Catalytic Enantioselective Syn-Hydroxy-Oxyacylation of Electron Deficient Alkenes

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Asymmetric syn-dihydroxylation and dioxyacylation of alkenes have been well established. A direct method for the enantioselective preparation of orthogonally protected syn-1,2-diols from alkenes is unprecedented. Here in, we report the first enantioselective hypervalent iodine catalyzed syn-hydroxy-oxyacylation of enones. The orthogonally protected diols were obtained with excellent diastereo- and regioselectivity under metal-free condition. For these electron-deficient alkenes, even the syn-dihydroxylation and dioxyacylation have remained yet an unfinished challenge.

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Catalytic Enantioselective *syn*-Hydroxy-Oxyacylation of Electron Deficient Alkenes

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This paper is dedicated to late Professor Kilian Muniz

ABSTRACT: Asymmetric *syn*-dihydroxylation and dioxyacylation of alkenes have been well established. A direct method for the enantioselective preparation of orthogonally protected *syn*-1,2-diols from alkenes is unprecedented. Here in, we report the first enantioselective hypervalent iodine catalyzed *syn*-hydroxy-oxyacylation of enones. The orthogonally protected diols were obtained with excellent diastereo- and regioselectivity under metal-free condition. For these electron-deficient alkenes, even the *syn*-dihydroxylation and dioxyacylation have remained yet an unfinished challenge.

Orthogonally protected diols and triols are privileged structural motifs in numerous biologically active natural products, pharmaceuticals, functionalized materials, and are important intermediates in many syntheses.¹ Therefore, numerous synthetic approaches have been developed to stereoselectively install double *syn* C-O bonds on alkenes (Scheme 1). The oxidative dihydroxylation of alkenes catalyzed by OsO₄, especially Sharpless dihydroxylation, has emerged as an extremely reliable variant.² However, the high toxicity, expensiveness and volatility of this catalyst led to the renewed interest in developing catalysts based on other transition metals, such as ruthenium,³ palladium,⁴ manganese⁵ and iron.⁶ The metal-free methods due to their intrinsic properties have also generated a great interest using peroxides,⁷ hydroxamic acids,⁸ hypervalent iodine reagents,⁹ organocatalysts¹⁰ and biocatalysts.¹¹ The group of Fujita reported the first asymmetric variant of Prevost and Woodward method for the dihydroxylation using chiral hypervalent iodine reagent in 2011.¹² Besides dihydroxylation, asymmetric diacetoxylation¹³ and dialkoxylation¹⁴ have also garnered significant importance for the asymmetric functionalization. However, for any effective direct chemoselective transformation, the difunctionalities are ideally desired to be in the differentiated/orthogonally protected form to avoid unproductive protection and deprotection steps in a multistep synthesis.

Enones are an important class of olefins which act as the surrogates for accessing triols after deoxygenation, followed by a selective reduction. It has surprisingly remained beyond the scope of almost all the known methods for enantioselective *syn*-dihydroxylation or diacylation. In 2002, the group of Brown pioneered the 1,2-dihydroxylation of enones using a phase transfer catalyst in a moderate yield of 19-52% and 60-80% ee (Scheme 1a).^{10b} This method is compatible with enones

Scheme 1. Asymmetric Hydroxy-Oxyacylation of Enones

(a) Asymmetric *syn*-Dihydroxylation/Diacylation

Alkenes: Well explored

Enones: Challenging
Brown

(b) Asymmetric *syn*-Hydroxy-Oxyacylation: Not Known

This Work: Enantioselective *syn*-Hydroxy-Oxyacylation of Enones

substituted with less bulky alkyl chains at the β -position, and the sterically demanding (hetero)aryls and polycyclic aryls are beyond its scope. To the best of our knowledge, (i) there is no report on asymmetric *syn*-hydroxy-oxyacylation of electron-deficient alkenes, and (ii) for enones, even the *syn*-dihydroxylation with a high enantioselectivity has remained unfinished task, whereas the dioxyacylation is yet to be reported (Scheme 1b). Herein, we describe the first highly enantio and regioselective *syn*-1,2-hydroxy-oxyacylation of enones using hypervalent iodine catalyst (Scheme 1b). Acetic acid/H₂O (residual water from the reagents) act as the source of acyloxy and hydroxy groups.

Our initial investigation focused on identifying a suitable hypervalent iodine catalyst, generated *in situ*, for the asymmetric

Table 1. Reaction Condition Optimization^a

entry	cat	oxidant	additive	yield (%) ^b	ee (%) ^c
1	-	oxone	Sm(OTf) ₃	0	-
2	A	oxone	Sm(OTf) ₃	42	-
3	B/C	oxone	Sm(OTf) ₃	0	-
4	D	oxone	Sm(OTf) ₃	33	98
5	E	oxone	Sm(OTf) ₃	51	96
6	F	oxone	Sm(OTf) ₃	36	96
7	G	oxone	Sm(OTf) ₃	31	65
8	E	selectfluor	Sm(OTf) ₃	0	-
9	E	<i>m</i> CPBA	Sm(OTf) ₃	62	96
10	E	<i>m</i> CPBA	Yb(OTf) ₃	78	82
11	E	<i>m</i> CPBA	HFIP	0	-
12	E	<i>m</i> CPBA	TfOH	56	97
13	E	<i>m</i> CPBA	BF ₃ .OEt ₂	56	97
14 ^d	E	<i>m</i> CPBA	BF ₃ .OEt ₂	96	95
15 ^e	E	<i>m</i> CPBA	BF ₃ .OEt ₂	84	93
16 ^f	E	<i>m</i> CPBA	BF ₃ .OEt ₂	56	96

^aReaction condition unless otherwise specified: **1a** (0.1 mmol), additive (20 mol %), I(III) catalyst **A-G** (20 mol %), oxidant (1.2 equiv.), solvent (2.0 mL, 1:1 ratio) at rt. ^bIsolated yield. ^cDetermined by HPLC analysis on chiral stationary phase. ^d50 mol % of BF₃.OEt₂ was used. ^eReaction performed at 0 °C. ^f30 mol % of catalyst loading was used.

syn-1,2-hydroxy-oxyacylation of chalcone **1a** (Table 1). Various class of chiral aryl iodides (**B-G**) were tested as the potential catalysts in the presence of oxone in AcOH:TFA (1:1) as the solvent and Sm(OTf)₃ as the additive. Initial breakthrough was observed in the presence of 20 mol % of achiral catalyst **A**, giving the desired hydroxy-oxyacetylated product **2a** as a single diastereomer in 42% yield (entries 1 and 2). Among the different catalysts screened, catalyst **E** provided **2a** with a decent yield of 51% and 96% ee (entry 5). We next evaluated various oxidants. The use of selectfluor was found to be unsuitable while *m*CPBA produced **2a** in 62% yield and 96% ee (entries 8-9). The variation of Lewis/Bronsted acids showed a dramatic effect on the yield and BF₃.OEt₂ was the optimal choice giving the desired product in 96% yield with 95% ee (entry 14). The structure and the absolute configuration was unambiguously confirmed through X-ray crystallographic analysis of **2d** (Scheme 2).¹⁵

