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Ru-Catalyzed Chemo- and Enantioselective Hydrogenation of 2,4-Pentadien-1-ones: Synthesis of Chiral 2,4-Pentadien-1-ols

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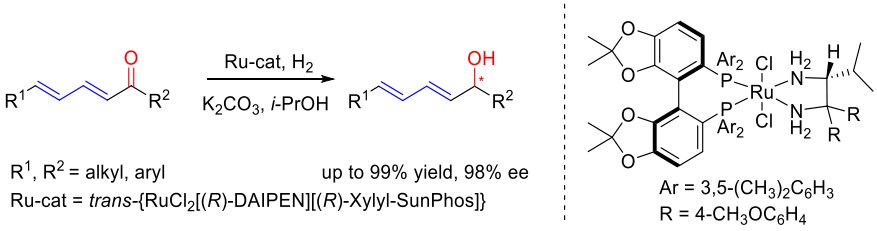
ABSTRACT



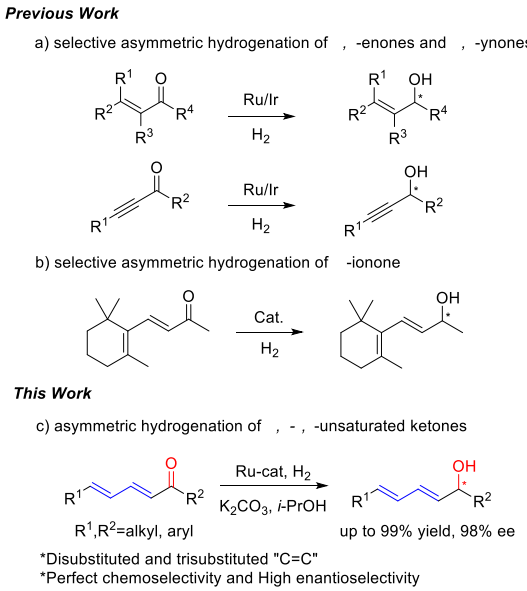
The asymmetric hydrogenation of 2,4-pentadien-1-ones has been achieved by using *trans*-$RuCl_2$[(*R*)-XylylSunPhos][(*R*)-Daipen] as catalyst under basic conditions. This hydrogenation demonstrated exclusive C1-carbonyl selectivity and thus the conjugated 2,4-diene motifs remained untouched, which provides a synthetically useful method for various chiral 2,4-pentadien-1-ols.

INTRODUCTION

Over the past few decades, homogeneous catalytic asymmetric hydrogenation of porchiral ketones has become a mature and powerful method for the synthesis of secondary chiral alcohols.[1] In this field, selective hydrogenation of carbonyl groups in unsaturated ketones has been considered difficult for a long time (Scheme 1a). The two hydrogenation systems, Ir-DIOP[2] and [Ir(BINAP)(COD)]BF_4-aminophosphine[3] gave good chemoselectivities but with only moderate enantioselectivities. Since the 1990s, Noyori and co-workers has made a great progress by introducing novel and efficient Ru-diphosphane-diamine bifunctional catalysts.[1b,4] This significant discovery characterized excellent compatibility of various functional groups and the reversion of the classical chemoseletivitity in the hydrogenation of C=C and C≡C over C=O groups. Subsequently, Ru-diphosphane-diamine catalyzed hydrogenation represents one of the most reliable approach to various types of valuable chiral allylic alcohols.[5] Besides, several other catalytic hydrogenation systems,[6] kinetic resolution,[7] enantioselective aldehydevinylation,[8] asymmetric transfer hydrogenation,[9] and other asymmetric reduction of unsaturated

ketones[10] have been developed for this purpose with high chemoselectivities and moderate to excellent enantioselectivities.

Scheme 1. The Asymmetric Hydrogenation of Conjugated Ketones



However, the asymmetric hydrogenation of α,β-γ,δ-unsaturated ketones, which possessed multiple unsaturated bonds conjugated carbonyl, is rarely explored. To the best of our knowledge, only the hydrogenation of β-ionone which contains a low activity tetrasubstituted double bond, has been reported (Scheme 1b).[3,4b,4d,6e] Furthermore, the polyene-conjugated chiral allyl alcohols are important units of a number of natural compounds and biologically active molecules (Figure 1). On the other hand, these motifs with conjugated polyenes could be further exploited through subsequent diverse transformations, for example, they could serve as both dienes and dienophiles in Diels-Alder rection.[11] Up to now, only a few methods are available for the synthersis of chiral secondary polyenols, such as asymmetric reduction,[10a,10d,10f] asymmetric addition,[12] reductive coupling[13] and (dynamic) kinetic resolution.[14] Nevertheless, these synthetic methods suffered from limited scope of substrates, low efficiency and/or poor enantioselectivity. Accordingly, the search for effective and highly selective approaches to synthesize enantiomerically pure polyenols is still a significant and challenging work.

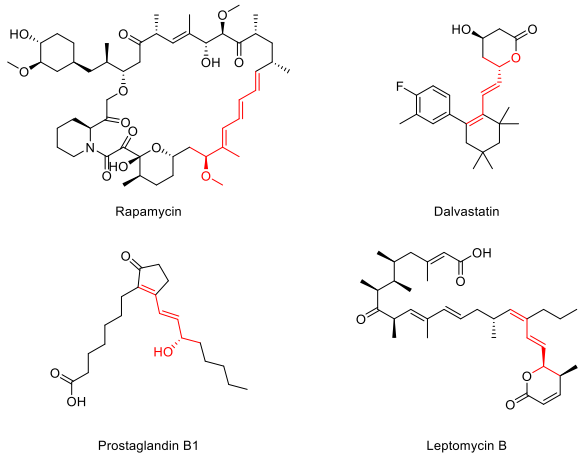


Figure 1. Selected Chiral 2,4-Pentadiene-1-ol Units in Drugs and Natural Products

Our group has been devoted to the Ru-catalyzed asymmetric hydrogenation of functionalized and

simple ketones using SunPhos and its derivatives as chiral ligands.[1j,15] As our continued interest, we reported herein an efficient and selective synthetic approach for polyene-conjugated chiral allyl alcohol through Ru-SunPhos-catalyzed asymmetric hydrogenation of *α,β-γ,δ*-unsaturated ketones.

RESULTS AND DISCUSSION

Inspired by the fact that in 1998 Noyori et al. adopted the weak base K_2CO_3, instead of conventional ^{t}BuOK, in the hydrogenation of some highly base sensitive unsaturated ketones with improvement of ee values,[4d] we chose the easily available (3*E*,5*E*)-6-phenylhexa-3,5-dien-2-one (**1a**) as the model substrate, and initially carried out the reaction in *i*-PrOH containing *trans*-$RuCl_2$[(*S*)-SunPhos][(*S*)-Daipen] and K_2CO_3 under 10 bar of H_2 at 30 °C for 15 h. To our surprises, the corresponding chiral alcohol **2a** was obtained with nearly quantitative yield and 91.3% ee (Table 1, entry 1). Next, various chiral diphosphines (shown in Figure 2) were also tested to explore the effect of the ligand structure on the reactivity and enantioselectivity for the asymmetric hydrogenation of *α,β-γ,δ*-unsaturated ketones. The results are showed in Table 1. Tol-SunPhos or DMM-SunPhos with matching configuration diamine-DAIPEN also gave good enantioselectivities but slightly lower than that using Xylyl-SunPhos as the ligand (Table 1, entries 1-4, 91.3%-95.6% ee). The matching/mismatching effect between diphosphine and diamine was also included here. Mismatching ligands led to disappointed result (Table 1, entries 5, 77.0% ee, 35% conv.). Employing other several commercially available diphosphine ligands, such as (*S*)-BINAP, (*S*)-SEGPhos, (*S*)-C3-TunePhos and (*S*)-MeO-Biphep with matching (*S*)-DAIPEN resulted in good ee values (Table 1, entries 6-9, 83.1%-92.9% ee). Overall, the diphosphine Xylyl-SunPhos was the ligand of choice in terms of enantioselectivity.

