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RuPHOX-Ru-Catalyzed Selective Asymmetric Hydrogenation of Exocyclic α,β-Unsaturated Pentanones

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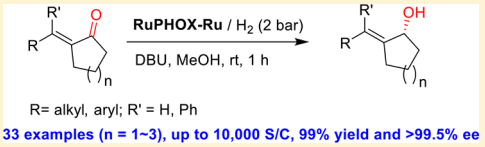
Supporting Information

ABSTRACT: A RuPHOX-Ru catalyzed selective asymmetric hydrogenation of exocyclic α,β-unsaturated ketones has been developed, furnishing the corresponding chiral exocyclic allylic alcohols in high yields and with up to >99.5% ee. The reaction could be performed on a gram scale with a relatively low catalyst loading (up to 10000 S/C) without any loss in reaction activity and enantioselectivity. The resulting hydrogenated products could be easily transformed to several biologically active compounds with high asymmetric performance. The asymmetric protocol provides an efficient methodology for the synthesis of chiral exocyclic allylic alcohols.



INTRODUCTION

Chiral allylic alcohols, particularly chiral cyclopentanols, are of great importance in organic synthesis because they are found not only in natural products but also in pharmaceuticals.[1] Some typical examples include the following (Figure 1): 16β-

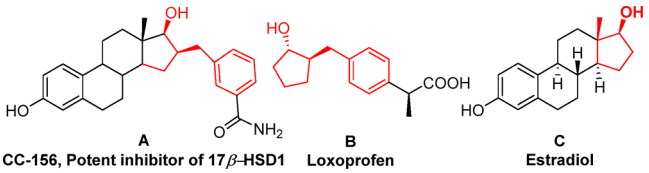


Figure 1. Chiral five-membered allylic alcohols and their derivatives.

m-carbamoylbenzyl-E2 (CC-156, **A**), identified as a promising inhibitor of 17β-hydroxysteroid dehydrogenase type 1 (17β-HSD1), which is involved in the conversion of estrone into estradiol, the most potent estrogen in women;[2] the propionic acid derivative of chiral exocyclic allylic alcohol, the non-steroidal anti-inflammatory drug loxoprofen (**B**);[3] estradiol (**C**), a female sex hormone that regulates many processes in the body, which is used to treat menopause symptoms such as hot flashes.[4]

The transition-metal-catalyzed asymmetric hydrogenation of exocyclic α,β-unsaturated ketones is one of the most powerful strategies for the synthesis of chiral exocyclic allylic alcohols, due to its atom efficiency and minimal environmental impact.[5] This protocol has been conducted using a diverse array of chiral iridium-based catalysts,[6] as exemplified by the independent pioneering studies of Bolm, Hou, Ding, Qiu, and our groups, who have developed Ir complexes bearing chiral P,N-ligands for the efficient asymmetric hydrogenation of the C═C double bond of exocyclic α,β-unsaturated ketones (Scheme 1, top). As a comparison, the asymmetric hydrogenation of the C═O double bond of such ketones is rare. In 2010, Zhou and co-workers realized an efficient asymmetric hydrogenation of C═O bonds in exocyclic α,β-unsaturated carbonyl compounds by using Ir complexes bearing chiral spiro aminophosphine ligands with good to excellent results (Scheme 1, middle).[7a] Just recently, we have developed a novel planar chiral ferrocene phosphine-oxazoline ligand, which has been successfully applied to the above reaction, with the desired products being obtained in up to 98% yield and 99% ee (Scheme 1, middle).[7b] It is obvious that the asymmetric hydrogenation of C═O double bonds of exocyclic α,β-unsaturated ketones has received much less attention and the substrate scope is somewhat limited. Therefore, the exploration of efficient metal-catalyzed asymmetric hydrogenation of the C═O double bond of various exocyclic α,β-unsaturated ketones remains worthy of further investigations.

We have previously developed a chiral phosphino-oxazoline ligand, RuPHOX,[8d] which has shown promising asymmetric catalytic behavior in several asymmetric reactions.[8] In particular, its Ru complex, RuPHOX-Ru,[9a] has been successfully applied in the asymmetric hydrogenation of many types of substrates containing C═C and/or C═O double bonds.[9] Just recently, we have achieved an efficient RuPHOX-Ru-catalyzed selective asymmetric hydrogenation of the C═O double bond of four-membered exo-α,β-unsaturated cyclobutanones.[10] In a continuation of our efforts concerning the synthesis of chiral exocyclic allylic alcohols, we herein report the efficient and mild RuPHOX-Ru catalyzed asymmetric hydrogenation of the C═O double bond of five-, six-, and seven-membered exocyclic α,β-unsaturated ketones (Scheme 1, bottom).

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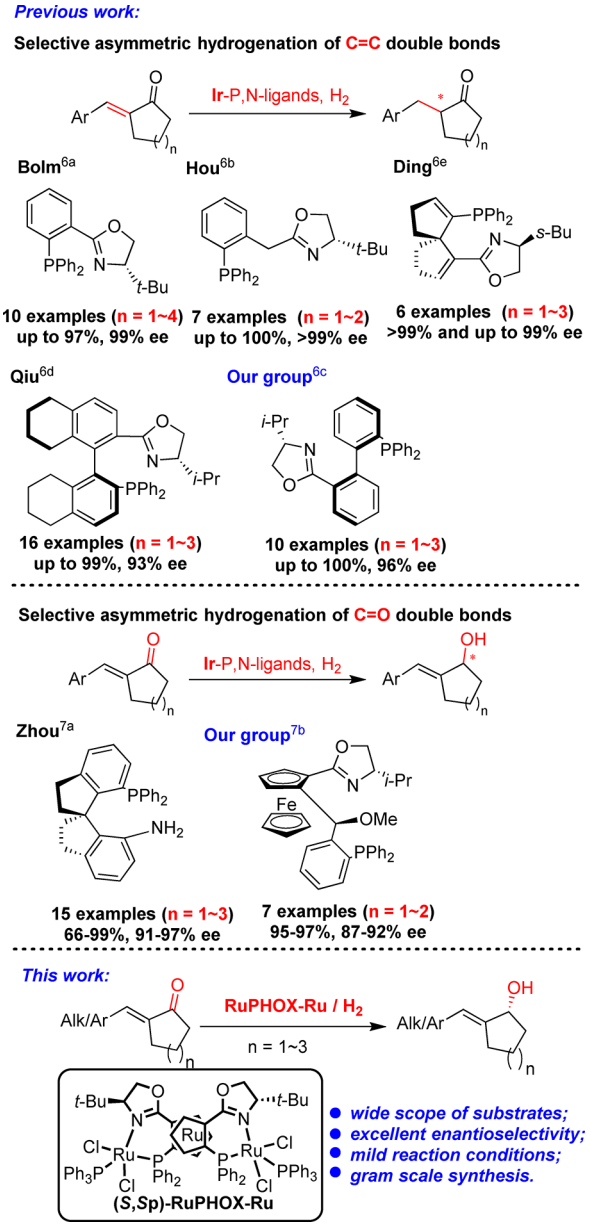
Scheme 1. Asymmetric Hydrogenation of Exocyclic α,β-Unsaturated Ketones

