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Ni-Catalyzed Highly Chemo-, Regio-, and Enantioselective Decarboxylative Aldol Reaction of β,γ-Unsaturated α-Ketoesters with β-Ketoacids

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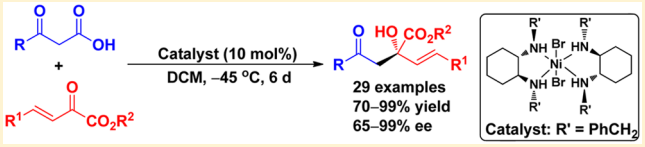
Supporting Information

ABSTRACT: A novel Ni-catalyzed decarboxylative aldol reaction of β,γ-unsaturated α-ketoesters with β-ketoacids is reported. The reaction proceeds smoothly with high chemo-, regio-, and enantioselectivity. This protocol provides a convenient approach to access enantioenriched chiral tertiary alcohols.



INTRODUCTION

The reactivity and functionality of β,γ-unsaturated α-ketoesters provide many possibilities for synthetic transformations involving the double bond, carbonyl group, and ester moiety. Over the past decade, asymmetric catalytic reactions of β,γ-unsaturated α-ketoesters using chiral metal complexes and organocatalysts have attracted considerable attention and evolved into an important tool for the construction of useful multifunctional chiral building blocks (Figure 1).[1] Among

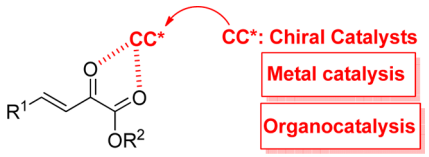
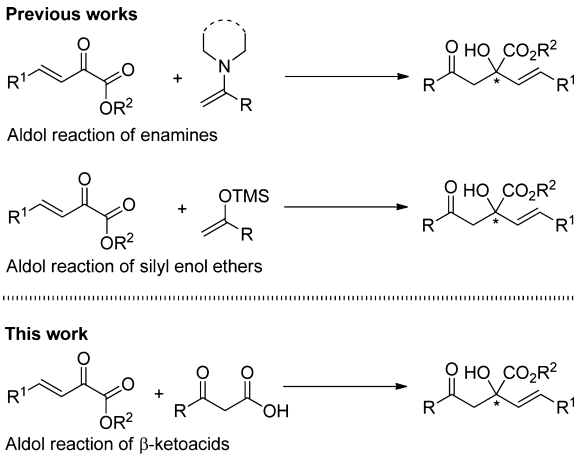


Figure 1. Two-point binding catalysis of β,γ-unsaturated α-ketoesters.

them, asymmetric catalytic aldol condensations of β,γ-unsaturated α-ketoesters with enolizable ketones provide facile access to enantioenriched chiral tertiary alcohols. However, in situ or preactivation of ketones is often required. For instance, enamine catalysis and silyl enol ethers of ketones have been widely employed in the enantioselective aldol reactions of β,γ-unsaturated α-ketoesters (Scheme 1, top).[2,3] Despite these impressive advances, the development and application of new enolate equivalents of ketones is still in high demand.

In recent years, asymmetric decarboxylative reactions of β-ketoacids with various electrophilic partners have been reported using chiral metal complexes and organocatalysts.[4−6] Although β-ketoacids are very attractive candidates for the generation of ketone enolate equivalents under very mild reaction conditions, there are no reports on the enantioselective decarboxylative reaction of β-ketoacids with β,γ-unsaturated α-ketoesters. During our ongoing studies in the field of asymmetric decarboxylative transformations,[7] we have developed a Ni-catalyzed decarboxylative aldol reaction of β-ketoacids with β,γ-unsaturated α-ketoesters. This reaction proceeds with excellent chemo-, regio-, and enantioselectivity to afford highly functionalized chiral tertiary alcohols (Scheme 1, bottom). Herein, we report the results of our studies on this subject.

Scheme 1. Aldol Reactions of β,γ-Unsaturated α-Ketoesters



RESULTS AND DISCUSSION

Optimization of Reaction Conditions. In an initial investigation, we conducted the reaction of 3-oxo-3-phenylpropanoic acid **1a** with β,γ-unsaturated α-ketoester **2a** using a series of chiral organo- and metal-catalysts, including cinchona alkaloids, aminothioureas, Cu, Zn, Sc, Pd and Ni complexes. It was found that Ni complexes were able to catalyze this model reaction to give the desired product in high yield with moderate enantioselectivity,[8] whereas the other chiral catalysts tested resulted in relatively low yields and/or poor enantioselectivities

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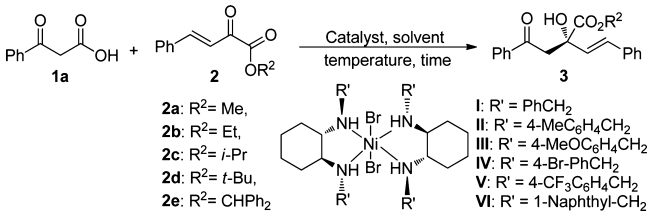
(see the Supporting Information). Accordingly, a series of chiral Ni-complex catalysts (**I**–**VI**, 10 mol %) were further screened, and the results are shown in Table 1. α-Ketoesters (**2a**–**e**)

Table 1. Optimization of Reaction Conditions[a]



entry	α-ketoester	catalyst (mol %)	solvent	temp (°C)/time (d)	yield (%)[b]	ee (%)[c]
1	**2a**	**I** (10)	DCM	−20/0.5	99	62
2	**2b**	**I** (10)	DCM	−20/0.5	99	65
3	**2c**	**I** (10)	DCM	−20/0.5	99	70
4	**2d**	**I** (10)	DCM	−20/0.5	99	74
5	**2e**	**I** (10)	DCM	−20/0.5	99	80
6	**2e**	**II** (10)	DCM	−20/3	91	45
7	**2e**	**III** (10)	DCM	−20/3	96	66
8	**2e**	**IV** (10)	DCM	−20/0.5	99	77
9	**2e**	**V** (10)	DCM	−20/2.5	90	68
10	**2e**	**VI** (10)	DCM	−20/1	95	66
11	**2e**	**I** (10)	DCE	−20/0.5	99	66
12	**2e**	**I** (10)	toluene	−20/2.5	43	63
13	**2e**	**I** (10)	Et_2O	−20/2.5	40	63
14	**2e**	**I** (10)	DME	−20/2.5	98	55
15	**2e**	**I** (10)	THF	−20/1	99	53
16	**2e**	**I** (10)	CH_3CN	−20/1.5	94	50
17	**2e**	**I** (10)	DCM	−40/5	99	89
18	**2e**	**I** (10)	DCM	−45/6	99	90
19	**2e**	**I** (10)	DCM	−50/8	77	90
20	**2e**	**I** (5)	DCM	−45/11	99	80
21	**2e**	**I** (15)	DCM	−45/6	99	90

[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.1 mmol), and catalyst **I**–**VI** (5–15 mol %) in solvent for the stated time. [b]Isolated yield was obtained from an average of two runs. [c]Determined by HPLC analysis using a chiral stationary phase; the absolute configuration was assigned analogous to that of **3d**.[9]

delivered the decarboxylative aldol products **3** in excellent yields with good enantioselectivities (62–80% ee) at −20 °C in dichloromethane. The reaction also exhibited excellent regio- and chemoselectivities; the 1,4-adducts and/or the Claisen condensation products were not observed (Table 1, entries 1–5). In addition, the substituent of the ligands on the Ni-complexes **I**–**VI** influenced the reactivity and enantioselectivity of the reaction (entries 6–10) with catalyst **I** giving the best performance (entry 5). Further optimization of the enantioselectivity was achieved with catalyst **I** by screening different solvents, lowering the reaction temperature, and changing the catalyst loading (entries 11–21). Thus, the decarboxylative aldol reaction of 3-oxo-3-phenylpropanoic acid **1a** with β,γ-unsaturated α-ketoester **2e** could be performed in dichloromethane at −45 °C to provide product **3a** in 99% yield with 90% ee (entry 18).

Scope of the Decarboxylative Aldol Reaction. With the optimal reaction conditions in hand, we explored the scope of this catalytic enantioselective decarboxylative aldol reaction with a series of γ-substituted β,γ-unsaturated α-ketoesters, and the results are shown in Table 2. In the presence of 10 mol % catalyst **I**, the reaction was readily extended to several γ-phenyl-substituted β,γ-unsaturated α-ketoesters, and both electron-withdrawing and -releasing substituents on the phenyl ring were well tolerated under the current reaction conditions, thus generating desired products **3a**–**g** in consistently high yield (92–99%) with good to high enantioselectivity (82–92% ee). 2-Thiophenyl- and styrene-substituted β,γ-unsaturated α-ketoesters were also found to be good substrates, delivering products **3h** and **3i**, respectively, in high yield and enantioselectivity. In addition, it was found that γ-alkyl-substituted β,γ-unsaturated α-ketoesters could also be used as electrophilic partners, and the decarboxylative aldol products **3j** and **3k** were obtained in high yields with good enantioselectivities.

Having established the scope of β,γ-unsaturated α-ketoesters, we turned our attention to the β-ketoacids. As shown in Table 3, the decarboxylative aldol reaction of ortho-, meta-, and para-substituted phenyl β-ketoacids proceeded smoothly to afford aldol adducts **3l**–**t** in excellent yields (95–99%) with high enantioselectivities (86–99% ee). 2-Naphthyl-, 2-thiophenyl-, and 2-furanyl-substituted β-ketoacids were also found to be good substrates, thus giving the aldol products **3u**–**w** in 90–99% yields with good to high enantioselectivities. To further define the scope of our methodology, we tested the reactions of a series of alkyl-substituted β-ketoacids with β,γ-unsaturated α-ketoester **2e**. Under the current reaction conditions, the reactivity of these substrates is lower than that of aryl-substituted β-ketoacid. Subsequently, at relatively higher temperatures, the decarboxylative aldol condensations of these alkyl-substituted β-ketoacids could proceed to give desired products **3x**–**c′** in good to high yields with moderate to good enantioselectivities.