With the optimized reaction condition in hand, chalcones bearing different electron-donating groups (EDG) as well as electron-withdrawing groups (EWG) at *ortho*, *meta* and *para*-position of the aryl rings were examined (Scheme 2). The EDGs

Scheme 2. Substrate scope

^aHPLC separation for **2z** was not achieved, see SI for further details.

like Me, Et, OMe, ⁱPr; and EWGs like fluoro, chloro, bromo on the aryl ring Ar₁ gave the desired products in good to excellent yields and high enantioselectivity. Substitution patterns on the β-aryl ring (Ar₂) were also compatible with the optimized reaction condition producing the desired products in good yields and excellent ee.¹⁶ Switching from acetic acid to higher analogues also furnished **2ab** and **2ac** in good yields without any loss in enantioselectivity.

Scheme 3. Proposed Reaction Mechanism

Our proposed reaction mechanism for this transformation is detailed in Scheme 3. The catalytic cycle begins with the *in situ* oxidative generation of I(III) in presence of *m*CPBA/TFA that reacts with $\text{BF}_3 \cdot \text{OEt}_2$ to produce intermediate II. This intermediate coordinates with the chalcones **1** to give adduct III. A regioselective substitution by an acetate generates intermediate IV. The regeneration of catalyst E takes place *via* reductive elimination to give either intermediate V (path a) or intermediate VII (path b). Subsequent regioselective hydrolysis of intermediate VI or VIII generates the desired product with excellent regio- and stereoselectivity. A detailed DFT calculation is underway to ascertain the preferred reaction pathway among the path a and path b.

In conclusion, we have achieved the first enantioselective *syn*-hydroxy-oxyacylation of electron deficient olefins using hypervalent iodine(III) catalysis. This method furnished the orthogonally protected *syn*-diols from alkenes with a wide substrate scope and excellent enantiocontrol. Further studies towards selective transformation of the products is under progress in our laboratory.

ASSOCIATED CONTENT

Supporting Information

Experimental procedure, characterization data and spectra (PDF)

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Notes

The authors declare no competing financial interests.

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15. CCDC 1946629 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/daa_request/cif.
16. HPLC separation for **2z** was not achieved, see SI for further details.

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Supplementary Information

Catalytic Enantioselective *syn*-Hydroxy-Oxyacylation of Electron Deficient Alkenes

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Table of Contents

I	<i>General information</i>	S2
II	<i>General procedures for the synthesis of Chalcones 1</i>	S2
III	<i>General Procedure for synthesis of Hydroxy-oxyacylation products 2</i>	S2
IV	<i>References</i>	S3
V	<i>Stereochemistry determination of 2d via X-ray crystallographic analysis</i>	S3
VI	<i>Characterization data of Hydroxy-oxyacylation Products, 2</i>	S4
VII	<i>¹H and ¹³C{¹H} spectra of Hydroxy-oxyacylation products, 2</i>	S12
VIII	<i>HPLC spectra of Hydroxy-oxyacylation products, 2</i>	S71

I. General Information

Commercially available aldehydes purchased from Alfa-Aesar or Sigma-Aldrich were used without further purification. The chalcones were synthesized from commercially available aryl aldehydes and aryl acetophenones following the literature procedure.¹ The chiral catalysts were synthesized using the reported literature procedure.² Solvents were dried and distilled following the standard methods. TLC was carried out on pre-coated plates (Merck silica gel 60, f254), and the spots were visualized with UV light and by charring the plates dipped in phosphomolybdic acid (PMA) solution. Column chromatography was accomplished using silica gel (230-400 mesh) with distilled solvents. Proton nuclear magnetic resonance (¹H) and proton decoupled carbon nuclear magnetic resonance (¹³C{¹H}) for compounds were recorded at 400 MHz and 800 MHz instruments using CDCl₃ as the solvent. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ 7.26, singlet). ¹H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the peaks. High-resolution mass spectral analysis (HRMS) was performed on “QTOF Premier mass spectrometer”. HPLC analysis was performed on “Agilent Technologies 1260 Infinity” using chiral stationary phase.

II. General procedures for the synthesis of Chalcones 1

Chalcones **1**, were synthesized by an Aldol-condensation reaction, following a literature procedure.^[1]

To a stirred solution of substituted acetophenone (20 mmol) in ethanol (50 mL) at 0°C, was added dropwise a solution of sodium hydroxide (26 mmol) in water (15 mL) followed by slow addition of substituted benzaldehyde (20 mmol). The resulting mixture was slowly warmed to room temperature and stirred for 6 h, then filtered and washed with ethanol to get the pure product **1**.

III. General Procedure for synthesis of Hydroxy-oxyacylation products 2

To a 25 ml round bottom flask containing magnetic bar was added catalyst **E** (0.02 mmol) and *m*-CPBA (0.12 mmol, 1.20 equiv.) followed by acetic acid (1.0 mL) and trifluoroacetic acid (1.0 mL) at room temperature. Chalcone **1** (0.1 mmol) was then added in one portion followed by BF₃·OEt₂ (0.05 mmol, 50 mol%) and the resulting mixture was allowed to stir at rt for 12 h. After completion, the reaction mixture was quenched with a saturated aqueous solution of NaHCO₃ and extracted

with CH₂Cl₂ (3 x 5 mL). The combined organic layers were dried over Na₂SO₄, and concentrated *in vacuo* to provide the crude product. The crude mixture was then purified by column chromatography to afford the pure product.

IV. References

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V. Stereochemistry determination of **2d** via X-ray crystallographic analysis

Absolute configurations of the products were assigned based on the crystal X-ray structures of **2d**. A colorless flaky crystal of **2d** was obtained by vaporization of a methanol solution of compound **2d** (96% ee). The absolute configuration of **2d** was determined by X-ray to be (1*S*,2*R*). CCDC 1946629 contains the supplementary X-ray crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

VI. Characterization data of Hydroxy-oxyacylation Products 2

(1*S*,2*R*)-2-Hydroxy-3-oxo-1,3-diphenylpropyl acetate (2a): Colorless gummy liquid, 96% yield

(27.3 mg); $[\alpha]_D^{20} = -27.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.93-7.87 (m, 2H), 7.64 (t, $J = 8.0$ Hz, 1H), 7.51 (t, $J = 8.0$ Hz, 1H), 7.42-7.28 (m, 5H), 6.09 (d, $J = 4$ Hz, 1H), 5.35 (dd, $J = 8$ Hz, $J = 2.9$ Hz, 1H); 3.84 (d, $J = 8.0$ Hz, 1H); 2.00 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.7, 169.4, 136.5, 134.1, 134.0, 128.8, 128.4, 128.3, 126.9, 75.5, 75.1, 20.6; HRMS (ESI) m/z calcd. for C₁₇H₁₆O₄Na [M+Na]⁺: 307.0941, found: 307.0939; HPLC analysis: 95% ee (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 46.5 min, R_t (major) = 33.5 min.