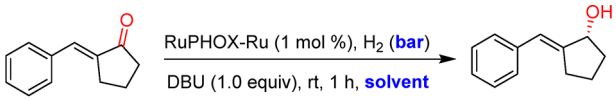


RESULTS AND DISCUSSION

Initially, the RuPHOX-Ru-catalyzed asymmetric hydrogenation of (*E*)-2-benzylidenecyclopentan-1-one (**1a**) was carried out under 20 bar of hydrogen pressure with 1 equiv of DBU as a base in different solvents at room temperature for 1 h.[11] As shown in Table 1, MeOH was first used as a solvent with the desired product (*R*,*E*)-2-benzylidenecyclopentan-1-ol (**2a**) being obtained in quantitative conversion and 99.5% ee (entry 1). The use of EtOH provided the same conversion but a slightly lower enantioselectivity in comparison to that of MeOH (entry 2). When *i*-PrOH was used as a solvent, quantitative conversion and 97% ee were obtained (entry 3). However, none of the desired product was formed when the reaction was conducted in CF_3CH_2OH (entry 4). As a comparison, aprotic solvents such as THF, acetone, and PhMe were used. Good to excellent enantioselecitvities but inferior activities were observed when the reaction was conducted in aprotic solvents (entries 5−7). Next, the asymmetric hydrogenation was carried out in MeOH under different hydrogen pressures. To our delight, the hydrogenation pressure did not affect the asymmetric behaviors and >99% conversions and 99.5% ees were obtained when the reactions were carried out at either a high or low hydrogen pressure (entries 8−10). To illustrate the role of the two Ru sites of the RuPHOX-Ru, asymmetric hydrogenation was conducted under a hydrogen balloon by using a catalytic system of RuPHOX-Ru, *mono*-RuPHOX/Ru (molar ratio 1/1) or RuPHOX/Ru (molar ratio 1/1). The reaction catalyzed by *mono*-RuPHOX/Ru gave low reaction activity as well as inferior enantioselectivity in comparison with that using RuPHOX-Ru as a catalyst (entry 11 versus entry 12). Asymmetric hydrogenation with the last catalytic system provided the desired product with more than 90% ee but in low conversion (entry 13). The results suggest that the two Ru atoms of the RuPHOX-Ru act as catalytic centers and are essential for the excellent catalytic behavior.

With the optimized reaction conditions in hand, exploration of the hydrogenated substrate scope was commenced (Scheme 2). First, substrates with different lengths of carbon chains (*n* = 0−2) between the phenyl ring and C═C double bonds were investigated (**1a**−**c**). As shown in Scheme 2, **1a** bearing the shortest link (*n* = 0) provided the highest ee value (**2a**, 99.5% ee). Next, substrates **1** bearing different substituted aryl rings were investigated. Compounds **1** with different substituents at the 2-position of the aryl rings were examined, and the desired products were obtained in high yields and with 95−98% ees (**2d**−**i**). Electronic properties had little effect on the reaction,

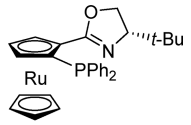
Table 1. Solvent and Hydrogen Pressure Screening[a]



1a **2a**

entry	solvent	H_2 (bar)	conversion (%)[b]	ee (%)[c]
1	MeOH	20	>99	99.5
2	EtOH	20	>99	99
3	*i*-PrOH	20	>99	97
4	CF_3CH_2OH	20	NR	
5	THF	20	72	79
6	acetone	20	38	89
7	toluene	20	47	96
8	MeOH	50	>99	99.5
9	MeOH	6	>99	99.5
10	MeOH	2	>99	99.5
11	MeOH	balloon	70	97
12[d]	MeOH	balloon	45	76
13[e]	MeOH	balloon	28	92

[a]Reaction conditions: **1a** (0.30 mmol), (*S*,*Sp*)-RuPHOX-Ru (1.0 mol %), and DBU (1.0 equiv) in a suitable solvent (2 mL) under a certain hydrogen pressure at room temperature for 1 h. [b]Determined by ^{1}H NMR. [c]Determined by chiral HPLC analysis of **2a** using an OD-H column. The absolute configuration of **2a** was determined according to reported data.[7a] [d]*mono*-RuPHOX/$RuCl_2(PPh_3)_3$ = 1/1 (molar ratio). [e]RuPHOX/$RuCl_2(PPh_3)_3$ = 1/1 (molar ratio).



mono-RuPHOX

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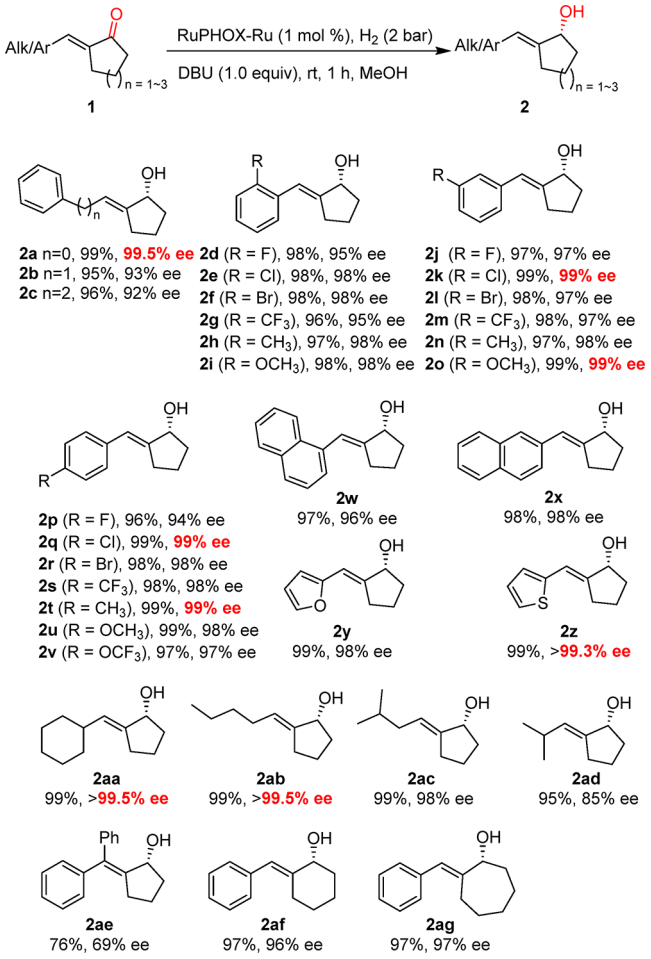
Scheme 2. Exploration of Substrates[a]

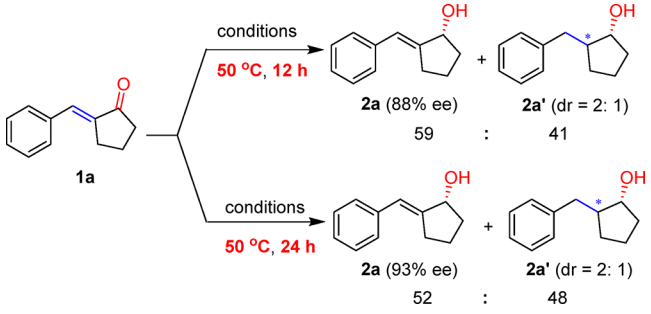


[a]Reaction conditions: **1** (0.30 mmol), (S,S_p)-RuPHOX-Ru (1 mol %), and DBU (1.0 equiv) in MeOH (2 mL) under 2 bar of hydrogen pressure at room temperature for 1 h. Isolated yields. ees were determined by chiral HPLC analysis of **2** using an OD-H, OJ-H, or AS-H column. The absolute configurations of **2** were determined according to reported data.[7a]

and excellent results were observed for all products. Similarly, when election-donating or electron-withdrawing groups were located at the 3-positions of the aryl rings, high yields and excellent enantioselectivities were still obtained (**2j−o**). Substrates bearing para substitutents on the phenyl rings also provided excellent asymmetric catalytic behaviors (**2p−v**). Replacing the electron-withdrawing substituent with an electron-donating group, such as MeO or Me, also had no effect on the reaction, with the desired products being obtained in quantitative yields and up to 99% ee. When the phenyl ring was replaced by naphthalene, high yields and excellent enantioselectivities were also obtained (**2w,x**). Pleasingly, this catalytic asymmetric hydrogenation system is also amenable to heterocyclic substrates (**2y,z**). The aryl group can be replaced by alkyl groups (Cy, *n*-Bu, *i*-Bu, and *i*-Pr) with the desired products **2aa−ac** being obtained in almost quantitative yields and with up to 99.5% ee. In addition, a substrate with a tetrasubstituted olefin unit was subjected to the reaction and the desired product was obtained in 76% yield and with 69% ee (**2ae**). Finally, the size of the alkyl ring was examined in the reaction. We were pleased to find that excellent results were obtained for all of the hydrogenated substrates, varying from five-membered to seven-membered alkyl rings (**2a,af,ag**).

