1} = 17.9 min, t_{R2} = 37.8 min], ee = 75%; $[\alpha]_{25}^{D}$ = +14.70 (*c* 0.50, $CHCl_3$).

*(R)-5-(3-Chloro-5-fluorophenyl)dihydrofuran-2(3H)-one (**2t**)*

Colorless oil (53.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14–7.11 (m, 1H), 7.08–7.04 (m, 1H), 6.98-6.93 (m, 1H), 5.47–5.43 (m, 1H), 2.73–2.63 (m, 3H), 2.18–2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 162.8 (d, *J* = 249.6 Hz), 143.3 (d, *J* = 8.1 Hz), 135.7 (d, *J* = 10.3 Hz), 121.2 (d, *J* = 3.2 Hz), 116.1 (d, *J* = 24.5 Hz), 110.8 (d, *J* = 22.7 Hz), 79.4, 30.7, 28.5; IR (KBr) cm^{-1}: 2830, 1787, 1657, 1366, 1119, 786, 774; HRMS (ESI): calcd for $C_{10}H_8ClFO_2$ $[M+Na]^+$: 237.0089, found 237.0095; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 10.1 min, t_{R2} = 12.6 min], ee = 81%; $[\alpha]_{25}^{D}$ = +18.36 (*c* 0.32, $CHCl_3$).

*(R)-5-(3,4-Difluorophenyl)dihydrofuran-2(3H)-one (**2u**)*

Colorless oil (49.5 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21–7.12 (m, 2H), 7.08–7.04 (m, 1H), 5.47–5.41 (m, 1H), 2.71–2.62 (m, 3H), 2.20–2.09 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.3, 151.5 (dd, *J* = 29.5, 13.0 Hz), 149.1 (dd, *J* = 29.0, 12.6 Hz), 136.4 (dd, *J* = 5.4, 3.6 Hz), 121.4 (dd, *J* = 6.5, 2.7 Hz), 117.7 (d, *J* = 17.5 Hz), 114.6 (d, *J* = 18.3 Hz), 79.8, 30.9, 28.8; IR (KBr) cm^{-1}: 2925, 2830, 2716, 1765, 1631, 1366, 1068, 785, 774; HRMS (ESI): calcd for $C_{10}H_8F_2O_2$ $[M+Na]^+$: 221.0385, found 221.0387; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 11.6 min, t_{R2} = 13.5 min], ee = 74%; $[\alpha]_{25}^{D}$ = +9.42 (*c* 0.44, $CHCl_3$).

*(R)-5-(3,4-Dichlorophenyl)dihydrofuran-2(3H)-one (**2v**)*[9a]

Colorless oil (57.4 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 14.8 Hz, 1H), 7.43 (d, *J* = 2.0 Hz, 1H), 7.17 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.47–5.43 (m, 1H), 2.71–2.64 (m, 3H), 2.18–2.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1, 139.6, 133.1, 132.5, 130.8, 127.3, 124.5, 79.5, 30.8, 28.7; HPLC [Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 75/25, 210 nm, 0.8 mL/min, t_{R1} = 14.1 min, t_{R2} = 19.6 min], ee = 74%; $[\alpha]_{25}^{D}$ = +18.60 (*c* 0.32, $CHCl_3$).

The synthesis of (*R*)-4-hydroxy-N-isopropyl-4-phenyl-butyramide (3)[8]

A mixture of **2a** (1 g, 6.2 mmol) and isopropylamine (5 mL, 58.7 mmol) was stirred at room temperature for approximately 10 hours. The additional isopropylamine was removed under reduced pressure to give 4-hydroxy-N-isopropyl-4-phenyl-butyramide **3** as a white solid (1.36 g, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.29 (m, 4H), 7.25–7.21 (m, 1H), 5.73 (d, *J* = 6.0 Hz, 1H), 4.73 (q, *J* = 4.0 Hz, 1H), 4.09–3.98 (m, 1H), 2.26 (t, *J* = 6.8 Hz, 2H), 2.04–1.93 (m, 2H), 1.11 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 144.6, 128.3, 127.2, 125.7, 73.5, 41.5, 34.5, 33.1, 22.6; HPLC [Daicel Chiralcel OX-H, *n*-hexane/*i*-PrOH = 95/5, 210 nm, 0.5 mL/min, t_{R1} = 85.0 min, t_{R2} = 123.6 min], ee = 86%; $[\alpha]_{25}^{D}$ = +38.95 (*c* 0.32, $CHCl_3$).