Further Synthetic Transformation of the Aldol Product. When the Ni-catalyzed decarboxylative aldol reaction was scaled up to the gram scale, condensation product **3d** was obtained in high yield with excellent optical purity after single recrystallization from ethyl acetate and petroleum ether (Scheme 2). Direct oximation of **3d** with hydroxylamine furnished intermediate **4** in 61% yield, and subsequent intramolecular etherification afforded isoxazoline **5** in good yield without any racemization. Also, reduction treatment of **3d** with $NaBH(OAc)_3$ gave rise to corresponding α,γ-dihydroxyester **6** in excellent yield and diastereoselectivity.[12] Then, intramolecular transesterification allowed access to α-hydroxy-γ-butyrolactone **7** in 62% yield. Furthermore, the stereoisomer of **7** proved to be crystalline, allowing the determination of the absolute configuration of the two stereogenic centers to be (3*S*, 5*S*) by means of X-ray crystallographic analysis.[9] Thus, the absolute configuration of decarboxylative aldol product **3d** is assigned as *S*.

^{13}C NMR Spectra and Reaction Mechanism. To cast some light on the mechanism, we conducted ^{13}C NMR spectroscopic experiments in $CDCl_3$ (Figures 2 and 3). When one equivalent of β-ketoacid **1a** was added to the Ni-complex **I**, new signals appeared in the ^{13}C NMR spectra, indicating that a coordination exchange of a diamine ligand with β-ketoacid had occurred (Figure 2b and c). Spectra b and c bear greater similarity to spectrum d (the HCl salt of diamine) than spectrum e (diamine itself). Thus, one of the diamine ligands could be exchanged from the Ni-complex **I** by the substrate, and the liberated diamine could then deprotonate the metal-bound β-ketoacid. In sharp contrast, diamine ligand displacement with α-ketoester cannot be observed when one equiv of

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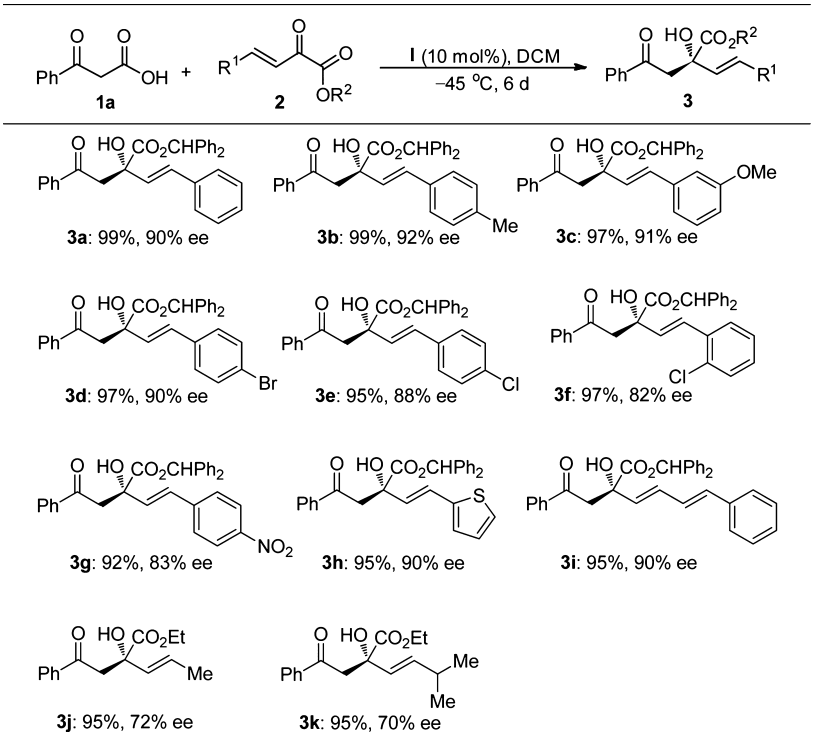
Table 2. Scope of the Ni-Catalyzed Asymmetric Decarboxylative Aldol Reaction with Various β,γ-Unsaturated α-Ketoesters 2[a]



[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.1 mmol), and catalyst **I** (10 mol %) in CH_2Cl_2 stirred for 6 days. Yield was isolated product from an average of two runs. The ee value was determined by HPLC analysis using a chiral stationary phase. The absolute configuration of other adducts was assigned analogous to that of **3d**.

α-ketoester **2e** was added to Ni-complex **I** (Figure 3). In addition, a control experiment in which acetophenone was used as a surrogate for 3-oxo-3-phenylpropanoic acid under otherwise identical reaction conditions did not afford aldol product **3a**. This observation suggests that the aldol reaction could occur prior to the decarboxylation step in this asymmetric decarboxylative transformation.

On the basis of our experimental results and previous studies,[6a] the decarboxylative aldol reaction is proposed to begin with the formation of intermediate **Int-1** upon treatment of β-ketoacid **1** with the Ni-complex followed by release of the HBr salt of diamine (Figure 4). The α-keto functionality of α-ketoester is coordinated to the metal center in the axial position with a concomitant hydrogen-bond interaction between the diamine ligand and α-ketoester, leading to square pyramidal transition states. For the binding of the β,γ-unsaturated α-ketoester, the substrate interacts with the metal center most likely in its *S*-cis form as the *S*-trans isomer is disfavored for steric reasons. In the favored transition state (**TS-1**), the N-benzyl group of the ligand is orientated away from the ester moiety of α-ketoester. Protonation of the product with the new reactant constitutes the final step of the catalytic cycle. However, the detailed mechanism of this decarboxylative aldol reaction remains to be elucidated.

CONCLUSION

In conclusion, we have successfully developed a highly chemo-, regio-, and enantioselective decarboxylative aldol reaction of β-ketoacids with β,γ-unsaturated α-ketoesters. In the presence of a Ni (II) complex, the reaction proceeded smoothly for a broad variety of β-ketoacids and β,γ-unsaturated α-ketoesters to afford highly functionalized chiral tertiary alcohols. Moreover, the aldol products obtained can be converted into optically pure isoxazoline and α-hydroxylactone derivatives. Further mechanistic investigation and extension of the reaction scope are underway in our laboratory.

EXPERIMENTAL SECTION

General Information. NMR were recorded at 400 or 600 MHz for ^{1}H NMR and at 100 or 150 MHz for ^{13}C NMR. Chemical shifts were reported in ppm from the solvent resonance as the internal standard ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), and dt (doublet of triplets). High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF-QII Instrument.

Materials. Tetrahydrofuran (THF), ether, and toluene were distilled from sodium/benzophenone. CH_2Cl_2 (DCM) was distilled from CaH_2; CH_3CN was distilled from P_2O_5. All commercially available reagents were used without further purification. Analytical thin layer chromatography was performed on 0.20 mm silica gel plates. Silica gel (200−300 mesh) was used for flash chromatography. The β,γ-unsaturated α-ketoesters were synthesized according to the literature.[10] All β-ketoacids were prepared according to the literature.[6a,7]

General Procedure for Preparation of Catalysts I−VI.[6a,11] Nickel(II)−bis[(*S*,*S*)-*N*,*N*′-dibenzylcyclohexane-1,2-diamine]Br_2 **I** and **IV** were prepared following reported procedures.[6a]

Nickel(II)−bis[(*S*,*S*)-*N*,*N*′-bis(4-methylbenzyl)-cyclohexane-1,2-diamine]Br_2 (II). A mixture of $NiBr_2$ (437 mg, 2 mmol) and (*S*,*S*)-*N*,*N*-bis(4-methylbenzyl)-cyclohexane-1,2-diamine (1.38 g, 4.3 mmol) in acetonitrile (50 mL) was refluxed for 5 h. Subsequent to solvent removal, the residue was dissolved in dichloromethane and filtered through a fritted glass funnel. The solvent was removed under reduced pressure, and the crude product was recrystallized from petroleum ether and ethyl acetate to yield the title compound as a microcrystalline pale green powder (1.38 g) in 80% yield. IR (KBr) ν:

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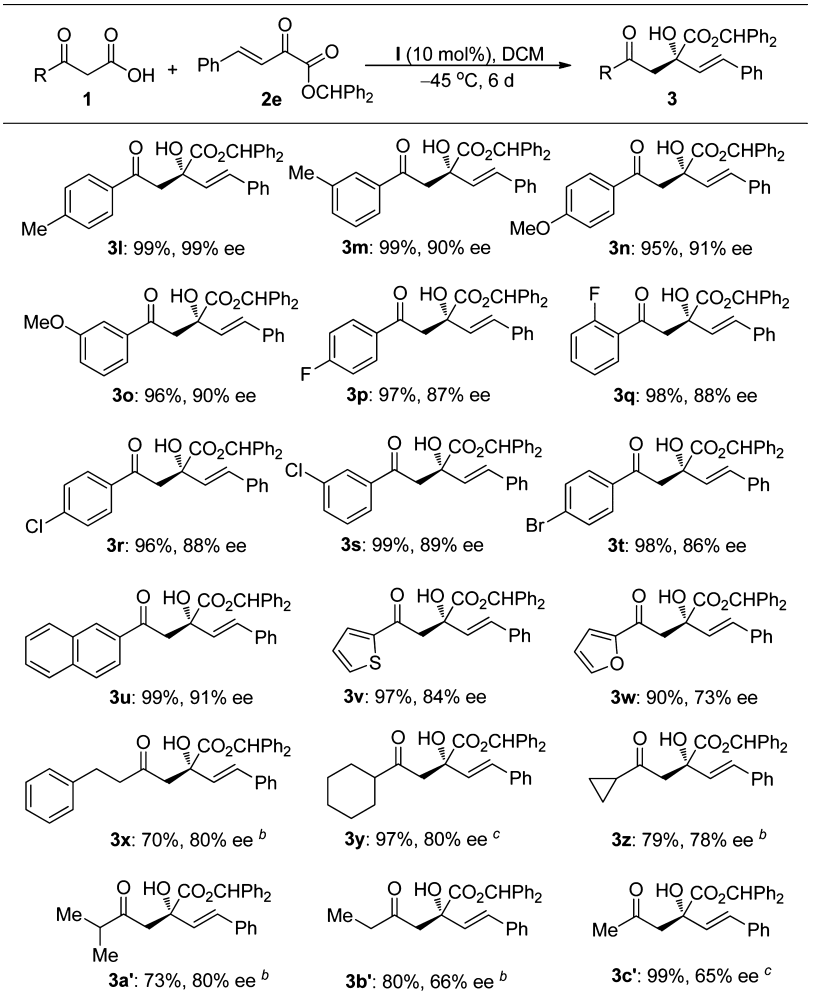
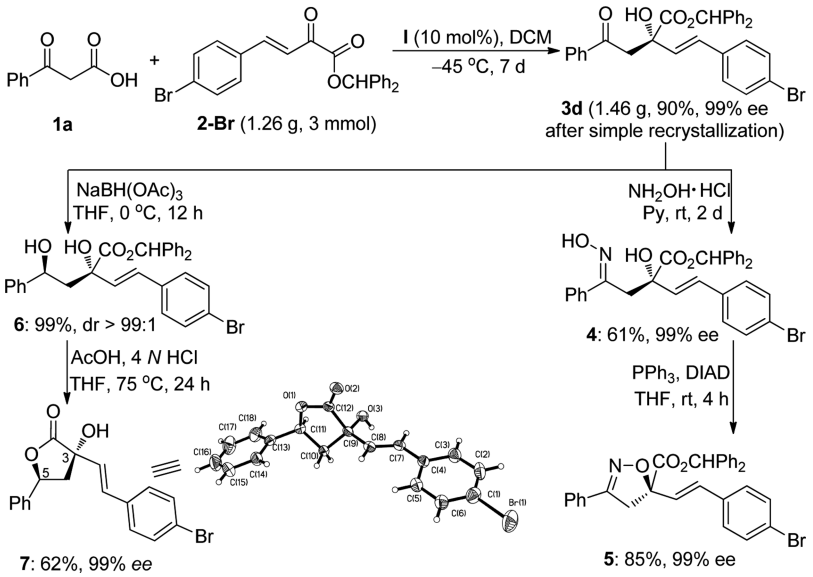
Table 3. Scope if the Ni-Catalyzed Asymmetric Decarboxylative Aldol Reaction with Various β-Ketoacids 1 and α-Ketoester 2e[a]



[a]Unless otherwise stated, the reaction conditions were as **1** (0.2 mmol), **2** (0.1 mmol), and catalyst **I** (10 mol %) in CH_2Cl_2 stirred for 6 days. Isolated yield was obtained from an average of two runs. The ee value was determined by HPLC analysis using a chiral stationary phase. The absolute configuration of other adducts was assigned analogous to that of **3d**. [b]Reaction temperature/time (°C/d): −35/5. [c]Reaction temperature/time (°C/d): −20/3.

Scheme 2. Scaled-up Version of the Decarboxylative Aldol Reaction and Synthetic Transformation



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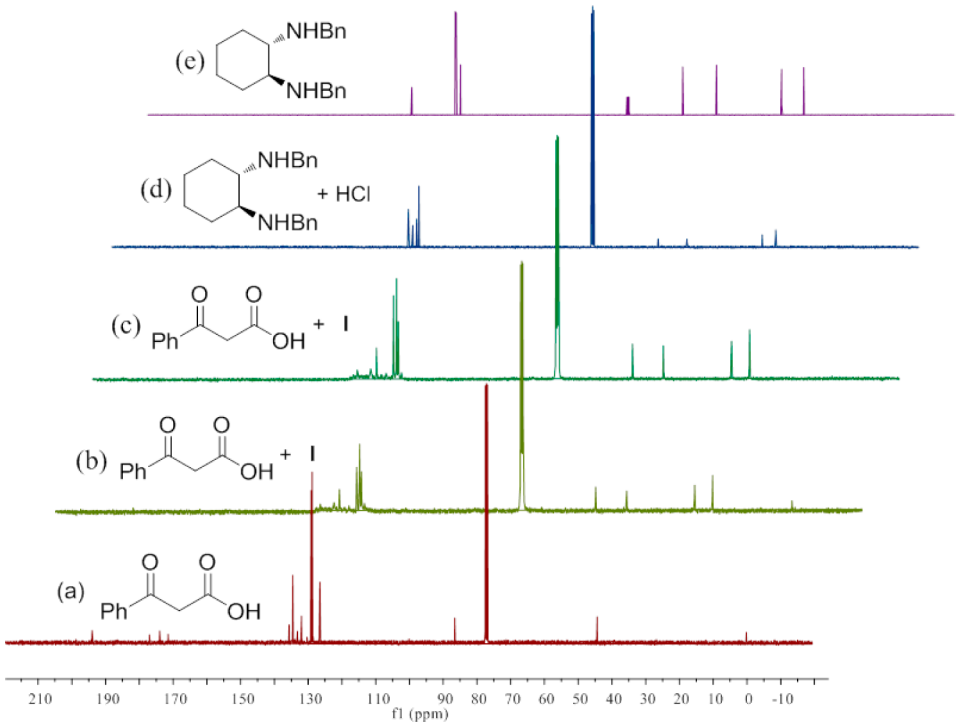

Figure 2. ^{13}C NMR spectra in $CDCl_3$ of (a) β-ketoacid **1a**, (b) a 1:1 mixture of Ni-complex **I** and β-ketoacid **1a** (10 min later), (c) a 1:1 mixture of Ni-complex **I** and β-ketoacid **1a** (2 h later), (d) diamine hydrochloride, and (e) diamine.

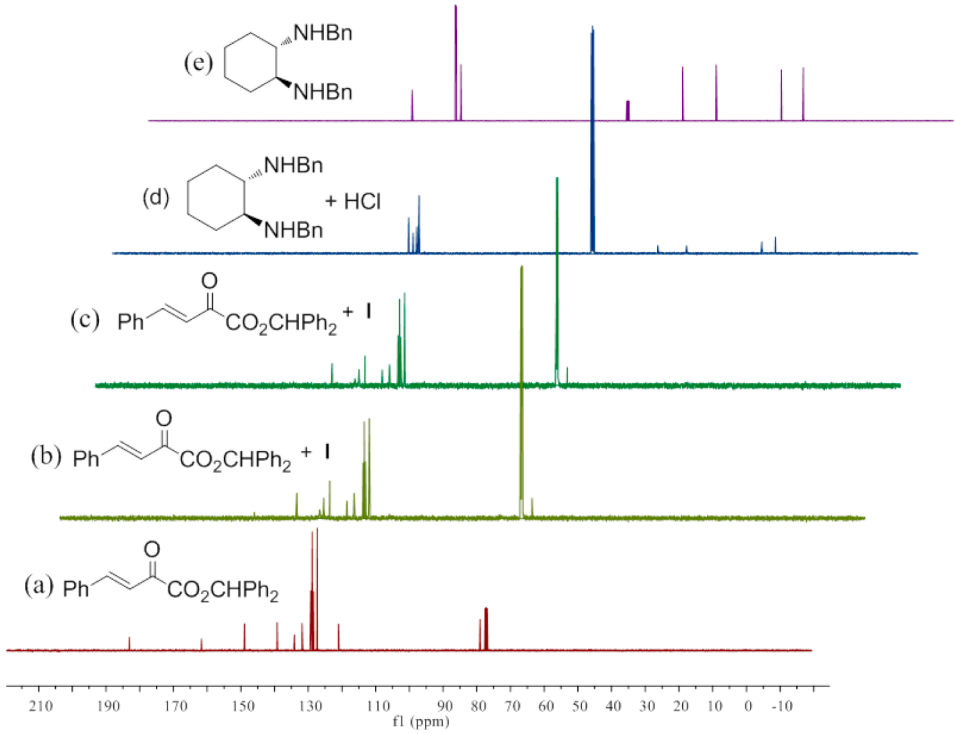

Figure 3. ^{13}C NMR spectra in $CDCl_3$ of (a) α-ketoester **2e**, (b) a 1:1 mixture of Ni-complex **I** and α-ketoester **2e** (10 min later), (c) 1:1 mixture of Ni-complex **I** and α-ketoester **2e** (1 h later), (d) diamine hydrochloride, and (e) diamine.

3354, 3286, 3048, 3014, 2932, 2857, 1572, 1515, 1447, 1384, 1159, 1116, 1058, 1033, 950, 895, 847, 753, 623 cm^{-1}; $[\alpha]_D^{25}$ + 30.1 (*c* 1.0, CH_2Cl_2).

Nickel(II)−bis[(*S*,*S*)-*N*,*N*′-bis(4-methoxybenzyl)-cyclohexane-1,2-diamine]Br_2 (III). A mixture of $NiBr_2$ (437 mg, 2 mmol) and (*S*,*S*)-*N*,*N*-bis(4-methoxybenzyl)-cyclohexane-1,2-diamine (1.52 g, 4.3 mmol) in acetonitrile (50 mL) was refluxed for 5 h. Subsequent to solvent removal, the residue was dissolved in dichloromethane and filtered through a fritted glass funnel. The solvent was removed under reduced pressure, and the crude product was recrystallized from dichloromethane/acetonitrile to yield the title compound as a blue crystal (1.67 g) in 90% yield. IR (KBr) ν: 3226, 3192, 3010, 2962, 2934, 2861, 1613, 1582, 1516, 1455, 1302, 1281, 1179, 1120, 1051, 985, 810, 704, 620 cm^{-1}; $[\alpha]_D^{25}$ + 34.4 (*c* 1.0, CH_2Cl_2).