The asymmetric hydrogenation was conducted under 20 bar of hydrogen pressure at 50 °C over 12 and 24 h, with the aim of completing the reduction of both the C═O and C═C double bonds (Scheme 3). It was found that the C═C double

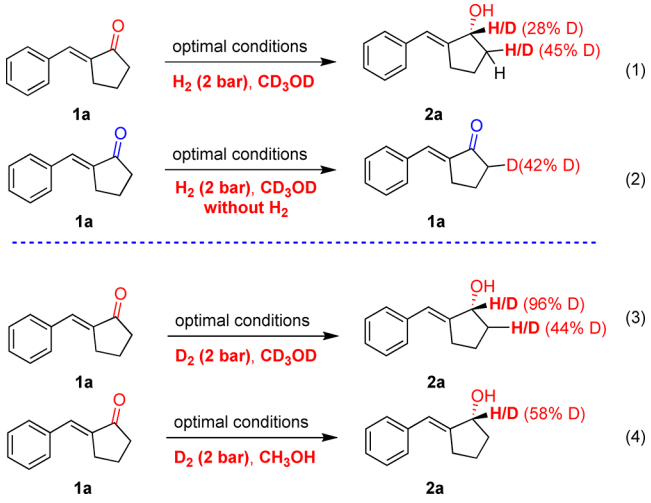
Scheme 3. Reduction of both C═O and C═C Double Bonds



bond could be hydrogenated together with the C═O double bond to give the desired hydrogenated product **2a′**. However, the C═C double bond could not be hydrogenated completely and a mixture of **2a** and fully hydrogenated product **2a′** was obtained, even after 24 h. The results reveal that the C═O and C═C double bonds can be hydrogenated together and the C═O double bond is more easily reduced in comparison with that of the C═C double bond in the current reaction.

To gain a better understanding of the reaction mechanism, we conducted deuterium labeling experiments by using D_2 and/or CD_3OD in place of H_2 and/or CH_3OH (Scheme 4).

Scheme 4. Deuterium Labeling Experiments



When the reaction was performed under a H_2 atmosphere in CD_3OD, 72% H was incorporated at the α-position of the hydroxyl group (eq 1). However, none of the desired product was observed if the above reaction was carried out in the absence of H_2 (eq 2). The results revealed that the reaction proceeds via reduction by H_2 rather than the reaction solvent MeOH. Additionally, approximately 50% H at the α position was deuterated when the reaction was carried out in CD_3OD, suggesting the presence of a keto−enol tautomerization equilibrium during the reaction (eqs 1−3). It was found that

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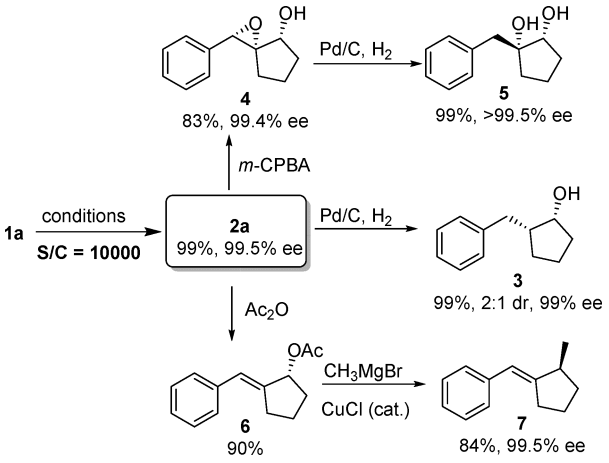
no deuteration of the α-position H atom occurred when the reaction was carried out with D_2 in MeOH, illustrating that the reaction process proceeds via an asymmetric hydrogenation of the C═O double bond of the ketone without including the C═C double bond of the enol equivalent (eq 4).

To examine the efficiency of the catalyst system, a gram-scale hydrogenation of **1a** (5.1 g) was carried out with a low catalyst loading of 0.01 mol % (S/C = 10000) and with modified reaction conditions of 30 bar of H_2 at room temperature for 72 h. To our delight, the desired product **2a** was obtained in quantitative yield without any loss in enantioselectivity (Scheme 5). The C═C double bond of **2a**

Scheme 5. Gram-Scale Synthesis of 2a and Its Transformations



could be further reduced using Pd/C as a catalyst in THF, affording the corresponding **3** in 99% yield, 2:1 dr, and 99% ee. The C═C double bond could also be oxidized by *m*-CPBA to give the corresponding epoxidation product **4** in 83% yield without any loss in enantioselectivity.[12] **4** was then hydrogenated with H_2 catalyzed by Pd/C and was further transformed to its adjacent dihydroxyl product **5** (99% yield, >99.5% ee). The hydroxyl group of **2a** could also be acetylated with Ac_2O easily to give **6**, which was then treated with CH_3MgBr, providing the alkylated product **7** in high yield and 99.5% ee (Scheme 5).[13]

CONCLUSION

In summary, we have developed an efficient RuPHOX-Ru-catalyzed selective asymmetric hydrogenation of exocyclic α,β-unsaturated ketones. Under the optimal reaction conditions, the corresponding chiral exocyclic allylic alcohols were obtained in almost quantitative yields and up to >99.5% ee. The reaction could be performed on a gram scale with a relatively low catalyst loading (up to 10000 S/C), and the resulting products were transformed to several biologically active compounds. The asymmetric protocol provides an efficient methodology for the synthesis of chiral exocyclic allylic alcohols.

EXPERIMENTAL SECTION

General Remarks. All reactions were performed in flame-dried glassware under an atmosphere of dry nitrogen, and the workup was carried out in air, unless otherwise noted. Solvents were dried and degassed by standard procedures. Commercially available reagents were used without further purification. The asymmetric hydrogenation substrates were synthesized according to the reported method.[7a] Column chromatography was performed using 100−200 mesh silica gel. Melting points were measured with an SGW X-4 micro melting point apparatus, and the thermometer was uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Ascend 400 (400 and 100 MHz), Bruker Ascend 500 (500 and 125 MHz), and Bruker Avance III600 spectrometers (600 and 151 MHz). ^{19}F NMR spectra were recorded on a Bruker Ascend 500 spectrometer (500 and 470 MHz). High-resolution mass spectra (HRMS) were obtained on a Fourier-transform mass spectrometer at the Instrumental Analysis Center of Shanghai Jiao Tong University. Enantioselectivity was measured by high-performance liquid chromatography (HPLC) using Daicel Chiralcel OD-H, OJ-H, and AS-H columns with *n*-hexane/*i*-PrOH as eluent. GC analysis was performed using a Shimadzu GC-2010 plus instrument with a chiral capillary column (β-dex-225 or β-dex-120, 30 m × 250 μm × 0.25 μm).

General Procedure for Asymmetric Hydrogenation of Exocyclic α,β-Unsaturated Ketones. In a nitrogen-filled glovebox, a hydrogenation tube was charged with a stirring bar, **1** (0.3 mmol), RuPHOX-Ru (5.2 mg, 1 mol %), and DBU (45.7 mg, 1.0 equiv), followed by the addition of MeOH (2 mL) using a syringe. The hydrogenation tube was then put into an autoclave. The system was evacuated and filled with hydrogen three times. The autoclave was then charged with hydrogen to 2 bar hydrogen pressure, and the reaction mixture was stirred at room temperature for 1 h. After the hydrogen was released, the reaction mixture was concentrated on a rotary evaporator. The conversion of the substrate was determined by ^{1}H NMR analysis of the above crude product. After purification via column chromatography (SiO_2, PE/EtOAc = 4/1), the ee value of the pure product was determined by HPLC using Chiralcel OD-H, OJ-H, and AS-H columns with *n*-hexane/*i*-PrOH as eluent.