(1*S*,2*R*)-2-Hydroxy-3-oxo-1-phenyl-3-(*p*-tolyl)propyl acetate (2b): Colorless gummy liquid,

73% yield (21.7 mg); $[\alpha]_D^{20} = +12.6$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, $J = 8.0$ Hz, 2H), 7.43-7.28 (m, 7H), 6.09 (d, $J = 2.6$, 1H), 5.31 (dd, $J = 8$ Hz, 2.6 Hz, 1H), 3.88 (d, $J = 8.0$ Hz, 1H), 2.44 (s, 3H), 2.01 (s, 3H), ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.1, 169.4, 145.2, 136.6, 131.4, 129.6, 128.5, 128.3, 126.9, 75.7, 75.0, 21.7, 20.6; HRMS (ESI) m/z calcd for C₁₈H₁₈O₄Na [M+Na]⁺: 321.1097, found: 321.1098; HPLC analysis: 98% ee (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 38.3 min, R_t (major) = 25.0 min.

(1*S*,2*R*)-2-Hydroxy-3-(4-methoxyphenyl)-3-oxo-1-phenylpropyl acetate (2c): Colorless

gummy liquid, 93% yield (29.2 mg); $[\alpha]_D^{20} = +4.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.80 (dd, $J = 8.0$ Hz, 4.0 Hz, 2H), 7.33-7.28 (m, 2H), 7.27-7.19 (m, 3H), 6.90 - 6.85 (m, 2H), 6.00 (d, $J = 4.0$ Hz, 1H), 5.21-5.16 (m, 1H), 3.82 (d, $J = 8.0$ Hz, 1H), 3.78 (s, 3H), 1.92 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 196.6, 169.4, 164.2, 136.7, 130.8, 128.3, 126.8, 126.7, 114.1, 75.8, 74.7, 55.4, 20.6; HRMS (ESI) m/z calcd for C₁₈H₁₈O₅Na [M+Na]⁺: 337.1046, found: 337.1046; HPLC analysis: 89% ee (Chiralcel IC, 10:90 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 54.6 min, R_t (major) = 44.0 min.

(1*S*,2*R*)-3-(4-Bromophenyl)-2-hydroxy-3-oxo-1-phenylpropyl acetate (2d): Colorless gummy

liquid, 76% yield (27.5 mg); $[\alpha]_D^{20} = +25.8$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, $J = 8.0$ Hz, 2H), 7.64 (d, $J = 12.0$ Hz, 2H), 7.40-7.27 (m, 5H), 6.05 (d, $J = 4.0$ Hz, 1H), 5.27 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.75 (d, $J = 8.0$ Hz, 1H), 2.02 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.8, 169.5,

136.2, 132.9, 132.2, 129.8, 129.4, 128.5, 128.4, 126.9, 75.5, 75.2, 20.7; HRMS (ESI) calcd for

$C_{17}H_{15}BrO_4Na$ $[M+Na]^+$: 385.0046, found: 385.0039; HPLC analysis: 96% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 65.1min, R_t (major) = 37.0min.

(1*S*,2*R*)-3-(4-Chlorophenyl)-2-hydroxy-3-oxo-1-phenylpropyl acetate (2e): Colorless gummy

liquid, 64% yield (20.4 mg); $[\alpha]_D^{20} = +68.8$ ($c = 0.1$ CHCl₃); 1H NMR (400 MHz, CDCl₃) δ 7.82 (d, $J = 8.0$ Hz, 2H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.38 - 7.28 (m, 5H), 6.05 (d, $J = 2.9$ Hz, 1H), 5.27 (dd, $J = 8.0$ Hz, 4.0

Hz, 1H), 3.73 (d, $J = 8.0$ Hz, 1H), 2.02 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CDCl₃) δ 197.6, 169.5, 140.6, 136.2, 132.5, 129.8, 129.2, 128.5, 128.4, 126.9, 75.5, 75.2, 20.7; HRMS (ESI) m/z calcd for $C_{17}H_{15}ClO_4Na$ $[M+Na]^+$: 341.0551, found: 341.0546; HPLC analysis: 96% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 61.8min, R_t (major) = 34.1min.

(1*S*,2*R*)-2-Hydroxy-3-(4-nitrophenyl)-3-oxo-1-phenylpropyl acetate (2f): Colorless gummy

liquid, 21% yield (7 mg); $[\alpha]_D^{20} = +19.8$ ($c = 0.1$ CHCl₃); 1H NMR (400 MHz, CDCl₃) δ 8.27 (d, $J = 8.0$ Hz, 2H), 7.96 (d, $J = 8.0$ Hz, 2H), 7.30 - 7.22 (m, 5H), 5.98 (d, $J = 3.3$ Hz, 1H), 5.26 (s, 1H), 3.56 (d, $J =$

8.0 Hz, 1H), 1.97 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CDCl₃) δ 197.9, 169.6, 150.6, 139.1, 135.8, 129.5, 128.8, 128.6, 126.9, 123.9, 75.9, 75.3, 29.6; HRMS (ESI) m/z calcd. for $C_{17}H_{15}NO_6Na$ $[M+Na]^+$: 352.0792, found: 352.0793; HPLC analysis: 92% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 58.6 min, R_t (major) = 32.9min.

(1*S*,2*R*)-2-Hydroxy-3-oxo-3-phenyl-1-(*p*-tolyl)propyl acetate (2g): Colorless gummy liquid,

68% yield (20.3 mg); $[\alpha]_D^{20} = +16.2$ ($c = 0.1$ CHCl₃); 1H NMR (400 MHz, CDCl₃) δ 7.81 (d, $J = 8.0$ Hz, 2H), 7.55 (t, $J = 8.0$ Hz, 3H), 7.43 (t, $J = 8.0$, 2H), 7.19 (t, $J = 8.0$, 2H), 7.07 (d, $J = 8.0$, 2H), 5.97 (d, $J =$

4.0, 1H), 5.24 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.72 (d, $J = 8.0$ Hz, 1H), 2.25 (s, 3H), 1.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CDCl₃) δ 198.8, 169.4, 138.2, 134.2, 134.0, 133.5, 129.0, 128.8, 128.4, 126.8, 75.5, 75.1, 21.1, 20.6; HRMS (ESI) calcd for $C_{18}H_{18}O_4Na$ $[M+Na]^+$: 321.1097, found: 321.1096; HPLC analysis: 83% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1mL/min), R_t (minor) = 29.8 min, R_t (major) = 43.8min.