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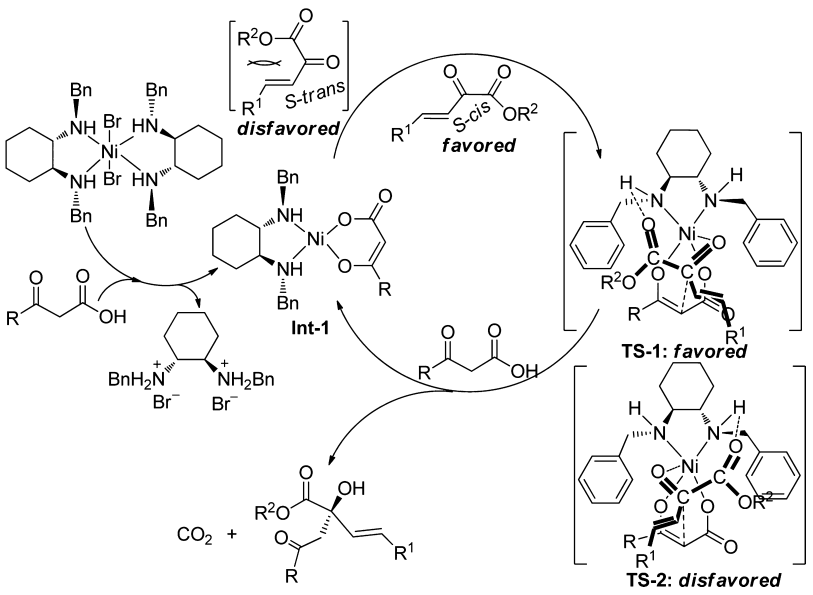

Figure 4. Proposed reaction mechanism.

Nickel(II)−bis[(*S,S*)-*N,N′*-bis(4-(trifluoromethyl)benzyl)-cyclohexane-1,2-diamine]Br_2 (V). A mixture of $NiBr_2$ (218.5 mg, 1 mmol) and (*S,S*)-*N,N*-bis(4-(trifluoromethyl)benzyl)-cyclo-hexane-1,2-diamine (0.93 g, 2.2 mmol) in acetonitrile (25 mL) was refluxed for 5 h. Subsequent to solvent removal, the residue was dissolved in dichloromethane and filtered through a fritted glass funnel. The solvent was removed under reduced pressure, and the crude product was recrystallized from petroleum ether and ethyl acetate to yield the title compound as a pale green powder (0.75 g) in 70% yield. IR (KBr) ν: 3413, 3271, 2940, 2864, 1620, 1459, 1328, 1168, 1123, 1018, 985, 841, 756, 645 cm^{-1}; $[\alpha]_D^{25}$ + 46.6 (*c* 1.0, CH_2Cl_2).

Nickel(II)−bis[(*S,S*)-*N,N′*-bis(naphthalen-2-ylmethyl)-cyclohexane-1,2-diamine]Br_2 (VI). A mixture of $NiBr_2$ (437 mg, 2 mmol) and (*S,S*)-*N,N*-bis(naphthalen-2-ylmethyl)-cyclohexane-1,2-diamine (1.70 g, 4.3 mmol) in acetonitrile (50 mL) was refluxed for 5 h. Subsequent to solvent removal, the residue was dissolved in dichloromethane and filtered through a fritted glass funnel. The solvent was removed under reduced pressure, and the crude product was recrystallized from dichloromethane/acetonitrile to yield the title compound as a pale green powder (1.71 g) in 85% yield. IR (KBr) ν: 3280, 3046, 3008, 2932, 2858, 1599, 1512, 1148, 1398, 1354, 1165, 1095, 974, 934, 895, 788, 769 cm^{-1}; $[\alpha]_D^{25}$ + 26.3 (*c* 1.0, CH_2Cl_2).

General Procedure for the Aldol Reaction of *β*-Ketoacids 1 and *β,γ*-Unsaturated *α*-Ketoesters 2. To a 10 mL Schlenk flask equipped with a stirring bar were added *β,γ*-unsaturated *α*-ketoesters **2** (0.1 mmol), Ni-complex **I** (10 mol %), and CH_2Cl_2 (2.0 mL). The mixture was stirred at −45 °C for 5 min. Then, *β*-ketoacid **1** (0.2 mmol) was added in one portion, and the resulting mixture was stirred at the same temperature. After completion of the reaction (monitored by TLC), the residue was purified by column chromatography on silica gel (eluted with 10:1 petroleum ether/ethyl acetate) to give product **3**.

Benzhydryl (*S,E*)-2-Hydroxy-2-(2-oxo-2-phenylethyl)-4-phenylbut-3-enoate (3a). Results in 45.7 mg, 99% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IA, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 53.6 min (major), and t_R = 30.5 min (minor)); mp 105−106 °C; $[\alpha]_D^{25}$ − 26.8 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.56; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.41−7.31 (m, 10H), 7.25 (s, 5H), 7.02 (s, 1H), 6.95 (d, *J* = 15.9 Hz, 1H), 6.34 (d, *J* = 15.9 Hz, 1H), 4.33 (s, 1H), 3.91 (d, *J* = 17.6 Hz, 1H), 3.57 (d, *J* = 17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 172.9, 139.4, 139.3, 136.4, 136.1, 133.7, 131.4, 128.7, 128.6, 128.5, 128.5, 128.40, 128.2, 128.1, 128.1, 128.0, 127.3, 127.3, 126.8, 78.7, 75.7, 47.3; IR (KBr) ν 3542, 3060, 3029, 2923, 2854, 1730, 1681, 1596, 1494, 1449, 1356, 1208, 1133, 975, 748, 697 cm^{-1}; HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{31}H_{26}O_4$+Na 485.1729, found 485.1729.

Benzhydryl (*S,E*)-2-Hydroxy-2-(2-oxo-2-phenylethyl)-4-(*p*-tolyl)but-3-enoate (3b). Results in 47.2 mg, 99% yield, and 92% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 13.0 min (major) and t_R = 15.2 min (minor)); mp 170−171 °C; $[\alpha]_D^{25}$ − 23.5 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.43; ^1H NMR (600 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.57 (s, 1H), 7.45 (s, 2H), 7.37−7.08 (m, 14H), 6.95 (s, 1H), 6.85 (d, *J* = 15.6 Hz, 1H), 6.23 (d, *J* = 15.6 Hz, 1H), 4.25 (s, 1H), 3.85 (d, *J* = 17.4 Hz, 1H), 3.51 (d, *J* = 17.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.0 173.0, 139.4, 139.3, 138.0, 136.3, 133.7, 133.3, 131.2, 129.4, 128.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.3, 127.3, 127.3, 126.7, 78.7, 75.6, 47.3, 21.3; IR (KBr) ν 3548, 3058, 3030, 2922, 2856, 1729, 1677, 1592, 1494, 1450, 1344, 1256, 1190, 1127, 988, 750, 698 cm^{-1}; HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{32}H_{28}O_4$+Na 499.1885, found 499.1885.

Benzhydryl (*S,E*)-2-Hydroxy-4-(3-methoxyphenyl)-2-(2-oxo-2-phenylethyl)but-3-enoate (3c). Results in 47.7 mg, 97% yield, and 91% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 17.0 min (major), and t_R = 19.9 min (minor)); mp 72−73 °C; $[\alpha]_D^{25}$ − 24.4 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.33; ^1H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.1 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.34−7.28 (m, 4H), 7.26−7.14 (m, 7H), 6.96 (s, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.88−6.83 (m, 2H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.28 (d, *J* = 15.9 Hz, 1H), 4.28 (s, 1H), 3.86 (d, *J* = 17.6 Hz, 1H), 3.79 (s, 3H), 3.51 (d, *J* = 17.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.9, 172.9, 159.8, 139.3, 139.2, 137.5, 136.3, 133.8, 131.3, 129.6, 128.7, 128.6, 128.6, 128.4, 128.3, 128.2, 128.1, 127.3, 127.3, 119.4, 113.9, 111.9, 78.7, 75.6, 55.3, 47.3; IR (KBr) ν 3538, 3060, 3031, 2920, 2834, 1734, 1682, 1592, 1492, 1453, 1349, 1233, 1201, 1127, 1038, 751, 695 cm^{-1}; HRMS (ESI) *m/z* $[M + Na]^+$ calcd for $C_{32}H_{28}O_5$+Na 515.1834, found 515.1834.

Benzhydryl (*S,E*)-4-(4-Bromophenyl)-2-hydroxy-2-(2-oxo-2-phenylethyl)but-3-enoate (3d). Results in 52.5 mg, 97% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IA, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 52.1 min (major), and t_R = 21.2 min (minor)); mp 133−134 °C; $[\alpha]_D^{25}$ − 25.0 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.47; ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.0 Hz, 1H), 7.35 (m, 4H), 7.26−7.17 (m, 5H), 7.15−7.05 (m, 7H), 6.88 (s, 1H), 6.73 (d, *J* = 15.8 Hz, 1H), 6.18 (d, *J*

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= 15.8 Hz, 1H), 4.21 (s, 1H), 3.76 (d, J = 17.5 Hz, 1H), 3.42 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 172.7, 139.3, 139.1, 136.2, 135.0, 133.9, 131.8, 130.3, 129.1, 128.8, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 127.3, 127.3, 122.0, 78.8, 75.6, 47.2; IR (KBr) ν 3549, 3060, 3029, 2938, 2908, 1724, 1670, 1591, 1491, 1358, 1212, 1173, 1066, 975, 809, 696 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}BrO_4$+Na 563.0834, found 563.0836.