*(R,E)-2-Benzylidenecyclopentan-1-ol (**2a**).*[7b] White solid (51.7 mg, 99%). Mp: 81−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.33 (m, 4H), 7.27−7.21 (m, 1H), 6.59 (q, J = 1.6 Hz, 1H), 4.59 (t, J = 5.6 Hz, 1H), 2.76−2.69 (m, 1H), 2.62−2.54 (m, 1H), 2.26 (br s, 1H), 2.02−1.91 (m, 2H), 1.77−1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 137.8, 128.4, 128.3, 126.5, 123.5, 77.2, 34.7, 29.3, 22.5. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 19.0 min (major) and t_{R2} = 20.5 min (minor), ee = 99.5%. $[\alpha]_D^{25}$ = −6.12 (c 0.40, $CHCl_3$).

*(R,E)-2-(2-Phenylethylidene)cyclopentan-1-ol (**2b**).* Colorless oil (53.7 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.27 (m, 2H), 7.21−7.18 (m, 3H), 5.73 (t, J = 7.2 Hz, 1H), 4.47−4.39 (m, 1H), 3.37 (d, J = 7.2 Hz, 2H), 2.56−2.46 (m, 1H), 2.37−2.27 (m, 1H), 1.95−1.84 (m, 2H), 1.73−1.61 (m, 2H), 1.48 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 140.7, 128.4, 128.3, 125.9, 122.6, 75.5, 35.6, 35.6, 27.1, 21.9. IR (KBr) cm^{-1}: 3430, 2957, 1716, 1451, 1176, 1025, 748, 698. HR-MS (ESI): m/z 171.1174, calcd for $C_{13}H_{16}O$ [M − OH]$^+$ 171.1168. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 80/20, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 6.4 min (minor) and t_{R2} = 7.2 min (major), ee = 93%. $[\alpha]_D^{25}$ = −16.06 (c 0.77, $CHCl_3$).

*(R,E)-2-(3-Phenylpropylidene)cyclopentan-1-ol (**2c**).*[14] Colorless oil (58.3 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.27 (m, 2H), 7.21−7.20 (m, 3H), 5.58 (t, J = 8.0 Hz, 1H), 4.41−4.34 (m, 1H), 2.70 (t, J = 7.6 Hz, 2H), 2.37−2.27 (m, 3H), 2.13−2.05 (m, 1H), 1.87−1.77 (m, 2H), 1.67−1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 142.0, 128.4, 128.2, 125.8, 123.1, 75.5, 35.5, 35.5, 31.2, 26.9, 21.9. HPLC (Chiralcel OJ-H, *n*-hexane/*i*-PrOH 90/10, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 7.9 min (major) and t_{R2} = 8.7 min (minor), ee = 92%. $[\alpha]_D^{25}$ = −17.66 (c 0.26, $CHCl_3$).

*(R,E)-2-(2-Fluorobenzylidene)cyclopentan-1-ol (**2d**).* Colorless oil (56.5 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (td, J = 8.0, 1.5 Hz, 1H), 7.24−7.19 (m, 1H), 7.13 (td, J = 7.5, 1.0 Hz, 1H), 7.08−7.04 (m, 1H), 6.79−6.73 (m, 1H), 4.68−4.59 (m, 1H), 2.72−2.66 (m, 1H), 2.57−2.50 (m, 1H), 2.03−1.93 (m, 2H), 1.79−1.65 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.1 (d, J = 246.75 Hz), 150.0, 129.1 (d, J = 2.875 Hz), 128.1 (d, J = 8.375 Hz), 125.5 (d, J = 12.625 Hz), 123.6 (d, J = 3.375 Hz), 115.4, 115.2 (d, J = 6.25 Hz), 77.0, 34.8, 29.1, 22.3. ^{19}F NMR (470 MHz, $CDCl_3$): δ −116.5. IR (KBr) cm^{-1}: 3354, 2961, 1485, 1455, 1095, 753. HR-MS (ESI): m/z

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215.0844, calcd for $C_{12}H_{13}FO$ $[M + Na]^+$ 215.0844. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 10.7 min (major) and t_{R2} = 12.8 min (minor), ee = 95%. $[\alpha]_D^{25}$ = −52.50 (*c* 0.63, $CHCl_3$).

(R,E)-2-(2-Chlorobenzylidene)cyclopentan-1-ol (**2e**).[7b] Colorless oil (61.4 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.40 (m, 1H), 7.36 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.24−7.20 (m, 1H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 6.82 (q, *J* = 1.6 Hz, 1H), 4.62 (t, *J* = 5.6 Hz, 1H), 2.67−2.59 (m, 1H), 2.51−2.43 (m, 1H), 2.02−1.88 (m, 2H), 1.80 (br s, 1H), 1.75−1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 135.6, 133.5, 129.4, 129.3, 127.8, 126.3, 120.0, 76.8, 34.7, 28.8, 22.3. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 80 20, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 6.5 min (major) and t_{R2} = 7.8 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −31.66 (*c* 1.39, $CHCl_3$).

(R,E)-2-(2-Bromobenzylidene)cyclopentan-1-ol (**2f**). Colorless oil (74.4 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.28−7.24 (m, 1H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 6.78−6.73 (m, 1H), 4.63 (t, *J* = 4.8 Hz, 1H), 2.65−2.56 (m, 1H), 2.48−2.40 (m, 1H), 2.03−1.87 (m, 3H), 1.72−1.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 137.3, 132.7, 129.4, 128.0, 126.9, 124.2, 122.6, 76.7, 34.7, 28.7, 22.2. IR (KBr) cm^{-1}: 2965, 1716, 1465, 1436, 1024, 749. HR-MS (ESI): *m*/*z* 235.0116, calcd for $C_{12}H_{13}BrO$ $[M - OH]^+$ 235.0117. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 10.1 min (major) and t_{R2} = 14.1 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −13.22 (*c* 0.56, $CHCl_3$).

(R,E)-2-(2-(Trifluoromethyl)benzylidene)cyclopentan-1-ol (**2g**). Colorless oil (69.7 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.0 Hz, 1H), 7.50−7.44 (m, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.82 (s, 1H), 4.63−4.55 (m, 1H), 2.59−2.53 (m, 1H), 2.42−2.33 (m, 1H), 2.02−1.95 (m, 1H), 1.91−1.85 (m, 1H), 1.79 (br s, 1H), 1.72−1.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7, 136.5, 131.3, 129.8, 127.9 (q, *J* = 32.1 Hz), 126.4, 125.7 (q, *J* = 5.6 Hz), 122.9, 119.7, 76.4, 34.7, 28.6, 22.1. ^{19}F NMR (470 MHz, $CDCl_3$): δ −60.184. IR (KBr) cm^{-1}: 3354, 2953, 1716, 1487, 1455, 1034, 768, 657. HR-MS (ESI): *m*/*z* 265.0815, calcd for $C_{13}H_{13}F_3O$ $[M + Na]^+$ 265.0811. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 7.9 min (major) and t_{R2} = 8.6 min (minor), ee = 96%. $[\alpha]_D^{25}$ = −19.09 (*c* 0.68, $CHCl_3$).

(R,E)-2-(2-Methylbenzylidene)cyclopentan-1-ol (**2h**).[15] White solid (54.8 mg, 97%). Mp: 72−73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 7.6 Hz, 1H), 7.20−7.09 (m, 3H), 6.67 (s, 1H), 4.64−4.58 (m, 1H), 2.67−2.56 (m, 1H), 2.49−2.38 (m, 1H), 2.31 (s, 3H), 2.03−1.87 (m, 2H), 1.71−1.64 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 136.5, 136.1,129.9, 127.9, 126.7, 125.5, 121.5, 76.7, 34.9, 28.7, 22.3, 19.9. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 9.5 min (major) and t_{R2} = 11.7 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −14.26 (*c* 0.41, $CHCl_3$).