(1*S*,2*R*)-1-(4-Chlorophenyl)-2-hydroxy-3-oxo-3-phenylpropyl acetate (2h): Colorless gummy liquid, 60% yield (19 mg); $[\alpha]_D^{20} = +61.6$ ($c = 0.1$ CHCl₃); 1H NMR (400 MHz, CDCl₃) δ 7.88

(d, $J = 8.0$ Hz, 2H), 7.65 (t, $J = 8.0$ Hz, 1H), 7.52 (t, $J = 8.0$ Hz, 2H), 7.31 (s, 4H), 6.03 (d, $J = 2.6$ Hz, 1H), 5.29 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.84 (d, $J = 8.0$ Hz, 1H), 1.98 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 198.4, 169.3, 135.0, 134.3, 134.2, 134.0, 128.9, 128.5, 128.4, 75.0, 74.9, 20.6; HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{15}\text{ClO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 341.0551, found: 341.0546; HPLC analysis: 94% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 33.8\text{min}$, $R_t(\text{major}) = 36.5\text{min}$.

(1*S*,2*R*)-1-(2-Bromophenyl)-2-hydroxy-3-oxo-3-phenylpropyl acetate (2i): Colorless gummy

liquid, 62% yield (22.6 mg); $[\alpha]_{\text{D}}^{20} = +14.2$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.77-7.73 (m, 2H), 7.67-7.63 (m, 2H), 7.38-7.30 (m, 5H), 6.05 (d, $J = 4.0$ Hz, 1H), 5.26 (d, $J = 8.0$ Hz, 1H), 3.75 (s, 1H), 2.02 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 197.9, 169.5, 136.3, 133.0, 132.2, 129.9, 129.5, 128.6, 128.5, 127.0, 75.6, 75.2, 20.7; HRMS (ESI) m/z calcd. for $\text{C}_{17}\text{H}_{15}\text{BrO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 387.0025, found: 387.0021; HPLC analysis: 96% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 64.4\text{min}$, $R_t(\text{major}) = 36.8\text{min}$.

(1*S*,2*R*)-1-(4-Bromophenyl)-2-hydroxy-3-oxo-3-phenylpropyl acetate (2j): Colorless gummy

liquid, 65% yield (23.7 mg); $[\alpha]_{\text{D}}^{20} = +36.4$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.56 (t, $J = 8.0$ Hz, 1H), 7.35-7.46 (m, 4H), 7.17 (d, $J = 8.0$ Hz, 2H), 5.93 (d, $J = 4.0$ Hz, 1H), 5.20 (d, $J = 4.0$ Hz, 1H), 3.78 (d, $J = 8.0$ Hz, 1H), 1.89 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 198.3, 169.2, 135.5, 134.2, 134.0, 131.4, 128.9, 128.7, 128.3, 122.5, 75.0, 74.8, 20.5; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{15}\text{BrO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 387.0025, found: 387.0026; HPLC analysis: 93% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 35.6\text{ min}$, $R_t(\text{major}) = 40.9\text{min}$.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-hydroxy-3-oxo-3-phenylpropyl acetate (2k): Colorless gummy

liquid, 72% yield (21.7 mg); $[\alpha]_{\text{D}}^{20} = +29.8$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.81 (d, $J = 8.0$ Hz, 2H), 7.57 (t, $J = 8.0$ Hz, 1H), 7.45 (t, $J = 8.0$ Hz, 2H), 7.33-7.27 (m, 2H), 6.95 (t, $J = 8.0$ Hz, 2H), 5.97 (d, $J = 2.3$ Hz, 1H), 5.22 (d, $J = 4.0$ Hz, 1H), 3.76 (d, $J = 8.0$ Hz, 1H), 1.91 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 198.6, 169.4, 162.7 (d, $J_{\text{C-F}} = 245$ Hz) 134.2, 134.1, 132.4, 132.3, 129.0, 128.9, 128.8, 128.4, 115.5, 115.2, 75.0, 20.6; HRMS (ESI) m/z calcd. for $\text{C}_{17}\text{H}_{15}\text{FO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 325.0847, found: 325.0839; HPLC analysis: 92% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 29.1\text{min}$, $R_t(\text{major}) = 22.8\text{min}$.

(1S,2R)-2-Hydroxy-3-oxo-1,3-di-*p*-tolylpropyl acetate (2l): Colorless gummy liquid, 60%

yield (18.7 mg); $[\alpha]_D^{20} = -1.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, $J = 8.0$ Hz, 2H), 7.33 (t, $J = 8$ Hz, 4H), 7.18 (d, $J = 8.0$ Hz, 2H), 6.10 (s, 1H), 5.32 (s, 1H), 3.89 (s, 1H), 2.47 (s, 3H),

2.36 (s, 3H), 2.02 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.2, 169.4, 145.1, 138.1, 133.7, 131.5, 129.5, 129.0, 128.5, 126.8, 75.6, 75.0, 21.7, 21.0, 20.6; HRMS (ESI) m/z calcd for C₁₉H₂₀O₄ [M+Na]⁺: 335.1254, found: 335.1247; HPLC analysis: 88% ee (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 24.6 min, R_t (major) = 20.0 min.

(1S,2R)-1-(4-Ethylphenyl)-2-hydroxy-3-oxo-3-(*p*-tolyl)propyl acetate (2m): Colorless gummy

liquid, 69% yield (22.5 mg); $[\alpha]_D^{20} = +31.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, $J = 4.0$ Hz, 2H), 7.33-7.27 (m, 4H), 7.17 (d, $J = 8.0$ Hz, 2H), 6.06 (d, $J = 4.0$ Hz, 1H), 5.30 (d, $J =$

8.0 Hz, 1H), 3.84 (d, $J = 8.0$ Hz, 1H), 2.63 (q, $J = 8.0$ Hz, 2H), 2.43 (s, 3H), 1.99 (s, 3H), 1.22 (t, $J = 8.0$ Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.2, 169.5, 145.1, 144.5, 133.9, 131.6, 129.6, 128.5, 127.9, 127.0, 75.7, 75.1, 28.5, 21.7, 20.7, 15.4; HRMS (ESI) m/z calcd for C₂₀H₂₂O₄Na [M+Na]⁺: 349.1410, found: 349.1411; HPLC analysis: 91% ee (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 22.3 min, R_t (major) = 18.7 min.

(1S,2R)-1-(4-Bromophenyl)-2-hydroxy-3-oxo-3-(*p*-tolyl)propyl acetate (2n): Colorless gummy

liquid, 64% yield (24.2 mg); $[\alpha]_D^{20} = -14.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 6.02 (d, $J =$

2.5 Hz, 1H), 5.25 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.88 (d, $J = 8.0$ Hz, 1H), 2.45 (s, 3H), 1.99 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.7, 169.3, 145.5, 135.7, 131.5, 131.3, 129.7, 128.7, 128.5, 122.5, 75.2, 74.7, 21.8, 20.6; HRMS (ESI) m/z calcd. for C₁₈H₁₇BrO₄Na [M+Na]⁺: 401.0182, found: 401.0177; HPLC analysis: 94% ee (Chiralcel OZ-H, 10:90 *i*PrOH/Hexane, 1 mL/min), R_t (minor) = 34.4 min, R_t (major) = 16.6 min.