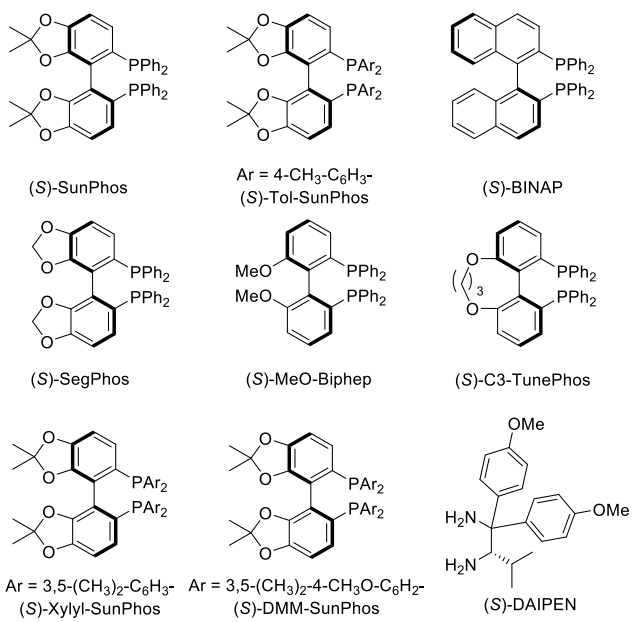
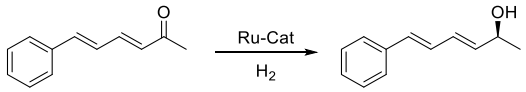


Figure 2. Structures of bidentate ligands.

Table 1. Effects of Ligands in Asymmetric Hydrogenation [a]



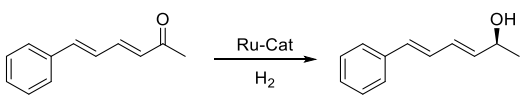
1a **2a**

entry	cat	ee (%)[b]
1	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-SunPhos]}	-91.3
2	*trans*-{$RuCl_2$[(*R*)-DAIPEN][(*R*)-Tol-SunPhos]}	94.7
3	*trans*-{$RuCl_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]}	95.6
4[c]	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*R*)-Xylyl-SunPhos]}	77.0
5	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-DMM-SunPhos]}	-95.2
6	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-BINAP]}	-83.1
7	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-MeO-Biphep]}	-90.0
8	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-SegPhos]}	-89.6
9	*trans*-{$RuCl_2$[(*S*)-DAIPEN][(*S*)-C3-TunePhos]}	-92.9

[a]Unless otherwise stated, all reactions were carried out with a substrate (0.25 mmol) in 1 mL *i*-PrOH under 10 bar H_2 at 30 °C for 15 h, substrate/catalyst/K_2CO_3 = 100/1/10. All in full conversion. [b]Determined by HPLC on a Chiralpak IA-3 column. [c]35% conversion by ^1H NMR..

Next, the effects of the solvent, reaction temperature, and hydrogen pressure were explored and the results were depicted in Table 2. Both protic solvents (*i*-PrOH, MeOH, EtOH, *i*-BuOH and isoamyl alcohol, Table 2, entries 1-5) and aprotic solvents (THF, DCM and toluene, Table 2, entries 5-7) were tested, and it turned out that *i*-PrOH was the best choice for this hydrogenation. The enantioselectivity of the hydrogenation was dramatically influenced by the reaction temperature. Increased the temperature caused an obvious drop of enantiomeric excess (Table 2, entry 9, 50 °C, 87.3% ee). Unexpectedly, the hydrogen pressures exhibited little effect on the reaction (Table 2, entry 10, 30 bar, 94.2% ee). Moreover, the transfer hydrogenation process was also excluded by the result that **1a** was fully recovered in the absence of hydrogen (Table 2, entry 11).

Table 2. Optimization of Solvent, Temperature, and Pressure[a]



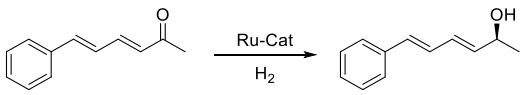
1a **2a**

entry	solvent	P (bar)	conv.(%)[b]	ee (%)[c]
1	*i*-PrOH	10	> 99	95.6
2	MeOH	10	90	92.4
3	EtOH	10	> 99	93.4
4	*i*-BuOH	10	> 99	92.3
5	Isoamyl alcohol	10	> 99	94.9
6	DCM	10	0	--
7	THF	10	0	--
8	Toluene	10	0	--
9[d]	*i*-PrOH	10	> 99	87.3
10	*i*-PrOH	30	> 99	94.2
11[e]	*i*-PrOH	0	0	--

[a]Unless otherwise stated, all reactions were carried out using *trans*-{$RuCl_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]} as the catalyst with substrate (43.0 mg, 0.25 mmol) in 1 mL solvent under 10 bar of H_2 at 30 °C for 15 h, substrate/catalyst/K_2CO_3 = 100/1/10. [b]Determined by NMR. [c]Determined by HPLC on a Chiralpak IA-3 column. [d]Reaction temperature 50 °C. [e]Without H_2.

Subsequently, we turned our attention to the effect of bases (Table 3). ^{t}BuOK, which was mostly used in Ru/diphosphine/diamine hydrogenation systems, gave very poor enantioselectivity (Table 3, entry 2, 5.2% ee). And it was investigated that the lack of enantioselectivity using ^{t}BuOK as base was not due to product racemization. When we treat the product **2a** in the presence of ^{t}BuOK in ^{i}PrOH, no racemization was observed. Other potassium bases (KOH, K_3PO_4 and KOAc) other carbonates (Cs_2CO_3, Na_2CO_3) and organic base (NEt_3) led to lower enantioselectivities and/or activities than using K_2CO_3 as the base.

Table 3. Screening of Base[a]



1a **2a**

entry	solvent	conv.(%)[b]	ee (%)[c]
1	K_2CO_3	> 99	95.6
2	^{t}BuOK	> 99	5.2
3	KOH	> 99	8.3
4	K_3PO_4	> 99	12.7

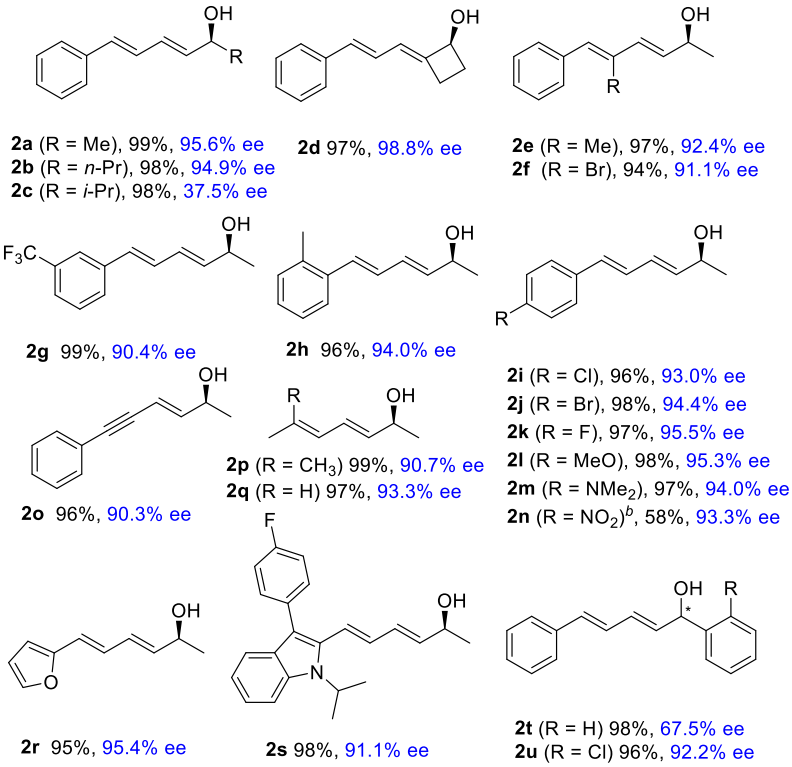
5	Cs_2CO_3	> 99	66.3
6	Na_2CO_3	48	95.3
7	Et_3N	0	--
8	KOAc	0	--

[a]Unless otherwise stated, all reactions were carried out using *trans*-{$RuCl_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]} as the catalyst with substrate (43.0 mg, 0.25 mmol) in 1 mL *i*-PrOH under 10 bar of H_2 at 30 °C for 15 h, substrate/catalyst/base = 100/1/10. [b]Determined by NMR. [c]Determined by HPLC on a Chiralpak IA-3 column.