(R,E)-2-(2-Methoxybenzylidene)cyclopentan-1-ol (**2i**).[15] Colorless oil (60.1 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.87−6.85 (m, 2H), 4.65−4.58 (m, 1H), 3.83 (s, 3H), 2.72−2.64 (m, 1H), 2.54−2.45 (m, 1H), 1.99−1.89 (m, 2H), 1.76−1.60 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 147.9, 128.7, 127.9, 126.5, 120.1, 117.8, 110.3, 77.1, 55.3, 34.7, 29.1, 22.5. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 80/20, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 9.2 min (major) and t_{R2} = 17.5 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −56.45 (*c* 0.63, $CHCl_3$).

(R,E)-2-(3-Fluorobenzylidene)cyclopentan-1-ol (**2j**). Colorless oil (55.9 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.08 (dt, *J* = 8.5, 2.0 Hz, 1H), 6.93 (dt, *J* = 8.5, 2.0 Hz, 1H), 6.56 (q, *J* = 1.5 Hz, 1H), 4.60 (t, *J* = 5.5 Hz, 1H), 2.76−2.69 (m, 1H), 2.62−2.55 (m, 1H), 2.03−1.95 (m, 2H), 1.79−1.71 (m, 1H), 1.70−1.62 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7, 161.8, 149.0, 140.0 (d, *J* = 7.6 Hz), 129.6 (d, *J* = 8.3 Hz), 124.2 (d, *J* = 2.6 Hz), 122.5 (d, *J* = 2.5 Hz), 114.7 (d, *J* = 21.5 Hz), 113.3 (d, *J* = 21.2 Hz), 34.7, 29.3, 22.3. ^{19}F NMR (470 MHz, $CDCl_3$): δ −113.4. IR (KBr) cm^{-1}: 2961, 1716, 1589, 1488, 1253, 787, 686. HR-MS (ESI): *m*/*z* 175.0928, calcd for $C_{12}H_{13}FO$ $[M - OH]^+$ 175.0918. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 0.5 mL/min): t_{R1} = 20.1 min (major) and t_{R2} = 22.1 min (minor), ee = 97%. $[\alpha]_D^{25}$ = −18.67 (*c* 0.39, $CHCl_3$).

(R,E)-2-(3-Chlorobenzylidene)cyclopentan-1-ol (**2k**).[7b] Colorless oil (62.0 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (s, 1H), 7.26−7.16 (m, 3H), 6.52−6.46 (m, 1H), 4.60−4.53 (m, 1H), 2.75−2.66 (m, 1H), 2.58−2.52 (m, 1H), 2.02−1.92 (m, 2H), 1.77−1.59 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 139.5, 134.1, 129.5, 128.1, 126.5, 126.5, 122.2, 77.1, 34.8, 29.3, 22.3. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 80/20, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 6.4 min (major) and t_{R2} = 6.9 min (minor), ee = 99%. $[\alpha]_D^{25}$ = −2.88 (*c* 0.50, $CHCl_3$).

(R,E)-2-(3-Bromobenzylidene)cyclopentan-1-ol (**2l**). Colorless oil (74.4 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.46 (m, 1H), 7.32 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.26−7.24 (m, 1H), 7.20−7.17 (m, 1H), 6. 49 (q, *J* = 1.6 Hz, 1H), 4.57 (t, *J* = 5.6 Hz, 1H), 2.74−2.65 (m, 1H), 2.61−2.51 (m, 1H), 2.04−1.91 (m, 2H), 1.77−1.70 (m, 2H), 1.67−1.57 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 139.8, 131.0, 129.7, 129.4, 126.9, 122.4, 122.1, 77.1, 34.8, 29.3, 22.3. IR (KBr) cm^{-1}: 3400, 2961, 1716, 1473, 1419, 783, 684. HR-MS (ESI): *m*/*z* 235.0116, calcd for $C_{12}H_{13}BrO$ $[M - OH]^+$ 235.0117. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 1.0 mL/min): t_{R1} = 12.2 min (major) and t_{R2} = 14.0 min (minor), ee = 97%. $[\alpha]_D^{25}$ = −3.91 (*c* 0.53, $CHCl_3$).

(R,E)-2-(3-(Trifluoromethyl)benzylidene)cyclopentan-1-ol (**2m**). Colorless oil (71.2 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58−7.53 (m, 1H), 7.49−7.40 (m, 3H), 6.62−6.55 (m, 1H), 4.64−4.55 (m, 1H), 2.79−2.68 (m, 1H), 2.60−2.55 (m, 1H), 2.00−1.97 (m, 2H), 1.87 (br s, 1H), 1.77−1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.7, 138.4, 131.4, 128.7, 124.8 (q, *J* = 3.7 Hz), 123.0 (q, *J* = 3.6 Hz), 122.8, 122.2, 77.1, 34.7, 29.2, 22.2. IR (KBr) cm^{-1}: 2962, 1716, 1330, 804, 696. HR-MS (ESI): *m*/*z* 265.0085, calcd for $C_{13}H_{13}F_3O$ $[M - OH]^+$ 265.0086. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/1, UV 230 nm, flow rate 0.5 mL/min): t_{R1} = 35.2 min (major) and t_{R2} = 37.3 min (minor), ee = 97%. $[\alpha]_D^{25}$ = −3.58 (*c* 0.47, $CHCl_3$).

(R,E)-2-(3-Methylbenzylidene)cyclopentan-1-ol (**2n**). Colorless oil (54.8 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.22 (m, 1H), 7.18−7.17 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.58−6.52 (m, 1H), 4.62−4.53 (m, 1H), 2.75−2.69 (m, 1H), 2.60−2.51 (m, 1H), 2.36 (s, 3H), 2.02−1.91 (m, 3H), 1.78−1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 137.7, 137,7 129.2, 128.2, 127.3, 125.4, 123.6, 77.3, 34.8, 29.3, 22.5, 21.5. IR (KBr) cm^{-1}: 2952, 1744, 1628, 910, 786, 695. HR-MS (ESI): *m*/*z* 171.1176, calcd for $C_{13}H_{16}O$ $[M - OH]^+$ 171.1168. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 12.8 min (major) and t_{R2} = 15.1 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −50.98 (*c* 0.64, $CHCl_3$).

(R,E)-2-(3-Methoxybenzylidene)cyclopentan-1-ol (**2o**).[15] Colorless oil (60.6 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.90 (s, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.54 (s, 1H), 4.61−4.55 (m, 1H), 3.80 (s, 3H), 2.77−2.69 (m, 1H), 2.60−2.54 (m, 1H), 2.01−1.90 (m, 2H), 1.77−1.59 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 148.1, 139.1, 129.2, 123.5, 121.0, 113.8, 112.1, 77.3, 55.1, 34.8, 29.4, 22.4. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90:/10, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 19.4 min (minor) and t_{R2} = 25.4 min (major), ee = 99%. $[\alpha]_D^{25}$ = −45.23 (*c* 0.59, $CHCl_3$).

(R,E)-2-(4-Fluorobenzylidene)cyclopentan-1-ol (**2p**).[15] Yellow solid (55.4 mg, 96%). Mp: 56−57 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32−7.28 (m, 2H), 7.04−6.99 (m, 2H), 6.53 (q, *J* = 1.5 Hz, 1H), 4.57 (t, *J* = 5.5 Hz, 1H), 2.69−2.49 (m, 3H), 2.00−1.91 (m, 2H), 1.76−1.61 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.3 (d, *J* = 244.8 Hz), 147.1 (d, *J* = 2.125 Hz), 133.9 (d, *J* = 3.25 Hz), 129.8 (d, *J* = 7.875 Hz), 122.4, 115.1 (d, *J* = 21.25 Hz), 77.1, 34.7, 29.2, 22.4. ^{19}F NMR (470 MHz, $CDCl_3$): δ −115.3. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 254 nm, flow rate 1.0 mL/min): t_{R1} = 8.7 min (minor) and t_{R2} = 9.9 min (major), ee = 94%. $[\alpha]_D^{25}$ = −2.82 (*c* 0.28, $CHCl_3$).