(1S,2R)-1-(4-Chlorophenyl)-2-hydroxy-3-oxo-3-(*p*-tolyl)propyl acetate (2o): Colorless

gummy liquid, 84% yield (28 mg); $[\alpha]_D^{20} = -19.6$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.33-7.30 (m, 6H), 6.03 (d, $J = 4.0$ Hz, 1H), 5.26 (dd, $J = 8.0$

Hz, 2.6 Hz, 1H), 3.88 (d, $J = 8.0$ Hz, 1H), 2.44 (s, 3H), 1.99 (s, 3H); ¹³C{¹H} NMR (100 MHz,

CDCl₃) δ 197.8, 169.4, 145.5, 135.2, 134.3, 131.3, 129.7, 128.6, 128.5, 128.4, 75.1, 74.8, 21.8, 20.6; HRMS (ESI) m/z calcd for C₁₈H₁₇ClO₄Na [M+Na]⁺: 355.0708, found: 355.0704; HPLC analysis: 95% *ee* (Chiralcel OZ-H, 10:90 ⁱPrOH/Hexane, 1 mL/min), R_t(minor) = 30.4 min, R_t(major) = 15.3min.

(1*S*,2*R*)-3-(4-Bromophenyl)-2-hydroxy-3-oxo-1-(*m*-tolyl)propyl acetate (2p): Colorless

gummy liquid, 68% yield (25.7 mg); [α]_D²⁰ = +32.2 (*c* = 0.1 CHCl₃);

¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.26-7.19 (m, 1H), 7.17-7.09 (m, 3H), 6.00 (d, *J* = 4.0

Hz, 1H), 5.26 (s, 1H), 3.74 (d, *J* = 4.0 Hz, 1H), 2.33 (s, 3H), 2.02 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.9, 169.5, 138.1, 136.1, 133.0, 132.2, 129.8, 129.4, 129.3, 128.4, 127.5, 123.9, 75.5, 75.3, 21.4, 20.7; HRMS (ESI) m/z calcd. for C₁₈H₁₇BrO₄Na [M+Na]⁺: 401.0182, found: 401.0184; HPLC analysis: 98% *ee* (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t(minor) = 40.9min, R_t(major) = 26.4 min.

(1*S*,2*R*)-3-(4-Bromophenyl)-2-hydroxy-3-oxo-1-(*p*-tolyl)propyl acetate (2q): Colorless

gummy liquid, 64% yield (24.2 mg); [α]_D²⁰ = +33.2 (*c* = 0.1 CHCl₃);

¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, *J* = 12.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 3H), 6.01

(d, *J* = 4.0 Hz, 1H), 5.25 (dd, *J* = 8.0 Hz, 4.0 Hz, 1H), 3.70 (d, *J* = 8.0 Hz, 1H), 2.33 (s, 3H), 2.01 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.0, 169.5, 138.5, 133.2, 133.0, 132.2, 129.9, 129.4, 129.1, 126.9, 75.5, 75.3, 21.1, 20.7; HRMS (ESI) m/z calcd. for C₁₈H₁₇BrO₄Na [M+Na]⁺: 401.0182, found: 401.0183; HPLC analysis: 91% *ee* (Chiralcel IC, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t(minor) = 32.7min, R_t(major) = 25.2min.

(1*S*,2*R*)-3-(4-Bromophenyl)-1-(4-ethylphenyl)-2-hydroxy-3-oxopropyl acetate (2r): Colorless

gummy liquid, 81% yield (31.6 mg); [α]_D²⁰ = -14.6 (*c* = 0.1 CHCl₃);

¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.01

(d, *J* = 4.0 Hz, 1H), 5.25 (dd, *J* = 8.0 Hz, 4.0 Hz, 1H), 3.72 (d, *J* = 8.0 Hz, 1H), 2.62 (q, *J* = 8.0 Hz, 2H), 2.01 (s, 3H), 1.21 (t, *J* = 8.0 Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.0, 169.6, 144.8, 133.4, 133.0, 132.2, 129.9, 129.3, 128.0, 127.0, 75.5, 75.3, 28.5, 20.7, 15.4; HRMS (ESI) calcd. for C₁₉H₁₉BrO₄Na [M+Na]⁺: 413.0359, found: 413.0361; HPLC analysis: 99% *ee* (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t(minor) = 28.4 min, R_t(major) = 23.8min.

(1*S*,2*R*)-3-(4-Bromophenyl)-2-hydroxy-1-(4-isopropylphenyl)-3-oxopropyl acetate (2s):

Colorless gummy liquid, 64% yield (26 mg); $[\alpha]_D^{20} = +29.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, $J = 8.0$ Hz, 2H), 7.61 (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 6.00 (d, $J = 4.0$ Hz, 1H), 5.25 (d, $J = 4.0$ Hz, 1H), 3.72 (d, $J = 8.0$ Hz, 1H), 2.91-2.81 (m, 1H), 2.02 (s, 3H), 1.22 (d, $J = 8.0$ Hz, 6H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.1, 169.6, 149.4, 133.6, 133.0, 132.1, 129.8, 129.3, 127.0, 126.5, 75.6, 75.3, 33.8, 23.8, 20.7; HRMS (ESI) m/z calcd. for C₂₀H₂₁BrO₄Na [M+Na]⁺: 429.0495, found: 429.0491; HPLC analysis: 95% *ee* (Chiralcel IC, 02:98 ⁱPrOH/Hexane 0.7 mL/min), R_t (minor) = 98.1min, R_t (major) = 92.1min.

(1*S*,2*R*)-3-(4-Chlorophenyl)-2-hydroxy-3-oxo-1-(*m*-tolyl)propyl acetate (2t): Colorless

gummy liquid, 81% yield (27 mg); $[\alpha]_D^{20} = -19.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, $J = 8.0$ Hz, 2H), 7.47 (d, $J = 12.0$ Hz, 2H), 7.27-7.20 (m, 1H), 7.17-7.09 (m, 3H), 6.01 (d, $J = 4.0$ Hz, 1H), 5.26 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.73 (d, $J = 8.0$ Hz, 1H), 2.33 (s, 3H), 2.02 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.7, 169.5, 140.6, 138.1, 136.2, 132.6, 129.8, 129.3, 129.2, 128.4, 127.6, 123.9, 75.6, 75.3, 21.4, 20.7; HRMS (ESI) m/z calcd for C₁₈H₁₇ClO₄Na [M+Na]⁺: 355.0708, found: 355.0708; HPLC analysis: 94% *ee* (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 37.3min, R_t (major) = 23.8min.