With the optimized conditions in hand, the scope of substrates was investigated and the results were summarized in Scheme 2. A series of polyene-conjugated chiral allyl alcohols were synthesized with perfect chemical selectivities, good to excellent ee values and wide functional group tolerance. The model substrate **1a** (R = Me) was hydrogenated in 99% yield and 95.6% ee. When the substrate with a longer chain, the activity and enantioselectivity was still remained (R = *n*-Pr, **1b**; 98% yield, 94.9% ee**)**. However, when the substrate **1c** containing a bulkier isopropyl group was subjected to the reaction, the corresponding product **2c** was obtained in only 37.5% ee. Substituents on the conjugated diene motifs had little influence on the selective hydrogenation reactions wherein the desired chiral alcohols **2d-f** were isolated with good enantioselectivities and high yields. When the substrates possessing *meta*-CF_3 (**1g**) or *ortho*-Me (**1h**) were subjected to this hydrogenation, the corresponding hydrogenation products **2g** and **2h** were obtained in 90.4% and 94.0% ee, respectively. Besides, a range of *para*-substituted substrates delivered universally high enantiomeric excess, and halogen (**1i-1k**), methoxyl (**1l**) and dimethylamino group (**1m)** were tolerated. Notably, the nitro group was also bearable in the reaction, affording the product **2n** in 93.3% ee, albeit in 62% conversion. Interestingly, compound **1o** with conjugated triple and double bonds was also hydrogenated in good chemo- and enantioselectivity. Moreover, under the reaction conditions, substrate **1p** and **1q** both gave high yield and Enantioselectivity. In addition, hydrogenation of heterocyclic compound **1r** and **1s** afforded the corresponding alcohols with good ee values in full conversion.

With *tarns*-$RuCl_2$[(*R*)-XylylSunPhos][(*R*)-Daipen]-K_2CO_3 as catalyst, hydrogenation of **1t** afforded **2t** in full conversion but only 67.5% ee. The *ortho*-Cl compound **1u** was attempted delivering desired alcohol with excellent enantioselectivity (**2u**, 92.2% ee). This phenomenon is under further investigation to find whether steric hindrance or electronic effect dominate the difference.

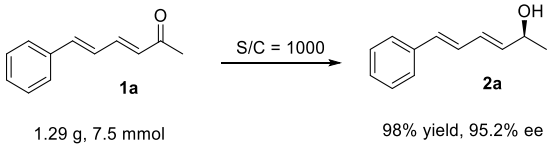
Scheme 2. Substrate Scope[a]



[a]Unless otherwise stated, all reactions were carried out using *trans*-{RuCl$_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]} as the catalyst with a substrate (0.25 mmol) in 1 mL *i*-PrOH under 10 bar of H_2 at 30 °C for 15 h, substrate/catalyst/K_2CO_3 = 100/1/10. All in full conversion. The ee values were determined by HPLC on a Chiralpak column. The absolute configurations of **2b-2s** were determined according to **2a**. [b]62% conversion by ^{1}H NMR.

Finally, to further evaluate the catalytic efficiency of this hydrogenation system, a gram scale hydrogenation of **1a** (7.5 mmol, 1.29 g) was carried out (S/C = 1000) under 30 bar of H_2 at 30 °C for 48 h, and the chiral product (*S*,3*E*,5*E*)-6-phenylhexa-3,5-dien-2-ol (**2a**) could be obtained in 98% yield and 95.2% ee (Scheme 3).

Scheme 3. Gram-Scale Asymmetric Hydrogenation of 1a



CONCLUSION

In summary, we realized a general and practical selective hydrogenation of 2,4-pentadiene-1-ones to 2,4-pentadiene-1-ols. The conjugated disubstituted C=C bonds remained untouched to afford a wide range of enantiopure 1,3-dieneols. The bifunctional catalyst *trans*-{RuCl$_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]} showed high enantioselectivity (up to 98% ee) and reactivity (S/C up to 1000) for a wide range of 2,4-pentadiene-1-ones under very mild conditions. Further applications of this protocol are currently under investigation in our group.

EXPERIMENTAL SECTION

General Procedures. Unless those noted below, commercially available reagents purchased from macklin chemical company were used throughout without further purification. EtOH and MeOH were distilled from magnesium under nitrogen. ^{i}PrOH and DCM were dried over CaH_2 under nitrogen. Toluene and THF were freshly distilled from Na-benzophenone under nitrogen. Unless otherwise noted, all reactions were performed using standard Schlenk techniques under an atmosphere of nitrogen. Oil bath was used in all experiments for reactions that require heating. Flash column chromatography was performed using 300-400 mesh silica gel. ^{1}HNMR spectra were recorded at 500 MHz with TMS as an internal standard. $^{13}C\{^1H\}$ NMR spectra were recorded at 125 MHz and referenced to the central peak of 39.52 ppm for *d*6-DMSO or 77.00 ppm for $CDCl_3$. Coupling constants (*J*) are reported in units (Hz) and refer to apparent peak multiplications. Specific rotation $[\alpha]_D$ were obtained in a 0.5 dm cell using the D-line (589 nm) of a sodium lamp. HRMS data were measured on an ESI-TOF mass spectrometer. IR data determinated from Perkin Elmer Spectrum 100 (KBr).

Typical Procedure for the Preparation of 1a, 1e, 1g-1n, 1q, 1r, 1s.

To a solution of the corresponding aldehyde (10 mmol) in acetone (10 mL) and H_2O (10 mL) was added dropwise 10 mL 5% NaOH aqueous solution slowly at room temperature; Upon completion of the reaction (monitored by TLC), the pH value was adjusted to 6-7 with 10% HCl, and the resulting solution was extracted with DCM (20 mL × 3). The combined organic phase was washed with saturated brine before dried over anhydrous Na_2SO_4, and the concentration was conducted under vacuum. The crude product was purified by flash column chromatography or recrystallized from DCM/ PE (petroleum ether).

Typical Procedure for the Preparation of 1b, 1t, 1u.

To a solution of the corresponding aldehyde (10 mmol) and ketone (11 mmol) in EtOH (10 mL) was added dropwise 10 mL 5% NaOH aqueous solution slowly at room temperature; Upon completion of the reaction (monitored by TLC), the pH value was adjusted to 6-7 with 10% HCl, and the resulting solution was extracted with DCM (20 mL × 3). The combined organic phase was washed with saturated brine before dried over anhydrous Na_2SO_4, and the concentration was conducted under vacuum. The crude product was purified by flash column chromatography or recrystallized from DCM/ PE.

(3*E*,5*E*)-6-Phenylhexa-3,5-dien-2-one (1a):[16] Recrystallized from DCM/ PE. Yellow solid: 1.41 g, 82% yield; mp: 60–61 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48–7.46 (m, 2H), 7.38–7.26 (m, 4H), 6.97 –6.85 (m, 2H), 6.26 (d, *J* = 15.5 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 198.3, 143.4, 141.2, 135.9, 130.4, 129.2, 128.8, 127.2, 126.6, 27.3.

(5*E*,7*E*)-8-Phenylocta-5,7-dien-4-one (1b):[17] Recrystallized from DCM/ PE. Pale yellow solid: 0.41 g, 21% yield; mp: 41–43 °C; ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.48–7.47 (m, 2H), 7.38–7.30 (m, 4H), 6.95 (d, *J* = 15.5 Hz, 1H), 6.88 (dd, *J* = 15.5 Hz, 10.5Hz, 1H), 6.29 (d, *J* = 15.5 Hz, 1H), 2.58 (t, *J* = 7.5 Hz, 2H), 1.73–1.65 (m, 2H), 0.97 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 200.6, 142.3, 141.1, 136.0, 129.7, 129.1, 128.8, 127.1, 126.7, 42.6, 17.8, 13.8.