(R,E)-2-(4-Chlorobenzylidene)cyclopentan-1-ol (**2q**).[7b] White solid (62.0 mg, 99%). Mp: 84−85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.30 (m, 4H), 6.54 (q, *J* = 1.6 Hz, 1H), 4.60 (t, *J* =

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5.2 Hz, 1H), 2.75−2.67 (m, 1H), 2.60−2.52 (m, 1H), 2.06−1.94 (m, 2H), 1.81−1.74 (m, 1H), 1.68−1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 136.2, 132.1, 129.5, 128.4, 122.4, 77.2, 34.8, 29.3, 22.4. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 7.8 min (minor) and t_{R2} = 8.6 min (major), ee = 99%. $[\alpha]_D^{25}$ = −88.89 (*c* 0.58, $CHCl_3$).

(R,E)-2-(4-Bromobenzylidene)cyclopentan-1-ol (**2r**).[7a] White solid (74.4 mg, 98%). Mp: 84−85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.47 (s, 1H), 4.58−4.51 (m, 1H), 2.70−2.62 (m, 1H), 2.52−2.43 (m, 1H), 2.02 (s, 1H), 1.97−1.88 (m, 2H), 1.75−1.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5, 136.6, 131.3, 129.8, 122.4, 120.2, 77.1, 34.7, 29.3, 22.3. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 11.8 min (major) and t_{R2} = 13.4 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −152.81 (*c* 1.038, $CHCl_3$).

(R,E)-2-(4-(Trifluoromethyl)benzylidene)cyclopentan-1-ol (**2s**).[15] Colorless oil (71.2 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 6.62 (q, *J* = 1.5 Hz, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 2.77−2.70 (m, 1H), 2.65−2.57 (m, 1H), 2.09−1.96 (m, 2H), 1.79−1.71 (m, 1H), 1.69−1.62 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.4, 141.2 (q, *J* = 1.25 Hz), 128.4, 128.1, 125.2 (q, *J* = 3.75 Hz), 124.2 (q, *J* = 270.0 Hz), 122.3, 77.1, 34.8, 29.4, 22.2. ^{19}F NMR (470 MHz, $CDCl_3$): δ −62.4. HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH 90/10, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 7.9 min (minor) and t_{R2} = 9.9 min (major), ee = 98%. $[\alpha]_D^{25}$ = −1.99 (*c* 0.32, $CHCl_3$).

(R,E)-2-(4-Methylbenzylidene)cyclopentan-1-ol (**2t**).[7b] Colorless oil (55.9 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 6.8 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.54 (s, 1H), 4.60−4.55 (m, 1H), 2.74−2.68 (m, 1H), 2.58−2.51 (m, 1H), 2.34 (s, 3H), 2.00−1.89 (m, 2H), 1.78−1.69 (m, 1H), 1.66−1.62 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 136.3, 134.9, 129.0, 128.3, 123.5, 77.3, 34.8, 29.3, 22.6, 21.1. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 8.4 min (minor) and t_{R2} = 10.2 min (major), ee = 99%. $[\alpha]_D^{25}$ = −17.58 (*c* 0.70, $CHCl_3$).

(R,E)-2-(4-Methoxybenzylidene)cyclopentan-1-ol (**2u**).[7a] White solid (60.6 mg, 99%). Mp: 80−81 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 6.54 (q, *J* = 1.5 Hz, 1H), 4.59 (t, *J* = 5.5 Hz, 1H), 3.82 (s, 3H), 2.74−2.67 (m, 1H), 2.58−2.52 (m, 1H), 2.03−1.90 (m, 3H), 1.79−1.72 (m, 1H), 1.69−1.63 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.2, 145.4, 130.6, 129.6, 123.1, 113.7, 77.4, 55.2, 34.8, 29.2, 22.6. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/5, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 16.2 min (major) and t_{R2} = 18.0 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −7.14 (*c* 0.59, $CHCl_3$).

(R,E)-2-(4-(Trifluoromethoxy)benzylidene)cyclopentan-1-ol (**2v**). Colorless oil (75.1 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.58 (q, *J* = 2.0 Hz, 1H), 4.61 (t, *J* = 5.5 Hz, 1H), 2.76−2.69 (m, 1H), 2.62−2.55 (m, 1H), 2.04−1.96 (m, 2H), 1.81−1.72 (m, 1H), 1.69−1.65 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.6, 147.5 (q, *J* = 1.8 Hz), 136.4, 129.5, 122.1, 120.7, 120.4 (q, *J* = 255.6 Hz), 77.2, 34.8, 29.2, 22.3. ^{19}F NMR (470 MHz, $CDCl_3$): δ −57.8. IR (KBr) cm^{-1}: 2891, 2637, 1507, 1362, 1261, 825. HR-MS (ESI): *m*/*z* 241.0839, calcd for $C_{13}H_{13}F_3O_2$ $[M - OH]^+$ 241.0835. HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH 90/10, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 7.3 min (minor) and t_{R2} = 11.3 min (major), ee = 97%. $[\alpha]_D^{25}$ = −35.92 (*c* 0.35, $CHCl_3$).

(R,E)-2-(Naphthalen-1-ylmethylene)cyclopentan-1-ol (**2w**).[15] White solid (65.3 mg, 97%). Mp: 92−93 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16−8.13 (m, 1H), 7.92−7.89 (m, 1H), 7.82−7.79 (m, 1H), 7.56−7.53 (m, 2H), 7.51 (s, 1H), 7.50 (d, *J* = 1.5 Hz, 1H), 7.24 (q, *J* = 2.0 Hz, 1H), 4.77 (t, *J* = 6.0 Hz, 1H), 2.68−2.62 (m, 1H), 2.51−2.44 (m, 1H), 2.29 (br s, 1H), 2.12−2.05 (m, 1H), 1.97−1.90 (m, 1H), 1.80−1.66 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.8, 134.7, 133.6, 131.7, 128.5, 127.2, 125.8, 125.8, 125.7, 125.3, 124.4, 120.6, 76.5, 35.1, 28.8, 22.2. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 98/2, UV 254 nm, flow rate 0.5 mL/min): t_{R1} = 111.3 min (minor) and t_{R2} = 117.9 min (major), ee = 96%. $[\alpha]_D^{25}$ = −29.54 (*c* 0.83, $CHCl_3$).

(R,E)-2-(Naphthalen-2-ylmethylene)cyclopentan-1-ol (**2x**).[7b] White solid (65.9 mg, 98%). Mp: 95−96 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84−7.81 (m, 4H), 7.54 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.51−7.46 (m, 2H), 6.76 (q, *J* = 1.5 Hz, 1H), 4.67 (t, *J* = 5.5 Hz, 1H), 2.90−2.83 (m, 1H), 2.75−2.68 (m, 1H), 2.08−1.98 (m, 2H), 1.83−1.68 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 135.3, 133.4, 132.1, 128.0, 127.8, 127.5, 127.2, 126.7, 126.1, 125.7, 123.7, 77.4, 34.9, 29.5, 22.6. HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, UV 230 nm, flow rate 0.8 mL/min): t_{R1} = 11.6 min (minor) and t_{R2} = 12.5 min (major), ee = 98%. $[\alpha]_D^{25}$ = −63.34 (*c* 0.70, $CHCl_3$).

(R,E)-2-(Furan-2-ylmethylene)cyclopentan-1-ol (**2y**). Colorless oil (48.8 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (s, 1H), 6.42 (d, *J* = 18.0 Hz, 2H), 6.23 (d, *J* = 2.8 Hz, 1H), 4.60−4.52 (m, 1H), 2.74−2.62 (m, 1H), 2.59−2.47 (m, 1H), 1.97−1.90 (m, 2H), 1.75−1.59 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 146.2, 141.4, 112.2, 111.3, 108.1, 76.6, 35.4, 29.6, 22.1. IR (KBr) cm^{-1}: 3439, 2958, 1715, 1600, 1362, 1261, 1019. HR-MS (ESI): *m*/*z* 147.0811, calcd for $C_{10}H_{12}O_2$ $[M - OH]^+$ 147.0804. HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH 75/25, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 5.8 min (minor) and t_{R2} = 6.6 min (major), ee = 98%. $[\alpha]_D^{25}$ = −55.28 (*c* 0.52, $CHCl_3$).