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References and notes

1. Selected reviews, see: (a) Takaya, H.; Ohta, T.; Noyori, R. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 1993; p 1; (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; Chapter 2; (c) Ohkuma, T.; Noyori, R. In *Transition Metals for Organic Synthesis*: *Building Blocks and Fine Chemicals*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 2, p 25; (d) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; (e) Knowles, W. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1998; (f) Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008; (g) Tang, W.; Zhang, X. *Chem. Soc. Rev.* **2012**, *41*, 4126; (h) Chen, Q.; Ye, Z.; Duan, Y.; Zhou, Y. *Chem. Soc. Rev.* **2013**, *42*, 497; (i) Zhang, Z.; Butt, N. A.; Zhang, W. *Chem. Rev.* **2016**, *116*, 14769; For selected papers, see: (j) Llorente, N.; Fernández-Pérez, H.; Núñez-Rico, J. L.; Carreras, L.; Martínez-Carrión, A.; Iniesta, E.; Romero-Navarro, A.; Martínez-Bascuñana, A.; Vidal-Ferran, A. *Pure Appl. Chem.* **2019**, *91*, 3; (k) Mazuela, J.; Antonsson, T.; Knerr, L.; Marsden, S. P.; Munday, R. H.; Johansson, M. J. *Adv. Synth. Catal.* **2019**, *361*, 578; (l) Seo, C. S. G.; Morris, R. H. *Organometallics*, **2019**, *38*, 47; (m) Yan, Q.; Xiao, G.; Wang, Y.; Zi, G.; Zhang, Z.; Hou, G. *J. Am. Chem. Soc.*, **2019**, *141*, 1749.
2. (a) Takaya, H.; Ohta, T.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Inoue, S.-I.; Kasahara, I.; Noyori, R. *J. Am. Chem. Soc.* **1987**, *109*, 1596; (b) Murahashi, E. I.; Nakota, T.; Kuwabara, T.; Saito, T.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1990**, *112*, 7820; (c) Kitamura, M.; Tokunaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1993**, *115*, 144; (d) Dobbs, D. A.; Vanhessche, K. P. M.; Brazi, E.; Rautenstrauch, V.; Lenoir, J. Y.; Genet, J. P.; Wiles, J.; Bergens, S. H. *Angew. Chem. Int. Ed.* **2000**, *39*, 1992; (e) Bulliard, M.; Laboue, B.; Lastanet, J.; Roussiasse, S. *Org. Process Res. Dev.* **2001**, 438; (f) Genet, J. P. *Acc. Chem. Res.* **2003**, *36*, 908; (g) Wu, J.; Chen, H.; Yeung, C. H.; Chan, A. S. C. *Tetrahedron Lett.* **2002**, *43*, 1539; (h) Utsumi, N.; Arai, N.; Kawaguchi, K.; Katayama, T.; Yasuda, T.; Murata, K.; Ohkuma, T. *ChemCatChem* **2018**, *10*, 3955.
3. (a) Gunasekera, S. P.; Isbrucker, R. A.; Longley, R. E.; Wright, A. E.; Pomponi, S. A.; Reed, J. K.; *J. Nat. Prod.* **2004**, *67*, 110; (b) Bandichhor, R.; Nosse, B.; Reiser, O. *Top. Curr. Chem.* **2005**, *243*, 43; (c) Kitson, R. R. A.; Millemaggi, A.; Taylor, R. J. K. *Angew. Chem. Int. Ed.* **2009**, *48*, 9426; (d) Xia, S.; Chen, Y.; Zhuo, J.; Xu, H. *Biocatal. Biotransfor.* **2013**, *31*, 66.
4. (a) Ohkuma, T.; Kitamura, M.; Noyori, R. *Tetrahedron Lett.* **1990**, *31*, 5509; (b) Benincori, T.; Rizzo, S.; Pilati, T.; Ponti, A.; Sada, M.; Pagliarini, E. *Tetrahedron*: *Asymmetry* **2004**, *15*, 2289; (c) Starodubtseva, E. V.; Turova, O. V.; Vinogradov, M. G.; Gorshkova, L. S.; Ferapontov, V. A.; Struchkova, M. I. *Tetrahedron* **2008**, *64*, 11713; (d) Arai, N.; Namba,