(4*E*,6*E*)-2-Methyl-7-phenylhepta-4,6-dien-3-one (1c): Under nitrogen atmosphere, to a pre-cooled solution of diisopropylamine (2.42 g, 12 mmol), THF (20 mL) was added *n*-butyl lithium solution dropwisely (11 mmol, 2.4 M, 4.6 mL) at -20°C, and the resulting solution was stirred at -20°C for 0.5 h. Then 3-methyl-2-butanone(0.86 g, 10 mmol) in 5 mL THF was added dropwisely, keeping the temperature at -20°C, after the addition the mixture was stirred for another 0.5 h, then cinnamaldehyde

(1.45 g, 11 mmol) in 5 mL THF added dropwise at -20°C. After completion of addition, the reaction was stirred for 1 h, then quenched with 3 mL 10% HCl at -20°C. The mixture was extracted by ethyl acetate (30 mL × 3).and the combined organic phase was washed by brine before dried using Na_2SO_4. Combined organic phase was washed by brine before dried using Na_2SO_4.

After removing the solvents under vacuum, Ac_2O (4 mL) and NaOAc (1 g) was added and the resulting mixture was stirred over night at room temperature under nitrogen atmosphere. Then the mixture was heated to 110°C for 10 minutes before ethanol (10 mL) was added at RT, then the mixture was stirred for another 2h. Finally the mixture was filtered and the solvent was evaporated before it was subjected to column separation.

Petroleum ether/ Ethyl acetate = 50/1 as the eluent. Then recrystallized from DCM/ PE. Pale yellow solid: 1.34 g, 67% yield; mp: 59.4–61.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48–7.46 (m, 2H), 7.41–7.29 (m, 4H), 6.97–6.87 (m, 2H), 6.37 (d, J = 15.0 Hz, 1H), 2.90–2.82 (m, 1H), 1.15 (d, J = 6.5 Hz, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 204.0, 142.4, 141.1, 136.1, 129.1, 128.8, 127.8, 127.1, 126.8, 39.1, 18.50. FT-IR (KBr, cm^{-1}): 3553, 3479, 3417, 3239, 2976, 2966, 1681, 1639, 1615, 1590, 1464, 1450, 1385, 1456, 1285, 1227, 1184, 1124, 1084, 1051, 1022, 760, 707, 690, 617, 511, 475. HRMS-ESI (m/z): $(M + H)^+$ calcd. for $C_{14}H_{17}O$, 201.1279; found 201.1272.

(*E*)-2-((*E*)-3-Phenylallylidene)cyclobuta-1-one (1d):[18] Petroleum ether/ Ethyl acetate = 100/1 as the eluent. Pale yellow solid: 0.59 g, 32% yield; mp: 104.1–105.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49–7.47 (m, 2H), 7.38–7.30 (m, 3H), 6.94 (d, J = 15.0 Hz, 1H), 6.84–6.72 (m, 2H), 3.03–2.99 (m, 2H), 2.80–2.77 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 199.2, 147.6, 142.5, 136.1, 129.2, 128.8, 127.2, 126.6, 123.4, 43.7, 20.8.

(3*E*,5*E*)-5-Methyl-6-phenylhexa-3,5-dien-2-one (1e):[19] Recrystallized from DCM/ PE. Pale yellow solid: 0.71 g, 38% yield; mp: 68.6–69.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40–7.28 (m, 6H), 6.89 (s, 1H), 6.26 (d, J = 16.0 Hz, 1H), 2.34 (s, 3H), 2.06 (d, J = 1.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 198.6, 148.7, 139.7, 136.6, 134.4, 129.4, 128.3, 127.8, 126.7, 27.5, 13.7.

(3*E*,5*Z*)-5-Bromo-6-phenylhexa-3,5-dien-2-one (1f):[20] Synthesized according to the literature.[20] Petroleum ether/ Ethyl acetate = 20/1 as the eluent. Yellow solid: 1.05 g, 42% yield; mp: 38.4–39.1 °C; ^{1}H NMR (500 MHz, DMSO): δ 7.83–7.81 (m, 3H), 7.60 (d, J = 15.0 Hz, 1H), 7.50–7.42 (m, 3H), 6.45 (d, J = 15.0 Hz, 1H), 2.34 (s, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO): δ 197.4, 143.6, 140.3, 134.6, 130.7, 129.8, 129.7, 128.5, 120.1, 28.0.

(3*E*,5*E*)-6-(3-(Trifluoromethyl)phenyl)hexa-3,5-dien-2-one (1g): Petroleum ether/ Ethyl acetate = 50/1 as the eluent. Yellow oil: 1.35g, 56% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.64–7.63 (m, 1H), 7.57–7.55 (m, 1H), 7.50–7.47 (m, 1H), 7.31–7.26 (m, 1H), 6.98–6.91 (m, 2H), 6.32 (d, J = 15.5 Hz, 1H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 198.2, 142.4, 139.1, 136.7, 131.5, 131.3 (q, J = 32.3 Hz), 130.1, 129.3, 128.3, 125.5 (q, J = 3.8 Hz), 123.8 (q, J = 270.8 Hz), 123.7 (q, J = 3.8 Hz), 27.50. ^{19}F NMR (471 MHz, $CDCl_3$): δ -62.9. FT-IR (KBr, cm^{-1}): 3551, 3479, 3417, 3041, 1669, 1619, 1436, 1363, 1327, 1281, 1254, 1207, 1125, 1098, 1073, 996, 962, 914, 877, 795, 695, 664, 641, 597, 561, 520. HRMS-ESI (m/z): $(M + H)^+$ calcd. for $C_{13}H_{12}F_3O$, 241.0840; found 241.0832.

(3*E*,5*E*)-6-(o-Tolyl)hexa-3,5-dien-2-one (1h):[19] Petroleum ether/ Ethyl acetate = 50/1 as the eluent. Yellow oil: 1.41g, 76% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57–7.55 (m, 1H), 7.33 (dd, J = 15.5, 10.5

Hz, 1H), 7.24–7.17 (m, 4H), 6.81 (dd, *J* = 15.5, 11.0 Hz, 1H), 6.26 (d, *J* = 15.5 Hz, 1H), 2.40 (s, 3H), 2.33 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.4, 143.7, 138.9, 136.6, 134.8, 130.7, 130.3, 129.0, 127.6, 126.3, 125.6, 27.4, 19.7.

(3*E*,5*E*)-6-(4-Chlorophenyl)hexa-3,5-dien-2-one (1i):[16] Recrystallized from DCM/ PE. Yellow solid: 1.31 g, 63% yield; mp: 73.5–74.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41–7.39 (m, 2H), 7.35–7.32 (m, 2H), 7.29–7.24 (m, 1H), 6.92–6.82 (m, 2H), 6.27 (d, *J* = 16.0 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.3, 142.9, 139.7, 134.9, 134.4, 130.8, 129.1, 128.3, 127.2, 27.4.

(3*E*,5*E*)-6-(4-Bromophenyl)hexa-3,5-dien-2-one (1j):[19] Recrystallized from DCM/ PE. Yellow solid: 1.97 g, 78% yield; mp: 100.7–102.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.48 (m, 2H), 7.35–7.33 (m, 2H), 7.29–7.24 (m, 1H), 6.91–6.83 (m, 2H), 6.27 (d, *J* = 15.5 Hz, 1H), 2.32 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.3, 142.9, 139.7, 134.9, 132.0, 130.9, 128.6, 127.3, 123.2, 27.5.

(3*E*,5*E*)-6-(4-Fluorophenyl)hexa-3,5-dien-2-one (1k):[14a] Petroleum ether/ Ethyl acetate = 20/1 as the eluent. Yellow oil: 1.70 g, 89% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47–7.43 (m, 2H), 7.30–7.24 (m, 1H), 7.08–7.03 (m, 2H), 6.91 (d, *J* = 15.5 Hz, 1H), 6.80 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.25 (d, *J* = 15.5 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.3, 163.1 (d, *J* = 250.6 Hz), 143.1, 139.8, 132.2 (d, *J* = 3.5 Hz), 130.4 (d, *J* = 1.1 Hz), 128.9 (d, *J* = 8.1 Hz), 126.3 (d, *J* = 2.5 Hz), 115.8(d, *J* = 21.8 Hz), 27.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ -111.2.