(1*S*,2*R*)-3-(4-Chlorophenyl)-2-hydroxy-3-oxo-1-(*p*-tolyl)propyl acetate (2u): Colorless

gummy liquid, 73% yield (24.2 mg); $[\alpha]_D^{20} = +38.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, $J = 8.0$ Hz, 2H), 7.47 (d, $J = 12.0$ Hz, 2H), 7.23 (d, $J = 8.0$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 2H), 6.02 (d, $J = 3.0$ Hz, 1H), 5.24 (d, $J = 4.0$ Hz, 1H), 3.72 (d, $J = 8.0$ Hz, 1H), 2.33 (s, 3H), 2.00 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 197.7, 169.5, 140.6, 138.4, 133.2, 132.6, 129.8, 129.2, 129.1, 126.9, 75.5, 75.3, 21.1, 20.7; HRMS (ESI) m/z calcd. for C₁₈H₁₇ClO₄Na [M+Na]⁺: 355.0708, found: 355.0707; HPLC analysis: 96% *ee* (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 31.2 min, R_t (major) = 23.0min.

(1*S*,2*R*)-3-(4-Chlorophenyl)-1-(4-ethylphenyl)-2-hydroxy-3-oxopropyl acetate (2v):

Colorless gummy liquid, 76% yield (26.3 mg); $[\alpha]_D^{20} = +34.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, $J = 8.0$ Hz, 2H), 7.46 (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.16 (d, $J = 8.0$

Hz, 2H), 6.01 (d, $J = 4.0$ Hz 1H), 5.26 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.72 (d, $J = 8.0$ Hz 1H), 2.62 (q, $J = 8.0$ Hz, 2H), 2.01 (s, 3H), 1.21 (t, $J = 8.0$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 197.8, 169.6, 144.8, 140.6, 133.5, 132.6, 129.8, 129.2, 128.0, 127.0, 75.6, 75.3, 28.5, 20.7, 15.4; HRMS (ESI) m/z calcd. for $\text{C}_{19}\text{H}_{19}\text{ClO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 369.0864, found: 369.0865; HPLC analysis: 94% *ee* (Chiralcel OD-H, 02:98 i PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 26.4\text{min}$, $R_t(\text{major}) = 22.0\text{min}$.

(1*S*,2*R*)-3-(4-Chlorophenyl)-2-hydroxy-1-(4-isopropylphenyl)-3-oxopropyl acetate (2w):

Colorless gummy liquid, 75% yield (27 mg); $[\alpha]_{\text{D}}^{20} = +24.0$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J = 8.0$ Hz, 2H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.30-7.24 (m, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 6.0 (d, $J = 4.0$ Hz, 1H), 5.30-5.23 (m, 1H), 3.73 (d, $J = 8.0$ Hz, 1H), 2.92-2.82 (m, 1H), 2.02 (s, 3H), 1.22 (d, $J = 8.0$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 197.9, 169.6, 149.4, 140.5, 133.6, 132.6, 129.8, 129.2, 127.0, 126.5, 75.6, 75.3, 33.8, 23.8, 20.7; HRMS (ESI) m/z calcd. for $\text{C}_{20}\text{H}_{21}\text{ClO}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 383.1021, found: 383.1021; HPLC analysis: 93% *ee* (Chiralcel IC, 02:98 i PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 42.1\text{ min}$, $R_t(\text{major}) = 46.3\text{min}$.

(1*S*,2*R*)-2-Hydroxy-3-oxo-1-phenyl-3-(thiophen-2-yl)propyl acetate (2x): Colorless gummy

liquid, 81% yield (23.5 mg); $[\alpha]_{\text{D}}^{20} = -59.4$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.76 (t, $J = 4.0$ Hz, 2H), 7.42-7.24 (m, 6H), 7.17 (t, $J = 8.0$ Hz, 1H), 6.16 (d, $J = 4.0$ Hz, 1H), 5.09 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.64 (d, $J = 8.0$ Hz, 1H), 2.06 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 190.7, 169.6, 140.1, 136.4, 135.3, 133.2, 128.5, 128.5, 128.4, 126.9, 76.4, 76.2, 20.8; HRMS (ESI) m/z calcd. for $\text{C}_{15}\text{H}_{14}\text{O}_4\text{SNa}$ $[\text{M}+\text{Na}]^+$: 313.0505, found: 313.0502; HPLC analysis: 95% *ee* (Chiralcel OD-H, 02:98 i PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 74.8\text{min}$, $R_t(\text{major}) = 52.3\text{min}$.

(1*S*,2*R*)-2-Hydroxy-3-(naphthalen-2-yl)-3-oxo-1-phenylpropyl acetate (2y): Colorless

gummy liquid, 78% yield (26 mg); $[\alpha]_{\text{D}}^{20} = +26.0$ ($c = 0.1$ CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 8.41 (s, 1H), 8.00-7.87 (m, 4H), 7.68-7.56 (m, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.38-7.27 (m, 3H), 6.16 (d, $J = 4.0$ Hz, 1H), 5.51 (s, 1H), 3.91 (s, 1H), 2.00 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 198.6, 169.5, 136.5, 135.9, 132.3, 131.5, 130.5, 129.6, 129.0, 128.9, 128.5, 128.4, 127.8, 127.1, 127.0, 123.7, 75.87, 75.1, 20.7; HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{18}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$: 357.1097, found: 357.1096;

HPLC analysis: 94% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 56.5$ min, $R_t(\text{major}) = 66.3$ min.

(1*S*,2*R*)-2-Hydroxy-1-(naphthalen-1-yl)-3-oxo-3-phenylpropyl acetate (2z): Colorless gummy

liquid, 73% yield (24.4 mg); $[\alpha]_D^{20} = +15.6$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, $J = 8.0$ Hz, 1H), 7.87-7.82 (m, 3H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.68-7.54 (m, 3H), 7.53-7.42 (m, 4H), 6.81 (d, $J = 3.1$ Hz, 1H), 5.47 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 3.86 (d, $J = 8.0$ Hz, 1H), 2.07 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 199.5, 169.5, 134.4, 134.0, 133.7, 132.2, 130.2, 129.1, 129.0, 128.8, 128.2, 126.6, 125.7, 125.6, 125.2, 122.5, 74.6, 72.3, 20.7; HRMS (ESI) m/z calcd for C₂₁H₁₈O₄Na [M+Na]⁺: 357.1097, found: 357.1094. HPLC analysis: Chiral separation was not achieved.