T.; Kawaguchi, K.; Matsumoto, Y.; Ohkuma, T. *Angew. Chem. Int. Ed.* **2018**, *57*, 1386.

5. For planar chiral RuPHOX ligands, see reviews: (a) Zhang W.; Liu, D. In *Chiral Ferrocenes in Asymmetric Catalysis: Synthesis and Applications*; Dai, L.-X.; Hou, X.-L. Eds.; VCH: Weinheim, Germany, **2010**; Chapter 14, pp 175; (b) Butt, N. A.; Liu, D.; Zhang, W. *Synlett* **2014**, *25*, 615; (c) Butt, N. A.; Zhang, W. *Chem. Soc. Rev.* **2015**, *44*, 7929; (d) Fu, J.; Huo, X.; Li, B.; Zhang, W. *Org. Biomol. Chem*. **2017**, *15*, 9747; See selective papers: (e) Zhao, X.; Liu, D.; Guo, H.; Liu, Y.; Zhang, W. *J. Am. Chem. Soc*. **2011**, *133*, 19354; (f) Huo, X.; Quan, M.; Yang, G.; Zhao, X.; Liu, D.; Liu, Y.; Zhang, W. *Org. Lett.* **2014**, *16*, 1570; (g) Huo, X.; Yang, G.; Liu, D.; Liu, Y.; Gridnev, I. D.; Zhang, W. *Angew. Chem. Int. Ed.* **2014**, *53*, 6776; (h) Huo, X.; He, R.; Fu, J.; Zhang, J.; Yang, G.; Zhang, W. *J. Am. Chem. Soc*. **2017**, *139*, 9819; (i) Huo, X.; Zhang, J.; Fu, J.; He, R.; Zhang, W. *J. Am. Chem. Soc*. **2018**, *140*, 2080; (j) Huo, X.; Fu, J.; He, X.; Chen, J.; Xie, F.; Zhang, W. *Chem. Commun*. **2018**, *54*, 599.
6. (a) Liu, D.; Xie, F.; Zhao X.; Zhang, W. *Tetrahedron* **2008**, *64*, 3561; (b) Wang, Y.; Liu, D.; Meng, Q.; Zhang, W. *Tetrahedron*: *Asymmetry* **2009**, *20*, 2510; (c) Guo, H.; Liu, D.; Butt, N. A.; Liu, Y.; Zhang, W. *Tetrahedron* **2012**, *68*, 3295; (d) Wang, J.; Liu, D.; Liu, Y.; Zhang, W. *Org. Biomol. Chem*. **2013**, *11*, 855; (e) Wang, Y.; Wang, J.; Liu, D.; Zhang, W. *Chin. J. Org. Chem*. **2014**, *34*, 1766; (f) Wang, J.; Wang, Y.; Liu, D.; Zhang, W. *Adv. Synth. Catal*. **2015**, *357*, 3262; (g) Li, J.; Shen, J.; Xia, C.; Wang, Y.; Liu, D.; Zhang, W. *Org. Lett*. **2016**, *18*, 2122; (h) Guo, H.; Li, J.;