(3*E*,5*E*)-6-(4-Methoxyphenyl)hexa-3,5-dien-2-one (1l):[14a] Recrystallized from DCM/ PE. Yellow solid: 1.82g, 90% yield; mp: 103.9–104.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44–7.41 (m, 2H), 7.31–7.26 (m, 1H), 6.92–6.88 (m, 3H), 6.79–6.74 (m, 1H), 6.22 (d, *J* = 15.5 Hz, 1H), 3.84 (s, 3H), 2.31 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.5, 160.6, 144.0, 141.1, 129.4, 128.8, 128.7, 124.5, 114.3, 55.4, 27.3.

(3*E*,5*E*)-6-(4-(Dimethylamino)phenyl)hexa-3,5-dien-2-one (1m): Recrystallized from DCM/ PE. Red solid: 1.70g, 79% yield; mp: 131.1–132.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.35 (m, 2H), 7.32–7.27 (m, 1H), 6.88 (d, *J* = 15.5 Hz, 1H), 6.73–6.66 (m, 3H), 6.16 (d, *J* = 15.5 Hz, 1H), 3.01 (s, 6H), 2.29 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.5, 151.1, 144.9, 142.2, 128.8, 127.9, 124.1, 122.1, 112.0, 40.2, 27.1. FT-IR (KBr, cm^{-1}): 3554, 3478, 3416, 1639, 1619, 1385, 1365, 1258, 1156, 1085, 994, 669, 618, 476. HRMS-ESI (m/z): $(M + H)^+$ calcd. for $C_{14}H_{18}NO$, 216.1388; found 216.1380.

(3*E*,5*E*)-6-(4-Nitrophenyl)hexa-3,5-dien-2-one (1n):[16] Recrystallized from DCM/ PE. Brown solid: 1.70 g, 78% yield; mp: 115.6–116.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25–8.22 (m, 2H), 7.64–7.60 (m, 2H), 7.32–7.26 (m, 1H), 7.05–6.97 (m, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 2.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.1, 147.6, 142.1, 141.7, 138.0, 132.6, 130.8, 127.6, 124.2, 27.7.

(*E*)-6-Phenylhex-3-en-5-yn-2-one (1o):[21] Synthesized according to the literature.[21] Petroleum ether/ Ethyl acetate = 20:1 as the eluent. Yellow solid: 0.63 g, 37% yield; mp: 40.1–42.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.48 (m, 2H), 7.40–7.34 (m, 3H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.57 (d, *J* = 16.0 Hz, 1H), 2.31 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 197.0, 137.7, 131.9, 129.4, 128.5, 123.8, 122.1, 99.6, 86.7, 27.6.

(3*E*,5*E*)-hepta-3,5-dien-2-one (1q): [17] Petroleum ether/ Ethyl acetate = 50:1 as the eluent. Pale yellow oil: 0.53 g, 48% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13–7.07 (m, 1H), 6.24–6.17 (m, 2H), 6.05 (d, *J* = 15.0 Hz, 1H), 2.26 (s, 3H), 1.88 (d, *J* = 5.0 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 198.7, 143.7,

140.2, 130.1, 128.5, 27.0, 18.7.

(3*E*,5*E*)-6-(Furan-2-yl)hexa-3,5-dien-2-one (1r):[14a] Petroleum ether/ Ethyl acetate = 10/1 as the eluent. Red solid: 1.18g, 73% yield; mp: 34.2–35.8°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (d, *J* = 1.5 Hz, 1H), 7.22 (dd, *J* = 15.0, 10.5 Hz, 1H), 6.81–6.70 (m, 2H), 6.48–6.44 (m, 2H), 6.24 (d, *J* = 15.5 Hz, 1H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 198.2, 152.1, 143.8, 142.9, 130.2, 127.6, 124.9, 112.2, 112.1, 27.4.

(3*E*,5*E*)-6-(3-(4-Fluorophenyl)-1-isopropyl-1H-indol-2-yl)hexa-3,5-dien-2-one (1s): Petroleum ether/ Ethyl acetate = 10/1 as the eluent. Yellow solid: 1.18g, 37% yield; mp: 104.3–105.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56–7.50 (m, 2H), 7.41–7.37 (m, 2H), 7.25–7.19 (m, 2H), 7.17–7.12 (m, 2H), 7.11–7.07 (m, 1H), 7.03 (d, *J* = 15.5 Hz, 1H), 6.38 (dd, *J* = 16.0, 11.5 Hz, 1H), 6.06 (d, *J* = 15.5 Hz, 1H), 4.94–4.86 (m, 1H), 2.27 (s, 3H), 1.70 (d, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 198.1, 161.7 (d, *J* = 246.5 Hz), 143.0, 136.2, 132.4, 131.8 (d, *J* = 7.9 Hz), 130.8 (d, *J* = 3.3 Hz), 130.7, 130.1, 129.8, 128.4, 123.1, 120.1, 120.0, 118.2, 115.6 (d, *J* = 21.4 Hz), 111.9, 47.9, 27.7, 21.8. ^{19}F NMR (471 MHz, $CDCl_3$): δ -115.6. FT-IR (KBr, cm^{-1}): 3555, 3479, 3417, 1663, 1639, 1609, 1525, 1358, 1343, 1225, 1156, 1142, 999, 749, 669, 618, 566, 476. HRMS-ESI (m/z): $(M + H)^+$ calcd. for $C_{23}H_{23}FNO$, 348.1764; found 348.1766.

(2*E*,4*E*)-1,5-Diphenylpenta-2,4-dien-1-one (1t):[22] Recrystallized from EtOH. Yellow solid: 1.61 g, 69% yield; mp: 93.8–94.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99–7.97 (m, 2H), 7.63–7.56 (m, 2H), 7.52–7.48 (m, 4H), 7.39–7.31 (m, 3H), 7.10 (d, *J* = 15.0 Hz, 1H), 7.07–7.00 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 190.4, 144.8, 141.9, 138.2, 136.1, 132.6, 129.2, 128.8, 128.5, 128.3, 127.3, 126.9, 125.4.

(2*E*,4*E*)-1-(2-Chlorophenyl)-5-phenylpenta-2,4-dien-1-one (1u):[23] Recrystallized from DCM/ PE. Yellow solid: 1.32 g, 49% yield; mp: 66.6–68.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48–7.31 (m, 9H), 7.22 (dd, *J* = 15.5, 9.5 Hz, 1H), 7.01–6.92 (m, 2H), 6.67 (d, *J* = 15.5 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 193.9, 146.4, 142.5, 139.2, 135.9, 131.19, 131.18, 130.2, 129.6, 129.4, 129.2, 128.9, 127.4, 126.8, 126.6.

Typical Procedure for the Asymmetric Hydrogenation.

To a 25 mL Schlenk tube were placed (*R*)-Xylyl-SunPhos (17.2 mg, 22 μmol) and$[RuCl_2(benzene)]_2$ (5.0 mg, 10 μmol), the tube was evacuated and purged with nitrogen three times before addition of freshly distilled and freeze-thaw degassed DMF (2 mL). The resulting mixture was heated at 100 °C for 10 min before it was cooled to room temperature, and then (*R*)-Daipen (7.5 mg, 24 μmol) in DMF (1 mL) was added. The tube was heated to 40 °C for 4 h before the solvent was removed to give a brownish yellow solid. The catalyst was dissolved in freeze-thaw degassed ^{i}PrOH (8 mL), and then the solution was equally charged into eight vials which contained 0.25 mmol of substrates, K_2CO_3 (3.5 mg, 0.025 mmol). Then the vials were transferred into a 300 mL autoclave. The autoclave was purged three times with H_2, and the required pressure of H_2 was set under specified reaction conditions. After cooling to ambient temperature and hydrogen was released carefully, the autoclaves were opened and the solvent was evaporated. The residue was filtered through a short pad of silica gel column, and the enantiomeric excess was directly determined by HPLC. The crude product was further purified by flash column chromatography on silica gel to provide the pure compound.