Benzhydryl (*S*,*E*)-4-(4-Chlorophenyl)-2-hydroxy-2-(2-oxo-2-phenylethyl)but-3-enoate (3e). Results in 47.2 mg, 95% yield, and 88% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 12.2 min (major), and t_R = 13.5 min (minor)); mp 139−140 °C; $[\alpha]_D^{25}$ − 24.0 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.47; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, J = 7.4 Hz, 2H), 7.51 (t, J = 7.0 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.26−7.09 (m, 14H), 6.88 (s, 1H), 6.76 (d, J = 15.8 Hz, 1H), 6.17 (d, J = 15.8 Hz, 1H), 4.20 (s, 1H), 3.77 (d, J = 17.5 Hz, 1H), 3.42 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.8, 172.8, 139.3, 139.2, 136.2, 134.6, 133.8, 133.8, 130.2, 128.9, 128.8, 128.7, 128.6, 128.4, 128.2, 128.2, 128.1, 128.0, 127.3, 127.3, 78.8, 75.6, 47.2; IR (KBr) ν 3551, 3062, 3032, 2956, 2917, 1732, 1673, 1593, 1492, 1340, 1343, 1281, 1220, 1132, 1091, 988, 749, 699 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}ClO_4$+Na 519.1339, found 519.1338.

Benzhydryl (*S*,*E*)-4-(2-Chlorophenyl)-2-hydroxy-2-(2-oxo-2-phenylethyl)but-3-enoate (3f). Results in 48.2 mg, 97% yield, and 82% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 17.5 min (major), and t_R = 14.7 min (minor)); mp 85−86 °C; $[\alpha]_D^{25}$ − 22.1 (c 1.0 CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.43; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.39−7.16 (m, 15H), 6.97 (s, 1H), 6.26 (d, J = 15.8 Hz, 1H), 4.29 (s, 1H), 3.87 (d, J = 17.5 Hz, 1H), 3.55 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 172.7, 139.3, 139.2, 136.2, 134.4, 133.8, 133.5, 131.4, 129.8, 129.1, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.3, 127.3, 127.2, 126.9, 78.8, 75.8, 47.2; IR (KBr) ν 3539, 3062, 3031, 2922, 2856, 1738, 1682, 1593, 1447, 1353, 1203, 1134, 1077, 1031, 986, 753, 698 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}ClO_4$+Na 519.1339, found 519.1343.

Benzhydryl (*S*,*E*)-2-Hydroxy-4-(4-nitrophenyl)-2-(2-oxo-2-phenylethyl)but-3-enoate (3g). Results in 46.7 mg, 92% yield, and 83% ee of a light yellow solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 61.2 min (major), and t_R = 48.3 min (minor)); mp 137−138 °C; $[\alpha]_D^{25}$ − 25.8 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.26; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, J = 8.5 Hz, 2H), 7.91 (d, J = 7.7 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.36−7.16 (m, 10H), 7.04−6.91 (m, 2H), 6.45 (d, J = 15.8 Hz, 1H), 4.36 (s, 1H), 3.89 (d, J = 17.5 Hz, 1H), 3.52 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.6, 172.4, 147.2, 142.5, 139.2, 139.0, 136.1, 134.0, 133.0, 129.5, 128.8, 128.6, 128.5, 128.3, 128.3, 128.2, 127.4, 127.3, 127.3, 124.1, 79.0, 75.7, 47.1; IR (KBr) ν 3535, 3067, 3031, 2929, 2844, 1740, 1664, 1595, 1514, 1340, 1180, 1144, 1069, 968, 839, 749, 696 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}NO_6$+Na 530.1580, found 530.1580.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-oxo-2-phenylethyl)-4-(thiophen-2-yl)but-3-enoate (3h). Results in 44.5 mg, 95% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AD, 50:50 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.5 mL/min, t_R = 155.9 min (major), and t_R = 80.7 min (minor)); mp 113−114 °C; $[\alpha]_D^{25}$ − 16.4 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.40; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.32−7.18 (m, 10H), 7.01 (d, J = 15.6 Hz, 1H), 6.95 (t, J = 5.0 Hz, 3H), 6.14 (d, J = 15.6 Hz, 1H), 4.24 (s, 1H), 3.82 (d, J = 17.6 Hz, 1H), 3.50 (d, J = 17.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 172.8, 141.1, 139.2, 139.2, 136.2, 133.8, 128.7, 128.6, 128.4, 128.2, 128.2, 128.1, 127.6, 127.4, 127.2, 127.0, 125.0, 124.8, 78.8, 75.3, 47.2; IR (KBr) ν 3542, 3059, 3028, 2947, 2917, 1733, 1677, 1593, 1450, 1349, 1263, 1201, 1121, 974, 750, 700 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{29}H_{24}O_4S$+Na 491.1293, found 491.1293.

Benzhydryl (*S*,*3E*,*5E*)-2-Hydroxy-2-(2-oxo-2-phenylethyl)-6-phenylhexa-3,5-dienoate (3i). Results in 46.5 mg, 95% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 220 nm UV detector, 0.8 mL/min, t_R = 14.1 min (major), and t_R = 20.3 min (minor)); mp 164−165 °C; $[\alpha]_D^{25}$ − 60.8 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, J = 5.6 Hz, 2H), 7.56 (s, 1H), 7.45−7.17 (m, 17H), 6.94 (s, 1H), 6.69 (dt, J = 24.7, 11.2 Hz, 2H), 6.54 (d, J = 15.2 Hz, 1H), 5.89 (d, J = 15.2 Hz, 1H), 4.21 (s, 1H), 3.79 (d, J = 17.3 Hz, 1H), 3.46 (d, J = 17.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.9, 172.8, 139.4, 139.3, 137.0, 136.4, 134.3, 133.7, 132.0, 131.8, 128.7, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.4, 127.4, 127.3, 126.6, 78.7, 75.5, 47.3; IR (KBr) ν 3558, 3060, 3025, 2913, 2667, 1741, 1671, 1592, 1492, 1450, 1352, 1279, 1223, 1187, 1002, 750, 695 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{33}H_{28}O_4$+Na 511.1885, found 511.1882.

Ethyl (*S*,*E*)-2-Hydroxy-2-(2-oxo-2-phenylethyl)pent-3-enoate (3j). Results in 24.9 mg, 95% yield, and 72% ee of a colorless oil as determined by HPLC analysis (Daicel Chiralpak AS, 90:10 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 12.4 min (major), and t_R = 21.9 min (minor)); $[\alpha]_D^{25}$ − 59.6 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.48; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, J = 7.7 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 6.02 (dd, J = 15.2, 6.7 Hz, 1H), 5.60 (d, J = 15.3 Hz, 1H), 4.25 (dd, J = 7.0, 2.5 Hz, 2H), 4.00 (s, 1H), 3.67 (d, J = 17.6 Hz, 1H), 3.40 (d, J = 17.6 Hz, 1H), 1.75 (d, J = 6.5 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.2, 174.3, 136.3, 133.6, 130.6, 128.7, 128.2, 127.3, 75.0, 62.0, 47.4, 17.7, 14.1; IR (KBr) ν 3524, 3032, 2980, 2918, 2853, 1735, 1685, 1597, 1562, 1449, 1388, 1359, 1264, 1206, 1144, 998, 855, 757, 690 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{15}H_{18}O_4$+Na 285.1103, found 285.1100.

Ethyl (*S*,*E*)-2-Hydroxy-5-methyl-2-(2-oxo-2-phenylethyl)hex-3-enoate (3k). Results in 27.6 mg, 95% yield, and 70% ee of a colorless oil as determined by HPLC analysis (Daicel Chiralpak AS, 90:10 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 9.8 min (major), and t_R = 14.5 min (minor)); $[\alpha]_D^{25}$ − 50.9 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.52; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J = 7.9 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.7 Hz, 2H), 5.99 (dd, J = 15.5, 6.6 Hz, 1H), 5.52 (d, J = 15.6 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.00 (s, 1H), 3.67 (d, J = 17.5 Hz, 1H), 3.39 (d, J = 17.6 Hz, 1H), 2.37−2.31 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.01 (dd, J = 6.7, 2.4 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.3, 174.4, 139.2, 136.5, 133.6, 128.7, 128.2, 126.7, 75.0, 62.0, 47.5, 30.7, 22.2, 22.1, 14.1; IR (KBr) ν 3520, 3062, 2961, 2930, 2871, 1733, 1686, 1598, 1451, 1360, 1249, 980, 856, 758, 691, 588 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{17}H_{22}O_4$+Na 313.1416, found 313.1412.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-oxo-2-(*p*-tolyl)ethyl)-4-phenylbut-3-enoate (3l). Results in 47.1 mg, 99% yield, and 99% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 16.3 min (major)); mp 131−132 °C; $[\alpha]_D^{25}$ − 32.0 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.60; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 7.8 Hz, 2H), 7.36−7.16 (m, 17H), 6.95 (s, 1H), 6.88 (d, J = 15.9 Hz, 1H), 6.27 (d, J = 15.9 Hz, 1H), 4.32 (s, 1H), 3.84 (d, J = 17.5 Hz, 1H), 3.48 (d, J = 17.5 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.6, 172.9, 144.7, 139.4, 139.3, 136.1, 133.9, 131.3, 129.4, 128.6, 128.6, 128.4, 128.4, 128.1, 128.1, 128.0, 127.3, 127.3, 126.8, 78.7, 75.7, 47.2, 21.8; IR (KBr) ν 3529, 3059, 3029, 2916, 1736, 1677, 1605, 1450, 1351, 1234, 1192, 1130, 980, 809, 748, 697 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{32}H_{28}O_4$+Na 499.1885, found 499.1889.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-oxo-2-(m-tolyl)ethyl)-4-phenylbut-3-enoate (3m). Results in 47.2 mg, 99% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 14.0 min (major), and t_R = 12.9 min (minor)); mp 107−108 °C; $[\alpha]_D^{25}$ − 27.5 (c 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum

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ether) R_f = 0.60; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (s, 2H), 7.42−7.16 (m, 17H), 6.96 (s, 1H), 6.89 (d, J = 15.9 Hz, 1H), 6.28 (d, J = 15.9 Hz, 1H), 4.30 (s, 1H), 3.85 (d, J = 17.6 Hz, 1H), 3.50 (d, J = 17.6 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.2, 172.9, 139.4, 139.3, 138.5, 136.4, 136.1, 134.6, 131.4, 128.8, 128.7, 128.6, 128.6, 128.4, 128.1, 128.1, 128.0, 127.4, 127.3, 126.8, 125.5, 78.7, 75.7, 47.4, 21.4; IR (KBr) ν 3485, 3059, 3030, 2922, 2859, 1733, 1676, 1600, 1493, 1354, 1245, 1200, 1109, 987, 746, 695 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{32}H_{28}O_4$+Na 499.1885, found 499.1885.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-(4-methoxyphenyl)-2-oxoethyl)-4-phenylbut-3-enoate (3n). Results in 46.7 mg, 95% yield, and 91% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 33.2 min (major), and t_R = 45.7 min (minor)); mp 104−105 °C; $[\alpha]_D^{25}$ − 31.4 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 8.7 Hz, 2H), 7.35−7.28 (m, 9H), 7.25−7.16 (m, 6H), 6.97−6.86 (m, 4H), 6.28 (d, J = 15.9 Hz, 1H), 4.39 (s, 1H), 3.88−3.81 (m, 4H), 3.44 (d, J = 17.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.5, 173.0 164.0, 139.4, 139.3, 136.1, 131.3, 130.6, 129.3, 128.7, 128.6, 128.4, 128.1, 128.10 128.0, 127.3, 127.3, 126.8 113.9, 78.6, 75.8, 55.6, 46.9; IR (KBr) ν 3525, 3060, 3029, 2937, 2839, 1739, 1669, 1600, 1453, 1353, 1176, 1025, 976, 747, 697 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{32}H_{28}O_5$+Na 515.1834, found 515.1833.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-(3-methoxyphenyl)-2-oxoethyl)-4-phenylbut-3-enoate (3o). Results in 47.3 mg, 96% yield, and 90% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 16.2 min (major), and t_R = 21.7 min (minor)); mp 40−41 °C; $[\alpha]_D^{25}$ − 19.6 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.51; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, J = 7.5 Hz, 1H), 7.32 (s, 1H), 7.28−7.19 (m, 9H), 7.19−7.15 (m, 2H), 7.13 (m, 5H), 7.04 (dd, J = 8.1, 1.9 Hz, 1H), 6.88 (s, 1H), 6.80 (d, J = 15.9 Hz, 1H), 6.19 (d, J = 15.9 Hz, 1H), 4.18 (s, 1H), 3.78−3.69 (m, 4H), 3.42 (d, J = 17.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.7, 172.9, 159.9, 139.4, 139.2, 137.6,136.1, 131.4, 129.7, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.3, 127.3, 126.8, 121.0, 120.5,112.2, 78.7, 75.6, 55.5, 47.4; IR (KBr) ν 3512, 3061, 3030, 2927, 2839, 1740, 1681, 1590, 1453, 1258, 1201, 1131, 967, 750, 696 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{32}H_{28}O_5$+Na 515.1834, found 515.1835.

Benzhydryl (*S*,*E*)-2-(2-(4-Fluorophenyl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3p). Results in 46.6 mg, 97% yield, and 87% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 20.5 min (major), and t_R = 17.4 min (minor)); mp 139−140 °C; $[\alpha]_D^{25}$ − 21.8 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.55; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87−7.80 (m, 2H), 7.26−7.10 (m, 15H), 7.03 (t, J = 8.2 Hz, 2H), 6.88 (s, 1H), 6.80 (d, J = 15.8 Hz, 1H), 6.19 (d, J = 15.8 Hz, 1H), 4.16 (s, 1H), 3.73 (d, J = 17.4 Hz, 1H), 3.39 (d, J = 17.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.2, 172.9, 166.2 (d, J_{C-F} = 255.0 Hz), 139.3, 139.2, 136.0, 132.8 (d, J_{C-F} = 1.5 Hz), 131.5, 131.0 (d, J_{C-F} = 9.0 Hz) 128.7, 128.6, 128.4, 128.2, 128.2, 128.1, 127.4, 127.2, 126.8, 115.9 (d, J_{C-F} = 21.0 Hz), 78.8, 75.6, 47.2; IR (KBr) ν 3538, 3059, 3031, 2956, 2918, 1747, 1663, 1596, 1500, 1373, 1340, 1221, 1168, 1005, 972, 749, 699 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}FO_4$+Na 503.1635, found 503.1641.

Benzhydryl (*S*,*E*)-2-(2-(2-Fluorophenyl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3q). Results in 49.2 mg, 98% yield, and 88% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 11.2 min (major), and t_R = 10.3 min (minor)); mp 100−101 °C; $[\alpha]_D^{25}$ − 21.3 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.55; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (t, J = 7.1 Hz, 1H), 7.44 (q, J = 6.0 Hz, 1H), 7.29−7.21 (m, 8H), 7.19 (m, 2H), 7.16−7.09 (m, 6H), 7.06−7.01 (m, 1H), 6.89 (s, 1H), 6.80 (d, J = 15.6 Hz, 1H), 6.18 (d, J = 15.6 Hz, 1H), 4.06 (s, 1H), 3.73−3.86 (m, 1H), 3.38−3.52 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.7, 173.0, 162.3 (d, J_{C-F} = 253.5 Hz), 139.3, 139.2, 136.1, 135.4, 135.4, 131.4, 130.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.3, 127.2, 126.8, 124.8, 124.7, 124.60 (d, J_{C-F} = 12 Hz), 116.8 (d, J_{C-F} = 24 Hz), 78.7, 75.5 (d, J_{C-F} = 1.5 Hz), 52.2 (d, J_{C-F} = 9 Hz); IR (KBr) ν 3474, 3067, 3029, 2928, 2859, 1716, 1609, 1487, 1451, 1349, 1255, 1204, 1130, 1071, 971, 748, 697 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}FO_4$+Na 503.1635, found 503.1635.

Benzhydryl (*S*,*E*)-2-(2-(4-Chlorophenyl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3r). Results in 47.7 mg, 96% yield, and 88% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 23.1 min (major), and t_R = 18.4 min (minor)); mp 147−148 °C; $[\alpha]_D^{25}$ − 21.6 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.61; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.26−7.08 (m, 15H), 6.88 (s, 1H), 6.80 (d, J = 15.8 Hz, 1H), 6.19 (d, J = 15.8 Hz, 1H), 4.12 (s, 1H), 3.72 (d, J = 17.5 Hz, 1H), 3.39 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.6, 172.8, 140.3, 139.2, 139.2, 136.0, 134.6, 131.5, 129.7, 129.1, 128.7, 128.6, 128.4, 128.2, 128.1, 127.4, 127.2, 126.8, 78.8, 75.6, 47.3; IR (KBr) ν 3527, 3058, 3029, 2962, 2872, 1747, 1667, 1592, 1492, 1452, 1404, 1250, 1171, 972, 808, 749, 699 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}ClO_4$+Na 519.1339, found 519.1339.

Benzhydryl (*S*,*E*)-2-(2-(3-Chlorophenyl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3s). Results in 49.2 mg, 99% yield, and 89% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IA, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 49.0 min (major), and t_R = 27.3 min (minor)); mp 96−97 °C; $[\alpha]_D^{25}$ − 15.0 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.62; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.41 (t, J = 7.9 Hz, 1H), 7.35−7.31 (m, 8H), 7.30−7.27 (m, 2H), 7.18−7.25 (m, 5H), 6.97 (s, 1H), 6.89 (d, J = 15.9 Hz, 1H), 6.27 (d, J = 15.9 Hz, 1H), 4.16 (s, 1H), 3.80 (d, J = 17.6 Hz, 1H), 3.49 (d, J = 17.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.6, 172.8, 139.3, 139.2, 137.9, 137.3, 137.2, 136.0, 135.1, 133.9, 133.7, 133.6, 131.6, 130.0, 128.8, 128.7, 128.6, 128.5, 128.5, 128.3, 128.2, 128.2, 128.2, 127.4, 127.2, 126.8, 126.3, 78.9, 75.6, 47.5; IR (KBr) ν 3482, 3131, 3065, 3030, 2946, 1730, 1681, 1569, 1400, 1353, 1251, 1199, 1106, 967, 746, 695 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}ClO_4$+Na 519.1339, found 519.1340.

Benzhydryl (*S*,*E*)-2-(2-(4-Bromophenyl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3t). Results in 52.5 mg, 98% yield, and 86% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IB, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 33.6 min (major), and t_R = 29.3 min (minor)); mp 149−150 °C; $[\alpha]_D^{25}$ − 24.0 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.48; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 7.6 Hz, 2H), 7.28−7.09 (m, 15H), 6.88 (s, 1H), 6.80 (d, J = 15.8 Hz, 1H), 6.19 (d, J = 15.8 Hz, 1H), 4.11 (s, 1H), 3.71 (d, J = 17.5 Hz, 1H), 3.39 (d, J = 17.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.8, 172.8, 139.2, 139.1, 136.0, 135.0, 132.0, 131.5, 129.7, 129.0, 128.7, 128.6, 128.4, 128.2, 128.2, 128.1, 127.4, 127.2, 126.8, 78.8, 75.6, 47.2; IR (KBr) ν 3439, 3059, 3030, 2921, 2855, 1743, 1671, 1586, 1492, 1451, 1372, 1178, 1071, 997, 911, 748, 700 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{31}H_{25}BrO_4$+Na 563.0834, found 563.0835.

Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-(naphthalen-2-yl)-2-oxoethyl)-4-phenylbut-3-enoate (3u). Results in 50.7 mg, 99% yield, and 91% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.7 mL/min, t_R = 34.4 min (major), and t_R = 46.9 min (minor)); mp 137−138 °C; $[\alpha]_D^{25}$ − 25.0 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.61; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.01−7.82 (m, 4H), 7.62 (t, J = 6.8 Hz, 1H), 7.56 (t, J = 6.8 Hz, 1H), 7.39−7.12 (m, 15H), 6.98 (s, 1H), 6.93 (d, J = 15.8 Hz, 1H), 6.33 (d, J = 15.8 Hz, 1H), 4.33 (s, 1H), 4.00 (d, J = 17.4 Hz, 1H), 3.66 (d, J = 17.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 173.0, 139.3, 139.2, 136.1, 135.9, 133.7, 132.4, 131.4, 130.3, 129.7, 128.9, 128.7, 128.6, 128.6, 128.4, 128.4, 128.1, 128.0, 127.9, 127.3, 127.3, 127.0, 126.8, 123.6, 78.7, 75.7, 47.4; IR (KBr) ν 3417, 3061, 3029, 2957, 2924, 2855, 1723, 1678, 1595, 1494, 1453, 1399, 1259, 1186, 1124, 966, 752, 699 cm^{-1}; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{35}H_{28}O_4$+Na 535.1885, found 535.1888.

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Benzhydryl (*S*,*E*)-2-Hydroxy-2-(2-oxo-2-(thiophen-2-yl)-ethyl)-4-phenylbut-3-enoate (3v). Results in 45.4 mg, 97% yield, and 84% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 22.1 min (major), and t_R = 30.0 min (minor)); mp 148−149 °C; $[\alpha]_D^{25}$ − 15.2 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 3.5 Hz, 1H), 7.68 (d, *J* = 4.8 Hz, 1H), 7.35−7.26 (m, 10H), 7.23 (s, 5H), 7.13 (t, *J* = 4.2 Hz, 1H), 6.95 (s, 1H), 6.87 (d, *J* = 15.9 Hz, 1H), 6.27 (d, *J* = 15.9 Hz, 1H), 4.27 (s, 1H), 3.78 (d, *J* = 17.0 Hz, 1H), 3.45 (d, *J* = 17.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 190.5, 172.7, 143.4, 139.3, 139.2, 136.0, 134.8, 132.9, 131.4, 128.7, 128.6, 128.4, 128.4, 128.2, 128.1, 128.1, 127.4, 127.2, 126.8, 78.9, 75.7, 47.6; IR (KBr) ν 3551, 3058, 3028, 2921, 1735, 1649, 1453, 1413, 1293, 1189, 1129, 970, 858, 799, 751, 734, 699 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{24}O_4S$+Na 491.1293, found 491.1293.

Benzhydryl (*S*,*E*)-2-(2-(Furan-2-yl)-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3w). Results in 40.7 mg, 90% yield, and 73% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 23.6 min (major), and t_R = 29.2 min (minor)); mp 67−68 °C; $[\alpha]_D^{25}$ − 17.8 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.30; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.35−7.28 (m, 9H), 7.27−7.22 (m, 6H), 7.20 (d, *J* = 3.3 Hz, 1H), 6.95 (s, 1H), 6.86 (d, *J* = 15.9 Hz, 1H), 6.54 (d, *J* = 2.0 Hz, 1H), 6.27 (d, *J* = 15.9 Hz, 1H), 4.23 (s, 1H), 3.69 (d, *J* = 17.1 Hz, 1H), 3.41 (d, *J* = 17.1 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.5, 172.7, 152.2, 147.0, 139.2, 139.2, 136.0, 131.4, 128.6, 128.6, 128.4, 128.2, 128.2, 128.1, 128.1, 127.4, 127.2, 126.8, 118.2, 112.6, 78.9, 75.6, 46.6; IR (KBr) ν 3444, 3061, 3029, 2922, 2858, 1740, 1666, 1567, 1465, 1397, 1258, 1178, 1138, 974, 911, 752, 698 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{24}O_5$+Na 475.1521, found 475.1521.

Benzhydryl (*S*)-2-Hydroxy-4-oxo-6-phenyl-2-(*E*)-styrylhexanoate (3x). Results in 34.4 mg, 70% yield, and 80% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.7 mL/min, t_R = 20.6 min (major), and t_R = 25.4 min (minor)); mp 100−101 °C; $[\alpha]_D^{25}$ − 21.6 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.56; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.23 (m, 17H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 2H), 6.94 (s, 1H), 6.79 (d, *J* = 15.6 Hz, 1H), 6.17 (d, *J* = 15.6 Hz, 1H), 4.10 (s, 1H), 3.27 (d, *J* = 17.4 Hz, 1H), 2.91 (d, *J* = 17.4 Hz, 1H), 2.85−2.64 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.8, 172.8, 140.7, 139.3, 139.2, 136.0, 131.3, 128.6, 128.6, 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 127.5, 127.1, 126.8, 126.2, 78.8, 75.5, 50.8, 45.0, 29.2; IR (KBr) ν 3557, 3061, 3026, 2949, 2895, 1731, 1712, 1560, 1495, 1451, 1405, 1254, 1197, 1090, 1046, 898, 752, 702 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{30}O_4$+Na 513.2042, found 513.2044.

Benzhydryl (*S*,*E*)-2-(2-Cyclohexyl-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3y). Results in 45.4 mg, 97% yield, and 80% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak OD, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.7 mL/min, t_R = 21.5 min (major), and t_R = 40.6 min (minor)); mp 115−116 °C; $[\alpha]_D^{25}$ − 17.2 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.63; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33−7.21 (m, 15H), 6.93 (s, 1H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.17 (d, *J* = 15.9 Hz, 1H), 4.19 (s, 1H), 3.34 (d, *J* = 17.7 Hz, 1H), 2.93 (d, *J* = 17.7 Hz, 1H), 2.26 (dd, *J* = 14.0, 7.1 Hz, 1H), 1.81−1.60 (m, 5H), 1.30−1.13 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.2, 172.9, 139.3, 139.3, 136.1, 131.1, 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 127.6, 127.1, 126.7, 78.6, 75.5, 50.9, 48.8, 28.1, 28.0, 25.8, 25.5; IR (KBr) ν 3546, 3060, 3029, 2929, 2853, 1736, 1691, 1596, 1495, 1384, 1287, 1174, 1140, 1026, 977, 750, 699 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{32}O_4$+Na 491.2198, found 491.2201.

Benzhydryl (*S*,*E*)-2-(2-Cyclopropyl-2-oxoethyl)-2-hydroxy-4-phenylbut-3-enoate (3z). Results in 33.7 mg, 79% yield, and 78% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak AS, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 13.8 min (major), and t_R = 16.7 min (minor)); mp 119−120 °C; $[\alpha]_D^{25}$ − 12.0 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.40; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32−7.24 (m, 15H), 6.93 (s, 1H), 6.81 (d, *J* = 15.9 Hz, 1H), 6.18 (d, *J* = 15.9 Hz, 1H), 4.18 (s, 1H), 3.48 (d, *J* = 17.6 Hz, 1H), 3.08 (d, *J* = 17.6 Hz, 1H), 1.92−1.85 (m, 1H), 1.08−1.02 (m, 1H), 0.94−0.82 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.8, 172.8, 139.3, 139.3, 136.1, 131.2, 128.6, 128.5, 128.5, 128.2, 128.1, 128.1, 128.1, 127.4, 127.2, 126.7, 78.6, 75.3, 51.4, 21.1, 11.5; IR (KBr) ν 3553, 3059, 3029, 2921, 2859, 1734, 1682, 1494, 1451, 1253, 1186, 1077, 979, 852, 748, 648 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{26}O_4$+Na 449.1729, found 449.1729.

Benzhydryl (*S*)-2-Hydroxy-5-methyl-4-oxo-2-(*E*)-styrylhexanoate (3a′). Results in 31.3 mg, 73% yield, and 80% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak OD, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.7 mL/min, t_R = 15.6 min (major), and t_R = 20.8 min (minor)); mp 110−111 °C; $[\alpha]_D^{25}$ − 18.9 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.59; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33−7.24 (m, 15H), 6.94 (s, 1H), 6.81 (d, *J* = 15.9 Hz, 1H), 6.18 (d, *J* = 15.9 Hz, 1H), 4.16 (s, 1H), 3.35 (d, *J* = 17.7 Hz, 1H), 2.96 (d, *J* = 17.7 Hz, 1H), 2.53 (heptet, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.7, 172.9, 139.3, 139.2, 136.0, 131.2, 128.6, 128.6, 128.5, 128.3, 128.2, 128.1, 128.1, 127.5, 127.1, 126.7, 78.7, 75.4, 48.6, 41.2, 17.8; IR (KBr) ν 3536, 3062, 3029, 2968, 2929, 2875, 1727, 1495, 1455, 1257, 1213, 1143, 1066, 975, 749, 698 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{28}O_4$+Na 451.1885, found 451.1885.

Benzhydryl (*S*)-2-Hydroxy-4-oxo-2-(*E*)-styrylhexanoate (3b′). Results in 33.1 mg, 80% yield, and 66% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak OD, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.7 mL/min, t_R = 17.9 min (major), and t_R = 33.9 min (minor)); mp 97−98 °C; $[\alpha]_D^{25}$ − 19.2 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.43; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34−7.23 (m, 15H), 6.93 (s, 1H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.18 (d, *J* = 15.9 Hz, 1H), 4.15 (s, 1H), 3.29 (d, *J* = 17.3 Hz, 1H), 2.91 (d, *J* = 17.3 Hz, 1H), 2.39 (dd, *J* = 7.0, 2.8 Hz, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.5, 172.8, 139.3, 139.2, 136.0, 131.2, 128.6, 128.6, 128.5, 128.2, 128.2, 128.1, 128.1, 127.5, 127.1, 126.7, 78.7, 75.5, 50.3, 36.7, 7.4; IR (KBr) ν 3549, 3060, 3030, 2966, 2929, 1735, 1598, 1495, 1453, 1249, 1209, 1141, 977, 896, 748, 700 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{26}O_4$+Na 437.1729, found 437.1728.