(1*S*,2*R*,*E*)-2-Hydroxy-3-oxo-1,5-diphenylpent-4-en-1-yl acetate (2aa): Colorless gummy

liquid, 62% yield (19.2 mg); $[\alpha]_D^{20} = +86.8$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, $J = 15.8$ Hz, 1H), 7.53 (d, $J = 7.5$ Hz, 2H), 7.43 (d, $J = 6.1$ Hz, 4H), 7.39-7.31 (m, 3H), 6.82 (d, $J = 15.8$ Hz, 1H), 6.15 (d, $J = 3.8$ Hz, 1H), 4.70 (s, 1H), 3.75 (d, $J = 5.9$ Hz, 1H), 2.10 (s, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 196.9, 169.6, 145.0, 136.3, 133.9, 131.2, 129.0, 128.7, 128.5, 128.5, 127.0, 120.7, 78.1, 75.4, 20.9; HRMS (ESI): calcd for C₁₉H₁₈O₄ (M+Na): 333.1097, found: 333.1095; HPLC analysis: 98% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 29.1$ min, $R_t(\text{major}) = 27.6$ min.

(1*S*,2*R*)-2-Hydroxy-3-oxo-1,3-diphenylpropyl propionate (2ab): Colorless gummy liquid,

66% yield (19.7 mg); $[\alpha]_D^{20} = -25.8$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, $J = 7.8$ Hz, 2H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 2H), 7.40-7.29 (m, 5H), 6.09 (d, $J = 2.6$ Hz, 1H), 5.34 (s, 1H), 3.81 (s, 1H), 2.28 (q, $J = 7.5$ Hz, 2H), 1.05 (t, $J = 7.6$ Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.7, 172.8, 136.6, 134.2, 134.1, 128.9, 128.4, 128.4, 126.9, 75.4, 75.2, 27.4, 8.9; HRMS (ESI): calcd for C₁₈H₁₈O₄ (M+Na): 321.1097, found: 321.1097; HPLC analysis: 93% *ee* (Chiralcel OD-H, 02:98 *i*PrOH/Hexane, 1 mL/min), $R_t(\text{minor}) = 27.5$ min, $R_t(\text{major}) = 20.3$ min.

(1*S*,2*R*)-2-Hydroxy-3-oxo-1,3-diphenylpropyl pentanoate (2ac): Colorless gummy liquid, 60%

yield (19.6 mg); $[\alpha]_D^{20} = -6.4$ ($c = 0.1$ CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, $J = 7.9$ Hz, 2H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.52 (t, $J = 7.6$ Hz, 2H), 7.40-7.29 (m, 5H), 6.10 (d, $J = 2.5$ Hz, 1H), 5.34 (s, 1H), 3.83 (d, $J = 5.5$ Hz, 1H), 2.25 (t, $J = 7.5$ Hz, 2H), 1.55-1.45 (m, 2H), 1.28-1.22 (m, 2H), 0.87 (t, $J = 7.3$ Hz, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 198.6, 172.2, 136.7, 134.1, 134.1, 128.9, 128.4, 128.4, 126.9, 75.3, 75.3, 33.8, 26.8, 22.0, 13.6; HRMS (ESI): calcd for C₂₀H₂₂O₄ (M+Na): 349.1410, found: 349.1416; HPLC analysis: 90% ee (Chiralcel OD-H, 02:98 ⁱPrOH/Hexane, 1 mL/min), R_t (minor) = 22.0 min, R_t (major)= 17.2min.

VII. ¹H and ¹³C{¹H} spectra of Hydroxy-oxyacylation products 2:

¹H NMR spectrum of compound **2b** (400 MHz/CDCl₃)

¹H NMR spectrum of compound **2c** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2c** (100 MHz/ CDCl_3)

^1H NMR spectrum of compound **2d** (400 MHz/ CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2d** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2e** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2e** (100 MHz/ CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2f** (100 MHz/ CDCl_3)

^1H NMR spectrum of compound **2h** (400 MHz/ CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2h** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2i** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2i** (100 MHz/ CDCl_3)

^1H NMR spectrum of compound **2j** (400 MHz/ CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2j** (100 MHz/ CDCl_3)

¹H spectrum of compound **2l** (400 MHz/CDCl₃)

¹H spectrum of compound **2m** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ spectrum of compound **2n** (100 MHz/ CDCl_3)

$^{13}\text{C}\{^1\text{H}\}$ spectrum of compound **2o** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2p** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2p** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2q** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2q** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2s** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2s** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2t** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2t** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2u** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2u** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2v** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2v** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2w** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2w** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2y** (400 MHz/CDCl₃)

¹H NMR spectrum of compound **2aa** (400 MHz/CDCl₃)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **2aa** (100 MHz/ CDCl_3)

¹H NMR spectrum of compound **2ac** (400 MHz/CDCl₃)

VIII. HPLC spectra of Hydroxy-oxyacylation products, 2:

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
33.557	MM m	1.36	28406.55	302.84	50.14	
44.539	MM m	2.18	28245.65	190.82	49.86	
		Sum	56652.20

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
33.574	MM m	1.41	28423.61	306.51	97.68	
46.536	MM m	1.17	675.56	7.26	2.32	
		Sum	29099.17

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
25.081	MM m	1.29	100236.04	1114.27	50.64	
35.768	MM m	2.08	97707.75	629.34	49.36	
Sum			197943.80

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
25.027	MM m	1.36	145516.86	1535.24	99.03	
38.371	MM m	1.15	1422.42	15.56	0.97	
Sum			146939.28

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
44.451	MM m	1.17	47172.78	590.72	50.09	
50.916	MM m	1.35	46996.74	532.21	49.91	
Sum			94169.51

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
44.075	MM m	1.24	78967.76	908.24	94.58	
54.688	MM m	1.34	4522.52	51.88	5.42	
Sum			83490.28

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
36.848	MM m	1.63	117249.81	1008.70	50.38	
61.661	MM m	2.71	115480.64	543.72	49.62	
Sum			232730.45

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
37.071	MM m	1.73	102748.32	878.53	98.25	
65.130	MM m	1.41	1834.09	15.79	1.75	
Sum			104582.42

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
34.149	MM m	1.43	44740.45	477.63	50.51	
59.780	MM m	2.12	43833.22	258.17	49.49	
Sum			88573.67

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
34.138	MM m	1.42	52200.33	557.72	98.07	
61.807	MM m	1.21	1027.70	10.10	1.93	
Sum			53228.03

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
33.660	MM m	1.36	4543.33	49.19	50.96	
59.373	MM m	2.03	4371.58	28.68	49.04	
Sum			8914.91

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
32.935	MM m	1.33	9618.28	107.53	96.15	
58.674	MM m	1.40	385.32	3.23	3.85	
Sum			10003.60

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
52.150	MM m	2.52	54880.51	298.81	50.68	
69.368	MM m	3.74	53408.47	179.30	49.32	
Sum			108288.98

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
52.307	MM m	2.62	119164.23	583.08	97.62	
74.838	MM m	2.27	2901.15	15.03	2.38	
Sum			122065.38