(*S*,3*E*,5*E*)-6-Phenylhexa-3,5-dien-2-ol (2a):[14a] White solid: 43.1 mg, 99% yield; mp: 70.5–71.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39–7.37 (m, 2H), 7.32–7.29 (m, 2H), 7.23–7.20 (m, 1H), 6.75 (dd, *J* = 16.0, 10.5 Hz, 1H), 6.54 (d, *J* = 15.5 Hz, 1H), 6.37 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.86 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.43–4.38 (m, 1H), 1.32 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 137.6, 137.1, 132.6, 129.8, 128.6, 128.2, 127.5, 126.3, 68.5, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 95/5, 1.0 mL/min, 254 nm): t_1 = 10.7 min, t_2 = 11.6 min. $[\alpha]_D^{25}$ = – 16.5 (*c* = 0.46 in $CHCl_3$) for (*S*)-enantiomer with 95.6% ee. (Lit.[10d] $[\alpha]_D^{24}$ = + 17.73 (*c*=2.82 in $CHCl_3$) for (*R*)-enantiomer with 90% ee.)

(*S*,5*E*,7*E*)-8-Phenylocta-5,7-dien-4-ol (2b):[24] White solid: 49.5 mg, 98% yield; mp: 44.9–46.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.37 (m, 2H), 7.31–7.28 (m, 2H), 7.23–7.19 (m, 1H), 6.75 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.53 (d, *J* = 15.5 Hz, 1H), 6.36 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.81 (dd, *J* = 15.5, 7.0 Hz, 1H), 4.22–4.17 (m, 1H), 1.62–1.36 (m, 4H), 0.94 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 137.1, 136.8, 132.5, 130.5, 128.5, 128.3, 127.5, 126.3, 72.4, 39.4, 18.6, 14.0. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 254 nm): t_1 = 11.4 min, t_2 = 12.5 min. $[\alpha]_D^{25}$ = – 1.7 (*c* = 0.23 in $CHCl_3$) for (*S*)-enantiomer with 94.9% ee.

(*S*,4*E*,6*E*)-2-Methyl-7-phenylhepta-4,6-dien-3-ol (2c):[14c] Pale yellow oil: 49.6 mg, 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39–7.37 (m, 2H), 7.31–7.28 (m, 2H), 7.23–7.20 (m, 1H), 6.77 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.53 (d, *J* = 16.0 Hz, 1H), 6.37 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.82 (dd, *J* = 15.0, 7.0 Hz, 1H), 3.95–3.93 (t, *J* = 6.5 Hz, 1H), 1.81–1.73 (m, 1H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 137.1, 135.0, 132.4, 131.5, 128.5, 128.3, 127.5, 126.3, 77.7, 34.0, 18.2, 18.0. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 280 nm): t_1 = 11.9 min, t_2 = 12.5 min. $[\alpha]_D^{25}$ = + 5.2 (*c* = 0.58 in $CHCl_3$) for (*S*)-enantiomer with 37.5% ee. (Lit.[14c] $[\alpha]_D^{20}$ = + 0.9 (*c*= 1.89 in $CHCl_3$) for (*S*)-enantiomer with 39.6% ee.)

(*E*)-2-((*E*)-3-Phenylallylidene)cyclobutan-1-ol (2d): White solid: 45.0 mg, 97% yield; mp: 99.4–101.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39–7.38 (m, 2H), 7.31–7.28 (m, 2H), 7.22–7.19 (m, 1H), 6.73 (dd, *J* = 16.0, 11.0 Hz, 1H), 6.50 (d, *J* = 15.5 Hz, 1H), 6.25–6.21 (m, 1H), 4.80–4.76 (m, 1H), 2.74–2.66 (m, 1H), 2.45–2.37 (m, 2H), 2.15 (brs, 1H), 1.91–1.82 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 149.5, 137.5, 131.3, 128.5, 127.3, 126.2, 124.4, 120.2, 71.7, 30.3, 22.5. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 254 nm): t_1 = 11.4 min, t_2 = 13.3 min. $[\alpha]_D^{25}$ = – 30.8 (*c* = 0.35 in $CHCl_3$) for (*S*)-enantiomer with 98.8% ee. FT-IR (KBr, cm^{-1}): 3554, 3478, 3417, 1639, 1619, 967, 669, 618, 477. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{13}H_{13}$, 169.1017; found 169.1010.

(*S*,3*E*,5*E*)-5-Methyl-6-phenylhexa-3,5-dien-2-ol (2e): Colorless oil: 45.6 mg, 97% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.32 (m, 2H), 7.29–7.27 (m, 2H), 7.24–7.20 (m, 1H), 6.52 (s, 1H), 6.40 (d, *J* = 15.5 Hz, 1H), 5.82 (dd, *J* = 16.0, 7.0 Hz, 1H), 4.47–4.41 (m, 1H), 1.99 (d, *J* = 1.0 Hz, 3H), 1.34 (d, *J* = 6.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 137.7, 135.0, 134.8, 132.8, 131.6, 129.1, 128.1, 126.6, 69.0, 23.5, 13.9. HPLC (Chiralcel OJ-H column, hexane/*i*-PrOH = 90/10, 0.9 mL/min, 280 nm): t_1 = 9.3 min, t_2 = 10.9 min. $[\alpha]_D^{25}$ = – 9.7 (*c* = 0.39 in $CHCl_3$) for (*S*)-enantiomer with 92.4% ee. FT-IR (KBr, cm^{-1}): 3400, 3081, 3023, 2972, 2923, 1638, 1598, 1491, 1445, 1385, 1367, 1303, 1145, 1058, 1013, 965, 947, 917, 861, 847, 824, 748, 699, 509. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{13}H_{15}$, 171.1174; found 171.1167.

(*S*,3*E*,5*Z*)-5-Bromo-6-phenylhexa-3,5-dien-2-ol (2f): Yellow oil: 59.2 mg, 94% yield; ^{1}H NMR (500

MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.38–7.34 (m, 2H), 7.32–7.28 (m, 1H), 6.96 (s, 1H), 6.43 (d, *J* = 15.0 Hz, 1H), 6.27 (dd, *J* = 14.5, 5.5 Hz, 1H), 4.55–4.49 (m, 1H), 1.36 (d, *J* = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 138.9, 135.6, 131.9, 129.8, 129.4, 128.2, 128.1, 122.6, 67.9, 23.5. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 280 nm): t_1 = 12.0 min, t_2 = 12.9 min. $[\alpha]_D^{25}$ = + 1.0 (*c* = 0.39 in $CHCl_3$) for (*S*)-enantiomer with 91.1% ee. FT-IR (KBr, cm^{-1}): 3434, 2920, 2849, 1645, 1446, 1384, 1265, 1066, 954, 751, 696. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{12}H_{12}Br$, 235.0122; found 235.0123.

(*S*,3*E*,5*E*)-6-(3-(Trifluoromethyl)phenyl)hexa-3,5-dien-2-ol (2g): Yellow oil: 60.2 mg, 99% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.47–7.40 (m, 2H), 6.81 (dd, *J* = 16.0, 10.5 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.39 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.93 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.46–4.41 (m, 1H), 1.34 (d, *J* = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.1, 137.9, 131.0 (q, *J* = 31.9 Hz), 130.9, 130.0, 129.3 (d, *J* = 0.9 Hz), 129.1, 129.0, 124.1 (q, *J* = 270.8 Hz), 123.9 (q, *J* = 3.6 Hz), 122.9 (q, *J* = 3.8 Hz), 68.4, 23.3. ^{19}F NMR (471 MHz, $CDCl_3$): δ -62.8. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 99/1, 0.9 mL/min, 280 nm): t_1 = 17.8 min, t_2 = 18.7 min. $[\alpha]_D^{25}$ = + 12.6 (*c* = 0.35 in $CHCl_3$) for (*S*)-enantiomer with 90.4% ee. FT-IR (KBr, cm^{-1}): 3400, 2974, 2929, 1620, 1448, 1384, 1331, 1204, 1165, 1125, 1096, 1072, 987, 946, 906, 791, 696, 663. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{13}H_{12}F_3$, 225.0891; found 225.0883.