Benzhydryl (*S*)-2-Hydroxy-4-oxo-2-(*E*)-styrylpentanoate (3c′). Results in 39.6 mg, 99% yield, and 65% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak OD, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 14.9 min (major), and t_R = 34.7 min (minor)); mp 126−127 °C; $[\alpha]_D^{25}$ − 16.2 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.23 (m, 15H), 6.93 (s, 1H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.17 (d, *J* = 15.9 Hz, 1H), 4.09 (s, 1H), 3.32 (d, *J* = 17.4 Hz, 1H), 2.94 (d, *J* = 17.4 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.8, 172.7, 139.2, 139.2, 136.0 131.2, 128.6, 128.5, 128.53, 128.2, 128.2, 128.1, 128.0, 127.4, 127.1, 126.8, 78.8, 75.5, 51.5, 30.7; IR (KBr) ν 3555, 3059, 3031, 3946, 2918, 1738, 1707, 1595, 1495, 1366, 1256, 1208, 975, 851, 748, 700 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{24}O_4$+Na 423.1572, found 423.1572.

Scaled-up Procedure of the Decarboxylative Aldol Reaction. To a 25 mL Schlenk flask equipped with a stirring bar were added β,γ-unsaturated α-ketoester **2-Br** (1.26 g, 3 mmol), Ni-complex **I** (240 mg, 10 mol %), and CH_2Cl_2 (15 mL). The mixture was stirred at −45 °C for 5 min. Then, β-ketoacid **1a** (0.98 g, 6 mmol) was added in one portion, and the resulting mixture was stirred at the same temperature. After completion of the reaction (7 days as monitored by TLC), the residue was purified by column chromatography on silica gel (eluted with 10:1 petroleum ether/ethyl acetate) and recrystallized from dichloromethane/petroleum ether to give product **3d** (mp 133−133.5 °C, 1.46 g, 90% yield, 99% ee).

Synthetic Procedure for Benzhydryl (*S*,*E*)-4-(4-Bromophenyl)-2-hydroxy-2-((*Z*)-2-(hydroxyimino)-2-phenylethyl)but-3-enoate (4). To a 10 mL Schlenk flask equipped with a stirring bar were added **3d** (108.2 mg, 0.2 mmol), hydroxylamine hydrochloride (28.0 mg, 0.4 mmol), and pyridine (2.0 mL). The resulting mixture was stirred at room temperature for 48 h. Then, pyridine was removed

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under reduced pressure. The residue was diluted with water (10 mL) and extracted with EtOAc (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by flash column chromatography (6:1 petroleum ether/ethyl acetate) to afford **4** in 67.8 mg, 61% yield, and >99% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IC, 90:10 *n*-hexane/*i*-PrOH, 220 nm UV detector, 0.8 mL/min, t_R = 18.4 min (major)); mp 176−177 °C; $[\alpha]_D^{25}$ − 57.6 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.27; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.38−7.23 (m, 15H), 7.04 (d, *J* = 8.2 Hz, 2H), 6.79 (s, 1H), 6.70 (d, *J* = 15.7 Hz, 1H), 6.35 (d, *J* = 15.7 Hz, 1H), 3.94 (s, 1H), 3.57 (d, *J* = 13.2 Hz, 1H), 3.48 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1, 155.7, 139.4, 139.2, 136.1, 135.3, 131.6, 130.0, 129.4, 129.1, 128.6, 128.6, 128.4, 128.30, 128.3, 128.2, 127.4, 127.0, 126.9, 121.6, 79.3, 76.4, 36.5; IR (KBr) ν 3500, 3239, 3087, 3063, 2930, 1724, 1551, 1531, 1490, 1256, 1214, 1137, 1072, 989, 813, 757, 697 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{26}BrNO_4$+Na 578.0943, found 578.0940.

Synthetic Procedure for Benzhydryl (*R*,*E*)-5-(4-Bromostyryl)-3-phenyl-4,5-dihydroisoxazole-5-carboxylate (5). To a 10 mL Schlenk flask equipped with a stirring bar were added **4** (55.6 mg, 0.1 mmol), PPh_3 (52.0 mg, 0.2 mmol), and THF (1.0 mL). The mixture was cooled to 0 °C. Then, diisopropyl azodicarboxylate (DIAD, 41.0 mg, 0.2 mmol) was added to the solution. The resulting mixture was stirred at room temperature for 4 h, diluted with water (10 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phase was dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography (20:1 petroleum ether/ethyl acetate) to afford **5** in 45.7 mg, 85% yield, and >99% ee of a white solid as determined by HPLC analysis (Daicel Chiralpak IC, 90:10 *n*-hexane/*i*-PrOH, 254 nm UV detector, 1.0 mL/min, t_R = 16.3 min (major)); mp 123−124 °C; $[\alpha]_D^{25}$ − 39.7 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.74; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.3 Hz, 2H), 7.43−7.25 (m, 15H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.94 (s, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.01 (d, *J* = 16.9 Hz, 1H), 3.47 (d, *J* = 16.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 156.3, 139.5, 139.4, 134.6, 131.8, 131.1, 130.6, 128.9, 128.8, 128.8, 128.6, 128.6, 128.4, 128.2, 128.1, 127.2, 126.9, 126.9, 126.6, 126.5, 122.4, 88.7, 78.8, 44.5; IR (KBr) ν 3060, 3032, 2924, 2853, 1736, 1591, 1451, 1399, 1357, 1246, 1072, 965, 907, 755, 695 cm^{-1}; HRMS (ProMALDI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{24}BrNO_3$+Na 560.0837, found 560.0833.

Synthetic Procedure for Benzhydryl (*S*,*E*)-4-(4-Bromophenyl)-2-hydroxy-2-((*S*)-2-hydroxy-2-phenylethyl)but-3-enoate (6).[12] To a 10 mL Schlenk flask equipped with a stirring bar were added **3d** (108.2 mg, 0.2 mmol) and anhydrous THF (4.0 mL). The mixture was stirred at 0 °C under nitrogen for 5 min. Then, $NaBH(OAc)_3$ (84.8 mg, 0.4 mmol) was added to the mixture in one portion. The mixture was then stirred at room temperature for 12 h. Upon completion of the reaction (monitored by TLC), the reaction mixture was cooled to 0 °C and quenched with successive additions of water (10 mL). Then, the reaction mixture was extracted with ethyl acetate (3 × 10 mL) and dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash column chromatography (6:1 petroleum ether/ethyl acetate) to afford **6** in 107.5 mg, 99% yield, and *dr* > 99:1 as a white solid; mp 115−116 °C; $[\alpha]_D^{25}$ − 17.2 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.30; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.36−7.26 (m, 15H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.93 (s, 1H), 6.82 (d, *J* = 15.8 Hz, 1H), 6.33 (d, *J* = 15.8 Hz, 1H), 5.06 (d, *J* = 10.3 Hz, 1H), 4.03 (s, 1H), 2.80 (s, 1H), 2.44 (dd, *J* = 14.2, 10.7 Hz, 1H), 2.20 (d, *J* = 14.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 144.0, 139.2, 139.1, 135.1, 131.8, 130.0, 129.9, 128.6, 128.6, 128.5, 128.3, 128.3, 128.3, 127.6, 127.5, 127.1, 125.7, 121.9, 79.3, 76.7, 70.4, 46.8; IR (KBr) ν 3358, 3205, 3060, 3029, 2958, 2926, 1742, 1590, 1490, 1451, 1373, 1216, 1122, 1060, 1005, 974, 744, 699 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{27}BrO_4$+Na 565.0990, found 565.0990.

Synthetic Procedure for (3*S*,5*S*)-3-((*E*)-4-Bromostyryl)-3-hydroxy-5-phenyldihydrofuran-2(3*H*)-one (7). To a 25 mL Schlenk flask equipped with a reflux condenser pipe and a stirring bar were added **6** (108.5 mg, 0.2 mmol), THF (2.0 mL), acetic acid (300 μL), and 4 *N* HCl (6.0 mL). The mixture was stirred at 75 °C for 24 h. Then, the mixture cooled down to room temperature, and the aqueous layer was extracted with DCM (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by flash column chromatography (10:1 petroleum ether/ethyl acetate) and recrystallized from ethyl acetate/petroleum ether to give **7** in 44.5 mg, 62% yield, and >99% ee as determined by HPLC analysis (Daicel Chiralpak IC, 70:30 *n*-hexane/*i*-PrOH, 254 nm UV detector, 0.8 mL/min, t_R = 9.6 min (major)); mp 119−120 °C; $[\alpha]_D^{25}$ + 10.9 (*c* 1.0, CH_2Cl_2); TLC (1:4 ethyl acetate/petroleum ether) R_f = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43−7.33 (m, 7H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.75 (d, *J* = 16.1 Hz, 1H), 6.29 (d, *J* = 16.1 Hz, 1H), 5.77 (t, *J* = 7.2 1H), 3.28 (s, 1H), 2.87 (dd, *J* = 13.7, 6.0 Hz, 1H), 2.41 (dd, *J* = 13.4, 8.9 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.2, 138.2, 134.4, 131.8, 131.4, 128.9, 128.8, 128.3, 127.5, 125.5, 122.4, 79.1, 76.5, 44.8; IR (KBr) ν 3429, 3170, 2925, 2856, 1738, 1634, 1487, 1399, 1208, 1075, 908, 863, 762, 696 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{15}BrO_3$+Na 381.0102, found 381.0102.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra, HPLC analytic results for new compounds **3a**−**3c**′ and **4**−**7**, screening of chiral catalysts, and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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