(R,E)-2-(Thiophen-2-ylmethylene)cyclopentan-1-ol (**2z**).[15] Colorless oil (53.5 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, *J* = 4.8 Hz, 1H), 7.03−6.95 (m, 2H), 6.80 (s, 1H), 4.63−4.54 (m, 1H), 2.69−2.62 (m, 1H), 2.53−2.47 (m, 1H), 2.05−1.92 (m, 2H), 1.81−1.61 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.8, 141.8, 127.0, 126.3, 125.1, 117.0, 76.8, 35.5, 29.7, 22.3. HPLC (Chiralcel AS-H, *n*-hexane/*i*-PrOH 75/25, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 5.9 min (minor) and t_{R2} = 7.1 min (major), ee = 99.3%. $[\alpha]_D^{25}$ = −24.61 (*c* 0.25, $CHCl_3$).

(R,E)-2-(Cyclohexylmethylene)cyclopentan-1-ol (**2aa**).[15] Colorless oil (53.5 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35 (d, *J* = 8.8 Hz, 1H), 4.38−4.29 (m, 1H), 2.38−2.33 (m, 1H), 2.23−2.13 (m, 1H), 2.06−1.98 (m, 1H), 1.85−1.75 (m, 2H), 1.69−1.59 (m, 7H), 1.45 (br s, 1H), 1.29−1.12 (m, 3H), 1.08−0.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 130.1, 75.6, 38.4, 35.4, 32.7, 32.6, 26.7, 26.0, 25.9, 22.0. HPLC (Chiralcel OJ-H, *n*-hexane/*i*-PrOH 98/2, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 5.8 min (major) and t_{R2} = 6.7 min (minor), ee = 99.98%. $[\alpha]_D^{25}$ = −288.68 (*c* 1.21, $CHCl_3$).

(R,E)-2-Pentylidenecyclopentan-1-ol (**2ab**).[16] Colorless oil (45.8 mg, 99%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.52−5.48 (m, 1H), 4.35−4.33 (m, 1H), 2.34−2.33 (m, 1H), 2.16−2.15 (m, 1H), 2.00−1.96 (m, 2H), 1.83−1.77 (m, 2H), 1.63−1.58 (m, 2H), 1.36−1.27 (m, 4H), 0.90−0.86 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.3, 124.2, 75.2, 35.4, 31.4, 28.9, 26.8, 22.3, 21.8, 13.8. The enantiomeric excess was determined by GC analysis using a chiral capillary column (β-dex-120, 30 m × 250 μm × 0.25 μm), initially 90 °C, 1 °C/min: t_{R1} = 42.5 min (major), ee >99.5%. $[\alpha]_D^{25}$ = −40.91 (*c* 1.01, $CHCl_3$).

(R,E)-2-(3-Methylbutylidene)cyclopentan-1-ol (**2ac**). Colorless oil (45.8 mg, 99%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.55−5.54 (m, 1H), 4.37−4.34 (m, 1H), 2.33−2.32 (m, 1H), 2.16−2.14 (m, 1H), 1.88−1.80 (m, 4H), 1.66−1.60 (m, 3H), 0.90−0.88 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 146.2, 122.9, 75.4, 38.5, 35.5, 28.5, 27.0, 22.3, 22.3, 21.9. IR (KBr) cm^{-1}: 3362, 2955, 2869, 1601, 1464, 1383, 1365, 1090, 1023, 976. HR-MS (ESI): *m*/*z* 137.1326, calcd for $C_{10}H_{18}O$ $[M - OH]^+$. 137.1336. The enantiomeric excess was determined by GC analysis using a chiral capillary column (β-dex-120, 30 m × 250 μm × 0.25 μm), initially 90 °C, 1 °C/min: t_{R1} = 37.5 min (major) and t_{R2} = 40.6 min (minor), ee = 98%. $[\alpha]_D^{25}$ = −22.54 (*c* 0.99, $CHCl_3$).

(R,E)-2-(2-Methylpropylidene)cyclopentan-1-ol (**2ad**).[14] Colorless oil (40.0 mg, 95%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.28−5.26 (m, 1H), 4.26−4.25 (m, 1H), 2.31−2.26 (m, 2H), 2.12−2.09 (m, 1H), 1.76−1.70 (m, 2H), 1.54−1.51 (m, 2H), 0.88 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 143.0, 131.2, 75.2, 35.3, 28.6, 26.5, 22.6, 22.5, 21.9. The enantiomeric excess was determined by GC analysis using a chiral capillary column (β-dex-120, 30 m × 250 μm × 0.25 μm), initially 90 °C, 1 °C/min: t_{R1} = 22.1 min (major) and t_{R2} = 24.4 min (minor), ee = 85%. $[\alpha]_D^{25}$ = −15.57 (*c* 0.34, $CHCl_3$).

(R)-2-(Diphenylmethylene)cyclopentan-1-ol (**2ae**). Colorless oil (57.1 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42−7.40 (m, 4H),

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7.38−7.36 (m, 2H), 7.34−7.32 (m, 1H), 7.31−7.27 (m, 3H), 4.82 (t, J = 4.8 Hz, 1H), 2.75−2.69 (m, 1H), 2.49−2.44 (m, 1H), 2.04−1.95 (m, 2H), 1.87−1.82 (m, 2H), 1.73−1.66 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.7, 142.5, 141.8, 137.4, 129.1, 128.9, 128.5, 128.1, 127.0, 126.7, 73.3, 35.3, 31.3, 23.0. IR (KBr) cm^{-1}: 3420, 2957, 1646, 1596, 1489, 1442, 765, 700. HR-MS (ESI): m/z 233.1328, calcd for $C_{18}H_{18}O$ [M − OH]$^+$ 233.1336. HPLC (Chiralcel OJ-H, n-hexane/i-PrOH 95/5, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 11.1 min (major) and t_{R2} = 12.7 min (minor), ee = 69%. $[\alpha]_D^{25}$ = −31.72 (c 1.19, $CHCl_3$).

(R,E)-2-Benzylidenecyclohexan-1-ol (2af).[7b] White solid (54.8 mg, 97%). Mp: 51−52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.30 (m, 2H), 7.22−7.19 (m, 3H), 6.54−6.50 (m, 1H), 4.25−4.22 (m, 1H), 2.75−2.69 (m, 1H), 2.15−2.08 (m, 1H), 2.03−1.97 (m, 1H), 1.90−1.82 (m, 1H), 1.69−1.43 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 137.6, 128.9, 128.0, 126.2, 120.7, 109.9, 73.7, 36.5, 27.3, 26.9, 23.1. HPLC (Chiralcel OD-H, n-hexane/i-PrOH 90/10, UV 254 nm, flow rate 0.8 mL/min): t_{R1} = 8.0 min (major) and t_{R2} = 9.7 min (minor), ee = 96%. $[\alpha]_D^{25}$ = +37.89 (c 0.56, $CHCl_3$).

(R,E)-2-Benzylidenecycloheptan-1-ol (2ag).[7a] Colorless oil (58.8 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35−7.20 (m, 5H), 6.57 (s, 1H), 4.40−4.36 (m, 1H), 2.49−2.40 (m, 2H), 2.14−2.08 (m, 1H), 1.87−1.80 (m, 1H), 1.76−1.67 (m, 4H), 1.64−1.46 (m, 2H), 1.43−1.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.3, 137.4, 128.5, 128.1, 126.7, 126.3, 76.9, 36.5, 29.0, 28.0, 26.5, 23.8. HPLC (Chiralcel OD-H, n-hexane/i-PrOH 90/10, UV 210 nm, flow rate 0.8 mL/min): t_{R1} = 7.6 min (major) and t_{R2} = 9.2 min (minor), ee = 97%. $[\alpha]_D^{25}$ = −117.55 (c 0.47, $CHCl_3$).