(*S*,3*E*,5*E*)-6-(o-Tolyl)hexa-3,5-dien-2-ol (2h): Yellow oil: 45.3 mg, 96% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 7.48–7.46 (m, 1H), 7.18–7.13 (m, 3H), 6.77 (d, *J* = 15.5 Hz, 1H), 6.66 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.41 (dd, *J* = 15.0, 10.0 Hz, 1H), 5.86 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.44–4.39 (m, 1H), 2.34 (s, 3H), 1.33 (d, *J* = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 137.4, 136.0, 135.5, 130.4, 130.3, 130.1, 129.3, 127.4, 126.1, 125.1, 68.5, 23.3, 19.8. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 99/1, 0.6 mL/min, 280 nm): t_1 = 39.4 min, t_2 = 41.7 min. $[\alpha]_D^{25}$ = – 11.5 (*c* = 0.33 in $CHCl_3$) for (*S*)-enantiomer with 94.0% ee. FT-IR (KBr, cm^{-1}): 3411, 3023, 2972, 2927, 1644, 1615, 1600, 1485, 1462, 1383, 1294, 1135, 1099, 1057, 989, 945, 866, 748, 715. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{13}H_{15}$, 171.1174; found 171.1167.

(*S*,3*E*,5*E*)-6-(4-Chlorophenyl)hexa-3,5-dien-2-ol (2i):[25] White solid: 50.1 mg, 96% yield; mp: 84.5–85.7 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.26 (m, 4H), 6.72 (dd, *J* = 16.0, 10.5 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 6.36 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.88 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.45–4.40 (m, 1H), 1.33 (d, *J* = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 138.2, 135.6, 133.1, 131.3, 129.4, 128.81, 128.76, 127.5, 68.5, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 95/5, 0.9 mL/min, 280 nm): t_1 = 14.1 min, t_2 = 15.8 min. $[\alpha]_D^{25}$ = + 0.6 (*c* = 0.36 in $CHCl_3$) for (*S*)-enantiomer with 93.0% ee.

(*S*,3*E*,5*E*)-6-(4-Bromophenyl)hexa-3,5-dien-2-ol (2j): White solid: 62.0 mg, 98% yield; mp: 90.1-91.0 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.44–7.41 (m, 2H), 7.26–7.23 (m, 2H), 6.73 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.47 (d, *J* = 15.5 Hz, 1H), 6.35 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.88 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.44–4.39 (m, 1H), 1.32 (d, *J* = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 138.4, 136.1, 131.7, 131.3, 129.4, 128.9, 127.8, 121.2, 68.4, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 280 nm): t_1 = 13.9 min, t_2 = 15.2 min. $[\alpha]_D^{25}$ = – 15.8 (*c* = 0.43 in $CHCl_3$) for (*S*)-enantiomer with 94.4% ee. FT-IR (KBr, cm^{-1}): 3555, 3478, 3417, 1639, 1619, 994, 669, 618, 480. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{12}H_{12}Br$, 235.0122; found 235.0114.

(*S*,3*E*,5*E*)-6-(4-Fluorophenyl)hexa-3,5-dien-2-ol (2k):[14a] Pale yellow solid: 46.7 mg, 97% yield; mp: 96.2–97.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.31 (m, 2H), 7.01–6.97 (m, 2H), 6.65 (dd, *J* = 16.0, 10.5 Hz, 1H), 6.49 (d, *J* = 15.5 Hz, 1H), 6.34 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.85 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.43–4.38 (m, 1H), 1.32 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 162.2 (d, *J* = 245.6 H), 137.7 (d, *J* = 0.8 Hz), 133.3 (d, *J* = 3.3 Hz), 131.3, 129.5, 128.0 (d, *J* = 2.4 Hz), 127.8 (d, *J* = 7.8 Hz), 115.5 (d, *J* = 21.5 Hz), 68.4, 23.3. ^{19}F NMR (471 MHz, $CDCl_3$): δ -114.2. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 95/5, 0.9 mL/min, 280 nm): t_1 = 13.4 min, t_2 = 14.9 min. $[\alpha]_D^{25}$ = – 18.0 (*c* = 0.40 in $CHCl_3$) for (*S*)-enantiomer with 95.5% ee.

(*S*,3*E*,5*E*)-6-(4-Methoxyphenyl)hexa-3,5-dien-2-ol (2l):[14a] Pale yellow solid: 50.2 mg, 98% yield; mp: 122.2–124.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33–7.30 (m, 2H), 6.86–6.83 (m, 2H), 6.62 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.49 (d, *J* = 15.5 Hz, 1H), 6.34 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.80 (dd, *J* = 15.0, 6.5 Hz, 1H), 4.42–4.37 (m, 1H), 3.80 (s, 3H), 1.31 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.2, 136.5, 132.2, 130.0, 129.9, 127.5, 126.2, 114.0, 68.6, 55.2, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 280 nm): t_1 = 16.6 min, t_2 = 18.2 min. $[\alpha]_D^{25}$ = – 26.2 (*c* = 0.29 in $CHCl_3$) for (*S*)-enantiomer with 95.3% ee.

(*S*,3*E*,5*E*)-6-(4-(Dimethylamino)phenyl)hexa-3,5-dien-2-ol (2m): Red solid: 52.7mg, 97% yield; mp: 67.2–70.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29–7.27 (m, 2H), 6.67–6.65 (m, 2H), 6.57 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.47 (d, *J* = 15.5 Hz, 1H), 6.33 (dd, *J* = 15.5, 10.5 Hz, 1H), 5.75 (dd, *J* = 15.0, 6.5 Hz, 1H), 4.40–4.35 (m,, 1H), 2.95 (s, 6H), 1.30 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 150.0, 135.1, 133.0, 130.6, 127.4, 125.6, 124.1, 112.4, 68.8, 40.4, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 290 nm): t_1 = 16.6 min, t_2 = 19.5 min. $[\alpha]_D^{25}$ = – 30.7 (*c* = 0.52 in $CHCl_3$) for (*S*)-enantiomer with 94.0% ee. FT-IR (KBr, cm^{-1}): 3434, 2969, 2873, 1610, 1522, 1442, 1384, 1357, 1228, 1190, 1156, 1128, 1060, 984, 941, 870, 825, 798, 669, 527. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{14}H_{18}N$, 200.1439; found 200.1433.

(*S*,3*E*,5*E*)-6-(4-Nitrophenyl)hexa-3,5-dien-2-ol (2n): Yellow solid: 31.8 mg, 58% yield; mp: 58.9–61.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19–8.16 (m, 2H), 7.52–7.49 (m, 2H), 6.91 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.59 (d, *J* = 15.5 Hz, 1H), 6.42 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.02 (dd, *J* = 15.5, 6.0 Hz, 1H), 4.48–4.45 (m, 1H), 1.35 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 146.7, 143.7, 141.0, 132.8, 130.0, 128.7, 126.7, 124.1, 68.3, 23.3. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 254 nm): t_1 = 31.6 min, t_2 = 35.7 min. $[\alpha]_D^{25}$ = + 22.2 (*c* = 0.45 in $CHCl_3$) for (*S*)-enantiomer with 93.3% ee. FT-IR (KBr, cm^{-1}): 3400, 2972, 2925, 1616, 1592, 1513, 1341, 1181, 1109, 1057, 990, 853, 825, 747, 691. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{12}H_{12}NO_2$, 202.0868; found 202.0860.

(*S*,*E*)-6-Phenylhex-3-en-5-yn-2-ol (2o):[25] Colorless oil: 41.3 mg, 96% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44–7.41 (m, 2H), 7.32–7.29 (m, 3H), 6.27 (dd, *J* = 16.0, 5.5 Hz, 1H), 5.92 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.44–4.39(m, 1H), 1.33 (d, *J* = 6.5 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 146.6, 131.5, 128.3, 128.2, 123.2, 109.2, 90.1, 87.2, 68.3, 23.0. HPLC (Chiralcel OJ-H column, hexane/*i*-PrOH = 95/5, 0.9 mL/min, 280 nm): t_1 = 31.5 min, t_2 = 33.1 min. $[\alpha]_D^{25}$ = + 3.5 (*c* = 0.34 in $CHCl_3$) for (*S*)-enantiomer with 90.3% ee.