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
53.163	MM m	2.61	103952.09	519.08	49.93	
65.675	MM m	3.00	104231.85	444.50	50.07	
Sum			208183.93

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
56.516	MM m	1.96	7034.02	43.21	2.88	
66.373	MM m	3.23	237102.32	888.04	97.12	
Sum			244136.34

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
28.529	MM m	1.22	115404.72	1436.67	50.58	
42.488	MM m	1.83	112778.01	845.00	49.42	
		Sum	228182.73

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
29.827	MM m	1.35	2389.89	24.08	8.49	
43.864	MM m	1.62	25772.04	246.19	91.51	
		Sum	28161.93

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
31.757	BV	4.48	127318.74	1055.40	45.65	
36.243	VB	7.03	151571.00	1148.91	54.35	
Sum			278889.73

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
33.823	MM m	1.08	4658.68	64.98	3.20	
36.598	MM m	1.89	140777.01	1036.33	96.80	
Sum			145435.69

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
37.463	MM m	1.53	39272.64	368.76	52.23	
62.624	MM m	2.34	35917.33	204.36	47.77	
Sum			75189.97

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
36.842	MM m	1.73	128924.31	1076.70	98.09	
64.462	MM m	1.59	2508.54	21.23	1.91	
Sum			131432.85

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
34.717	MM m	1.90	99194.00	708.61	50.03	
41.104	MM m	2.16	99065.71	612.90	49.97	
		Sum	198259.71

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
35.665	MM m	1.30	1172.64	12.33	3.58	
40.965	MM m	1.86	31608.13	236.36	96.42	
		Sum	32780.78

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
22.634	MM m	0.55	55011.17	1539.17	50.22	
28.418	MM m	0.68	54524.11	1219.04	49.78	
		Sum	109535.28

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
22.852	MM m	0.54	43239.70	1233.84	95.79	
29.125	MM m	0.62	1900.18	48.22	4.21	
		Sum	45139.87

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
19.902	MM m	1.08	164279.25	2219.76	50.66	
23.322	MM m	1.43	159968.80	1648.27	49.34	
		Sum	324248.06

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
20.092	MM m	1.22	175994.91	2166.91	93.99	
24.688	MM m	1.10	11246.43	153.58	6.01	
		Sum	187241.34

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
20.405	MM m	0.94	15663.77	251.77	53.25	
23.020	MM m	1.07	13750.21	193.19	46.75	
	Sum		29413.98

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
18.795	MM m	1.10	242047.25	2976.46	95.55	
22.360	MM m	1.02	11276.88	175.01	4.45	
	Sum		253324.13

Signal: DAD1E,Sig=280,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.842	MM m	0.55	4579.94	129.40	50.66	
33.504	MM m	1.17	4460.03	55.45	49.34	
Sum			9039.97

Signal: DAD1E,Sig=280,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.637	MM m	0.59	15530.27	400.50	97.12	
34.426	MM m	0.98	459.90	6.52	2.88	
Sum			15990.17

Signal: DAD1E,Sig=280,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
15.514	MM m	0.49	3648.32	115.77	49.52	
29.990	MM m	1.06	3719.21	53.43	50.48	
		Sum	7367.53

Signal: DAD1E,Sig=280,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
15.361	MM m	0.51	10836.14	328.64	97.27	
30.468	MM m	0.78	303.83	5.16	2.73	
		Sum	11139.97

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
25.490	MM m	1.37	123069.64	1346.20	49.89	
36.357	MM m	2.19	123632.07	768.63	50.11	
		Sum	246701.71

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
26.489	MM m	1.46	129945.43	1289.98	98.77	
40.924	MM m	1.38	1617.01	15.58	1.23	
		Sum	131562.45

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
25.992	MM m	1.22	26353.71	323.86	49.07	
32.656	MM m	1.64	27351.50	243.51	50.93	
Sum			53705.22

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
25.200	MM m	1.12	10962.23	145.28	95.43	
32.799	MM m	0.97	524.57	6.58	4.57	
Sum			11486.79

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
24.492	MM m	1.13	31829.27	418.06	50.69	
28.163	MM m	1.39	30966.04	329.94	49.31	
Sum			62795.30

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.826	MM m	1.39	162392.76	1772.57	96.96	
28.487	MM m	1.10	5090.86	68.45	3.04	
Sum			167483.61

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
91.530	MM m	1.88	62164.19	512.78	51.63	
95.884	MM m	2.16	58231.93	412.34	48.37	
		Sum	120396.13

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
92.187	MM m	2.20	109353.96	729.79	98.09	
98.134	MM m	1.42	2131.54	18.37	1.91	
		Sum	111485.50

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.922	MM m	1.18	84693.43	1053.71	50.44	
34.981	MM m	1.91	83204.22	597.31	49.56	
Sum			167897.65

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.872	MM m	1.19	99632.64	1215.85	99.51	
37.369	MM m	0.86	486.93	6.86	0.49	
Sum			100119.57

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.457	MM m	1.06	50547.21	688.97	50.39	
30.627	MM m	1.44	49766.87	476.09	49.61	
		Sum	100314.09

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
23.078	MM m	1.27	171699.01	2006.07	96.94	
31.269	MM m	1.13	5410.81	71.44	3.06	
		Sum	177109.83

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
22.801	MM m	1.21	91183.64	1132.91	50.53	
26.503	MM m	1.42	89286.42	917.60	49.47	
Sum			180470.05

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
22.057	MM m	1.20	129223.57	1615.06	97.30	
26.496	MM m	0.96	3589.63	56.57	2.70	
Sum			132813.20

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
42.165	MM m	1.20	82174.37	954.66	52.09	
49.380	MM m	2.42	75594.22	404.81	47.91	
		Sum	157768.59

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
42.143	MM m	1.07	3017.52	41.82	3.60	
46.390	MM m	1.40	80894.69	781.20	96.40	
		Sum	83912.21

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
27.299	MM m	0.57	26392.91	746.41	53.45	
28.573	MM m	0.75	22983.54	489.78	46.55	
		Sum	49376.45

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
27.611	MM m	0.67	20159.93	467.22	98.77	
29.192	MM m	0.54	251.74	7.33	1.23	
		Sum	20411.67

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
20.251	MM m	0.77	43018.14	843.23	50.02	
26.610	MM m	1.17	42975.55	553.79	49.98	
		Sum	85993.69

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
20.365	MM m	0.83	61702.63	1131.34	96.53	
27.531	MM m	0.84	2221.27	40.47	3.47	
		Sum	63923.90

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
17.121	MM m	0.73	106235.30	2214.97	49.83	
21.237	MM m	1.10	106962.97	1462.41	50.17	
		Sum	213198.27

Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
17.204	MM m	0.70	78239.19	1701.52	95.09	
22.071	MM m	0.72	4035.58	89.30	4.91	
		Sum	82274.77			

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