Transformation of 2a: (1*R*,2*R*)-2-Benzylcyclopentan-1-ol (3).[17] A hydrogenation tube was charged with a stirring bar, **2a** (0.6 mmol, 104.5 mg) and Pd/C (10 mol %), followed by the addition of THF (5 mL) using a syringe. The hydrogenation tube was then put into an autoclave. The system was evacuated and filled with hydrogen 3 times. The autoclave was then charged with hydrogen to 10 bar hydrogen pressure, and the reaction mixture was stirred at room temperature for 2 h. After releasing the hydrogen and filtered carefully, the solution was concentrated in vaccuo to remove solvent, affording **3** as colorless oil (104.7 mg, 99%, 99.0% ee). *dr* (2:1) was determined by ^{1}H NMR analysis of **3**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.17 (m, 5H), 4.13−4.05 (m, 1H), 2.88−2.83 (m, 1H), 2.71−2.66 (m, 1H), 2.06−1.96 (m, 1H), 1.88−1.79 (m, 2H), 1.74−1.62 (m, 2H), 1.60−1.46 (m, 2H), 1.36 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 128.7, 128.3, 125.7, 74.3, 47.6, 35.4, 34.8, 28.7, 21.8; HPLC (Chiralcel OD-H, n-hexane/i-PrOH 99:1, UV 220 nm, flow rate 0.8 mL/min), t_{R1} = 16.7 min (major), t_{R1} = 31.1 min (minor), ee = 99.0%; $[\alpha]_D^{25}$ = −326.89 (c 2.26, $CHCl_3$).

(2*S*,3*S*,4*R*)-2-Phenyl-1-oxaspiro[2.4]heptan-4-ol (4).[18,19] *m*-CPBA (6.0 mmol) was added to a stirred solution of **2a** (418.1 mg, 2.4 mmol) in DCM (10 mL) at 0 °C, and the reaction was quenched with saturated aqueous $Na_2S_2O_3$ at 0 °C over 1 h. The resulting mixture was extracted with DCM (10 mL × 3). The combined organic phase was washed with saturated aqueous $NaHCO_3$ and brine and dried with anhydrous Na_2SO_4. Then the solvent was evaporated to provide the crude product, which was then purified by column chromatography (SiO_2, PE/EA 20/1) to afford pure **4** as a white solid (377.1 mg, 83%, 99.4% ee). Mp: 62−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.25 (m, 5H), 4.07 (s, 1H), 4.05 (q, J = 6.8 Hz, 1H), 2.49−2.33 (m, 1H), 2.06−2.01 (m, 1H), 1.92−1.84 (m, 1H), 1.83−1.66 (m, 2H), 1.64−1.57 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.8, 128.2, 127.8, 126.1, 72.3, 72.3, 61.7, 33.9, 25.6, 19.4. HPLC (Chiralcel OD-H, n-hexane/i-PrOH 90/10, UV 220 nm, flow rate 0.8 mL/min): t_{R1} = 8.6 min (major), t_{R1} = 10.0 min (minor), ee = 99.4%. $[\alpha]_D^{25}$ = −60.96 (c 0.49, $CHCl_3$).

(1*R*,2*R*)-1-Benzylcyclopentane-1,2-diol (5).[20] A hydrogenation tube was charged with a stirring bar, **4** (0.9 mmol, 190.2 mg), and Pd/C (10 mol %), followed by the addition of THF/MeOH (10 mL/5 mL) using a syringe. The hydrogenation tube was then put into an autoclave. The system was evacuated and filled with hydrogen three times. The autoclave was then charged with hydrogen to 10 bar hydrogen pressure, and the reaction mixture was stirred at room temperature for 3 h. After the hydrogen was released and the mixture filtered carefully, the solution was concentrated in vaccuo to remove solvent, affording **5** as a white solid (179.1 mg, 99%, >99.5% ee). Mp: 72−73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.29 (m, 2H), 7.26−7.23 (m, 3H), 3.86 (q, J = 6.8 Hz, 1H), 2.85−2.78 (m, 2H), 2.22 (s, 1H), 2.03−1.95 (m, 1H), 1.89 (d, J = 5.2 Hz, 1H), 1.87−1.74 (m, 1H), 1.71−1.61 (m, 3H), 1.54−1.44 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.5, 130.0, 128.4, 126.6, 79.8, 77.0, 44.6, 35.6, 31.4, 18.9. HPLC (Chiralcel OD-H, n-hexane/i-PrOH 95/5, UV 220 nm, flow rate 0.8 mL/min): t_{R1} = 14.9 min (major), ee >99.5%. $[\alpha]_D^{25}$ = −4.29 (c 0.41, $CHCl_3$).

(*R*,*E*)-2-Benzylidenecyclopentyl Acetate (6).[13] Et_3N (2.2 mmol) and 4-dimethylaminopyridine (DMAP, cat.) was added to a stirred solution of **2a** (350.0 mg, 2.0 mmol) in DCM (10 mL), followed by the addition of acetic anhydride (2.4 mmol) at 0 °C. The reaction mixture was stirred until the disappearance of **2a**. The reaction mixture was diluted with water, and the aqueous phase was extracted with DCM (10 mL × 3). The combined organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL × 3) and brine (10 mL × 3) and dried with anhydrous Na_2SO_4. Then the solvent was evaporated to provide a crude product, which was then purified by column chromatography (SiO_2, PE/EA 20/1) to afford pure **6** as a colorless oil (393.4 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.32 (m, 4H), 7.24−7.20 (m, 1H), 6.63 (q, J = 1.2 Hz, 1H), 5.68−5.66 (m, 1H), 2.78−2.70 (m, 1H), 2.61−2.53 (m, 1H), 2.09 (s, 3H), 2.03−1.90 (m, 2H), 1.84−1.72 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 142.8, 137.4, 128.6, 128.2, 126.8, 126.4, 79.1, 32.2, 29.6, 23.4, 21.4.

(*S*,*E*)-((2-Methylcyclopentylidene)methyl)benzene (7).[13] In a 50 mL two-neck round-bottom flask was placed MeMgBr (2.5 equiv), and CuCl (20 mol %) was added quickly when the reaction mixture was cooled to 0 °C. Fifteen minutes later, compound **6** (1.0 mmol, 1.0 equiv) in dry THF was added dropwise. The reaction mixture was quenched by 2 M HCl after 6 h and extracted with DCM (10 mL × 3). The combined organic layer was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography (SiO_2, 100% hexane) to give the corresponding product **7** (144.6 mg, 84%, 99.5% ee) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.33 (m, 4H), 7.21−7.17 (m, 1H), 6.28 (q, J = 2.0 Hz, 1H), 2.73−2.58 (m, 3H), 1.99−1.91 (m, 1H), 1.90−1.84 (m, 1H), 1.73−1.62 (m, 1H), 1.33−1.22 (m, 1H), 1.23 (q, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 138.9, 128.1, 128.0, 125.6, 120.1, 40.9, 34.6, 31.5, 24.7, 19.4. The enantiomeric excess (99.5% ee) was determined by GC analysis using a chiral capillary column (β-dex-225, 30 m × 250 μm × 0.25 μm), initially 90 °C, 1 °C/min: t_{R1} = 55.4 min (minor) and t_{R2} = 56.1 min (major), ee = 99.5%. $[\alpha]_D^{25}$ = −10.07 (c 1.01, $CHCl_3$).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.9b00366.

Synthesis of hydrogenated substrates and NMR spectra and HPLC data of both hydrogenated substrates and products (PDF)

Accession Codes

CCDC 1918858 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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