(*S*,*E*)-6-Methylhepta-3,5-dien-2-ol (2p): Colorless oil: 31.1 mg, 99% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.41 (dd, *J* = 15.0, 11.0 Hz, 1H), 5.81 (d, *J* = 11.5 Hz, 1H), 5.60 (dd, *J* = 15.0, 7.0 Hz, 1H),

4.39–4.34 (m, 1H), 1.78 (s, 3H), 1.76 (s, 3H), 1.29 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 136.1, 134.2, 126.3, 124.2, 68.9, 26.0, 23.4, 18.3. HPLC (Chiralcel AS-H column, hexane/*i*-PrOH = 99/1, 0.9 mL/min, 254 nm): t_1 = 7.7 min, t_2 = 8.2 min. $[\alpha]_D^{25}$ = + 6.8 (c = 1.53 in $CHCl_3$) for (*S*)-enantiomer with 90.7% ee. FT-IR (KBr, cm^{-1}): 3548, 3475, 3417, 2978, 2934, 1637, 1619, 1457, 1385, 1260, 1147, 1084, 618, 476. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for C_8H_{13}, 109.1017; found 109.1011.

(S,3*E*,5*E*)-hepta-3,5-dien-2-ol (2q): [14a] Colorless oil: 27.2 mg, 97% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 6.16 (dd, J = 15.5, 10.5 Hz, 1H), 6.06–6.00 (m, 1H), 5.74–5.67 (m, 1H), 5.60 (dd, J = 15.0, 6.5 Hz, 1H), 4.31–4.29 (m, 1H), 1.83 (s, 1H), 1.75 (dd, J = 6.5, 1.0 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 134.4, 130.7, 129.85, 129.81, 68.5, 23.3, 18.0. HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 99/1, 0.6 mL/min, 210 nm): t_1 = 8.2 min, t_2 = 8.8 min. $[\alpha]_D^{24}$ = + 1.6 (c = 0.50 in $CHCl_3$) for (*S*)-enantiomer with 93.3% ee.

(*S*,3*E*,5*E*)-6-(Furan-2-yl)hexa-3,5-dien-2-ol (2r):[14a] Yellow oil: 38.9 mg, 95% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 7.35 (d, J = 1.5 Hz, 1H), 6.66 (dd, J = 15.5, 11.0 Hz, 1H), 6.38–6.25 (m, 4H), 5.84 (dd, J = 15.5, 6.5 Hz, 1H), 4.41–4.36 (m, 1H), 2.11 (brs, 1H), 1.30 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 152.9, 142.1, 137.8, 129.2, 126.8, 120.1, 111.5, 108.3, 68.4, 23.2. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 95/5, 0.6 mL/min, 280 nm): t_1 = 17.2 min, t_2 = 18.8 min. $[\alpha]_D^{25}$ = – 15.2 (c = 0.58 in $CHCl_3$) for (*S*)-enantiomer with 95.4% ee.

(*S*,3*E*,5*E*)-6-(3-(4-Fluorophenyl)-1-isopropyl-1H-indol-2-yl)hexa-3,5-dien-2-ol (2s): Yellow solid: 85.4 mg, 98% yield; mp: 43.8–45.7 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.55–7.52 (m, 2H), 7.43–7.39 (m, 2H), 7.21–7.17 (m, 1H), 7.14–7.06 (m, 3H), 6.58 (d, J = 15.5 Hz, 1H), 6.36–6.23 (m, 2H), 5.68 (dd, J = 15.0, 6.5 Hz, 1H), 4.92–4.84 (m, 1H), 4.41–4.37 (m, 1H), 1.67 (d, J = 7.0 Hz, 6H), 1.54 (d, J = 3.5 Hz, 1H), 1.30 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4 (d, J = 243.3 Hz), 138.1, 135.5, 134.0, 133.7, 131.7 (d, J = 7.8 Hz), 131.4 (d, J = 3.3 Hz), 129.5, 128.4, 121.9, 121.5, 119.7, 119.4, 115.3 (d, J = 21.1 Hz), 115.2, 111.7, 68.3, 47.6, 23.4, 21.6. ^{19}F NMR (471 MHz, $CDCl_3$): δ -116.6. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 95/5, 0.9 mL/min, 280 nm): t_1 = 9.0 min, t_2 = 9.8 min. $[\alpha]_D^{25}$ = – 0.2 (c = 0.99 in $CHCl_3$) for (*S*)-enantiomer with 91.1% ee. FT-IR (KBr, cm^{-1}): 3551, 3478, 3417, 1640, 1619, 1385, 1222, 1157, 669, 650, 618. HRMS-ESI (m/z): $(M + H)^+$ calcd. for $C_{23}H_{25}FNO$, 350.1920; found 350.1924.

(2*E*,4*E*)-1,5-Diphenylpenta-2,4-dien-1-ol (2t):[26] White oil: 57.8 mg, 98% yield; ^1H NMR (500 MHz, $CDCl_3$): δ 7.40–7.34 (m, 6H), 7.31–7.27 (m, 3H), 7.23–7.20 (m, 1H), 6.76 (dd, J = 15.5, 10.5 Hz, 1H), 6.56 (d, J = 15.5 Hz, 1H), 6.45 (dd, J = 15.0, 10.5 Hz, 1H), 5.98 (dd, J = 15.0, 6.5 Hz, 1H), 5.29 (d, J = 6.5 Hz, 1H), 2.13 (brs, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 142.7, 137.0, 135.5, 133.2, 130.9, 128.6, 128.0, 127.7, 127.6, 126.4, 126.3, 74.8. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 90/10, 0.6 mL/min, 254 nm): t_1 = 16.5 min, t_2 = 18.7 min. $[\alpha]_D^{25}$ = – 13.7 (c = 0.48 in $CHCl_3$) with 67.5% ee.

(2*E*,4*E*)-1-(2-Chlorophenyl)-5-phenyl-1l3-penta-2,4-dien-1-ol (2u): Yellow solid: 64.9 mg, 96% yield; mp: 78.4–79.9 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.60–7.58 (m, 1H), 7.38–7.35 (m, 3H), 7.32–7.28 (m, 3H), 7.24–7.20 (m, 2H), 6.77 (dd, J = 15.5, 10.5 Hz, 1H), 6.58 (d, J = 15.5 Hz, 1H), 6.51 (dd, J = 15.5, 10.5 Hz, 1H), 5.96 (dd, J = 15.5, 6.5 Hz, 1H), 5.75–5.73 (m, 1H), 2.16 (d, J = 4.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 140.1, 137.0, 133.5, 133.4, 132.2, 131.4, 129.5, 128.7, 128.6, 128.0, 127.63, 127.57,

127.2, 126.4, 71.1. HPLC (Chiralcel IA-3 column, hexane/*i*-PrOH = 98/2, 0.9 mL/min, 280 nm): t_1 = 42.2 min, t_2 = 45.7 min. $[\alpha]_D^{25}$ = + 75.6 (*c* = 0.46 in $CHCl_3$) with 92.2% ee. FT-IR (KBr, cm^{-1}): 3369, 3024, 1469, 1449, 1436, 1390, 1328, 1276, 1208, 1191, 1122, 1074, 1042, 1023, 993, 947, 785, 754, 738, 693, 660. HRMS-ESI (m/z): $(M + H - H_2O)^+$ calcd. for $C_{17}H_{14}Cl$, 253.0779; found 253.0788.

Typical Procedure for the Gram-Scale Asymmetric Hydrogenation.

Under a nitrogen atmosphere, the substrate **1a** (1.29 g, 7.5 mmol), the *trans*-{$RuCl_2$[(*R*)-DAIPEN][(*R*)-Xylyl-SunPhos]} catalyst (9.5 mg, 7.5 μmol), K_2CO_3 (210 mg, 1.5 mmol) was dissolved in freeze-thaw degassed *i*-PrOH (8 mL) in a 30 mL vial, Then the container was transferred into a 125 mL autoclave. The autoclave was purged three times with H_2, and the specified reaction conditions (30 bar H_2, 30 °C, 48 h) was set. After careful release of hydrogen, the autoclaves were opened and the solvent was evaporated. The residue was purified by flash column chromatography (PE/EA=10/1 as the eluent) to provide chiral product **2a** as white solid (1.28 g, 98% yield, 95.2% ee).

SUPPORTING INFORMATION

The Supporting Information is available free of charge on the ACS Publications website.

NMR spectra for compounds **1-2** (PDF)

HPLC data for racemic and chiral compounds **2** (PDF)

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